XL ANNUAL MEETING OF INDIAN ACADEMY OF NEUROSCIENCES (IAN-2022)

Theme : Neurosciences Research: Current Trends and Future Needs

ABSTRACT BOOK



Organised by

Department of Biomedical Engineering
North-Eastern Hill University, Shillong
India

Website: www.ian2022nehu.com

Organizing Committee

Chief Patron



Prof. Prabha Shankar Shukla

Honble' Vice-Chancellor,
North-Eastern Hill University
Shillong 793022, Meghalaya, India

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Dean, School of Technology
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MESSAGES



Brig. (Dr.) B. D. Mishra (Retd.)
Governor



RAJ BHAVAN
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MESSAGE

Over a period of time, the field of biomedical engineering has expanded exponentially. This growth is supported by the advances in biological science, neurobiology, computational neuroscience, medical instrumentation, bio imaging, bioengineering and biomaterials. The ongoing progress in these fields has created new opportunities for the development of tools for diagnosis and therapy for human diseases.

To keep abreast with these developments, it is imperative that students, researchers, academicians and the connected industry have access to platforms where they can share their knowledge and expertise from time to time.

I am pleased to know that XL Annual Meeting of Indian Academy of Neurosciences (IAN-2022) is being organized by the Department of Biomedical Engineering (BME), North-Eastern Hill University (NEHU), Shillong, Meghalaya from December 8-10, 2022 under the theme '*Neuroscience Research: Current Trends and Future Needs".*

I am sanguine that the presence of the luminaries and experts, in various disciplines, from our country and abroad, would amply enlighten the participants on the theme of the meeting.

I wish the Indian Academy of Neurosciences and the North Eastern Hill University all success in their endeavour. I compliment the organisers of this mega event and admire their effort for the dissemination of the latest knowledge and good practices in the field of neuroscience.

Brig. (DR.) B.D Mishra (Retd.)

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MEGHALAYA
Golden jubilee celebration

सत्यमेव जयते

Conrad K. Sangma
Chief Minister
Meghalaya



MESSAGE

It gives me immense pleasure to write about the XL Annual Meeting of Indian Academy of Neurosciences (IAN-2022) during December 7 - 10, 2022 being organized by the Department of Biomedical Engineering (BME), North-Eastern Hill University (NEHU), Shillong, Meghalaya. We are grateful to the Indian Academy of Neurosciences (IAN) for holding its 40th Annual meeting at NEHU, Shillong and giving this wonderful opportunity to NEHU. The field of biomedical engineering has expanded markedly in the past ten years. This growth is supported by advances in biological science, neurobiology, computational neuroscience, medical instrumentation, bio imaging, bioengineering and biomaterials which have created new opportunities for development of tools for diagnosis and therapy for human diseases. This workshop and conference have been planned with the motive to provide platform for the students, researchers, academicians, industry to abreast themselves with latest developments in the field and share their knowledge and expertise. It is a mega event for the dissemination of progress and practices in the field of neuroscience that sees the participation of luminaries and experts from and outside the country. The theme for the XL Annual Meeting of the Indian Academy of Neurosciences (IAN-2022) is *Neuroscience Research: Current Trends and Future Needs.*

Indian Academy of Neurosciences is the most prestigious academy in India having eminent scientists from within India and abroad. Ever since its inception, the Academy has been active in promoting neurosciences and has been holding its annual meetings at different centers of excellence in neuroscience research. It is our pleasure that the opportunity to hold the IAN meeting in the current year has been bestowed upon us.

The annual meeting this year is special because a North-Eastern Institute is hosting this mega event for the first time. The 4-days long event is packed with pre-conference workshops, round-the-clock invited talks, panel discussions, and oral and poster sessions running in three parallel panels. Ademo-cum exhibition of health care devices and prototypes is also scheduled during the workshop. The IAN annual meeting record the approximate participation of 350-400 delegates including guests from India and abroad like- Singapore, Malaysia, and the USA. The participation institutes include DRDO, DIPAS, INMAS, NBRC, NIMANS, CDRI Lucknow, CSIR labs, IITs, NITs, Central Universities, Institute of National Importance, NIPER, etc. The event will be sponsored by NEHU, Govt. funding agencies like- SERB, DBT, and DRDO, Company sponsors like- Gentech, Marsap, GenX, and JB Corporation, and Sponsor from Indian Overseas Bank, Shillong.

(Conrad K. Sangma)

आचार्य प्रभा शंकर शुक्ल
कुलपति
पूर्वोत्तर पर्वतीय विश्वविद्यालय
जिला:पूर्वी खासी हिल्स,शिलांग-793022
मेघालय, भारत

Professor Prabha Shankar Shukla
Vice-Chancellor
North-Eastern Hill University
District: East Khasi Hills, Shillong - 793022
Meghalaya, India

Message



It gives me immense pleasure to write this message for the **XL Annual meeting of Indian Academy of Neurosciences** (IAN 2022) organized by the Department of Biomedical Engineering, North-Eastern Hill University, Shillong, India which will be held from December 7 - 10, 2022

I am glad to know that the theme of the meeting is "*Neuroscience Research: Current trends and future needs*" and along with the annual meeting, a pre-conference workshop on Science Communication, School Children interaction have also been planned to provide opportunity to the young researchers and school going children to develop their skills.

As a multidisciplinary field, biomedical engineering offers numerous avenues for research. It must be noted that it is now necessary to keep up with the most recent technological advancements, with a focus on improvements in the healthcare industry. The significance of technological advancements multiplies when healthcare is included in the technology.

I extend my best wishes for the success of the annual meeting and pre-conference workshop. I hope that it will create an interactive platform for the participating scientists, researchers and the students.

On behalf of the North-Eastern Hill University, I congratulate the organisers especially the Department of Biomedical Engineering and wish this event all the success.

Prof. P.S. Shukla

प्रो. मो. इफ्तेखार हुसैन
संकायाध्यक्ष, प्रोद्योगिकी संकाय
पूर्वोत्तर पर्वतीय विश्वविद्यालय
जिला: पूर्वी खासी हिल्स, शिलांग - 793022
मेघालय, भारत

Prof. Md. Iftekhar Hussain
Dean, School of Technology
North-Eastern Hill University
District: East Khasi Hills, Shillong - 793022
Meghalaya, India

Message



In the golden jubilee year of our University, I feel privileged to invite you all to the **XL Annual Meeting of the Indian Academy of Neurosciences** scheduled to be held during December 7-10, 2022, in the Department of Biomedical Engineering under the School of Technology, NEHU, Shillong. This four-day-long event is expected to witness a massive attendance from India and abroad to explore the scientific paths of neurosciences.

Biomedical Engineering is a bourgeoning discipline of enormous significance to our day-to-day lives. The impacts of neurological diseases and disorders can be significantly reduced using technology-based solutions. Engineering education and research can play a vital role in developing such solutions. The Biomedical Engineering Department under the School of Technology, NEHU, is committed to contributing to these issues. Their endeavours to explore and develop such technologies can significantly help our nation-building process. The leading technologists need to share their ideas and stimulate emerging researchers and technologists in this domain.

The Pre-conference Workshop planned on 7th December 2022 would focus on experimental and computational neuroscience through some accomplished researchers' lectures in the areas such as the modelling of neurons, neural systems and behaviour, the analysis of state-of-the-art neural data, and the development of theories to explain experimental observations, etc.

I would like to heartily congratulate Dr. Sudip Paul and his team for organising such an important event.

28.11.2022

Prof. Md. Iftekhar Hussain
Dean, School of Technology, NEHU, Shillong

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School of Studies in Neuroscience
Jiwaji University, Gwalior, India
Training Brains for the Brain

MESSAGE

Due to the pandemic, we had the meetings of the Academy for past 2 years on virtual mode. The advantage was we could meet leading neuroscientists of the world and listen to ground breaking advances in neuroscience but the disadvantage has been we started missing each other. Each of us now have a great urge to meet and share academic and personal experiences.

The past two virtual meetings organized by Prof. Anita Jagota and Prof. Shashi Bala Singh in 2020 and Prof. Jayashree Das Sarma in 2021 were great successes.

40th Annual Meeting of the Academy is being organized at Shillong, under the patronship of Prof. Prabha Shankar Shukla, Hon'ble Vice Chancellor of North-Eastern Hill University, Shillong and the dynamic organizational skills of Dr. Sudip Paul, during 7-10th December 2022. The theme of the Conference has been set as "Neuroscience research: Current trends and Future Needs". I am sure the meeting will provide opportunities for all the participants, present, to interact and even win several awards of the Academy. The major attractions have always been the posters from young Neuroscientists of the country and the Young Neuroscientists Colloquia. We will also have several lead lectures. This year we will have the Prof. P.N. Tandon Oration and Dr. S.S. Parmar Oration for the first time in addition to the Dr. K.T. Shetty Memorial Oration and Prof. B.K. Bachhawat Memorial Oration.

I wish a great success of the meeting.

20th November 2022

Ishan Patro

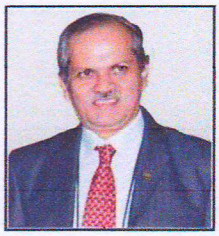
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INDIAN ACADEMY OF NEUROSCIENCES

(Registered Under Societies Registration Act XXI 1860)

Dr Vinay K. Khanna
PhD, FNASc, FIANS, FST, FAEB
Secretary HQ, Indian Academy of Neurosciences

November 19, 2022.



MESSAGE

I am happy to note that North-Eastern Hill University, Shillong is the host of **XL Annual Meeting of Indian Academy of Neurosciences** from December 8 - 10, 2022.

Increase in neurological and psychiatric diseases have aroused great concern due to associated burden on the caregivers and society at large. Prevalence of infections of the nervous system leading to neurological deficits further aggravates the situation. Although technological advances have made it possible to understand the intricacies of certain CNS disorders, understanding the functioning of brain still remains a greater challenge and mystery due to its complexity.

The theme Neuroscience Research: Current Trends and Future Needs is aptly chosen by the organizers. I am sure that the scientific deliberations during the meeting will provide insight and acquaint the young researchers with advances in different domains / compartments of neuroscience and their appropriate applications in basic and clinical research and treatment. This will also help to formulate strategies for the future to unravel the mysteries of brain. The participants will find it a rewarding experience and build new network to move forward in the pristine environment of Shillong, famous for its waterfalls, manicured gardens and music.

I wish the organizers and specially the dynamic Organizing Secretary Dr Sudip Paul to have successful and fruitful meeting.

Vinay Kumar Khanna

* Secretary HQ, Indian Academy of Neurosciences, Chief Scientist & Professor AcSIR, Adjunct Professor, NIPER-Hyderabad, Developmental Toxicology Laboratory, Area Coordinator - Systems Toxicology & Health Risk Assessment Group & Food, Drug and Chemical Toxicology Group CSIR - Indian Institute of Toxicology Research, Vishvigyan Bhavan, 31, Mahatma Gandhi Marg, Lucknow - 226 001, Uttar Pradesh, India

राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
(जैव एवं प्रौद्योगिकी विभाग का स्वायत् संस्था,
विज्ञान एवं तकनीकी मंत्रालय, भारत सरकार)
एन0 एच0–08, नैनवाल मोड़, मानेसर – 122 050 (हरियाणा)

National Brain Research Centre
(An Autonomous Institute of Deptt. of Biotechnology,
Ministry of Science & Technology, Govt. of India)
NH-08, Nainwal Mode, Manesar - 122 050 (Haryana)

November 4, 2022



Message

I am very happy to note that the XL Annual meeting of the Indian Academy of Neurosciences (IAN) is being hosted by The North East Hill University (NEHU) Shillong, India. This is for the first time that IAN is holding its meeting in North East state which is rich in cultural diversity. This is also the first in-person post-pandemic meeting of IAN hence we are expecting huge participation from neuroscientists around globe. The theme of the meeting – ***Neuroscience Research: Current trends and future needs*** is very timely and apt as there have been significant advancements in brain research.

As in previous years IAN meetings have been great forum for showcasing wonderful research carried out by Indian neuroscientists to the delegates from various other countries, foster collaborations and networking.

I wish great success for the XL annual meeting of the Indian Academy of Neurosciences at NEHU, Shillong, India.

Pankaj Seth

Pankaj Seth, Ph.D
Professor and Scientist -VII,
Molecular and Cellular Neuroscience,
National Brain Research Centre (N.B.R.C.),
Nainwal more, Near NSG Campus,
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डॉ. सुदीप पॉल

पूर्वोत्तर पर्वतीय विश्वविद्यालय
जिला: पूर्वी खासी हिल्स, शिलांग - 793022
मेघालय, भारत

Dr. Sudip Paul

North-Eastern Hill University
District: East Khasi Hills, Shillong - 793022
Meghalaya, India

MESSAGE FROM THE ORGANIZING SECRETARY



It is my pleasure to welcome you all to the XL Annual Meeting of the Indian Academy of Neurosciences (IAN-2022) during December 7 - 10, 2022. It is a mega event for the dissemination of progress and practices in the field of neuroscience that sees the participation of luminaries and experts from and outside the country. The theme for the XL Annual Meeting of the Indian Academy of Neurosciences (IAN-2022) is ***Neuroscience Research: Current Trends and Future Needs.*** Indian Academy of Neurosciences is the most prestigious academy in India having eminent scientists from within India and abroad. Ever since its inception, the Academy has been active in promoting neurosciences and has been holding its annual meetings at different centers of excellence in neuroscience research. It is our pleasure that the opportunity to hold the IAN meeting in the current year has been bestowed upon us. The main objective of our programme is to prepare young scholars/scientists and equip them with practical experience of the advanced techniques in neuroscience and neurobiology. This would also provide the participants, with possible career options in the future so that they are able to offer solutions on different neurodegenerative disorders such as Alzheimer's, Parkinson's and related motor neuron disorders.

I take this opportunity to express my sincere and deep sense of gratitude to **Prof. Prabha Shankar Shukla**, Hon'ble Vice-Chancellor, NEHU, Shillong, **Prof. Md. Iftekhar Hussain**, Dean, School of Technology, NEHU, Shillong, for providing all the help and assistance to organize this event. The IAN annual meeting records the approximate participation of 350-400 delegates including guests from India and abroad like- Singapore, Malaysia, and the USA. The participation institutes include DRDO, DIPAS, INMAS, NBRC, NIMANS, CDRI Lucknow, CSIR labs, IITs, NITs, Central Universities, Institute of National Importance, NIPER, etc. The event will be sponsored by NEHU, Govt. funding agencies like- SERB, DBT, and DRDO, Company sponsors like- Gentech, Marsap, GenX, and JB Corporation, and Sponsor from Indian Overseas Bank, Shillong. At last but not least, I sincerely thank all the faculty members, staffs, research scholars and students of the Department of Biomedical Engineering for their painstaking efforts and contributions to make this event grand success. Wish you all the best and have a wonderful and fruitful time during the meeting.

S. Paul

Dr. Sudip Paul
Organizing Secretary
IAN 2022

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SCHEDULE



XL Annual Meeting of
Indian Academy of Neurosciences

Pre-conference Workshops
December 07, 2022

XL Annual Meeting of
Indian Academy of Neurosciences
Theme: Neuroscience Research: Current Trends and Future Needs

December 8-10, 2022

Programme



Organized By:

Department of Biomedical Engineering
School of Technology
North-Eastern Hill University
Shillong - 793022, Meghalaya, India



XL Annual Meeting of
Indian Academy of Neurosciences

Wednesday, December 07, 2022	
(Multi-Use Convention Hall) **08.30 – 9.00 hrs.**	**Workshop Registration**
(Multi-Use Convention Hall) **09.00 – 09.30 hrs.**	**Inaugural Function**
09.30–11.00 hrs.	**Workshop – I** **Brain Signal Analysis using EEG** ***(Sponsored by Gentech Marketing & Distribution (P) Ltd, New Delhi)*** **Conveners:** **Anita Talwar,** Managing Director, Gentech **Richard Mills,** Vice President of Stoeting Co, USA
11.00 -12.30 hrs.	**Workshop – II** **Computational Neuroscience and Neurorehabilitation** ***(Sponsored by Gentech Marketing & Distribution (P) Ltd, New Delhi)*** **Conveners:** **Sandip Majumder,** Country Manager **Richard Mills,** Vice President of Stoeting Co, USA
13.30–16.00 hrs.	**Workshop – III** **Scientific Communication** **Conveners:** **Poonam Thakur,** IISER, Thiruvananthapuram **Sudip Paul,** NEHU, Shillong
(Community Hall) **10.30 – 12.30 hrs.**	**School Children–Scientist Interaction Meet** ***(Sponsored by The National Academy of Sciences, India)*** **Panelists:** **UC Srivastava,** Prayagraj **SR Joshi,** Shillong **IK Patro,** Gwalior **PK Seth,** Lucknow **VK Khanna,** Lucknow **P Seth,** Manesar **S Paul,** Shillong **SK Barik,** Shillong
(Multi-Use Convention Hall) **12.30 – 13.30 hrs.**	**Lunch**
(Community Hall) **17.00 – 18.30 hrs.**	**IAN 2022 - Opening Ceremony**
(Community Hall) **19.00 - 20.00 hrs.**	**Welcome Dinner**
(Multi-Use Convention Hall) **20.00 hrs. onwards**	**IAN Executive Committee Meeting**



XL Annual Meeting of
Indian Academy of Neurosciences

Day 1: Thursday, December 08, 2022	
(Multi-Use Convention Hall) **08.00 – 14.00 hrs.**	**Conference Registration**
(Multi-Use Convention Hall)	**Chairpersons:** **IK Patro,** Jiwaji University, Gwalior **TR Raju,** Sankara Academy of Vision, Bengaluru
09.00 – 09.45 hrs.	**BK Bachhawat Memorial Lifetime Achievement Award Lecture** **UC Srivastava,** The National Academy of Sciences, India, Prayagraj, Uttar Pradesh, India *Evolutionary diversity of cortical neurons in reptiles, birds and mammals*
09.45 – 10.30 hrs.	**KT Shetty Oration** **Suresh L. Mehta,** University of Wisconsin, Madison, USA *Noncoding RNAs and post-stroke functional outcomes*
10.30 – 11.00 hrs.	**Plenary Lecture – I** **Tuck Wah Soong,** Yong Loo Lin School of Medicine, NUS, Singapore *Modulation of RNA editing of Cav1.3 channels: Implications in learning and memory*
11.00 – 11.30 hrs.	**Tea**



XL Annual Meeting of
Indian Academy of Neurosciences

	Symposium – I (Multi-Use Convention Hall)	Symposium – II (Community Hall)	Symposium - III (Auditorium, Old Guest House)
11.30 – 13.00 hrs.	***Topic: Identify Novel Targets to Protect Neurotoxicity and Neurodegenerative Diseases*** **(Dedicated to the memory of Professor Ravindra Nath)** **Chairpersons:** **Prahlad K. Seth,** ILSI-India, Lucknow **Gurcharan Kaur,** GNDU, Amritsar **Aamir Nazir,** CSIR-Central Drug Research Institute, Lucknow *Studies on neuronal development, degeneration and repair employing transgenic C. elegans model* **Sharmili Vidyadaran,** Universiti Putra Malaysia *Microglia-induced neurotoxicity: the paradigm and the reality* **Vinay K. Khanna,** CSIR-Indian Institute of Toxicology Research, Lucknow, Uttar Pradesh *Role of inflammatory changes in dopaminergic alterations in nigrostriatal region on exposure to lambda-cyhalothrin in rats* **Rajat Sandhir,** Panjab University, Chandigarh, Panjab, *Identification of molecular targets of hydroxytyrosol, a neuroprotective molecule in Parkinson's disease* **Subhas C. Biswas,** CSIR-Indian Institute of Chemical Biology, Kolkata *Neuroprotective efficacy of proteins of A2-like astrocytes in a transgenic mice model of Alzheimer's disease*	***Topic: Experimental and Computational Approaches to Olfactory Sensory Processing*** **Chairpersons:** **Collins Assisi,** IISER, Pune **Joby Joseph,** UoH, Hyderabad **Nixon Abraham,** Indian Institute of Science Education and Research, Pune *Olfaction as a tool to study the brain in health and disease* **Varsha Singh,** Indian Institute of Science, Bangalore *Olfaction drives flight or fight response in Caenorhabditis elegans* **Joby Joseph,** University of Hyderabad, India *What of the olfactory code of an odor is learned by the honeybees?* **Collins Assisi,** Indian Institute of Science Education and Research, Pune *Intermittent inputs reveal invariant odor representations.* **Runa Hamid,** CSIR-Centre for Cellular and Molecular Biology, Hyderabad *Choline transporter: Channeling the Fly Olfactory Behavior*	***Topic: Therapeutic Intervention of CNS Diseases*** **Chairpersons:** **Suman Jain,** AIIMS, New Delhi **Akshay Anand,** PGIMER, Chandigarh **Jackson James,** Rajiv Gandhi Center for Biotechnology, Thiruvananthapuram *A unique stem cell niche in SVZ maintains neural stem cells during early neurogenesis and in the adult cortex* **Ravi Shankar Akundi,** South Asian University, New Delhi *P2 receptor-dependent cyclooxygenase 2 (COX-2) signaling enhances migration and invasion of the human neuroblastoma cell-line, IMR-32* **Malancha Ta,** Indian Institute of Science Education and Research, Kolkata *Identifying the Different Roles of Vitronectin in Human Mesenchymal Stem Cells under Microenvironment Stress* **Dharmendra Kumar Khatri,** National Institute of Pharmaceutical Education and Research, Hyderabad *Neuroepigenetic Alterations in the Prefrontal Cortex of Type 2 Diabetic Mice through DNA Hypermethylation*
(Community Hall) **13.00 – 13.45 hrs.**	**Group Photograph followed by Lunch**		
(Community Hall) **13.30– 15.15 hrs.**	**Poster Session – I**		



XL Annual Meeting of
Indian Academy of Neurosciences

	Symposium - IV (Multi Use Convention Hall)	Symposium - V (Community Hall)	Oral Session –I (Auditorium, Old Guest House)
15.15 – 16.45 hrs.	***Topic: Natural Extracts in the Treatment of Brain disorders: Promises and Challenges*** **(IAN - FAONS Symposium)** **Chairpersons:** **Tuck Wah Soong,** Yong Loo Lin School of Medicine, NUS, Singapore **SK Barik,** NEHU, Shillong **Gurcharan Kaur,** Guru Nanak Dev University, Amritsar *Tinosporacordifolia as a potential agent to ameliorate aging -related decline cognitive and locomotor impairments: cell survival and plasticity pathways as targets in female rat brain* **S.K. Trigun,** Institute of Science, Banaras Hindu University, Varanasi *Modulation of adult neurogenesis and bioenergetic deficits by Bacopa monnieri extract (CDRI-08) in the cortex of the hepatic encephalopathy rat model of neuro-excitotoxicity* **Surya Pratap Singh,** Department of Biochemistry, Institute of Science, Banaras Hindu University, Varanasi, Uttar Pradesh, India *Neuroprotective Potential of Phytomedicine against Parkinson's Disease* **Meenakshi Bawari,** Assam University, Silchar *Inherent phytochemical constituents in Mussaendaroxburghii Hook. f. A medicinal plant used in Tripura (India): A spectrum of neurotoxicological consequencesNeurotherapeutics* **Mohandas Rao KG,** Manipal Academy of Higher Education, Manipal. Karnataka *Treatment with*	***Topic: Neuromodulation in Health and Disease*** **Chairpersons:** **Hina Kauser,** VMMC and Safdarjung Hospital, Delhi **Trina Sengupta,** AIIMS, Jodhpur **Afreen Begum H Itagi,** All India Institute of Medical Sciences, Mangalagiri *Neuroactive steroids on Mozart effect for Spatial intelligence: An EEG Study* **Archana Gaur T,** AIIMS Bibinagar, Hyderabad *High-fat diet combined with exercise in anxiety-like behaviour of adolescent rats* **Trina Sengupta,** All India Institute of Medical Sciences (AIIMS), Jodhpur *Dietary glutamate in rats causes changes in medial preoptic area neuronal activity* **Suman Das,** All India Institute of Medical Sciences, Bilaspur *Cerebellar transcranial direct current stimulation: A new dimension for neuromodulation?* **Hina Kauser,** VMMC and Safdarjung Hospital, Delhi *Brain wave entrainment in sleep and cognitive functions*	***Topic: Neurodegenerative disorders*** **Chairpersons:** **Savita Gaur,** DIPAS, DRDO **Pankaj Seth,** NBRC, Manesar **Rajnikant Mishra,** Banaras Hind University, Varanasi *Expression and Interactions of Pax6 in brain of MPTP-treated mice* **Jitendra Narain Singh,** National Institute of Pharmaceutical Education and Research *The Elucidation of the Role of 2-Aminoethoxydiphenyl Borate in Preventing Mitochondrial Dysfunctions in MPTP model of Parkinson 's Disease* **Debapriya Garabadu,** Central University of Punjab, Bathinda *Ang (1-7)/Mas axis in the brain: A potential therapeutic target in the management of Alzheimer's disease* **Dibashree Tamuli,** Gauhati University, Assam *Autonomic brain atrophy as a neurodegenerative biomarker in spinocerebellar ataxia*



	Tinosporacordifolia reduces amygdaloid neuronal damage caused by prenatal stress and maternal separation in rats Neurotherapeutics **Sharmili Vidyadaran,** Universiti Putra Malaysia *Concluding Remarks*		
16.45 – 17.00 hrs.	**Tea**		
17.00 – 18.30 hrs.	**Oral Session - II** **(Multi Use Convention Hall)** ***Topic: Brain Pathology*** **Chairpersons:** **Suresh L. Mehta,** UoW, Madison, USA **Aamir Nazir,** CSIR-CDRI, Lucknow **Prabhakar Singh,** All India Institute of Medical Sciences, New Delhi *Localization of MHC-II expressing cells in the hippocampus of Aβ injected Alzheimer's rat model* **Masaraf Hussain,** All India Institute of Medical Sciences, Guwahati *Applying SABV (Sex as a biological variable) in research and clinical care* **Ashutosh Kumar,** All India Institute of Medical Sciences, Patna *Prevalence of long term sequelae of neuropsychiatric illness in COVID-19 survivors: a follow-up study* **Sudhi Shrivastava,** CMP College University of Allahabad *Vocal cognition in birds and underlying neuronal dynamics*	**Oral Session - III** **(Community Hall)** ***Topic: CNS Disorders*** **Chairpersons:** **Usha Panjwani,** DIPAS, Delhi **Jayasri Das Sarma,** IISER, Kolkata **Dinesh Upadhya,** Centre for Molecular Neurosciences, Kasturba Medical College *Prevalence of CNS infections: three years of data from a single centre study* **Jyotirmoy Banerjee,** All India Institute of Medical Sciences, New Delhi *α4-containing GABAA receptors: "Old" receptor as new target for drug-resistant epilepsy?* **Goutam Chandra,** Mahatma Gandhi University Campus *Lysosomal abnormalities and autophagic deficit contribute to the pathogenesis of infantile Batten disease* **Suman Das,** All India Institute of Medical Sciences, Bilaspur *Cerebellar transcranial direct current stimulation (tDCS): A new dimension as neuro-modulation therapy?*	**Oral Session - IV** **(Auditorium, Old Guest House)** ***Topic: Cognition*** **Chairpersons:** **Rajnikant Mishra,** BHU, Varanasi **Manorama Patri,** Ravenshaw University, Cuttack **Kolar Sridara Murthy Meena and Thiruchengodu Raju Kanmani,** NIMHANS, Bengaluru *Puppetry as a platform for increasing awareness on brain and its functions among school children in rural village of Karnataka State* **SS Tiwari,** IIT-Roorkee *Delayed cortical astrogliosis corelates with cognitive protection in a tauopathy environment following trauma in a cohort study* **Sudip Sen,** All India Institute of Medical Sciences, New Delhi *Hypoxic brain injury in cerebral palsy: an in vitro disease model for a complex disease* **Priyaranjan Maral,** National Forensic Sciences University, Gandhinagar *Cognitive Flexibility and Response Conflict of Emotion Laden Texts and Faces in PTSD: A Study on Nepal Earthquake*
18:30 - 19:15 hrs.	**Panel Discussion – Lessons for successful career**		
(Community Hall) 19.30 hrs. onwards	**Dinner**		



XL Annual Meeting of
Indian Academy of Neurosciences

Day 2: Friday; December 09, 2022	
(Multi-Use Convention Hall) **08:30 - 09:00 hrs.**	**Technical Talk** **Richard Mills,** Vice President, M/s. Stoelting Co, USA *Measuring Behavior in Neuroscience: ANY-maze Software is more than just another video tracking system*
(Multi-Use Convention Hall) **09:00 - 09:45 hrs.**	**Chairpersons:** **IK Patro,** Jiwaji University, Gwalior **Prahlad K. Seth,** ILSI-India, Lucknow **SS Parmar Oration** **Subhash C. Pandey,** University of Illinois at Chicago & Jesse Brown VA Medical Center, USA
09:45 - 10:30 hrs.	**PN Tandon Oration** **Ashok K. Mahapatra,** Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar
10:30 - 11:00 hrs.	**Plenary Lecture – II** **Jayasri Das Sarma,** Indian Institute of Science Education and Research, Kolkata *ERp29 Regulates Murine β-coronavirus Infectivity and Replication by limiting Endoplasmic Reticulum Stress and facilitating Connexin 43 trafficking to the cell surface*
11.00 – 11.30 hrs.	**Tea**



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11.30 – 13.00 hrs.	**Symposium - VI** **(Multi Use Convention Hall)** ***Topic: Multiple facets of Neurodevelopmental Disorders*** **Chairpersons:** **Ravi Muddashetty,** IISc, Bengaluru **James P Clement,** Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore **Anindya Ghosh Roy,** National Brain Research Center, Manesar *Role of Muscleblind-like (MBLN) protein MBL-1 in axon growth and synapse formation* **Bhavana Muralidharan,** Institute for Stem Cell Science and Regenerative Medicine, Bangalore *Chromatin regulation of human neural stem cells by putative causative of intellectual disability- LSD1* **Ramkumar Sambasivan,** Indian Institute of Science Education and Research, Tirupati *Left-right asymmetry patterning of the mammalian body* **Sarayu Ramakrishna,** Centre for Brain research, IISc, Bangalore *Stitching together the domains of FMRP to elucidate its function* **Sonal Nagarkar Jaiswal,** CSIR-Centre for Cellular and Molecular Biology, Hyderabad *dIER3IP1: a novel player in vesicle trafficking*	**Symposium - VII** **(Community Hall)** ***Topic: Emotion and Cognition*** **Chairpersons:** **Laxmi T Rao,** NIMHANS, Bengaluru **Balaji Jayaprakash,** IISc, Bangalore **Sreedharan Sajikumar,** National University of Singapore, Singapore *Inhibitory metaplasticity in juvenile stressed rats restores associative memory in the adulthood by regulating epigenetic complex G9a/GLP* **Smitha Karunakaran,** IISc, Bangalore *Locus coeruleus integrity determines the longevity of fear memory in APPswe/PS1dE9 mice* **Suhita Nadkarni,** Indian Institute of Science Education and ResearchPune *Neuromodulation by acetylcholine preserves activity patterns at hippocampal synapses* **Balaji Jayaprakash,** IISc, Bangalore *Uncertainties in Older Memory Creates Rapidly Consolidating Memories of Unreal Events* **Kaviraja Udupa,** National Institute of Mental Health and Neurosciences, Bengaluru *Exploring the utility of Neuromodulation in novel therapeutic regimens in the management of Neurodegenerative disorders*	**Oral Session – V** **(Auditorium, Old Guest House)** ***Topic: Behaviour Modulation*** **Chairpersons:** **Jayasri Das Sarma**, IISER, Kolkata **Subhash C. Pandey**, UIC, Chicago **Arpita Konar**, Institute of Health Sciences, Presidency University, Kolkata *Early life trauma and pathological aggressive behaviour: Local thyroid hormone Connect?* **Pavan Agrawal**, Kasturba Medical College, Manipal Academy of Higher Education *Transcriptional and epigenetic mechanisms underlying social isolation stress in Drosophila* **Archana Gaur T**, All India Institute of Medical Sciences, Hyderabad *The effect of a high-fat diet combined with exercise on biochemical and anxiety-like behaviour in adolescent male and female rats* **Prem Chand**, T.D. P.G. College, V.B.S. Purvanchal University, Jaunpur *Electrophysiological and anatomical correlates for the ethological hand use in the primary somatosensory cortex of macaque monkeys*
(Community Hall) **13.00 – 13.45 hrs.**	**Lunch**		
(Community Hall) **13.30 – 15.00 hrs.**	**Poster Session - II**		



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	Invited Lecture Session- I **(Multi Use Convention Hall)**	Invited Lecture Session - II **(Community Hall)**	Invited Lecture Session - III **(Auditorium, Old Guest House)**
15.00 – 16.30 hrs.	**Chairpersons:** **TR Raju,** Sankara Academy of Vision, Bengaluru **Surya P. Singh,** BHU, Varanasi **Akshay Anand,** Post Graduate Institute of Medical Education & Research, Chandigarh *Neuromodulatory and proteinopathy molecules in the ALS plasma and CSF and the in-vitro validation* **Madhav Bhatia,** University of Otago, Christchurch, New Zealand *Substance P and Neurogenic Inflammation in Inflammatory Diseases* **KP Mishra,** Defence Institute of Physiology and Allied Sciences, Delhi *Repeated exposure of cytokines and alarmin may lead to differential neuroimmune modulation* **Prem N. Yadav,** CSIR-Central Drug Research Institute, Lucknow *TGR5 Receptor Modulation Alleviates Sensory Motor Functions & Cognition in Ischemic Cerebral Stroke* **Hiyaa Ghosh,** Tata Institute of Fundamental Research, Bangalore *Adult brain homeostasis: how do cells and circuit in the adult brain change or adapt to maintain normalcy?*	**Chairpersons:** **Shukla Prasad,** BHU, Varanasi **UC Srivastava,** NASI, Prayagraj **Pramod Avti,** Post Graduate Institute of Medical Education and Research, Chandigarh *Age related neurovascular changes and vulnerability towards neurodegenerative diseases* **Shyamanta M. Hazarika,** Indian Institute of Technology Guwahati *Influence of Affordance-driven Action Observation on Motor Imagery* **Shubha Srivastava,** KNGPG College, Gyanpur *Neural networks that control vocal communication in non-human animals and human language* **Tapas Chandra Nag**, All India Institute of Medical Sciences, New Delhi *Vulnerability of the aging human photoreceptor cells and its consequences* **Shubha Shukla,** CDRI Lucknow *Chronic unpredictable stress negatively regulate hippocampal neurogenesis and promote anxious depression-like behavior via upregulating apoptosis and inflammatory signals in adult rats*	**Chairpersons:** **SK Trigun,** BHU, Varanasi **AK Agrawal,** Lucknow **Usha Panjwani,** Defence Institute of Physiology and Allied Sciences, Delhi *Mental health in the modern world and the role of Meditation* **Suman Jain,** AIIMS, New Delhi *Modulation of synaptic plasticity and oxidative stress in streptozotocin induced Alzheimer's disease rats by magnetic field exposure* **Manorama Patri,** Ravenshaw University, Cuttack *Early life environment influences the mental health through gut microbiota* **Savita Gaur,** Defence Institute of Physiology and Allied Sciences, Delhi *Immediate changes in Brain Event related potentials in response to steep HDTBR in young healthy females* **James P Clement,** Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore *Understanding fundamental mechanisms and finding therapeutics to treat Autism Spectrum Disorder*
16.30 – 17.00 hrs.	**Tea**		



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	Symposium –VIII (Multi Use Convention Hall)	Oral Session - VI (Community Hall)	Oral Session - VII (Auditorium, Old Guest House)
17.00 – 18.30 hrs.	***Topic: Translational and Cellular Approaches in Neurodegeneration*** **Chairpersons:** **Phalguni A. Alladi,** NIMHANS, Bengaluru **Ravi Manjithaya,** Jawaharlal Nehru Centre for Advanced Scientific Research, Bengaluru **Poonam Thakur,** Indian Institute of Science Education and Research-Thiruvananthapuram *Factors guiding the selective vulnerability of dopaminergic neurons in Parkinson's disease* **Sangeeta Nath,** Manipal Academy of Higher Education, Yelahanka *Long-range intercellular transfer of organelles via tunneling nanotubes: implications in neurodegenerative and neurological diseases* **Ravi Manjithaya,** Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore *Regulation of synaptic autophagy In neurodegenerative diseases* **Phalguni A. Alladi,** National Institute of Mental Health and Neurosciences, Bengaluru *Fibrinogen and Complementary factor H are capable of inducing cognitive deficits in Parkinson's disease: A study vide a translational approach* **Yarreiphang Haorei,** Hansraj College, University of Delhi, Delhi *Apoptotic factors assist determination of strain-specific susceptibility of mice to Parkinsonian neurotoxin MPTP*	***Topic: Neurogenetics and immunology*** **Chairpersons:** **Nisha Patro,** Jiwaji University, Gwalior **Rajesh A Shenoi,** Mahatma Gandhi University Campus, Kerala **Trina Sengupta,** All India Institute of Medical Sciences (AIIMS), Jodhpur *Intragastric administration of dietary glutamate in the rats causes changes in medial preoptic area neuronal activity* **Priyankar Sanphui,** CSIR-Indian Institute of Chemical Biology, Kolkata *Novel small molecule inhibitors of Cdc25A protect neuronal cells in neurodegenerative disease models.* **Saroj Kumar Das,** Centre for Biotechnology, Siksha 'O' Anusandhan, Bhubaneswar *Understanding the decisive role of immunity related gtpase M (Irgm1) in regulating neuroinflammation and neurodegeneration in clinically relevant knockout mice model* **Subash Chandra Bose Chinnathambi,** CSIR-National Chemical Laboratory, Pune *Purinergic receptor P2Y12 involves in Tau oligomers-induced*	***Topic: Neurophysiology*** **Chairpersons:** **Anindya Ghosh Roy,** NBRC, Manesar **Subhas C. Biswas,** CSIR-IICB, Kolkata **Mehdi Hayat Shahi,** Aligarh Muslim University, Aligarh *Sonic hedgehog-Gli1-Pax6 cell signaling axis regulation of neurogenesis to brain tumor* **Ashutosh Shrivastava,** Center for Advance Research, Faculty of Medicine, Lucknow *Antiproliferative activity of ArsenicumIodatum and Arsenicum Album in Glioblastoma Multiforme* **Paramdeep Singh,** AIIMS, Bathinda *Role of diffusion-weighted MR imaging in evaluation of intracerebral Hemorrhage (ich)* **Ganesh Kumar C,** Kasturba Medical College, Mangalore *Effect of Spondiaspinnata (SP) bark extract on the hippocampus in etoposide induced mucositis rat model: Histological findings* **Yogananda S. Markandeya,** National Institute of Mental Health & Neurosciences, Bengaluru *Caveolin-1 Regulates Excitotoxic Signaling in Hippocampal Neurons*
(Community Hall) 18.30 – 19.30 hrs.	**General Body Meeting**		
(Community Hall) 19.45hrs.onwards	**Cultural Night and Networking Dinner**		



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Day 3: Saturday; December 10, 2022

(Multi Use Convention Hall) **09:00 - 09:30 hrs.**	**Plenary Lecture – III** **Chairpersons:** **Shukla Prasad,** BHU, Varanasi, India **Madhav Bhatia,** University of Otago, Christchurch, New Zealand **Laxmi T. Rao,** National Institute of Mental Health and Neurosciences, Bengaluru *Sensation-seeking behavior at adolescence – why and how?*
(Multi Use Convention Hall) **09:30 - 11:00 hrs.**	**Young Scientist' Colloquium - I** **Presentations for DM Kar Prize** **Chairpersons:** **Vinay K. Khanna,** CSIR-IITR, Lucknow **Sharmili Vidyadaran,** Universiti Putra, Malaysia **Apoorva Bettagere Shivakumar,** Department of Cell and Molecular Biology, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal, Karnataka, India *Compulsive like behaviours in Aβ 1-42 induced Alzheimer's disease in mice are associated with hippocampo-cortical neural circuit dysfunction* **Archana Mehta,** National Brain Research Centre, Manesar *SARS-CoV-2 mediated neuronal loss: Deciphering the mechanisms* **Biru B. Dudhabhate,** Department of Pharmaceutical Sciences, RashtrasantTukadoji Maharaj Nagpur University, Nagpur, Maharashtra, India *Deep brain stimulation of LH-MFB ameliorates depression by reversing the neuropathology in dorsal raphe nuclei-medial prefrontal cortex serotonergic circuit* **Devyani Sharma,** Department of Anatomy, All India Institute of Medical Sciences, New Delhi *Impact of iron overload on mitochondrial dynamics, autophagy, and ferroptosis in aging retinal photoreceptor cells* **Krishna S. Nair,** Centre for Development & Ageing Research (CDAR), Inter University Centre for Biomedical Research & Super Speciality Hospital (IUCBR & SSH), MG University Campus at Thalappady, Rubber Board PO, Kottayam, Kerala, India *Saccades in young adults with autism spectrum disorder (ASD) and attention deficient hyperactivity (ADHD) traits: Indications of reduced social preference in ASD* **Chaithanya Leon,** Department of Physiology, All India Institute of Medical Sciences, New Delhi *Resting EEG microstate as a state marker in children with attention deficit hyperactivity disorder.* **Sumela Basu**, School of Biological Sciences, National Institute of Science Education and Research, Jatni, Bhubaneswar *Transient receptor potential vanilloid 2 (TRPV2) in the rat brain: role in modulation of the nigrostriatal dopaminergic pathway*
11:00 - 11:30 hrs.	**Tea**
(Community Hall) **11:00 - 13:00 hrs.**	**Poster Session – III**
(Community Hall) **13.00 – 13.45 hrs.**	**Lunch**



(Multi Use Convention Hall) **13.45 – 15.00 hrs.**	**Young Scientist' Colloquium - II** **Presentations for Tulsabai Somani Educational Trust Award** **Chairpersons:** **KP Mishra,** DIPAS, Delhi **Rajat Sandhir,** Panjab University, Chandigarh, Panjab **Akash Gautam,** Centre for Neural and Cognitive Sciences, University of Hyderabad, Hyderabad, India *Nootropic effects of Curcumin: Modulation of synaptic plasticity genes in amnesic mice model* **Aliya Mufti,** Department of Physiology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India *Cortical Transcranial Magnetic Stimulation a Promising Biomarker and therapeutic modality to induce Synaptic Plasticity in Cerebral Palsy Children with Single and Paired Pulses Paradigm* **Anamika,** Department of Zoology, University of Delhi, Delhi *SIRT3 activation normalizes neuronal derangements by restoring mitochondrial integrity in hippocampus of the moderate grade hepatic encephalopathy rats* **Ankita Srivastava,** Department of Biochemistry, University of Lucknow, Lucknow, Uttar Pradesh, India *A proteomic approach to investigate unmasking of neurotoxicity in rechallenged adult rats prenatally exposed to lindane* **Madhav Sharma,** Department of Biological Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur, West Bengal, India *Interferon-Induced Tetratricopeptide Repeat Protein (Ifit2) Ifit2 restricts murine Coronavirus spread and demyelination in the spinal cord* **Tanaya Batabyal,** Faculty of Psychology, University of Warsaw, Poland 2- Institute of Psychology, Polish Academy of Sciences, Warsaw, Poland *Is there any relationship between temperament of an infant and social attentional network development within 1st year of life? - A longitudinal study.* **Punit Kumar,** Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India *L-Arginine induced chronic visceral pain in mice*



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15.00 – 16.30 hrs.	**Symposium - IX** **(Multi Use Convention Hall)** ***Topic: Acute Brain Injury: Long-Term Sequalae and Interventions*** **Chairpersons:** **Samba Reddy,** Texas A&M University College of Medicine, Texas, USA **Thota Ganesh,** Emory University School of Medicine, Atlanta, USA **Samba Reddy**, Texas A&M University College of Medicine, Texas, USA *Traumatic brain injury and its long-term consequences on dementia and neurological comorbidities* **Rama Maganti,** *University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA* *Sleep Disorders and Other Sequelae after Traumatic Brain Injury: Medical Therapeutics* **Thota Ganesh,** *Emory University School of Medicine, Atlanta, USA* *Prostaglandin-E2 receptor EP2antagonistattenuatesinflammationinvitro andaltersseizuresin atraumatic brain injury model* **Awanish Mishra,** *National Institute of Pharmaceutical Education and Research, Guwahati* *Psychoneuro-pharmacological Updates on Pathobiology of Cognition Deficits in Epilepsy*	**Oral Session - VIII** **(Community Hall)** ***Topic: Neurotherapeutics*** **Chairpersons:** **SK Trigun,** BHU, Varanasi **Debapriya Garabadu,** Central University of Punjab, Bathinda **Dushyant Kumar,** All India Institute of Medical Sciences, New Delhi *MRI evaluation of physiotherapy induced corticospinal tract changes in ischemic stroke patients* **Hannah P. Priyanka,** Institute of Advanced Research in Health Sciences, Tamil Nadu *Neurobehavioral toxicity by formulated Favipiravir and the restorative impact of Vitamin D supplementation in adult Zebrafish* **Nantu Das**, North-Eastern Hill University, Shillong *Running pace analysis and graphical representation of 1500- meter female middle-distance runners* **Rajesh A Shenoi,** Mahatma Gandhi University Campus, Kerala *Polymeric nanoparticles for mitochondrial targeting: In vitro assessment on mitochondrial localization and toxicity in neuronal cells* **Anushree Tripathi,** Umeå University, Sweden *Organization of Streams in the Mouse Orbitofrontal Cortex along the Mediolateral Axis: Role in Emotional Regulation*
(Multi Use Convention Hall) **17.00 hrs. onwards**	**Closing Ceremony** **Prize Distribution and Valedictory Ceremony**	



Poster Session – I
Day 1: Thursday; December 08, 2022
(Community Hall)

Abinaya Raghavan	Parkinson's pathology induced mitochondrial toxicities promote biogenesis of tunneling nanotubes and proliferation of glial cells	P001	08-Dec-22
Banashree Chetia Phukan	Unveiling the dopamine-rescue potential of a novel phytoconstituent of Garcinia sp. in Parkinson's disease	P002	08-Dec-22
AbhijnaBallal R	Intranasal administration of GABA-loaded extracellular vesicles from GABA progenitors reduces seizures in temporal lobe epilepsy	P003	08-Dec-22
Gouri Jadhav	Psychobiotics shape epigenetic reprogramming in the hippocampus via NF-kB-mediated histone acetylation: A role in trauma-induced learning and memory deficits	P004	08-Dec-22
Varshith MR	Genome Diversity and genetic interplay of Burkholderiapseudomallei causing Neuromelioidosis in patients from Indian setup	P005	08-Dec-22
Ananya Shukla	Identification of common biological pathways between Alzheimer's Disease and Metabolic Disorders through transcriptomic analysis	P006	08-Dec-22
Dr. Mukesh Kumar	White matter microstructural changes in early onset schizophrenia Using Diffusion tensor imaging (DTI) Study	P007	08-Dec-22
Kumari Nidhi	Assessment of Gut microbiota of Parkinson's disease patient and observe the activity of specific bacteriophages on pathological features of patient.	P008	08-Dec-22
Suramya Malhotra	Identification of common biological pathways between Alzheimer's Disease (AD) and Metabolic Disorders (MD)through transcriptomic analysis	P009	08-Dec-22
Monika Sharma	Effect of six-degree Head Down Tilt (HDT) on Event Related Function (ERPs) and cognitive functions in humans.	P010	08-Dec-22
RonysonKharkongor	Preserved cognitive and neural profile through intervention with a novel combination of Fucoidan and environmental enrichment in the rat model of transient global cerebral ischemia	P011	08-Dec-22
Durga Jeyalakshmi Srinivasan	The impact of social rank on vulnerability to stress	P012	08-Dec-22
Bhuvanesh Baniya	Network Pharmacological Evaluation of Origanum Vulgare Bioactivephytochemicals for Identifying Novel Potential Inhibitors Against Alzheimer Disease	P013	08-Dec-22
Kirti Arora	Psychological stress exacerbates neurological deficits in experimental model of irritable bowel syndrome.	P014	08-Dec-22
Suravi Sasmita Dash	Astaxanthin Regulates Ionotropic Glutamate Receptors and Mitochondrial Calcium Uptake in Cortical Neurons	P015	08-Dec-22
Priti Gupta	The status of vernier acuity following late sight onset	P016	08-Dec-22
Shiffali Khurana	Role of exosomal miRNAs in Amyotrophic lateral sclerosis	P017	08-Dec-22
Bandana Kumari Sahu	Effect of nootropics on SOD1-based cell model of Amyotrophic Lateral Sclerosis	P018	08-Dec-22
Sagar Verma	Deciphering disease mechanism in FUS-driven Juvenile Amyotrophic Lateral Sclerosis: a family quartet analysis	P019	08-Dec-22
Shyamal Mandal	Wristband for Position Tracking of Alzheimer's Patients with Health Condition Monitoring	P020	08-Dec-22



Jhilik Dey	Seizure-associated, aberrant neurogenesis in adult mice characterized by alteration of the hippocampal neurogenic niche	P021	08-Dec-22
Navneet Shahi	The Calsyntenin orthologue, CASY-1, affects neuromodulation to regulate sensorimotor output in C. elegans.	P022	08-Dec-22
Sneha Tiwari	Role of genistein (GEN) in mild unpredictable stress exposed mouse	P023	08-Dec-22
Farheen Nasir	Hydrogen sulphide enhances synaptic plasticity and restores cognitive dysfunction in traumatic brain injury induced mouse model	P024	08-Dec-22
Meghana BK	: Functional connectivity disturbances in psychogenic non-epileptic seizures: A machine learning study using Resting State fMRI	P025	08-Dec-22
Premchand Rajeev	Nanoscale regulation of Ca2+ dependent phase transitions and real-time dynamics of SAP97/hDLG	P026	08-Dec-22
Sandhya G	Comparison of ACE III scores between amnestic and non-amnestic MCI	P027	08-Dec-22
Devika Chopra	Zingerone (Zingiber Officinale) in combination with temozolamide inhibits glioma cell proliferation in rats: A neurobehavioral and neurochemical study	P028	08-Dec-22
Ankur Kumar Srivastava	Role of TrkA signaling in the Monocrotophos induced neurotoxicity in rat brain neural stem cell derived neuronal cells	P029	08-Dec-22
Rahul Chittora	Short duration, early exposure to low intensity magnetic field stimulation ameliorates cognitive deficits and restores delta power in Alzheimer's disease rat model	P030	08-Dec-22
Mrudula Kambhampati	Autonomic functions as a window to identify the severity of disease in patients with Alcohol use disorder with Adult ADHD	P031	08-Dec-22
Lakshmi Jaya Madhuri B	Pb and Î²-amyloid peptide induced toxicity leads to the mitochondrial alterations in the mitophagy and apoptosis in the human neuronal cells	P032	08-Dec-22
Bindu	Role of zika virus induced autophagy in neural stem cell fate determination	P033	08-Dec-22
Jimna Mohamed Ameer	Honokiol prevents MPTP neurotoxicity in differentiated SH-SY5Y cells and in C57BL/6 mice	P034	08-Dec-22
Sana Sarkar	Identification of novel miRNA-protein regulatory modules and their implications in arsenic-induced neurodegeneration	P035	08-Dec-22
Chinthu V Saji	PLGA-based Centella asiatica nanoformulation: In vitro preclinical findings on its effects against Parkinson's disease pathogenesis	P036	08-Dec-22
Renu Negi	Human iPSCs derived spheroid: A human brain specific 3D tool to study the developmental neurotoxicity potential of xenobiotics	P037	08-Dec-22
Pankhi Vatsa	PC 12 secretome enhances neuronal differentiation of human mesenchymal stem cells and protects against toxic insult of Monocrotophos	P038	08-Dec-22
Shivangi Sharma	miR-9 Regulates the Fate of Neural Stem/Progenitor Cells Following Japanese Encephalitis Virus Infection	P039	08-Dec-22
Mr Anuj Pandey	Expression of miR-29b regulates Sirtuin-1-mediated apoptosis and cellular bioenergetics in Parkinson's disease	P040	08-Dec-22
Uzair Ahmad Ansari	Towards the development of human iPSCs derived TDP43 linked model of ALS: Critical involvement of autophagy and lysosomal dynamics	P041	08-Dec-22
Abhinav Srivastava	Secretagogin, a calcium binding protein in the brain of Indian wall lizard Hemidactylus leschenaultti	P042	08-Dec-22



Harsha P J	In vitro assessment of mimosine as a brain iron chelator: Its potential for iron binding, antioxidant activities and SH-SY5Y neuronal toxicity in culture	P043	08-Dec-22
TulikaRajawat	Pre-Stimulus EEG Microstates and its Cortical Sources during an Emotional Interference Task	P044	08-Dec-22
SANDEEP	NADPH oxidase inhibitor apocynin attenuates Paraquat-induced motor deficits in the rat model of Parkinsonism	P045	08-Dec-22
Neeraj Rawat	Effect of chlorpyrifos and cypermethrin exposure on the expression of Î±-synuclein, cyclooxygenase-2 and tyrosine hydroxylase in rat nigrostriatal tissue	P046	08-Dec-22
Raj Amarlal Katariya	Role of Central Agmatine In Etiopathogenesis of Huntington's Disease In Rats	P047	08-Dec-22
Mahima Kapoor	The Purinergic receptor P2Y12 signalling in Tau aggregates-induced ECM degradation and microglial migration	P048	08-Dec-22
NaqiyaAmbareen	Understanding the role of Sertad1 in autophagy dysfunction in Alzheimer's disease	P049	08-Dec-22
Akanksha Mishra	Expression of Neurotrophins (BDNF and NT-3) in Adult Human Cochleae	P050	08-Dec-22
Sagar Tyagi	Delineating the role of TNF-Î± & JAK-STAT signaling pathways in promoting oligodendrocyte differentiation in vitro	P051	08-Dec-22
Akash Mangal Waghade	Intracranial self-stimulation of LH-MFB ameliorate impaired reversal learning in schizophrenic like condition in rat: role of neuronal nitric oxide synthase	P052	08-Dec-22
Guneet Kaur	Envelope protein of Zika Virus alters properties of Brain Microvascular Endothelial Cells and Astrocytes in an in vitro human Blood Brain Barrier	P053	08-Dec-22
Siraj Fatima	A natural small molecule inhibits alpha-synuclein aggregation, maintains native monomeric structure and prevents neuronal degeneration	P054	08-Dec-22
Debarati Rakshit	Evaluation of the protective effect of fisetinnanoformulation in an experimental model of Alzheimer's disease	PA001	08-Dec-22
Sudipta Nayak	Evaluation of fisetinnanoformulation in experimental model of temporal lobe epilepsy	PA002	08-Dec-22
Snehashis Kundu	Protective effect of fisetin on arsenic and fluoride induced neurotoxicity	PA003	08-Dec-22
Raja Babu	American ginseng attenuates astrocytopathy in cell culture study	PA004	08-Dec-22
Amarjeet	American Ginseng exhibits anti-neuroinflammatory activity in LPS-stimulated microglia in an in-vitro study	PA005	08-Dec-22
Deshdeepak Ratna	Activation of cholinergic REM-ON neurons in PPT projecting to VTA increases REMS in rats: implications with intermittent appearance of REMS	PA006	08-Dec-22
Grishma Kasle	Proinflammatory and anti-inflammatory mediators regulate the host response to viral infection by altering the connexin 43 mediated gap junctional communication	PA007	08-Dec-22
Soumya B S	Comprehending the molecular cascade promoting motor neuron degeneration in a stem cell model of Amyotrophic Lateral Sclerosis	PA008	08-Dec-22
Aniket Aman	Effect of cardiovascular risks on Brain Structure Volumetry with Aging in Cognitively Normal, Mild Cognitive Impairment and Dementia Patients: Advanced Neuroimaging Investigations in ADNI Cohort	PA009	08-Dec-22
Adla Zubair	Dream Detector: Decoding Multivariate EEG pattern between dream recall and no recall from High-density PSG data	PA010	08-Dec-22



Prabhat Sharma	Personality or hunger states: What determines rationality in zebrafish (Danio rerio)?	PA011	08-Dec-22
Thasya Harsha Shetty	Single-dimensional multi-alternative shoal choice decoy space map of zebrafish (Danio rerio)	PA012	08-Dec-22
Nicky Singh	The neuroinflammatory markers in the frontal cortex are correlated with some memory impairments in intracerebroventricular streptozotocin injected rats in a time dependent study.	PA013	08-Dec-22
Archana Choudhary	Neurosteroid basis of molecular mechanism of Chronic Immobilization Stress: Systematic literature analysis	PA014	08-Dec-22
Rahul S. Nair	Correlative effects of distressed-body image scores on metastatic markers and depression in Indian women with breast cancer	PA015	08-Dec-22
Raj Kamal Srivastava	CB1 receptor in the catecholaminergic neurons: A â€œbrakeâ€ for exaggerated stress response	PA016	08-Dec-22
Palkin Arora	Traumatic brain injury leads to acute changes in systemic metabolism in rats	PA017	08-Dec-22
Tushar Ranjan Bhatta	Monoaminergic and neuropeptide interaction in mammalian brain cerebral cortex during immobilization stress: Systematic literature analysis.	PA018	08-Dec-22
Kumar Neelabh	Population encoding of meaning in the avian auditory cortex	PA019	08-Dec-22
Bhanuteja T	Neuronal Correlates of effects of Sleep deprivation induced Neuroinflammation on Fear Extinction Memory Consolidation	PA020	08-Dec-22
Aditya Fulluke	Single-dimensional multi-alternative shoal choice decoy space map of zebrafish (Danio rerio)	PA021	08-Dec-22
Megha Kumari	Metabolic and behavioral assessment of moderate blunt TBI at sub-acute time point	PA022	08-Dec-22
Monika Patel	The effect and mechanism of CXCL10 modulation of neuroinflammation and its consequences on synaptic plasticity and cognition	PA023	08-Dec-22
Sujay Daniel	Achievement Motivation During Adolescence: A Case Study on Siddi Children	PA024	08-Dec-22
Jemimah N.	Effect of methyl paraben on serotonin levels governing autistic behavior in zebrafish larvae.	PA025	08-Dec-22



Poster Session – II
Day 2: Friday; December 09, 2022
(Community Hall)

Ankita Namdeo	The Purinergic receptor P2Y12 in Tau aggregate clearance by endocytosis and degradation in microglia	P055	09-Dec-22
Rajitha Narayanasamy	Prevalence of MCI and Dementia and Its Association with Sociodemographic Factors	P056	09-Dec-22
SAFREENA N	"Animal models with behavioural distinctions in full blown and prodromal Alzheimer's disease"	P057	09-Dec-22
Phoolmala	Targeting Mitochondrial Trafficking by Environmental Toxicant Bisphenol-A in the Rat Hippocampus	P058	09-Dec-22
Khushi Jain	Rule-Based Categorization of Tactile Textures Using Linguistic Labels	P059	09-Dec-22
Hemant Subhashrao Kanhere	Deep brain stimulation of lateral habenula reverses depressive phenotype in the chronic unpredictable mild stress induced depressed rats	P060	09-Dec-22
Ankita Vijay Thul	Protocatechuic acid attenuate NR2B-mediated excitotoxic cell death post ischemic reperfusion injury	P061	09-Dec-22
Bhavesh Verma	Intra-habenular effect of cerebrolysin on ethanol dependence in mice	P062	09-Dec-22
Utkarsh Prakash Patil	Neuropeptide S facilitates reward by enhancing the activity of CARTergic neurons in lateral hypothalamus	P063	09-Dec-22
Niraj Kumar Gupta	Regional distribution of White Matter Hyperintensity and its implication in Brain Structure and Cognition with Aging	P064	09-Dec-22
Manasi D. Deorankar	Effect of medial forebrain bundle deep brain stimulation on affected reward motivation due to chronic stress model of depression	P065	09-Dec-22
Abdul Naeem	MCC950 boosts cognition and lowers anxiety through inhibiting NLRP3 and autophagy	P066	09-Dec-22
Rehana Khatoon	Chronic Vitamin D3 administration rescues working memory and attention in MK-801 induced mouse model of schizophrenia	P067	09-Dec-22
Pankaj	Cerebellar volumetric changes in Spinocerebellar ataxia type 12 patients	P068	09-Dec-22
Kumari Sarita Pandey	Pax6 and CTCF are inversely regulated in brain of Streptozotocinâ€“treated hyperglycemic mice	P069	09-Dec-22
Soni Kumari	Proteomics Spotlight on Biomarkers of Parkinson's Disease	P070	09-Dec-22
Bhaskar Sharma	Choroidal capillary death in aging rat eye with emphasis on involvement of immunocompetent cells	P071	09-Dec-22
Saurabh Kumar	Yoga: as a tool to enhance the Neuropsychology and Biochemical profiling in the newly recruited Police Personnel	P072	09-Dec-22
Roana Liz George	Preliminary investigation on the effect of serum vitamin D status in young adults on serotonin and neurobehavioral symptoms typical of autism spectrum disorder and attention deficit hyperactivity disorder	P073	09-Dec-22
Richa Singh	Oleuropein protects from rotenone-induced nigrostriatal neuronal death in mice model by activating PI3K-Akt signalling pathways.	P074	09-Dec-22
Priya Mishra	Medicinal Preparations of Nux Vomica Seed Extracts and Cicuta Virosa Root Extracts can Potentiate Neuronal Fortification by Upregulating Mitochondrial Biogenesis Pathways in PTZ induced Kindling Mice Model of Epilepsy	P075	09-Dec-22



Hagera Dilnashin	Tinospora cordifolia Protects Dopaminergic Neurons from Mitochondrial Dysfunction and Attenuates Rotenone-Mediated Parkinson's Disease	P076	09-Dec-22
S K Venkata Manjari	Vitamin D3 administration decreases oxidative stress induced by 3-nitropropionic acid and alleviates native immune receptor, T-cell receptor beta subunit expression in a mouse model of Huntington's disease	P077	09-Dec-22
Kanupriya Sharma	Mind body techniques-based amelioration of stress through neurogenic molecular mechanism	P078	09-Dec-22
Pinky	Pathophysiological alterations of the prefrontal cortex in a rat model of Alzheimer like disease with a preferential role of "Propranolol"	P079	09-Dec-22
Priya Battu	Role of candidate genes (ARMS2, COL10A1, RAD51B, and TGFBR1) Single nucleotide polymorphisms and protein levels in Age-related Macular Degeneration	P080	09-Dec-22
Shambhu Kumar Prasad	A deep proteome study of the rat hippocampus reveals crucial proteins involved in the pathogenesis of Moderate Hepatic Encephalopathy	P081	09-Dec-22
Ravi Prakash	MCC950 modulates the SIRT3-NLRP3 inflammasome dynamics in oxygen glucose deprived stem cells	P082	09-Dec-22
Aaina Singh Rathore	Curcumin activates selective autophagy through p62-mediated Nrf2-Keap1 pathway in Parkinson's disease	P083	09-Dec-22
Kajol Rustage	An Alzheimer's disease Domain-Specific network pharmacology of Nelumbo nucifera and specific targets identification responsible for Alzheimer's disease	P084	09-Dec-22
Kalyan Maity	Molecular, cell survival and neuro-cognitive effects of yoga intervention in stress induced cognitive impairment in prisoners	P086	09-Dec-22
Priya Mehra	Potential of stem cells in rescue of retinal injury and visual memory by subretinal transplantation of UCB derived Lineage negative stem cells in mice.	P087	09-Dec-22
Arushi Chauhan	To discover a novel investigational molecule towards serotonin receptor modulation for targeting neurodegenerative disorders.	P088	09-Dec-22
Manish Prajapat	Artificial Activation of Hippocampal Subfield CA1 drives the memory-driven Perception which interferes with the Sensory Perception	P089	09-Dec-22
Priyanka Kumari Keshri	18-Î^2 Glycyrrhetinic acid ameliorates alpha-synuclein aggregation targeting the ER-stress pathway in the Parkinsonian mouse model.	P090	09-Dec-22
Namrata Sangwan	Identification of a novel agonist and anti-ferroptotic small molecule for ferroptosis cascade receptor glutathione peroxidase (GPX4) targeting acute ischemic stroke	P091	09-Dec-22
Vaishali yadav	Glial niche and its function in central nervous system development	P092	09-Dec-22
Annapoorna P K	A novel histone lysine demethylase of the KDM7 family is implicated in chronic stress-induced depression-like phenotype in mice with specific involvement in adult neurogenesis	P093	09-Dec-22
Abu Junaid Siddiqui	Oxidative Stress-induced Impairment in human Mesenchymal Stem Cells	P094	09-Dec-22
Radhika Khosla	Altered patterns of angiogenic and neuroprotective molecules in CSF and plasma of ALS patients leads to degeneration of NSC 34 cells	P095	09-Dec-22



Manas Ranjan Sahu	Treatment with novel Hippo Signaling inhibitor, Xmu-mp-1, ameliorates cognitive impairments in sporadic Alzheimer's disease	P096	09-Dec-22
Nirupam Das	Parvalbumin interneurons (PV-IN) of dCA1 preserves details of episodic memories	P097	09-Dec-22
Athira M Menon	Establishing a 3D Coculture System to Mimic the Tumor Micro-Environment to study the Role of Neural Stem Cells in Prostate Cancer Cell lines	P098	09-Dec-22
Rajesh Kumar Ojha	Chronic defeat stress stimulates the RFRP-3 system in the hypothalamus and adrenal glands of adult mice	P099	09-Dec-22
B.Sindhusree	Identification of miRNA that targets EIF4EBP1 which is involved in protein translation.	P100	09-Dec-22
Megha Bhat Agni	Evaluation of the potential of Astaxanthin and DHA to mitigate the perinatal stress induced cognitive deficit and synaptic plasticity in the adult life	P101	09-Dec-22
Vanika Dhingra	Role of sub-synaptic molecular organization in modulating synaptic transmission	P102	09-Dec-22
Yogesh Sharma	Light injury to the retina: the protective role of ghrelin and its receptor GHSR-1a	P103	09-Dec-22
Nidhi Ghosh	Pax6 gets downregulated due to LPS-mediated Neuroinflammation in mouse brain	P104	09-Dec-22
Zubin Singh Rana	Epileptiform activity impairs bidirectional plasticity in the rat hippocampus	P105	09-Dec-22
Radhika Dhawan	Tetrahydroxy flavonoid class of anti-cardiovascular compound as a potential regulator towards Glutathione peroxidase (GPX4) in Ischemic stroke.	P106	09-Dec-22
Meghnaa Sakthi Ashok Kumar	Acute Dexamethasone Exposure Induces Developmental Toxicity and Alters Antioxidant Enzyme Activity in Zebrafish Embryo	PA026	09-Dec-22
Saathwick S	Role of Vitamin C In Restoring the Impaired Neural Behavior, Metabolic Enzyme, Antioxidant Enzyme Status In Adult Zebrafish Exposed To Dexamethasone	PA027	09-Dec-22
Usha Rani Balu	Toxicological effects on serotonergic system and its neuro-behavioural changes on chronic triclosan exposure in adult zebrafish	PA028	09-Dec-22
Aishika Datta	Apelin-13 alleviates post-stroke depression via regulating BDNF mediated phosphorylation of forkhead box O 3A protein in rat model of ischemic stroke	PA029	09-Dec-22
Prince Upadhyay	Human Brain Detects and Responds Against the Filarial SERPINS; A Way Forward Towards Theragnostic of Neuropathies	PA030	09-Dec-22
Madhura Milind Nimonkar	In silico analysis of two novel variants of the voltage-gated sodium channel encoding gene SCN1A involved in epilepsy	PA031	09-Dec-22
Tejal Pravin Yeole	Poor regulation of mitochondrial dynamics exacerbates stroke outcome in rodent model of chronic kidney disease-stroke complex	PA032	09-Dec-22
Dipali Machhindra Rahane	Stroke in pregnancy: An exploration towards altered epigenetic regulation in offspring	PA033	09-Dec-22
Akundi Soumya Shesharao	Stroke in pregnancy: An exploration towards altered epigenetic regulation in offspring	PA034	09-Dec-22
Pathulothu Vinod	Endoplasmic Reticulum Stress Exacerbates Stroke Outcome in Rodent Model of Chronic Kidney disease	PA035	09-Dec-22
Kaveri Sanjay Wagh	Post-stroke inosine therapy regulates inflammasome mediated microglial polarization in rodent model of ischemic stroke.	PA036	09-Dec-22



Swagata Bhattacharya	Poor regulation of mitochondrial dynamics exacerbates stroke outcome in rodent model of chronic kidney disease-stroke complex	PA037	09-Dec-22
Tannu Dhingra	Post-stroke inosine therapy alleviates inflammasome activation and modulates microglial polarization in rodent model of ischemic stroke	PA038	09-Dec-22
Bhurle Gangadhar	Stroke in pregnancy: An exploration towards altered epigenetic regulation in offspring	PA039	09-Dec-22
PratikshaDilip Godse	Endoplasmic Reticulum stress exacerbates stroke outcomes in rodent model of chronic kidney disease	PA040	09-Dec-22
Chandrima Saha	Endoplasmic Reticulum Stress exacerbates Stroke Outcome in Rodent Model of Chronic Kidney Disease	PA041	09-Dec-22
Tazeen Qureshi	HDAC6 promotes podosome-mediated migration in neurons	PA042	09-Dec-22
Muskaan Sharma	Post-stroke inosine therapy alleviates inflammasome activation and modulates microglial polarization in rodent model of ischemic stroke	PA043	09-Dec-22
Chalavadi Guruswamy	Poor regulation of mitochondrial dynamics exacerbates stroke outcome in rodent model of chronic kidney disease-stroke complex	PA044	09-Dec-22
Bijoyani Ghosh	Role of Statin in Regulating Endoplasmic Reticulum Stress in Stroke	PA045	09-Dec-22
Ashwini L S	Neuroprotective potential of Tinospora cordifolia in attenuating hippocampal CA3 neuronal damage induced by prenatal stress and maternal separation	PA046	09-Dec-22
Chalavadi Sivaraju	Major visual processing centres of Hieroglyphus banian	PA047	09-Dec-22
Anwesha Bhattacharyya	Evaluation of Cortical Vision with Next Generation Optogenetic Tools	PA048	09-Dec-22
Deepak K V	The role of p21 activated kinase in the repair of oligomeric amyloid-Î² induced plasma membrane damage and its implication in pathology spreading in Alzheimer's disease	PA049	09-Dec-22
Divya C	An In-Vitro Approach in Understanding Interneuron Migration	PA050	09-Dec-22



Poster Session – III
Day 3: Saturday; December 10, 2022
(Community Hall)

Mir Hilal Ahmad	Naringenin modulates oxidative stress and promotes mitochondrial perturbation in paraquatinduced parkinsonism in rat	P107	10-Dec-22
Mithila Ashok Kamble	Inducible Nitric Oxide Synthase deficiency protects against murine coronavirus induced demyelination	P108	10-Dec-22
Ahmad Raza Khan	NMR based Metabolomics of Mild and Repetitive Brain injury in a realistic rat model	P109	10-Dec-22
Bhagyashree Senapati	A Neural mechanism of Malaise learning in Fruit fly	P110	10-Dec-22
Seema Dhariwal	Comparative Lipid Profiling of Blast and Blunt Induced Traumatic Brain Injury in Preclinical Model	P111	10-Dec-22
Muneesh Pal	Identification of disease-relevant roles of Kalrn locus long non-coding RNAs in the mammalian brain	P112	10-Dec-22
Nisha Sarkar	An in-vitro study on the role of Oligodendroglia in sporadic Amyotrophic Lateral Sclerosis	P113	10-Dec-22
Ruchi Baghel	Plasma metabolic profiling based altered metabolic signatures and pathways in blast-related Mild TBI	P114	10-Dec-22
Shuvadeep Maity	Identification of the complex molecular signatures behind the differential vulnerability between ALS-resistant and sensitive motor neurons â€" a multi-omics approach	P115	10-Dec-22
SuvadeepMaiti	Neural responses of zebra finches to various interpersonal calls are influenced by social relationships	P116	10-Dec-22
Remya V R	Design and development of Ayurvedic nutraceutical-based food formulations for the treatment of Parkinson's disease	P117	10-Dec-22
Sneha Sanjay Vatte	Effect of alaternin on ischemic reperfusion injury	P118	10-Dec-22
Soumita Goswami	ICAM1 reduces amyloid-Î² induced gliosis and improves synaptic plasticity in 5xFAD mice model of Alzheimer's Disease	P119	10-Dec-22
Anima Roy	Methylcobalamin recovers demyelination-associated decline in neuronal arborization & cognitive functions in the MoHE rat model of neuroexcitotoxicity	P120	10-Dec-22
Aashima Jain	Omega-3 fatty acid polarizes microglial cells towards anti-inflammatory pathway	P121	10-Dec-22
Swati Kumari	The epigenetic effect of Cardiac Yoga Protocol on coronary artery disease patients and its impact on neuropsychological and molecular profile of CAD Patients	P122	10-Dec-22
Ashwini Anil Patil	The nitrergic projection from SC to VTA plays an essential role in the modulation of cognitive flexibility in rats	P123	10-Dec-22
Somasish Ghosh Dastidar	Deciphering if Senataxin, a gene whose mutation leads to Amyotrophic lateral Sclerosis 4, may act as a genetic modifier for sporadic Amyotrophic Lateral Sclerosis and familial Amyotrophic Lateral Sclerosis.	P124	10-Dec-22
Ratnesh Kumar Soni	Anatomical and morphological characterization of neurons responsible for cognition in pigeon (Columba livia)	P125	10-Dec-22
Manjari Rain	Differential role of autophagy in dry and wet age-related macular degeneration	P127	10-Dec-22
Archita Khanna	SIRT1 activation dependent transcriptional regulation of NMDAR subunits (NR2A and NR2B) by HIPK2 in animal model of major depressive disorder	P128	10-Dec-22



Sruthi Susan Kuriakose, Aishwarya Swamy	A simple seizure prediction approach running on a single board computer	P129	10-Dec-22
Swapna K K	Caveolin-1 Over Expression Mitigates Glutamate Mediated Excitotoxicity By Modulating Ionotropic Glutamate Receptor Function	P130	10-Dec-22
Pooja Nadholta	Efficacy of Mind- Body practice in maintaining good psychological health among pregnant women.	P131	10-Dec-22
Subhajit Jana	Fear conditioning leads to enduring alteration in RNA transcripts in hippocampal neuropil that is dependent on EphB2 forward signaling	P132	10-Dec-22
Nivedita Singh	Fluorescence Lifetime imaging by stochastic labelling using fluorogen activated FAST tags	P133	10-Dec-22
Madhumita P. Ghosh	Insulin like growth factor-1 with dopamine is neuroprotective against proliferative diabetic retinopathy	P134	10-Dec-22
Venkata Surya Kumar	In-vitro characterization of EIF4EBP2 using CRISPR-Cas9 mediated knock out and lentiviral mediated knockdown in HEK 293T and SHSY5Y cell lines	P135	10-Dec-22
Anshita Singh	Predicting White Matter abnormalities in Children Bipolar disorder	P136	10-Dec-22
Prijesh K	SRF-deficient reactive astrocytes are neuroprotective in the aging mouse brain	P137	10-Dec-22
Vaishali Kumar	Understanding the proteomic signature responsible for the Vitamin D3-mediated restoration of spatial memory in a mouse model of Huntington's disease	P138	10-Dec-22
Savita Kumari	Development of a chronic kindling model of adult zebrafish with clinical correlation	P139	10-Dec-22
Ajit Kumar Thakur	Comparative Study of Low-Dose Antibiotics in MPTP-Induced Parkinson's Disease: Pre-clinical Study	P140	10-Dec-22
Preeti Khera	Sweep Screening of Working Professionals using parametric MMSE domains	P141	10-Dec-22
Niyamat M A Chimthanawala	Neuroprotective role of daidzein, a phytoestrogen in rotenone-induced Parkinson's Disease	P142	10-Dec-22
Harish Mohan Kawade	Neuropeptide S facilitates fear extinction learning and memory by enhancing the activity of mesolimbic dopaminergic circuitry	P143	10-Dec-22
Manubhav Yadav	Activation of Kappa Opioid Receptor epigenetically regulates BDNF expression in the prefrontal cortex	P144	10-Dec-22
Dr. Vinod Tiwari	Behavioral and Pharmacological Validation of New Clinically MimickableModel of Chemotherapy-induced Neuropathic Pain	P145	10-Dec-22
Nikhitha Sreenivas	Peripheral neuropathy in alcohol use disorder patients: Exploring the role of oxidative and nitrosative stress pathway	P146	10-Dec-22
Kaushik Kumar Dey	Proteomic landscape: novel insights into pathogenesis and toward biomarker discovery for Alzheimer's disease	P147	10-Dec-22
Yogesh Sahu	Transcriptional Control of Mammalian Axon Regeneration - Role of Nuclear Receptors (NR) family of Transcription factors	P148	10-Dec-22
Subhajit Jana	Fear conditioning leads to enduring alteration in RNA transcripts in hippocampal neuropil that is dependent on EphB2 forward signaling	P149	10-Dec-22
Koyel Das	A Comparative Study of Vemp and vHIT in Vestibular Migraine andOther Variants Of Migraine	P150	10-Dec-22
Jaansi Bhansali	Study on the ameliorative potential of Methyl cinnamate in Alzheimer's disease model of Drosophila melanogaster	P151	10-Dec-22



Chelsea Rumao	Assessing The Therapeutic Potential of Methyl Cinnamate on park13 Mutants, a Parkinson's Disease Model of Drosophila melanogaster	P153	10-Dec-22
Arun Shankar Nair	Evaluation of Anti-Parkinson's activity of Silver herbomineral (Rajat bhasma) on MPTP induced Parkinson's disease in C57BL/6 mice	P154	10-Dec-22
Aneesa PA	A metagenomic approach to investigate the alterations in the gut microbiome of patients with Parkinson disease compared to Healthy controls	P155	10-Dec-22
Sumukha Hegde	Evaluation of lipid composition at various stages of neurodevelopment	PA051	10-Dec-22
Stuti Mohapatra	Role of lncRNA Gm20559 in flaviviral infection and associated inflammation in microglia	PA052	10-Dec-22
Haseena P A	Post synaptic density 95 (PSD95)â€“Actin interaction: A critical regulator of synaptic strength and plasticity.	PA053	10-Dec-22
Neha Dhiman	Identification of PPAR modulators as therapeutic targets in Alzheimer's Disease	PA054	10-Dec-22
Sonam Deshwal	Identification of non-steroidal LXR modulators as a key regulator of cholesterol homeostasis against Alzheimer's diseases.	PA055	10-Dec-22
Tripti Seth	Are claudins involved in synapse function in vertebrate neurons?	PA056	10-Dec-22
Shrilaxmi M S	Molecular analysis of the pathophysiology and virulence determinants of Burkholderiapseudomallei from Neuromelioidosis patients in Indian setup	PA057	10-Dec-22
Saradindu Banerjee	Characterizing the antidepressant potential of RXFP3 agonists in mice and rats	PA058	10-Dec-22
Medha Kaushik	Computational Markers for Validation of Long-Term Memory Consolidation Utilizing Behavioral Tagging and In Vivo Electrophysiology	PA059	10-Dec-22
Jyoti Tyagi	Alterations in the Expression of PNPO, FOXO3, and GABRA Affect the Electro-Behavioral and Spatial Learning in FeCl3-Induced Epileptic Rats	PA060	10-Dec-22
Neha Yadav	Advanced Neuroimaging and Event Based Modeling of Brain Structures and Microstructures: Development of Imaging based artificial intelligence platform predictive of Cognitive status and Dementia	PA061	10-Dec-22
Anuradha Mangla	Contributing role of Bisphenol A in augmenting the oxidative stress in brain of obese female rats	PA062	10-Dec-22
Rachagolla Sai Prathap Yadav	Identification of novel genes regulating social isolation induced behaviors in Drosophila.	PA063	10-Dec-22
Rachana Kashyap A N	Role of actin signalling pathways in Î±-synuclein induced tunneling nanotubes mediated transformation of neuroglial cells into cancer stem-like cells	PA064	10-Dec-22
Nisha	Role of genistein in cognitive impairment through SOD and CAT manifested in behavioral test of stressed mice	PA065	10-Dec-22
Hiba Khan	Repurposed Drug Exerts Neuroprotective Effect In Sub Arachnoid Hemorrhage Via Restoring Mitochondrial Dysfunction	PA066	10-Dec-22
Neha	Amelioration of cognitive deficit by atorvastatin in AÎ²1-42 induced Alzheimer's disease in a rat model	PA067	10-Dec-22
Malvika Ganesh Iyer	Brain tumor segmentation using multimodal neuroimaging techniques: a deep convolutional neural network approach.	PA069	10-Dec-22



SumelaBasu	Transient receptor potential vanilloid 2 (TRPV2) in the rat brain: role in modulation of the nigrostriatal dopaminergic pathway	PA070	10-Dec-22
Priyanka Gautam	Evaluation of gut microbiota diversity in Amyotrophic Lateral Sclerosis	PA071	10-Dec-22
S. Indira Priya	Elucidating The Anti-Inflammatory Role of SCFA in Jev Mediated Neuroinflammation In Mice	PA072	10-Dec-22
Saba Afsheen	Neurotoxicity Assessment of Fenpropathrin in Drosophila Melanogaster	PA073	10-Dec-22
Hannah Priscilla	Mitophagy in retinal cells after experimental iron accumulation in rats	PA074	10-Dec-22
Abir Mondal	G6PD deficiency mediated dysregulation of redox equilibrium contributing to Covid-19-mediated neuroinflammation	PA075	10-Dec-22
Ariyanachi Kaliappan	Morphometric analysis of anterolateral triangle of cavernous sinus with its clinical significance – a cadaveric study	PA076	10-Dec-22
Ankit	Reduced cortical activation and functional connectivity in attention deficit hyperactivity disorder during working memory task: A QEEG study	PA077	10-Dec-22
Urmila John	CSPG upregulation causes impaired dendritogenesis and spinogenesis, leading to synaptic dysregulation and inhibition of plasticity in a double-hit rat model of protein malnutrition (PMN) and bacterial infection (LPS)	PA078	10-Dec-22



XL Annual Meeting of
Indian Academy of Neurosciences

Theme: Neuroscience Research: Current Trends and Future Needs

North-Eastern Hill University
Shillong, Meghalaya, India

December 08-10, 2022

Guidelines for
Award Session and Poster Presentation

Dr. D.M. Kar Prize

Number of Prize – 1, Age limit - 35 years, Mode of presentation – **Oral**

TulsabaiSomani Educational Trust Award

Number of Award – 1, Age limit - 40 years, Mode of presentation – **Oral**
The presenter should be member of the Academy.

The presentation will be for 8 minutes followed by discussion/question(s) if any for 2 minutes. Multimedia facilities will be available for presentation.

The presenters are advised to organize their presentation in the following way-
Prior art, Rationale/Hypothesis, Methods, Salient observations (Figures/Tables) with discussion and conclusion.

Judgment is made on the following points:

Clear objectives

Approach to the problem

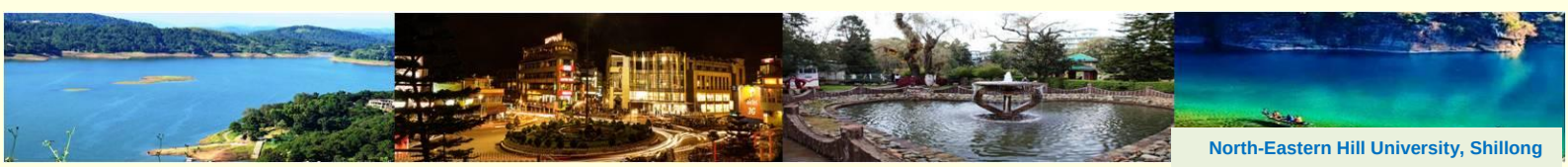
Findings in relation to aims and objectives

Conclusion

Clarity of presentation

Ability to answer the question(s)

There will be minus points for candidates if aided by mentors or colleagues and / or not keeping time. The decision of the referees will be final.



SS Parmar Research Foundation (USA) Prize

Number of Prizes – 2, Age limit - 35 Years, Mode of presentation – **Poster**

Suttee Nag Prize

Number of Prizes – 2, Age limit - 35 Years, Mode of presentation – **Poster**

*Sf*N Bangalore Chapter

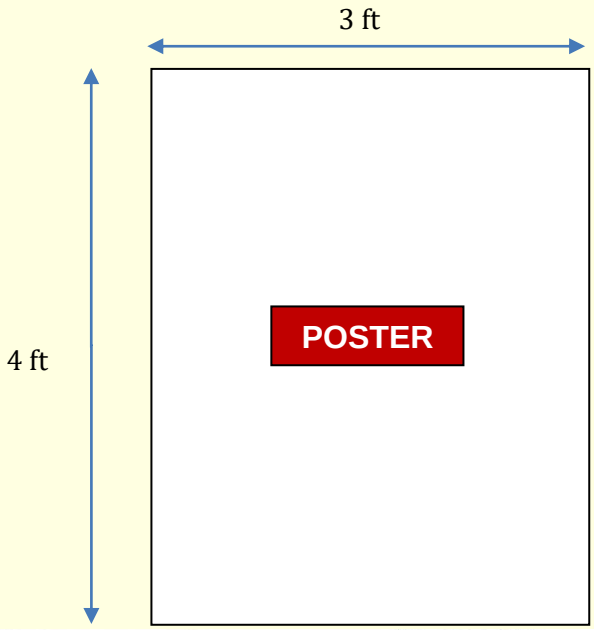
Number of Prizes – 2, Age limit - 35 Years, Mode of presentation – **Poster**

Best Paper Award from the Organizers

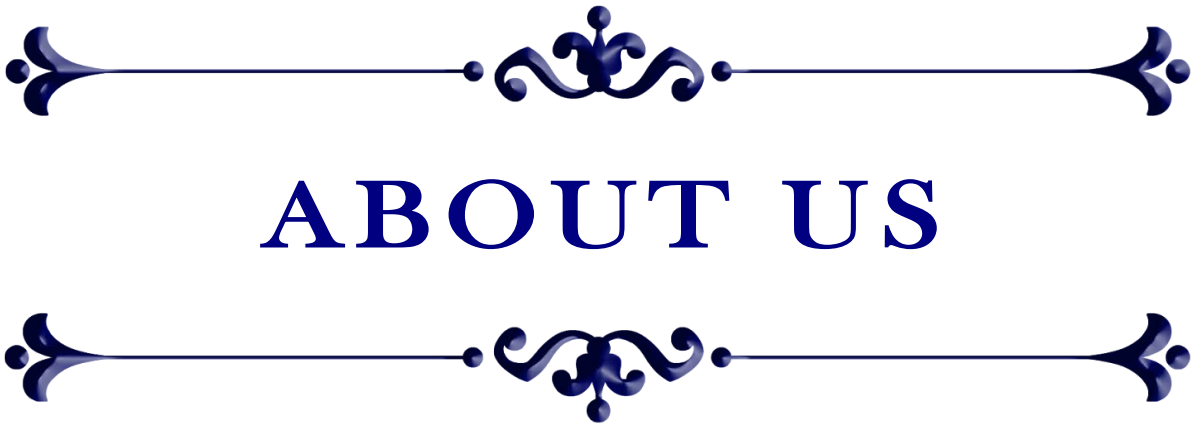
Number of Prizes – 2, Age limit - 35 Years, Mode of presentation – **Poster**

Guidelines

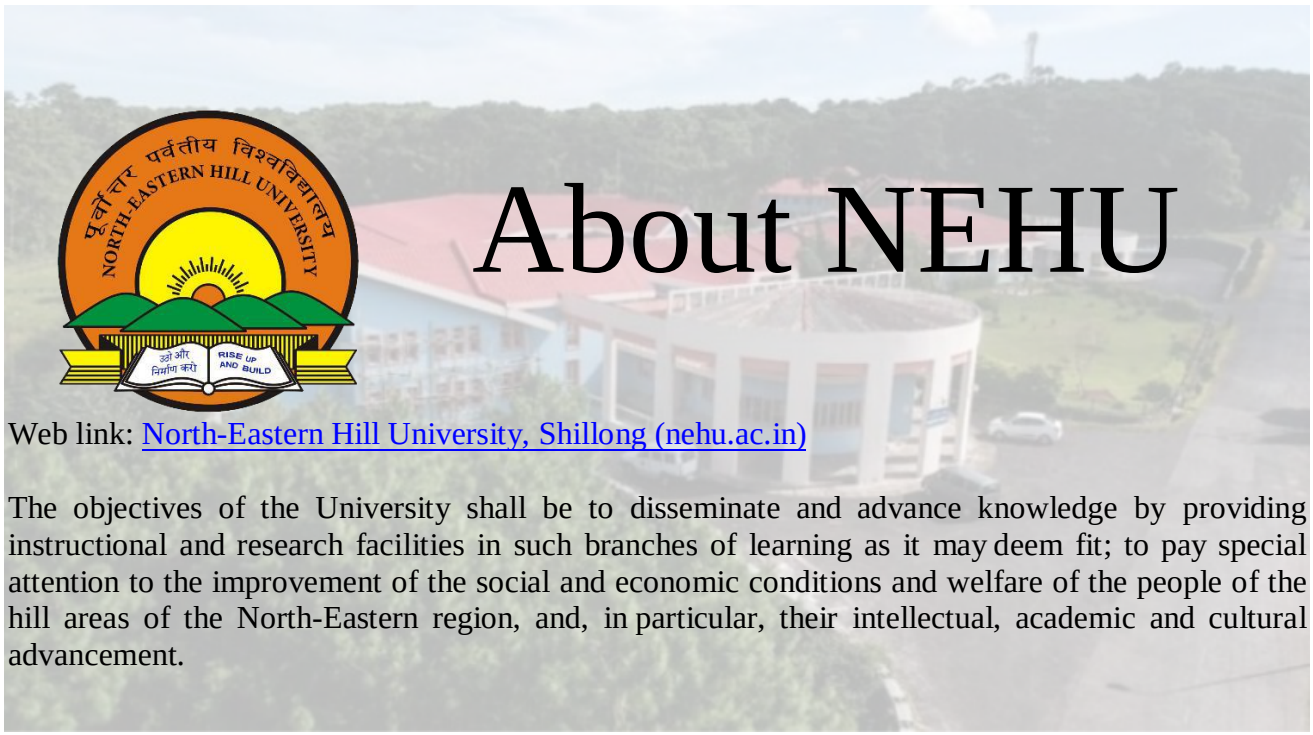
1. The presenter should be member of the Academy [for details please visit: Indian Academy of Neurosciences: (neuroscienceacademy.org.in)]
2. The content in the poster should be arranged – [Poster No. (mentioned in the confirmation email), Title of the paper, Authors and Affiliation, Brief Background, Materials and Methods, Observations (Tables / Figures) and Conclusion].
3. Please ensure that the work being presented should not have received award earlier or not presented elsewhere.
4. The poster must be placed at least one hour before the schedule time and remove till end of the day.
5. The judge's decision will be final for award category.
6. Please prepare the poster as per following dimensions.







ABOUT US



About NEHU

Web link: North-Eastern Hill University, Shillong (nehu.ac.in)

The objectives of the University shall be to disseminate and advance knowledge by providing instructional and research facilities in such branches of learning as it may deem fit; to pay special attention to the improvement of the social and economic conditions and welfare of the people of the hill areas of the North-Eastern region, and, in particular, their intellectual, academic and cultural advancement.

History

The North-Eastern Hill University Act (24 of 1973) passed by both Houses of Parliament received the assent of the President of India on May 26th, 1973. It was published in the Gazette of India (Extraordinary) on May 26th, 1973 together with the First Schedule of the Act incorporating the Statutes of the University. The objectives of the University, as laid down in the act, are "to disseminate and advance knowledge by providing instructional and research facilities in such branches of learning as it may deem fit; to pay special attention to the improvement of the social and economic conditions and welfare of the people of the hill areas of the North-eastern region, and in particular, the intellectual, academic and cultural advancement". The jurisdiction of the University extended originally to the states of Meghalaya and Nagaland and the erstwhile Union Territories of Arunachal Pradesh and Mizoram. With the establishment of the Nagaland University on 6th September 1994, the jurisdiction of NEHU ceased over Nagaland.

Likewise with the establishment of the Mizoram University the jurisdiction of NEHU over Mizoram also ceased from June, 2001. Arunachal Pradesh has its own university. However the North-Eastern Regional Institute of Science and Technology located in Arunachal Pradesh is affiliated to NEHU. Initially, the academic departments and administration of the University at Shillong functioned from hired buildings. Very soon, however, NEHU acquired two prime properties in the city, one belonging to the former Maharaja of Mayurbhanj and the other to the Rani of Bijni. The academic departments then moved to these two sites. Meanwhile, the Government of Meghalaya acquired, for the University, a substantial plot of land (measuring about 1225 acres) in Umshing, a little outside the city limits, for setting up its permanent campus. This picturesque land, gently undulating and thickly wooded - a perfect location for the University - was a gift from the Government of Meghalaya. The survey of the land and the master plan for the University were completed during the VI Five Year Plan; and construction activities began in a modest way during the VII Plan period. By the year 1991, with the completion of the construction of several residential quarters for the faculty, hostels for men and women, a ring road, a modern workshop for the University Scientific Instruction Centre, a building for the Regional Sophisticated Instrumentation Centre, and Guest House-cum-Seminar Complex, a complex of buildings for the science departments and with our own electricity and water supply system in place, the campus took the visible shape of an attractive University in the making. In 2005, following the shifting of the departments to the Permanent Campus at Umshing, Mayurbhanj

Compexat Nongthymmai was disposed off to the Government of Meghalaya. At the moment, barring a few Centres located at Bijni Compex, almost all departments of the University are housed in the buildings on the permanent campus. We now have Internet connectivity through our own VSAT to which all the departments located on the campus are linked. Efforts are on to enhance the range of our Internet connectivity. The telecommunication department has set up a fully automated telephone exchange on the campus. This is first of its kind in any University in the region. Much of the developmental work on the campus in the past couple of years or so has been made possible by the generous grant that the University has received from the Government of India from its "non-lapsable pool". It is hoped that in about another couple of years or so, the University would have developed sufficient infrastructure facilities for all its Centres (presently located at Bijni Complex) to move into permanent locations in the campus. The University has also allowed, with the permission of the Government of Meghalaya, the Department of Tourism to set up an Institute of Hotel Management, Indira Gandhi National University and the Indian Council of Social Science Research to set up their regional centres on its land. The Sports Authority of India has also been given permission to create modern sporting facilities in the University. Thus, in the verynear future, the campus will grow into a suitably diverse, but coherent, University Township. It has also the potential of being a University of striking scenic beauty. In spite of serious constraints of communication and the general lack of infrastructure facilities in the region, NEHU has established itself as an institution of higher learning and research of very high quality. It has been able to attract persons of proven academic excellence from almost all parts of the country to serve in its faculty; and its student community is drawn not only from the different parts of North-East but also from otherparts of the country. In February 1996, the University set up a campus at Tura with the Departments of English, Garo and Education. Very recently a Department of Rural Development and Agricultural Production has been added to the existing three departments at Tura. A number of departments of the University now receive special grants from University Grants Commission under its Special Assistance Programme. Four of the Science departments including Geography also receive grants under the UGC's SAP/COSIST Programme. The Departments of Science and Technology has extended financial help to five of our science departments including Geography as part of its scheme for funding infrastructure development in higher academic institution.

Some of the departments have also received grants under the UGC's Departmental Research Support Scheme. In addition, a huge number of research projects have been awarded to individual members of faculty notably by the CSIR, DST, DAE, UGC, ICSSR, Ford Foundation and DBT, DF & E, and MoEF. The University is also the recipient of a number endowments donated by various organisations and individuals including by Dr. Shankar Dayal Sharma, former President of India and Justice Krishna Aier. NEHU was also chosen for the prestigious Rajiv Gandhi Chair for research into protective discrimination. Several individual members of the faculty have been honoured with the highest academic awards in the country. Many of our teachers are also involved in collaborative research projects with Universities of Europe and Asia. One of the basicways in which the University endeavours to fulfil its "local" responsibilities, as enshrined in its Act is by focussing its attention on the North-East in its curricular programme including research. The fulfilment of its "global" responsibilities, as a member of the global academic community, is evident from the number of research publications by its teachers in journals of high international repute and the national and international seminars and conferences which are a regular feature of the University's academic life. At present there are fifty-three undergraduate colleges affiliated to the University including eight professional colleges. The University Central Library whose membership includes university and college teachers, postgraduate and undergraduatehonours students and members of the non- teaching staff has a collection of close to 2,00,000 books, 38,000 bound periodicals and it subscribes to 316 foreign and 366 Indian current journals. Our students have done well in life after leaving the University.Many have been taken into the Central Civil Services, Banking Services and into the University System. Several have been awarded scholarships and fellowships by both national and

foreign organisations. The percentage of our students clearing the NET, GATE and other national tests is quite high. The number of students turning for their Master's degrees and research students working for their M.Phil. and Ph.D. degrees is close to 1700. The undergraduate colleges affiliated to the University enrol about
18,000 students.
Our faculty strength is just over 300. In a short span of about 30 years NEHU has matured into an institution with a serious academic and social and cultural agenda and a clear vision for its future growth.

About Biomedical Engineering Department

Head: Dr. Sudip Paul

Address
Department of Biomedical Engineering North-Eastern Hill University
Shillong 793 022 Meghalaya
Web link: North-Eastern Hill University, Shillong ::Departments Biomedical Engineering Department(nehu.ac.in)



History

The Department of Biomedical Engineering (BME) was established in the year 2012, under the School of Technology, NEHU, Shillong, funded by MHRD, Government of India, with the specific purpose to promote studies in new emerging areas of medical sciences employing advancements in technology for the benefit of masses. In addition, the Department of the University intends to provide education to young minds to achieve better health care solutions with an emphasis on learning new techniques, developing innovative ideas through learning, skill development, Research and Development (R&D),and Industry-Institution interaction in the field.

Profile

The Department is one of the few institutes in the North-Eastern region offering U.G. and Ph.D. programs in Biomedical Engineering. The Department aims to focus on strengthening R&D activities to develop products and services that can be transferred to society for the benefit of humankind. The students are being prepared to face the emerging challenges in Biomedical Engineering by faculty members having rich expertise, diversity, and experience in this field. The core part of the curriculum embodies scientific and engineering knowledge essential to the profession. In addition to the core courses, the program also incorporates current and emerging technologies relevant to Biomedical Engineering. To tackle unknown medical problems with engineering technology, the curriculum has been designed by balancing various core, specialized and elective courses by offering several practical papers and challenging projects. The curriculum is also enriched with management papers to give students exposure in the field of corporate management. The Department has faculty with rich research and teaching experience drawn from different parts of the country. In addition, the Department has m

Infrastructure Facilities

Over the years, the Department has developed one of the best infrastructure facilities for its various teaching and research programs. The Department has spacious lecture halls, tutorial rooms, and specialized laboratories to provide the requisite environment for students' overall growth and development. The lecture halls are equipped with audio- visual, e-learning, and internet facilities to impart quality teaching. In addition, the Department is well connected with high-speed internet facilities through the university'scentralized VSAT network.

Major Equipment / Facilities available in the Department:

- Department has specialized laboratories with quality research facilities. Students perform experiments on different subjects such as Biomedical instrumentation, Medical Signal, Image Processing, Anatomy and Physiology, Medical Biochemistry, Biomechanics, Rehabilitation, Physiological systems modeling & Simulations, Biomaterials, and Nanomedicine, etc.

Equipment's / facilities available in the Department:

- Measuring, Recording, and Monitoring Instruments: Physiological recording system comprising of ECG, EEG, EMG, PCG, GSR, pulse-oxymeters, pulse rate, blood pressure, body temperature, respiration measurements, stress test with spirometry, wireless EMG recorder
- Analytical Equipment: UV-Vis Spectrophotometer, pH meters, ultra cooling centrifuge (-20 0C), probe sonicator, high-resolution microscopes, digital weighing balance, Quartz double distillation

unit, magnetic stirrer, and Oven.

- Spectrofluorometer
- Cutting plotter
- Multiple position magnetic stirrers
- Data acquisition system and amplifiers modules for the bio-signal recording
- Demonstration modules for cardiac pacemakers and defibrillators
- Microprocessor and microcontroller modules
- Workbench for Hardware designing
- Computer laboratory facilities with internet facility
- Universal Testing Machine loading up to 200KN
- Motion Analysis software for body modeling.
- 3D Printer-PLA, ABS, UV-Vis
- GAIT Laboratory- Force plate and Motion sensor camera
- Wireless EMG
- Data acquisition system and amplifiers modules for the bio-signal recording
- Demonstration modules for cardiac pacemakers
- Demonstration module for Ventilators
- Holter Monitor
- Demonstration module for Heart-Lung Machine
- Bioelectric amplifiers kits
- Cardiac stress test machine
- Digital Storage Oscilloscope
- Function Generators
- Work station set up
- Blood Pressure measuring instruments (Digital and analog)
- Multipara Monitoring SystemThrust Areas of Research
- Biomechanics and Rehabilitation Engineering
- Biomedical devices and signal processing
- Bio-nanotechnology and drug delivery
- Medical Image analysis and processing
- Biomaterials and artificial organs
- Medical Informatics and Telemedicine
- Virtual Instrumentation
- 3D Bio-printing, 3D Printing, and design for medical implants
- Computer-Aided Tissue Engineering
- Signal and Image Processing
- Marketing, International Business
- Environment Sustainability
- Electrophysiology
- Biomedical Instrumentation
- Machine Learning and ANN
- Biomedical Signal Processing

- Neural mechanism and motor neural
- Cognitive disorders
- Cancer drug delivery
- Magnetic nanoparticles
- Hyperthermia

About The Academy (Indian Academy of Neurosciences)

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The Indian Academy of Neurosciences (IAN) came to existence in 1982 with the efforts of Late Prof. K.P. Bhargava, Late Prof. Mahdi Hasan, Prof. S.S. Parmar, Late Prof. B.N. Dhawan, Prof. P.K. Seth and other eminent neuroscientists. Ever since its inception the Academy has been active in promoting neurosciences. It has been holding meetings regularly at different centres involved in neuroscience research in the country. Besides, the Academy has organized and sponsored symposia, workshops and conferences in areas of current interest.

The Academy recognizes eminent Neuroscientists by electing them as Fellows and Honorary Fellows. The Academy has instituted BK Bachhawat Life Time Achievement Award and KT Shetty Memorial Oration which are conferred on the scientist for his/her outstanding contributions in neurosciences. To encourage young scientists, the Academy has instituted awards for poster andoral presentations and published work. The Academy also provides Travel Fellowships to candidates seeking support for participation in the annual conference of Indian Academy of Neurosciences. The Academy publishes a Newsletter and a Journal - Annals of Neurosciences. A Membership Directory is also available which is updated from time to time.

Indian Academy of Neurosciences has good amalgamation of basic and clinical researchers. Started with few neuroscientists in 1982, the Academy has grown into a sizable organization of dedicated members. At present, the Academy has over 900 life members from India, Germany, Japan, Poland, Saudi Arabia, Sri Lanka, South Africa, UK and USA. Annual meetings of the Academy are also attended by foreign members and thus provide a unique forum for interaction among the neuroscientists from India and abroad.

The Academy invites you to join the league of neuroscientists and become Academy member andhelp the Academy achieve its goals and objectives.

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PRE-CONFERENCE WORKSHOP



XL Annual Meeting of Indian Academy of Neurosciences

December 8-10, 2022

Theme: Neuroscience Research : Current Trends and Future Needs

Pre Conference Workshop: December 7: 2022

Organized by:

Departments of Biomedical Engineering
North-Eastern Hill University, Shillong, India

Email id: **ian2022.nehu@gmail.com** **Visit us:** https://ian2022nehu.com/

Workshop - I
Brain Signal Analysis using EEG Workshops

Date- December 7, 2022
Time- 9:30 AM - 11 AM

Program Details:

Part 1 : General overview of Workshop and welcome Note – Dr. Anita Talwar, PhD in Physiology, Director of Gentech Marketing & Distribution (P) Ltd, New Delhi

9:30 AM - 10 AM



Part 2 : Brain Mapping Using Stereotaxic Techniques – Richard Mills, Vice President of Stoelting Co, USA

10 AM – 11 AM



This workshop will cover an introductory overview of Neuroscience study and relative brain functions and how to use Stereotaxic Apparatus to map animal's brain and its application in the field of Neuroscience.

Workshop - II
Computational Neuroscience and Neurorehabilitation

Date- December 7, 2022
Time- 11 AM – 12:30 PM

Program Details:

Part 1 : Tools and Techniques for Brain Signals Measurement – Sandip Majumder, Country Manager, Gentech Marketing & Distribution (P) Ltd, New Delhi

11 AM – 11:30 AM



Part 2 – Role of Behavioral Studies in Neuroscience – Richard Mills, Vice President of Stoelting Co, USA

11:30 AM – 12:30 PM



This workshop will cover the details application of brain signals acquisition and analysis brain waves and importance of assessing different behavioral aspects of animals in different conditions in the field of neuroscience.

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Email id: **ian2022.nehu@gmail.com** **Visit us:** https://ian2022nehu.com/

Scientific communication Workshop

Date- December 7, 2022
Time- 1.30 pm- 4 pm

Program Details:

General overview and welcome — Dr. Poonam Thakur1:30-
1:40 pm

Workshop 1- Effective literature review by Dr. Collins Assisi, Assistant Professor,IISER Pune
1.40 pm- 2:30 pm



This workshop will cover how to choose relevant papers to read, and how to choosewhich papers should be included in citations.

Workshop 2- Effective poster presentation by Dr. Poonam Thakur, AssistantProfessor, IISER Trivandrum

2:30-3:15 pm



This workshop will cover how to design an effective layout for a poster, how to presentconcise information and how to present it effectively in 5-10 minutes.

Workshop 3- Effective podium presentation by Dr. Vinay Khanna, Chief Scientist,IITR Lucknow

3:15 pm- 4 pm



This workshop will cover how to make an effective presentation in a short time and howto weave an effective narrative of the research story.



ORATIONS

Evolutionary diversity of cortical neurons in reptiles, birds and mammals

U. C. Srivastava
The National Academy of Sciences, India, 5, Lajpatrai Road, Prayagraj 211 002

Abstract

Evolutionary diversity of neurons in various classes of chordates namely: amphibian, reptiles, birds and mammals have been our interest for about 5 decades now. Tissue homologues of hippocampus within different vertebrates were explored. 9 different types of neuronal classes have been observed within the medial and dorsal cortex; 8 in dorsomedial cortex and 6 in lateral cortex of *H. flaviviridis* (Common Indian wall Lizards), *M. carinata* (Bamaniya Lizard) and *C. versicolor* (Garden Lizard). Along with neuronal diversity parameters such as dendritic thickness, spine density, spine morphology have also been explored in birds namely: *Lonchura punctulata* (Spotted munia), *Estrilda amandava* (Strawberry finch), *Psittacula krameri* (Indian ring neck parrot), *Eudynamys scolopaceus* (Koel) *and Ploceus phillipinus* (Baya weaver). The effect of seasons on the brain has also been investigated. The findings revealed the interesting changes in neuronal parameter across breeding and non- breeding phases of birds. The results suggested that changing season leads to modification in behavior and endocrinology of birds which imposes its effect on the neurons thereby preparing the animal to adapt/cope with changing behavior across season. Mammalian cortex has been observed to be highly evolved in form of structure and function. The neurons of cortex region in *R. lapidus* (Indian Bat), *F. pennanti* (Indian Squirrel) *and H. edwardsii* (Indian Grey Mongoose) were also observed and it was noticed that there was dominance of pyramidal neurons which is novelty of mammalian brain. It was interesting to note that many pyramidal neurons were deviated from "typical" neurons, designated as Atypical Pyramidal neurons with one or more of following characters: inverted somata, bifurcation of apical dendrite close to soma, poorly developed basal dendritic skirt and lack of terminal bouquet in layer I.

Overall we have proposed that the dorsomedial cortex neurons of the lizards were morphologically comparable with the neurons of the hippocampus of mammals. The neuronal morphology of neurons of parahippocampal (APH) area of dorsomedial forebrain of birds are comparable to the dorsomedial cortex neurons of the lizards. The neurons of APH in birds and CA3 (Cornu ammonis 3) area of hippocampus of mammals are directly evolved from the reptilian dorsomedial cortex. Dominant projection neurons of hippocampal region were *bitufted* in reptiles**;** *multipolar* in birds and *pyramidal* in mammals. Such marked regional differences in their phenotype are believed to influence their functional characteristics. All the findings suggest that cell structure is not necessarily correlated with the brain size but reflect specialization during evolution of the cortex. Findings also indicate that many diverse type of nonpyramidal and pyramidal neurons already emerged as discrete morphological entities in the vertebrate cortical evolution at the time of divergence of reptile, birds and mammals.

Noncoding RNAs and post-stroke functional outcomes

Suresh L Mehta[1] and Raghu Vemuganti[1, 2]
Department of Neurological Surgery, University of Wisconsin-Madison and [2]William S. Middleton Veterans Hospital, Madison, WI

Abstract

The mammalian brain expresses various classes of noncoding RNAs (ncRNAs), such as long ncRNAs (lncRNAs), microRNAs (miRNAs), and circular RNAs (circRNAs) that play crucial roles in modulating transcription and translation by RNA/protein scaffolding, sponging, and epigenetic changes. Stroke rapidly and significantly alters the expression of many of these ncRNAs in the brain, which affects the functional prognosis following a stroke. Using examples of each class of ncRNAs, we observed that a brain-specific lncRNA called Fos downstream transcript (FosDT), which is developmentally regulated, the adult cerebral cortex shows significantly higher FosDT expression than neonates, is induced rapidly in the rodent brain following ischemic stroke. When subjected to ischemic stroke, rats of both sexes deficient in FosDT showed enhanced sensorimotor recovery and reduced brain damage through curtailing induction of inflammatory genes, reduced apoptosis, mitochondrial dysfunction, and oxidative stress. We also observed that ischemic stroke induces a sustained downregulation of miR-7, leading to derepression of its target α-synuclein (α-Syn), which promotes neuronal death. When subjected to even a mild ischemic stroke, the miR-7 deficient mice showed exacerbated brain damage and worsened motor function. Replenishing the levels of miR-7 with a mimic restored miR-7 mediated neuroprotection and motor recovery. Similarly, circRNA CDR1as, which is known to regulate miR-7 abundance and function, is downregulated in a sustained manner in the peri-infarct cortex of the brain following ischemic stroke. Overexpression of CDR1as with an adenoviral vector containing a CDR1as gene significantly increased CDR1as levels, and CDR1as overexpressed mice subjected to ischemic stroke showed a significant increase in miR-7 levels and CDR1as binding to Ago2/miR-7, and suppressed post-stroke α-Syn protein induction, promoted motor function recovery, decreased infarct size and curtailed the pathological markers of apoptosis, autophagy mitochondrial fragmentation, and inflammation in the post-stroke brain. In tandem, these results suggest that ncRNAs induction and their interactive mechanisms play a crucial role in determining the post-stroke functional outcome. The fine-tuning of these ncRNAs is a viable strategy to promote post-stroke recovery and survival.

SS Parmar Oration

LEVERAGING GENOMIC AND EPIGENOMIC APPROACHES TO DEFINE THE NEUROBIOLOGY OF ANXIETY AND ALCOHOL USE DISORDER

Subhash C. Pandey

Center for Alcohol Research in Epigenetics, Dept. of Psychiatry, University of Illinois at Chicago & Jesse Brown VA Medical Center, Chicago IL 60612, USA

Abstract

Adolescent binge drinking represents a major public health concern, and use of alcohol during this critical window of brain maturation increases the susceptibility for psychiatric disorders in adulthood. Adolescent alcohol exposure produces long lasting impacts on the epigenome (based on ATAC-seq) and transcriptome (based on RNA-seq) and modulates synaptic gene network pathways in the amygdala underlying adult psychopathology. Furthermore, an enhancer region of activity-regulated cytoskeleton-associated protein (Arc) known as the synaptic activity response element (SARE) regulates Arc expression via epigenetic mechanisms in the adult amygdala after adolescent alcohol exposure in humans and rats. Using CRISPR-based epigenetic editing, we demonstrated that adolescent alcohol exposure induced anxiety and alcohol drinking behaviors in adulthood, which was causally linked to specific epigenetic changes at a genomic location within the rat amygdala. It is also known that alcohol produces anti-anxiety effects both in humans and animal models. Evidence will be presented to show that acute alcohol exposure rapidly opened chromatin and produced transcriptomic changes in the rat amygdala, which were associated with the observed anti-anxiety effects. Taken together, this presentation will provide evidence that a dynamic interplay exists between epigenomic and genomic changes that regulates synaptic plasticity, which may be responsible for the pathophysiology of anxiety and alcohol use disorder.

PN Tandon Oration

DEVELOPMENT OF NEUROSCIENCES IN INDIA

Ashok K. Mahapatra, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar



PLENARY TALK

ERp29 Regulates Murine β-coronavirus Infectivity and Replication by limiting Endoplasmic Reticulum Stress and facilitating Connexin 43 trafficking to the cell surface

Abhishek Bose, Grishma Kasle, Rishika Jana, Mahua Maulik, Deepthi Thomas, Vaishali Mulchandani, Priyanka Mukherjee, Michael Koval, and Jayasri Das Sarma* Department of Biological Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur, West Bengal, India
Email: dassarmaj@iiserkol.ac.in
Presenting author: *Jayasri Das Sarma**

Abstract

Background and rationale: Astrocytes are inter-connected by gap junctional intercellular communication (GJIC), which is important for metabolic coupling in the panglial system. Infection with a neurotropic murine- β-coronavirus (m-CoV), mouse hepatitis virus (MHV-A59) in primary neonatal mouse astrocytes causes intracellular retention of the predominant astrocytic GJ protein, Connexin43 (Cx43), thus impairing GJIC. The study investigated the role of coronavirus- induced ER stress in causing the intracellular retention of Cx43 and revealed an antiviral role for Cx43 and ERp29.

Methods: Primary astrocytes were isolated from neonatal pups of C57BL/6 mice, and DBT cells were infected with MHV-A59. The ER stress markers and an established Cx43 chaperone were checked in the infected cells. Inhibition of ER stress using a well-studied ER stress inhibitor, 4-sodium phenylbutyrate (4-PBA), in infected cells was adopted to check for the rescue of Cx43 trafficking. ERp29 overexpressing cell line DBT-ERp29 was generated to study the importance of Cx43 trafficking in modulating viral spread.

Results: Our studies highlight that intracellular retention of Cx43 in MHV-A59 infected primary astrocytes is associated with increased ER stress marked and reduced expression of ER-resident chaperone, ERp29. Treatment of MHV-infected primary astrocytes with a well- studied ER stress inhibitor 4-sodium phenylbutyrate (4-PBA) rescued their ability to transport Cx43 to the cell surface and increased GJIC by upregulating ERp29 expression. Furthermore, studies on mouse astrocytoma-derived DBT cells stably transfected with exogenous ERp29 showed increased Cx43 trafficking and assembly into GJ plaques. Interestingly, exogenous ERp29 expression in DBT cells restricted mCoV infectivity. Using a 4-PBA and mimetic peptides known to inhibit Cx43 mediated GJIC by binding to extracellular loops of Cx43 and thus demonstrated that ERp29 significantly reduces mCoV infectivity by reducing ER stress and rescuing the trafficking of Cx43 to the cell surface.

Conclusion and Discussion: The current study thus identifies ERp29 as a potential antiviral host factor that can be therapeutically targeted for curbing CoV infection by targeting Cx43 trafficking.
Ethics statement: All experimental procedures and animal care and use were strictly regulated and reviewed per animal ethics approved by the Institutional Animal Care and Use Committee at the Indian Institute of Science Education and Research Kolkata (AUP no. IISERK/IAEC/AP/2019/28.01). Experiments were performed following the guidelines of the Committee for Control and Supervision of Experiments on Animals (CPCSEA), India.

Acknowledgment: This work is supported by research grants from the Department of Biotechnology (DBT), India (DBT/PR20922/MED/122/37/2016) and the Council for Scientific and Industrial Research (CSIR), India (27(0356)/19-EMR-II) to JDS and research funds from IISER-K. Senior

Research Fellowships from CSIR supported AB and GK. VM and DT received Institutional Fellowships from IISER-K. MM was supported by DBT-Wellcome Trust India Alliance Early Career Fellowship (Grant no. IA/E/17/1/503659). The authors thank Dr. Kenneth
S. Shindler, University of Pennsylvania Scheie Eye Institute, Philadelphia, Pennsylvania, the US, for critically reviewing the work, and Dr. Julian Leibowitz (Texas A&M University College of Medicine, TX, US) for kindly providing the anti-N antibody, and Dr. Stanley Perlman (University of Iowa, Iowa City, IA, US) for his kind gift of DBT cells. The authors also thank the IISER-K confocal imaging facility.

Sensation-seeking behavior at adolescence – why and how?

Laxmi T Rao

Professor of Neurophysiology, NIMHANS, Bengaluru – 560 029

Abstract

Why some adolescents are highly vulnerable to sensation seeking behavior and some are not. These behavioral changes are not permanent. As they cross the adolescence age, these sensation-seeking behavior also subsides. Most of the times, it is believed that the hormones released during the puberty and abnormal change in the connectivity in cortico-amygdala- hippocampal-nucleus accumbens circuit at this critical developmental period is likely to contribute for such sensation seeking behavior. However, it is not clear yet why the sensation seeking behavior does not get terminated in all individuals after they cross the adolescence/puberty age.

Previous studies from our lab have shown that experience at early life can have major influence on adulthood behavior and thus on their performance. The changes in brain and behavior due to maternal separation and isolation (MS) stress during early postnatal days are mainly during the pre-weaning period. We showed that MS stress causes changes in anxiety, fear memory, fear extinction, spatial learning and memory, attention at young adulthood. In addition, we have also showed that increased anxiety was most often associated with increased REM sleep duration with not much impact on total sleep time. These changes on the REM sleep behavior were associated with changed synchronized activities between medial prefrontal cortex, amygdala, and hippocampus. Altogether, it is evident that early MS stress has long-lasting impact by increasing both anxiety at both adolescence and adulthood age.

In the present lecture I am going to provide some more evidence to show that how early life stress can cause individual differences in behavior. For example, the rodents exposed to early life stress at stress hyporesponsive period (SHRP) show a substantial increase in anxiety and curiosity at adolescence age. These behavioral changes were associated with increased basal plasma corticosterone and plasma dopamine level. However, it is yet unclear whether enhanced curiosity-like behavior at adolescence can have any impact on sensation seeking behavior and thus effecting the cognitive functions. Our preliminary findings indicate that animals that exhibit increased curiosity-like behavior show more risk-taking behavior and thus on sensation seeking behavior such as sucrose consumption or nicotine addiction, causing them highly vulnerable to substance use disorders. Finally, we conclude that brain plasticity and subsequent changes in sensation-seeking behavior at adolescence age could be under the influence of hormones.

Modulation of RNA editing of Cav1.3 channels: Implications in learning and memory

Tuck Wah Soong

Department of Physiology, Healthy Longevity and cardiovascular Translational Research Programmes, Yong Loo Lin School of Medicine, National University of Singapore

Abstract

Our lab has a long-standing interest in understanding the diversification of structure and function of voltage-gated calcium channels via alternative splicing. Here, I will present our discovery of Cav1.3 RNA editing and how editing of the IQ-domain affects Ca2+-dependent inactivation of the Cav1.3 channels. Unexpectedly, we uncovered that RNA editing of the Cav1.3 is neuron-selective and that restricted editing of Cav1.3 channel is due to the alternative splicing of an editing repressor which is a ubiquitously expressed splicing factor, SRSF9. To address the physiological significance of Cav1.3 RNA editing, we generated editing complementary sequence null (Cav1.3□ECS) mice that were genetically targeted to produce unedited Cav1.3 channels. Electrophysiological hippocampal slice recordings showed enhanced late-LTP and the Cav1.3□ECS mice have better spatial learning and memory as demonstrated by behavioural tests using the Morris Water-maze. The next question we hope to address is whether there are trade-offs to the loss of Cav1.3 RNA editing.



INVITED TALKS

Neuromodulatory and proteinopathy molecules in the ALS plasma and CSF and the in- vitro validation.

Akshay Anand*#$
* Neuroscience Research Lab, Department of Neurology, PGIMER, Chandigarh.
#CCRYN-Collaborative Center for Mind Body Intervention through Yoga, Post Graduate Institute of Medical Education and Research, Chandigarh, India $Centre of Phenomenology and Cognitive Sciences, Panjab University, Chandigarh, India

Abstract

Background: ALS is a neurodegenerative disease with severe health consequences to the patients. So far there are no specific biomarkers for the diagnosis or prognosis of ALS. Plasma and CSF can reflect the patients' physiology by showing the altered levels of various bio molecules. Similarly such changes can be reflected upon in *in-vitro* systems. The targeted molecules were neuromodulatory (neuroprotective, VEGF, VEGFR2, ANG and neuroinflammatory MCP1) and were involved in proteinopathy (TDP43, OPTN).

Aim: The study aimed to analyse alterations in such molecules in the CSF and plasma of ALS patients that can potentially act as biomarkers for early diagnosis and prognosis. It also aimed at analysing the effects of these fluids in *in-vitro* system.

Methodology: The molecules level was analysed in the CSF and plasma by ELISA. Risk predictive statistical model was developed using the binomial likelihood regression model from the bio molecule levels and socio-demographic data. NSC34 cells were induced using the CSF and plasma of patients and further cell viability and gene expression for the same molecules was analysed.

Results: All the molecules were observed to be significantly decreased in the plasma of patients in comparison to controls except ANG. In case of CSF, VEGF, and ANG were observed to be significantly decreased and the VEGFR2 was found to be significantly increased. VEGFR2 has also come up as a major molecule of contribution in the predictive statistical model. Further plasma was found to be toxic for the NSC34 cells and was found to be downregulating the gene expression of VEGF in the cells.

Conclusion: Since a single molecule can-not be found to act as a biomarker for a multifactorial disease such as ALS, a panel of different molecules involved in the different mechanisms of disease may be helpful in predicting the risk of disease. It can further help in early diagnosis. Alterations in these molecules can be verified and validated in the *in-vitro* system for further clarification and for assigning these molecules as targeted biomarkers for the disease.

Substance P and Neurogenic Inflammation inInflammatory Diseases

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Abstract:

Substance P is an 11 amino acid neuropeptide from the tachykinin family. Substance P is present in neuronal terminals, and when released, it acts as a neurotransmitter or a neuromodulator. In the peripheral nervous system, substance P acts as a neurotransmitter in the primary sensory neurons with cell bodies in the dorsal root ganglia and cranial sensory ganglia. Neurogenic inflammation is the process by which mediators are released directly from nerves to initiate an inflammatory reaction. Transient receptor potential vanilloid type 1 (TRPV1) polymodal transducer, a non-selective cation channel found predominantly in primary sensory neurons, plays a key role in neurogenic inflammation involving substance P. Neurogenic inflammation, is characterized by vasodilation and increased vascular permeability. Substance P is major mediator in neuro- immune interactions, and an extensive neuro-immune intersystem crosstalk exists between substance P and the inflammatory response to injury. We have shown that substance P acts as a mediator of inflammation in different disease conditions, including acute pancreatitis, sepsis, and severe burn injuries. Studies on the mechanism of action of substance P in inflammation show that it acts downstream of hydrogen sulfide, and acts through chemokines, adhesion molecules, MAP kinase ERK, and transcription factor NF-□B. Based on the studies with *in vitro* cell culture systems, isolated cells, and *in vivo* experimental models of disease, we now have a good understanding of the contribution of substance P to inflammation. Recent clinical studies have substantiated a key role of substance P in inflammatory diseases. These studies can lead to the development of novel therapeutic approaches for several clinical conditions, which are major health problems.

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Repeated exposure of cytokines and alarmin may lead to differential neuroimmunemodulation

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Abstract

Innate immune training and tolerance is a crucial mechanism of epigenetically mediated myeloid cellplasticity, that may alter subsequent immune responses. In the present study, we aimed to evaluate the type of immunological imprinting (training/tolerance), underlying mechanisms and subsequent effects on inflammatory responses within the CNS of animals. We demonstrated that the pattern of immune response generation, induced by peripheral administration of recombinant alarmin HMGB1, alone andin combination with other recombinant cytokines, is affected by prior exposure. The experimental outcomes revealed that recombinant HMGB1 exposure for seven consecutive days exhibit inflammatory response as evidenced by enhanced expression of inflammatory biomarkers and neurodegeneration. In contrary, combined doses of HMGB1and IL-1β, for three and seven consecutive days, exhibited lower inflammatory state compared to HMGB1 alone via differential epigenetic reprogramming, specially by involving HDAC and TAK1, majorly within brain-resident macrophages, microglia, and astrocytes. Thus, we concluded that additionally administered IL-1β as an important inducer of tolerance in the brain which may be beneficial in controlling the inflammation induced neurodegenerative diseases and subsequent memory impairment.

TGR5 Receptor Modulation Alleviates Sensory Motor Functions & Cognition in Ischemic Cerebral Stroke

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Abstract

G protein bile acid receptor1 (GPBAR1), also known as TGR5, is a Gαs proteincoupled receptor (GPCR) for bile acids that mediates many of the rapid, non-genomic actions. TGR5 is widely expressed in peripheral tissues (liver, pancreas, and gastrointestinal tract) and the central nervous system. It is now established that TGR5 modulate glucose homeostasis by increasing energy expenditure, modulating liver microcirculation. Although TGR5 role in anti-diabetic effects and anti-depressant effects have been shown, still these beneficial effects don't account for such wide expression throughout CNS. To further expand horizons of TGR5 functions in CNS, we investigated the role of this receptor in Middle Cerebral Artery Occlusion (MCAO) SD rats, a model of ischemic cerebral stroke. We discovered that sub-chronic treatment with TCG 1005, a TGR5 agonist improved neurobehavioral performance in MCAO rats, including neuromuscular functions (Rotarod test, Grip strength test), sensory and motor functions (Adhesive removal test), and acute spatial learning memory (Y-maze test). Furthermore, immunohistochemical analysis revealed that TGR5 agonist decreases the activated glia and neuronal loss in the MCAO rat brain. To further delineate the molecular mechanisms of TGR5 signalling, we performed oxygen-glucose deprivation (OGD) in rat primary cortical neurons to mimic ischemia and reperfusion and observed a decrease in phospho-CREB and increased active caspase3 and total oxygen free radical's levels which were reversed by treatment of TCG 1005. Further detailed mechanistic studies revealed the involvement of PKA- PPARγ-p65 signaling axis, and inhibition NR2B-NMDA function in salutary effects ofTGR5 agonist.

Adult brain homeostasis: how do cells and circuit in the adult brain change oradapt to maintain normalcy?

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Abstract

Proper functioning of a healthy brain depends on precisely coordinated actions of thedifferent cell-types; neuron, glia and others, that comprise the adult brain. The specified roles played by each of these cell-types are governed by carefully orchestrated genetic programs that control both the 'dynamic' as well as the 'housekeeping' properties of these cells. We investigated neural stem cells and mature neurons in the adult brain, to gain insights into the genetic programs that underlie the proper fate and functions of these cells throughout a lifespan. In this talk, I will present our recent findings; two studies that reveal that cells in the adult brain depend on sustained fate-maintenance to carry out their intended functions through a lifespan, and this active maintenance require continual proactive suppression of alternative cell-fates. I will place these findings in the context of adult brain homeostasis, and discuss how elucidation of homeostatic regulations can help gain better insights into pathological conditions.

Age related neurovascular changes and vulnerability towards neurodegenerative diseases

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Abstract

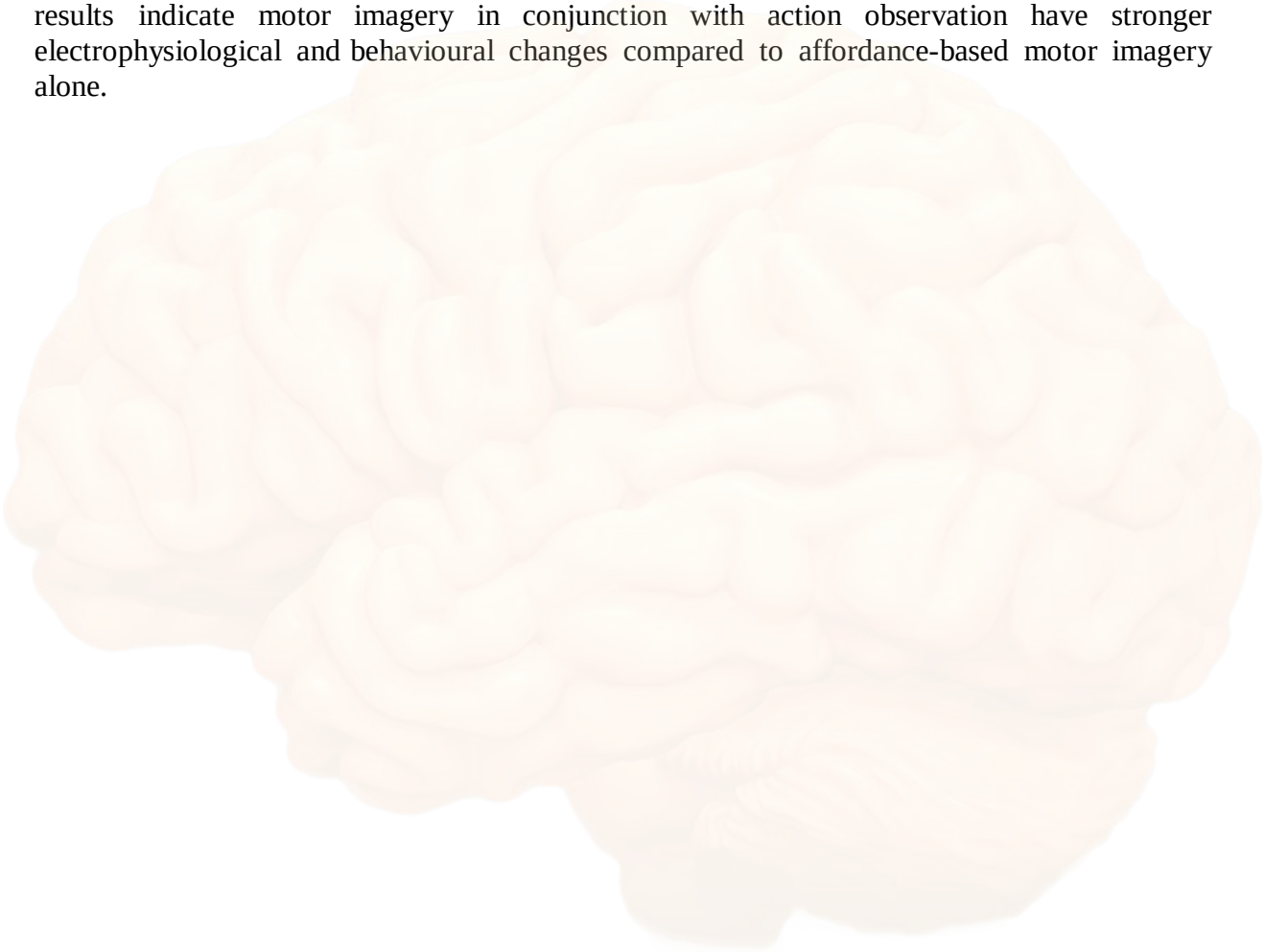
Age related changes in the brain has scare information and is one of the areas of great concern in the field of cognition and neurodegenerative disorder. However, emerging independent research suggest the role of vascular changes, capillary blood flow and related dynamics, tissue oxygen distribution. However, there are no direct extensive evidences which correlate these data. Hence, the need is to understand and evaluate these changes in the aging brain. The aging brain imaging suggests the grey matter and white matter changes in terms of their refractive indices. Futher, the capillary blood flow parameters measurements suggest the increased capillary volumetric blood flow and RBC velocity with a large vessel diameter in the aged brains under anesthesia as compared to unanaesthetized brains without affecting the RBC flux. This suggest that anesthesia affects the vessel diameter and related blood kinetics. Further, the distribution of the tissue partial pressure of oxygen measurements shows reduced levels of oxygen with hypoxic micro pockets. Further the vascular finger print pattern in the aging brain varies as compared to the young brains. Therefore, evaluating such parameters in much detail under various conditions would help overcome the age-related changes and prevent the neurodegenerative.

Influence of Affordance-driven Action Observation on Motor Imagery

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Abstract

Object affordance plays a significant part in priming motoric actions. The current study focused on investigating the influence of affordance-driven action observation on motor imagery. Our results indicate motor imagery in conjunction with action observation have stronger electrophysiological and behavioural changes compared to affordance-based motor imagery alone.



Neural networks that control vocal communication in Non- human animals and human language

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Abstract

Vocal learning, the capability of modifying, memorizing and producing complex auditory and syntactic sounds, is an indispensable requirement of human spoken language. This capability is considered as a significant innovation for the evolutionary origin of human speech. Latest revelations of unusual features in the neural substrates, and specialized neuroarchitecture for vocal acquisition can provide the clues about presence of exclusive neural specification necessary to collect information and its transmission essential for vocalization.

The present proposal is aimed to understand how evolution designed brain circuits for acquiring language and speech and also highlight the role of altered specialized neural components in language deficit disorders like Autism, Alzheimer's etc.

In this talk neural architecture, anatomical, and neuroimaging studies of the different areas of the brain related to vocal control, in non-human animals, and speech in humanswill be discussed.

Vulnerability of the aging human photoreceptor cells and its consequences

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Abstract

Photoreceptor cell death is a visible event in aging human retina and is unparalleled by instances seen elsewhere in the aging human central nervous system. Beginning in the second decade, it continues throughout our entire life-span. The light-sensitive rod photoreceptor cells are lost earlier than the cones; the latter are stable initially, but develop susceptibility later on, which leads to their death with advanced aging. This study examined the morphological and neurochemical changes in aging photoreceptor cells, especially the cones, and analyses the possible associated factors. Post-mortem human retinas from donors (age: 35-98 years) with no history of ocular diseases were procured via informed consent from relatives of the donors.They were preserved and then examined by electron microscopy, TUNEL, and immunohistochemistry for photoreceptor associated markers. The results show prominent changes in cone mitochondria, cone axons and pedicles than in rods. Oxidative stress appears to be involved in photoreceptor alterations, markers of lipid peroxidation (4-hydroxy 2-nonenal) and protein tyrosine nitration (nitro-tyrosine) are detected in aging cone outer- and inner segments, respectively. There is a redistribution of calbindin D-28K, a calcium-binding protein, in cone axon terminals in the parafovea and abnormal location of long/middle wavelength-sensitive opsin in the parafoveal and perifoveal cones, especially away from their outer segments, indicating an age-related defect involved in the intracellular trafficking and mislocalisation of those proteins (unusually in their somata, axons and axon terminals). These features are strong predictors of the increasing cone vulnerability with aging. Signs of reduced autophagy, with autophagosomes containing organelle remnants (of mitochondria) are seen in aging photoreceptor synapses, indicating that dysfunctional/defective autophagy may be involved in photoreceptor cell death. Some evidence favours apoptosis as a mechanism of photoreceptor cell death, which can be detected sporadically in the macula by TUNEL at an advanced age (ninth decade). Because cones appear to be altered fairly slowly, there is an opportunity of reversing those adverse cellular changes before they become susceptible and ultimately die. Thus, an understanding of how cones exist late through aging via the survival (molecular) pathways that they utilize must be the future research goal, for use of potential molecules in neurotherapeutics.

Chronic unpredictable stress negatively regulate hippocampal neurogenesis and promote anxious depression-like behavior via upregulating apoptosis and inflammatory signals in adult rats

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Abstract

Psychological and physical stress play a pivotal role in etiology of anxiety and depression. Chronic psychological and physical stress modify various physiological phenomena, as a consequence of which oxidative stress, decreased neurotransmitter level, elevated corticosterone level and altered NSC homeostasis is observed. However, the precise mechanism by which chronic stress induce anxious depression and modify internal milieu is still unknown. Herein, we show that exposure to CUS increase oxidative stress, microgliosis, astrogliosis while it reduces hippocampal NSC proliferation, neuronal differentiation and maturation in adult rats. CUS exposure in rats reduce dopamine and serotonin level in cortex and hippocampus, which result in increased anxiety and depression-like phenotypes. We also found elevated level of NF-κB and TNF-α while decreased anti-inflammatory cytokine IL-10 level, that led to increased expression of Baxand cleaved Caspase-3 whereas down regulation of antiapoptotic protein Bcl2. Additionally, CUS altered adult hippocampal neurogenesis, increased gliosis and neuronal apoptosis in cerebral cortex and hippocampus which might be associated with reduced AKT and increased ERK signaling, as seen in the rat brain tissue. Taken together, these results indicate that CUS induce oxidative stress and neuroinflammationwhich directly affects NSC dynamics, monoamines levels and behavioral functions in adult rats.

Mental health in the modern world and the role of Meditation

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Abstract

Yoga is an ancient Indian science, philosophy and way of life, which has become popular worldwide. Studies have shown that meditation practice optimizes sleep architecture and cognitive functions leading to optimal brain functioning in both normal and diseased states. Meditation practice is effective for disorders related to stress, sleep and cognitive functions, when practiced as an adjunct to conventional drug therapy.

Cognitive functions across age-groups are enhanced by yoga and meditation practice, leading to improved mental health and well-being, among young healthy adults, middle- aged and elderly. It has a beneficial effect on the age-related cognitive decline. Meditation may be beneficial for maintaining cognitive functions during physiological stress. During night sleep deprivation in normal healthy participants, meditation practitioners had a better attention, vigilance and a lesser decline in cognitive functions. It is reported to have a positive impact in neurological diseases. Drug-resistant epileptics who practiced meditation for 6 months showed a reduction in seizure frequency accompanied by changes in EEG.

Recent studies have shown that Meditation modulates brain function by changes in autonomic function, brain electrical activity, structural and functional changes in specific brain regions, changes in blood flow and metabolism, changes in neurochemical milieu andbetter functional connectivity in brain networks especially in key areas involved in sleep- wakefulness, attention, new learning and consolidation of memory.

Meditation practice enhances cognitive functions in young and elderly, in stressful conditions and in patients of neurological disorders by modulating brain activity.

Key words: Meditation—Cognitive functions—Mental health—Neuro-physiological mechanisms

Understanding fundamental mechanisms and finding therapeutics to treat AutismSpectrum Disorder

Abstract:

A cardinal feature of human brain development is that sensory, cognitive, and emotional experiences shape synapses and neural-circuit development. Neuronal activity triggers changes at the synapse, altering the composition, shape and strength of the synapse that are altered in Intellectual Disability (ID) and Autism Spectrum Disorder (ASD), which affects
~1% of the world's population. Using, *Syngap1* heterozygous mouse model (*Syngap1*$^{+/-}$) leads to aberrant neuronal development and function that causes various symptoms observed in the patients. Besides, the current therapeutics is aimed at co-morbidities of ASD/ID and lack a proper treatment for ASD/ID. Our recent publication demonstrates a novel compound that can provide better treatment for ASD/ID.

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Early life environment influences the mental health through gut microbiota

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Abstract

The detrimental effect of benzo[a]pyrene on central nervous system and to disrupt intestinal barrier and permeability leading to dysbiosis has been well documented in literature. As gut-brain axis is directly regulating the brain homeostatic environment, an imbalance in gut microbial composition following B[a]P exposure is maleficent. Zebrafish is gaining significant attention in translational modelling of disease conditions. In this line, involvement of probiotics as prophylactic intervention against B[a]P-induced neurotoxicity is elusive in literature. Therefore, the current study was aimed to determine the impact of acute B[a]P exposure on neurobehavioral response of zebrafish and possible neuroprotection through co-supplementation of probiotic *Lactobacillus rhamnosus* GG (LGG). Zebrafish were divided into naive, control, B[a]P treated, probiotic (LGG), B[a]P treated co-supplemented with probiotic (LGG) groups. Neurobehavioral assessment was carried out after seven days of acute exposure to B[a]P with probiotic co-supplementation followed by histopathological study. The basic findings indicated that there was a clear altercation in locomotor activity and habitat preference, with animals preferentially responding towards altered zone on exposure to B[a]P. However, co-supplementation of LGG showed restoration against B[a]P-induced neurobehavioral alteration and cognitive dysfunction. Brain tissue pyknosis and intestinal epithelial disruption was significantly mitigated on LGG co-supplementation against B[a]P exposure in zebrafish. Our present study deciphers a novel approach towards supplementation of probiotics in modulation of gut commensal microbiota influencing neurobehavior in zebrafish. Our findings delineating the possible role of probiotic as a curative administration against B[a]P-induced neurobehavioral alteration and might be a novel intervention to counter exposome persuaded neurological outcomes.

Keywords: Exposome**,** Benzo[a]pyrene; Gut microbiota; *Lactobacillus rhamnosus* LGG; Behavior; Zebrafish

Immediate changes in Brain Event related potentials in response to steep HDTBR in young healthy females

Savita Gaur, Monika Sharma, Sanjiv Kumar, Ruma Dutta, Bhanu Teja, Neha Yadav, Harsh Powar, Koushik Ray, Krishna Kishore, KK Deepak , Usha Panjwani, Rajesh Arora

Abstract

Microgravity-related changes in the space environment may affect cognitive functioning of astronauts, which is crucial for mission success. The aim of the present study was to determine the effect of 20 degree head down tilt bead rest (HDTBR) on brain ERPs, cognitive interference and subjective feeling in healthy young female volunteers. The Event related potentials P300 & CNV, color Stroop test and simulator sickness questionnaire data were measured for baseline, microgravity exposure and post recovery period of the study in n=13 Participants. The mean age of the participants was 26.5 ±4.1 years. The anthropometric parameters Head circumference and Neck circumference values were 54.3± 1.09 cm and 32.47±2.01cm respectively. The average head length of participants was 17.46±0.5 cm and head breadth was 14.55±0.7 cm. Results suggest immediate degradation in ERP P300 and feeling of fullness of head due to cephalad shift under influence of Head down tilt. The ERP P300 data were normally distributed ($p>0.05$) on Shapiro-Wilk test. There was a significant increase in the latency of P300 wave ($p< 0.05$) (5.7%) as compared to the baseline. The changes in latency didn't return to baseline post recovery period of 10 minutes. The latency was significantly different from Baseline ($p<0.05$) (3.8%) indicating that for the allotted recovery time of the experiment was inadequate. There was insignificant change in the CNV mean reaction time ($p>0.05$) post 20° HDTBR for samples in the study. The selective attention capacity on Stroop test was found increased for simulated gravity exposure and can be attributed to the practice effect. On simulator sickness questionnaire (SSQ) scale, 62% participants recorded fullness of head during head down tilt. It was concluded that microgravity environment hampers cognitive performance. The study has immense potential in understanding and application of neurocognition in outer space.

Methods

In this observational cohort study n=13 young healthy female volunteers were subjected to HDTBR of 20 deg for 30 minutes followed by 10 min recovery. They had no known history of any neurological disorders. No history of head or ear injuries. The study was approved by the Human Ethics Committee of the Institute. The experimental protocols were explained to the participants and informed consent was taken.

Inclusion criteria: Women between the ages of 20 and 40 who were generally healthy met the inclusion requirements. The subjects voluntarily agreed to take part in the study. All of the participants were Indian nationals. The subjects had no physical or mental health issues. Their body physiology and anthropometry data, medical history and sleep and wake time were documented.

Exclusion criteria: The study did not include any participants who were under the age of 18 or older than 40. Volunteers with any medical or mental conditions that might be exacerbated by microgravity exposure were not allowed to participate.

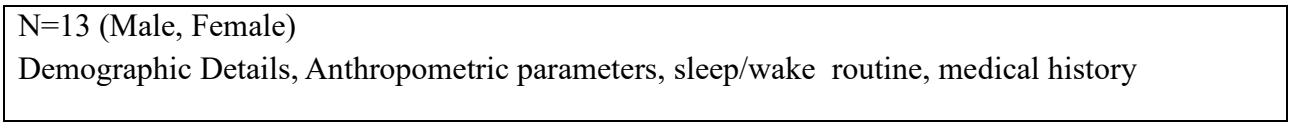
Assessment Tools and Experimental Protocol

Head down tilt Bed rest (HDTBR): A head-down tilt table is a widely used tool to replicate microgravity in a lab setting. To simulate microgravity, studies were conducted at a 20-degree head-down tilt, a relatively uncommon inclination. In the neurophysiology lab, recordings were standardized on a motorized tilt table. A standard working temperature was maintained, and the experimental lab was noise-proof. The experiment was conducted supine, with no head, hand, or leg movement other than during patient response.

At 11 am, all pertinent information, including blood pressure, SpO2, temperature, ERP P300 and CNV, response to the Color Stroop test, and a simulator sickness questionnaire, was meticulously recorded (Time-1). After 30 minutes of microgravity exposure at a 20-degree angle (Time-2) and a 10-minute recovery interval (Time-3), all of these values were recorded again.

10-20 Electrode placement system

The 10-20 system is an internationally accepted standard for defining and positioning scalp electrodes for polysomnography, EEG testing, and ERP recording. Participants were instructed to wash their hair prior to the experiment in order to keep their scalp clean and oil-free. Ten20TM conductive EEG paste was applied to a specific location after carefully cleaning the scalp with NuPrepTM skin preparing gel (Weaver and Company USA). Recordings were made using Ag-Agcl disc electrodes (Natus, Biomedical USA). Prior to beginning baseline ERP recording, measurements of blood pressure, SpO2, and temperature were taken in supine position. Through headphones, the audio stimulus was delivered to both ears. The first baseline recording (Time-1) was performed at 11 a.m. in the morning, prior to microgravity exposure. After that, the motorised tilt table was inclined to -20 degrees HDT, and the participant was exposed to a 30-minute simulated microgravity. The data recording were repeated (Time). After 10 minutes of rest, often known as the study's physiological recovery phase, the bed was again put to sleep at 0 degrees. The readings were then repeated (Time-3). The experimental study design is presented in Figure 1.



Time 1	Time 2	Time 3
Baseline 0 ° Supine-Bed Rest	HDT- Simulated microgravity exposure (-20) °, 30 min	Recovery (-20) ° 10min after exposure end.
Blood Pressure, SpO2, Temperature,P300, CNV, CANTAB, Simulator Sickness questionnaire (SSQ), Color Stroop Test		

ERP P300: To instrument participants for ERP data, electrodes were put at A1, A2, FPz (common ground), C3, C4, Cz, and Pz. Using the standard auditory oddball paradigm, the subjects were presented with two different click sounds—one non-target stimuli (Frequncy) and the other target Stimuli (Rare). The stimuli characteristics were- Intensity 80 dB, Impedance 5KΩ, HF 50Hz, LF 0-0.5Hz, Acquisition duration: 750ms, amplifier range: 500µV, sweep limit 25.

CNV: This tests involved audio visual stimuli. The First warning stmuli (S1) was a signle tone sound. After the duration of a second, the second imperative stimulus (S2) was presented in the form of a flash on the response button. Subject was asked to respond on the flash of flight. The time that has elapsed between S2 and motor response was recorded as the reaction time. A motor response after 2s was rejected and marked by the system as rejection. Stimulus characteristics: HF30Hz, LF 0.2Hz, Acquisition duration 5sec, amplifier range 500 µV, sweep limit 16.

Result

The Anthropometric details of the participant's are presented in Table 1. The descriptive statistics of body physiological parameters viz Blood pressure, SPO2 and temperature for baseline 20 deg HDT and post recovery are detailed in Table 2. There was no significant change in blood pressure , SpO2 and temperature from baseline to head down tilt condition. There was a significant ($P<0.001$)change in the Simulator sickness questionnaire (SSQ) score after exposure to 20 den , 30 min HDT simulated microgravity (Table 3). There was immediate significant change in the P300 wave latency ($p<0.05$) as observed on ANOVA. The post -hoc analysis revealed that Under head down tilt condition p300 latency was significantly different ($p<0.05$) then that of Baseline and allowed recovery period. The statistical analysis results are presented in Table4.

Discussion

The current study is pertinent in assessing the effects of acute exposure to simulated microgravity on human neurophysiological functioning. We observed significant increase in the latency of P300 during 20 degree head down tilt bed rest as compared to baseline. Post 10 min of recovery time, the elevated P300 latency did not match up to the baseline.

There are very few articles on the subjective response as assessed on simulator sickness questionnaire brought out that Head down tilt bed rest primarily caused discomfort, headache and fullness of head, whereas head and fullness of head persisted when measured as post recovery time.

Conclusion

The Event Related Potential P300 is found to be impaired in a simulated microgravity environment of 20 deg HDTBR for 30 min. Increased reaction time and delayed latency suggest diminished working memory, mental acuity, and stimulus evaluation. By using a well-known spaceflight analogue (HDTBR), it was possible to obtain a better understanding of the neurophysiological mechanism and operational hazard of microgravity-induced behavioral changes. The findings of this research may aid researchers in understanding the recovery time and developing targeted remedies for detrimental effects of long-duration spaceflight on neurocognitive function.

Descriptive Statistics

	Age	Height	Weight	HC	NC	HL	HB
Mean	26.53	158.78	61.22	54.34	32.47	17.46	14.55
Std. Deviation	4.10	4.83	13.77	1.10	2.01	0.57	0.70
IQR	6.10	8.00	18.60	1.50	3.00	0.70	1.00

Table 1: Anthropometric data of participants (Age, Height, Weight, Head Circumference, Neck Circumference, Head Length, Head Breadth)

Descriptive Statistics

	Baseline					HDTBR					Recovery				
	BP sys	BP Dy	Pulse	SpO2	T	BP sys	BP Dy	Pulse	SpO2	T	BP sys	BP Dy	Pulse	SpO2	T
Mean	108.1	65.8	71.6	98.9	36.5	111.9	67.7	68.7	99.0	36.5	114.3	72.2	72.6	98.6	36.5
SD	9.7	6.3	11.9	0.7	0.2	11.8	5.1	12.7	0.8	0.2	14.3	9.8	14.6	1.3	0.2
IQR	7.7	10.3	11.2	0.5	0.3	13.4	6.6	15.8	0.6	0.2	15.1	10.4	14.4	0.8	0.3

Table 2: Body physiology parameters, Systolic and Diastolic Blood pressure, SPO2 and temperature for study volunteers

Post Hoc Comparisons – SSQ

		Mean Difference	SE	t	p bonf		p holm	
Baseline	HDTBR	-157.2	36.8	-4.3	< .001	***	< .001	***
	RECOVERY	-48.7	36.8	-1.3	0.6		0.2	

* p < .05, *** p < .001

Table 3: Simulator sickness questionnaire assessment

Post Hoc Comparisons – ERP P300 Latency

		Mean Difference	SE	t	p bonf		p holm	
Baseline	HDTBR	-18.2	5.7	-3.2	1.1e -2	*	1.1e -2	*
	RECOVERY	-12.3	5.7	-2.2	0.1		8.1e -2	

* p < .05

Table 4: ERP P300 Latency

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Modulation of synaptic plasticity and oxidative stress in streptozotocin induced Alzheimer's disease rats by magnetic field exposure

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Abstract

Alzheimer's disease (AD) is the most commonest form of age related dementia that worsens with each passing year. Clinically it is characterized by cognitive impairment, deposition of neurofibrillary tangles(NFT) and amyloid ß(Aß) in brain parenchyma. As AD is a multifaceted condition and patients are often resistant to pharmacotherapies which generally provide transient symptomatic relief, alternative therapeutic strategies are imperative. Over the last few years non- invasive and non-lesional brain neuromodulation procedures have gained attention as they can alter the activity of neuronal cells/ tissue to repair, regenerate and restore the structure and function. In the present study, we have planned to investigate the role of extremely low frequency magnetic field (ELF-MF, 17.96µT, 50Hz, 2hr/day) exposure on i.c.v. streptozotocin (STZ, 3mg/kg bw, bilaterally, single bolus) induced rat model of AD. A group of rats were exposed to ELF-MF, 24h after STZ injection for 60 days in a customized MF chamber. A set of behavioural tests followed by Golgi Cox staining and assessment of oxidative stress was done at the end of study. A significant loss of spatial memory in Morris water maze (MWM) and recognition memory in one trial object recognition task (OTORT) was observed in STZ injected rats. However, in rats exposed to ELF-MF, a significant decrease in the distance travelled to the goal quadrant ($p=0.05$) as well as in latency to the first entry was observed. Similarly, recognition index ($p=0.003$) and discrimination index ($p<0.0001$) in the OTORT showed a significant increase when compared with AD rats on day 60 after ELF-MF exposure, suggesting an improvement in cognitive function upon exposure to ELF-MF. Further, GSH content and catalase activity was decreased and 8-OHdG increased significantly ($p<0.05$) in hippocampus and frontal cortex in AD rats, which was restored after MF stimulation. Scholl profile of CA1 pyramidal cells of hippocampus exhibited a significant increase ($p<0.05$) in length, bifurcations, and intersections as a function of distance from soma both in apical and basal dendrites in spatial dendritic complexity after ELF-MF MF treatment in AD rats. The scientific evidences from the present study strengthens the notion that, ELF-MF treatment has a potential to combat cognitive impairment seen in i.c.v. STZ (3mg/kg bw) animal model of AD through prevention of synaptic dysfunction and oxidative stress.



ORAL TALKS



Expression and Interactions of Pax6 in brain of MPTP-treated mice

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Abstract

Background: Pax6, a Paired box protein and transcription factor, is a neurogenic determinant during development, in adult neural progenitor cells and expressed in neurons, glia and selective populations of dopaminergic neurons. Pax6 shows age-dependent modulation, interacts with several critical proteins and binds to promoters of genes involved in neurogenesis and neurodegeneration, synaptic plasticity, memory, and immunological surveillance. Pax6 interacts with Bdnf, Iba1, GFAP, S100β, Ngn2, TGF-β and p53 that alter during Parkinson's disease (PD), but mechanisms of Pax6 functions are not clear. Parkinson's disease (PD) is a slowly developing neurodegenerative disease characterized by loss of nigro-striatal dopaminergic neurons and aggregation of the α-synuclein-rich inclusions called as Lewy bodies. Pax6 also interacts with Parkin that is enriched at glutamatergic synapses and its mutation/loss-of-function causes PD by disrupting excitatory neurotransmission. Therefore, it has been intended to evaluate the status of expression (transcriptome and proteome), distribution, co-expression and interactions of Pax6 to genes and proteins after MPTP-treatment as compared to the respective control in mice.
Materials and Methods: The brains of mouse (15±4 weeks, weight range=20-25g) from controls and MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; 20mg/kg for 21days)-induced Parkinson's models were used for experimental works. The expression and co-localization of Pax6 and co-expressed genes (Pax6 and Parkin, α-Synuclein, Gfap, S100β, TGFβ, p53, Ngn2 and Iba1) in different regions and cell-types of brain were evaluated from mouse model of Parkinson's disease. Pax6 interacting proteins were predicted by neural network server STRING, and binding of Pax6 to promoter sequences were analysed by Eukaryotic Promoter Database. The expression, co-localization and interactions of Pax6 were evaluated by qPCR, western blotting, Fluorescence Activated Cell Sorting (FACS) and immunofluorescence assay, ChIP and Co-IP, respectively. The expression of was analysed by real-time PCR and Western blotting.
Results: Significant alterations were observed in the numbers of immune-reactive/positive (Pax6 and Parkin, α-Synuclein, Gfap, S100β, TGFβ, p53, Ngn2 and Iba1) cells and their distribution in the brains of control and in MPTP treated mice. The MPTP-treated Parkinson's model of mice shows region specific alterations of Pax6 in brain. At the transcript level, expressions of S100β, SPARC, *P73ð, p73α* decrease, while the other genes like *Pax 6, α-Synuclien, Parkin, Iba1, P53, Gfap, Tgf- β, Pcna, Sparc,* were increased in MPTP- treated mice compare to control mice. The multiple binding sites of Pax6 to promoters of *α-Syn, Parkin, Bdnf* and *Tgf-β* were observed as compared to *Tmem119, Iba1, Ifn-γ,* and *Tnf-α*. At protein level, expression of Pax6, α-Syn, Parkin, S100β and Iba1 were increased in MPTP- treated mice compare to control mice.
Conclusion: The altered expression of Pax6 in different cell types of cerebral cortex, dorsal ventricle, hippocampus and cerebellum indicated their role in the regulation of motor functions as well as neuronal/axonal path findings, emotions, reward and cognitive

functions. Preliminary results are in agreement that Pax6 may have protective impact against dopaminergic cell loss inthe Parkinson's disease.

Keywords: Pax6, Brain, Parkinson 's disease, Protein-Protein Interaction

Ang (1-7)/Mas axis in the brain: A potential therapeutic target in the management of Alzheimer's disease

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Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder. It has been well reported that a single molecule with a specific target is not sufficient to ameliorate the progression of this disease. Thus, there is a need to develop a promising alternate drug molecule in the pharmacotherapy of AD. Recently, it has been suggested that Angiotensin (Ang (1-7))/Mas axis attenuates oxidative stress, neuroinflammation, and mitochondrial dysfunction in the D-galactose-ovariectomized model of AD. Therefore, our first aim of the present study was to estimate the level of expression of HO-1 and degree of amyloid deposition, mitochondrial function, integrity, and bioenergetics in memory-sensitive brain regions such as the hippocampus, pre-frontal cortex, and amygdale of amyloid beta (Aβ) challenged rats. Subsequently, we explored the effect of Ang(1-7) with or without Trigonelline, Nrf2 inhibitor, on the extent of amyloid beta accumulation, mitochondrial function, integrity, and bioenergetics in memory-sensitive rat brain regions. At last, we evaluated the therapeutic potential of Naringin with or without A779, Mas receptor inhibitor on the Aβ level, calcium accumulation, mitochondrial function, integrity, and bioenergetics in memory-sensitive brain regions of Aβ challenged rats. Experimentally dementia was induced by the ICV administration of Aβ (1-42) (1µg/µL) and the Morris water maze and Y maze were used for the evaluation of memory impairment in cognitive deficits rats.

In the first objective, Ang(1-7) attenuated the Aβ-induced behavioral abnormalities in the cognitive deficit animals. Further, it significantly restored the level of expression of HO-1 in above brain regions of Aβ-challenged AD-like rats. Moreover, the Ang(1-7) ameliorated the Aβ-induced apoptosis and impaired mitochondrial function, integrity, and bioenergetics in all the rat brain regions. The Mas receptor antagonist, A779, abolished the therapeutic effectiveness of Ang(1-7) on Aβ-challenged cognitive deficit animals. These observations indicated the fact that Ang(1-7) could exert a therapeutic effect perhaps through the Mas-receptor-mediated mechanism in the animals.

In the next study, Trigonelline abolished the therapeutic effect of Ang(1-7) on the level of expression of HO-1 in memory-sensitive brain regions of Aβ-induced cognitive deficit animals. Further, Trigonelline abolished the Ang(1-7)-mediated attenuation of apoptosis and impairment in mitochondrial function, integrity, and bioenergetics in all selected rat brain regions.

In the last objective, Naringin facilitated the neuroprotective potential by decreasing the level of expression of HO-1 and MCU in all selected brain regions. Moreover, it also mitigated the Aβ-induced mitochondrial calcium accumulation, function, integrity, and bioenergetics in all selected brain regions. Interestingly, Mas receptor antagonist, A778 also abolished the therapeutic activity of naringin in the Aβ-induced cognitive deficit animals.

In conclusion, the Ang(1-7)/Mas/Nrf2 mediated pathway could be a potential target to attenuate the Aβ-induced mitochondrial toxicity and thereby cognitive dysfunctions in the animals. Further, Naringin exhibited a significant therapeutic effect on Aβ-induced

mitochondrial toxicity and thereby cognitive dysfunctions in the animals through Ang(1-7)/Mas/Nrf2-dependent mechanism. Hence, brain Ang(1-7)/Mas could be a potential therapeutic target in the management of AD.

Autonomic brain atrophy as a neurodegenerative biomarker in spinocerebellar ataxia

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Abstract

Background: Spinocerebellar ataxia (SCA) is a progressive neurodegenerative disorder having autonomic manifestation. The differential autonomic abnormality was quantified using Composite Autonomic Severity Score (CASS) in the most common SCA subtypes – SCA1 and SCA2. We have assessed the probable neurodegeneration in the autonomic brain areas correlated with CASS to know the sympathetic and parasympathetic autonomic brain atrophy in SCA subtypes.

Method: MRI was performed using a 3T scanner (Philips, Achieva) to obtain 3D T1-weighted scans of the whole brain and analyzed by FreeSurfer (version 5.3 and 6 dev.) software. We recruited genetically proven SCA1 (n = 18) and SCA2 (n = 25) patients with age-matched healthy controls (n = 8). We have evaluated autonomic function - heart rate variability (HRV), systolic blood pressure variability (BPV), systolic baroreflex sensitivity (BRS) and composite autonomic severity score (CASS) in SCA patients. To know the differential pattern of atrophy, the SCA subtypes were compared using ANOVA/ Kruskal Wallis test and followed by correlation analysis with multiple corrections.

Result: There was autonomic brain atrophy, comprising parasympathetic brain areas - left cuneus, right cuneus, right isthmus cingulate and sympathetic brain area -left lingual that form the core of the central autonomic network in both SCA1 and SCA2 patients. The autonomic brain atrophy was seen more in SCA1 as compared to SCA2.

Conclusion: The study states the differential autonomic brain atrophy in SCA1 and SCA2 patients. This could be act as neurodegenerative biomarker to diagnose SCA subtypes early in their course, when therapy is likely to be most effective, and to record responses for new effective therapies.

Applying SABV (Sex as a biological variable) in research and clinical care

Abstract

SABV (sex as a biological variable) has to be recognized in both preclinical (basic) and clinical research [1], as a major contributor to disease risk, phenomenology, natural history, treatment and adverse effects, and disease severity.

To consider sex as a biological variable in research, it is necessary to appreciate the following:

1. To define and distinguish sex from gender: "Sex" originates from sex chromosome complement and is involved in all aspects of physiological functioning.

The term "gender" refers to the human male and female traits in the context of social, cultural and psychological factors.

2. There are differences between the sexes at the cellular, molecular and genetic levels.

3. Without applying SABV in research there will be gaps in our knowledge of how similarly or differently the sexes function or respond to treatment.

4. Research findings in men cannot necessarily be applied to women, and vise- versa.

For many decades, in preclinical neuroscience research, male rodents had been the default model organism, which most likely contributed to higher rates of adverse effects of drug treatment in women. Studies have shown male rodents only were used in 80% or more animal studies in the fields of neuroscience, pharmacology, endocrinology, immunology, and physiology [2].Several drugs would have been recalled because of severe adverse effects in women, as theclinical trials were carried out often without sufficient population of women [3].

To deliver gender appropriate medical care for both women and men, and to fill in the gaps of our knowledge of male and female biology, studying both sexes in clinical and preclinical research is necessary.

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Prevalence of long term sequelae of neuropsychiatric illness in COVID-19survivors: a follow-up study

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Abstract

Background: The pathological involvement of the nervous system in COVID-19 patients poses a long term risk for the development of a neurpsychiatric illness in survivors, the prevalence of which needs to be assessed.

Methods: A total of 207 hospitalized patients with COVID-19 were followed up post-discharge. The patients were verbally interviewed through a telephonic call and were asked about the persistence or new appearance of any neurological/psychiatric illness from a set list. Data was tubulated and statisticallyanalyzed.

Results: A neuropsychiatric illness was noted to be present in ~ 38 % (79/207) of the followed-up patients. Diminished vision (28/79) and difficulty in speech or walking (24/79) were the most frequent symptoms followed by memory loss (17/79), and loss of smell and taste (11/79). Giddiness (8/79), difficulty in concentration (7/79), loss of conciousness (6/79), depression or anxietyv(2/79), headache(1/79), derranged orientation (1/79), and irrelevant talk (1/79) were less frequent symptoms.

Conclusion: The presence of a neuropsychtric illness in a significant proportion of COVID-19 survivors indicatesfor a looming public health crisis. A longer time follow up study involving larger population is advised.

Keywords: Neuropsychiatric symptoms, long covid, prevalence, public health

Vocal cognition in birds and underlying neuronal dynamics

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Abstract

Certain avian species, including corvids and parrots, might share an extremely sophisticated and surprising cognive skills, which are comparable to those of large-brained mammals. This includes several processes, such as reasoning, behavioral complexities, vocalization, and imagination. Extensive research has illuminated the mechanisms underlying human spoken language, a rare and complex cognitive task found only in three distantly related groups of birds and some distantly related groups of mammals. The full complexies involved in human speech development, like the integrated process by which humans perceive, learning and memories, are all to be understood. Interpreting the neural mechanism, such as localization and morphological characterization of neurons driving vocal learning are technical and ethically not possible in humans. For this reason, avian animal models like parrot and songbirds in which controlled experiments can analyse the behavioral, neurological, and genetic components of language-relevant traits, are of great importance. The avian pallial domain consists of four divisions called hyperpallium, mesopallium, nidopallium and the arcopallium. The nidopallium caudolateral (NCL), an area in the avian pallium, shows important neural similaries to the mammalian prefrontal cortex and generates executive functions without displaying any visible lamination. Present study was designed to idenfy the possible shared neural features of avian pallium that may generate higher levels of consciousness and cognion in birds.

Prevalence of CNS infections: three years of data from a single centre study

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Abstract

Pathogenic infection of the central nervous system is highly fatal. In the literature, information about the incidence of multiple CNS infections caused by various etiological agents affecting the Indian population is limited. We have conducted a retrospective study among patients admitted with central nervous system infections for 3 years in Kasturba hospital, Manipal, India. A total of 882 patient case sheets have been evaluated, and 593 subjects have met the inclusion criteria. Demographic details, clinical presentation, etiological agents, and outcome were evaluated. Among all the patients, 368 (62.1%) male and 225 (37.9 %) female subjects were present, and 22.1% were of age below 12 years. Most common pathogens causing CNS infection were bacteria (52.6%) followed by viruses (14%), fungi (4%) and parasites (0.3%). Etiological agent was unidentified in 172 (29%) subjects. Common causative pathogens were *Mycobacterium tuberculosis*, Scrub typhus, Kyasanur forest disease virus and *Cryptococcus neoformans*. Pneumonia, sepsis and acute kidney injury were the common complications, with a mortality rate of 6.6%. Widespread epidemiological studies are required for useful and accurate information on several causative agents of CNS infections. More sensitive diagnostic methods for early and effective diagnosis must be devised and implemented.

Cerebellar transcranial direct current stimulation (tDCS): A new dimension as neuro- modulation therapy?

Abstract

In recent years, transcranial direct current stimulation (tDCS), as a non-invasive therapeutic tool, has gained attention due to its low-risk administration procedure and high cost-effectiveness. A wide range of medical fields, from stroke to schizophrenia patients, have considered tDCS for treating patients with limited options. In spite of this, tDCS is rarely applied to treat cerebellar disorders. We realized that an optimal use is only possible when mechanistic pathways are understood thoroughly. In order to decipher this, we created a mouse model, for the first time, to investigate cerebellar tDCS-induced behavioral changes. Our results provided evidence that the acute effect of anodal tDCS on cerebellar dependent VOR adaptation in mice was disrupted by genetic ablation of long-term plasticity in Purkinje cells (PCs). Based on our animal study, we expected to observe similar effects in humans. To our surprize, neither offline nor online anodal tDCS had an effect on VOR adaptation. However, anodal tDCS of the cerebellum facilitated locomotor adaptation in humans. It is plausible that the electric field strength in the flocculus was insufficient to affect neuronal firing and VOR adaptation is exceedingly more complex in humans than in mice. In future, we will have to consider (i) anatomical location of the preferred stimulation site, (ii) neuronal firing profile and dynamics of the network and (iii) behavior paradigm before administering tDCS as a therapeutic tool in cerebellar disorders.

Puppetry as a platform for increasing awareness on brain and its functions among schoolchildren in rural village of Karnataka State

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Abstract

Introduction: Educators and clinicians are always looking at innovative methodologies to impart health education which would promote positive health behaviour that is culturally specific and age- appropriate. Puppetry is India's traditional method of storytelling among children and a creative methodology that stimulates learning, attention, motivation, and interest that fashions joyful learning. The International Brain Research Organization [IBRO] awarded the authors a brain awareness grant for this unique methodology to increase brain awareness among school children.

Method of dissemination: The Department of Mental Health Education collaborated with the Department of Psychiatric Social Work, Neuropathology, Clinical Psychopharmacology and Toxicology and identified theatre actors from a well-known School of Drama in Karnataka State. The theatre actors were oriented to the brain's functions, followed by a traditional form of puppetry developed. In the first phase, the script was drafted, and the script's content was given to subject experts and validated. In the second phase, the play of 30-45 minutes, five characters, a young boy and a grandmother in the leading role and supporting characters, were shaped, and the awareness of the brain and its functions were narrated. In the Third phase, a puppetry show was organized for the Institute faculty and staff, feedback was taken, and modification was incorporated. In the fourth phase, a rural village was identified in Kolar District after due permission was obtained by the local panchayath leader and school principal. Around 75 students in 4 batches were permitted to view the show. Post the session, the students had many doubts, and the authors clarified them. In addition, Brain samples were displayed and a live interactive session with the students to enrich their knowledge.

Conclusion: Most students expressed that education about the brain and its functions through puppetry made learning enjoyable and easy to understand the concept and the content. Further, it strengthened their knowledge about the brain and its functions. This medium provides a practical approach to disseminating vital health messages. It effectively promotes behaviour change in understanding our body's functions and preventing the diseases caused due to them.

Hypoxic brain injury in cerebral palsy: an in vitro disease model for a complex disease

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Abstract

Cerebral palsy (CP) is a disease arising in neonates because of hypoxic brain injury *in utero* or during birth. Interestingly, premature neonates are more vulnerable to hypoxic injury. To elucidate the pathogenesis of CP, fetal neural stem cells (FNSCs) isolated from the subventricular zone of aborted fetal brains (n=5) were allowed to differentiate into premyelinating oligodendrocytes (pre-OL) and mature OL over a period of 4 weeks to mimic normal oligodendrocyte (OL) development in the fetal brain. Different cell types were characterized by stage-specific markers. It is known that premyelinating OL (pre-OL) are more prevalent in premature neonates and are more vulnerable to hypoxic injury. Pre-OL and mature OL were exposed to 0.2% hypoxia for 48 hours (hypoxia was validated using a panel of markers). RNA sequencing (Illumina platform) of the cells was done before and after exposure to hypoxia, to elucidate the mechanism(s) and the impact of hypoxia on the etiopathogenesis of CP. Some of the differentially expressed genes / pathways that were shown to be affected, were validated. Interestingly, analysis of our results indicate that hypoxic injury to the cells in pre-OL stage may result in blocking OL maturation, leading to the manifestation of CP in premature neonates.

Cognitive Flexibility and Response Conflict of Emotion Laden Texts and Faces in PTSD: AStudy on Nepal Earthquake

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Abstract

In the last few decades, earthquakes, which can be the most dangerous and destructive, have become more common. Gigantic earthquakes bring attention to the fact that survivors often have problems with their mental health. This study aimed to investigate mechanisms of cognitive flexibility and response to conflict in emotion-laden texts and faces using an emotion word stroop paradigm in people with and without symptoms of PTSD after the earthquakes in Nepal.The sample consisted of 84 participants (42 PTSD and 42 nonPTSD) aged 18 to 55 years from Kathmandu city and the Chautara district (Sindhupalchowk), Nepal. Most of them experienced at least two major earthquakes and aftershocks. The PCL-5 and IES scales were used to segregate the participants into two groups (PTSD and nonPTSD). Findings showed that, on the basis of accuracy score, PTSD individuals indicated the semantic processing of emotion-laden texts did not interfere or influence the recognition of emotion-laden faces due to cognitive impairments. In addition, PTSD individuals performed better in the recognition of emotion-laden faces than in texts because of inadequate semantic processing of emotion-laden texts. On the other hand, due to intact cognitive functions of nonPTSD individuals, the semantic processing of emotion-laden texts interferes with or influences the recognition of emotion-laden faces or vice-versa. On the basis of reaction time, it was also predicted that the cognitive flexibility of nonPTSD individuals in task switching for focus (face or text) was found intact. PTSD individuals not only showed less response conflict in recognition of emotion, but also showed task shifting from text to face one direction unconsciously for recognition and processing of emotional text and faces. This showed an impairment in cognitive flexibility in PTSD individuals. However, the emotional Stroop effect was found in both types of focus conditions in nonPTSD. These results suggest that people with PTSD automatically and unconsciously process emotional faces more than they do emotional texts.

Keywords: Cognitive Flexibility, Emotion, Posttraumatic Stress Disorder, Response Conflict

Early life trauma and pathological aggressive behavior: Local thyroid hormone Connect?

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Abstract

Pathological aggressive behavior is an aberrant form of aggression that has detrimentalimpact on health and society. Early life traumatic experiences leads to adulthood pathological aggression, anti-social personality disorders and criminality, though molecular mechanisms are obscure. Here, we provide brain region and sex specific transcriptome profiles of peripubertal stress (PPS) exposed adult pathological aggressive male and resilient female mice. We identify transthyretin (TTR) as a key regulator of PPS induced pathological aggression in males. TTR mediated long-term perturbation in hypothalamic thyroid hormone (TH) availability contributed to male aggression without affecting circulating hormone. Further, we deciphered Ttr promoter hyper methylation in hypothalamus of pathological aggressive males as compared to control counterparts. Our findings reveal that trauma during puberty trigger lasting aberrant aggressive behavior by epigenetic programming of TTR and consequent impaired thyroid availability in brain. TTR-TH signalling in hypothalamus can serve as potential target in reversal of pathological aggression. Gender differences are less explored in majority of behavioral neuroscience and psychiatry research and thus women's mental health is not being protected equally. In order to reduce such gap, my core research aims in understanding gender differences in early life trauma induced lasting behavioral deficits and risk for psychoses. Being an early career principle investigator and guiding students, I attempt to maintain a balanced workforce. I have included male and female students of diverse geographic region, socio-economic status and culture. I also wish to take people of arts and humanities studying sociology and psychology in my research team. Our collaborators even include persons with disabilities but high scientific acumen. My project in studying violent aggressive behavior has a huge societal impact due to rise in crime incidences and anti-social activities. Further, I aim to extend the animal model work in human cohort of diverse countries, ethnicity, age and sexual orientation.

The effect of a high-fat diet combined with exercise on biochemical and anxiety-likebehaviour in adolescent male and female rats

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Abstract

Lifelong repercussions result from childhood exposure to a high-fat diet on metabolism. Exercise and switching to a normal low-fat diet during adulthood could reverse most but not all biochemical and behavioral implications due to a high-fat diet paradigm. In this study, whether exercise coupled with a high-fat diet is able to influence the biometric, biochemical and anxiety-like behavior in adolescent male and female rats was addressed. After obtaining approval from the Institutional Animal Ethics Committee 12 female and 12 male Wistar adolescent rats, aged 35 days and weighing between 30-50 g were obtained. They were divided into two groups control group and HFD group of 6 female and male in each group. The control group received standard diet and HFD group received HFD for 10 weeks coupled with exercise in last three weeks. We found that 10-week administration of a high-fat diet increased body weight in both male and female rats, which was comparable to control in males and got lowered in females after 3-week of exercise. Exercise in high-fat-fed female rats showed comparable liver lipid levels to control, while the serum glucose and lipid profile was raised in both males and females. The exercise was able to ameliorate the anxiogenic behavior in high-fat diet-fed adolescent female rats, but not in male rats. Taken together, these results reflect upon the gender-specific differential effect of high-fat diet and exercise during adolescence which influences the biometric, biochemical, and anxiety-like behavioral outcomes.

Electrophysiological and anatomical correlates for the ethological hand use in the primary somatosensory cortex of macaque monkeys

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Abstract

The macaque monkeys have an opposable thumb like humans, to initiate their ability to execute precision grip, and object manipulation. Monkeys use the thumb (D1) and index finger (D2) in a pincer-like grasp called precision grip. The evolution of opposable thumb may lead to change in the brain organization such that inputs from thumb processed differently as compared to other fingers. To address this question we have done two sets of experiments. In electrophysiological experiments, we determined the extent of neurons from each digit representations in cortical area 3b, respond to touch on the other fingers of the hand. We recorded neuronal responses in different digit representation at the same time as stimulating different locations on the hand. The results showed that neurons in the digit 1 (D1) representation responded to the tactile stimuli almost entirely on the thumb, and were mostly unresponsive to touch on other fingers. Instead, neurons located in other digit representation (D2-D5) had more widespread receptive fields and responded when touched any of these fingers.

In separate set of anatomical experiments, we determined the intrinsic connections of different digit representations in area 3b using small amount of neuroanatomical tracers. The locations of retrogradely labeled neurons in the hand representation were plotted using Neurolucida cell plotting system. The objective was to determine if neurons in the digit 1 representation and the other digits have differential intrinsic cortical connectivity. The results showed that the intrinsic connection of digit 1 are largely confined within the same digit whereas digit 2-5 were more widespread and showing cross connectivity.

These results point toward the tactile inputs from digit 1 are processed largely independent from other digits, while inputs from other digits are significantly more cross-talked. These results conform to behavioral use of the opposable thumb independent of other fingers, which are used to execute precise grip or manipulation of the objects.

INTRAGASTRIC ADMINISTRATION OF DIETARY GLUTAMATE IN THE RATSCAUSES CHANGES IN MEDIAL PREOPTIC AREA NEURONAL ACTIVITY

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Place where work was done: AIIMS, New Delhi

Abstract

Brown adipose tissue (BAT) thermogenesis occurs after intragastric administration of dietary glutamate. The brain senses glutamate intake in the gut by the stimulation of gut glutamate receptors leading to activation of gastric afferent vagal fibers. Neuro-imaging techniques revealed activation of medial preoptic area (mPOA) in rats after intragastric glutamate administration. Nonetheless, to establish that the brain activity induced by dietary stimulus, it is important to confirm results obtained from imaging techniques with recordings made at the neuronal level. In this study we have investigated the neuronal activity of mPOA after intragastric infusion of glutamate. The recording was obtained from 48 neurons of adult male/female Wistar rats weighing between (200-250) g. Rats were urethane anesthetized and fixed onto stereotaxic apparatus. A glass microelectrode of 1-5µm tip diameter was lowered at mPOA in steps of 1µm with motorized microdrive. An Ag-Cl wire was inserted into the microelectrode, which was connected to high input impedance probe. One min baseline neuronal recording and five min recording was done after glutamate (0.12M, 1.5 ml) was infused intragastrically via a polyethylene tube. Out of the 48 neurons studied, 39 responded to the intervention. Intragastric glutamate increased the firing rate of 28 out of 39 responding POA neurons; while 4 of the responding neurons showed a decrease in firing rate. The latency of response ranged from 1-5 min after the glutamate was delivered. Dietary glutamate probably triggers the neurons of the mPOA bringing about an increase in the BAT thermogenesis.

Novel small molecule inhibitors of Cdc25A protect neuronal cells in neurodegenerative disease models.

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Abstract

Alzheimer's disease (AD) and Parkinson's disease (PD) are progressive neurodegenerative diseases that presently have no cure. Research has shown activation of cell cycle pathways in neurodegenerative diseases. We have previously reported the activation and necessary role of Cdc25A in models of neurodegenerative diseases. The present study was aimed to test the efficacy of a small library of novel synthetic molecules that target Cdc25A in cellular models of neurodegeneration. Neuronally differentiated PC12 cells were used as cellular model. NGF deprivation and 6OHDA treatment were used as insult relevant to neurodegeneration. NGF deprivation is a major cause of developmental neuron deathand has been implicated in AD. 6-OHDA, a PD mimetic, is a highly oxidizable dopamine analog that can be taken up by the dopamine transporters in catecholaminergic neurons and can induce cell death by ROS generation. For synthesis of the inhibitors, simple Buchwald reaction and amid coupling were used as key steps. A number of these designed small molecule inhibitors significantly prevented neuronal cell death evoked by NGF deprivation as well as 6-hydroxydopamine (6-OHDA). Molecular dynamics stimulation with water as an explicit solvent indicated stability of enzyme inhibitor complex in water. Computational chemistry and molecular docking studies indicated that the inhibitors bind to the catalytic site of CDC25A indicating competitive inhibition. A number of our newly synthesized molecules inhibit Cdc25A phosphatase activity, loss of mitochondrial integrity, and Caspase3 activation caused by NGF deprivation and 6-OHDA. Hence, it may be proposed thatCdc25A inhibition would be a therapeutic choice for neurodegenerative diseases, and thesesynthesized Cdc25A inhibitors could lead to effective treatments for AD and PD.

Understanding the decisive role of immunity related GTPase M (Irgm1) in regulating neuroinflammation and neurodegeneration in clinically relevant knockout mice model

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Abstract

Inflammation of central nervous system (CNS) is the fundamental host defence response to CNS injury, pathological invasion and toxic insult. However, a sustained inflammatory response in CNS is detrimental and associated with neurodegeneration and demyelination in brain. Recent reports advocated that immunity related GTPase M (IRGM) and its mouse orthologue (LRG-47/Irgm1) act as a principal negative regulator of inflammatory and type I interferon response to check the viral proliferation by strong induction of viral restriction factors and related cascades. In this context, a heightened inflammatory response through microglial and astrocytic activation in brain is detrimental for neuronal microenvironment. To understand the regulatory role of Irgm1 towards neuroinflammation-instigated neurodegeneration and demyelination, Irgm1 WT ($Irgm1^{+/+}$) and KO ($Irgm1^{-/-}$) male mice as animal model were considered for the present study. Our preliminary findings showed a significant delay in consolidation of reference memory as well as retrieval of memory in $Irgm1^{-/-}$ mice as compared to $Irgm1^{+/+}$ mice under basal condition. Since aberrant microglial activation is linked with neurodegeneration and memory impairment, our observation also showed heightened GFAP and Iba1 expression in brain of $Irgm1^{-/-}$ mice. Additionally, necroptosis-associated neurodegeneration was further verified by upregulation of pMLKL and pTau in $Irgm1^{-/-}$ mice brain. Further, we were fascinated to understand the association of heightened neuroinflammation with progressive demyelination through the regulatory role of Irgm1. In this regard, our preliminary findings showed a significant down-regulation of myelin basic protein (MBP) and Olig2 with corresponding upregulation of GFAP and Iba1 in $Irgm1^{-/-}$ mice brain as compared to $Irgm1^{+/+}$ mice following cuprizone supplementation. Increasing evidence advocated that heightened inflammatory response in CNS is the precondition for demyelination and neurodegeneration through impaired oligodendrogenesis. Thus, our findings suggests the neuroprotective role of Irgm1 against CNS demyelination by keeping heightened neuroinflammation under check in $Irgm1^{+/+}$ mice. As reactive microglia and macrophages are responsible for impaired neurogenesis, oligodendrogenesis and myelin plasticity through induction of specific cytokines/chemokines, our further study will focus on screening of specific population of cytokines/chemokines by microglial/astrocytes reactivity in mice brain. Therefore, understanding the role of IRGM in neuroprotection provides a new insight into the therapeutic intervention against neurodegenerative diseases.

Ethics statement:

All experiments conducted on mice were in accordance to the guidelines of the institutional animal ethics committee (IAEC), Siksha 'O' Anusandhan (Deemed to be University) [IAEC/SPS/SOA/101/2022].

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Sonic hedgehog-Gli1-Pax6 cell signaling axis regulation of neurogenesis to brain tumor

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Abstract:

Brain development is tightly regulated process. In the process of brain development various cell signalingpathways are involved and these pathways further act upon various downstream targets genes including many transcription factors. Therefore, in this study we investigated the role of Shh cell signaling pathwayin neurogenesis to brain tumor. It has been reported that Shh control the neural tube development by regulating the homeodomain transcription factors (HDTFs) Pax6 and Nkx2.2 on the gradient basis. Our study revealed that when cerebellum was damaged by cadmium treatment then its neural cells showed high expression of Shh and also downstream HDTFs Pax6 and Nkx2.2. Moreover, these two transcription factors also showed their role in brain tumor development. SiRNA-mediated knockdown of Shh cell signaling main transcription factor Gli1 showed the down-regulation of Pax6 and upregulation of Nkx2.2. Even, this pathway specific inhibitor GANT61 also showed the similar results. Henceforth, it suggests that these HDTFs are not only regulate in the early neurogenesis but also contribute in the brain tumor development. However, mode of regulation is differential in brain tumor as compared to neural tube development and neurogenesis. Therefore, our study concludes that brain development genes including Shh-Gli1-Pax6 axis have potential significant in the brain tumor development. Hence, understanding the neurogenesis may provide lead to better understand the therapeutic targets of brain tumoriogenesis.

Antiproliferative activity of Arsenicum Iodatum and Arsenicum Album in GlioblastomaMultiforme

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Abstract:

Glioblastoma multiforme (GBM) is the most malignant brain tumors with the poorest prognosis, has a median survival time of 14.6 months and a 5 year survival rate of <10% . GBM is the primary tumor of glial cells that form the tissue surrounding nerve cells found within the brain and spinal cord. Despite progress in neurosurgery of brain tumors, complete resection of GBM is not possible due to its highly invasive nature to the surrounding brain tissue. The potential effects of radiotherapy on GBM are limited by the associated toxicity to normal tissues. In addition, the efficiency of chemotherapy is also limited, as chemotherapeutic agents are unable to efficiently cross the Blood Brain Barrier. Therefore, novel therapeutic strategies to eliminate invasive tumor cells without damaging the normal brain parenchyma are urgently required.

Homeopathic medicines are produced from healing substances, neutral substances, or highly toxic substances like Arsenic. Arsenicum iodatum is a homeopathic ingredient that is chemically prepared from metallic arsenic and iodine. Arsenicum album has also been known for a long time for its anticancer properties. In-depth understanding of mechanism is essential to further categorize the Arsenicum iodatum and Arsenicum album as an independent chemotherapeutic agent or facilitator molecule in conjunction with other chemotherapeutic agents. We started with investigating the anti-proliferative activity of Arsenicum Iodatum and Arsenicum Album in GBM Cell lines namely U-87 and LN-229. There was a dose dependent decrease in the cell viability of U-87 and LN-229 cells when treated with increasing concentration of Arsenicum iodatum and Arsenicum album. Cell viability assay using Trypan Blue staining confirmed Arsenicum iodatum and Arsenicum album induced cell death indicating antiproliferative activity of these compounds. We wanted to understand the underlying metabolic changes in the Arsenicum iodatum and Arsenicum album treated GBM cells. We used untargeted, semiquantitative Gas Chromatography-Mass Spectrometry to unearth semi quantitative changes in the metabolite levels of various classes and different metabolic pathways. We found that a total of 19 pathways were modulated in U-87MG cells by these compounds. Out of them Pyrimidine metabolism, Glutathione metabolism, TCA cycle were significantly impacted. In the LN229 cells, alterations in 14 metabolic pathways were reported. Pyrimidine metabolism, Starch and sucrose metabolism and TCA cycle showed highest impact after the drug treatment. Given the antiproliferative activity of Arsenicum iodatum and Arsenicum album, the targeting of pyrimidine metabolism and TCA cycle in GBM cells could provide a therapeutic opportunity.

ROLE OF DIFFUSION-WEIGHTED MR IMAGING IN EVALUATION OF INTRACEREBRAL HEMORRHAGE (ICH)

Paramdeep Singh, AIIMS, Bathinda

Abstract

Background and Aim: Diffusion-weighted imaging (DWI) is well known for its diagnostic utility in stroke; yet, recent attention has focused on other disorders that also show restricted diffusion on DWI. DWI of blood clot is of particular interest as hemorrhage maycomplicate the appearance of stroke. The aim of this study is to evaluate the role of diffusion-weighted MR imaging in detection and characterization of Intracerebral Hemorrhage.

Material and Methods: 90 patients with ICH underwent MRI that comprised DWI, T1-and T2-weighted, T2* gradient-echo images and fluid-attenuated inversion recovery (FLAIR) sequences. According to the time interval between commencement of symptoms and initial MRI, five phases were characterized: hyperacute (n=20); acute (n=25); early subacute (n=15); late subacute (n=20); and chronic (n=10). We examined the signal intensity and apparent diffusion coefficient (ADC) of ICH and compared the signal intensities of hematomas at DWI and on conventional MR images.

Results: Diffusion was reduced in hyperacute, acute, and subacute clots with ADCs being reduced compared with normal brain tissue during all phases. The hematomas were bright on DWI in hyperacute and late subacute clots due to reduced ADC and hypointense at the acute, early subacute and chronic stages because of T2- induced hypointensity of clot (ie, “T2 dark-through”).

Conclusions: In patients with acute stroke, an understanding of the distinctive features of ICH seen at DWI can be useful in both the categorization of intracranial hemorrhagic lesions and the delineation of hemorrhage from ischemia.

MRI Evaluation of Physiotherapy Induced Corticospinal Tract Changes in Ischemic Stroke Patients

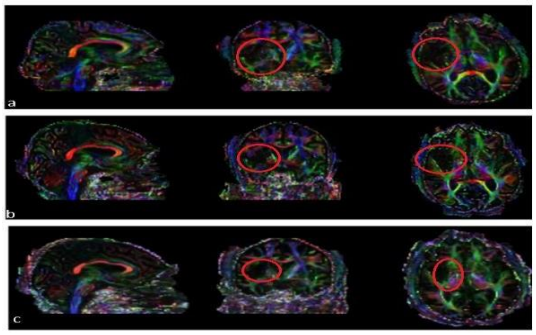
Dushyant Kumar[1], Rajesh Mishra[1], Priyanka Bhagat[2], Surbhi Kaura[2], Padma Srivastava[2], Rama Jayasundar[1*] Departments of [1]NMR, [2]Neurology, All India Institute of Medical Sciences, New Delhi, India
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Abstract

Introduction: Stroke is a leading cause of disability worldwide and affects economy and work productivity of countries.[1] Physiotherapy is the conventional rehabilitation technique. The present study evaluates the effect of physiotherapy in post-stroke rehabilitation by Magnetic Resonance imaging (MRI)

Materials and methods: Eleven first-ever stroke patients (18-60 years) with ischemia in left hemisphere were enrolled for the study after obtaining approval from Institute Ethics Committee and written informed consents. Qualified physiotherapists gave standard physiotherapy to all patients, one hour every day for six consecutive months. National Institutes of Health Stroke Scale was determined at 0, three and six months post-intervention. Diffusion Tensor Imaging (DTI) was carried out at 3T (Ingenia, Philips MR scanner), using the following parameters: repetition time 12210 ms, echo time 83 ms, acquisition matrix 112 X 110, flip angle 90^0, number of slices 66, gradient direction 32. DTI images were acquired and processed with FSL 5.0.9. Color coding of tractography pathways was based on a standard red-green-blue (RGB) code that was applied to the vector in each brain area (red for right to left, blue for dorsal to ventral, and green for anterior to posterior). Comparisons between groups (pre- and post-physiotherapy) for longitudinal changes were carried out.

Results: Percentage improvement in NIHSS score was observed for all the patients after three (71.5%) and six (80%) months of physiotherapy. Representative images of processed DTI data shown in Figure-1 shows the physiotherapy induced mean changes in fractional anisotropy of corticospinal tract for left and right hemisphere separately. The fractional anisotropy of left corticospinal tract decreased between on 3 and 6 months, whereas increased in the right corticospinal tract. This shows that the contralateral region has taken the activity and resulted in increase in CST tract volume.



Persuassive image. Representative image of physiotherapy group showing longitudinal changes in DTI FA 3a= 0 Month, 3b= 3 Months, 3c= 6 Months

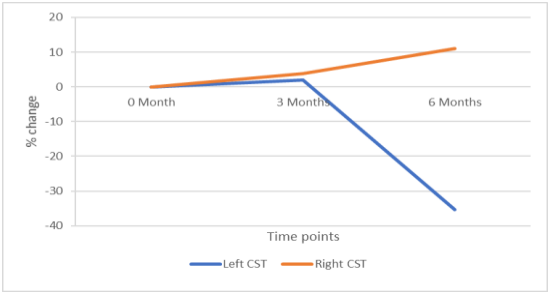


Figure 1: Mean percentage of physiotherapy

Conclusion

Physiotherapy plays a major role in post stroke rehabilitation. Although there are reports on physiotherapy induced changes in physiological functions,[2] to the best of our knowledge there are no studies to assess the white matter changes effected by physiotherapy in post-stroke recovery. The current study has evaluated for the first time physiotherapyinduced corticospinal tract changes in post-stroke recovery using DTI. The results have shown that DTI can play a crucial role in understanding the effects of physiotherapy in post-stroke recovery.

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Organization of Streams in the Mouse Orbitofrontal Cortex along the Mediolateral Axis: Role in Emotional Regulation.

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Abstract

The Orbitofrontal cortex (OFC) is a multisensory hub, integrating exteroreceptive information from the sensory associative cortices with the dopaminergic inputs from the midbrain conveying hedonic value to the sensory stimuli and the amygdalar projections relaying information of the emotional context. These input- output connectivity from the different subdivisions of the rodent OFC are behind the OFC´s role in emotional regulation.

The OFC has been divided into distinct anatomical and functional subdivisions along the mediolateral axis. Here we have used a retrograde tracer to topographically map the afferents to these subdivisions and then compared them to the established efferents in the mice. We show the presence of OFC substreams that correspond to the functional differences in affective regulation as observed in rodents.

We have also investigated the corticocortical connectivity relaying acoustic information to mouse OFC. Indeed, acoustic hallucinations are a hallmark for psychosis in several mood and thought disorders, also associated with affective dysregulation. We measured clear acoustic responses in the OFC by local field potentials and live animal imaging. These responses were abolished by pharmacological and chemogenetic inactivation of the above identified pathway. Noticeably this pathway was also sensitive to neuromodulators wherein the auditory responses were reduced by local application of dopaminergic agonist and neurosteroids. Finally, the OFC acoustic responses reverberated to auditory cortex via feedback connections and displayed sensory gating, a phenomenon of local origin not detectable in input auditory cortices.

Together, our data supports the existence of distinct OFC pathways implicated in emotional and goal directed behaviour.

Ang (1-7)/Mas axis in the brain: A potential therapeutic target in the management of Alzheimer's disease

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Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder. It has been well reported that a single molecule with a specific target is not sufficient to ameliorate the progression of this disease. Thus, there is a need to develop a promising alternate drug molecule in the pharmacotherapy of AD. Recently, it has been suggested that Angiotensin (Ang (1-7))/Mas axis attenuates oxidative stress, neuroinflammation, and mitochondrial dysfunction in the D-galactose-ovariectomized model of AD. Therefore, our first aim of the present study was to estimate the level of expression of HO-1 and degree of amyloid deposition, mitochondrial function, integrity, and bioenergetics in memory-sensitive brain regions such as the hippocampus, pre-frontal cortex, and amygdale of amyloid beta (Aβ) challenged rats. Subsequently, we explored the effect of Ang(1-7) with or without Trigonelline, Nrf2 inhibitor, on the extent of amyloid beta accumulation, mitochondrial function, integrity, and bioenergetics in memory-sensitive rat brain regions. At last, we evaluated the therapeutic potential of Naringin with or without A779, Mas receptor inhibitor on the Aβ level, calcium accumulation, mitochondrial function, integrity, and bioenergetics in memory-sensitive brain regions of Aβ challenged rats. Experimentally dementia was induced by the ICV administration of Aβ (1-42) (1µg/µL) and the Morris water maze and Y maze were used for the evaluation of memory impairment in cognitive deficits rats.

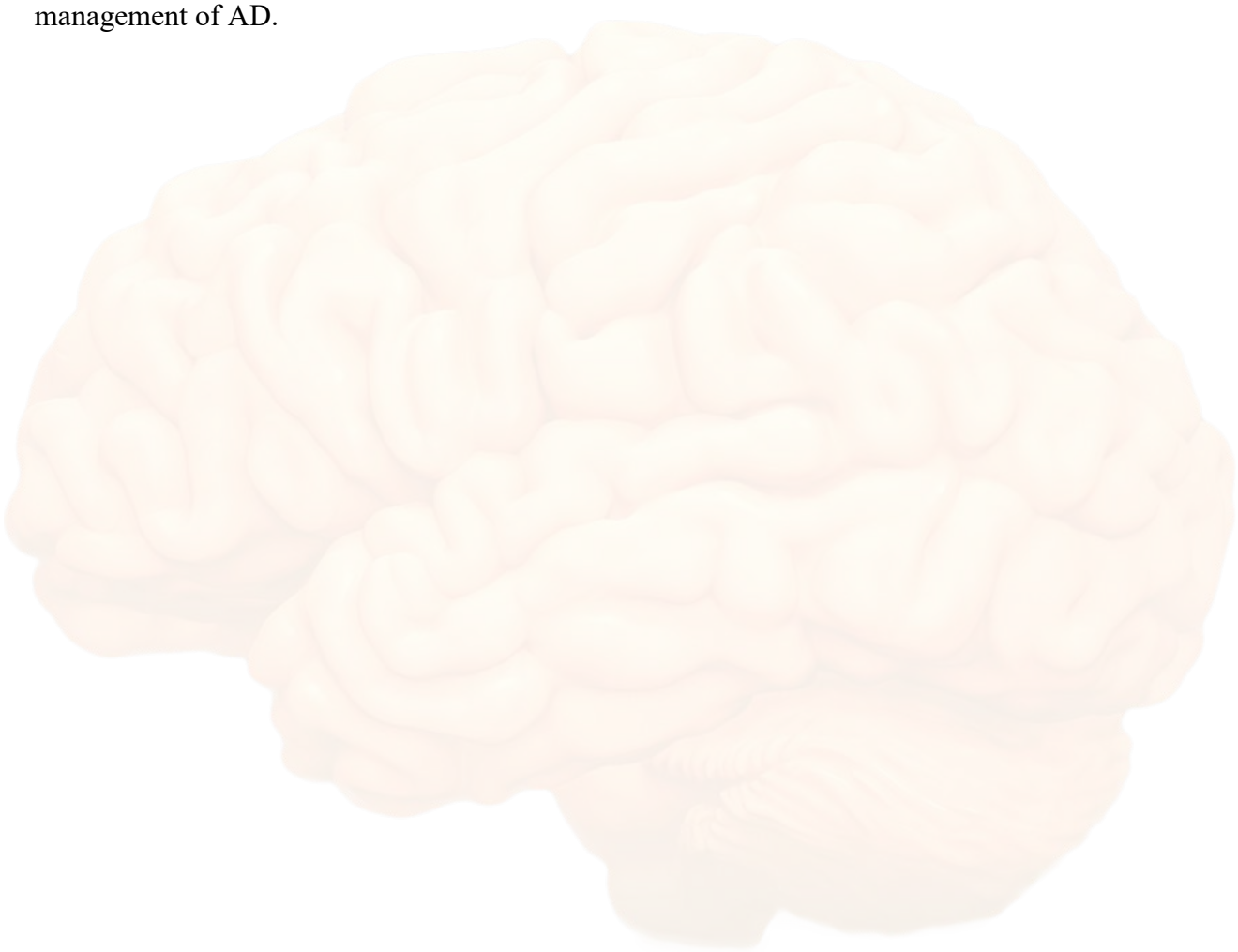
In the first objective, Ang(1-7) attenuated the Aβ-induced behavioral abnormalities in the cognitive deficit animals. Further, it significantly restored the level of expression of HO-1 in above brain regions of Aβ-challenged AD-like rats. Moreover, the Ang(1-7) ameliorated the Aβ-induced apoptosis and impaired mitochondrial function, integrity, and bioenergetics in all the rat brain regions. The Mas receptor antagonist, A779, abolished the therapeutic effectiveness of Ang(1-7) on Aβ-challenged cognitive deficit animals. These observations indicated the fact that Ang(1-7) could exert a therapeutic effect perhaps through the Mas-receptor-mediated mechanism in the animals.

In the next study, Trigonelline abolished the therapeutic effect of Ang(1-7) on the level of expression of HO-1 in memory-sensitive brain regions of Aβ-induced cognitive deficit animals. Further, Trigonelline abolished the Ang(1-7)-mediated attenuation of apoptosis and impairment in mitochondrial function, integrity, and bioenergetics in all selected rat brain regions.

In the last objective, Naringin facilitated the neuroprotective potential by decreasing the level of expression of HO-1 and MCU in all selected brain regions. Moreover, it also mitigated the Aβ-

induced mitochondrial calcium accumulation, function, integrity, and bioenergetics in all selected brain regions. Interestingly, Mas receptor antagonist, A778 also abolished the therapeutic activity of naringin in the Aβ-induced cognitive deficit animals.

In conclusion, the Ang(1-7)/Mas/Nrf2 mediated pathway could be a potential target to attenuate the Aβ-induced mitochondrial toxicity and thereby cognitive dysfunctions in the animals. Further, Naringin exhibited a significant therapeutic effect on Aβ-induced mitochondrial toxicity and thereby cognitive dysfunctions in the animals through Ang(1-7)/Mas/Nrf2-dependent mechanism. Hence, brain Ang(1-7)/Mas could be a potential therapeutic target in the management of AD.



Neurobehavioral Toxicity by Formulated Favipiravir and The Restorative Impact of Vitamin D Supplementation in Adult Zebrafish

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Abstract:

Background: Neurorestorative effects of Vitamin D supplementation may help reverse neuroendocrine deficits induced by COVID 19 therapy using combination of antivirals including favipiravir.
Purpose: To assess the effects of Vitamin D supplementation in Favipiravir-induced adverse drug effects seen as neuro psychological stress and altered neurobehavior in adult zebrafish model.
Methods: Fishes were exposed to three different sub-lethal concentrations of favipravir (High Dose: 60.54mg/l, Moderate Dose: 6.05mg/l, and Low Dose: 0.6mg/l; based on LC50: 600.54 mg/l) with or without concomitant Vitamin D exposure (3000IU/g). Acute exposure for 5 days was given and then exposure was ceased and the fishes were maintained for 10 days to study the long-term effects of the drug.
Results: High dose favipiravir treatment showed significant increase in oxidative stress parameters, upregulation of CRH, cortisol and TSHβ gene and reduced BDNF gene expression, serotonin levels and AChE activity. Exposure to favipiravir also caused gut dysbiosis thus altering the gut – brain axis. These changes led to the neurobehavior changes in the fishes and caused reduced locomotion, impaired memory function and anxiety and depression like state in the fishes. Concomitant Vitamin D supplementation with high dose favipravir significantly enhanced serotonin levels, decreased oxidative stress parameters, cortisol and CRH levels.

Conclusion: Favipiravir exposure in sublethal doses caused neurotoxicity in the zebrafish model and vitamin D showed supplementary effect by restoring homeostasis.

Effect of Spondias pinnata (SP) bark extract on the hippocampus in etoposide induced mucositis rat model: Histological findings

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Abstract:

Several regions of the brain are involved in processing of cognition but in particular, the hippocampus is essential in various memory functions. A number of chemotherapy drugs, either as monotherapy or combination regimen cause sustained long-term cognitive deficits. The mechanism causing cognitive impairment are thought to be peripheral toxic effects causing downstream structural and functional changes in the brain. Etoposide (EP), an anti-cancer drug, is used for the treatment of wide range of malignancies and one of its common side effect is mucositis. Hence, there is a need for the development of drugs which could minimise the side effects of chemotherapy. As plant products are gaining more importance since some time, it could be a safe and effective alternative. Spondias, is one among such plants belonging to the cashew family (Anacardiaceae). Plants of this genus comprises many species and is used in traditional medicine. Plants belonging to Spondias have antioxidant, anti-inflammatory, hepato-protective, anti-dementia effects. These properties of plant extract might minimise the side effects of chemotherapy and also help in preventing degenerative changes in the brain. Therefore, this study proposes to view the effect of Spondias pinnata (SP) bark extract on the neurodegenerative changes of hippocampus in etoposide induced mucositis rat model. In this study adult wistar rats were divided into 3 groups. Group 1: Normal control, Group 2: Mucositis model: Administered with single dose of Etoposide (45mg/Kg body weight) intra-peritoneally (i.p),Group 3: SP treatment group (EP+SP) – Etoposide administered initially (i.p)followed by 200mg/kg, body weight of the plant extract (per oral).Neuronal assay of the brain tissue, stained with Cresyl violet, of all three groups was done and the expression of neurons in the hippocampus and dentate gyrus was noted.

Histological findings of different regions of hippocampus regions showed that the mucositis induced animals had more degenerated neurons in comparison to that of normal control animals, whereas the treated group animals exhibited improvement in comparison to that of the EP induced group animals. From this result it can be concluded that the SP bark extract provides protection from degeneration of neurons in the hippocampus to certain extent, which can be confirmed by further studies with more samples and different dosages of the extract.

Lysosomal abnormalities and autophagic deficit contribute to the pathogenesis of infantile Batten disease

Goutam Chandra

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Abstract:

Infantile neuronal ceroid lipofuscinosis (INCL), also known as infantile Batten disease, is a devastating neurodegenerative lysosomal storage disease caused by inactivating mutations in the *CLN1* gene. *CLN1* encodes palmitoyl-protein thioesterase-1 (PPT1), a lysosomal enzyme that catalyzes the deacylation of S-palmitoylated proteins to facilitate their degradation and clearance by lysosomal hydrolases. Despite the discovery more than three decades ago that *CLN1* mutations causing PPT1-deficiency underlies INCL, the precise molecular mechanism(s) of pathogenesis has remained elusive. Our previous work on INCL patient cells and PPT1 knock-out (KO) mice demonstrated substantial lysosomal proteolytic defect involving mistargeting of vacuolar ATPase V0A1, elevation of lysosomal pH and cathepsin D processing deficit. Here we show that chronic lysosomal deficits in PPT1-KO cells cause permeabilization of lysosomal membrane, lysosome-autophagosome fusion defect and reduced autophagic flux. Since maintenance of neuronal autophagic function plays crucial role in intraneuronal proteostasis as well organelle quality control, deficient autophagy in PPT1-KO cells might be responsible for accumulation of lysosomal ceroids leading to INCL pathogenesis. Our findings signify the role of *CLN1*/PPT1 in autophagy and suggest that pharmacological up regulation of autophagy in PPT1-KO/INCL cells may have therapeutic value.

The Elucidation of the Role of 2-Aminoethoxydiphenyl Borate in Preventing Mitochondrial Dysfunctions in MPTP model of Parkinson 's Disease

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Abstract

Parkinson's Disease (PD) is the most common movement disorder and the second most common age-related neurodegenerative disorder after Alzheimer's disease. It affects more than ten million people worldwide. The disease usually begins in the fifth or sixth decade and frequency increases with advancing age. Mitochondrial dysfunction is closely linked to the pathophysiology of numerous neurodegenerative diseases, including PD. Despite numerous therapeutic advances related to PD, mitochondrial dysfunction-targeting strategies remain largely elusive. Transient receptor potential (TRP) channels have been shown to play a crucial role in the regulation of mitochondrial and neuronal functions in PD. This study investigated the effect of 2-aminoethoxydiphenyl borate (2-APB), a broad-spectrum TRP channels blocker, in the context of mitochondrial dysfunctions in Sprague Dawley rats with MPTP-induced PD.

Methods: 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) was administered to the male Sprague-Dawley rats by bilateral intranigral administration with the help of stereotaxic apparatus and assessment of behavioral and biochemical parameters were done. Using protein expression studies, its effects on behavioural deficits and mitochondrial biogenesis were also investigated in the midbrain and striatum of MPTP-lesioned rats.

Results: Bilateral intranigral administration of MPTP in rats induced PD as evident from significant decrease in motor and anxiety like behavior. It is also associated with the significant alterations in molecular (tyrosine hydroxylase) parameters. Two weeks of 2-APB treatment improved behavioral parameters while also increasing Complex-I activity and mitochondrial potential in isolated mitochondria from the midbrain and striatum. In addition, 2-APB treatment also increased the expression of tyrosine hydroxylase and proteins involved in mitochondrial biogenesis, including Peroxisome proliferator-activated receptor-gamma coactivator-1 alpha (PGC-1α) and mitochondrial transcription factor A (TFAM). Treatment with 2-APB inhibitors significantly ameliorated motor and cognitive deficits accompanied with improvement in biochemical and molecular parameters in the MPTP administered animals.

Conclusion: Thus, our findings indicate that 2-APB has a neuroprotective effect in the MPTP rat model of PD by targeting mitochondrial dysfunctions. The present study demonstrates the beneficial role of TRP inhibitor in PD rat model.

Acknowledgements: Authors are thankful to Department of Health Research, Government of India (Start UP grant No. R.12020/02/2017-HR) for the financial support. The authors declare that they have no competing interests.

α4-containing GABAA receptors: "Old" receptor as new target for drug-resistantepilepsy?

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Abstract

Background: $GABA_A$ receptor is heteropentamerid and - gated ion channel consisting of 2α, 2β, and a δ/γ subunit. Subunit composition and receptor stoichiometry $GABA_A$ receptors impact its biophysical and pharmacological properties $GABA_A$ receptors are acknowledged target for ant-I seizuredrugs like benzodiazepines (BZDs). BZDs bind at the interface of α-and γ- subunit of the $GABA_A$ receptors, with selectivity of BZD determined by the type of α subunit. α1-, α2-, α3-, and α5-containing $GABA_A$ receptors are sensitive, while α4-, and α6- containing $GABA_A$ receptors are insensitive to BZDs. We investigated subunit configuration of $GABA_A$ receptors in various drugresistant epilepsy (DRE) pathologic and its possible contribution to pharmaco- resistance.

Materials & Method: Cortical specimens were obtained from patients with various DRE pathologies like temporal lobe epilepsy, focal cortical dysplasia, Rasmussen's encephalitis, dysembryoplastic neuroepithelial tumor and ganglioglioma undergoing respective surgery. Differential gene and cellular expression of $GABA_A$ receptor subunits were evaluated using qPCR and immunohistochemistry. Wh-oclell patch-clamp recordings were performed on pyramidal neurons in slice preparations of cortical sample obtained from patients with DRE to measure the effect of BZD - binding site antagonist, flumazenil, on spontaneous GABAergic activity.

Results: We observed upregulation of α4-and γ2-containing $GABA_A$ receptors both t and mRNA and protein levels in DRE samples as compared to the non-seizure controls, whilelevels of other α-subunitsand δ subunit remain unaltered. Flumazenil did not affect the kinetics of GABAergic events in cortical samples of DRE pathologies, but significantly reduced the frequency and amplitude of GABAergic activity recorded from pyramidal neurons of non seizure control samples.

Discussion & Conclusions: Altered configuration of $GABA_A$ receptor subunits is known to contribute to a aberrant GABAergic activity associated with DRE pathologies. Our results suggest that α4-containing $GABA_A$ receptors may be predominant in patients with DRE, which could contribute to altered synaptic transmission and BZD resistance in these patients. Current $GABA_A$ receptor-targeting drugs have limited subunit selectivity, therefore there is a need to develop selective α4-containing $GABA_A$ receptor pharmaceuticals for DRE pathologies.

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RUNNING PACE ANALYSIS AND GRAPHICAL REPRESENTATION OF 1500- METER FEMALE MIDDLE DISTANCE RUNNERS

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Abstract

The 1500-meters middle distance running events are contested at all global athletics championships including India. The purpose of the paper is to analyze the pacing strategies of foreign elite female athlete and Indian female athlete in 1500-meter middle distance race. The study is to exhibit whether split 100 meter and 400 meter times of 1500-meter are varied in between foreign elite female athlete and Indian female athlete. Ten female leading foreign athletes are selected as foreign athletes from readily publically available data of the International Association of Athletic Federation (IAAF) World Athletics Championship 2017 and ten female Indian athletes are selected as Indian athletes from the Association of Indian Universities (AIU) All India Inter University Athletics Championship 2020.

The results section commences with assessing the velocity variations, speed variations of female 1500 meter runners. The research brings forth how the variations occurs among the Indian 1500 meter athletes of female population. The constant variation in their running pace, velocity of the Foreign athletes is exhibited in accordance with their distance parameter. The mean values of Foreign female athletes seem to be higher than the zonal mean values of running time of Indian athletes in 1500 meters.

Keywords: Pacing Strategies · Data Analysis · Middle Distance Runner · Zonal Velocity. Championship

Transcriptional and epigenetic mechanisms underlying social isolation stress in *Drosophila*

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Abstract

Social isolation is stressful and profoundly alters behaviors as observed globally during the lockdowns induced by the recent CoVID19 pandemic. Social isolation has been shown to disrupt multiple behaviors across animal kingdom including sleep, violence, feeding, mental health etc. Given the public health problem posed by social isolation it is important to understand responsible molecular mechanisms.

To approach this problem my group is using fruit fly Drosophila melanogaster as a model. Social isolation in Drosophila, similar to mammals, induces robust changes in behaviors including aggression and sleep. My earlier work has identified both whole brain and cell-type-specific transcriptional and epigenetic changes in Drosophila using cutting-edge genomic methods. Insights gained from these approaches were combined with high-throughput quantitative behavioral assays to identify causal mechanisms in the brain that shape these behaviors. By modulating group size and isolation length, we identified a graded response in aggressive behaviors. RNA-seq and subsequent behavioral assays revealed a neuropeptide Dsk whose modulation alters social isolation induced aggressive behavior. To identify cell-type specific changes due to social isolation we developed 'mini-INACT' method, which helped us purify ~100 dopaminergic neurons/brain (<0.1% of total neurons). This enabled identification of epigenetic signatures in dopaminergic neurons due to social isolation vs. enrichment.

Here, I will present our findings from optogenetic, and machine vision based behavioral assays which reveal how a neuropeptide regulates behavioral changes due to social isolation. I will also present our work on cell type specific epigenetic modulation that will help identify causal relationship between epigenetic changes and altered behaviors.

Keywords: Social isolation, aggression, epigenomics, dopamine, optogenetics.

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Localization of MHC-II expressing cells in the hippocampus of Aβ injected Alzheimer's rat model

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Abstract

Alzheimer's disease (AD) is a most common cause of elderly dementia. The disease is morphologically characterized by presence of intracellular neurofibrillary tangles and extracellular senile plaques in the brain regions primarily involved in memory function. Senile plaques are formed by deposition of amyloid beta (Aβ) peptides. Aβ injection in the hippocampus induces gliosis and inflammatory response. Expression of major histocompatibility complex type II (MHC -II)) is directly involved in antigen presentation and used as a marker for phagocytic microglia in the brain. Antigen presentation by type II MHC is dependent on interaction with T-cells which are infiltrated from blood circulation to the brain in injury and diseases. In AD brain, activated T cells are abundant and suggested to have auto-aggressive property. Use of active and passive vaccination against Aβ are very successful in animal models of AD and AD patients with a significant lowering Aβ load in the brain. However, the trial was stopped due to showing adverse serious side effects in few patients. It was thought that use of antibodies against Aβ caused over-activation of immune response and phagocytic activity. We have used OX-6 antibody to stain MHC-II expressing cells in the Aβ injected hippocampus to understand the persistent microglia associated immune response.

Materials and Methods: Three months old male Wistar rates were anesthetized and stereotaxic injection of Aβ (rPeptide, USA) was performed. Rats were allowed to survive for 30 days after recovery and then they were perfused trans-cardially with 4% paraformaldehyde in PBS. Fixed brain samples were processed for histology, 30µm thick sections were cut and immunohistochemistry was performed for MHC-II by incubating free floating sections with a primary monoclonal antibody OX-6. Sections were counterstained with 1.0% cresyl violet solution (Nissl's staining) and qualitatively analyzed using Ziess Axiophot research microscope**.**

Results and Discussion: The Aβ retained in the brain for one month and caused neuronal loss and an accumulation of MHC-II positive cells near injection site in the hippocampus. The MHC-II expressing microglia were also present in the other regions of the hippocampus such as hilus and CA3 however, there was no marked neuronal loss observed. Most of the activated microglia are associated with the pyramidal cell layer of CA3 region. In many cases, the dentate gyrus was completely collapsed near injection site and there was intensive accumulation of MHC-II positive amoeboid cells. MHC-II immunopositive microglia were amoeboid near granular layer of degenerating dentate gyrus however they were bushy and heterotrophic in CA3 region. Furthermore, CA2 and CA1 regions were devoid of microgliosis. In case of AD the functional importance of immune cells are more complex as their activation is needed to remove Aβ while phagocytosis may enhance degradation resistance of Aβ by converting it into more complex fibrils. Microglial activation is functionally complex as it may be neuroprotective and neurotoxic at a same time therefore, more attention must be given to the heterogeneity of microglial response in the brain for Aβ based therapeutic remedies.

Polymeric nanoparticles for mitochondrial targeting: *In vitro* assessment on mitochondriallocalization and toxicity in neuronal cells

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Abstract

Mitochondrial dysfunction is implicated in various human diseases including neurodegenerative, Huntington disease, etc. The currently available drugs for these diseases are symptomatic and suffer from severe side effects requiring its withdrawal, and change of the class of the drug. One of the causes could be undue higher dose of the drug, inefficient cellular internalization and inability to reach selective targets including the mitochondria. In order to achieve improved mitochondrial targeting, where mitochondria are a target of any drug, conjugation of drug to a lipophilic triphenylphosphonium cation (TPP) is employed. However, very high doses of the TPP-conjugated drugs required for therapeutic efficacy result in the accumulation of the highly cationic TPP in the mitochondria, thereby imparting toxicity. Attachment of TPP to nanocarriers such as liposomes and polymers is employed in order to reduce the amount of TPP required for drug targeting. But these nanocarriers have limited clinical utility due to their inherent cationic nature that leads to toxicityat higher concentrations. Hence there is a need to develop alternative and safer nanocarrier systems for improved drug targeting to the mitochondria with reduced toxicity. Here, we have developed a polymer-TPP nanoparticle based on a neutral dendritic polymer, hyperbranched polyglycerol and optimized them for physicochemical properties such as size, molecular weight, surface charge and TPP density. The nanoparticles were assessed for their cellular internalization, mitochondrial localization, effect on mitochondrial functions and toxicity, if any in SH-SY5Y neurons. We report here that optimization of the physicochemical properties of the nanoparticles is crucial for achieving mitochondrial targeting with reduced toxicity.

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Delayed cortical astrogliosis corelates with cognitive protection in a tauopathyenvironment following trauma in a cohort study

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Abstract

Tauopathy is a hallmark of a broad category of neurodegenerative conditions and Traumatic Brain Injury (TBI). Progression of tau pathology may lead to impaired cognitive conditions leading to dementia. However, previous studies have reported cognitively healthy patients with cortical tau pathologies. The mechanism for this cognitive protection in a tauopathy environment is being investigated by various groups. Astrocytes are essential for physiological homeostasis of brain and reactive astrogliosis is an associated pathology in neuroinflammation associated with TBI. The corelation between levels of cortical astrogliosisand dementia status of TBI patients at similar tau pathology staging is an unanswered problem. In our investigation we addressed this question by studying hippocampal and parietalcortex tissues from a subset of open access ACT study patient dataset. In our investigation, the cohort was grouped according to the tauopathy status based on Braak staging analysis and dementia status following trauma. We analysed the astrogliosis and microgliosis using GFAP and IBA1 as marker, respectively. Our work identified a significantly lower level of astrogliosis in cohort with early tauopathies and no associated dementia. This was missing inlate stage tauopathies with no dementia and also with microgliosis. In summary, our analysis hints towards a possible protective role of reduced astrogliosis in dementia associated with tauopathies following TBI.

Caveolin-1 Regulates Excitotoxic Signaling in Hippocampal Neurons

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Abstract

Background: Excitotoxicity is known to associate with neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, Huntington's disease, as well as aging, stroke, trauma, ischemia and epilepsy. Caveolins are a group of cholesterol binding scaffolding proteins associates with lipid rafts. The caveolin family consists of Caveolin-1, 2 and 3, Cav-1 & 2 are expressed in almost all cell types including neurons, whereas Cav-3 is muscle specific. Cav-1 known to associates with synaptic proteins SNAP-25, PSD-95, Gαs, PLA2, AC, nNOS, iNOS, L-type calcium channel, VDAC, modulates ERα, 5-HT2A, and Dopamine (D1) receptors. Loss of Cav-1 is reported in Alzheimer's disease, aging, cancers, Huntington's disease, schizophrenia and cerebral ischemia. Cav-1 over expression suggested to increase dendritic arborization, neurite sprouting and reactive synaptogenesis. However, the role of Cav-1 in excitotoxic neuronal death is not elucidated.

Objective: To investigate the effect of Cav-1expression on excitotoxic signaling in hippocampal neurons.

Methods: We have assessed intracellular calcium $[Ca^{2+}]i$, mitochondrial membrane potential, Reactive Oxygen Species (ROS), using live cell fluorescence imaging in 13-15 day *in-vitro* hippocampal neurons. Primary rat neuronal cultures were prepared from postnatal day 0 Wistar rat pups.

Results: Cav-1 knockdown (Cav-1KD) increases mitochondrial depolarization, ROS formation intracellular calcium influx along with sustained secondary calcium response, whereas the Cav-1 over-expressors (Cav-1OE) displayed fast intracellular calcium buffering, decrease in mitochondrial depolarization and ROS generation. Cav-1 affects both NMDA and Non-NMDA receptor mediated Ca^{2+} influx and irreversible secondary calcium response. Immunostaining results suggest Cav-1 co-localizes with NMDA and AMPA. CO-IP results suggest that Cav-1 associates with glutamate receptor and synaptic proteins. Apart from this, Cav-1 OE inhibits *in-vitro* epileptiform calcium oscillations.

Conclusion: Overall our data demonstrates that Cav-1 regulates excitotoxic neuronal signaling by modulating ionotropic glutamate receptors.

Ethics: Approved by NIMHANS IAEC. **Funding:** CRG-SERB-DST for YSM, UGC fellowship for SKK. **Conflict of interest**: None



ORAL AWARD SESSIONS



Compulsive like behaviours in Aβ 1-42 induced Alzheimer's disease in mice areassociated with hippocampo-cortical neural circuit dysfunction

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Abstract

Besides memory deficits, patients with Alzheimer's disease (AD) experience neuropsychiatric disturbances as well. Recent studies have suggested the association of obsessive compulsive disorder (OCD) with the early stages of AD. However, there is a lack of understanding of the neurobiological underpinnings of compulsive like behaviours and their relationship with AD. We have addressed this issue in Aβ 1-42 induced mouse model for AD and studied compulsive like behaviours. Here, our findings show that AD mice exhibit compulsive like behaviours as evidenced by the enhanced marble burying, nest building and burrowing behaviours. In addition, AD mice displayed depression like behaviour and reduced novelty-seeking behaviour, two comorbid behavioural states that are often accompanied by OCD. Further, AD mice exhibited hippocampo-cortical circuit dysfunction, demonstrated by decreased power of rhythmic oscillations at the theta (4-12Hz) and gamma frequency (25-50Hz) in the hippocampus and the medial prefrontal cortex (mPFC), two functionally interconnected brain regions involved in compulsive behaviors. Importantly, coherence between the hippocampus and mPFC in the theta band of AD animals was significantly reduced. Furthermore, we found reduced cholinergic and glutamatergic neurotransmission in the hippocampus and mPFC of AD mice. We conclude that the hippocampo-cortical functional alterations may play a significant role in mediating thecompulsive like behaviours observed in AD mice. These findings may help in understanding the underlying circuitry mechanisms of OCD like phenotypes associated with AD.

Keywords: Alzheimer's disease, Compulsive behaviors, Hippocampo-cortical neuralcircuit, Theta coherence, Neurotransmitters

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SARS-CoV-2 mediated neuronal loss: Deciphering the mechanisms

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Abstract

Globally, COVID-19 presents a diverse disease profile, including mild, moderate and severe manifestations reported in 30-60% of Long COVID-19 patients. Neurons undergo significant death in experimental systems such as neuronal cultures, brain organoids, as well as in COVID-19 patient brain autopsies. While the direct viral invasion of the brain is debatable, multiple lines of evidence suggest both direct and indirect neuronal injury and death in COVID-19 patients. No study has yet explored the molecular mechanisms involved in neuronal loss in physiologically relevant models.

In this work, we have screened 29 SARS-CoV-2 proteins for cell death andhave identified Orf6 and Nsp2 as the proteins causing maximum death in primary neurons. Further, we have identified necroptosis as the predominant molecular pathway that is induced in primary human neurons derived from the fetal neural progenitor cells. These findings were replicated in neurons treated with the whole SARS-CoV-2 virus, and later validated in post-mortem brain tissue sections from COVID-19 patients, using histological staining techniques. We found these SARS-CoV-2 proteins interact with specific mitochondrial proteins, leading to significant mitochondrial dysfunction in infected cells, resulting in alterations in fission/fusion machinery, mitochondrial membrane potential, mitochondrial reactive oxygen species. In summary, our work uncovers previously unknown mechanisms by which neuronal death occurs in COVID-19 patients. We are currently exploring the pharmacological modulation of these cells using molecules for therapeutic intervention.

Work was supported by NBRC core funds.

Deep brain stimulation of LH-MFB ameliorates depression byreversing the neuropathology in dorsal raphe nuclei-medial prefrontal cortex serotonergic circuit

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Abstract

Background: The dysfunction in dorsal raphe nucleus (DRN)-medial prefrontal cortex (mPFC) serotonergic circuit is a major causal factor for the cognitive deficit attributed to depressive state. Despite the fact that pharmacological medications are widely used to treat the condition, some people do not respond and are considered to have treatment-resistant depression (TRD). Deep brain stimulation (DBS) targeted at lateral hypothalamus-medial forebrain bundle (LH-MFB) shows a promising antidepressant effects in TRD patients; however, the underlying molecular mechanism is enigmatic.

Aim and Objective: To understand the molecular mechanisms of DBS of LH-MFB responsible for the antidepressant effect in chronic unpredictable mild stress (CUMS) induced depressed rats.

Methods: The depression was induced by applying 42 days different chronic unpredictable mild stressors to adult male Wistar rats. The CUMS induced depressed rats were subjected to DBS via an electrode implanted in the right LH-MFB for 4 h/day for 14 days. Rats were then assessed for anhedonia, behavioral despair, locomotor counts, memory deficit, change in body weight, corticosterone blood levels, dendritic arborization of mPFC neurons, and 5-HT and 5- HIAA level in the mPFC.

Results: DBS targeted at LH-MFB reversed anhedonia, behavioral despair, reduced body weight, memory deficit, decreased level of corticosterone in blood and the level of 5-HT and 5-HIAA in mPFC of CUMS rats. DBS also arrests the degeneration of serotonergic cells in the DRN and decreased mPFC dendritic branching in CUMS rats.

Conclusion: The DBS of LH-MFB restored the CUMS-induced neuropathology in DRN-PFC serotonergic circuit and reversed cognitive deficit associated with depressive state.

Impact of iron overload on mitochondrial dynamics, autophagy, and ferroptosis in agingretinal photoreceptor cells

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Abstract

Iron is essential for proper retinal functioning but excessive iron is toxic and causes diseases, such as age-related macular degeneration. We aimed to establish the impact of long-term iron administration on mitochondrial dynamics, autophagy and cell death in rat retina through aging. To achieve this, male Wistar rats were grouped into 4-month control (baseline control), 8-month control, 8-month experimental, 12-month control and 12-month experimental groups. After initial determination of safety dose, rats were administered orally with ferrous sulphate (500 mg/kg body weight/week) from 4 months of age onwards until 12 months of age, the control rats received water as a vehicle. They were sacrificed at 4, 8, and 12 months of age. Retinal levels of iron and lipid peroxidation product, mitochondrial fission-fusion events, signs of autophagy and ferroptosis in photoreceptor cells were assessed. The retinal iron levels and lipid peroxidation were significantly increased in 8-month (370µM and 3.66 nmol/g protein, $p<0.001$) and 12-month iron-fed rats (540µM and 6.30 nmol/g protein, $p<0.001$) respectively. TEM revealed degenerated mitochondria and ongoing mitochondrial fission in 8- and 12-month experimental rats in comparison to normal photoreceptor mitochondria in control rats. Increased expression of Drp-1 (fission) and Mnf-2 (fusion) depicted an imbalance in mitochondrial dynamics, although there was no correlation with parkin and PINK 1 expressions. Compared to that in age-matched controls, the presence of autophagosomes with disorganized mitochondria in parallel to increased LC3B and decreased p62 expressions in experimental rats suggests autophagy initiation. The decrease in the expression of glutathione, glutathione peroxidase-4, and mitochondrial ferritin in experimental rats led to redox imbalance, triggering photoreceptor cell death (17% to 45%; $p<0.005$) by ferroptosis in 12-month experimental rats. This study concludes that iron overload causes an imbalance in mitochondrial dynamics, induces parkin and PINK 1-independent mitophagy and triggers photoreceptor death by ferroptosis.

Saccades in young adults with autism spectrum disorder (ASD) and attention deficient hyperactivity (ADHD) traits: Indications of reduced social preference in ASD

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Abstract

Neurodevelopmental disorders ASD and ADHD manifest overlapping behavioral symptoms. When ASD probands show deficits in social communication and repetitive behavior, ADHD phenotypes are inattention, impulsivity, and hyperactivity. During the early stages of development, differential diagnosis of ADHD and ASD is complicated. Although these disorders share atypicality in communication and attention, both show distinct differences in their response to social stimulation. Based on this information, we hypothesize that social and non-social visual stimuli elicit unique responses in ASD and ADHD. Therefore, the present study investigated the utility of gaze behavior tracking in response to social and non-social visual signals. We screened young adults from the general population in Kerala using an online self-assessment questionnaire (SAQ) for ASD and ADHD. Based on the scores of the autism spectrum quotient (AQ) and adult ADHD self-report scale (ASRS) included in the SAQ, we categorized the young adults into typically developing (TD) controls and with ASD/ADHD traits. We subjected them to a preferential-viewing task on social/non-social signals and recorded their gaze behavior while they freely viewed simultaneous presentation of 30 pairs of images. A scrambled version of these stimuli was used to control the impact of low-level visual features. The AQ scores that followed a Gaussian distribution were classified into Groups I-III. Group I and III are the two extreme ends of the Gaussian Curve, with the lowest and highest AQ scores respectively. The five social attention and communication sub-phenotypes of AQ showed significant changes between Groups I and III. Additionally, the eye tracking data revealed that the proportion of gaze duration towards social image to total viewing time on social, non-social, and blank spaces together showed a significant decrease in Group III compared to Group I. For the screening of ADHD traits, we used the ASRS scores; 3 and below are taken as TD controls, scores 4 and above indicated ADHD traits. Unlike the young adults with ASD, ADHD traits did not show any preferential viewing of social, non-social, and blank areas. However, the percentage of trials omitted due to track loss significantly increased in adults with ADHD. However, the percentage omission was insignificant among Group III with ASD traits. The preliminary results indicated that the young adults with ASD have lesser social visual attention and awareness than ADHD subjects, which could be developed into a potential biomarker for ASD once validated in a

greater sample size. The higher level of track loss in ADHD indicated impulsivity, inattention, and hyperactivity. In brief, our results suggested eye tracking analysis to be an efficient tool to decipher the bias toward social attention and preferences; and could be used for differential diagnosis of ASD and ADHD.

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Resting EEG microstate as a state marker in children with attention deficit hyperactivity disorder.

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Abstract

Background and rationale: Studying resting-state large-scale brain dynamics, depicted in the form of functional EEG brain microstates, can be a useful tool to characterize neurodevelopmental disorder such as Attention deficit hyperactive disorder. We investigated whether resting state EEG microstate alterations and their neural generators could be used as a novel approach to capture large-scale cortical dynamics in ADHD compared to neurotypical controls.

Method: Thirty-five ADHD (12.3±2.7 yrs.; 30:5 (Male: Female)) and thirty-five age matched neurotypical controls (12.9±3.5 yrs.; 23:12 (Male: Female)) participated in the study. 128 channel electroencephalography was acquired during three-minute eyes open state. Artifactually clean data was then subjected to microstate analysis in Cartool software to determine best map representative for both groups based on meta-criterion. Further, map parameters (frequency of occurrence, global explained variance (GEV), mean duration, and time coverage) for each microstate map were ascertained between the groups which were then compared using one sample t-test. Intracranial generators of each map were found using sLORETA software and statistical non-parametric mapping comparisons were done between the groups.

Results: Microstate analysis using k-means clustering revealed four dominant maps (Map1-Map4) which explained 79.73% of the total variance. Significant differences were seen in temporal parameters of Map3 between both the groups. Map 3 exhibit occipito-central topography which resemble Map F reported in literature that play role in saliency network and acts as switch between DMN and executive areas.

As compared to typically developing controls, longer mean duration (28.92±2.6 vs 26±3.2 ms), higher number of time frames (4484 ±1234 vs 3761± 1632) and time coverage (18.28% ± 4.6 vs 13.94% ± 6.03) was seen in children with ADHD. The intracranial generators of Map 3 using sLORETA revealed significantly higher cortical activity in parietal, temporal and occipital cortices which form a part of central executive network and saliency network.

Discussion: Map 3 emerged out to be a state marker in the current study which could distinguish ADHD from neurotypical controls in terms of its temporal parameters. The cortical sources show higher cortical activation in post central gyrus (primary somatosensory cortex), middle temporal gyrus (that subserve language and semantic memory processing, visual perception, and multimodal sensory integration), superior temporal gyrus (involved in auditory processing, including language also a critical structure in social cognition), middle occipital (object recognition) and inferior occipital (processing of faces) gyrus, lingual gyrus (identification and recognition of words),

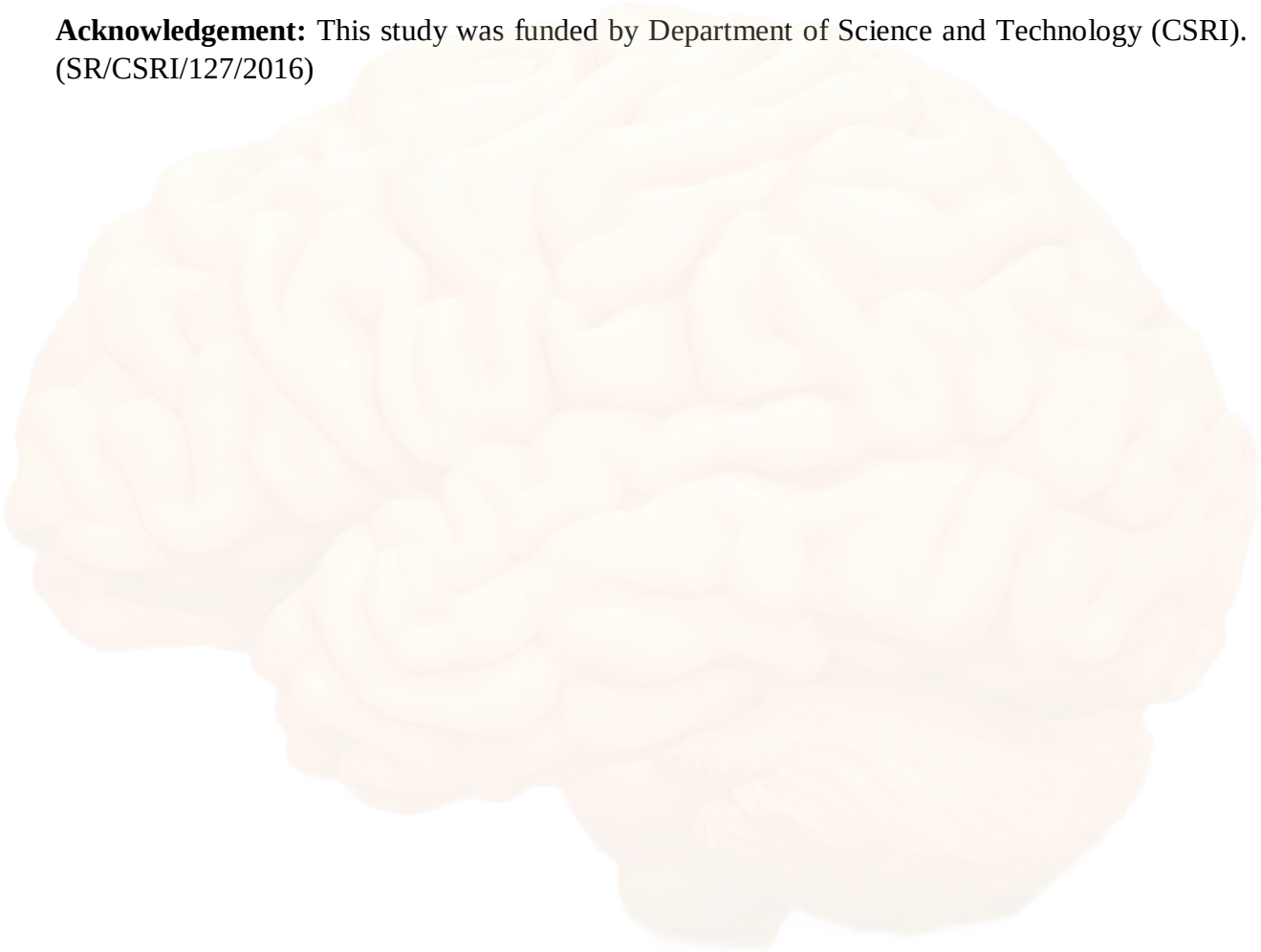
fusiform gyrus (face perception, object recognition and reading) and cuneus (visual processing and default mode network).

The results of the present study are in line with the available literature and indicate towards structural differences in ADHD that could probably indicate towards the pathology of ADHD and may be related to inattentive and hyperactive symptoms.

Conclusion: Resting EEG microstate can elucidate reliable features to distinguish ADHD from neurotypical controls, thereby serving as a promising state marker for ADHD.

Ethics statement: This study was approved by the institute ethical committee of AIIMS Ref No. IEC-582/05.01.2017, RP-11/2017

Acknowledgement: This study was funded by Department of Science and Technology (CSRI). (SR/CSRI/127/2016)



Transient receptor potential vanilloid 2 (TRPV2) in the rat brain: role in modulation of the nigrostriatal dopaminergic pathway

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Abstract

TRPV-subfamily of cationic channels are abundantly expressed in the brain and emerged as novel regulators of neuronal function and behaviour. Among the thermosensitive TRPVs, TRPV2 is activated beyond noxious threshold temperature, expressed in the brain, but its significance in neural regulation is poorly understood. The midbrain dopamine (DA)-ergic neurons in rodents are thermosensitive and in a pilot study on rats, we observed TRPV2 neurons in the substantia nigra pars compacta (SNc). We have therefore hypothesized that TRPV2 in SNc regulate nigrostriatal DA-ergic pathway. Immunofluorescence using anti-TRPV2 specific antisera on the rat brain sections showed TRPV2-ir neurons widely distributed in the brain. We observed TRPV2-mRNA expression in midbrain tissue, and TRPV2-ir neurons in the ventral tegmental area (VTA) and SNc. While TH neurons in VTA as well as SNc co-expressed TRPV2, SNc TH neurons were more TRPV2 enriched than those in VTA. Retrograde neuronal tracer iontophoresed in the dorsal striatum accumulated in TH/TRPV2 SNc neurons. Intra-SNc TRPV2-agonist, Probenecid increased DA release in dorsal striatum and locomotor activity, whereas prior intra-dorsal striatal administration of DA-D2 receptor antagonist reduced Probenecid-induced response. In *ex vivo* midbrain slice superfusion, compared to control, Probenecid treatment increased TH-ir in SNc neurons. Parkinson (PD)-like condition was induced by 6-Hydroxy dopamine (6-OHDA, intra-SNc). Compared to controls, intraperitoneal (i.p.) apomorphine injection produced contralateral rotations in 6-OHDA-treated rats. Intra-SNc Probenecid prior to apomorphine injection further enhanced contralateral movements in PD-like condition. The results suggest that the widely expressed TRPV2 in brain regions regulate a range of physiological functions.

TRPV2 in SNc may serve as novel regulator of nigrostriatal DAergic pathway and a potential drug target for Parkinson’s disease.

Nootropic effects of Curcumin: Modulation of synaptic plasticity genes in amnesic micemodel

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Abstract

Rationale: Curcumin [(1E,6E)-1,7-bis (4-hydroxy- 3-methoxyphenyl) -1,6- heptadiene-3,5-dione] is a naturally occurring phytochemical, obtained from the rhizome of the plant *Curcuma longa* (turmeric). This yellow-coloured compound is used in Ayurvedic medicine, generally for inflammation-related disorders. Recently, lab studies on rodents have shown its effectiveness against cognitive dysfunctions. However, there are no clear reports on the molecular mechanisms elicited by curcumin against neurological disorders, particularly amnesia or memory loss.

Hypothesis: As the process of memory is an interplay of different synaptic plasticity genes, we hypothesize that the curcumin modulates the expression of **particular** synaptic plasticity genes in **specific** brain regions of amnesic mice to reverse the memory loss.

Objective: To prove this hypothesis, we have analyzed the effect of curcumin treatment on cognition as well as the expression of synaptic plasticity genes (Arc, FMRP, c-fos and zif-268) in the hippocampus and prefrontal cortex of scopolamine-induced amnesic mice.

Methodology: 24 Swiss albino male mice were randomly divided into control, amnesic, pre- and post-treated with curcumin amnesic mice groups. A standardized dose of saline, scopolamine hydrobromide and/or curcumin was administered intraperitoneally to all mice for a week. Their spatial memory was assessed daily using the Morris Water Maze test. On the 7th day, their hippocampus and prefrontal cortex were isolated to check the synaptic plasticity gene's mRNA level (through real-time PCR) and protein level (through Western blotting).

Results: We observed a significant downregulation of synaptic plasticity genes (Arc, FMRP and c-fos) during scopolamine-induced amnesia, which gets reversed by the pre- and post-treatment of curcumin in both the brain regions. Interestingly, synaptic plasticity gene expression showed better recovery in the hippocampus than the prefrontal cortex, and the pre-treatment with curcumin was more effective than the post-treatment.

Significance of the study: Our study reveals a molecular pattern of how curcumin ameliorates amnesia. However, additional research on upstream signalling pathways can support the extract's medicinal use in memory problems.

Cortical Transcranial Magnetic Stimulation a Promising Biomarker and therapeutic modality to induce Synaptic Plasticity in Cerebral Palsy Children with Single and Paired Pulses Paradigm

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Abstract

Background: Infantile Cerebral Palsy(CP) is the most common neuro congenital disorder caused by the injury in the immature fragile developing brain usually before birth or due to perinatal stroke, resulting in impairment of motor function, cognition, communication and sensory perception. As the brain is plastic in nature, it has innate capacity to adapt to altered activity. Thus neuromodulating strategies like rTMS, can be used to investigate the coherence of the fast-conducting corticomotor pathways and induce recovery in CP patients. The aim of the present study is to understand the effect of low frequency repetitive transcranial magnetic stimulation on cortical excitability and plasticity in infantile hemiplegic cerebral palsy patients.

Method: Infantile hemiplegic cerebral Palsy patients were recruited from Pediatric Neurology, OPD AIIMS Delhi and consent for the study was taken. Low frequency rTMS was administered at primary motor cortex for 4 weeks in 10 sessions, following which QUEST scoring was done to assess sensory and motor function, Modified spasticity score (MAS) assessed extent of spasticity. Cortical excitability and plasticity was recorded using single and paired pulse paradigms of TMS.

Result: After 10 sessions of intervention there was a significant increase in QUEST score, CP-Quality of life Child score, grip strength and decrease in MAS Score in the Active rTMS group as compared to Sham. Single pulse paradigm revealed significant decrease in resting and active motor threshold as well as reduction in short and long intracortical inhibition in intervention group of patients.

Conclusion: Our findings suggest therapeutic potential of rTMS in alleviating symptoms of patients with neurodevelopmental disorders like Cerebral Palsy (CP).

SIRT3 activation normalizes neuronal derangements by restoring mitochondrial integrity in hippocampus of the moderate grade hepatic encephalopathy rats

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Abstract

Sirtuins are a class of NAD^+ dependent class III histone deacetylases involved in regulating critical cell functions mainly by deacetylating a number of non-histone proteins. Out of many homologues, the mitochondrial SIRT3 is considered as the master regulator of mitochondrial bioenergetics, cytoplasmic- mitochondrial metabolite trafficking and mitochondrial structure-function integrity in health and diseases. Involvement of SIRT3 in various neurological and age-related disorder is an evolving concept as most of the neurodegenerative events either converge at or diverge from mitochondrial dysfunction.

The moderate grade hepatic encephalopathy (MoHE) is a neuropsychiatric brain disorder developed due to persistent hyperammonemia led elevated extracellular glutamate leading into NMDAR overactivation led excitotoxic neuronal damage. The present study was undertaken in the hippocampus of the neurobehavioral characterized MoHE rats, developed by administration of 100 mg/kg bw of thioacetamide
i.p. for 10 days. Experiments were performed in control, the MoHE and the MoHE rats post treated with honokiol (HKL) 10 mg/Kg b.w. for 7 days. The results suggested that HKL could recover the MoHE associated declined expression and activity of SIRT3 in hippocampus. Also, as compared to the control rats, the MoHE associated compromised mitochondrial bioenergetics could be normalized back due to the HKL treatment. This was consistent with the restoration of neuroprotective NR2A dominated NMDAR composition from a neurodegenerative NR2B dominated receptor combination seen in the hippocampus of the MoHE rats. At mechanistic level, SIRT3 activation could also restore MoHE associated deranged Ca^{2+} influx, mPTP and ROS load thereby inhibiting apoptosis. Concordantly, SIRT3 activation upregulated the levels of mitochondrial integrity regulators, PGC1α & Foxo3a, and could also deacetylate its immediate target Mn-SOD in the hippocampus of MoHE rats. As end point assay, the neuroarchitectural parameters of the CA1 pyramidal neurons; the MoHE associated declined dendritic length and arborization vis a vis neurobehavioral deficit could also be normalized back due to SIRT3 activation. The findings suggest SIRT3 as a potential therapeutic target for managing mitochondrial dysfunction led neurodegeneration.

Ethical Statement: The animal-based study plan was approved by the institutional animal ethical committee (IAEC) of Banaras Hindu University, for the care and use of Laboratory animals.

Acknowledgement: This work was financially supported by a DST project to SKT and award of CSIR-SRF to Anamika.

Conflict of interest: The authors declare no conflict of interest.

A proteomic approach to investigate unmasking of neurotoxicity in rechallenged adult ratsprenatally exposed to lindane

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Abstract

Lindane is a broad-spectrum organochlorine pesticide and well known neurotoxicant. A proteomic approach using nLC-HRMS and 2D gel electrophoresis was used to investigate responsiveness of proteins related to various neuronal functions and neurodegeneration in brain regions [Substantia Nigra (SNi) and Hippocampus (Hi)] of rat offspring prenatally exposed to lindane (orally; 0.25 mg/kg) from gestation day 5 (GD5) to GD21 and subsequently rechallanged with lindane (orally; 2.5mg/kg for 21 days) at adulthood (12 weeks). Proteomic data revealed significantly greater magnitude of alterations in the expression of proteins related to synaptogenesis, synaptic structure and function, neurotransmission, myelination, cytoskeleton and calcium binding in brain regions of rechallenged rats when compared to age matched controls or rats prenatally exposed to lindane or control offspring treated postnatally to lindane. Further, a much higher magnitude of downregulation in expression of protein related to mitochondrial and energy metabolism, ubiquitin proteosome pathway (UPP) and chaperons in rechallanged offspring indicated increased oxidative stress in rechallanged offspring. This increased oxidative stress was further demonstrated by relatively higher magnitude of alterations in antioxidant enzymes and lipid peroxidation in Hi and SNi isolated from rechallanged offspring. Higher magnitude of alteration in expression of proteins related to apoptosis (cyto C), necrosis (RIP3 and RIPK1) and marker proteins of Alzheimer's disease and Parkinson's disease in the Hi and SNi of rechallenged offspring also revealed trigger of cell death processes and neurodegeneration. Ultrastructural analysis of brain regions demonstrating disrupted mitochondrial integrity, synaptic and myelin structures along with greater magnitude of alterations in neurobehavioral learning-memory and motor parameters in rechallanged rats were found in support of proteomic data. In conclusion, the present data suggests that prenatal low dose exposure of lindane induces persistent silent changes in the nervous system of offspring with no overt sign of toxicity which are unmasked leading to massive molecular damage and neurodegeneration following rechallenge at adulthood.

Key words: neurotoxicity, rechallange, lindane, unmaking
Competing interest: The authors have no conflicts of interest.
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Corresponding author: Ankita Srivastava

Interferon-Induced Tetratricopeptide Repeat Protein (Ifit2) Ifit2 restricts murine Coronavirus spread and demyelination in the spinal cord

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Presenting author: Madhav Sharma

Abstract

Background and rationale: The interferon-induced tetratricopeptide repeat protein (Ifit2) protects mice from lethal neurotropic viruses. Neurotropic coronavirus MHV-RSA59 infection of Ifit2$^{-/-}$ mice caused pronounced morbidity and mortality accompanied by rampant virus replication and spread throughout the brain. In spite of the higher virus load, induction of many cytokines and chemokines in the brains of infected Ifit2$^{-/-}$ mice were similar to that in wild-type mice. In contrast, infected Ifit2$^{-/-}$ mice revealed significantly impaired microglial activation as well as reduced recruitment of NK1.1 T cells and CD4 T cells to the brain, possibly contributing to the lack of viral clearance. These two deficiencies were associated with a lower level of microglial expression of CX3CR1, the receptor of the CX3CL1 (Fractalkine) chemokine, which plays a critical role in both microglial activation and leukocyte recruitment.

Methods: Ifit2$^{-/-}$ and Ifit2$^{+/+}$ (WT) mice were intracranially inoculated with RSA59. Mice were observed for neuropathogenic outcomes at day 5 -8 post-infection (acute inflammation) and day 30 p.i. (chronic inflammation).

Results: Ifit2 deficiency causes professed viral spread throughout the spinal cord without respecting the gray and white matter distribution with significantly impaired CD4$^+$ T cell infiltration upon RSA59 infection. CLN of RSA59 infected Ifit2$^{-/-}$ mice showed reduced activationand priming of CD4$^+$ T cells along with reduced IFNγ expression at the acute phase of neuroinflammation. This reduced leukocyte infiltration could also be ascribed to the reduced BBB permeability in Ifit2 deficiency as evidenced via intact, tight junction protein ZO-1 expression surrounding the meninges and blood vessels and decreased Texas red dye uptake. Furthermore, Ifit2 deficiency induces severe demyelination at the chronic phase of neuroinflammation even at asignificantly lower dose of 500 PFUs.

Conclusion: Ifit2 is required for efficient T cell priming in the CLN and also protects mice from developing severe chronic demyelination.

Ethics statement: All studies were carried out in strict accordance with all provisions of the Animal Welfare Act, the Guide for the Care and Use of Laboratory Animals, and the PHS Policy on Human Care and Use of Laboratory Animals. All animal experiments were performed in compliance with protocols approved by the Cleveland Clinic Institutional Animal Care and Use Committee (PHS assurance number A3047-01).

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Word count- Background+Methods+Results+Conclusion:131+27+112+20=290 words

Is there any relationship between temperament of an infant and social attentional network development within 1st year of life? – A longitudinal study.

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Funded by Horizon 2020, Marie Sklodoswka Curie Innovative Training Networks- project SAPIENS, European Commission.

Abstract

The role of individual differences in attentional efficiency and its contribution in the development of successful self-regulation (Posner & Rothbart, 1998, 2000, 2007; Rueda, Posner, & Rothbart, 2004) has been a widely explored research domain.It has established a close relationship between attention regulation and temperament along development (Reuda, Rothbart and Rothbart, 2011). Temperament refers to intrinsic individual differences in emotional, motor, and attentional reactivity in conjunction with the self-regulatory processes that modulate such reactivity, which are observable from birth (Rothbart and Bates,2006). Reactivity is classified along a negative/avoidant (i.e. negative affectivity, NA) and a positive/approaching (i.e. surgency, SUR) axis, whereas regulation has been linked to executive attention (Rothbart and Bates, 2006). The general trend shows that higher temperamental reactivity and poorer self-regulation are associated with deficits in attention control (Compton,2000). Different temperamental profiles have been linked to differences in children's executive attention.Prefrontal structures associated with the control of attention (e.g., ACC, DLPFC, or VLPC) modulate the activation of limbic structures (essentially amygdala, hippocampus, and nucleus accumbens), so that the interaction among these neural circuits is proposed to explain individual variability in temperament (Rohr et al., 2015; Whittle et al.,2006). Overall, these studies suggest that temperamental measures can in fact be a predictor of later executive attention skills (Ursache et al., 2013).
In the current study, we tried to explore how individual temperamental measures at infancy within 1st year of life relate to oscillatory features of brain electrophysiological activity in specific channel groups associated with attentional networks. A longitudinal study was designed to investigate parent reported measures of Infant Behavior Questionnaire-Revised (IBQ-R) data from 51 typically developing infants (m=28, f=23) recruited at 5 months and 11 months of age and relate it to the EEG (64 channel) power spectral measures obtained at 11 months of age while looking at dynamic faces and dynamic objects on screen. The results show a negative correlation between IBQ-R surgency scores with power spectral measures of beta (r=-.278,p=.049), lower gamma(r=-.277,p=.049), upper gamma (r=-.335,p=.016) in frontal and beta (r=-.378,p=0.006), lower gamma (r=-.314,p=.025), upper gamma (r=-310,p=0.027) in central channels during dynamic object viewing and negative correlation between IBQ-R surgency scores with power spectral measures of beta (r=-.295,p=0.036)in central electrodes and upper gamma (r=-.283,p=.044)

in frontal electrodes during dynamic faces viewing. Thus, characteristic involvement of beta and gamma frequency in frontal and central electrodes indicate the possible relation of surgency measures of temperament with attentional control mechanism across varying conditions of social attentional demand.

L-Arginine induced chronic visceral pain in mice

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Abstract

Background: Chronic pain is defined as that which lasts for more than three months after the resolution of the causative injury. Chronic pancreatitis (CP) is a common cause of chronic visceral pain and the abdominal pain is one of its most upsetting symptoms. Its pathogenesis is poorly understood. Studies based on magnetic resonance imaging have reported that there is structural reorganization in the brain areas involved in visceral pain processing. Here, we used repetitive injections of L-arginine to induce CP in mice and report on the measurement of visceral pain and the morphology of the dorsal root ganglion and spinal cord, both of which are implicated in the transmission and regulation of chronic visceral pain.

Methods: After obtaining ethical clearance, CP was induced in adult male Swiss albino mice by intra-peritoneal injections of two doses (4.5gm/Kg) of L-Arginine one-hour apart for 4 weeks on days 0,7,14 and 21. Mice were sacrificed on days 7, 14, 21 and 28. Control mice received equivalent volumes of normal saline intraperitoneally.
We assessed pain by von Frey filaments on the antepenultimate day of sacrifice.The ascending stimulus method was used. Thereafter, mice were sacrificed in a carbon-dioxide chamber and fixed by trans-cardiac perfusion with 4% paraformaldehyde in 0.1M phosphate buffer (PB), pH 7.4. The vertebral column was dissected out, decalcified in 10% ethylene diamine tetra acetic acid, cryoprotected in 30% sucrose, mounted in a cryomedium and cryosectioned to obtain 20µm-thick sections. The sections were stained either with cresyl violet (CV) or haematoxylin and eosin (H & E) stain, mounted and studied with a light microscope.

Results: L-Arginine treated mice showed significantly decreased in pain threshold (0.008g) and increase in total percentage of responses by different von Frey hairs indicating progressive mechanical allodynia. Dorsal root ganglia were identified by their presence in the vicinity of spinal cord and presence of pseudounipolar neurons surrounded by satellite glial cells. The spinal cord, had outer white matter containing myelinated fibers and inner grey matter containing cell bodies of neurons and glia.

Conclusions: The L-arginine model of CP produces chronic visceral pain and the morphology of the spinal cord and dorsal root ganglia can be investigated further by other morphometric and molecular techniques to investigate the central effects of chronic visceral pain.



SYMPOSIUMS



Studies on Neuronal Development, Degeneration and Repair EmployingTransgenic *C. elegans* Model

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Abstract:

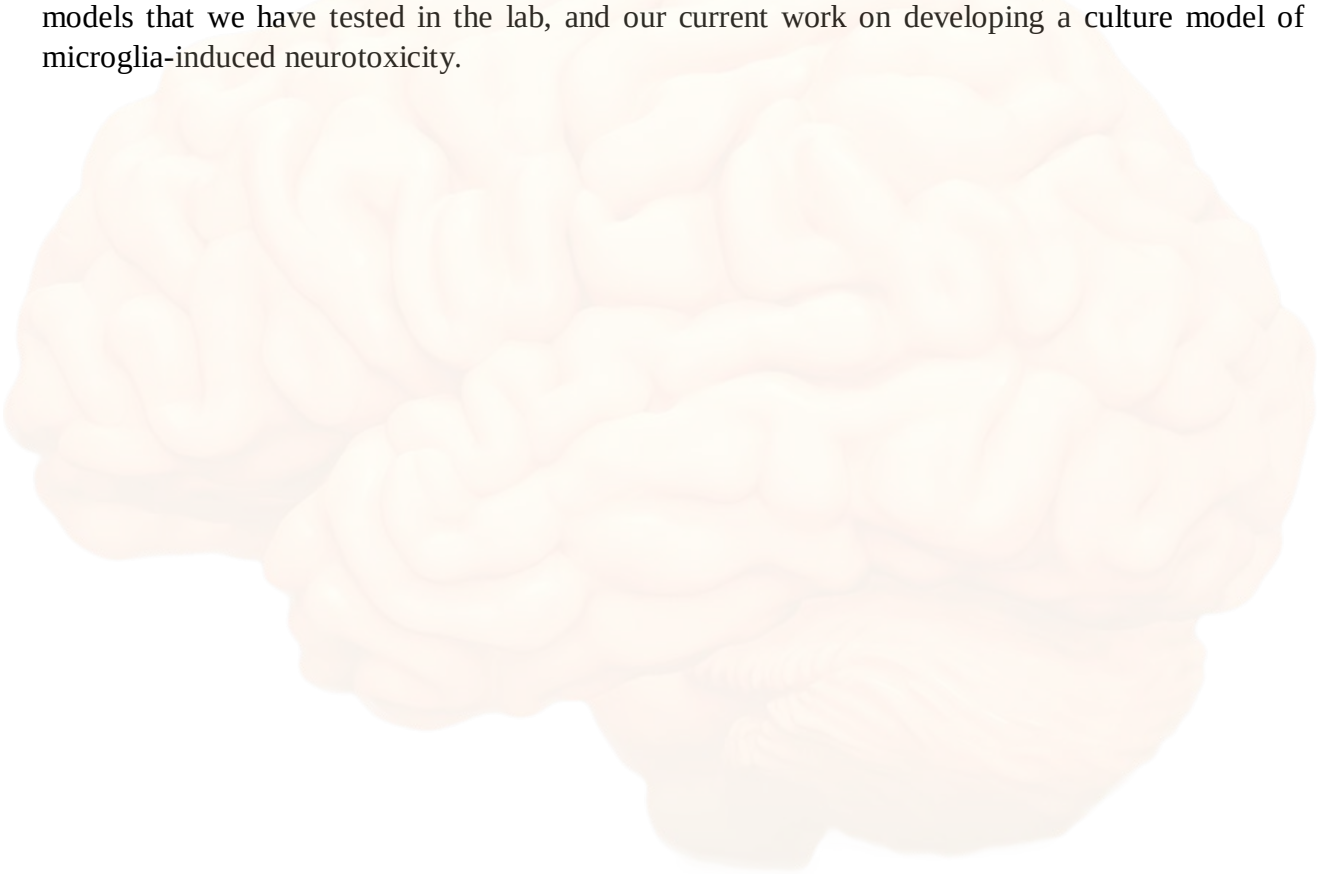
The advancement in research on disease physiology and pathophysiology has generated significant interest in the aspects of functional genomics and epigenetics pertaining to specific disease conditions. Studying neurodegenerative diseases, the importance of protein quality control and role of non-neuronal cells like glial cells, have provided intriguing insights. In *C. elegans* model, the glial cells are enriched with specific genes like patch related family gene *ptr-10*. We endeavored to study the role of this specific "enrichment" in neuronal function, especially in development of neurons orin healing of damaged neurons. We assayed the expression pattern of PTR-10 across various developmental stages, employed RNAi induced silencing and knock-out based studies towards carrying out functional, behavioural and transcript profiling studies in *C.elegans* model. We also established a model for studying neuronal damage and repair towards exploring the role of *ptr-10*. We extended the studied towards identifying functional genomics and epigenetic modulators associated with ageing and related processes. Our studies revealed that PTR-10 has an increased expression during the stages of neurogenesis and eventually the expression declines as the worm's age. Lossof *ptr-10* led to partial loss of anterior dopaminergic neuron ADE and associated neuronal processes. Neuronal damage as a result of catecholaminergic-toxicant assaultwas not effectively repaired by neuroprotectant when *ptr-10* was absent. The transcriptomic analysis of *ptr-10* knockout revealed changes in the expression a subset of 5 genes having role in axonal regeneration. We also identified a novel chromatin modulator and studied functional genomics associated with protein quality control. The studies provide interesting insights on why PTR-10 is enriched in glial cells and that the understanding can be employed towards exploring possible ways of exploiting its protective or repair functions during the conditions of neuronal demise associated with ailments like Parkinson's disease.

Microglia-induced neurotoxicity: the paradigm and the reality

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Abstract

The paradigm of microglia-induced neurotoxicity has long been considered. It describes the neuronal damage caused by the inflammatory responses of microglia. However, where this paradigm has failedto deliver is in neuroinflammation-targeted therapies. Clinically-trialled drugs that have targeted microglia have largely failed. In this session, I share what is known thus far about microglia, neuroinflammation and neurotoxicity. I also review BV2 microglia stimulation models that we have tested in the lab, and our current work on developing a culture model of microglia-induced neurotoxicity.



Identification of molecular targets of hydroxytyrosol, a neuroprotective molecule inParkinson's disease

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Abstract:

3-Hydroxytyrosol (HXT) is a natural polyphenol present in extra-virgin olive oil and is Itis a key component of Mediterranean diet. The present study evaluated the potential of HXT as an anti-parkinsonian molecule through *in-silico, in-vitro* and *in-vivo* approach. In-silico molecular docking study followed by MMGBSA binding free energy calculation revealed that HXT has a strong binding affinity for MAO-B in comparison to MAO-A. Moreover, rasagiline and HXT interacted with the similar binding sites and modes of interactions. Additionally, molecular dynamics simulation studies revealed stable nature of HXT-MAO-B interaction and also provided information about the amino acid residues involved in binding. Moreover, *in vitro* studies revealed that HXT inhibited MAO-B in human platelets with IC50 value of 7.78 μM. In vivo studies using MPTP-induced mouse model of PD revealed increase in DA levels with concomitant decrease in DA metabolites (DOPAC and HVA) on HXT treatment. Furthermore, MAO-B activity was also inhibited on HXT administration to PD mice. In addition, HXT treatment prevented MPTP-induced loss of DA neurons in substantianigra and their nerve terminals in the striatum. HXT also attenuated motor impairments in PD mice assessed by catalepsy bar, narrow beam walk and open field tests. Analysis in various transgenic mutant strains of *C. elegans* revealed that HXT mitigates Parkinson's disease (PD) pathology by preventing □-synuclein accumulation and dopaminergic neuronal degeneration. *In-vivo*also revealed HXT prevented MPTP-induced mitochondrial dysfunctions and enhances mitochondrial biogenesis. The study suggests HXT as a possible anti-parkinsonian molecule, with pleiotropic properties, which may be used as a lead molecule for the development of therapeutics for PD.

Neuroprotective efficacy of proteins of A2-like astrocytes in a transgenic mice model of Alzheimer's disease

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Abstract:

Two distinct reactive astrocyte subtypes with their unique transcriptomic signatures have been proposed in CNS disorders. The two subtypes are termed as A1 astrocyte (detrimental) and A2 astrocyte (beneficial). Recent studies allude to the presence of A2-like astrocytes at the prodromal stage of Alzheimer's disease (AD) releasing a plethora of beneficial cytokines. Our studies identified intercellular adhesion molecule-1 (ICAM-1) and tissue inhibitor of matrix metalloproteinase-1 (TIMP-1) as major neuroprotective candidates of astrocyte origin that protect neurons and ameliorate memory deficits in 5XFAD mice. We show that amyloid-β (Aβ) induces a state of reactivity and elicits a cytokine pool from primary astrocytes as early as 6h. We found ICAM-1 and TIMP-1 as major neuroprotective molecules in this secretome through neuron-astrocyte co-culture studies. In primary neurons, TIMP-1 inhibited both Aβ-induced - FOXO3a-mediated apoptosis and impaired autophagy flux - by increasing Akt phosphorylation. Furthermore, we detected CD63 expression is essential for TIMP-1's attachment on neurons and for mediating downstream Akt phosphorylation through knockdown studies. Interestingly, intracerebroventricular TIMP-1 injection in transgenic 5xFAD mice not only reduced apoptosis and prevented autophagic dysregulation in the hippocampus but also decreased Aβ plaque burden. ICAM-1 and TIMP-1 enhanced learning and memory in cognitive behavioral tests in these mice. We found that synaptic protein expressions, spine density and spine shape were improved in whole tissue and in pure synaptosomal isolations/preparations from hippocampi and cortices of TIMP-1 treated 5xFAD mice. TIMP-1 increased long term potentiation (LTP) at the Schaffer collateral-CA1 synapses in acute hippocampal slices from 5xFAD in electrophysiology experiments. Biochemically, Akt/GSK3β signaling was detected as an underpinning mechanism for TIMP-1 mediated LTP induction. In conclusion, ICAM-1 and TIMP-1 are major neuroprotective cytokines secreted by reactive astrocytes early in AD that ameliorates memory deficits and therefore has an exciting prospect in AD therapeutic research.

Olfaction as a tool to study the brain in health and disease

NixonAbraham
IISER , Pune

Abstract:

A cardinal question in neuroscience is how the brain perceives the ever-changing external world and generates specific behavior. Our sense organs collect information from the external environment and convert the physical/chemical energy to neural representations. Pre- cortical and cortical regions refine these representations facilitating sensory perception that leads to decisions and required actions. In the Laboratory of Neural Circuits and Behavior at IISERPune, we study the key question of how different neuronal circuits shape perception and decision-making ultimately leading to well-defined behaviors. We use olfaction as a model and combine state-of-art automated behavioral training, electrophysiology and optogenetics. In the first part of my talk, I will cover the basics of olfactory information processing and decision-making. In the second part, I will explain how we use optogenetic tools for modulating specific behaviors in rodents. Our experiments using optogenetic activation of olfactory bulb inhibitory circuits during and after stimulus provide novel spike-dependent mechanisms explaining learning and long-term memory formation. Finally, I will discuss howthe olfactory decision-making is impaired in different models to study brain dysfunctions.

Olfaction drives flight or fight response in Caenorhabditis elegans

Varsha Singh
Indian Institute of Science, Bangalore

Abstract:

Olfaction is one of the oldest sensory modalities utilized by animals to find food, mate, and avoid predators. We utilize *Caenorhabditis elegans* as a model host to ask whether olfaction drives pathogen sensing, by serving as a non-canonical mode of pattern recognition in organisms lacking classical pattern recognition receptors (PRRs). By careful analysis of worm behavior, we determined that olfaction is necessary for the avoidance of Pseudomonas aeruginosa, a pathogenic bacterium. Using gas chromatography-mass spectrometry, we identified six prominent volatiles released by this bacterium. A specific volatile, 1-undecene, activates nematode odor sensory neurons inducing flight as well as fight responses in worms. In behavioural assays, worms are repelled by 1-undecene, and this aversion response is driven by the detection of this volatile through AWB odor sensory neurons. Furthermore, 1-undecene odor can induce immune effectors specific to P. aeruginosa via AWB neurons and brief pre-exposure of worms to the odor enhances their survival upon subsequent bacterial infection. Thus, 1-undecene derived from P. aeruginosa serves as a pathogen associated molecular pattern for the induction of protective responses in C. elegans. Can we harness volatile molecular patterns from various pathogens and gut microbiota to modulate the immune response and behavior of animals? I will discuss strategies to delve into this emerging area of research.

What of the olfactory code of an odor is learned by the honeybees?

Joby Joseph
Center for Neural and Cognitive Sciences, University of Hyderabad, India

Abstract:

A steady olfactory stimulus causes spatio-temporal representation in the brain at different stages in the olfactory pathway. The code is also often characterised by oscillatory synchronization of subpopulations of neurons at certain stages in the pathway. Though there are various proposals on how this code is used to form associations, there is no definite answer yet. PER conditioning in honeybees is one of the popular assays used to investigate olfactory associative learning. PER conditioning paradigm has phenomena happening at two timescales, within a trial and across trials. In this work we use behavioural physiological measurements during learning in a variety of probing stimuli to improve our understanding of what of the olfactory code of an odour is learned by the honeybees.

Intermittent inputs reveal invariant odor representations

Collins Assisi
IISER Pune

Abstract:

Steady odor streams are typically encoded as robust spatiotemporal spike trains by olfactory networks. However, odorants often come riding upon chaotically pulsed plumes of air. Consequently, the spike sequences must also be different every time an animal encounters the odorant. Nevertheless, animals can decode sensory cues and navigate highly complex and turbulent 'odorscapes'. Here, we attempt to find the neural invariants of stable olfactory percepts in a computational model of the locust olfactory system. We show that when time-varying odor inputs intermittently perturb subsets of neurons in the antennal lobe network, the activity of the network reverberates in a manner that depends on both the nature of the inputs it receives and the structure of the neuronal sub-network that these inputs stimulate. We demonstrate that it is possible to decipher the structure of the perturbed sub-network by examining transient synchrony in the activity of the neurons. We find that the ability to reconstruct the sub-network structure is vastly improved when odor inputs arrive or are sampled in an intermittent manner. Thus, the structure of the stimulated sub-network itself serves as a unique invariant code that represents the odor.

Choline transporter: Channeling the Fly Olfactory Behaviour

Runa Hamid
CSIR-Centre for Cellular and Molecular

Abstract:

Neurotransmitter transporters (NTTs) belong to the specific solute carrier family (SLC) of membrane transporters present either on the pre-synaptic membrane or the glial cells. They facilitate the re-uptake of neurotransmitters (NT) into the pre-synaptic terminal, thus regulating the duration of synaptic activity by controlling the levels of NT in the synaptic cleft.Due to their property to modulate NT levels at synapses, NTTs are an important class of protein that plays a crucial role in regulating various cognitive behaviors. A large amount of valuable clinical data from patients and animal models indicates that malfunctioning of NTTshas a strong correlation with disruption of cognition and behavior at various levels of their function. Choline Transporter (ChT) is one such transporter which is essential for uptake of choline into the presynaptic terminals of cholinergic neurons. Choline is an essential substrate for Acetylcholine synthesis and is a critical molecular determinant of cholinergic signalling. There is intriguing evidence that associates ChT with neurodevelopmental delay, attentional disorder, depression, and other cognitive disorders. Despite several reports that highlight the cognitive significance of ChT, it remains functionally uncharacterised.
In the talk, I will present our recent work on expression and functional characterization of ChTin *Drosophila* central nervous system. We have used olfaction-based paradigms to demonstrate that ChT facilitates 'Habituation' and regulates incoming olfactory stimuli.
Additionally, I will discuss the proposed significance of ChT in psychiatric and neurodevelopmental disorders.

A unique stem cell niche in SVZ maintains neural stem cells during early neurogenesisand in the adult cortex

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Abstract

We have demonstrated the existence of a new subclass of NIHes-1 expressing neural stem cells and NDHes-1 expressing neural progenitors/RGCs in the developing neocortex. The new subclass of NIHes-1 expressing neural stem cells are quite unique since they are not dependent on cell-cell interaction as observed with NDHes-1 expressing RGCs. Therefore, it is important to completely characterize this unique subpopulation of NIHes-1 expressing neural stem cells which will have profound implications in terms of maintenance/expansion of neural stem cells in the ventricular zone of developing neocortex. We asked the following question. A) What is the role of NIHes-1 and NDHes-1 expressing cells in the developing neocortex? B) Are the quiescent neural stem cells maintained in adult SVZ of embryonic origin and maintained through NIHes-1 expression?

To address these questions we have custom generated a new conditional Knockout mice model Nestin CreERT2: NIHes-1f/f for knocking out non-canonical Hes-1 promoter region (NIHes-1) in Nestin positive neural stem cells. This will be the most appropriate tool to understand the functional significance of this newly identified subclass of NIHes-1 expressing neural stem cells in the ventricular zone of developing neocortex. From our immunohistochemical (IHC) and transcriptomic analysis it appears that knocking out Hes-1 from the NIHes-1 cells shows an upregulation of Hes5 in the KO neocortex which indicated a possible shift from non-canonical Notch activation to canonical Notch activation which was evident from the increased radial glial morphology upon knocking out. More specifically, we were interested in the fate of neural stem cells (NSCs) and radial glial cells (RGCs) upon knocking out of NIHes-1 promoter region. From meta-analysis of all published single cell RNA-Seq data, we found that there was a significant reduction of embryonic cortex neural stem cell population whereas radial glial markers and Cajal Retzius neuron were upregulated. IHC of control and cKO E18 sections also showed a decrease in proliferating Ki67 positive cells in the knockout compared to the control. We could also observe a decrease in proliferating AUKB positive cells. We found a prominent decrease in GFAP positive glial cells than of mature neurons in cKO sections. Thus, we can conclude that NIHes-1 promoter activation at the embryonic stages maintains the cycling neural stem cell population and in the absence of NIHes-1, early maturation of the primitive stem cell pool is taking place. Next to understand if the quiescent neural stem cells maintained in adult SVZ are maintained through NIHes-1 expression we injected BrdU at the embryonic stages and electroporated pmtCBF1-Hes1-d2EGFP reporter at the adult stage to track the NIHes-1 neural stem cells. Here, we observed that few of the NIHes-1 expressing neural stem cells in adult cortex are in a quiescence state and are of an embryonic origin.

Funding: Supported by intramural funding from RGCB and extramural funding from DST-SERB (CRG/2021/005847)

P2 receptor-dependent cyclooxygenase 2 (COX-2) signaling enhances migration and invasion of thehuman neuroblastoma cell-line, IMR-32

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Abstract:

The tumor microenvironment plays a major role in the ability of the tumor cells to undergo metastasis. A major player of tumors gaining metastatic property is the inflammatory protein, cyclooxygenase 2 (COX-2). Several tumors show upregulation of this protein, which has been implicated in mediating metastasis in various cancer types such as of colon, breast and lung. In this report, we show that the concentration ofextracellular ATP (eATP) is increased in response to cell death mediated by chemotherapeutic agents such as doxorubicin. We show that in the human neuroblastoma cell-line, IMR-32, the eATP goes on to act on purinergic (P2) receptors. Among the various P2 receptors expressed in these cells we identified P2X7 as important in modulating cell migration and invasion. Downstream of the P2 receptor activation, both p42/44 mitogen-activated protein kinase (MAPK) and the p38 MAPK are activated in these cells.

These result in an increase in the expression of COX-2 mRNA and protein. We also observe an increase in the activity of matrix metalloproteinase 2 (MMP-2) enzyme in these cells. Blocking the P2 receptors not only blocks migration and invasion, but also COX-2 synthesis and MMP-2 activity. Our results show the link between purinergic receptors and COX-2 expression. Increased levels of ATP in the tumor microenvironment, therefore, leads to increased COX-2 expression, which, in turn, affords migratory and invasive properties to the tumor cells. This opens a new avenue for P2 receptor-based anti-inflammatory drugs (PBAIDs) as potential cancer therapeutics.

Identifying the Different Roles of Vitronectin in Human Mesenchymal Stem Cells under Microenvironment Stress

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Abstract:

Due to their immunomodulatory and trophic support roles, mesenchymal stem cells (MSCs) are attractive targets in the field of cell-based regenerative medicine. However, post transplantation they are challenged by various microenvironmental stress factors, nutrient deprivation being one of them.

On subjecting human umbilical cord-derived MSCs to nutrient deprivation *in vitro*, a marked upregulation in ECM glycoprotein, vitronectin (VTN) expression was noted with arrest in G0/G1 phase of cell cycle, but no appreciable apoptotic change. Pro-survival PI3kinase pathway inhibition led to further increase in VTN expression, yet no apoptotic change. However, siRNA-mediated inhibition of VTN resulted in reversal in G0/G1 cell cycle arrest and a strong increase in apoptosis, suggesting a role of VTN in preventing serum deprivation-induced apoptotic cell death. Moreover, autophagy was implicated as an underlying mechanism in this pro-survival role of VTN.

Additionally, a significant increase in cell spread area and cell-matrix adhesion was observed, while, cellular migration got adversely impacted under serum starvation stress. The changes in adhesion and migration characteristics were accompanied by formation of a large number of super mature focal adhesions along with extensive stress fibres. VTN knockdown also resulted in reduction of super mature focal adhesions and extensive stress fibres, which were formed under serum starvation stress. Further, NF-κβ and ERK pathways were identified as positive and negative regulators of VTN expression, respectively. Thus, along with its pro-survival role, VTN was also established as a possible key player which regulated the adhesion and migration properties of umbilical cord-derived MSCs under serum starvation stress via focal adhesion signalling.

Neuroepigenetic Alterations in the Prefrontal Cortex of Type 2 Diabetic Mice throughDNA Hypermethylation

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Abstract

Background: DNA methylation changes have known to downregulate several regulatory proteins epigenetically during various neurodegenerative disorders. Our study aims to understand the effect of this global DNA methylation on the cerebral complications of type 2 diabetes mice, and its notable effect on maintaining the synaptic fidelity.

Methods and Results: Chronic high fat diet and streptozotocin (STZ)-induced diabetic mice were studied for the neurobehavioral and neuroanatomic parameters pertaining to prefrontal cortex, subsequently elucidating the associated changes in DNA methylation within these diabetic brains. Further, the impact of this epigenetic dysregulation on HSF1, BDNF and PSD95 were studied by assessing the binding affinity and level of % methylation within the promoter site of their respective genes. Our study suggest increased DNMT aberrations within the prefrontal cortex, with increased MeCP2 levels, confirming DNA hypermethylation. This was in accordance with the altered neurobehavioral changes. Further, the hypermethylation was found to participate in gene silencing of HSF1, BDNF and PSD95 proteins, responsible for maintaining the synaptic fidelity.

Conclusion: Overall, our study concludes the plausible involvement of neuroepigenetic alterations in the prefrontal cortex (PFC) of the type 2 diabetes mice, specifically DNA hypermethylation. PFC plays a central role in modulating cognitive and other executive functions through its connection with several brain regions, and thus therapeutic strategies targeting epigenetic modulations in it, can pave a way in controlling several neurological alterations in the brain.

Keywords: DNA Methylation, Diabetes, Prefrontal Cortex, Synaptic Transmission, Epigenetic Modulation

ACKNOWLEDGMENTS

The authors would like to acknowledge the Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Government of India for funding and supporting this work.

Tinospora cordifolia as a potential agent to ameliorate aging-related decline cognitive and locomotor impairments: cell survival and plasticity pathways as targets in female rat brain

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Abstract

Biological aging in women is accelerated with the cessation of reproductive phase which is mainly attributed to the decline in sex hormones reserves. During the midlife transition, various deleterious neurological health outcomes become prevalent in ageing women thus leading to increased disability- adjusted life years (DALYs) count. In clinical practices, hormone replacement therapy (HRT) is prescribed to manage these complications during and/or post midlife transition period. However, the increased susceptibility to coronary heart diseases, heart attacks, breast cancer etc. due to side effects of HRT calls for safer alternatives with least or no side effects. *Tinospora cordifolia*, an important medicinal herb has captured the interest of various research groups worldwide, owing to its different ethano- pharmacological properties. Cognitive impairment and reduced bone mineral density, as well as muscle strength are the hallmark of aging-related deficits and related neuropathologies in women. In a recent study in our lab, we have tested the dry stem powder of *Tinospora cordifolia* (TCP) as a dietary supplement to explore its efficacy to attenuate age-associated cognitive impairments and locomotor dysfunctions using intact acyclic middle aged female rats as the model system of the mid-life transition phase of women. Normal chow or 30% High Fat Diet (HFD) feed, supplemented with or without TCP fed for 12 weeks to these animals resulted in improvement of anxiety like behavior, learning and memory functions and locomotor performance on rotarod of these middle-aged animals. Post-sacrifice protein expression studies identified the neuroinfammation, apoptosis, cell survival and plasticity pathway markers as targets of actives from this herb which may be attributed to its multicomponent nature of this herbal formulation. These findings suggest that TCP supplementation in the diet may be a potential interventional strategy for the management of neurological deficits and fall-associated morbidities in ageing post-menopausal women.

Modulation of adult neurogenesis and bioenergetic deficits by *Bacopa monnieri* extract(CDRI-08) in the cortex of the hepatic encephalopathy rat model of neuroexcitotoxicity

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Abstract

The moderate grade hepatic encephalopathy (MoHE) is a neurological complication developed in the patients with chronic liver failure. Since it involves primarily the NMDAR over activation led neuroexcitotoxicity as its primary neurochemical aberration, it derives the merit of a module pathogenic event for a number of neurodegenerative brain diseases. We have developed MoHE rat model for neuroexcitotoxicity and used it to identify certain non-NMDAR targets for therapeutic management of HE. The modulation of pannexin1 (Pnx1), an ATP exit channel accountable for causing bioenergetic deficit in the brain cells by the Bacopa extract (Branhmi: CDRI-08), was identified as one of those relevant targets. Bacopa is also known to modulate adult neurogenesis, an evolving concept in neuroprotection. We studied the effect of CDRI-08 treatment on the comparative profile of adult neurogenesis vs Panx1 neurochemistry in the cortex/hippocampus of the neurobehavioral characterized MoHE rats, developed by administration of 100 mg/kg bw of thioacetamide i.p. for 10 days. Experiments were performed in control, the MoHE and the MoHE rats post treated with bacopa extract (CDRI-08)) for 7 days. The results suggested that CDRI-08 treatment could recover the MoHE associated enhanced level and activity of Panx1 vis a vis declined level of bioenergetic deficits in those rats. This was consistent with normalization of the NMDAR composition and its activity in those MoHE rats. Concordantly, as compared to the control rats, the hippocampus DG region of the MoHE rats showed significantly compromised status of adult neurogenesis in terms of producing the nascent NSCs (Neuronal stem cells) and the cells expressing the neuronal lineage, its maturation and differentiation markers. However, all the markers of adult neurogenesis were observed to be recovered back in the DG region of the MoHE rats treated with CDRI-08. This was consistent with recovery in the MoHE associated neuroarchitectural and neurobehavioral deficits due to treatment with CDRI-08. The findings suggest that CDRI-08 is able to recover the rats from MoHE pathogenesis mainly by normalizing Panx1 led bioenergetic deficits and activating adult neurogenesis.

Ethical Statement: The animal-based study plan was approved by the institutional animal ethical committee (IAEC) of Banaras Hindu University, for the care and use of Laboratory animals.

Acknowledgement: This work was financially supported by the DBT project to SKT and award of ICMR SRF to DM.

Conflict of interest: The authors declare no conflict of interest.

Neuroprotective Potential of Phytomedicine against Parkinson's Disease

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Abstract

In recent years, phytomedicine has been intensively explored and studied for its therapeutic potential for various neurodegenerative diseases including Parkinson's disease. Parkinson's disease is characterized by progressively losing the structure and function of dopaminergic neurons, which led to cell death. Phytomedicine has emerged as a potential neuroprotective agent for the treatment of Parkinson's disease. In vivo evidence has demonstrated that oral administration of phytomedicinal plant extracts (*Mucuna pruriens*, *Withania somnifera*, and *Tinospora cordifolia*) may protect against dopaminergic cell death, striatal neurotransmitter dysregulation, and motor deficits in Parkinsonian mouse models. The underlying mechanisms of their action include regulation of survival-related kinases (AKT and ERK), antioxidant effects, upregulation of anti-apoptotic proteins, as well as modulation of the NF-κB pathway, and inhibition of excessive proinflammatory responses. In addition, *in vivo* studies have revealed that phytomedicinal plant extracts may affect the aggregation of α-synuclein. Our study focuses on the therapeutic potential of phytomedicine to exert a neuroprotective effect on Parkinson's disease pathology. Moreover, we have shown recent evidence on the novel therapeutic opportunities of these phytomedicines against PD, indicating additional mechanistic aspects that should be explored, and potential obstacles/limitations that need to be overcome, for its inclusion in experimental PD therapeutics.

Keywords: Plant extracts; *Tinospora cordifolia*; Phytomedicine; *Mucuna pruriens*; *Withania somnifera*; PI3K/AKT Signaling.

Inherent phytochemical constituents in *Mussaenda roxburghii* Hook.f. a medicinal plant used in Tripura (India): A spectrum of neurotoxicological consequences

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Abstract

Introduction : Traditional medicinal practice used worldwide is being increasingly accepted and utilised by larger population for treating various kinds of diseases. *Mussaenda roxburghii* Hook.f. which belongs to the family Rubiaceae is a perennial shrub abundant in wet regions and grows in the the hilly tracks in Tripura and other North Eastern states of India. It is used to cure mouth sores , bacterial & fungal infections and wound healing by the indigenous tribes of Tripura. This study targets to investigate the neurotoxicity induced by *Mussaenda roxburghii* Hook.f. in albino mice.

Material and Methods : Oral acute toxicity test in albino mice was performed according to the Organisation for Economic Co-operation and Development (OECD) guidelines for the testing of chemicals . Methanolic extract of leaves of *Mussaenda roxburghii* Hook.f. (MEMR) was administered to different groups of mice in various doses and behavioural study & transmission electron microscopy (TEM) of the brain was performed. Qualitative phytochemical analysis and gas chromatography mass spectrometry (GCMS) analysis of MEMR was done.

Result: Our study shows that high dose of MEMR induced augmented behavioural abnormality in mice subjected to morris water maze test and open field test. TEM images of brain depicted ultrastructural damage. GCMS chromatogram analysis of MEMR indicates the presence of 22 phytochemical constituents.

Discussion and Conclusions: The medicinal plants represent reservoir of phytoconstituents having immense structural diversity responsible for the array of pharmacological properties. Its improper preparation and consumption may lead to undesired neurotoxic symptoms. Further exhaustive study on the phytoconstituents will be useful for delineating the neurochemical pathwaysinvolved in the toxicity.

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GCMS analysis – AIRF , JNU, N.Delhi.
TEM analysis – SAIF, NEHU, Shillong , Meghalaya.

Treatment with *Tinospora cordifolia* reduces amygdaloid neuronal damage caused by prenatal stress and maternal separation in rats

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Abstract

Background: Prenatal stress induced during pregnancy affects brain development by altering neuronal proliferation, synaptic connections, and by inducing dendritic pruning in developing offspring. Amygdala: a subcortical set of nuclei is responsible for emotional processing, fear conditioning, and stress management. *Tinospora cordifolia* (TC); one of the *medhya* drugs in *Ayurveda* is believed to act against oxidative stress and enhance learning and memory. However, there is no experimental evidence to suggest its efficacy against neuronal damage caused by prenatal vibratory stress and maternal separation. Therefore, the aim was to assess the ability of TC to reduce the amygdaloid neuronal damage in rat neonates subjected to prenatal vibratory stress and maternal separation.

Materials and Methods: Pregnant Wistar rats were divided into normal control (NC_M), vehicle control (VC_M), 3 hour / day vibratory stress (VS_M) groups and TC treated group (VS+TC_M) which received 6 mg/kg body weight of TC extract orally before subjecting them to vibratory stress. The neonates born to mothers of control groups were allocated into NC_N and VC_N groups. The neonates born to VS_M group were further categorised into prenatally stressed control (VS_N control) and prenatally stressed and postnatal maternal separation (VS+MS_N) group and prenatally stressed with postnatal TC treated group (VS+PNTC_N). Neonates born to VS+TC_M were divided into VS+TC_N control, maternal separation (VS+TC+MS_N) and maternal separation followed by postnatal TC treatment (VS+TC+MS+PNTC_N) groups. After 6 weeks, animal brains were dissected and processed for Golgi cox staining to study the amygdaloid neuronal arborization.

Results: The dendritic branching points were significantly ($p<0.01$) increased in amygdaloid neurons of stressed group mothers and neonates compared to TC treated groups, but they seldom intersected beyond 80µ from the soma. Significant ($p<0.001$) increase in dendritic intersections were observed at 20µ to 60µ circles from the soma in TC treated mothers and neonates. The number of processes arising from amygdaloid neurons were significantly ($p<0.001$) higher in TC treated mothers. Both prenatally stressed and maternal separation neonatal groups showed significant ($p<0.01$) increase in number of processes after prenatal and postnatal TC treatments.

Conclusion: Treatment with TC extract reverses amygdaloid neuronal damage caused by prenatal vibratory stress and maternal separation in rats.

Key words: Prenatal stress, herbal extract, maternal separation, amygdala

Neuroactive steroids on Mozart effect for Spatial intelligence: An EEG Study

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Abstract

Focusing on subtle changes in EEG by spectral analysis, the modulation of large-scale, synchronous, neocortical oscillations reflecting brain circuits can be predicted. Listening to music serves to strengthen the neuronal pathways subsequently leading to the execution of spatial tasks.Neuroactive steroids (NAS) interact with neurotransmitter receptors and alter the excitability and synaptic transmission to modulate learning and cognitive processes.Since there is paucity of literature on neuronal oscillations and neuroactive steroids influencing effect the Mozart music effect on directed attention, our study urges to continue examining the effect of patterned Mozart music and any underlying neuronal processes involved to demonstrate its role in spatial task performance. This cross-sectional Analytical study was undertaken at EEG Laboratory, AIIMS Mangalagiri, 30 healthy individuals above 18 years of age, who consent to participate were included and excluded the participants with history of neurologic or psychiatric illness. The temporal and frequency properties of EEG: Power/ERSP of EEG bands were recorded at rest and soft music of Mozart is played for 6 minute using external speakers. An event was marked in the continuous EEG data for the better analysis of data to see the effect of music on EEG bands. While playing music, subjects were asked to close their eyes for 3 minute and followed by eyes open for 3 minutes. Blood sample was collected for measurement of Neuroactive steroids: cortisol and DHEA-S before and after exposure to music. Exposure to mozart music leads to changes in Power/ERSP of EEG bands: delta, theta, alpha, beta and gamma and alteration of NAS: Cortisol and DHEA-S. The accuracies and latencies showed improvement in Spatial task performance by increased directed attention due to mozart effect. These changes show probability of growth and development of new communication in brain circuits leading to changes in neuronal rhythmsin turn reflects specific pathways and cortical areas involved in Mozarteffect. Alteration of NAS: Cortisol and DHEA-Sleads to variation in synaptic transmission and neuronal excitability suggesting possible role of Neuronal oscillations predicting cortical communications reflected by Electroencephalogram record analysis and Neuroactive steroids in mozart effect for Spatial attention.

High-fat diet combined with exercise in anxiety-like behaviour of adolescent rats

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Abstract

Lifelong repercussions result from childhood exposure to a high-fat diet on metabolism. Exercise and switching to a normal low-fat diet during adulthood could reverse most but not all biochemical and behavioral implications due to a high-fat diet paradigm. In this study, whether exercise coupled with a high-fat diet is able to influence the biometric, biochemical and anxiety like behavior in adolescent male and female rats was addressed. After obtaining approval from the Institutional Animal Ethics Committee 12 female and 12 male Wistar adolescent rats, aged 35 days and weighing between 30-50 g were obtained. They were divided into two groups control group and HFD group of 6 female and male in each group. The control group received standard diet and HFD group received HFD for 10 weeks coupled with exercise in last three weeks. We found that 10-week administration of a high-fat diet increased body weight in both male and female rats, which was comparable to control in males and got lowered in females after 3-week of exercise. Exercise in high-fat-fed female rats showed comparable liver lipid levels to control, while the serum glucose and lipid profile was raised in both males and females. The exercise was able to ameliorate the anxiogenic behavior in high-fat diet-fed adolescent female rats, but not in male rats. Taken together, these results reflect upon the gender-specific differential effect of high fat diet and exercise during adolescence which influences the biometric, biochemical, and anxiety-like behavioral outcomes.

Dietary glutamate in rats causes changes in medial preoptic area neuronal activity

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Abstract

Brown adipose tissue (BAT) thermogenesis occurs after intragastric administration of dietary glutamate. The brain senses glutamate intake in the gut by the stimulation of gut glutamate receptors leading to activation of gastric afferent vagal fibers. Neuro-imaging techniques revealed activation of medial preoptic area (mPOA) in rats after intragastric glutamate administration. Nonetheless, to establish that the brain activity induced by dietary stimulus, it is important to confirm results obtained from imaging techniques with recordings made at the neuronal level. In this study we have investigated the neuronal activity of mPOA after intragastric infusion of glutamate. The recording was obtained from 48 neurons of adult male/female Wistar rats weighing between (200-250) g. Rats were urethane anesthetized and fixed onto stereotaxic apparatus. A glass microelectrode of 1-5μm tip diameter was lowered at mPOA in steps of 1μm with motorized microdrive. An Ag-Cl wire was inserted into the microelectrode, which was connected to high input impedance probe. One min baseline neuronal recording and five min recording was done after glutamate (0.12M, 1.5 ml) was infused intragastrically via a polyethylene tube. Out of the 48 neurons studied, 39 responded to the intervention. Intragastric glutamate increased the firing rate of 28 out of 39 responding POA neurons; while 4 of the responding neurons showed a decrease in firing rate. The latency of response ranged from 1-5 min after the glutamate was delivered. Dietary glutamate probably triggers the neurons of the mPOA bringing about an increase in the BAT thermogenesis.

Cerebellar transcranial direct current stimulation: A new dimension for neuromodulation?

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Abstract

In recent years, transcranial direct current stimulation (tDCS), as a non-invasive therapeutic tool, has gained exponential attention due to its low-risk administration procedure and high cost effectiveness. A wide range of medical fields, from stroke to schizophrenia patients, have considered DCS for treating patients with limited options. In spite of this, tDCS is rarely applied to treat cerebellar disorders. We realized that an optimal use is only possible when mechanistic pathways are understood thoroughly. In order to decipher this, we created a mouse model, for the first time, to investigate cerebellar tDCS-induced behavioral changes. Our results provided evidence that the acute effect of anodal tDCSoncerebellar dependent VOR adaptation in mice was disrupted by genetic ablation of long-term plasticity in Purkinje cells (PCs).Based on our animal study, we expected to observe similar effects in humans. To our surprize, neither offline nor online anodal tDCS had an effect on VOR adaptation. However, anodal tDCS of the cerebellum facilitated locomotor adaptation in humans. It is plausible that the electric field strength in the flocculus was insufficient to affect neuronal firing and VOR adaptation is exceedingly more complex in humans than in mice. In future, we will have to consider (i) anatomical location of the preferred stimulation site, (ii) neuronal firing profile and dynamics of the network and (iii) behaviour paradigm before administering tDCS as a therapeutic tool in cerebellar disorders.

Brain wave entrainment in sleep and cognitive functions

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Abstract

Brain wave entrainment has been shown to improve various aspects of cognition in health and disease. Recently various scientifically proven and non-invasive techniques i.e. transcranial direct current stimulation and transcranial magnetic stimulation are used for this purpose. In the present study, we planned to evaluate the efficacy of acoustic stimulation in sleep and cognitive functions by modifying the relative power of the brain waves during sleep. The subjects were young adults in age group of 18-28 years. They were screened for their sleep by PSQI and ISI. Cambrige brain sciencies neuropsychological test battery was used to assess the key cognitive abilities i.e. working memory, attention, reasoning and planning. The neurophysiological correlates of cognition were assessed by P300 test utilizing auditory odd ball paradigm. The participants were undergone acoustic stimulation for 60 minutes before sleep each day for four weeks. The outcome measures were obtained at baseline, after 2 weeks and 4 weeks of intervention. There was association in impaired cognitive performance, delayed P300 latency and poor sleep quality. The assessment of cognitive domains demonstrated that memory, attention and executive function improved after 4 weeks of acoustic stimulation. P300 measures, i.e., amplitude and latency both increased significantly with the given intervention. A significant improvement in sleep quality with brain wave entrainment was reflected on all sleep scores. These results indicate that brain wave entrainment with acoustic stimulation during sleep has a potential to improve sleep and cognitive functions.

Role of Muscleblind-like (MBLN) protein MBL-1 in axon growth and Synapse formation

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Abstract

Regulation of microtubule cytoskeleton is fundamental for the development and maintenance of neuronal architecture. Recent studies have shown that regulated RNA processing is also critical for the establishment and maintenance of neural circuits. In a genetic screen using mechanosensory neurons of *C. elegans*, we identified a mutation in *muscleblind-1* as a suppressor of loss of kinesin-13 family microtubule destabilizing factor *klp-7*. Muscleblind-1(MBL-1) is an RNA-binding protein that regulates the splicing, localization, and stability of RNA. We found that *mbl-1* is required cell-autonomously for axon growth and synapse formation in the posterior lateral microtubule (PLM) neuron. Loss of *mbl-1* affects stability and plus-end-out organization of microtubules in the anterior process of PLM. These defects are also accompanied by abnormal axonal transport of the synaptic protein RAB-3 and loss ofgentle touch sensation in *mbl-1* mutant. Our data showed that *mbl-1* is genetically epistatic to *mec-7* (β tubulin) and *mec-12* (a tubulin) for axon growth. The immunoprecipitation of MBL-1 pulls down the *mec-7*, *mec-12*, and *sad-1* mRNAs. Additionally, the *mbl-1* mutants show a reduction in the level and stability of *mec- 7* and *mec-12* transcripts. Independently, *mbl-1* is epistatic to *sad-1* for synapse formation. Our work elucidated a previously unknown link between RNA binding protein and cytoskeletal machinery for the development and maintenance of the nervous system.

Left-right asymmetry patterning of the mammalian body

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Abstract

Vertebrates display left-right (LR) asymmetry with respect to the organisation of internal organs. The LR asymmetry is established in the embryos prior to the formationof organs. In mammals, LR asymmetry is orchestrated by the node, a midlineembryonic structure. Failure of LR pathway causes a range of LR defects known as heterotaxy syndrome. Fundamental questions such as the mechanism timing the induction of the LR pathway during development remain poorly addressed. Mouse embryos mutant for *Tbx6*, encoding a T-box transcription factor, manifest severe LR defects; the mechanism of action is unclear. *Tbx6* is an early developmental gene with a central role in mesoderm germ layer specification and in progenitors generating posterior spinal cord and musculoskeletal tissues. We have identified global targets of Tbx6. Together with our analysis of mutant mouse embryos, our findings suggest that Tbx6 controls LR pathway at multiple key regulatory steps. Based on this evidence, we propose that Tbx6 is pivotal to determine left-right asymmetry and that it could bea part of the mechanism to time the induction of the LR pathway.

Stitching together the domains of FMRP to elucidate its function

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Abstract

The Fragile-X Mental Retardation Protein (FMRP) is an RNA binding protein that regulates the translation of mRNAs essential for synaptic development and plasticity. The loss of FMRP results in neurodevelopmental disorder Fragile X Syndrome (FXS). Though the pathology of FXS is well studied, the physiological function of FMRP is yet to be fully uncovered. In this context, we focused on investigating the functional role of the individual domains of FMRP (N-terminal domain, KH domains and C-terminal domain). Our recent study reveals that the C-terminus domain is essential and sufficient for FMRP-mediated neuronal translation repression and ribosome binding, similar to the full length FMRP. However, the microtubule association of FMRP is a function of the synergistic combination of all the domains rather than the contribution by an individual domain. Additionally, we highlight the importance of phosphorylation of FMRP at Serine-500 as a fundamental mechanism governing the size/number of FMRP puncta, ribosome association and translation regulation. Finally, through the use of patient identified FMRP mutations, we emphasize the hierarchical contribution ofFMRP's domains in translation regulation.

dIER3IP1: a novel player in vesicle trafficking

Sonal Nagarkar Jaiswal
CSIR-Centre for Cellular and Molecular Biology, HyderabadAbstract:

Abstract

De-regulated neural stem cell maintenance has profound consequences on brain development that can lead to neurodevelopmental disorders. To unveil the molecular players maintaining neural stem cell homeostasis, we performed genetic screens using *Drosophila* neural stem cells, neuroblasts, as a model system. We isolated an evolutionarily conserved gene named *CG32069/dIER3IP1*, homolog of human IER3IP1, a gene associated with microcephaly in human. *IER3IP1* is an uncharacterized protein-coding gene and its role in brain development is still unclear. We developed a fly model to study the role of *dIER3IP1* in brain development. We show that *dIER3IP1* loss in neuroblasts results in their premature differentiation into neurons leading to a developmental delay and larval lethality with a small brain phenotype. Our preliminary data suggests that these defects could be due to a perturbance in vesicle trafficking.

Inhibitory metaplasticity in juvenile stressed rats restores associative memoryin the adulthood by regulating epigenetic complex G9a/GLP

Sreedharan Sajikumar, Dept. Physiology, National University of Singapore,Singapore

Abstract

Exposure to juvenile stress was found to have long-term effects on plasticity and the quality of associative memory in adulthood, but the underlying mechanisms are still poorly understood. We demonstrate that even long after the elimination of actual stressors, an inhibitory metaplastic state is evident, which promotes synaptic competition over synaptic co-operation and decline in latency of associative memory in the behavioural paradigm despite the exposure to novelty. Mechanistically, juvenile stress led to a heightened expression of the epigenetic marker G9a/GLP complex which is thus far ascribed to transcriptional silencing and goal directed behaviour. The blockade of the G9a/GLP complex was found to alleviate deficits in long-term plasticity and associative memory during the adulthood of animals that were exposed to juvenile stress. My talk will provide insights on the long-term effects of juvenile stress that involve epigenetic mechanisms, which directly impact long-term plasticity, synaptic tagging and capture and associative memory.

Locus coeruleus integrity determines the longevity of fear memory in APPswe/PS1dE9mice

Smitha Karunakaran, Assistant Professor, Center for Brain Research, IISc, Bangalore

Abstract

Alzheimer's disease (AD) is a neurological disorder that slowly impairs memory and higher cognitive functions. Extracellular amyloid β plaques and intracellular neurofibrillary tangles are the neuropathological hallmarks of AD. In familial forms of AD, subtle cognitive deficits develop <25 years before they develop dementia. The brainstem noradrenergic nuclei, locus coeruleus (LC) is known to modulate cognitive and behavioural deficits that are associated with prodromal AD. However, the pathological consequences of dysregulation of noradrenergic transmission in AD remains to be elucidated. In this study, we demonstrate that male 2-month-old APPswe/PS1dE9 (APP/PS1) mice, a transgenic amyloidogenic model of AD, display loss of noradrenergic terminals in the hippocampus, have low levels of β-adrenergic receptors (β-AR) and exhibit long-term memory loss in Pavlovian hippocampal - dependent contextual fear conditioning task. Intra hippocampus infusion of isoproterenol hydrochloride, a β-AR agonist, immediately before fear conditioning restored long-term contextual fear memory in the male APP/PS1 mice. However, female APP/PS1 mice did not display these deficits. We report that there are inherent gender dependent differences in the LC noradrenergic system which afford protection to female APP/PS1 mice during early stagesof AD.

Neuromodulation by acetylcholine preserves activity patterns at hippocampal synapses

Suhita Nadkarni, Associate Professor, Department of Biology, IISER Pune.

Abstract

Acetylcholine is a crucial neuromodulator for memory formation and recall. It acts on a family of ionotropic and metabotropic receptors with distinct expression loci over multiple timescales and has diverse downstream targets and outcomes. We construct a biophysical model of Schaffer-collateral (SC) synapses to study the effect of acetylcholine receptors on synaptic transmission and plasticity. Acetylcholine M1 receptors primarily expressed in the post-synaptic regions on the soma and dendrites are known to broadly enhance neuronal excitability. The M4 acetylcholine receptors, on the other hand, are most densely populated in the presynaptic regions and suppress neurotransmitter release via their action on voltage-gated calcium. We show that the seemingly paradoxical effect of acetylcholine on pre and postsynaptic terminals enhances transmission of relevant information. The suppression of the vesicle release rate via M4 receptors enables the limited vesicle resource to sustain release for a longer time. The prolonged release of vesicles creates a stronger correlation between the amount of neurotransmitter released and the pre-synaptic firing rate. Additionally, the activation of M1 receptors amplifies the weaker neurotransmitter signal to generate a stronger correlation of the post-synaptic response with pre-synaptic activity. In the hippocampus, theta-band activity coincides with elevated levels of acetylcholine. We investigate the action of cholinergic receptors on SC synapses during theta-entrained activity in CA3 neurons. Interestingly we see that the encoding mediated by acetylcholine is optimally tuned to respond to theta-rhythmic firing activity in CA3 neurons. The modulatory actions of acetylcholine on synaptic transmission filter out noise to support efficient transmission and encoding of information. Our model elucidates the subtle interplay between the M1 and M4 receptors and their role in orchestrating synaptic function.

Uncertainties in Older Memory Creates Rapidly Consolidating Memories of Unreal Events

Balaji Jayaprakash, Associate Professor, Centre for Neuroscience, IISc, Bangalore.

Abstract

Our brain encodes novel information in the form of new memories. However, most often the brain integrates new information such as those resulting from everyday experiences with related, existing memories. Remarkably, the neurobiology of such related learning is fundamentally different as they are typically acquired in absence of direct reinforcement and are based on previous memories of reward or punishment. Core to this process is our brain's ability to compare the current sensory perception to past experiences and establish a plausible relationship. Little is known about how the current ongoing experience dictated by sensory perception interact with events perceived through memory retrieval ("memory perception"). With recent advent of targeted activation and inactivation through opto/chemo genetic approaches we now could create mixed perception where perceived memory is different from the ongoing experience. I would be discussing the experiments performed in our laboratory to probe such perceptions specifically when the sensory experience a) is congruent to a related memory and b) conflicts with a related memory. Our results indicate that such interactions between related memories result in creation of new memories for events hitherto unexperienced by the organism (unreal events) and unlike memories of realistic events such memories are rapidly consolidated.

Exploring the utility of Neuromodulation in novel therapeutic regimens in the management of Neurodegenerative disorders

Kaviraja Udupa, Departments of Neurophysiology, National Institute of Mental Health & Neuro Sciences (NIMHANS),Bengaluru, India

Abstract

There is expanding interest in understanding various neurodegenerative disorders utilizing gut-brain axis and brain stimulation techniques such as non-invasive brain stimulation (NIBS): repetitive TMS and transcranial direct current stimulation (tDCS), transcranial alternating brain stimulation (tACS) and transcutaneous auricular vagal nerve stimulation (taVNS). Transcranial magnetic stimulation (TMS) has been utilized in the investigation and treatment of many neurological and psychiatric disorders forthe last three decades. TMS is shown to be non-invasive, safe and effective mode of investigation to explore the physiology of cortical circuits in health and disease. TMS usually delivered to motor cortexto obtain characteristic response from the muscles of hand, which is having maximal motor cortical representation along with face as observed in motor homunculus. Generally, single or paired pulses of TMS could be used to investigate cortical excitability functions, which are altered in various neuropsychiatric disorders. rTMS and various patterns of stimuli delivered over length of time alters the excitability of stimulated region for extended period of time (so called plasticity effects) thus providing therapeutic potentials. In this review, I'll be describing emerging trends of other modes of stimulation as well as their therapeutic implications in neurodegenerative disorders such as Parkinsonian disorders.

In ongoing studies, we are investigating factors REM sleep behavior disorders with Parkinsonian disorders, the efficacy of dual stimulation of tDCS and high frequency rTMS in patients with Major depression (commonest mental health disability) and investigate the medical refractoriness in depression by using a comprehensive battery of clinical and investigative modalities of TMS. Further,we are investigating mechanisms of potential Ayurvedic add-on therapies in couple of projects involving patients with depression or Duchene Muscular Dystrophy. In these projects we are exploring various neurochemical factors to understand the interaction between excitatory and inhibitory neurotransmitter systems using paired pulse TMS protocols and neurochemical investigations. I shall briefly discuss these neurophysiologic perspectives of brain stimulation, possible combination of various modes of brain stimulation and mechanistic basis of these stimulation protocols.

Although rTMS treatment has been successfully considered as add-on to physiotherapies in management of unilateral stroke, clinical depression and various other neuropsychiatric disorders, we are still lacking the clear understanding of their mechanisms of action in neurodegenerative conditions.Many studies involving clinical & behavior changes, imaging measures, molecular and animal modelsof neurological conditions have looked into various modes of mechanisms of action of these brain stimulation modalities. Further, based on scientific studies, we know brain stimulation alter the excitability and plasticity of stimulated region and its connected regions based on polarity, frequency and patterns of stimulation. Further, newer protocols of stimulation, tailor made protocols depending onthe genetic and clinical profiles of patients, newer brain stimulation techniques and possible combination of various modes of brain stimulation, which are emerging in research and clinical practice of these neuropsychiatric conditions. These newer protocols or combination of brain stimulation techniques may potentially augment both understanding the pathophysiology as well as treatment strategies for various disabling neurodegenerative disorders.

Factors guiding the selective vulnerability of dopaminergic neurons in Parkinson's disease

Poonam Thakur
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Abstract

Parkinson's disease is associated with α-synuclein aggregation and progressive loss of substantia nigra dopaminergic neurons (SN DA-neurons). The precise mechanism(s) behind the selective vulnerability of SN DA-neurons to α-synuclein aggregation in comparison to ventral tegmental area (VTA) DA neurons is not known. Even within SN, DA-neurons in ventro-lateral tier degenerate earlier and to a larger extent compared to the neurons in dorso-medial tier.

In our lab we focus on the cellular mechanisms by which α-synuclein aggregates cause toxicity to the cells as well as why different cell populations have a different response to them. In my talk, I will focus on the involvement of the K-ATP channel as a molecular player in determining α-synuclein's toxicity to dopaminergic cells.

Long-range intercellular transfer of organelles via tunneling nanotubes: implications in neurodegenerative and neurological diseases

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Sangeeta Nath

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Abstract

Cytoplasmic inclusions of α-synuclein (α-SYN) or Lewy bodies are the major hallmark of Parkinson's disease (PD). The contribution of extracellular α-SYN in PD pathology development and progression has been implicated by several studies. Additionally, exogenous α-SYN is known to activate neuroglial cells resulting in inflammatory microenvironments. We show that, upon exposure to α-SYN protofibrils, cancerous glial cells and primary astrocytes transfer toxic organelles through tunneling nanotubes (TNTs) and that aid in survival and proliferation. This TNT-mediated cell-to-cell transfer process not only accelerated degradation of α-SYN protofibrils, but helped cells to eliminate toxic dysfunctional mitochondria and curb ROS (reactive oxygen species) levels. Our studies delineate the contribution of TNTs in clearance of α-SYN protofibrils induced toxic organelles,which leads to transformation of neuroglial cells into hyperproliferative state.

Several studies have shown, neurodegenerative aggregates (including amyloid-β and α-SYN) induced endo-lysosomal toxicities promote biogenesis of TNTs in neurons. We have shown in our previous study, that internalization of amyloid-β aggregates into lysosomes via an actin- dependent endocytic pathway, promotes the formation of TNTs and cell-to-cell propagation of pathogenic aggregates. On the other hand, neuroglial-cells (glioblastoma and primary astrocytes) adapt to alternate TNT-mediated rescue mechanism and cell proliferation to get rid of toxic burdens. Interestingly, epidemiological and clinical evidences also suggest an increased risk of brain tumours in PD patients, the associations are noticeable in certain ethnicgroup pool. However, it is not known how TNT mediated cell-to-cell transfer of organelles can inversely work in these diseases, where one develops due to gradual cell death of neurons and other by rapid proliferation of cancer cells. Our studies reveal the contribution of TNTs in long range transfer of organelles in the brain cells and their implications in neurodegenerativeand neuroglial disease models.

Regulation of synaptic autophagy In neurodegenerative diseases

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Abstract

In many neurodegenerative diseases (NDs), including Alzheimer's, Huntington's and prion diseases, the cellular manifestation of disease pathology is seen earliest at the presynapse. Simultaneously, compromised proteostasis, including autophagy, is a hallmark of these NDs. Autophagy in neurons is highly compartmentalized and subtle modulation of presynaptic autophagy may confer neuroprotective effects against synaptopathies associated with such NDs. To investigate this idea, we first characterized synaptic dysfunction in vivo in a Drosophila model of Spinocerebellar Ataxia Type 3 (SCA3) using locomotion-based behavioural assays as surrogate readouts of presynaptic function. Further detailed characterization of glutamatergic synapses of motor neurons, the neuromuscular junctions (NMJs), revealed defects in the morphology and function of these synapses, with a concomitant defect in the autophagy pathway as a result of mutant Ataxin-3 overexpression. Our work aims to understand how modulation of the autophagy pathway can rescue defects associated with synaptopathies in vivo.

Fibrinogen and Complementary factor H are capable of inducing cognitive deficits inParkinson's disease: A study vide a translational approach.

Phalguni Anand Alladi
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Abstract:

Our previous non-targeted label free proteomics-based biomarker study, evidenced that fibrinogen and complement factor H (CFAH) were maximally upregulated in CSF of Parkinson's disease (PD) patients with cognitive impairment (PDCI). We therefore set out to investigate the pathogenic potential of these two proteins in bringing about or simulating PDCI- like symptoms, using the C57BL/6J mice strain as a model. We found that, fibrinogen induced a loss of dopaminergic neurons in the substantia nigra, compensatory hypertrophy of the surviving neurons, and reduction in striatal TH expression; thus reminiscing PD pathology. Hypertrophy of the surviving DA neurons implicates compensation against the neuronal loss, which was noted in case of both the proteins. The reduction in stride length in fibrinogen and CFAH injected mice indicates shuffling of gait, an important motor deficit in PD. In addition, we observed hypertrophic neurons in CA1 and subiculum indicating degenerative effects on cognitive functions. The low discrimination index in NOR test in the fibrinogen-group imply impaired working (recognition) memory deficits. Thus, our study provides objective evidence that fibrinogen and CFAH bear the potential to induce motor and cognitive impairments in mice, akin to the PDCI-associated neuropathological deficits. These proteins need to be studied in detail to understand their application as biomarkers in the PD patients.

Apoptotic factors assist determination of strain-specific susceptibility of mice to Parkinsonian neurotoxin MPTP

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Abstract:

Identification of genetic mutations in Parkinson's disease (PD) promulgates the genetic nature of disease susceptibility. Resilience-associated genes being unknown till date, the normal genetic makeup of an individual may be considered as determinative too. Our earlier studies comparing the substantia nigra (SN) and striatum of C57BL/6J, CD-1 mice and their F1-crossbreds demonstrated neuroprotective role of admixing, against the neurotoxin MPTP. Further, the differences in levels of mitochondrial fission/fusion proteins in the SN of parent strains, imply effect on mitochondrial biogenesis. Our present investigations suggest that the baseline levels of apoptotic factors Bcl-2, Bax and AIF differ across the three strains and, are differentially altered in the SN following MPTP-administration. The reduction in complex-I levels exclusively in MPTP-injected C57BL/6J, reiterate mitochondrial involvement in PD pathogenesis. The MPTP-induced increase in complex-IV, in the midbrain of both parent strains may be compensatory in nature. Ultrastructural evaluation showed fairly preserved mitochondria in the dopaminergic neurons of CD-1 and F1-crossbreds. However, in CD-1, the endoplasmic reticulum demonstrated distinct luminal enlargement, bordering onto ballooning, suggesting proteinopathy as a possible initial trigger. The increase in α-synuclein in the pars reticulata of crossbreds suggests a supportive role for this output nucleus in compensating for the lost function of pars compacta. Alternatively, since α-synuclein over-expression occurs and is an indicator of degeneration in different brain regions in PD, the its increase here may suggest similar pathogenic outcome. Further understanding is required to resolve this biological contraption. Nevertheless, admixing reduces the risk against MPTP by favouring anti-apoptotic consequences. Similar neuroprotection may be envisaged in the admixed populace of Anglo-Indians.

Traumatic brain injury and its long-term consequences on dementiaand neurological comorbidities

D. Samba Reddy
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Abstract:

Traumatic brain injury (TBI) causes death and disability in young and aged people worldwide. TBI is a leading cause of acquired epilepsy referred to as post-traumatic epilepsy (PTE), characterized by spontaneous recurrent seizures (SRS) that start in the months or years following TBI. TBI is often associated with dementia and related memory dysfunction. An estimated 2.87 million people experience a TBI each year and over 280,000 victims are hospitalized due to a TBI in USA. About 5 million people in the US are living with a TBI-related disability. In India, the cases may be grossly underestimated since many mild TBI cases go untreated in the clinic. However,there are few treatment options for TBI and related damage. There is a critical need to develop animal models for advancing the neurotherapeutics of PTE, which accounts for 20% of all acquired epilepsy cases. Despite many attempts to create PTE in animals, success has been limited due to a lack of consistent spontaneous "epileptic" seizures after TBI. Recently, we developed an advanced cortical contusion model in mice that elicits a chronic state of PTE with SRS and robust epileptiform activity, along with cognitive comorbidities. Here we present a comprehensive phenotype of PTE after contusion brain injury in mice, which exhibit robust spontaneous seizures along with neuronal loss, inflammation, and cognitive dysfunction. Our broad profiling of a TBI mouse reveals features of progressive, long-lasting epileptic activity, unique contralateral hippocampal sclerosis, and comorbid mood and memory deficits. Though incidence was higher in the severe cohort, moderate injury elicited a robust epileptogenesis. Progressive neuronal damage, neurodegeneration, and inflammation signals were evident in many brain regions; comorbid behavior and cognitive deficits were observed for up to 4-months. SRS onset was correlated with the inception of interneuron loss after TBI. Contralateral hippocampalsclerosis was unique and well correlated with SRS, confirming a potential network basis for epileptogenesis. Collectively, this mouse model exhibits several hallmarks TBI sequelae reminiscent of human PTE and dementia This model provides a vital tool for probing molecular pathological mechanisms and therapeutic interventions for post-traumatic epileptogenesis and dementia.

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Sleep Disorders and Other Sequelae after Traumatic Brain Injury:Medical Therapeutics

Rama Maganti
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Abstract:

Traumatic brain injury (TBI) is a global problem from various causes including motor vehicle accidents and sports injuries commonly in civilians but also in military personnel from multiple causes including explosive injuries. The sequelae of TBI include posttraumatic epilepsy (PTE), sleep disorders, cognitive and motor deficits, and mood disorders such as depression or posttraumatic stress disorder (PTSD). The sequelae of TBI not only require long-term medical care but also cause a huge economic toll on patients, their families, and the society. Epidemiological data show that PTE constitutes 5% of all epilepsy and over 20% of cases of acquired epilepsy. Sleep disturbances can begin immediately after TBI and persist long after the injury. Epidemiological evidence also shows that sleep disturbances, mood disorders occur in 30-50% of the patients, requiring chronic health care. Sleep complaints in TBI patients range from insomnia to hypersomnia with polysomnographic studies showing sleep fragmentation and multiple sleep latency tests showing reduced latencies. Sleep disturbances and PTE often occurin the same patient after TBI. Moreover, sleep disruptions and epilepsy have a complex bidirectional relationship where each can exacerbate the other. Here, I will show how the sequelae of TBI can be studied mouse models to tease out the mechanisms of these sequelae. I will also show how treating sleep disturbances after TBI can be beneficial for the other sequelae. The data will underscore potential therapeutics for TBI with sleep aids having a specific mechanism of targeting orexin receptors in the brain.

Prostaglandin-E2 receptor EP2 antagonist attenuates inflammation in vitro and alters seizures in a traumatic brain injury model

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Abstract

Traumatic brain injury (TBI) affects everyone from children to older adults. TBI leads to long-term disability in the form of neuropsychiatric or neurological disorders. Moreover, TBI patients are at high risk for developing post traumatic epilepsy. In patients, TBI induces massive inflammatory reaction, oxidative-stress and disruption of blood-brain-barrier in the brain and these features lead to emergence of posttraumatic epilepsy. We hypothesize that targeting these pathways with pharmacological agents could be an effective therapeutic strategy to prevent epileptogenesis and to mitigate the other long-term consequences of TBI. Prostaglandin-E_2 receptor EP2 subtype has emerged as an important biological target that mediates much of the inducible cyclooxygenase-2 (COX-2) driven inflammation following the brain injuries such as TBI and status epilepticus. We recently identified and developed a novel class of EP2 antagonists. We tested one of the lead antagonists TG8-260 and found that it is anti-inflammatory in in vitro cellular models (BV2 cells overexpressing *human* EP2 receptors) and in vivo models of status epilepticus. We further utilized a fluid percussion injury (FPI) rat model of TBI to study temporal expression of neuroinflammatory and oxidative-stress markers from 3-24 hours following FPI injury and found that FPI results in increased protein and mRNA expression of inflammatory mediators including COX-2 and EP2 receptor, NOX2 as a marker of oxidative-stress, astrogliosis and microgliosis in cortex and hippocampus. To derive the proof-of- concept for anti-epileptogenesis, we tested EP2 antagonist TG8-260 and found that it reduces distribution of seizure duration in rats post FPI, and trends towards reduction in seizure incidence, seizure frequency and duration. Overall, my presentation will discuss the EP2 receptorpharmacology, biology and therapeutic opportunities for targeting the EP2 with small molecules to mitigate TBI induced co-morbidities.

Psychoneuropharmacological Updates on Pathobiology of CognitionDeficits in Epilepsy

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Abstract

The cognitive deficit appears as one of the major comorbid conditions affecting majorly in children with epilepsy which results in poor learning, school dropouts and social stigma in these patients. The management of cognitive impairment often gets complicated due to negative effect of antiepileptic drugs on learning and memory consolidation. The adjuvant therapy with cognitive enhancers poses significant risk of seizure precipitation. The basic understanding regarding the molecular mechanisms of cognitive impairment in epilepsy is still poorly understood. We evaluated the occurrence of learning and memory in pentylenetetrazol induced kindling in mice and attempted to evaluate the neurochemical alterations in cortex and hippocampus of kindled brain. We identified specific reduction in cortical and hippocampal serotonin level and elevation in cortical and hippocampal acetylcholinesterase (AChE) levels. Based upon these preliminary findings, an attempt was made for AChE inhibitor along with phenytoin. However, this adjuvant treatment resulted in enhanced seizure severity score possibly via reducing the cortical and hippocampal serotonin level. Meanwhile, role of 5-HT1A/5-HT2A/2C/5-HT3 receptor modulation was investigated on cognitive function in kindled brain. It was observed that antagonism of 5-HT3 receptor (with ondansetron) resulted in improvement in memory deficit along withreduction in seizure severity, possibly via improving excitatory/inhibitory neurotransmitter balance and simultaneous reduction in AChE activity in cortex and hippocampus. Further, agonism of 5-HT2A/2C receptor also resulted in improvement of memory impairment in kindled animals. Overall, the modulation of serotonergic receptors in kindled animals, suggested the possible involvement ofserotonergic receptors in pathobiology of cognitive comorbidity in epilepsy. Thus, the findings of the study further advocate the use of serotonergic modulators for the management of cognitive deficit in epilepsy after systematic investigations.



POSTER SESSIONS



Parkinson's pathology induced mitochondrial toxicities promote biogenesis of tunneling nanotubes and proliferation of glial cells

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Abstract

Epidemiological studies reported since 1980s that Parkinson's disease (PD) negatively correlates with most of the cancers, except melanoma and breast cancer. Later accumulative evidences established significant positive association between PD patients and brain tumor, including meningioma, astrocytoma and glioblastoma multiforme. It is not known how molecular pathogenesis can inversely work in these two diseases. We have observed that exposure of α-synuclein (α-SYN) protofibrils causes increase in biogenesis of f-actin-based membrane conduits and tunneling nanotubes (TNTs) in the human glioblastoma-astrocytoma cell line U-87MG (GBM), for a transient period of time. The nascent f-actin nano-sized membrane networks were characterized and distinguished from tumor microtubes interms of negative β-tubulin staining and the hovering nature of the TNTs between two neighboring cells, using 3D-volume view with confocal Z-stacks. The TNTs facilitate transfer of α-SYN, and organelles such as lysosomes and mitochondria between neighbouring cells. TNT mediated cell-to-cell transfer eases degradation of α-SYN protofibrils and helps GBM cells to cope up with the toxic aggregates, induced ROS (reactive oxygen species) levels and toxic dysfunctional mitochondria. Eventually, TNT-mediated transfers promote GBM cell proliferation generating a CD133 positive cancer stem cell population. A recent study showed, mitochondria are transferred in astrocytes via TNTs to facilitate cell proliferation, supporting our observation. This study could open up potential therapeutic strategies to treat resistant cancer cell population targeting biogenesis of TNTs. The study will also explain possible molecular basis to support epidemiological correlation between PD and glioblastoma multiforme.
Key words: cell-cell transfer, Parkinson's disease, α- synuclein, glioblastoma multiforme, tunneling nanotubes, reactive oxygen species (ROS), mitochondria, cancer stem cells.

Unveiling the dopamine-rescue potential of a novel phytoconstituent of *Garcinia sp.* in Parkinson's disease

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Abstract

Introduction: Parkinson's disease (PD) is characterized by the progressive degeneration of dopamine containing neurons of substantia nigra pars compacta region of the midbrain. Loss of dopaminergic neurons results in significant depletion of dopamine levels in the striatum thereby leading to motor abnormalities in PD. Despite intensive research, the exact aetiology of disease still remains obscure, while the therapies provide only symptomatic relief. Studies brought to light the efficacy of different bioactive components in neurodegenerative diseases including PD. Garcinol-one of the active phytoconstituent of *Garcinia sp.* is recently reported to have beneficial effect in different diseases, however, its role in Parkinson's disease is yet to be revealed.

Main methods: To test the efficacy of the biomolecule-garcinol, it was administered into the neurotoxin- induced PD mice as well as naïve animals. Mice were than subjected to motor behavioural assessment, following which they were sacrificed for analyses of nigro-striatal dopaminergic pathway. Different parkinsonian motor-behavioural parameters were studied. While the status of dopaminergic neurons was assessed by immunohistochemistry.

Results: This bioactive molecule garcinol was found to significantly ameliorate the motor behavioural anomalies observed in the parkinsonian mice. Interestingly, in the garcinol administered PD mice, degeneration of dopaminergic neurons was significantly prevented. The underlying mechanism for neuroprotection was found to be due to amelioration of neuroinflammation.

Significance of the study: The findings of this study for the first time highlighted the efficacy of the biomolecule garcinol, to attenuate the motor behavioural dysfunctions and dopaminergic neurodegeneration in the neurotoxin-induced mice model of PD. Thus, the present study puts forward a plausible anti-parkinsonian bioactive compound garcinol, which might serve as a potent drug candidate in Parkinson's disease therapeuticsin the near future.

Intranasal administration of GABA-loaded extracellular vesicles from GABA progenitors reduces seizures in temporal lobe epilepsy

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Abstract

Medial Ganglionic eminence (MGE) cells are the main precursors of GABA-producing interneurons. Studies reveal that abnormal GABA-mediated inhibition leads to imbalance in excitatory-inhibitory neurotransmission and is considered as one of the reasons for chronic temporal lobe epilepsy. Transplantation of GABA producing cells reduces spontaneous recurrent seizures in chronic epilepsy. However, cell transplantation in epilepsy has several barriers. Herein, we have tested the hypothesis that whether exogenously loaded GABA in extracellular vesicle (EVs) from MGE cells could control seizures in chronic epilepsy. GABA was loaded to isolated EVs at room temperature and intranasally administered once a day for a week to repeated low-dose Kainic acid-induced chronic epileptic rats. The total number of seizures and time spent in seizures before and after the treatment were observed. The frequency of stage III, IV and V seizures were also compared before and after treatment. Chronic epilepsy-related comorbidities were evaluated by behavioral tests like novel object recognition test (NORT), Object location test (OLT) and novelty suppressed feeding test (NSFT). A significant reduction in frequency and duration of SRMS was seen in rats treated with GABA-loaded MGE-EVs. Evaluation of behavior tests reveal that, in NORT and OLT, no significant improvements was observed, while NSFT showed a significant decrease in the latency time to first bite before and after treatment. Our results demonstrates that treatment with GABA loaded EVs from MGE cells control seizures while behavior improvements were observed partially in chronic epilepsy.

Psychobiotics shape epigenetic reprogramming in the hippocampus via NF-kB-mediated histone acetylation: A role in trauma-induced learning and memory deficits

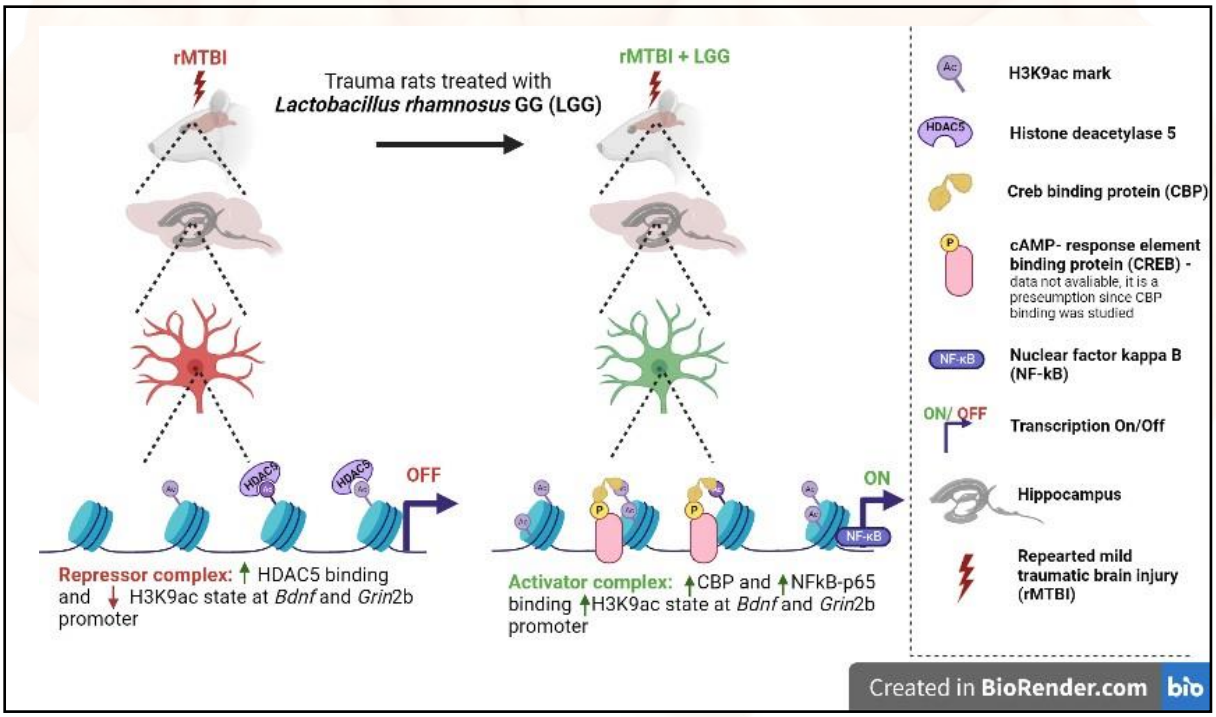
Gouri Jadhav and Amul Sakharkar
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Abstract

Cognitive loss is fairly common among patients with mild traumatic brain injuries. Experience-dependent epigenetic remodelling shapes activity-dependent neuroplasticity via gene expression. Hence, neuro-epigenetic aberrations in hippocampal plasticity are central to understanding the molecular basis of learning and memory impairments. While gut microbiota is studied widely for its role in the gut-brain axis; clinical manifestations of trauma display gut dysbiosis and its repercussions on host metabolism, health and behaviour. Therefore, microbiota emerges as potential psychobiotics to serve as non-invasive therapeutics for neuropsychiatric disorders. In the current study, repeated mild traumatic brain injury (rMTBI) was inflicted in adult male Wistar rats (n=8) by closed head weight- drop injury model. Five hits on alternate days were applied to induce long-term cognitive deficits. rMTBI caused learning and memory deficits in novel object recognition (NOR) and 8-arm radial maze tests. rMTBI reduced gut motility accompanied by dysbiosis, attributing to low colonization of short-chain fatty acid (SCFA), butyrate producers. We hypothesize that butyrate producing psychobiotics may reverse rMTBI-induced chromatin remodelling in the hippocampus, thereby restoring synaptic plasticity and deficits in learning and memory. After 30 days of rMTBI, a single strain probiotic – *Lactobacillus rhamnosus* GG (LGG at 10^8 CFU/ml) was administered 10 times, one dose each on alternate days by oral gavage. Trauma decreased brain-derived neurotrophic factor (*Bdnf*) and glutamate receptor (*Grin* 2B subunit) gene levels indicating hypofunction of synaptic plasticity in the hippocampus. Chromatin status at both *Bdnf* exon IX (*Bdnf* IXp) and *Grin* 2B promoter suggested the formation of repression complex, as observed in the form of hypoacetylated state (low H3K9ac levels) with high binding of histone deacetylases 5 (HDAC5) at promoters. Trauma decreased expression of NF-kB subunits, NF-kB1 and Rel A. Role of NFkB-p65 in the facilitation of CBP binding at *Bdnf* promoter is shown previously to induce histone acetylation. NFkB-p65 shows synaptic activity detection and relay of information to nuclease as a transcription factor for synaptic plasticity encoding gene expression. Trauma attenuated the binding of

both NFkB-p65 and CBP at *Bdnf* IXp and Grin2Bp. Gut probiosis in rMTBI rats using LGG restored trauma-induced decrease in *Bdnf* IX and *Grin* 2B expression. Formation of activator complex at *Bdnf* IXp and G*rin* 2Bp was observed with increased binding of NFkB-p65 and CBP with concomitant improvement in histone acetylation (H3K9ac levels). Hence, LGG treatment in trauma rats could improve synaptic plasticity by undertaking epigenetic changes at *Bdnf* and *Grin* 2B promoters, which might normalize learning and memory behaviour. The study implicates gut dysbiosis in shaping the behaviour by undertaking epigenetic remodelling to alter the synaptic plasticity. The notion is supported by the observation that the treatment with psychobiotic, such as LGG, could reverse the dramatic changes in plasticity and behaviour. Hence, psychobiotics may prove as a promising therapeutic intervention that might be effective in the management of neuropsychiatric disorders.

Graphic abstract:



[#] Supported by RUSA, DST-SERB, UGC

Genome Diversity and genetic interplay of *Burkholderia pseudomallei* causing Neuromelioidosis in patients from Indian setup.

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Abstract

Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*, a gram-negative soil saprophyte. The disease is endemic to Northern Australia, Northeast Thailand, and South Asian tropical regions such as the Indian subcontinent, but it is underreported in many other equatorial regions. Neuromelioidosis is a rare clinical complication that is most often undiagnosed or misdiagnosed. We have diagnosed a significant number of neuromelioidosis cases in India. *B. pseudomallei* genome is reported to be vast comprising two chromosomes consisting of 4.07 and 3.14 Mbp respectively. Considering the potential to be used as a bioweapon, *B. pseudomallei* and *B. mallei* are classified in the United States as Tier 1 selects agent as they can be used for bioterrorism. Apparently, the genome is complex with a high rate of horizontal gene transfer. Any considerable variation among the genomes is likely to impart differential virulence which is often interpreted geographically.

We isolated and characterized *B. pseudomallei* strains from clinical samples of patients with Melioidosis. The genome of these clinical isolates were sequenced using Illumina HiSeq 2500 platform and the raw data was bioinformatically analysed using a custom analysis pipeline. Virulome profiling and comparative genome analysis between different species belonging to the Burkholderia genus and the clinical isolates of *B. pseudomallei* reveal that few genes related to Burkholderia virulence are considerably different. We have found functionally different genes such as *sugC, LPS-rfb* and *cysC1* of native *B. pseudomallei* strains as compared to the global reference strain. We note the presence of genomic islands which is indicative of horizontal gene transfers. Notably few virulent genes, *gmhA* and *gmhB2* proteins associated with bacterial pathogenesis during the escape of host phagosome were found in the genome island elements. Further *in silico* proteomic analysis indicated two genes *lolA* and *ompV* as potential candidates for vaccine development. In our ongoing studies, we would like to decipher the etiology behind the pathophysiology of melioidosis especially Neuromelioidosis using *in vitro* systems.

Keywords: Neuromelioidosis, Melioidosis, *B. pseudomallei*, Genome Islands, Virulent genes, outer membrane proteins, Vaccine candidates, Bioweapon, India.

Identification of common biological pathways between Alzheimers Disease and Metabolic Disorders through transcriptomic analysis

Abstract

Alzheimer's Disease (AD) is a prominent age-related neurodegenerative disorder, which leads to deterioration in cognitive ability, progressive loss of memory and major behavioural changes. It is the most common form of dementia and approximately accounts for 60-70% of total dementia cases reported all over the world. Recent evidence has revealed that people afflicted with metabolic disorders like Diabetes and Obesity have a higher chance of developing AD than the normal population. As number of individuals affected by metabolic disorders reaches epidemic proportions in developed and developing nations, the patients impacted by AD will also exponentially grow. However, the exact mechanism responsible for this association is not fully understood. Therefore, it is essential to discover the underlying pathways and molecular targets which might aid in unravelling this mystery. The current study aimed to discover novel associations between AD, Diabetes and Obesity through in-silico means. Briefly, gene expression datasets from NCBI Gene Expression Omnibus (GEO) were downloaded and subjected to transcriptomic analysis to discover Differentially Expressed Genes (DEGs) in all three diseases through GEO2R (a R package to determine significant DEGs in datasets). Additionally, pathway enrichment analysis was carried out by MolSig database to discover common pathways and categorize the DEGs into significant pathways. From MolSig, a hub of pathways, mainly linked through MAPK signalling, was shortlisted for further studies. The pathways identified included Neurotrophin signalling pathway, Chemokine signalling, Insulin signalling pathway, Calcium signalling, Endocytosis, Focal Adhesion and Lysosome. Further, these pathways were categorized into wider sub-headings to get a clearer idea about the overall related functioning of the systems involved. Moreover, we also discovered common genes between the datasets to delineate the reason behind AD progression and understand it's pathophysiology better. The results obtained from this study have identified novel cellular and molecular mechanisms that might link AD progression with metabolic disorders and will further aid in formulating new treatment regimens.

White matter microstructural changes in early onset schizophrenia Using Diffusion tensorimaging (DTI) Study

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Abstract

The aim of this study is to investigate micro-structural disruption of white matter tracts in early-onset Schizophrenia (EOS). Our finding revealed decreased fractional anisotropy (FA) and increased radial, axial and mean diffusivity in corticospinal tracts (CST), Anterior thalamic radiation (ATR), Inferior fronto-occipital fasciculus (IFO), Superior longitudinal fasciculus (SLF), Inferior longitudinal fasciculus (ILF), Superior longitudinal fasciculus (SLFT), Forceps major (FM) and Uncinate fasciculus (UF) in early onset schizophrenia (EOS) as compared to controls. The results are suggestive of thinner packing of axon and fiber bundle and impairment in axonal integrity, visuospatial processing, motor function, emotional and social withdrawal behavior in EOS.

Introduction: The Schizophrenia appearing between 13-18 years of age is referred as early onset schizophrenia (EOS). It is a chronic disorder and affect nearly 1% of the world's population with cognitive impairment. EOS have premorbid neurodevelopmental abnormalities and worse long-term outcome, cytogenetic anomalies. Hallucinations, delusions, altered thoughts, social withdrawal, loss of speech are some of the symptoms in EOS. Diffusion tensor imaging (DTI) study reported white matter abnormalities of the bilateral corticospinal (CST), left inferior longitudinal fasciculus (ILF) and left inferior fronto-occipital fasciculus (IFOF), optic radiations, internal cap right ALIC in EOS[1-3]. In present study, we used Tract-Based Spatial Statistics (TBSS) of DTI measures to investigate micro-structural disruption of white matter tracts in EOS.

Materials and Methods: Eighteen EOS patients (mean age 17.68±2.15 years; 7F/11M) who met ICD-10 (code F20) criteriawere recruited from the psychiatric clinics. Seventeen healthy subjects (age=20.9±0.99, 6F/11M) with no history of neurological and psychiatric disorder were recruited from local community. The study was approved by the institutional ethics committee. DTI data were acquired on a 3T MRI (Ingenia 3.0 T, M/s Philips Health Care, Netherlands) using 32-channel head coil, with parameters: b-values=0, 1000 s/mm^2, 64 diffusion directions, slice thickness=3 mm with no inter-slice gap, number of slices=50, TR/TE = 6642/86 ms. Data was processed using FSL[4].

Results: Decreased fractional anisotropy (FA) and increased radial, axial and mean diffusivity was observed in corticospinal tracts (CST), Anterior thalamic radiation (ATR), Inferior fronto-occipital fasciculus (IFO), Superior longitudinal fasciculus (SLF), Inferior longitudinal fasciculus (ILF), Superior longitudinal fasciculus (SLFT), Forceps major (FM) and Uncinate fasciculus (UF) in EOS with respect to that in controls (Figure 1, Table 1).

Discussion: Atrophy in the white matter regions (especially in the CST, ATR, IFOF), decreased FA, increased MD and RD in EOS maybe suggestive of thinner packing of axon and fiber bundle[3,5]. Increased AD suggests impairment in axonal integrity[3]. Altered connection IFOF fiber suggest impaired visuospatial processing. CST fiber connection may be attributed to impaired motor function, and ATR fibers connection to impaired emotional and social withdrawal behavior in EOS.

Conclusion: Our findings suggest that EOS demonstrated widespread reduction of FA, MD, RD, AD in major white matter pathways and such abnormal white matter structure may be linked to cognitive and behavioural impairment.

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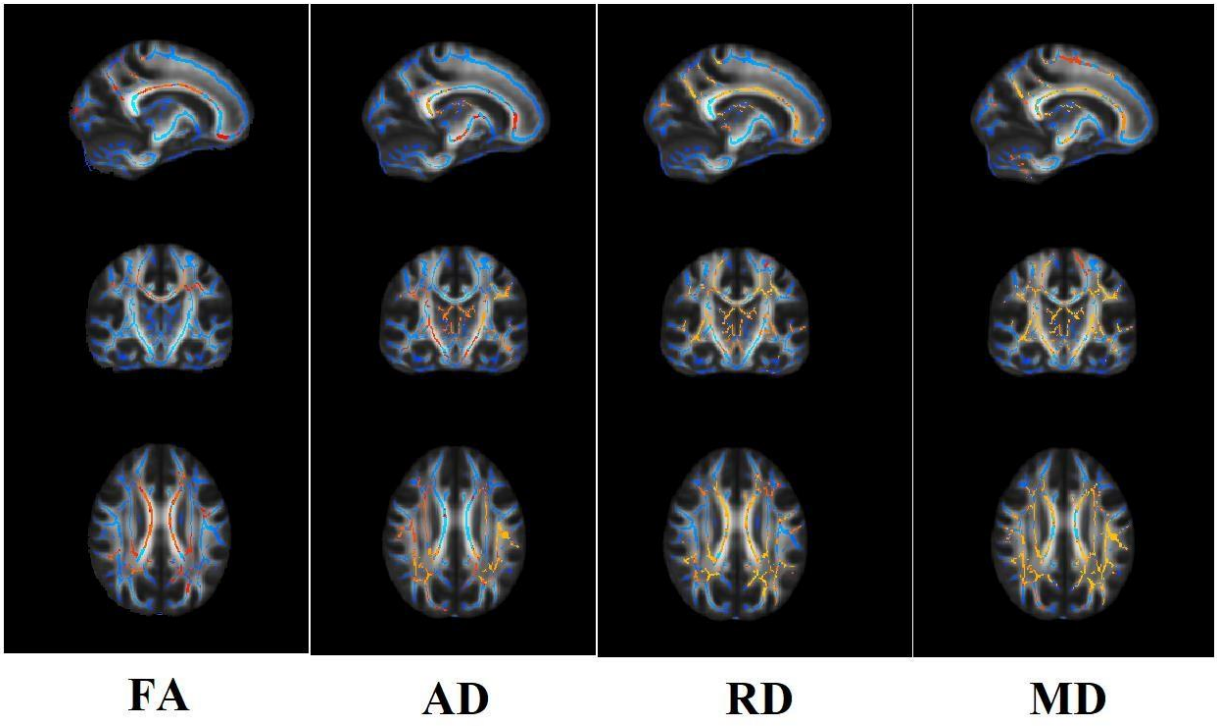


Figure 1: Figure showed the decrease FA and increase RD, AD and MD diffusivity in EOS as compared to control in the following white matter tract: ATR, CST, IFO, FM, ILF, SLF, UF, Cingulum (cingulate gyrus)

Table 1. Fractional anisotropy (FA), radial diffusivity (RD) and axial diffusivity (AD) and Mean diffusivity (MD) values from the white matter tracts of the brain in early onset schizophrenia (EOS) as compared to controls.

Diffusion metrics	Fibers	Control (N=17)	EOS (N=18)	P value		Control (N=17	EOS (N=18)	p-value
FA	RATR	0.463±0.033	0.428±0.041	.009	MD	0.780±0.032	0.904±0.15	.003
	LATR	0.474±0.037	0.435±0.043	.007		0.773±0.037	0.869±0.10	.001
	RCST	0.555±0.029	0.516±0.041	.003		0.692±0.023	0.721±0.03	.004
	LCST	0.538 ±0.033	0.498±0.033	.001		0.673±0.024	0.703±0.02	.001
	RIFO	0.465 ±0.028	0.432±0.038	.007		0.767±0.022	0.799±0.04	.004
	LIFO	0.539 ±0.037	0.502±0.039	.006		0.749±0.027	0.784±0.03	.002
	FM	0.607±0.032	0.570±0.045	.009		0.742±0.028	0.784±0.04	.001
	RSLF	0.516 ±0.035	0.485±0.043	.024		0.715±0.024	0.754±0.04	.021
	LSLF	0.535±0.031	0.494±0.036	.001		0.700±0.029	0.735±0.03	.002
	RILF	0.467 ±0.023	0.430±0.030	.000		0.725±0.023	0.740±0.03	.007
	LILF	0.492±0.028	0.456±0.023	.000		0.703±0.027	0.735±0.03	.002
	RUF	0.509±0.033	0.473±0.047	.015		0.758±0.022	0.788±0.03	.003
	LUF	0.537±0.040	0.497±0.050	.014		0.744±0.03	0.777±0.02	.002
RD	RATR	0.606±0.03	0.720±0.13	.002	AD	1.10±0.04	1.27±0.22	.005
	LATR	0.608±0.04	0.716±0.11	.001		1.15±0.04	1.26±0.13	.001

	RCST	0.425±0.03	0.464±0.03	.001		1.31±0.03	1.36±0.05	.007
	LCST	0.425±0.03	0.466±0.03	.001		1.33±0.03	1.37±0.04	.001
	RIFO	0.540±0.03	0.578±0.04	.004		1.27±0.03	1.30±0.06	.03
	LIFO	0.502±0.03	0.546±0.03	.000		1.20±0.02	1.25±0.05	.002
	FM	0.411±0.04	0.454±0.05	.006		1.53±0.05	1.61±0.06	.000
	RSLF	0.476±0.03	0.513±0.05	.015		1.12±0.04	1.16±0.06	.048
	LSLF	0.475±0.03	0.518±0.04	.002		1.13±0.04	1.17±0.04	.019
	RILF	0.536±0.03	0.577±0.04	.001		1.09±0.03	1.12±0.05	.008
	LILF	0.504±0.03	0.543±0.03	.001		1.10±0.03	1.14±0.04	.005

Abstract

Parkinson's disease (PD) is the most common neurodegenerative disorder after Alzheimer's disease. Worldwide, it affects a broad range of populations over the age of 60 years. Around 3 million populations all over the world suffer from the devitalizing symptoms of Parkinson's like tremors, muscle rigidity, bradykinesia, and impaired gait.

Apart from these symptoms, some of the studies have also established the fact that the Gut microbial community plays a major role in the onset and progression of the disease and that the gut microbiota of PD patients is different from that of a healthy human being. A decrease in the abundance of the family *Prevotellaceae*, with genus *Prevotella* and species *Prevotella copri*, has been found. Also, some of the bacteria have been found to increase prominently in PD patients' guts like *Akkermansia, Proteus species, Enterobacter* and there are many more.

Our study aims to analyze the composition of gut microbiota of PD patients in the Indian population using stool samples from the patient. The identification of the microbes will be done through phenotypic and genotypic processes i.e. by biochemical tests and by applying ERIC and RAPD-PCR respectively. Along with this, 'Rotenone' induced mice model for Parkinson's will be developed and its gut microbiota will be analyzed relative to human samples. Further, we plan to apply Phage therapy to the animal using some specific bacteriophage against the bacteria of our interest from PD patients which differ from the control group.

We hope to find a positive correlation between the gut flora and the disease onset and progression and we expect a result like an improvement in motor coordination after the application of phage therapy as this would help to balance the gut microbiota of the patient. The result would be analyzed through the brain sections of a model and using an immunofluorescent labeling technique to identify the effect of phage in the phage-treated mice.

Identification of common biological pathways between Alzheimers Disease (AD) and Metabolic Disorders (MD) through transcriptomic analysis

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Abstract

Alzheimer's Disease (AD) is a prominent age-related neurodegenerative disorder, which leads to deterioration in cognitive ability, progressive loss of memory and major behavioural changes. It is the most common form of dementia and approximately accounts for 60-70% of total dementia cases reported all over the world. Recent evidence has revealed that people afflicted with metabolic disorders like Diabetes and Obesity have a higher chance of developing AD than the normal population. As number of individuals affected by metabolic disorders reaches epidemic proportions in developed and developing nations, the patients impacted by AD will also exponentially grow. However, the exact mechanism responsible for this association is not fully understood. Therefore, it is essential to discover the underlying pathways and molecular targets which might aid in unravelling this mystery. The current study aimed to discover novel associations between AD, Diabetes and Obesity through in-silico means. Briefly, gene expression datasets from NCBI Gene Expression Omnibus (GEO) were downloaded and subjected to transcriptomic analysis to discover Differentially Expressed Genes (DEGs) in all three diseases through GEO2R (a R package to determine significant DEGs in datasets). Additionally, pathway enrichment analysis was carried out by MolSig database to discover common pathways and categorize the DEGs into significant pathways. From MolSig, a hub of pathways, mainly linked through MAPK signalling, was shortlisted for further studies. The pathways identified included Neurotrophin signalling pathway, Chemokine signalling, Insulin signalling pathway, Calcium signalling, Endocytosis, Focal Adhesion and Lysosome. Further, these pathways were categorized into wider sub-headings to get a clearer idea about the overall related functioning of the systems involved. Moreover, we also discovered common genes between the datasets to delineate the reason behind AD progression and understand it's pathophysiology better. The results obtained from this study have identified novel cellular and molecular mechanisms that might link AD progression with metabolic disorders and will further aid in formulating new treatment regimens.

Preserved cognitive and neural profile through intervention with a novel combination ofFucoidan and environmental enrichment in the rat model of transient global cerebral ischemia.

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Abstract

Acute global loss of cerebral blood flow results in selective neural damage, especially to the CA1 pyramidal neurons of the dorsal hippocampus followed by progressive cognitive impairment. This study was designed to understand the efficacy of a novel combination of intervention with Fucoidan extracted from brown seaweed - Fucus vesiculosis and exposure to an enriched environment. The cognitive profile, neuro-inflammation, and angiogenesis in the hippocampus, primarily the CA1 region was assessed. Adult male Wistar albino rats of 250-300 gram body weight were used for this study, and the rats were exposed to 4VO, i.e., four-vessel occlusion for 15 minutes (Permanent occlusion of vertebral arteries followed by clamping of both common carotid arteries for 15 minutes to create transient global cerebral ischemia in rats), then randomly divided into five groups: Sham, Lesion (4VO), 4VO+ EE, 4VO+Fucoidan 50mg/kg, 4VO+Fucoidan 50mg/kg+ EE. All the aforementioned groups were evaluated for their cognitive ability through the Morris water maze, Novel object recognition task, T- Maze; the exploratory and anxiety level were assessed using the Open field test, Hole board task, and elevated plus maze. The CA1 region of the hippocampus was subjected to histopathological assessment, the expression of a pro-inflammatory marker, (IL1-β, IL6, NFκB, TNF-α, CD68) and the expression of angiogenic markers (HIFα, AngI, MMP2, MMP9, VEGFR) was assessed through western blot assessment. The outcome of the study implies that combined intervention of Fucoidan, and enriched environment exposed to the 4VO rats, showed better cognitive behavioural outcomes. The cytoarchitecture of CA1 pyramidal neurons was well preserved in the combination treatment group than others. The proinflammatory markers were found to be downregulated, while the angiogenic markers were seen to be upregulated in the combination treatment groups when compared to the lesion group and sham alone group. In conclusion, this intervention of a combination of Fucoidan in an enriched environment provided a better outcome in preserving the neural and cognitive profile of transient global cerebral ischemic rats.

Network pharmacological evaluation of origanum vulgare bioactivephytochemicals for identifying novel potential inhibitors against alzheimer disease

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Abstract

Due to the complexity of the pathogenic pathways behind Alzheimer disease (AD), mounting research suggests that treating diseases with complicated aetiology using traditional medicine may be more effective when using many components and targets. The goal of the study was to use an integrated network pharmacology approach to preliminary understand the bioactive components and probable mechanisms of Origanum vulgare for AD prevention and treatment. To fulfill this objective, Network pharmacology approach, gene ontology, pharmacokinetic analysis, molecular docking and molecular dynamic stimulation (MDS) studies were performed. A total of 176 active component in Origanum vulgare, 7 predicted Alzheimer disease target of *origanum vulgare*, and 11400 Alzheimer related target were identified from different database. The network analysis showed that the top 10 targets APP, GSK3B, AXIN1, APBB1, HSD17B10, FRAT1, CTSD, NUMB, APLP1, GAPDH were found as significant target related to Alzheimer disease. On the basis of gene ontology and topology analysis results, APP was found as a significant target to Alzheimer disease pathways. Molecular docking results found that Elemol ,Selin-11-en-4-ol, (-)-alpha-Cadinol, Spathulenol, Caryophyllene oxideshowed the best binding affinities -6.59, -6.46, -7.06, -7.39, -7.39kcal/mol. Further, MDS results suggested that Spathulenol, Caryophyllene oxidecould be used as potential inhibitors against APP protein and could be useful for the treatment of Alzheimer disease.

Keywords: Origanum vulgare, Alzheimer disease, Network pharmacology, Molecular docking, ADME.

The status of vernier acuity following late sight onset

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Abstract

Background and rationale: A widely used index of clarity of vision is Snellen acuity, which characterises an observer's ability to resolve closely separated stimuli. 'Normal' 20/20 vision corresponds to a resolution acuity of 1 minute of arc. A complementary assay of visual function is vernier acuity, which measures how well a person can detect misalignments between extended contours. This is generally considered a kind of 'hyper-acuity' since the detectable misalignments are typically finer than the diameter of single retinal cones. The ability to resolve such small misalignments is believed to reflect cortical processing. This makes vernier acuity a potentially useful index to study the status of cortical function, and longitudinal changes therein.

Methods: We examined resolution and vernier acuities in an unusual population of observers – those who had been blind for the first several years of life and then had received sight surgeries. Given the advanced ages of these subjects, past studies on critical periods of brain plasticity would posit that there would be little, if any, change in the functional status of the visual cortex following sight surgery. We sought to test this prediction empirically by examining whether there were any discernible changes in vernier acuity as a function of time post surgery. As part of Project Prakash, we collected data from 17 late-sighted participants ranging in age from 7 to 21 years (mean 11.29 years). Over a period of a year, we longitudinally assessed their visual function.

Results: Our data reveal that although the subjects do not reach typical levels of resolution and vernier acuities, they do exhibit a surprising amount of improvement as a function of time. These findings point to the availability of significant neural plasticity in the primary visual cortex even several years following birth.

Conclusion: The results have basic scientific implications for our conceptions of the timelines of cortical plasticity, and applied implications for the prospects of visual rehabilitation in childrenfollowing treatment for congenital blindness.

Ethics statement: The study was approved by the IRBs of MIT and SCEH. Informed consent/assent was obtained from all participants.

Role of exosomal miRNAs in Amyotrophic lateral sclerosis.

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Abstract

Amyotrophic lateral sclerosis (ALS) is a fatal, adult-onset neurodegenerative disorder characterized by lossof upper and lower motor neurons. It results in progressive muscle weakness leading to atrophy and finallydeath within 3-5 years of onset of symptoms. Despite a plethora of evidence, cellular and molecular mechanisms underlying ALS pathogenesis still remain elusive. Recent evidence suggests that extracellular vesicles such as exosomes secreted by mammalian cells are likely responsible for the spread of interconnected neuronal cell death found in ALS pathogenesis. To identify ALS-associated exosomal miRNAs involved in communication between motor neurons and skeletal muscle cells, isolation of exosomes was done from the conditioned media of NSC-34 cells expressing wild type and mutant SOD1s. Characterization of exosomes using flow cytometry, nanoparticle tracking analysis and western blotting was performed by exosome specific markers such as CD9, CD81 and CD63. Exosomal miRNome was carried out by Illumina 150 bp paired end sequencing. For identification of target genes of significantly dysregulated miRNAs, miRWalk database (http://mirwalk.umm.uni-heidelberg.de/) was exploited. Molecular pathway analysis was performed using Gene Set Enrichment Analysis to identify enriched pathways. Pathways and GO (Gene Ontology) processes with p value ≤ 0.05 were considered significant. Several miRNAs including miR-34a-5p, miR-335-5p, miR-146b-5p, miR-205-5p and miR-196b-5p previously associated with ALS were identified. In-depth analysis is being carried out and the findings willbe presented.

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Effect of nootropics on SOD1-based cell model of AmyotrophicLateral Sclerosis

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Abstract

Background: Mutations in Superoxide Dismutase (SOD1) gene are associated with Amyotrophic Lateral sclerosis (ALS), a fatal neurodegenerative disease affecting upper and lower motor neurons. Toxicity of mutant SOD1 causes aberrant folding and formation of large insoluble aggregates of the protein. This results in increased oxidative stress, mitochondrial dysfunction leading to severe disease progression. Currently, there is no cure for ALS.
Rationale: Nootropics, the brain booster molecules are known to cross blood-brain barrier and have good bioavailability. Nootropics have been shown to have neuroprotective role in many neurodegenerative diseases including Alzheimer's disease, Parkinson Disease. However, role of various nootropics in ALS remains unexplored. In this study, we are using motor neuronal cell model to check the potential role of nootropics as therapeutics in ALS-linked SOD1 mutation.
Methods: Human mutant SOD1 fused with GFP exhibited aggregates in motor neuronal cell line. Nootropics were screened for their anti-aggregation potential by immunoblotting and fluorescent microscopy. Cell toxicity was determined by flow cytometry, lipid peroxidation by malondialdehyde and protein carbonylation by DNPH assay. Neurite outgrowth was observed by fluorescent microscopy where images were captured and analyzed using Sholl's analysis. To determine the molecular targets of nootropic, microarray was performed.
Results: Few nootropics have been screened for the effect on mutant SOD1 aggregation. Significant decrease in SOD1 aggregation was observed on treatment with one nootropic. This potent nootropic decreased celular toxicity, oxidative stress due to mutant SOD1. In addition, there was significant increase in neurite outgrowth on treatment. Microarray analysis shows interesting findings which will be presented.
Conclusion: A pilot screen has led to identification of a potent nootropic which exhibits neuroprotective effect and can be exploited to develop effective therapies for ALS. Expression analysis will helpto define the mechanism of action of this nootropic.
Acknowledgement: Authors acknowledge ICMR for funding. BKS and MM acknowledge ICMR for fellowships.SV acknowledges CSIR fellowship.

Deciphering disease mechanism in FUS-driven Juvenile Amyotrophic Lateral Sclerosis: a family quartet analysis

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Abstract

Amyotrophic lateral sclerosis (ALS) is a fatal adult onset neurodegenerative disorders characterized by loss of motor neurons. Juvenile ALS (JALS) is a rarer form of ALS which involves early age of onset (<25years). Molecular mechanisms underlying JALS pathology are still obscure. In this study, we have attempted to understand disease mechanisms in a 14-year-old boy with an aggressive sporadic JALS phenotype by multiomics approach in a family quartet. Whole exome sequencing led to identification of a novel *de-novo* variation in *FUS* gene in proband. This variation causes premature truncation and cytoplasmic mislocalization of FUS protein. Interestingly, co-occurrence of multiple rare and potentially deleterious mutations in other genes implicated in ALS and JALS, neuromuscular disorders and rare variants suggested oligogenic etiology of sporadic JALS. Transcriptome analysis showed abnormal expression of genes involved in inflammatory response, synaptic transmission, axonal regeneration and muscle contraction. In addition, metabolomics has been carried out for family quartet and the findings willbe presented.

Acknowledgments

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Seizure-associated, aberrant neurogenesis in adult mice characterized by alteration of the hippocampal neurogenic niche.

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Abstract

Background: Adult Hippocampal Neurogenesis participates in learning, memory and cognition and in the control of stress and anxiety. It is hypothesized that the impairment of some of these aforesaid functions following a seizure is promoted by alteration of neuronal activities at the neurogenic niche. Induction of seizure by the convulsant, Kainic Acid (KA) produces a well- established model of epilepsy to study adult neurogenesis as a response to excitotoxicity. Our present study demonstrates how the neurogenic niche of the dentate gyrus in the hippocampus is altered and is associated with aberrant neurogenesis, in response to KA-mediated seizure.
Methodology: KA was administered once intraperitoneally at a dose of 30mg/kg of animal body weight. The seizure-associated behavioural phenotypes were monitored for consecutive 2 hours following KA (IP) and based on seizure severity, the seizure score was given (based on a modified Racine scale; Luttjohann et al. BrdU was injected for 7 consecutive days following KA injection at dose 100 mg/kg mark the new-born neurons. Transcardial perfusion was performed and the brain sample was fixed and further processed by cryosection. Immunofluorescence was performed using a routine procedure.
Result: Enhanced proliferation of BrdU+ neuronal progenitors following KA-induced excitotoxicity in the adult brain is observed. Our result showed activation-dependent conversion of radial glial-like NSCs to reactive-like and gliogenic neural stem cells (NSCs) in the sub-granular zone (SGZ) that are associated with reactive morphologies i.e., loss of radial glial-like processes, hypertrophied, and change in their polarity at SGZ. In addition, significant aberrant neurogenesis is observed. Ectopic growth of newborn immature granular neurons and its abnormal migration in the dentate gyrus occurred. These newborn-immature neurons have their morphological features i.e., elongated basal dendrites and their polarity, altered.
Conclusion: In response to neuronal hyperexcitation following seizure, robust proliferation of neuronal progenitors at the neurogenic niche, SGZ of the dentate gyrus of adult mice has taken place. This contributes to the activation of the NSCs following reactive gliosis, leading to the depletion of the neurogenic niche. This phenomenon further is responsible for aberrant hippocampal neurogenesis.
Keywords: Adult Neurogenesis, neurogenic niche, neural stem cells, Aberrant neurogenesis

Role of genistein (GEN) in mild unpredictable stress exposed mouse

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Abstract

GEN is a phytoestrogen belongs to group flavonoids and showed estrogenic functions. GEN has potential to modulate inflammatory responses involving in neurodegenerative disorders. It is abundantly found in fava beans and soybeans. Further, GEN has antioxidant, anti-inflammatory anticancer and neuroprotective properties. Stress is a nonspecific response stimulated by several social and psychological factors. During stress, hippocampus, hypothalamus, amygdala *etc.* are affected and linked to anxiety, depression and cognitive deficits. In this study, seven mild stressors were given to 30weeksold male *Swiss Albino* mice for 1week followed by treatment with GEN 1mg/kg bw orally. Briefly, mice were placed into 4 groups; Control, Mild Stress (MS), MS+Vehicle and MS+GEN. For behavioral analysis, forced swimming test (FST), Rotarod test (RRT) and sucrose preference test (SPT) were performed. Further, acetylcholine esterase (AChE) activity was measured. Moreover, FST monitored depressive like behavior measured by immobility time of mouse in water. Results showed immobility time was increased in MS and MS+Vehicle whereas MS+GEN showed decrease in the immobility time as compared to control. Further, SPT measured anhedonia like behaviour in mice. Sucrose preference percentage was decreased in MS and MS+Vehicle whereas increased in MS+GEN group as compared to control. Furthermore, RRT was performed to evaluate motor coordination of mice. The latency to fall time was decreased in MS and MS+Vehicle and increased in MS+GEN as compared to control. Finally, AChE activity was lowered significantly in MS as compared to control whereas a slight increase was observed in vehicle and GEN. Several studies suggested involvement of estrogen mediated cholinergic system in neuronal functions such as memory, attention, anxiety and cognition. In conclusion, the present study may be helpful to understand cholinergic system related neurodegenerative diseases and abnormal brain functions.

Key words: Genistein, Mild Stress, Forced swimming test, Rotarod test, Sucrose preference test, Acetylcholine

Hydrogen sulphide enhances synaptic plasticity and restores cognitive dysfunction intraumatic brain injury induced mouse model

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Abstract

Introduction: Traumatic brain injury (TBI) affects millions of people annually, but effective treatments are lacking due to poor understanding of how injury impacts, persists and progresses to deteriorate neuronal function. H_2S has always been regarded as a toxic gas however, accumulating evidences suggest that it can execute neuroprotection in brain. Therefore, the present study focusses on the role of hydrogen sulphide (H_2S) on TBI induced neurological dysfunctions in mouse brain cortex.

Methods: Swiss albino male mice (16±2 weeks) were subjected to weight drop method of TBI. Animals were grouped into sham, TBI and TBI+NaHS groups. Mice of sham group were treated with intraperitoneal injections of saline (0.9% NaCl) and TBI+NaHS group was treated with NaHS (50µM/kg body weight) for 7 days. We estimated acetylcholinesterase enzyme (AChE) activity, assessed brain edema and performed reactive oxygen species (ROS) assay along with neurological severity score. Assessment of cognition were done using radial arm maze and Barnes maze test. The level of H_2S and various oxidative stress markers in the brain cortex was measured using ELISA kits. Immunoblotting studies and qRT-PCR were conducted for TBI biomarkers and synaptic biomarker proteins.

Results: TBI causes a drastic decrease in AChE activity, an increase in the brain edema, an elevated ROS production and a higher neurological severity score. The level of H_2S in the mouse brain cortex exhibited a dynamic decrease in parallel with glutathione and malondialdehyde levels. The increased expression of NSE, GFAP and UCH-L1 in TBI group validated the model. Moreover, the decreased expression of Bdnf, Arc, PSD-95 and synaptophysin reflects cognitive dysfunction which was also confirmed in the radial arm maze and Barnes maze test. H_2S ameliorates the aforementioned dysfunctions associated with TBI.

Conclusion: These findings suggest that hydrogen sulphide might have a potential protectiveeffect in a weight drop model of TBI.
Acknowledgements: CSIR-SRF and UGC- SEED grant for financial assistance.

Nanoscale Regulation of Ca^{2+} Dependent Phase Transitions and Real-time Dynamics of SAP97/hDLG

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Abstract

Real time molecular arrangement of modular complexes of scaffolding molecules and membrane molecules are involved in the orchestration of events that decides the formation, maintenance, and elimination of cellular interfaces. Progressive changes in molecular organizations results in ordered separation of molecules both in the membrane and cytoplasmic compartments. Such phase separations have known to play an important role in the formation of modular scaffolds that allows the positioning of receptors and cell adhesion molecules, stable signalling complexes that are responsible for regulated exchange of molecules and in some cases, nucleation disorders and synaptopathy related disorders. Here using SAP97/hDLG, a cardinal member of the family of membrane associated guanylate kinases (MAGUKS), we understand how changes in the concentration of cytosolic calcium results in antagonistic outcomes in phase transitions and underlying nanoscale heterogeneity.

Synapse associated protein-97/Human Disk Large (SAP97/hDLG) is a conserved, alternatively spliced, modular protein critical in regulating the molecular organization of cell-cell junctions in vertebrates. It is one of the many proteins that function as scaffolds at the postsynapse to fixate the receptor proteins adjacent to the presynaptic region. The loss of function of this protein has been linked to various psychiatric disorders, including schizophrenia, autism spectrum disorders and bipolar disorder. In this study, we investigated the nanoscale organization of SAP97 in vivo and in vitro conditions and provided a model for the organization mechanism to extract the biophysical characteristics of the protein aggregates. We confirm that the molecular determinants of first order phase transition of SAP97/hDLG is controlled by morpho-functional changes in its nanoscale organization. This molecular aggregation driven transitions is dependent on the nanoscale organization of the endogenous SAP97/hDLG where they are organized in a dispersed phase, and a condensed phase with increased packing density per unit area. These different phases have distinct nanoscale signatures which in turn is controlled by local variability of spliced isoforms present in the phase separated compartments.

Furthermore, the molecular signatures of these signalling islands and phase transitions are altered in response to changes in cytosolic Ca2+. Additionally, exchange kinetics of alternatively spliced isoforms of the intrinsically disordered region in SAP97/hDLG C-terminus shows differential sensitivities to Ca2+ bound Calmodulin, affirming that the molecular signatures of local phase transitions of SAP97/hDLG depends on their nanoscale heterogeneity and compositionality of isoforms. This work provides insights into the molecular interactions and biophysical properties of SAP97/hDLG enabling us to close in on its isoform specific differential dynamics, nanoscale distribution and the molecular signatures in cell systems and solutions, opening opportunities to explore more into its impacts on the receptor dynamics that controls the firing properties of synaptic signals, which ultimately determines the efficacy of neural signaling.

Zingerone *(Zingiber Officinale)* in combination with temozolamide inhibitsglioma cell proliferation in rats: A neurobehavioral and neurochemical study

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Abstract

Background: Glioma forms craniocerebral tumour derived from glial cells; epitomises prominent cellular heterogeneity and constitutes 70% of all brain tumours. The major causeof complicated drug resistance and survival mechanism could be attributed to the vigorous infiltration in the adjacent brain tissue resulting in high mortality followed by poor prognosis. Emerging evidence suggests that medicinal plants have been used by researchers and scientists in understanding several ailments as they are cost-effective, safe and well tolerated. Among various active components found in ginger, zingerone is a polyphenolic alkanone and nontoxic compound and an active phenolic compound with several pharmacological properties which include antioxidantive, anti-inflammtory, anti-cancer, immunomodulation.

Purpose*:* For our better understanding of relevant clinical features and mechanisms underlying the aggressiveness of the disease, it is of great significance for discovery of new and effective therapeutic agents striking multiple targets and aids in managing the eclectic nature of glioma. Hereunder, we evaluated the usefulness of zingerone as an adjunct to temozolamide in mitigating the proliferation of glioma cells in animal model.

Methods*:* The animals were divided into five groups namely Group1 (Sham control), Group 2 (transfected with C6 cells), Group 3 (C6 glioma inflicted + Zingerone administered at a dose of 50mg/kg b.w.), Group 4 (C6 glioma infliction+ combined treatment with zingerone and temozolamide) and Group 5 (glioma inflicted + temozolamide treatment at a dose of 10mg/kgb.w).The animals were assessed for body weight changes with survival time, neurobehavioraltests to assess short-term memory evaluated by performing passive-avoidance test, novel-object recognition and Y-maze test, key antioxidants indices (reduced glutathione, catalase, superoxide dismutase, lipid peroxidation, reactive oxygen species), protein expression profile of NF-KB, COX-2, TNF-alpha, IL-8 and GFAP, histo-architectural changes using haematoxylin and eosin staining method.

Results: The histo-architectural analysis showed, C6 inflicted animals established brain tumours indicating increased hyperplasia at the site of transfection. Further,

researchers and clinicians have also encountered decline in neurocognitive functioning in malignant gliomas. Tumour bearing animals also showed impairment in memory functions and increased oxidative stress in terms of enhanced reactive oxygen species, lipid peroxidation, lowered reduced glutathione levels, superoxide dismutase and catalase activities which interestingly were appreciably modulated upon zingerone and temozolamide supplementation. The protein expressions of NF-KB, COX-2, TNF-alpha, IL-8 and GFAP were increased in glioma bearing animals and upon zingerone supplementation these expressions were suppressed in animals bearing gliomas. In conclusion, our results clearly suggested that zingerone has the capacity to modulate the tumour environment and can effectively contain the proliferation of glioma cells by modulating the expressions of key biochemical indices.

Conclusion*:* The study concludes that zingerone when given in combination temozolamide aids in containing the growth of gliomas and mitigates oxidative stress.

Role of TrkA signaling in the Monocrotophos induced neurotoxicity in rat brain neural stem cell derived neuronal cells

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Abstract

Monocrotophos (MCP) a widely used an organophosphate is known to induce neurotoxicity, however the underlying mechanisms are still explored precisely. The present study was aimed to investigate the involvement of TrkA activation and its downstream signaling pathways in MCP induced neurotoxicity in cultured rat brain neural stem cell (rBNSCs) derived neuronal cells. Nerve Growth Factor (NGF) induced neuronally differentiated neural stem cell (rBNSCs) derived neuronal cells were exposed to non-cytostatic doses of MCP. It was found that MCP induced apoptosis and subsequent neurotoxicity in neuronal cells derived from rBNSC via trigger of TrkA signaling. Our results demonstrate a significant inhibition in the phosphorylation of TrkA and subsequent inhibition in the TrkA mediated downstream key signaling molecules that lead to inhibition of pro-survival ERK1/2 and Akt signaling in stem cell derived neuronal cells exposed to MCP. Such MCP induced inhibition in the expression of TrkA and other signaling molecules was found to be associated with the altered expressions of neural markers (Tuj1, NF-M, GAP43, Neu-N) including cholinergic (ChAT) expression. The increased expression of cytochrome-c, Bax, caspase-3/9 and reduced expression of BCl_2 in our studies have also confirmed the mitochondria mediated caspase cascade induced apoptosis due to MCP exposure. Further, a significant DNA damage, oxidative stress and subsequent loss of cell viability also supports the MCP induced apoptotic changes. The p75NTR has a complex role in regulating neural survival and death that is dependent on its binding to ligands. The involvement of TrkA/p75NTR dependent signaling cascades including ERK1/2, Akt and JNK1/2 signaling pathway in MCP induced neurotoxicity was reconfirmed by significant downregulated expression of pERK1/2, pAkt, pCREB along with upregulation of activated pJNK. We are reporting that MCP mimics TrkA receptor ligand and binds to the ATP binding domain of TrkA receptor, thereby inhibits its activation. The findings shed the light on mechanistic insights of MCP mediated neuronal damage under strictly controlled experimental conditions, which infers the possible neurodegeneration via change in mitochondrial membrane potential, activation of signaling cascade TrkA receptor ligand and finally cell death. The exposure to MCP could be a potential threat for further neurodegeneration in patients of AD, PD and other neurodegenerative diseases.

Keywords: Neural Stem Cells, neuronal subtypes, Nerve Growth Factor, MCP

Autonomic functions as a window to identify the severity of disease inpatients with Alcohol use disorder with Adult ADHD

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Abstract

Background and Rationale: Alcohol use disorder (AUD) is a chronic disease characterized by uncontrolled drinking and preoccupation with alcohol. Patents with AUD have propensity to develop attention deficit hyperactivity disorder in adults (AADHD). Central autonomic network and frontal cortex plays an important role as Neurophysiological link for behavioral traits between AUD and AADHD. We hypothesized in patients with AADHD there will be cardiac, autonomic, cognitive dysfunction compared to AUD patients and Healthy control subjects (HCS).

Materials and Methods: 90 male subjects aged 18-50 years admitted to deaddiction department of NIMHANS were divided into 3 groups with 30 subjects in each group: AUD per se, AUD with co morbid AADHD and compared with HCS admitted from hospital staff and students of NIMHANS. Study groups were subjected to Heart rate variability, Echocardiography, Conventional autonomic function tests, Pupillometry.

Results: In patients with AUD with AADHD there is: decreased parasympathetic activity with sympathovagal imbalance with sympathetic dominance evident from reduced HF power and RMSSD, Moderate to severe autonomic dysfunction evident from AFT and delayed pupil reactivity to light evident from reduced velocity of pupil constriction speed and delayed release amplitude, cardiac pathology evident from left ventricular diastolic dysfunction evident from 2D-echocardiography, compared to patients with AUD per se and HCS.
Conclusion: Our study demonstrates the importance of including cardiac and autonomic evaluation in routine screening in deaddiction clinics in patients with AUD which can help them in early diagnosis of the disease severity and suggesting strategies to cope up withthe behavioral outcomes which can improve the quality of life and increase the life expectancy in these patients.

Keywords: ADHD, Alcohol, Heart rate variability, Autonomic functions.

Ethics statement: The experimental protocols were approved by the institutional human ethics committee, NIMHANS.

Acknowledgements: We thank NIMHANS institutional fellowship

Conflicts of interest: Authors declare no conflicts of interest in this study.

Role of Zika virus induced autophagy in neural stem cell fate determination.

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Abstract

Zika virus (ZIKV) is a mosquito-borne virus belonging to the Flavivirus genus that induces microcephaly in new-borns. The cellular and molecular mechanism of ZIKV-induced microcephaly remain poorly understood. Proliferation arrest and premature differentiation of neural stem cells (NSC) are key mechanisms linked to microcephaly. As autophagy also controls NSC proliferation and differentiation, we are interested to study the effects of ZIKV on autophagy and its impact on NSC fate. Using human fetal NSCs as a model system, we found co-transfection with ZIKV non-structural protein NS4A and NS4B significantly altered the NSC fate by arresting its proliferation and inducing them towards premature neurogenesis as evident from reduced neurosphere size and increased expression of neurogenesis markers.

Augmented expression of LC3II and reduced p62 expression depicted enhanced autophagy in NSCs. As autophagy controls NSC fate by regulating key signalling pathways like Wnt and Notch, expression of Wnt and Notch receptors was assessed and found that the protein expression of Notch1 was downregulated following co-transfection with NS4A and NS4B. We also found altered gene expression of the notch target genes. To further confirm that reduced notch1 expression is due to autophagy-mediated degradation, we treated our cells with an autophagy inhibitor (3 methyladenine) along with Co-transfection with NS4A and NS4B. We found rescuein notch1 expression, enhanced proliferation and reduced differentiation of NSCs. Further experiments are in progress to validate these findings through siRNA-mediated knockdown of autophagy genes.

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Honokiol prevents MPTP neurotoxicity in differentiated SH-SY5Y cells and in C57BL/6 mice

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Abstract

Parkinson's disease (PD) is a complex geriatric neurodegenerative disease in which both genetic and environmental factors are thought to contribute to its etiology. 1-methyl-4-phenyl 1,2,3,6-tetrahydropyridine (MPTP) has been reported to cause PD-like phenotype in humans, primates and lower mammals. Although PD is a chronic debilitating condition, many of its pathogenic phenotypes including specific dopaminergic neurodegeneration can be mimicked by acute MPTPadministration. Here, we show that Honokiol, a naturally occurring pleotropic lignan, can prevent neurotoxic effects of MPTP in differentiated SH-SY5Y neuroblastoma cells by amelioration of the neurotoxin-induced mitochondrial and lysosomal deficits. Moreover, Honokiol treatment on MPTP-treated mice protected against motor behavioural deficits and dopaminergic neurodegeneration in the nigrostriatal pathway. We are presently working on the molecular pathways by which honokiol mitigated the loss of DA neurons caused by MPTP. Our preliminary results indicate that honokiol may have therapeutic value for treating PD.
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Human iPSCs derived spheroid: A human brain specific 3D tool to study the developmental neurotoxicity potential of xenobiotics

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Abstract

Background: Rapid and reliable experimental model for human brain specific developmental neurotoxicity (DNT) is a need of hour for all the stake holders including academia, researchers, regulators and industries. Results obtained from three-dimensional (3D) spheroid cultures haveshown promising path towards more human mimicking physiology and functionality, and responses against xenobiotics. The neural progenitor cell (NPCs) derived spheroids have also been suggested as a close representation of neurodevelopmental model system under in vitro condition. Present study aims to investigate the applicability of human-iPSC derived neural progenitor spheroids as high throughput 3D tool to study the DNT potential of drugs and chemicals.
Materials and methods: Following the characterization and bulk production, the primary cultures of hiPSCs were allowed to differentiate into neural progenitor cells (NPCs) under specific growth conditions. The characterized NPCs were then grown in 2D culture and 3D spheroids. Both models were exposed with sub-toxic concentration of 5µM sodium arsenite (SA) for 24 h and compared for morphological changes, cellular physiology, respiratory kinetics, and translational alterations via LC-MS/MS analysis.
Result: The NPCs in 2D monolayers under the influence of SA had compromised neurites as compared to the control. Further, a significant decrease in MMP was seen in SA exposed 2D cells with reference to control group. However, no significant changes in MMP were observed in SA exposed spheroids. Furthermore, the results of MMP were validated by Seahorse based bioenergetic analysis, where we found decreased mitochondrial oxygen consumption rate in SA exposed 2D group. The SA exposure also induced morphological deformities in the cells along with dose-dependent reduction in viability. The comparative global proteomic profiling between the 2D and spheroids showcase an upregulation in proteins responsible for axon guidance, synapse formation and other metabolic pathways. The results also revealed the downregulation in the expression of proteins involved in the ribosome, glyoxylate decarboxylate metabolism.
Conclusion: The results of the present investigations revealed that the magnitude of SA induced detrimental effects was more in 2D cultures than in 3D spheroids. The results obtainedthus so far are very promising and further studies will shed light on the mechanistic insights ondeveloping stem cell-based 3D spheroid systems for assessing the DNT.

PC 12 secretome enhances neuronal differentiation of human mesenchymal stem cells andprotects against toxic insult of Monocrotophos

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Abstract

Introduction: The plethora of literature strongly indicates that stem cell-mediated regeneration is majorly due to their paracrine activity; however the role of non-stem cells is abeyant. The present study aims at investigating the role of conditioned medium (CM) of non-stem cells i.e. neuronally differentiated rat pheochromocytoma-PC 12 cells in neuronal differentiation of human mesenchymal stem cells (hMSCs).

Method: The CM of neuronally differentiated PC 12 cells was harvested and its role in neuronal differentiation of human mesenchymal stem cells (hMSCs) was assessed via immunocytochemistry and immuno-blotting. Additionally, the MSC derived neuronal cells and SHSY-5Y cells were exposed to Monocrotophos (MCP) and further subjected to the CM for investigating its restoration potential in mitigating MCP induced neurotoxicity.

Results: The results manifested an increased expression of neuronal markers *viz.* β-III tubulin, synaptophysin, NF-M and NeuN in the MSCs exposed to the conditioned medium along with increase in the neurite length when compared to NGF induced neuronal differentiation. The co-exposure of NGF and CM depicted an additive response and directed cholinergic differentiation of MSCs. The MCP exposed neuronally differentiated MSCs and SHSY-5Y cells showed a significant restoration post exposure to the CM in terms of cell viability, oxidative stress, and apoptotic cell death.

Conclusion: Results demonstrate that the CM of differentiated PC 12 cells aids in neuronally differentiation and also mediates neuroprotection against MCP induced damages via the activation of autophagy. The propensity of CM to augment the neuronal properties of stem cells may greatly assist in their rapid differentiation into neuronal subtypes in the particular circumstances of stem cell transplantation for neuronal injuries, thereby expanding the range of non-stem cell-based applications in the field of secretomics.

miR-9 Regulates The Fate of Neural Stem/Progenitor Cells Following Japanese Encephalitis Virus Infection

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Abstract

Aims and Introduction: Japanese Encephalitis Virus (JEV), a member of the Flaviviridae family is prevalent in South and South-east Asia with nearly 25%mortality rate . Neuroinvasion by the virus is responsible for acute flaccid paralysis and encephalitis leading to deleterious long term effects. In the brain, JEV infects mitotically active neural stem/ progenitor cells (NSPCs), decreases their proliferation capacity and changes the NSPC fate by differentiating them more into glial lineage. The present study aims to identify the mechanism by which NSPC fate and thereby neurogenesis is being regulated upon JEV infection. microRNAs(miRNAs) are well established as key regulators of genes expressions. miRNAs are known to play a role in regulating host cell response to viral infection. Specifically, miR-9-5p is reportedly known to play the role of a versatile regulator of neurogenesis in the sub-ventricular zone (SVZ) by repressing the expression of anti-neuronal genes.

Results: In silico analysis predicted Onecut2 (O2) as a target for miR-9-5p. Further, we confirmed the dynamic interaction between the miR-9 and its target in vitro and ex vivo. Decreased miR-9 levels led to increased expression levels of OC2 . We have also observed that if these neuronal stem cells are provided with the differentiation media containing growth factors such as BDNF and NGF, the expression levels of OC2 somewhat coincided with the increase in abundance of glia-related genes. Transfection with miR-9 mimic in differentiated NSPCs expressed more of neuronal phenotype and less of glial cells. Upon JEV infection, the loss in neuronal cell type post differentiation was somewhat rescued by miR-9 mimic expression.
The same was validated in ex vivo primary NSPC culture. Conclusion:
Our study is the first to establish a functional relationship between miR-9-5p and its predicted target OC2 in NSPC model post Flavivirus infection. This study elucidates the mechanism underlying the loss of neurogenesis and subsequently gliogenesis induced in NSPC upon JEV infection.
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Towards the development of human iPSCs derived TDP43 linked model of ALS: Critical involvement of autophagy and lysosomal dynamics

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Abstract

Background: The cause of pathogenesis of Amyotrophic Lateral Sclerosis (ALS), a fatal neurodegenerative disorder, has been suggested to be altered expression of over 20 genes. Mutation in Transactive response DNA-binding protein 43 (TARDBP encoding TDP43) gene has recently been reported as one of the prominent causes of sporadic ALS. Though the progressive etiology of the disease is unclear, autophagy and lysosomal dysfunctions have been postulated as potential contributors. The present investigation aims to investigate the possible involvement of autophagy and lysosomal activity in the accumulation of misfolded TDP43 in human iPSCs derived neural progenitor cells (NPCs). Further, we explored the anti-TDP43 protein (misfolded) aggregation potential of Mitoxantrone drug.

Materials and Methods: Human iPSCs were transfected using CRISPR Cas9 system to develop TDP43 mutated NPCs. Following the characterization, the normal NPCs and TDP43-Mutated NPCs were assessed for lysosomal and autophagy markers at both transcriptional and translational level. The similar markers were also studied in the cells exposed to Mitoxantrone drug, an anthracenedione, for its potential as anti-TDP43 protein aggregation.

Results: The results revealed a significant increase in the expression levels of lysosomal and autophagy markers (LAMP1, LC3B, and P62) along with the stress granule markers (G3BP1 and TIA1) in the NPCs mutated for TDP43, when compared with normal NPCs. The experimental exposure to mitoxantrone drug (1µM) has shown a significant recovery in the altered expression of markers studied, hence suggests a possible therapeutic potential against ALS.

Discussion and Conclusion: The findings are indicative of regulatory response of autophagy and lysosomal dynamics in human iPSC-derived in vitro model of ALS. The experimental exposure of Mitoxantrone drug has also inferred its potential as promising therapeutic intervention in ALS by mitigating the misfolded protein aggregation.

In vitro assessment of mimosine as a brain iron chelator: Its potential for iron binding,antioxidant activities and SH-SY5Y neuronal toxicity in culture

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Abstract

Iron is an essential element in brain for performing several functions such as mitochondrial respiration, myelin and neurotransmitter synthesis and metabolism. Brain iron homeostasis is tightly controlled by a set of iron storage, import and export proteins in which the iron is mostly in the bound form to the proteins. But disruption of brain iron homeostasis results in unbound or labile iron pool that accumulates in the brain. This labile iron pool can cause oxidative stress by generation of reactive oxygen species *via* Fenton's reaction. Iron accumulation in specific brain regions and the resulting oxidative stress-mediated cell death are implicated in several neurodegenerative diseases. Hence chelating the labile iron pool in the brain has been considered as a therapeutic approach for the treatment of neurodegenerative diseases. In the present work, we have examined the iron binding and antioxidant potential of a phytochemical, mimosine in an initiative to develop it as a potential brain iron chelator. The iron binding potential of mimosine was evaluated using ferrozine assay. Mimosine showed 84% iron binding at a concentration of 60 µM and this was comparable to that of the clinically used iron chelator, deferiprone. The effectiveness of mimosine to bind iron and inhibit iron-mediated Fenton reaction was assessed using deoxyribose degradation assay. Mimosine exhibited concentration-dependent inhibition of malondialdehyde generation in the deoxyribose degradation assay. The antioxidant potential of mimosine was also confirmed by its ability to reduce ferric to ferrous using the ferric reducing antioxidant power assay. Mimosine was found to be non-toxic to the cells up to a concentration of 10 µM as revealed by MTT assay in differentiated SH-SY5Y cells.

Key words: Mimosine, Iron chelation, Parkinson's disease

Acknowledgements: The study was conducted with financial assistance from Indian Council of Medical Research, New Delhi (Senior Research Fellowship) and Department of Higher Education, Government of Kerala.

Pre-Stimulus EEG Microstates and its Cortical Sources during an Emotional Interference Task

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Abstract

Introduction: Integration of emotional valence and semantic information plays pertinent role in social interactions. Emotional interference is reflected as a decline in executive function in the presence of an emotional stimuli We hypothesize apart from what we perceive, the intrinsic brain activity may also influence the behavioural outcome. Thus, we investigated the role of pre-stimulus EEG microstate in determining performance of an individual in an emotional interference task.

Material: Twenty healthy right handed participants, mean age 27.25±4.77 years, performed two variants of emotional interference task i.e. Face-word interference (FwI) and Word-face interference (WfI) designed using E- Prime version 2.0. Emotional stimuli consisted of valenced pictures from International Affective Picture System (IAPS) and words from Affective Norms for English Words (ANEW). Sixty trials of each variant were presented, wherein emotion of face had to be categorized neglecting the valence of word (FwI) and categorizing the valence of word, neglecting the valence of face (WfI). Simultaneous acquisition of single trial EEG was done using 128-channel dense array. After preprocessing, data was segmented into 60 artifact free segments of 100 ms pre stimulus epochs from correct and incorrect trials. Further, microstate analysis was done using Cartool software and number of time frames, global explained variance (GEV), mean duration and time coverage were computed based on the spatial correlation for each template map. The cortical sources for each of the significant microstate maps were further identified using sLORETA software using Statistical non parametric mapping based on statistical nonparametric mapping method (SnPM) for analysis of current source density based on Fisher's permutation method (with the threshold set at the 5% probability level).
Result: Four maps during FwI and six maps during WfI could represent the response accuracy of the preceding behavioural response in respective variants. Statistically significant difference was found in number of time frames in all the four maps of FwI while mean duration of Map1 was significantly higher in correct vs incorrect trials ($p<0.001$). No significant difference was seen in GEV and time parameters. For the WfI, no significant difference was seen in temporal microstate parameters of six topographical maps obtained. Significant cortical sources for each of the maps (threshold value- 4.387 & extreme p value- 0.00020) were explored using sLORETA software. The intracranial generators of the pre-trial microstate during FwI revealed areas related phonological processing (middle temporal gyrus and superior temporal gyrus), emotional processing (Inferior Parietal Gyrus, Parahippocampal gyrus, Transverse Temporal), conflict resolution (Inferior frontal gyrus and Insula) and motor responses (Pre-central); while in WfI areas activated were involved in phonological processing (Temporal gyrus),emotional engagement (Superior temporal gyrus, middle occipital gyrus and cingulate gyrus, lingual gyrus, fusiform gyrus) and motor response (post central gyrus).
Conclusion:Pre-stimulus microstate alterations during correct versus incorrect trials revealed the preparation related to the upcoming emotional stimuli in both FwI and WfI, as reflective in microstate topography and cortical sources.Thus, in addition to valence and semantics, pre-stimulus microstate may also determine the performance of an individual in an emotional interference task.

Effect of chlorpyrifos and cypermethrin exposure on the expression of α-synuclein,cyclooxygenase-2 and tyrosine hydroxylase in rat nigrostriatal tissue

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Abstract

Background:
Selective degeneration of dopaminergic neurons in the nigrostriatal tissue reduces dopamine content in the striatum and onset of symptomatic hallmarks of Parkinson's disease (PD). Reduced expression of tyrosine hydroxylase (TH) and augmented expression of *α*-synuclein and cyclooxygenase-2 (COX-2) have been found to be associated with PD. Cypermethrin acts as a Parkinsonian neurotoxicant while chlorpyrifos is shown to produce neurotoxicity.
Objective:
The study aimed to assess whether chlorpyrifos affects the cypermethrin-induced alterations in the expression of TH, *α*-synuclein and COX-2 in the rat nigrostriatal tissue.
Methods:
Rats were exposed to chlorpyrifos for 4, 8, and 12 weeks in the presence/absence of cypermethrin along with controls. Animals were sacrificed and expression of TH, *α*-synucleinand COX-2 proteins and the number of TH-positive cells were checked in the nigrostriatal tissue.
Results:
Chlorpyrifos or cypermethrin augmented the expression of *α*-synuclein and COX-2 while reduced the expression of TH and number of TH-positive cells after 12 weeks of exposure. The alterations produced by half of the combined exposure were more pronounced than that of individual ones.
Conclusion:
The results suggest that chlorpyrifos induces the cypermethrin-mediated toxicity to dopaminergic neurons in the nigrostriatal pathway.

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ROLE OF CENTRAL AGMATINE IN ETIOPATHOGENESIS OF HUNTINGTON'S DISEASE IN RATS

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Abstract

Background: The physical, cognitive, and behavioral health symptoms of Huntington's Disease (HD), a hereditary neurological condition, advance over many years and eventually result in death. Despite the fact that the HTT gene mutation that leads to the toxic Huntingtin protein (mHTT) is now established as the precise cause of the disease, there are currently no disease-modifying medications that can stop or even slow this fatal disorder. Agmatine, an endogenous polyamine, has a variety of biological characteristics and shows therapeutic promise.

Aim and objectives: The present study was designed to elucidate the therapeutic effect of central agmatine in quinolinic acid-induced HD.

Methods: This investigation would focus on the beneficial effects of agmatine in treating behavioral dysregulation associated with neurodegenerative disorders like HD.

Results: It has been shown in numerous studies that agmatine has a role in a variety of neurological conditions, including acute attacks (stroke and traumatic brain damage) and chronic neurodegenerative conditions (Parkinson's disease, Alzheimer's disease). In this study, the possible therapeutic benefits of agmatine in the management of HD are discussed, along with its associated complications such as motor irregularities, cognitive impairments, and psychiatric symptoms like depression, apathy, suicidal ideation, and anxiety.

Summary and Conclusion: Agmatine is safe and has a low rate of side effects, which points to its enormous potential as a treatment for neurodegenerative illnesses. Our data, in particular, stimulate further research into agmatine as a potential novel medication for the treatment of HD.
Keywords: Huntington's Disease, Agmatine, Quinolinic acid, Parkinson's disease, Alzheimer's disease.

The Purinergic receptor P2Y12 signalling in Tau aggregates-induced ECM degradation and microglial migration

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Abstract

Microglia are resident immune custodians entrusted with the responsibility of survelling, maintaining and defending the central nervous system against all invaders. They are known to undertake actin remodelling for generation of varied microstructures such as lamellipodia, filopodia, podosomes, focal adhesions and stress fibers to aid in chemotaxis, internalization and degradation of toxic extracellular Tau seeds. Podosomes, particularly, are complex and dynamic micro-assemblies with an actin-rich core surrounded by ring of accessory proteins majorly mediating extracellular matrix adhesion and degradation in migratory microglia. Previous studies in our lab have associated P2Y12, a chemotactic purinergic receptor with microglial podosomes and established a key role for these receptors in degradation of Tau monomers and oligomers as ECM depositions. The current study was undertaken to elaborate the same for Tau aggregates. Time-dependent comparative analysis was carried out to adjudge the potential of microglial P2Y12-linked-podosomes for Tau-ECM degradation in conjunction with metalloproteases like MMP9 and ADAM. This study will help us elucidate the significance of P2Y12 signalling in Tau aggregates-induced ECM degradation and microglial migration.

Expression of Neurotrophins (BDNF and NT-3) in Adult Human Cochleae

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Abstract

Background:
Sensorineural hearing loss is the most prevalent type of hearing loss and encompasses pathologies of the inner ear and auditory nerve. Its definitive management is cochlear implantation, contingent on the presence of adequate spiral ganglion neurons (SGN) and auditory nerve function. Age-related degeneration of the hair cells in the organ of Corti and SGNs are limiting factors in cochlear implant efficacy.
Neurotrophins help in the development and differentiation of neurons, their synaptic connections and plasticity. Neurotrophin-3 (NT-3) is expressed developmentally in supporting and hair cells of mice. NT-3 and BDNF are also expressed postnatally. They show reversed expression gradients along the cochlear tonotopic axis. In experimental animal studies, BDNF induces physiological properties in SGNs characteristic of those of basal cochlea; NT-3 of apical cochlea. Reliable studies on the expression of NT-3, BDNF in adult human cochleae are lacking.

Novelty/ Innovation:
Neurotrophins are potential therapeutic agents for rekindling synapses and maintaining optimal nerve function and signaling. This beneficial effect is yet to be extended to the ageing human auditory pathway.

Methods:
After obtaining ethical clearance, seven human temporal bones containing the cochlea and auditory nerve were derived from the mortuary within 6-12 hours of death, during winter months. The bones were fixed in 4% paraformaldehyde, and decalcified with 10% EDTA for ten to twelve weeks.
Decalcified specimens were cryoprotected in sucrose, mounted and sectioned on a cryotome to obtain30µm thick coronal sections of the cochlea.
The cryosections were used for H&E and CV staining for studying cochlear morphology. They were also used for determining the expression of BDNF and NT-3 using immunohistochemistry. We retrieved antigens using heat shock in citrate buffer (0.01M, pH 6), thereafter, the sections were blocked in normal serum, quenched in 5% hydrogen peroxide (in methanol). The sections were then incubated in primary antisera against either BDNF or NT-3 followed by species-specific secondary antibodies. Avidin-biotin-peroxidase complex was used to amplify the signal, and antigen-antibody binding sites were visualized using 3,3-diaminobenzidine tetrahydrochloride.
Results/ Conclusion:
Inner and outer hair cells, and SGNs were identified on stained sections. The hair cells and SGNs expressed NT-3 and BDNF.
This study will be extrapolated to cochlear samples across different age groups and can serve to be a qualitative observational study of neurotrophin expression across different age groups. If this research holds significant, supplementation of receptor agonists/neurotrophins around the age of onset of presbycusis could be therapeutic.

Delineating the role of TNF-*α* & JAK-STAT signaling pathways in promotingoligodendrocyte differentiation *in vitro*

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Abstract

White matter injury (WMI) is a common consequence of preterm birth and may result in neurological sequelae like cerebral palsy. This appears to be related to the failure of cell survival and maturation of oligodendrocytes (OL) in hypoxic injury of cerebral white matter. Impaired differentiation of pre-OL and aberrant myelination are possibly implicated in the pathogenesis. The developmental stages of oligodendrocytes (OL) in fetal brain are oligodendrocyte progenitor cells (OPC), pre-OL, immature-OL and mature-OL. The pre-OL that are prevalent between 24 and 32 weeks of gestational age (in pre-term babies) are more vulnerable to hypoxic injury. Information about signaling pathways involved in terminal OL maturation needs to be elucidated to allow their modulation to influence OL development. Involvement of pro-inflammatory pathways in terminal OL differentiation was reported earlierby our group, using transcriptional datasets in primary OL. In the present study, the role of pro-inflammatory pathways in OL maturation and the effect of hypoxia were independently evaluated. MO3.13 cell line was used for this work as it resembles pre-OL. Initially, MO3.13 were differentiated into mature-OL over 7 days, using PMA. Undifferentiated MO3.13 cells were exposed to various grades of hypoxia (20%, 6%, 2%, 0.2%) for 48 hours. Characterizationof MO3.13 was done by qPCR & ICC with the help of pre-OL markers (NG2 & O4) and mature-OL marker (MBP). The differentiation of MO3.13 into mature-OL was confirmed by the increased expression of MBP (qPCR & ICC) and decreased expression of NG2 & O4 (ICC). Critical genes involved in TNF- α and JAK-STAT signaling pathways were evaluated using qPCR. During differentiation, the expression of TNF- α, IL-6 along with transcription factors (STAT1, STAT2, and STAT3) of the JAK-STAT pathway were found to be elevated. Interestingly, exposure of undifferentiated MO3.13 (pre-OL) to severe hypoxia (0.2%) decreased the expression of TNF-*α* and IL-6 as well as STAT1 and STAT2. The present data indicates the involvement of TNF-α and JAK-STAT signaling pathway during hypoxia and OL maturation. The novel findings of this study may help in designing new therapeutic strategiesto ameliorate the manifestations of hypoxic white matter injury in preterm infants.

Envelope protein of Zika Virus alters properties of Brain Microvascular Endothelial Cells and Astrocytes in an *in vitro* human Blood Brain Barrier

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Abstract

The blood brain barrier (BBB) is a regulated interface between peripheral and central nervous system which prevents access of various toxins and pathogens into the brain. While presence of BBB protects the CNS from viral infection, many viruses are able to access the brain and establish CNS infection. Zika virus (ZIKV) is an arthropod-borne *Flavivirus*, known for worldwide outbreaks in 2015-2016 and emerged as the cause of fetal microcephaly and encephalitis. Thesurface envelope (E) protein is involved in host cell binding and facilitating viral entry. In the current study, we investigated the effects of ZIKV E protein on theproperties of human brain microvascular endothelial cells (hBMECs) and human progenitor derived astrocytes using an *in-vitro* BBB model. Here we employed use of physiologically relevant dual cell model of BBB using transwell apparatusto closely recapitulate the *in vivo* microenvironment. We found exposure of E protein resulted in activation of hBMECs and astrocytes. E protein resulted in reduced expression of characteristic tight junction proteins of hBMECs. This resulted in altered state of BBB integrity and permeability. BBB integrity was also influenced by increased levels of inflammatory cytokines and chemokines in BMECs. Furthermore, ZIKV E protein resulted in activation of astrocytes as depicted by increased levels of GFAP and Vimentin and dysregulated extracellular glutamate levels in astrocytes. Our findings suggests that BBB cellsare highly vulnerable to ZIKV E protein, resulting in their activation.
Work was partially supported by DBT grant and NBRC core funds.

Prevalence of MCI and Dementia and Its Association with Sociodemographic Factors

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Abstract:

Background:
With demographic ageing in India, the prevalence of Mild Cognitive Impairment (MCI) and Dementia in the population is predicted to see a drastic increase. Dementia is a neurodegenerative condition with a deterioration in cognitive function and MCI is regarded as the intermediate stage between normal ageing and dementia. MCI can also be used to understand the cognitive status of individuals at risk of converting to dementia. At present, there are very few population-based studies in India to understand the prevalence of MCI and dementia and its association with various sociodemographic factors. With dementia predicted to become an epidemic among elderly in the coming decades, research in the Indian context keeping in mind the sociodemographic factors, along with being pertinent to the realities and challenges of our country is imperative.

Aim:
To estimate the prevalence of MCI and dementia among individuals aged 45 years & above and its association with selected demographic variables from a sample of healthy individuals in urban Bangalore.

Methods:
This study consists of baseline data collected from 923 participants who are part of the ongoing study titled 'Tata Longitudinal Study of Ageing (TLSA)', Bangalore, India. Clinical Dementia Rating Scale (CDR) scores were used to estimate the prevalence of MCI and dementia in the population. The study also looked into the association between MCI and dementia with the following factors: age, gender, language and years of education. Shapiro-Wilk test was used to assess the normality of the continuous variables. Kruskal-Wallis test was used to assess the difference between continuous variables whereas

Chi square test was used to investigate the association between categorical variables in the study.

Results:
Estimated prevalence for MCI and dementia were 7.5% and 1.7%, respectively. There was a significant difference in age and years of education among people with normal cognition, MCI and dementia. Language (monolingual, multilingual) was found to be associated with cognitive functioning (p=0.01). There was no significant association found between gender and cognitive functioning.

Conclusion:
People with dementia are more likely to be monolinguals and have lower years of education.

Keywords: ageing, dementia, mild cognitive impairment, prevalence



Targeting Mitochondrial Trafficking by Environmental Toxicant Bisphenol-A in the Rat Hippocampus

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Abstract

This study summarized the neuronal death following Bisphenol-A (BPA) exposure linked impaired mitochondrial trafficking in rat brain hippocampus. For the correct neuronal function and survival, it is important to proper transport and distribution of mitochondria to specific location along axon and near synaptic terminals where ATP supply and calcium buffering are in high demand. The motor proteins (Kinesin and Dynein) and motor-adaptor protein (Miro and Milton) help in mitochondrial trafficking (bidirectional transportation of mitochondrial along microtubule) in the neurons. Environmental Toxicant Bisphenol-A is a known xenoestrogen, found in consumable plastics products, causes neurodegeneration in the developing and adult brain, potentially contributing to cognitive and motor deficits after chronic exposure in the rat. Any damage in mitochondria and mitochondrial trafficking complex is responsible for impaired mitochondrial trafficking, which is directly associated with cognitive impairment. Our earlier studies suggested that Bisphenol-A exposure reduces neurogenesis by abnormal mitochondrial dynamics (fission/fusion) and mitochondrial biogenesis through impaired mitochondrial fission protein DRP1 and import protein GFER respectively, which leads to neurodegeneration, and cognitive deficits in the rats. Herein, we have investigatedthe gene expression and protein levels of main factors of mitochondrial trafficking complex motor protein (KIF5C, Dynein etc.) and motor-adaptor protein, Miro (RhoT1, RhoT2), Milton (TRAK1, TRAK2), Syntabulin, Syntaphilin etc. after BPA exposure in the adult rat hippocampus and in NSC derived neuronal culture. Our result showed increased protein levels of KIF5C and RhoT2 which helps in mitochondrial anterograde transport (from cyton to axonal terminal), and reduced protein level of Dynein which help in mitochondrial retrograde transport (from axonal terminal to cyton) and Syntaphilin which is static anchor of mitochondria. Thus, the above findings suggest that, for high energy need of ATP to the axonal terminal anterograde transporter motor and motor adaptor protein level increases while reduced the level of retrograde transporter motor protein. So, it may reduce the transport of unhealthy, exhausted and damaged mitochondriafrom terminal to cyton for their renewal, repair and mitophagy, may create aggregations to neuronal terminal,causes apoptosis and may results in neurodegenerations after exposure of BPA.

Keywords Bisphenol-A(BPA); Neurogenesis; Hippocampus; Mitochondrial trafficking; neurodegeneration; Neurotoxicity.

Deep brain stimulation of lateral habenula reverses depressive phenotype in the chronic unpredictable mild stress induced depressed rats

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Abstract

Background: Patients with major depressive disorder (MDD) shows disturbed mood, anhedonia, cognitive impairment, and suicidal behavior. A range of strategies like pharmacotherapy, psychotherapy and electroconvulsive therapy has been employed to treat the depressive condition, but 10- 30% of populations with MDD are unresponsive, which is known as treatment-resistant depression (TRD). Deep brain stimulation (DBS) a novel surgical strategyused for treatment of TRD patient and showing antidepressant effect when targeted in various neuroanatomical sites includes subcallosal cingulate cortex (SCC), ventral capsule/ventral striatum (VC/VS) and medial forebrain bundle (MFB). Recently, evolved DBS target such as lateral habenula (LHb) have greater importance in the brain stimulation surgical therapy because it's robust antidepressant effect. Herein, we have done preclinical evaluation of DBS of LHb using chronic unpredictable mild stress (CUMS) model of depression.

Aim & Objectives: To investigate the effect of DBS targeted at LHb on CUMS induced depression in rat.

Methods: Adult male Wistar rats were exposed to CUMS for 6 weeks with the different unpredictable mild stressors. The electrodes were implanted into the LHb area of different groups of rats (Control, CUMS and CUMS+DBS). The rats in the CUMS+DBS group were treated with DBS for 1 h/day for 14 days. Subsequently animals were tested for behavioral despairs, anhedonia, recognition memory and locomotor activity by using forced swim test (FST), sucrose preference test (SPT), novel object recognition test (NOR) and open field test (OFT), respectively.

Results: The DBS of LHb partially or totally reversed the affected locomotor activity, behavioral despairs, decreased sucrose consumption and deficit in recognition memory in the CUMS-induced depressed rats.

Conclusion: DBS of LHb reversed depressive phenotype induced due CUMS in rats. It can be used as a novel effective DBS target for the treatment of severe depression.

Protocatechuic acid attenuate NR2B-mediated excitotoxic cell death post ischemicreperfusion injury

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Abstract

Background: Protocatechuic acid (PCA) is widely distributed in most edible plants used in folk medicine. PCA possess potential antioxidant activity, suggesting that it could be used as a complementary medication to prevent oxidative burst in various degenerative diseases.

Aim and Objective: To investigate, if PCA exhibit its neuroprotection by influencing NR2B mediated excitotoxic cell death involved in ischemic reperfusion injury.

Methods: Adult male Wistar rats (200-250g) were used for induction of ischemic stroke by MCAO surgery in stereotaxically cannulated rat. PCA (50 mg/kg, i.p.) was administered at 1 h post ischemia and NR2B antagonist (Ro-256981 2 µl i.c.v.30 min before occlusion). Neurological deficit score and beam walk test was used to assess neurological functions after administration of PCA. To determine the effect of Ro-256981 alone or in combination with PCA (1hr) on cerebral infarction, TTC staining was performed. Time-dependent study of PCA (1 hr & 2hr) was also done. For biochemical analysis, MTT assay, LDH assay and H & E assay was performed.

Result and discussion: In this study, significant group effect of PCA (50 mg/kg) was observed in neurological deficit test and beam walk test. PCA produced the significant increase in cell viability as compared with the vehicle group. LDH assay revealed that PCA treatment significantly reduced the cell death compared to the vehicle group. In H & E staining, PCA treated group 50 mg/kg at 1 h of I/Rinjury showing improvement as compared to vehicle treated group. Previous study showed that PCA exhibits antiapoptotic effect by restoring imbalance of cell survival/death signalling.

Conclusion: In present study, PCA treatment showed reduction in NR2B mediated excitotoxic cell death in MCAO induced focal cerebral ischemia model of stroke in rats. PCA may act as a potential adjuvant in the early hours of I/R injury in ischemic stroke.

Intra-habenular effect of cerebrolysin on ethanol dependence in mice

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Abstract

Background: Cerebrolysin (CBL) acts as endogenous neurotrophic factor. Previous study had shown its neuroprotective efficacy in morphine dependence and withdrawal induced brain damage. Role of CBL cocaine, morphine and nicotine in addiction induced neurodegeneration but remains unexplored in ethanol addiction.

Aim and Objective: Intra-habenular effect of cerebrolysin on ethanol dependence in mice

Methods: Adult male Swiss Albino mice (25-30 g) were used for induction of ethanol dependence (4 g/kg (i.g.); 20% w/v; 10 days) and withdrawal in stereotaxically cannulated mice. Acute administration (on 11^{th} day) and chronic administration (for 10 days) treatment study of CBL was performed on ethanol dependent mice through intra-LHb (0.5 & 1 µg; i.c.v.) administration. Somatic signs and behavioral effects were assessed by open field test (OFT), elevated plus maze (EPM) and light-dark chamber.

Result and discussion: In this study, the ethanol (4 g/kg; 20% w/v) administration for 10 days significantly produced withdrawal symptoms in ethanol dependent mice. The anxiolytic effect of CBL (0.5 & 1 µg i.c.v.) was observed in OFT, EPM, & light-dark chamber. CBL produced a significant reduction in the ethanol associated withdrawal symptoms as compared to vehicle group.

Conclusion: The present study, demonstrated the intra-LHb effect of CBL on ethanol dependence and withdrawal symptoms in mice. This study suggests the beneficial role of CBL and also depicts the anti-addictive potential of CBL.

Regional distribution of White Matter Hyperintensity and its implication inBrain Structure and Cognition with Aging

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Abstract

Cerebral Small Vessel Disease (CSVD) is among the most common pathologies of the aging brain, which occurs due to infarcts in small perforating arteries and arterioles. Chronic ischemia associated with CSVD is seen as White Matter Hyperintensity (WMH) on the T2-FLAIR MR images. Here we aim to understand the effect of load and regional distribution of WMH on brain structure health and cognition in cognitively normal (CN), cognitively impaired (CI) and subjects with etiological diagnosis of Alzheimer's disease (AD) using the National Alzheimer's Coordinating Center (NACC) cohort.

T2- FLAIR and T1-weighted MR images obtained on 3T whole-body-scanner were segmented using UBO Pipeline to determine white matter hyperintensity volume in the periventricular and deep white matter regions. Regional load of WMH was obtained across frontal, parietal, temporal and occipital regions. Load and kinetics of WMH increase with age were investigated across CN, CI and AD groups. Multivariate analysis was conducted to understand the plausible association of WMH with structural volumetry and episodic and executive memory performance.

WMH load increases with age across all three groups CN, CI and AD. However, the rate of increase of WMH volume with age is significantly higher in CI and AD subjects compared to CN. Periventricular WMH load accrues significantly higher than the DWMHs. Periventricular WMH deposition exhibits significant decline in cognitive performance, mainly affecting executive functions and global cognition($p<0.0001$). Intriguingly, WMH is inhomogeneously distributed on the brain with aging. Parietal lobe of the brain possesses significantly higher WMH load in all groups, while MCI and AD subjects additionally showed increased WMH load in the Frontal lobe.
Vascular insult because of increased PV-WMH and DWMH may elicit an early and enhanced rate of cognitive deficit and structural atrophy with aging.

Keywords: Cerebral Small Vessel Disease, White Matter Hyperintensity, Aging, Cognition, Brain lobes

MCC950 boosts cognition and lowers anxiety through inhibiting NLRP3 and autophagy

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Abstract

Despite Alzheimer's disease (AD) being the most common form of dementia, ourunderstanding of the molecular mechanisms that underlie the severe cognitive impairments of AD patients remains very incomplete. The development of extracellular amyloid-beta (Aβ) plaques and neurofibrillary tangles in the intracellular environment, neuronal death, and synaptic loss are the defining characteristics of AD. These symptoms all gradually worsen cognitive function. Inflammation in AD has been linked to cognitive dysfunction, increased tauphosphorylation, increased Aβ generation, and neuronal damage. Activating the inflammasome NLRP3 causes pro-IL-1 and pro-IL-18 to break down into their active forms. Aβ fibrils cause the NLRP3 inflammasome to be activated, which causes the production of the pro- inflammatory cytokine IL1 in microglia and the worsening of NLRP3 inflammasome signaling following the impairment of autophagy. Here, we used an intracerebroventricular (ICV) injection of streptozotocin (STZ) to produce a rat model of sporadic AD, which increased cognitive impairment, NLRP3-mediated neuroinflammation, autophagy deregulation, and enhanced anxiety. In this study, we showed that the NLRP3 inflammasome and autophagy are regulated in parallel. Interestingly, supplementation of MCC950 reduces autophagy along with inhibiting NLRP3. In the current study, treatment with MCC950 not only slowed the development of AD pathology but also improved cognition in STZ- induced AD rats. NLRP3 may therefore represent a promising therapeutic target for the management of AD.

Keywords: Alzheimer's disease; NLRP3; Inflammation; amyloid-beta; autophagy; MCC950

Chronic Vitamin D3 administration rescues working memory and attention in MK-801 induced mouse model of schizophrenia

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Abstract

Schizophrenia (SCZ) is a neuropsychiatric disorder, characterized by positive, negative, and cognitive symptoms. Recently available medications for SCZ have shown an affirmative effect on positive symptoms but these are less effective on negative or cognitive symptoms. In this regard, Vitamin D3 (VD) has drawn keen attention because of its modulatory effect on neurotransmission, neurodevelopment,and neuroinflammation (Kaviani et al., 2020; Juwita et al., 2021; Jiang et al.,2022). In the present study, we used MK-801 (0.5 mg/kg) to recapitulate some of thenegative and cognitive symptoms of SCZ and explored the effect of VD on locomotion, anxiety, working memory, and attention. We have previously demonstrated the neuroprotective effects of VD in a mouse model of HD (Manjari et al., 2022). Here we performed behavior tests like an open field, elevated plus maze and novel object recognition on four groups of C57BL/6J miceto explore the modulation of VD on prefrontal cortex function. Mice were divided into four groups namely: **(1)** control (saline), **(2)** SCZ (MK-801, 0.5 mg/ kg), **(3)** Only Vitamin D3 (VD, 500IU/kg) and **(4)** SCZ +VD **(**MK-801, 0.5 mg/kg + VD, 500IU/kg). A reverse transcription- polymerase chain reaction was conducted (RT-PCR) from the prefrontal cortex brain tissue sample extracted on the 30th day, from the respective groups of mice. Our preliminary data show that pre-supplementation of VD significantly improves MK-801-induced alteration in the elevated plus maze, locomotor activity, and memory and attention function of the PFC circuitry. The rescue effect of VD on various behavior tasks was paralleled with restoration in the mRNA expression of NR2B and NR2A subunit of N-Methyl-D-Aspartate (NMDA) receptor in PFC. Collectively, our data suggest a novel function of VD in restoring PFC dysfunction in SCZ.

Keywords, MK-801, neurotramission, oxidative stress, Vitamin D3, NMDA, NR2A, NR2B.

Cerebellar volumetric changes in Spinocerebellar ataxia type 12 patients

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Abstract

Introduction: Spinocerebellar ataxia (SCA) is characterized by progressive cerebellar ataxia with oculomotor dysfunction, dysarthria, pigmentary retinopathy, peripheral neuropathy, cognitive impairment symptoms and pyramidal, extrapyramidal signs[1]. Cerebellum plays a role in motor control, voluntary activity (such as balance, speech, posture, tremors) and cognitive functions[2]. SCA is associated with progressive degeneration, the CAG repeat expansion on chromosomes and the atrophy of the cerebellum, varying across different types of SCA[3]. SCA type 12 is a very rare disease and more prevalent in the Indian subcontinent[4]. It is characterized by a slow progression of ataxia and tremor of the head and hand[5]. We usedstructural MRI data and a cerebellum volumetrics pipeline using brain stem atlas-based template to isolate and characterize atrophy in SCA12 in comparison with healthy controls[6-8].

Methodology: The study was carried out in twenty-one symptomatic SCA12 (mean age 52±10 years; 7F/14M) patients (after genetic confirmation from the ataxia clinic) without head tremor and fourteen healthy controls (HC, age=36±14, 6F/8M). 3D T1W images were acquired on a 3T MR scanner using a circular 32- channel head coil. After reorientation and cerebellar volume correction, 28 anatomical lobules were generated. Voxel-based morphometry (VBM) was carried out using the SUIT toolbox (in SPM version 12). Flat maps were used to visualize the 3D space of the cerebellum and brainstem area. Inter-group analyses were performed using an independent two sample t-test between the SCA12 and HC, with p-value ≤ 0.05. SPSS statistical software was used for Pearson correlation between age and cerebellum lobule volumes.

Result: Atrophy was observed in the bilateral cerebellum and brainstem in SCA12 patients. SCA12 group revealed prominent gray and white matter atrophy with a significant difference in bilateral posterior cerebellar lobules (lobule V, VI, Crus l and Crus ll, Vll B) in comparison with the HC. SCA12 group also revealed a reduced volumetric loss in Corpus Medullare, right lobule VIII B and right lobule lX in comparison with the controls. Total cerebellar volume was reduced in SCA12 group with respect to the HC group. We observed a negative correlation of cerebellum anterior lobule IV with age in SCA12 group.

Discussion and conclusion: Motor control and voluntary activity such as balance, speech and posture are controlled predominantly by the cerebellum. Lobules V and VI of the left and right hemispheres are associated with motor learning[9], and the primary motor cortex[10]. Crus l, Crus ll and VIIB are correlated with anterior cerebellar lobules[11]. Atrophy in the cerebellum, brainstem, basal ganglia and thalamus areas reported in SCA[12] and atrophy in bilateral posterior lobules in SCA12 patients[13] has been associated with motor dysfunction. Our results of atrophy in cerebellum, especially the posterior lobules and reduced cerebellar volume in SCA12 patients with respect to HC may be attributed to motor and cognitive dysfunctions. Cognitive or psychological illnesses can arise with cerebellar impairment, including gait ataxia, however these conditions are often not very disabling.

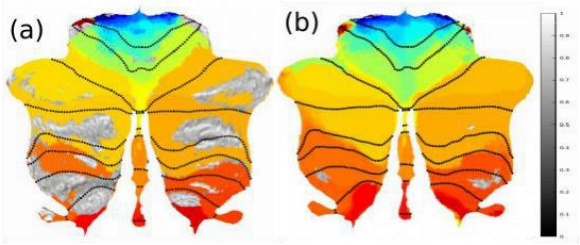


Figure1: Cerebellum atrophy of (a) SCA12 and (b) HC displayed on SUIT Flat map view (color map: jet and threshold 0:0.1)

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Proteomics Spotlight on Biomarkers of Parkinson's Disease

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Abstract

Background: Parkinson's disease (PD) is characterized by dopaminergic neurodegeneration in the nigrostriatal region of the brain. Neurodegeneration extends well beyond dopaminergicneurons. It is also characterized by pathogenic protein aggregates that correlate with the progressive degeneration of neurons and loss of behavioral functions. PD lack biomarkers for diagnosis and treatment efficacy. Proteomics is an unbiased qualitative/quantitative tool capable of the high throughput quantitation of thousands of proteins from minimal volume of complex. Therefore, it has been intended to evaluate the impact of MPTP (1-methyl-4-phenyl-1,2,3,6- tetrahydropyridine) on proteome of brain in MPTP-induced Parkinson mouse model.
Methods: PD was induced by intra-peritoneal injection of MPTP (20mg/kg body weight) in 4-6 weeks old AKR strain mice for consecutive 21 days. Normal saline was given as vehicle control. Further, the brain from control and treated groups were taken for the experiments. To gain a better understanding of the molecular changes relevant to PD, we applied 2DE and HRLCMS to analyze alterations of the proteome in brain using a MPTP-induced PD mouse model. In-silico studies were performed to see the protein-protein interaction (http://string-db.org) and pathway enrichment by KEGG.
Results: Proteomic profiling by 2DE showed alteration of various proteins in treatment group. The combined analyses resulted in the identification of 2,383 proteins with at least two unique peptides per protein. A total of 12 protein spots were selected for the analysis. Out of that, 7 protein spots were upregulated and 5 were downregulated in MPTP-treated mice. The relative abundance changes in both control and treated were estimated based on the spectral count information. Alpha synuclein, apoptosis, stress related proteins were also increased in the treatment group. Depletion of transmembrane protein 65 (tmem65) leads to oxidative stress, apoptosis which further enhance the progression of PD.
Conclusion: Our results provide the insight into the protein profiles of MPTP-induced PD mice brain and the underlying dysregulated pathways arising from the MPTP treatment.
Keywords: Neurodegeneration, MPTP, Parkinson disease, in-silico
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Choroidal capillary death in aging rat eye with emphasis on involvement of immunocompetent cells.

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Abstract

Choroidal capillaries die significantly with aging and in age-related ocular diseases. This limits the supply of nutrients and oxygen to outer retina, resulting in geographic atrophy characterized by loss of retinal pigment epithelium and photoreceptor cells. The mechanisms leading to capillary death in the choroid with aging are currently speculative. Microglia are abundant around capillary remnants in aged choroid, but it is unclear whether they are protective or detrimental. The purpose of this study was to look into the phenotypes of microglia in aged choroid as well as other immunocompetent cells (such as macrophages, dendritic cells, and monocytes) and their involvement in capillary death to see if they are pro-inflammatory. Male Wistar rats were reared on a regular diet until they were eight months old. They were sacrificed at four- and eight months of chronological age, and the eyes enucleated. ELISA was performed to measure the levels of proinflammatory cytokines, and histochemistry and immunohistochemistry were used to analyse the distribution and immunophenotypic markers of microglia/macrophages and other immunocompetent cells in the choroid. TEM was used to evaluate capillary damage and loss in the choroid of young and aged animals. The control group showed fenestrated capillaries with large luminal diameter measuring about 12±2.5 µm in mean diameter, whereas in experimental group capillaries were with uneven luminal diameter and partly enlarged in size (mean diameter: 16.7-19.4 µm). The endothelium and pericyte of most vessels were intact in control group, whereas the endothelial layer was vacuolated in experimental group, the pericyte layer, though intact, was electron-dense. The levels of TNF-α and IL-1β in serum and choroidal homogenates in young healthy rats showed an increased concentration but compared to control group, their levels were lower in the aged group (8 months of age). Whole-mounted choroid showed mast cells in central choroid that were aligned parallel to the length of the blood vessels. Immunohistochemical expression for Iba-1 revealed the choroidal microglia were much larger than those present in the retina. In the choroid, many of them showed few processes, compared to that seen in the retinal counterpart, a feature suggestive their activated state. The number of Iba-1 immunopositive microglial cells increased in number from 12-15 in four-month-old rats to 20-23 in eight-month-old rats. These data suggest mast cells as well as microglia to play a role in capillary damage.

Yoga: as a tool to enhance the Neuropsychology and Biochemical profiling in the newly recruited Police Personnel

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Abstract

Background: Police personnel are the backbone of anysociety responsible for maintaining law and order. The work environment and nature of duty play a major role incontributing to a stressful life in the regimented forces. Likewise, the newly recruited police personnel have to face a significant shift in their lifestyle by undergoing restless professional training, which is necessary for dealing with crimes in society. This affects their physical and mental health. Yoga, a holistic mind-body intervention, has been shown to improve both the physical and mental well-being of an individual.

Aim: We aimed to evaluate the effectiveness of the Common Yoga Protocol (CYP) in improving the Neuropsychology and Biochemical profiling in the newly recruited Police Personnel's

Methods: This single-centre randomized controlled trial was carried out at the Police Training Academy of Chandigarh Police, Hoshiarpur, Punjab. The participantsincluded newly recruited naïve police constables of Chandigarh Police. 478 police personnel of both genders were divided into Yoga (N=264) and non-Yoga control (N=214) groups. The 45-minute CYP practicewas administered along with their professional policetraining, whereas the Control group underwent only professional police training. The assessments were done at the baseline and after three months of the intervention.

Results: The analysis was performed through SPSS software, and normality was checked by Kolmogorov- Smirnov (K-S) test. A significant ($p \leq 0.05$) change was observed in the various Neuropsychology parameters (like WHOQOL-BREF, forward/backward scoring, trail-making test)

and also in the biochemical parameters (like cholesterol, LDL, sugar, and HDL) of the Yoga group compared to the Control.

Conclusion: 3 months of Yoga practice effectively help improve the physical and mental health of newly recruited police personnel undergoing professional training.

Keywords: Yoga, Police Personnel, Neuropsychology, Biochemical, RCT

Preliminary investigation on the effect of serum vitamin D status in young adults on serotonin and neurobehavioral symptoms typical of autism spectrum disorder and attention deficit hyperactivity disorder

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Abstract

Calcitriol, the active form of the vitamin D hormone, is a soluble vitamin that plays a vital role in overall health. To initiate genomic functions, it first binds to its target tissue vitamin D receptor (VDR) and forms a heterodimer with retinoid-X-receptor (RXR). Vitamin D-mediated action is elicited once the vitamin D- bound VDR-RXR complex binds to the vitamin-D response elements (VDRE) on target genes, regulating their transcription. Among the many VDR target genes are tryptophan hydroxylase 1 & 2 (TPH1, TPH2) genes, the rate-limiting enzyme in serotonin biosynthesis. Serotonin (5-HT) modulates various physical, physiological, and psychological functions. Therefore, vitamin D and VDR polymorphisms possibly affect TPH gene expression and controls the serotonin level in the CNS and periphery. Furthermore, there are studies linking vitamin D deficiency with various brain-related diseases, which are currently on the rise. At the same time, Vitamin D deficiency is also a significant concern globally. Based on this, we hypothesize that vitamin D, through the regulation of TPH, affects serotonin synthesis and modulates brain development and function. Thus, its deficiency may lead to neurobehavioral problems. Therefore, the objective of the study is to investigate the effect of serum vitamin D levels on platelet serotonin levels and ASD/ADHD-specific behaviour assessed using AQ and ASRS scores. Our survey on 172 young adults from the local population revealed that 23% are only vitamin D sufficient (VDS), and the rest, 77% are either deficient (VDD) or insufficient (VDI). Even though platelet serotonin level in participants with VDD was lower than that of the VDI and VDS, it was statistically insignificant. The genotypes of five VDR polymorphisms also did not show any differences in the serum vitamin D level. When the score of the participants showed an insignificant negative correlation with serum vitamin D levels, the AQ score showed a little positive correlation. The platelet serotonin also did not correlate with the AQ and ASRS scores. The preliminary results of this investigation suggest that vitamin D is unlikely to influence serotonin and neurobehavioral phenotypes specific to ASD and ADHD.

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Oleuropein protects from rotenone-induced nigrostriatal neuronal death in mice model by activating PI3K-Akt signalling pathways.

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Abstract

Background : One of the prevalent neurodegenerative conditions, Parkinson's disease (PD) is characterised by the gradual loss of dopaminergic neurons in the substantia nigra, causes muscular rigidity, bradykinesia and tremor. The major pathological condition of PD belongs to the fibrillar aggregation of α-synuclein that form Lewy body. The pathogenesis of Parkinson's disease (PD) is associated with impaired redox signalling, mitochondrial dysfunction, chronic neuroinflammation and apoptosis. Moreover, the pharmacokinetic effect of L-DOPA shows several side effects including dyskinesia. Therefore, new therapeutic strategies which modulates the cellular pathways that lead to neuronal cell death and dysfunction are needed. According to several research, polyphenols in plants and fruits contain antioxidant properties and can aid in the prevention of oxidative stress. One such compound, Oleuropein (OLE) is a polyphenolic compound found in Olive leaves and fruits exhibits anti-oxidative and anti- inflammatory properties. Present work is intended to investigate the neuroprotective role of OLE in rotenone-induced mice model by activating PI3K-Akt signalling pathways.

Methods and Materials: All protocols for animals (Swiss albino mice) on which the experiments were carried out was approved by the Animals Ethics Committee of our institute. Mice were divided into four groups: Control, Rotenone administrated with OLE and OLE group. The treatment group were first pre-treated with Oleuropein for 7 days and further the doses continue with dose of rotenone for 35 days. After completion of dosing, the mice were sacrificed and behaviour test was performed. The protein expression related with neuronal survival in PD was also detected through western blot analysis and immunohistochemistry.

Results: The Behaviour analysis showed the increase in motor impairment was observed in rotenone group as compared to control and the treatment group shows significant decrease in motor impairment. The expression of α-synuclein and several kinases protein like- Akt, PI3K and GSK-3β reduced in case of rotenone group than control and significantly increased in case of treated group. The immunohistochemistry analysis also revealed the decrease in expression of GSK-3β in rotenone group and decrease in treatment group and number of tyrosine hydroxylase positive cells was less in rotenone group and significantly more in OLE treated group.

Medicinal preparations of Nux vomica seed extracts and Cicuta virosa root extracts can potentiate neuronal fortification by upregulating mitochondrial biogenesis pathways in PTZ induced kindling mice model of epilepsy

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Abstract

Background and rationale: Conventional Anti-epileptic Drugs (AEDs) focus primarily on the ion channel failure while not addressing the potent neurochemical alterations responsible for chronic epileptic condition. Herbal remedies have accrued great interest in this regard owing to their competent efficacy without side effects.

Methods: The medicinal formulations (30CH; pre-treatment) of Nux vomica (NV) and Cicuta virosa (CV) were produced as per Homeopathic Pharmacopoeia of India. PTZ induced Kindling was (29 days; 35 mg/kg; i.p. alternate dose) followed by biochemical (MDA, GSH and SOD levels) and molecular (SIRT1/PGC1-α protein expression; Glutamate/GABA ratio) investigations. Gabapentin (GBP; 200 mg/kg;
i.p. pre-treatment) was used as the reference drug. Data were expressed as Mean ± SD and analyzed using ANOVA one-way ($\alpha = 0.05$) and Tukey's post hoc test ($n = 6$).

Results: Medicinal formulations significantly delayed the kindling [NV30CH; $F(1,28)=15.27$; $p<0.001$: CV30CH; $F(1,28)=11.38$; $p<0.01$] and enhanced the seizure latency [NV30CH; $F(1,10)=9.41$; $p<0.05$: CV30CH [$F(1,10)=7.57$; $p<0.05$]. Biochemical investigation revealed downregulated MDA [NV30CH; $F(1,10)=14.37$; $p<0.01$: CV30CH; $F(1,10)=10$; $p<0.05$] levels and enhanced GSH [NV30CH; $F(1,10)=7.5$; $p<0.05$: CV30CH; $F(1,10)=3.75$; $p>0.05$] and SOD [NV30CH; $F(1,10)=9.43$; $p<0.05$: CV30CH; $F(1,10)=9.01$;
$p<0.05$] levels in the pre-treatment groups. Furthermore, PTZ induced SIRT1 [$F(1,10)=620.76$; $p<0.001$] and PGC1-α [$F(1,10)=327.20$; $p<0.001$] degradation was ameliorated by NV30CH [SIRT1; $F(1,10)=5.52$, $p<0.05$: PGC1-α; $F(1,10)=1.59$; $p>0.05$] and CV30CH [SIRT1; $F(1,10)=0.70$; $p>0.05$: PGC1-α; $F(1,10)=1.26$;
$p>0.05$). Also, PTZ led increase in Glutamate/GABA ratio [$F(1,10)=326.04$; $p<0.001$] was notably restored by NV30CH [$F(1,10)=16.37$; $p<0.01$] and CV30CH [$F(1,10)=3.33$, $p>0.05$].

Conclusion: The activation of SIRT1/PGC1-α pathway was observed to be accompanied with restored excitation-inhibition balance (glutamate/GABA ratio) in the neuronal circuit along with decreased free radical activity and downregulated lipid peroxidation.

Ethics statement: The IAEC guidelines were strictly adhered throughout the study.

Acknowledgement and conflict of interest: None.

Tinospora cordifolia Protects Dopaminergic Neurons from Mitochondrial Dysfunction and Attenuates Rotenone-Mediated Parkinson's Disease

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Abstract

Background: Oxidative stress-induced mitochondrial dysfunction and disturbed mitochondrial dynamics were found to be common phenomena in the pathogenesis of Parkinson's disease (PD). Tinospora cordifolia (Guduchi) has emerged as a novel medicinal plant that protects neurons from oxidative stress.
Objective: In the present study, we investigated the autophagy/mitophagy-enhancing effect of Tinospora cordifolia and explored its neuroprotective mechanism in the rotenone-intoxicated PD model.
Material and Methods: Mice were divided into four experimental groups: control, rotenone (2 mg/kg body wt., subcutaneous), Tinospora cordifolia extract (TCE, 200 mg/kg body wt., oral) + rotenone, and TCE only]. Mice were pre-treated with TCE for a week and then simultaneously injected with ROT for 35 days.
Results & Discussion: Tinospora cordifolia rescued the rotenone-induced loss of dopaminergic neurons and mitochondrial membrane potential. Subsequently, the accumulation of mitochondrial reactive oxygen species (ROS) was balanced by an increase in the expression of antioxidant enzymes. Furthermore, Tinospora cordifolia restored rotenone-impaired autophagy and mitophagy regulators PINK-1 and Parkin in Parkinsonian mice. In addition, Tinospora cordifolia reduces α-synuclein accumulation and increases the autophagy marker LC3-II compared to the rotenone-intoxicated group. These results demonstrated that Tinospora cordifolia exerted neuroprotective effects by upregulating autophagy and PINK-1/Parkin mediated mitophagy in PDmice.
Conclusion: Taken together, our findings indicate that Tinospora cordifolia has beneficial neuroprotective effects in PD and it might be a potential therapeutic agent for the treatment of PD.In light of its favorable neuroprotective properties, Tinospora cordifolia should be evaluated in the treatment of PD as well as related neurologic disorders.
Keywords: Parkinson's disease; Tinospora cordifolia; rotenone; α-synuclein; mitophagy; reactive oxygen species

Vitamin D3 administration decreases oxidative stress induced by 3-nitropropionic acid and alleviates native immune receptor, T-cell receptor beta subunit expression in a mouse model of Huntington's disease

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Abstract

Recent scientific evidence has established that the nervous and immune systems have shared molecular signaling components and proteins native to the immune system are also expressed in the cells of the central nervous system. One such immune molecule is the T-cell receptor beta (TCR-β) subunit, whose expression was documented by Syken and colleagues in 2003. However, whether neuropathological conditions characterized by increased oxidative stress and neuroinflammation cause an enhancement in the gene expression of a brain-resident immune molecule like TCR-β is presently unknown. In the present study, we utilized 3-nitropropionic acid (3-NP) to induce HD-like symptoms in mice and explored if such a neurotoxic environment leads to an increase in the TCR-β mRNA expression of the cortex and striatum. We found a substantial enhancement in the gene expression of the TCR-β subunit in HD. Interestingly, Vitamin D3 (VD) supplementation alleviated the TCR-β subunit expression with the concomitant restoration of acetylcholine in both cortex and the striatum in HD mice. Recent findings from our lab showed a neuroprotective effect of VD in restoring motor function in HD (Manjari et al., 2022). Komal and colleagues also documented a negative functional interaction between TCR and α7 nicotinic acetylcholine receptors (Komal et al., 2014). In addition, administration of VD to 3-NP treated mice rescued the expression of antioxidants (Superoxide dismutase 1 [SOD1], Superoxide dismutase 2 [SOD2], Catalases [Cat], and Glutathione peroxidase [GpX4]) in both the brain regions. Collectively, our data decipher a novel function of VD in combating immune protein, the TCR-β subunit in HD.

Pathophysiological alterations of the prefrontal cortex in a rat model of Alzheimer like-disease with a preferential role of "Propranolol"

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Abstract

Propranolol is a well-known antagonist for beta-adrenoceptors, and exerts activity on the cholinergic system and modulates the memory disturbance in the animal model of cognitive deficit. Propranolol is also involved in the direct inhibition of AChE and has an innovative role in adrenergic pathways in memory modulation. Through this study, we have evaluated the effect of memory performance at different doses of propranolol and taken donepezil as a positive control. In this study, the nootropic and anti-amnesic effects of propranolol on scopolamine-induced amnesia in wistar rats were evaluated. Rats were treated once daily with propranolol (10 mg/kg, 30 mg/kg, and 50 mg/kg) and donepezil (1 mg/kg) orally for 17 days. During the final 9 days of treatment, a daily I.P injection of scopolamine (3 mg/kg) was administered to induce cognitive deficits. Besides that, behavioural analysis was carried out to assess the rats' learning and memory functions. Meanwhile, prefrontal cortex tissues were extracted for protein expression, neurotransmitter analysis, and histopathological studies. Results suggested that propranolol was found to significantly improve the recognition (NOR) and elevated plus maze (EPM) tests, respectively. Furthermore, propranolol at certain doses (10 mg/kg, 30 mg/kg, and 50 mg/kg) significantly exhibited a memory-enhancing effect in the absence of scopolamine, besides improving the recognition index when challenged with chronic scopolamine treatment. Moreover, in the EPM test, propranolol-treated rats showed an increase in inflection ratio in nootropic activity. In addition, propranolol contributed towards the elevated expression of BDNF, CREB1 and lowered the oxidative markers (SOD and LPO) expression. Pre-treatment of rats with propranolol mitigated scopolamine-induced neurochemical and histological changes in a manner comparable to donepezil. These findings suggest that propranolol is a nootropic compound, possesses an anti-amnesic ability that is displayed against scopolamine-induced memory impairment in rats.

Key words: Alzheimer's disease (AD), Scopolamine, Propranolol, Learning and Memory and Neuroprotection.

Role of candidate genes (ARMS2, COL10A1, RAD51B, and TGFBR1) Single nucleotide polymorphisms and protein levels in Age-related Macular Degeneration

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Abstract

Background: Age-related macular degeneration (AMD) is a sight debilitating disease involving progressive degeneration of RPE and neuroretina. It is a complex multifactorial disease involving genetic, environmental, and sociodemographic components. GWAS studieshave identified genes that harbour risk SNPs for AMD. But the role of these genes remains elusive in the context of the Indian population. This study was done with the aim of exploringthe status of the SNPs and related proteins in Indian AMD patients.
Methods: The present study was carried out on 238 individuals (150 AMD patients and 88 controls. ELISA was used for the estimation of proteins in the serum of the participants. Taqman genotyping assay was used for SNP genotyping of the samples. SPSS version 21 wasused for statistical analysis.
Results: We found that the genotypic frequency of ARMS2 and COL10A1 is significantly different between cases and controls (p=.0001). Also, the protein levels of COL10A1 were significantly higher and level of RAD51B and TGFBR1 was significantly lower in AMD as compared to controls. The level of RAD51B was found to be increased post-follow-up in AMD

patients. AUROC analysis revealed that these SNPs also have high sensitivity and specificity in predicting AMD. Also, the protein levels of COL10A1 were found to be significantly associated with lifestyle factors like sleeping hours. Also, the AMD treatment with Vitamin/mineral supplements altered the level of these proteins to some extent. A significant and positive correlation was also found between these molecules.

Conclusion: We conclude that the SNPs in the above genes are implicated in AMD in the Indian population and AMD risk can be predicted on the basis of lifestyle factors, protein levels, and genotypic frequencies of studied genes.

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A deep proteome study of the rat hippocampus reveals crucial proteins involved in the pathogenesis of Moderate Hepatic Encephalopathy

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Abstract

Patients with liver disease develop a serious neurological disorder known as hepatic encephalopathy (HE), which is associated with a broad spectrum of neurological or psychiatric abnormalities and motor dysfunction. 80% of cirrhotic patients develop minimal HE (which involves subtle changes in cognition and motor coordination), while 30–50% develop overt HE. Patients with overt HE have a high mortalityrate and is a cause of great concern amongst clinicians and researchers. Studies in the last few decades identified increased glutamate-led overactivation of NMDAR receptors as the key pathogenic factor responsible for neurological dysfunction in moderate HE. However, NMDAR as a therapeutic target isnot a viable option. So, to discover new non-NMDAR therapeutic targets, we have used high-resolutionmass spectrometry-based proteomic profiling of the MoHE rat model brain. The most malleable brain region, the hippocampus (involved in learning and memory), was selected for our study.

Adult Charles Foster rats were categorized into two groups: (a) control (n = 6) and (b) MoHE (n = 6), each administrated with 1X PBS and thioacetamide (100 mg/kg body wt) i.p., respectively, once daily for 10 days. Rat hippocampal protein was extracted by urea lysis buffer from both groups, the protein was estimated, and 50µg protein was trypsin digested. The desalted peptides were analyzed by label- free, LC-MS/MS mass spectrometry on the tribrid mass spectrometer Thermo Scientific Orbitrap Fusion. Proteome Discoverer was used to identify the proteins in both the groups, followed by Statistical analysis by MetaboAnalyst, Gene Ontology (GO) enrichment, and protein-protein interaction analysis by Metascape and StringDB, respectively. Some significantly upregulated proteins were validated by qPCR, western blot, and immunofluorescence (IF).

In LFQ analysis, we found 2175 proteins. After performing missing value imputation (>30%), 1898 proteins were taken for statistical analysis. The volcano plot showed 47 dysregulated proteins, of which5 were downregulated and 42 upregulated in the MoHE group. A few critical proteins among the top 10 upregulated proteins are Homer-2, Y-box-binding protein 3, Autophagy-related protein 9A, Focal adhesion kinase 1, Tetraspanin 2 and CD9 antigen. IF and western blot analysis of Homer-2, Focal adhesion kinase 1, Tetraspanin 2, and CD9 antigen validated the increased expression in MoHE rat hippocampus compared to control. Network analysis on Metascape showed that a few enriched biological processes necessary for the CNS to be perturbed during MoHE, such as gliogenesis, astrocyte differentiation, regulation of myelination, and post-translational protein phosphorylation. The role of these proteins in the pathogenesis of MoHE is being studied.

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Curcumin activates selective autophagy through p62-mediated Nrf2-Keap1 pathway in Parkinson's disease

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Abstract

Background: Parkinson's disease (PD), a motor disease, is caused due to aggregation of abnormally misfolded alpha-synuclein protein in cytoplasm of dopaminergic neurons. These aggregated proteins are cleared by a process called autophagy which degrades long-lived and damaged proteins and organelles from the cell. Curcumin, a polyphenol, is known to be a potent autophagy inducer.
Objective: To study the effect of curcumin on autophagy and Nrf2-Keap1 pathway as a potential treatment therapy in Parkinson's disease.
Methodology: The mice were divided into four groups, Control group; Rotenone group; Rotenone + Curcumin group and; Curcumin alone group. The mice were subcutaneously injected with rotenone (2.5mg/kg bw) and co-treated with oral administration of curcumin (80mg/kg bw) for 35 days.
Results: The results revealed the downregulation of Nrf2 in the rotenone-intoxicated mice along with decrease in tyrosine hydroxylase (TH) level. However, the level of both Nrf2 and TH were significantly restored on the treatment with curcumin. Autophagy was evaluated by the change in expression of autophagic markers, p62 and LC3-II. Increased p62 expression and decreased LC3 expression in the rotenone mouse model of PD confirmed the compromised autophagy pathway, consequently increasing the aggregation of misfolded protein α-syn. Whereas, curcumin treatment showed a significant decrease in the expression of autophagy substrate p62 along with down-regulation of α-syn expression and increased level of LC3-II.
Conclusion: The findings reveal the neuroprotective role of curcumin in rotenone-intoxicated mice by activating p62-dependent Keap1-Nrf2 autophagy pathway.

An Alzheimer's disease Domain-Specific network pharmacology of Nelumbo nucifera and specific targets identification responsible for Alzheimer's disease

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Abstract

Background: Alzheimer's disease (AD) is one of the most complicated progressive neurodegeneration diseases that involve many genes, proteins and their complex interaction. No effective medicines or treatment are available yet to stop or revert the progression of AD due to its polygenic nature. Form last three decades herbal drugs have been used as role model in the field of drug discovery. The herb Nelumbo Nucifera (NN) is a common prescribed herb for various neurological disorders such as Parkinson, Huntington and Alzheimer's. However, the underlying mechanism between AD and NN is unclear.

Objective: In this study we aimed to explore the active photochemical, target predictions, blood brain barrier crossers, gene ontology, pharmacokinetics analysis (absorption, distribution, biotransformation and excretion), and network construction between NN and AD to find out the targets that can be targeted specifically in order to have best approachable treatment possible for AD.

Material and methods: DRUG BANK, GENE CARD, BATMAN-TCM and literature were searched thoroughly for targets prediction of NN and AD. Further CYTOSCAPE were used to build the network. Additionally, Swiss ADMET was used to screen pharmacokinetics profile of 255 photochemical of NN and other criteria for being a drug such as Lipskie rule, BBB crossers, solubility, partion coefficient, lead likeness and pain. Selected phytochemicals were used for Molecular Docking.

Results: Search system/database extracted total 93 targets of NN and 11504 targets of AD out of them 4 genes were found to be common. Further from network construction, top 10 genes such as APP, GSK3B, AXIN1.APBB1, HSD17B10, CTSD, FRAT1, GAPDH, APLB1, and
NUMB were found as significant targets related to AD and on the basis of pharmacokinetics profile 5 best phytocheimicals such as nuciferine, lotusine, pycnarrhine, geraniol and isosinomenine were screened from 255 compounds for being a drug to target AD.

Conclusion: Our work illuminates the multicompounds, multitargets and curative action of NN in the treatment of AD by network pharmacology.

Molecular, cell survival and neuro-cognitive effects of yoga intervention instress induced cognitive impairment in prisoners

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Abstract

Background: Cognitive impairment is a pre-stage of memory loss. The most common factors thatcan be considered responsible for cognitive impairment are stress, depression, and anxiety. Stress can lead to cognitive decline and memory loss in severe stages. Prison populations show high levels of stress due to social isolation and other factors. Yoga has been showed proven effect on stress and cognitive variables. However, there is lack of mechanistic studies on effect of Yoga to combat stress and cognitive impairment on prison inmates.

Aim: To evaluate the effect of AYUSH Common Yoga Protocol to manage stress induce memoryloss in the prison population.

Methodology: Different Neuropsychological, Biochemical, and Molecular Assessments will be done at baseline and after intervention to analyse the changes in different variables of stress and cognitive impairments. Comparison will be done to determine levels of significance with respect to control subjects.

Hypothesis: Common Yoga Protocol alleviates stress-induced cognitive impairment by increased expression of neurotrophic factors.

Keywords: Yoga, Stress, Cognitive Impairment, Prisoners. Acknowledgement: Authors are thankful to the authorities for permission.Conflict of Interest: No conflict of interest.

Potential of stem cells in rescue of retinal injury and visual memory by subretinaltransplantation of UCB derived Lineage negative stem cells in mice.

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Abstract

Background- Visual pathway involves synaptic signalling to amplify the neuronal signals resulting in visual image formation. Disruption in the pathway leads to visual impairment, cognition decline and memory loss. Although, various studies have been carried out to reversethe injury by therapeutic intervention but these have not clinically translated successfully.

Purpose- To evaluate the effect of retinal injury on visual spatial memory by establishing a laser injury model using laser photocoagulator and its rescue by subretinal transplantation of Lineage negative stem cell derived from Umbilical cord blood in mice model.

Methods- C57BL/6J male mice were used for the study. The retinal injury was given around the optic disc using laser photocoagulation with defined parameters that disrupted the RPE layer of the retina. The specific number of laser spots were given into the mice each eye such as 2 laser spots, 4 laser spots and 8 laser spots were given into the mice eye. The Fundus Fluorescein Angiography was done to confirm the establishment of injury model. Subsequently, visual-spatial memory was analysed by neurobehavioral tests and short-term memory by using Morris Water Maze (MWM) and Passive Avoidance followed by molecularassay by RT-PCR and Immunohistochemistry.

Results- In neurobehavioral experiments, we measured the escape latency time in all groups such as Healthy group, Vehicle group, laser injury (2, 4 and 8 laser injury) and stem cell transplantation group (2,4 and 8 laser) followed by passive avoidance test, the latency time wasrecorded. We found learning behaviour in the stem cell transplantation group after injury AND in RT-PCR and IHC specific genes were upregulated after transplantation of stem cell such as BDNF, CNTF, Ki67 and other markers that shows neuronal activity was found be higher aftertransplantation. This implies the

positive efficacy of stem cell to rescue the injury.

Conflict of Interest- None

To discover a novel investigational molecule towards serotonin receptor modulation for targeting neurodegenerative disorders.

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Abstract

Background: Neurodegenerative diseases are a category of conditions caused by gradual degradation to cells and nervous system connections that are necessary for movement, coordination, strength, sensation, and cognition affecting millions globally. Neurodegenerative disorders either include age related disorders such as Alzheimer's disease, Parkinson's disease, multiple system atrophy, Huntington's disease, Stroke or disorders arising due to neurodegeneration caused by chronic diseases such as epilepsy. Because neurodegenerative illnesses are so complicated, the aetiology of many of them is unknown. The serotonin receptors are linked to various neurodegenerative disorders like Parkinson's, Amyotrophic lateral sclerosis, multiple sclerosis, attention-deficit hyperactivity disorder, and autism spectrum disorder.

Aim: To identify novel investigational molecules that can regulate the $5HT_{2B}R$ and neurotransmitter release, as well as target neurodegeneration therapeutically.

Methods: The target is a mutant chimera at RCSB, so homology modelling is performed and the 3D structure is validated (Ramachandran plot, enrichment analysis), virtual screening of the investigational library (compounds-2029) is performed to determine the lead medications, and shortlisting is also based on pharmacokinetic and toxicology (ADMET/QSAR) studies. A molecular dynamic simulation technique is utilised to test the drug-receptor complex stability.

Results: The 3D-structure of receptor is modelled and validated, only after recording that a maximum number of residues favour the 3D structure existence and stability, the modelled receptor is considered for further experimentation. After screening and ADMET/QSAR analysis of the investigational library, three compounds are shortlisted based on docking score, blood brain permeability, mutagenicity as well as carcinogenicity profile, and stable RMSD, RMSF values as compared to Apo. The RMSD values resemble to that of the Apo state clarifying a stable and strong binding between the top chosen drug molecules and target receptor. The top three compounds belong to the benzenoids class and the trajectory analysis- radius of gyration show better compaction and thus stable binding even better than Apo. Further, DCCM and PCA also points out a strongly positive correlation between the residues on drug-binding.

Conclusion: The strong and stable binding of the top three drugs can be involved in regulating $5HT_{2B}R$ and might target some neurodegenerative disorders.
Keywords: $5HT_{2B}R$, Benzenoids, Investigational drugs, Molecular dynamics, Radius of gyration, Serotonin receptors.

Artificial Activation of Hippocampal Subfield CA1 drives the memory-driven Perception, which interferes with the Sensory Perception

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Abstract

Episodic memories are the memories of everyday experiences, such as what happened, when, and where, which can be stated explicitly. Episodic memories are not just retrieved as a fact or information but are accompanied by the perception of the particular episode. Such memory-driven perceptions also invoke the emotional states experienced during the episode along with the factual and sensory information. The hippocampal formation, specifically the subfield CA1, is critical for encoding, consolidation, and retrieval of episodic memories. Sensory information from different sensory regions finally converges to CA1, making it ideal as an integrator of multi-modal sensory information. Memories are stored in a population of sparse neurons, also known as engrams, which undergo physical and chemical changes during and after the experience of an event. In this study, we hypothesize that the Hippocampal subfield CA1 is the seat of memory-driven perception; if artificially activated, it can interfere with the sensory perception to create a mixed perceptual reality. We have used state-of-the-art optogenetic tools to activate the CA1 neuronal population, encoding a specific memory under various testing conditions. We found that the memory-associated behavior is enhanced when CA1 is activated to invoke a memory of particular context A when animals are also present in context A. In order to understand how vital is incoming sensory information to CA1 during memory retrieval, we chemogenetically inhibited the Retrosplenial cortex (RSC), which feeds information to CA1. We report a reduction in memory-associated behavior upon blocking the sensory input to CA1, but when the memory engram of CA1 is activated optogenetically, it can overcome the deficiency of sensory information, and behavior is restored to normal. These results suggest that the memory-driven perception arises in the CA1, and it should align with sensory perception to invoke the associated behavior. Moreover, any conflict between memory and sensory perceptions creates a perception of mixed reality, suppressing the behaviors associated with the sensory or memory-based information alone. These results shed light on the cognitive processes of memory and perception and how these interact to modulate behavior.

18-β Glycyrrhetinic acid ameliorates alpha-synuclein aggregation targeting the ER-stress pathway in the Parkinsonian mouse model.

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Abstract

Introduction: Alpha-synuclein aggregation mediated endoplasmic reticulum (ER) stress is the major factor that is involved in the apoptosis of dopaminergic neurons in Parkinson's disease (PD). PD is the second mostcommon form of neurodegenerative disorder after Alzheimer's disease, affecting the population worldwide. To date, the only treatment options available are either dopamine agonist or L-dopa with several side effects. In the present study, we have evaluated the neuroprotective effect of a pentacyclic triterpenoid aglycone compound 18-β Glycyrrhetinic acid (GA) on a-synuclein aggregation and endoplasmic reticulum stress- mediated apoptosis in the parkinsonian mouse model.

Methodology: Swiss albino mice weighing 25±5 g was used in the study. Experimental animals were randomized into four groups: control, MPTP, GA+MPTP, and GA. Control group received saline/probenecid. The diseased (MPTP) and treatment (GA+MPTP) groups received chronic doses of MPTP/probenecid whilethe treatment (GA+MPTP) and only compound (GA) group received GA for 5 weeks. After the completion of dosing, the behavioral test was performed and mice were sacrificed and brains were isolated for further western blot analysis.

Results: The results indicate that the GA treatment significantly improved motor coordination of MPTP- intoxicated mice. It also reduced the overexpression of alpha-synuclein protein. Further, GA inhibits the activation of ER-stress marker Grp-78 and pro-apoptotic protein Bax while elevating the activation of anti- apoptotic protein Bcl2, thus playing a major role in inhibiting the further death of dopaminergic neurons.

Conclusion: The findings signify that the GA has pharmacological properties which contribute to neuroprotection against MPTP-induced alpha-synuclein aggregation, ER stress, and cell death. GA treatmentcan further arise as a potential therapeutic candidate for ER-stress-mediated apoptotic death of DA neurons inPD.

Keywords: Parkinson's disease, Endoplasmic reticulum stress, Apoptosis, Alpha-synuclein aggregation,Grp-78

1

Identification of a novel agonist and anti-ferroptotic small molecule for ferroptosis cascade receptor glutathione peroxidase (GPX4) targeting acute ischemic stroke

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Abstract

Background: Acute Ischemic Stroke, accounts for ~85% of all stroke cases, occur due to the obstruction of the blood supply to the brain, causing hypoxia and ultimately neuronal apoptosis. Nowadays, an iron cell dependent pathway i.e., ferroptosis is emerging cascade playing a vital role in ischemic stroke pathophysiology. The iron dependent cascade isassociated with critical events such as excess iron accumulation, disruption of blood brain barrier, increased reactive oxygen species (ROS), impairment of cystine/glutamate antiporter, depletion of glutathione and Glutathione peroxidase (GPX4), mitochondrial damage and neurodegeneration. GPX4, an antioxidant, is a key regulator of ferroptosis cascade and converts glutathione into oxidized glutathione, causing transformation of cytotoxic lipid peroxides to the corresponding alcohols. However, in ischemic condition the aggregation of iron and ROS reduces glutathione synthesis which eventually causes suppression of GPX4. In contrast, activation of GPX4 leads to the inhibition of ferroptotic neurodegeneration and provides a promising approach for ischemic stroke therapeutics. Therefore, an in-silico investigation is hypothesised to find out a potent agonist for GPX4 and emphasizing their preferential bindingacross varied species 6HN3 for Homo sapiens and 5L71 for Mus musculus.
Aim: A computational analysis to identify the potent agonist for ferroptosis cascade receptor GPX4 in acute ischemic stroke therapeutics.
Methods: In the present study, the 3D structure of 6HN3 and 5L71 for two distinct species(Homo sapiens and Mus musculus) were considered. A set of 723 ferroptosis ligand library virtual screening was conducted at extra precision. Top one compound with higher negative docking score were shortlisted and further subjected to molecular dynamic simulations and trajectory analysis.
Results: The virtual screening results imply a common/ multi-target compound for 6HN3 and 5L71 i.e., Secoisolariciresinol diglucoside (SDG) having docking score of -8.627 and -7.544 respectively. The compound SDG, is a plant lignan extracted from flaxseed and possessstrong antioxidant, neuroprotective and anti-hyperlipidemia characteristics. It forms stable H- bonds with 6HN3 and 5L71, comprising some of the alike interacting amino acid residues suchas Asp21, Asp23, Lys99, and Asp101. MD trajectory analysis i.e., RMSD(~1.35Å and 1.60Å),RMSF(~2.3Å and 2.4Å), Rgyr(~5.4Å and 5.25Å) and B-factor(24Å and 60Å) of SDG with 6HN3 and 5L71 respectively; provides greater stabilisation, firm binding and compact structures. DCCM & PCA analysis shows positive correlation, atomic displacements and residual clustering among residues of protein-ligand

complexes.

Conclusion: The stable and firm binding of multi-target compound SDG can be considered as a potent agonist and anti-ferroptotic agent for GPX4. Thus, SDG might anticipate as promising therapeutics in ischemic stroke for further translational studies.

Keywords: Acute Ischemic Stroke, Ferroptosis, Glutathione peroxidase (GPX4), Molecular Dynamics.

Glial niche and its function in central nervous systemdevelopment

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Abstract

Stem cell does not always function in isolation. They are surrounded by cells that serve as a niche and help them communicate with their surroundings. This cross-talk between signals intrinsic and extrinsic to stem cells is also essential in regulating its correct fate. Drosophila neural stem cells (NSCs) or NBs are popular models to understand how this communication occurs. In a screen, we have identified several genes that non-autonomously influence the NSC homeostasis. During different stages of development, the NSCs can switch fates back and forth from proliferation to quiescence. We are exploring the extent to which the glia niche is involved in decision-making for various stem cell fates. We have found that knockdown of the candidate genes through RNAi affect the glial. We are currently exploring several signaling pathways that could be pivotal in establishing the cross-talk between NBs and their microenvironement.

A novel histone lysine demethylase of the KDM7 family is implicated in chronic stress- induced depression-like phenotype in mice with specific involvement in adult neurogenesis

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Abstract:

Chronic psychological stress causes widespread epigenetic changes in the brain and these changes are known to precipitate the development of neuropsychiatric disorders, including depression. Depression involves dysregulations of several functional regions of the brain primarily those involved in mood, reward perception and cognition. Among the various brain regions involved, functions of the hippocampus, widely known for its role in long-term memory and mood regulation, have been illustrated more recently. It has a niche called the dentate gyrus (DG) which is one of the very few brain regions known to have adult neurogenesis. Dysregulations of adult hippocampal neurogenesis have been observed in depression; however, its functions and the molecular mechanisms involved remain elusive.

Epigenetic alterations in response to chronic stress have been observed in the DG in animal models of depression and some other neuropsychiatric disorders. Changes in histone post translational modifications and some associated enzymes have been shown to be involved in stress and depression. Among these, the KDM7 family of lysine demethylases are well characterised for their roles in neurodevelopment and neural and glial differentiation. However,their exact role in mediating the effects of stress on DG neurogenesis, which may contribute to depression-like phenotype and comorbid cognitive impairment, is not yet known.

To investigate this, we used chronic social defeat stress (CSDS) mouse model. We found that the expression levels of the KDM7 family genes were dysregulated in the hippocampus including the DG of the defeated C57bl/6 mice. A putative demethylase of this family, 49…Rik, that was uncovered in a previous high-throughput ChIP-Chip study from the mouse brain, was also found to be dysregulated in the DG of defeated mice. On probing in vitro in cultured neural stem/progenitor cells derived from the DG, results indicate its involvement in neural stem cell differentiation. Interestingly, upon its overexpression in the mouse DG using recombinant Adeno Associated Virus 2 (rAAV2), the animals showed depression –like phenotype even without CSDS. We, for the first time report the involvement of this novel demethylase in depression and have also identified its tentative histone lysine methyl targets.

Oxidative Stress-induced Impairment in human Mesenchymal Stem Cells

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Abstract

Stem cell treatments have become a potential treatment for numerous disorders, including ischemic stroke. Cell survival, post-transplantation, remains a serious problem post-treatment. In this context, we studied the effect of oxidative stress on human mesenchymal stem cells (hMSC). Oxidative stress was induced in hMSC using oxygen-glucose deprivation (OGD). OGD-induced production of $O2^{\bullet-}$ or H2O2 enhanced autophagy by enhancing the expression of the activating molecule in the BECN1-regulated autophagy protein1 (Ambra1) and Beclin1 in hMSC. However,. We further observed that autophagy was affected by $O2^{\bullet-}$ or H2O2, and the process was unidirectional. Reactive oxygen species (ROS) scavengers were used to pre-condition hMSCs and this drastically reduced the expression of Ambra1 and Beclin1, as well as inactivated autophagy. Furthermore, our results demonstrated ROS-p38-Erk1/2 involvement in stressed hMSCs. SB202190 and PD98059, which are specific inhibitors of the p38 and Erk1/2 pathways, pre-treatment reversed the effects of OGD on the expression of Ambra1 and Beclin1, indicating that oxidative stress-mediated autophagy was activated by these mechanisms. These discoveries helped us understand why hMSCs die after transplantation and might lead to the development of preventative measures against therapeutic cell loss caused by oxidative stress.

Key words: oxygen-glucose deprivation; human mesenchymal stem cell; autophagy; $O2^{\bullet-}$ or H2O2; Ambra1; Beclin1

Altered patterns of angiogenic and neuroprotective molecules in CSF and plasma ofALS patients leads to degeneration of NSC 34 cells

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Abstract

Introduction: Amyotrophic Lateral Sclerosis (ALS) is a devastating neurodegenerative disorder and progressively leads to degeneration of motor neurons at the neuromascular junctions, resulting in paralysis to the patients. VEGF, VEGFR2 and ANG are important neuroprotective molecules and work in tandem for neuroprotection. Observing all the three molecules as a panel in CSF and plasma of patients may have diagnostic importance. Further testing the effect of the alterations found on NSC34 cells provided evidence of alteration of VEGF mRNA expression in cells exposed to media having plasma of ALS patients.

Method: Protein levels of VEGF, VEGFR2 and ANG were analysed in the CSF and plasma of ALS patients using ELISA. Neuroblastoma Spinal Cord hybridoma cell line (NSC34) was cultured under appropriate conditions. 10% ALS patients' plasma and CSF was added to the media and cells were conditioned for 12 hours. Cell survival analysis and differential gene expression of VEGF, VEGFR2 and ANG was investigated.

Results: All the three molecules were found to be decreased in ALS patients' plasma. VEGF and ANG were decreased in the CSF of patients. However, VEGFR2 was found to be elevated in the CSF of patients. ALS patients' plasma impacted the cell viability and reduced the survival to nearly 50% after induction. VEGF was found to be significantly down- regulated in the cells which can be explained as a reason for reduced cell survival.

Conclusion: The altered levels of angiogenic and neuroprotective molecules in the surrounding media, affects the survival of the cells via mRNA expression alteration in the cells.

Treatment with novel Hippo Signaling inhibitor, Xmu-mp-1, ameliorates cognitive impairments in sporadic Alzheimer's disease.

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Abstract

Alzheimer's disease (AD), the most common form of dementia, is a progressive neurodegenerative disorder associated with aging. Persons with Alzheimer's face some serious problems related to memory, thinking, motor movements, language, and behavior due to neurodegeneration in the brain. Apoptosis is one of the mainstream mechanisms driving neuronal death. The Hippo signaling pathway has recently emerged as a critical pathway influencing cell survival, proliferation, and apoptotic-related pathophysiological conditions. Previous studies have highlighted the contributions of a hyper-activated Hippo signaling pathway in executing cellular death in various neurodegenerative disorders, including AD. However, it remains unknown whether suppressing the Hippo pathway can rescue neuronal death in AD and its impact on other AD-driven pathophysiological changes. In this study, we investigated the beneficial role of the novel Hippo signaling inhibitor, Xmu-mp-1, on Streptozotocin (STZ)-induced cognitive deficits in the rat AD model. Intracerebroventricular STZ administration induces cognitive impairment. As revealed by the Morris water maze test,the deficits in spatial and learning memory were found to be alleviated with Hippo signaling inhibition. Further, the open field test and novel object recognition test revealed that Hippo signaling inhibition improves the exploratory and object recognition memory. The current findings of this ongoing study indicate the promising therapeutic and ameliorative potential ofHippo pathway inhibition via Xmu-mp-1 in managing AD pathophysiology. Future studies willshed light on the molecular implications behind this therapeutic potential of Hippo signaling inhibition.

Parvalbumin interneurons (PV-IN) of dCA1 preserves details of episodic memories

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Abstract

We acquire new information or experience things from our surroundings daily, and we store this information in the form of memory. This stored information helps us to plan better for the future. The newly acquired memory, known as recent memory, is specific and detailed. Over time memories get generalized, and our Brain keeps only the abstract or schematic form of these memories. The underlying mechanism which maintains memory specificity is still unknown. It has been shown that inhibitory neurotransmitter such as Gamma−Aminobutyric Acid (GABA) plays a role in preserving the specificity of memory in mice. Inhibitory interneurons are the primary sources of GABA, but their individual contributions in maintaining memory specificity have not been studied. Our study sought to investigate the role of parvalbumin interneurons (PV− IN) of CA1 (subregion of the hippocampus) and ACC brain regions in maintaining recent memory specificity. We used PV−Cre Knock−in mice (n=8 and n=10) and a chemogenetic−based approach to specifically label and inhibit the PV−IN population of HPC and ACC, respectively. Animals were trained in the Contextual Fear Conditioning behavior (CFC) paradigm and probed for memory specificity in different contexts under different test conditions. The freezing behavior exhibited by the animals in the contexts is a proxy for memory retention. We found that PV−IN of CA1 subregion plays a role in maintaining recent memory specificity without hindering memory retrieval. Animals in which hippocampal PV−IN were inhibited throughchemo−genetics showed as much freezing percentage (%F) in a similar but not the same context as it was inthe training context. Our data indicate that animals were unable to discriminate between contexts when PV−IN of CA1 were inhibited. In other words, animals cannot recall detailed contextual information about the context in which they were trained. However, we did not find such an effect in animals where PV−IN of ACCwere silenced through chemo−genetics.

Establishing a 3D Coculture System to Mimic the Tumor Micro-Environment to study the Role of Neural Stem Cells in Prostate Cancer Cell lines

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Abstract

Solid tumors are known to manipulate their microenvironment to optimize their growth and metastatic potential. Neurons have recently been discovered to be important components of this tumor microenvironment that promote the initiation and progression of various cancers. Evidence suggests that the neurological systemis involved in all phases of cancer. In this study, a 3D coculture system was established using collagen type 1 and fibrinogen-thrombin matrix forming a dual compartment. The pancreatic cancer cells (PC3) were embedded in the collagen gel and the Neuronal Stem cells (NSC) isolated from Sub-Ventricular Zone were cultured in the fibrin gel with the aid of growth factors. The cellular morphology and viability were investigated by microscopic imaging, Hematoxylin-Eosin staining, andfluorescently labelled live cell tracking. The gene expression in the tumor microenvironment were studied using Real-Time PCR. The developed coculture method mimicked in vivo patterning of the cells by forming spheroids and eminent protrusions in the gel. It also showed neuro-cancer cell connections by invading mutually. The gene expression studies showed differentially expressed ECM and metalloproteases genes that further establishes in-vivo conditions. In conclusion, the study establishes a 3D co-culture systemthat can be used to study the cancer-neuro crosstalk by investigating the neurocrine micro-niche signals in cancerdevelopment and dormancy, as well as the changes in niche signals following neuro-modulations.

Chronic defeat stress stimulates the RFRP-3 system in the hypothalamus and adrenal glands of adult mice

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Abstract

Background: Stress is a fight-or-flight response that causes aberrant alterations in the body's physiological activity. Chronic defeat stress (CDS) in mice is a useful model to study the pathophysiology of stress-related diseases since it is an etiologically valid stressor. The victors develop more attacking behaviors, whereas the losers develop more protective and territorial tendencies. RFRP-3 neurons are located in the dorsomedial hypothalamus of the brain and project to the preoptic area where it inhibits the release of gonadotropin-releasing hormone (GnRH) by acting mainly through its receptor, GPR 147. Chronic stress affects the release of various hormones regulating their reproductive and social behaviour. RFRP-3 acting through its central and peripheral targets can mediate the effects of stress. Therefore, in the present study, we studied the changes in RFRP-3 and GPR147 expressions in the hypothalamic-pituitary-adrenal axis of male mice under CDS.
Methodology: Various tests like 1) Tube dominance test, 2) Food deprivation test, 3) Water deprivation tests, 4) Sucrose preference test, and 5) Offensive defensive test to identify the dominant and submissive mice. After selection, the dominant mouse was placed to interact with the resident/submissive mouse for 10 minutes. This procedure was repeated every day for a week with the different dominant mice. Once the experimental mice were physically defeated (by six-seven attacks), the resident and the intruder were separated.
Results: To investigate whether the changes in RFRP-3 expression related to stress are important for HPA function, we performed real-time PCR and immunohistochemistry. We found that CDS leads to increased RFRP-3 and its receptor GPR147 mRNA levels in the HPA axis of submissive mice compared with dominant mice. Our results further indicated the role of adrenal glands in the stress-induced increase in the expression of RFRP-3 and GPR147.
Conclusion: In the present study, we observed that CDS stimulates the RFRP-3 and GPR147 expression in the HPA axis. We found a causative link between stress-induced changes in RFRP-3 expression and social behaviour. Our findings further showed that CDS-induced changes in the RFRP-3 system in the adrenal can potentially modulate the synthesis of steroid hormones.
Keywords: Stress, Chronic defeat stress, RFRP-3, HPA axis, social dominance

Funding: We acknowledge the financial support from SERB-CRG (CRG/2021/001717) and the DBT Ramalingaswami fellowship.

Evaluation of the potential of Astaxanthin and DHA to mitigate the perinatal stressinduced cognitive deficit and synaptic plasticity in the adult life

Abstract

Background: Early life experiences and environmental conditions such as maternal undernutrition during perinatal life induce retardation of brain development leading to cognitive impairment in offspring. However, little is known about the long-term impact of perinatal stress on cognition and synaptic plasticity in the postnatal life. Hence, we questioned whether perinatal undernutrition will affect cognitive function and genes responsible for synaptic plasticity and Can Astaxanthin (AsX) and Docosahexaenoic acid (DHA) will ameliorate the effects of undernutrition stress? Therefore, the present study was designed to investigate the mechanism of AsX and DHA on cognitive function and synaptic plasticity in the postnatal life of perinatally undernourished Wistar rats.

Materials and Methods: The body weights of the pups from all the experimental groups were measured at postnatal day 1 to 56. The cognitive function was assessed by Recognition Memory and Spatial learning memory using Novel Object Recognition (NOR) and Radial Arm Maze (RAM) task respectively using ETHOVISION-XT software. The mRNA levels of BDNF, NT-3, CREB, and UCP-2 genes at hippocampus were assessed by RT-qPCR. Gene expressions were expressed as relative expression normalized to the expression of internal control β-actin, and are presented as fold change (2^-ΔΔCT) as compared to controls. Data were expressed as Mean ± SEM and analyzed using one-way ANOVA or two-way repeated measures ANOVA. The P value <0.05 was considered significant.

Results: The weight on postnatal day-1 (PD1) was significantly reduced in PeriUN group when compared with that of PeriUN-AD ($p< 0.0001$). Similarly, PeriUN rats showed significantly decreased percent correct choice in retention test at 2 Months (Control vs PeriUN: $p = 0.0017$; PeriUN VS PeriUN-AD: = 0.0060 and 12 Months (Control vs PeriUN: p
= 0.0376), and increased WME at 2 Months (Control vs PeriUN: p= 0.0069; PeriUN VS PeriUN-AD: = 0.0065), and RME at 2 Months (Control vs PeriUN: p = 0.0239), 12 Month; Control vs PeriUN: p = 0.0466). There was no significant change in the WME and RME at 12-months of postnatal life ($p<0.05$) when compared to controls.
Discrimination index (DI) was calculated to evaluate recognition memory. The DI wassignificantly declined in PeriUN animals when compared to control, and PeriUN-AD ($p=0.0243$) at 2-months group. Further, we found that hippocampal mRNA expressions of BDNF, NT-3, CREB, and UCP-2 genes were up-regulated by maternal AsX and DHAsupplementation which was down-regulated in undernourished groups.

Conclusion: We demonstrated the mechanism of AsX and DHA in mitigating the cognitive deficit caused by perinatal undernutrition. AsX and DHA effectively modulated the recognition memory, spatial learning and memory deficits as indicated by the up-regulation of hippocampal mRNA expressions of BDNF, NT-3, CREB, and UCP-2 genes.

Role of sub-synaptic molecular organization in modulating synaptic transmission

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Abstract

For a long time, the synapse has been considered as the smallest independent unit of information transfer in the brain. The advent of microscopic paradigms that provide nanoscale resolution have allowed researchers to visualise the localization and exchange of proteins within individual synapses. This has served as a powerful tool for detailed investigation of synapses at 1-100 nm leading to the identification of an elaborate organization of molecular machines within and across the synapses. Recently, researchers have used these advanced imaging techniques to show that in the chemical synapses, presynaptic release sites are positioned precisely opposite the postsynaptic reception machinery. This trans-synaptic organization termed as the nanocolumn is believed to be the finest independent unit of signal computation in the brain and proposedly regulates the cellular correlates of learning and memory. Over the past one year, we have employed various forms of super resolution microscopy, to evaluate the heterogeneous distribution of core synaptic proteins (PSD95 and AMPARs). We have dissected the localization and diffusion parameters of these proteins within the subcompartments of excitatory synapses. The results imply a progressive increase in the density of molecules as subcompartments become more constricted within the spine heads and a parallel shift in mobility from freely diffusive to reversibly immobilised at a millisecond time scale. We have also been able to show that clusters of high density or nanodomains of PSD95 scaffold protein within the spine head are majorly occupied by the post-translationally modified, more precisely, the palmitoylated fraction of PSD95. Moving forward, we intend to employ plasticity paradigms and correlate the changes in the nanoscale machinery to the subtleties of synaptic transmission. We believe that our results will pave the way for understanding the role of experience and pathology in attuning the trans-synaptic nanocolumns and subsequently modulating the efficacy of information transfer in the brain.

Light injury to the retina: the protective role of ghrelin and its receptor GHSR-1a

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Abstract

Photoreceptors are rich in peroxidation-susceptible polyunsaturated fatty acids, which can oxidize easily upon intense light exposure and injure the retina. Free radicals and reactive oxygen species are physiological indicators of oxidative stress. Ghrelin is an endogenous hormone which acts as an antioxidant and free radical scavenger. It is produced locally in the retina and its receptor GHSR-1a is expressed in vascular endothelial cells and Müller cells. Intense light-induced oxidative stress in photoreceptor cells may likely to be minimized under the influence of potent endogenous antioxidants. Keeping these points under hypothesis, this study was focused on investigating the role of ghrelin and its receptor in the rat retina after intense light exposure. Two-month-old male Sprague- Dawley rats (N= 27) were maintained on a 12-hour light: 12-hour dark cycle at 300 Lux for two days. They were then divided into control (12L: 12D, 300 Lux) and experimental group (24L:0D), where light intensity was increased to 3000 Lux. Retinal samples were collected for histological assessment, TUNEL and immunohistochemistry. In response to continuous light, GFAP expression was increased in Müller cells. Also, Iba-1 immuno-positive microglial cells with short thick processes increased in number and concentrated towards the outer retina. GHSR-1a showed significant upregulation in Müller cells after exposure to continuous light in the experimental group, suggestive of the increased activity of ghrelin under stress produced by intense continuous light. TUNEL-positive photoreceptor nuclei in the outer nuclear layer were more in the experimental group as compared to that in the control, which is suggestive of increased photoreceptor cell death after exposure to high-intensity light, resulting in thinning of the retina. Histological assessment of the retina also showed retinal thinning and loss of photoreceptor cells after exposure to continuous light. The upregulation of ghrelin under light insult may play an important role in the protection of the retina under stress conditions, which is hitherto unreported.

Pax6 gets downregulated due to LPS-mediated Neuroinflammation in mouse brain

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Abstract

Background: Neurological diseases are caused by progression of chronicneuroinflammationinduced by activation of microglia, alterations in microenvironment or chemical insults. The activation of microglia and astrocyte drives release of cytokines and sometimes infiltration of peripheral leukocytes in the Central Nervous System.Lipopolysaccharide (LPS), a component from gram-negative bacterial cell wall is widely used to create neuroinflammatory mouse models. The LPS challenges the immune system of the body mainly through TLR4 signalling pathway. In-silico studies suggest that Pax6, a transcription factor and a multi-functional proteinbinds to promoter sequences of genes associated with inflammatory, anti inflammatory response and TLR signalling pathway.Butroles of Pax6 in neuroinflammation are unexplored. It has been intended to study Pax6 expression and its interaction with genes of TLR pathway, inflammatory and anti inflammatory in brains of Control and LPS induced Mice.

Materials and Methods: Neuroinflammatory mouse model was developed by injecting LPS (1mg/kg body weight) intraperitonially for five days in AKR strain of mice. Equal volume of saline was injected as a vehicle control. Status of expressions of Pax6, Inflammatory(Ifn-γ, Tnf-α, NF-κB), anti-inflammatory (Tgf-β1), microgliamarker (Iba1) and astrocyte marker (S100β) geneswere evaluated from brain ofLPS-treated neuroinflammatory mousemodel.RT- PCR and Western Blotting were performed to study expressions at transcript and protein levels.Binding sites of Pax6 on promoter sequences of TLR4 and Inflammasome (NLRP3) genes was also evaluated through Eukaryotic promoter database.

Results: Theexpressions of Pax6, Iba1, and Tgf-β1were reduced but expressions of Tnf-α, NF-κB and Ifn-γ were increased in brains of LPS-treated mice as compared to respective controls. Multiple binding sites of Pax6were observed on promoter sequences of TLR4 (- 1836, -1833, -1582, -445, -170, +876) ,NLRP3 (-1866, 1012, -1009, -371), Ifn-γ (-1545, -1013, -419),NF-κB(-395, -735, -940, -1182, -1571, -1798, -1091, -1171), TGF-β1 (-1136, -963, -549,-462, 452, -371,98, 376, 559, 562, 952),Iba1 (1534, -1196, -54). Two binding sites forTnf-α (810, -196) and one binding site for S100β (+13) were also observed. **Conclusion:**Reduced Pax6expression in LPS-treated mice indicates its role in regulation of neuroinflammation. The increased expression of Tnf-α, NF-κB and Ifn-γ and reducedexpression of Pax6 may suggest that Pax6 negatively regulates pro inflammatory genes undernormal conditions. From In-silico analysis it is presumed thatPax6 may be regulatingTLR, NLR, anti and pro inflammatory genes and thus regulating neuroinflammation.

Keywords: Pax6, Neuroinflammation, Brain, Lipopolysaccharide

Epileptiform activity impairs bidirectional plasticity in the rat hippocampus

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Abstract

Epilepsy is one of the most common neurological disorders, affecting about 1% of India's population. Temporal lobe epilepsy (TLE) is one of the most common types of epilepsy which majorly affects the hippocampus, parahippocampus, and amygdala. The reason behind epilepsy is mainly due to the disturbance of the inhibitory to excitatory ratio. It is commonly observed that patients with epilepsy have memory-related problems. Hippocampus is the region that is majorly associated with learning and memory. Long term potentiation (LTP) and long term depression (LTD) are the two well characterized cellular models of memory. LTP has been extensively studied both in animal models as well as in patients, but very little is known aboutLTD in epilepsy. Here, we studied the effect of epileptiform activity in LTD by studying the Schaffer collateral pathway in the rat brain hippocampal slices. We induced LTD in the Schaffer collateral pathway by the application of low frequency protocol (1Hz, 900 pulses), which induced 20% LTD in control hippocampal slices. But when we induced epileptiform activity in the hippocampal slices, application of the same protocol induced 20% LTP instead of LTD. Next, we induced LTD using a different protocol to confirm the findings. We used 30µM NMDA for 3 minutes to induce LTD in control and epileptiform slices and observed the same results as in the 1Hz protocol. We also performed whole cell patch clamp experiments onCA1 pyramidal neurons to study the excitatory and inhibitory currents in control and epileptiform slices. We found that epileptiform activity reduced the GABA A current amplitude and interevent interval significantly when compared with control slices. Our results showed that epileptiform activity impairs the excitatory to inhibitory ratio in the hippocampus. These results show that the loss of LTD may be the reason behind learning and memory impairment in epilepsy.

Tetrahydroxy flavonoid class of anti-cardiovascular compound as a potential regulatortowards Glutathione peroxidase (GPX4) in Ischemic stroke.

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Abstract

Background: Comorbid conditions such as hypertension, atherosclerosis, myocardial infarction, arrhythmia, etc. are the hallmarks associated with neurodegenerative disorder ischemic stroke. Neurocardiology an emerging field examines the connection of the heart and brain, and how cardiovascular diseases affects the brain causing neurodegeneration, neuroinflammation and vice versa. Thus, the comorbid conditions leading to the ischemia affects the brain causing neurodegeneration, neuroinflammation and severe neurological deficits. Nowadays an iron dependent apoptotic cascade is prominently explored for comorbidities and ischemia. The iron dependent pathway is under the regulatory control of a selenoprotein antioxidant i.e., glutathione peroxidase (GPX4). Accumulating evidences suggests that GPX4 assists in suppressing the increased reactive oxygen species, formation of free radicals, mitochondrial dysfunction and eventually inhibiting the ferroptotic neurodegeneration. A substantial amount of clinical and experimental data also points that GPX4 levels gets depleted during ischemia due to increased ROS, inflammation and reduced glutathione. Hence, activating GPX4 inhibits iron accumulation, reducing inflammation and prevents neurodegeneration can be a potential strategy for related comorbidities and ischemic stroke therapeutics.
Aim: Investigating the regulatory role of anti-cardiovascular compounds towards glutathione peroxidase (GPX4) in ischemic stroke via in silico analysis.

Methods: Virtual screening of 698 anti-cardiovascular compounds library against the 3D structure of 20BI was carried out at extra precision. Top hit compound exhibiting highest binding affinity, as well as docking score was shortlisted. ADME and ProTox analysis for drug likeable characteristics followed by molecular dynamics and trajectory analysis for drug- receptor complex stability of shortlisted compound was also performed.

Results: Hyperoside exhibited the best docking score of -8.097 in the virtual screening against 2OBI out of all compounds. Stable and firm binding interactions such as hydrogen bond, hydrophobic interactions, salt bridge, pi-pi stacking were observed within the binding pocket. ADMET/QSAR and ProTox analysis showed that the shortlisted hit is non-mutagenic, non- carcinogenic, and non-cytotoxic. Furthermore, MD and trajectory analysis including RMSD (~1.50 Å), RMSF (~2.4 Å), Rgyr (~4.05 Å) and B-factor (~25 Å) of Hyperoside with target receptor 2OBI states that they exhibit high stability, strong binding, and compact structures. Moreover, significant Positive association as well as residual grouping between complex residues are revealed by DCCM and PCA

analysis.

Conclusion: Hyperoside might be a possible therapeutic candidate for GPX4 due to its excellent binding affinity, ADME, toxicity-free profile, as well as optimal number of aromaticrings present in its structure and can be used in treating cerebral ischemia.

Keywords: Acute Ischemic stroke, Anti-cardiovascular, Comorbid conditions, Glutathione Peroxidase (GPX4), Molecular Dynamics simulation, Virtual Screening.

Inducible Nitric Oxide Synthase deficiency protects against murine coronavirus induceddemyelination

Abstract

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Introduction: Inducible nitric oxide synthase (iNOS) catalyses production of nitric oxide during an inflammatory stimuli and is a signature marker of M1-like microglia/macrophages. It can be induced during neuroinflammation and the presence of both iNOS mRNA and protein is reported in brain lesions of Multiple sclerosis (MS) patients. We employed RSA59, a mild hepatoneurotropic strain of Mouse hepatitis virus (MHV) which in 4-weeks-old C57BL/6 mice causes biphasic CNS disease characterised by acute neuroinflammation (day5 p.i.) and chronic demyelination and axonal loss (day30 p.i.). It is a widely used animal model for MS and wasused to study the role of iNOS in neuroinflammatory demyelination.

Methods: 4–5-weeks-old MHV-free wildtype C57BL/6 (WT) and iNOS knockout (iNOS-/-) mice were infected intracranially with 20000 or 10000 pfus of RSA59 and assessed daily for weight loss and disease score. The mice were sacrificed at day 10 and day 30 p.i. and checked for neuropathological outcomes.

Results: iNOS expression was upregulated in macrophages, natural killer cells, and natural killer T cells in WT mice, indicating involvement of iNOS in RSA59-induced acute neuroinflammation. iNOS-/- mice infected with RSA59 at 20000 pfus exhibited aggravated disease and high mortality at the acute-adaptive transition stage i.e., day10 p.i. as compared to wildtype controls despite being no differences in virus clearance by the CNS. Infected iNOS-/- mice also showed increased CNS infiltration of macrophages and neutrophils and exhibited enhanced demyelination in spinal cords, marked with morphologically defined microglia and macrophages in the demyelinating plaques. Additionally, the phagocytic markers CD206, and TREM2, were increased in the CNS of infected iNOS-/- mice.

Conclusion: Our studies reveal a protective role of iNOS against RSA59 induced demyelination by regulating the CNS inflammatory phenotype of microglia and macrophages.

Ethics approval: All experimental procedures and animal care and use were strictly regulated and reviewed per animal ethics approved by the Institutional Animal Care and Use Committee at the Indian Institute of Science Education and Research Kolkata (AUP no. IISERK/ IAEC/AP/2019/45). Experiments were performed following the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), India.

Acknowledgments: We thank Dr. Bhaskar Saha, the National Centre of Cell Science, Pune, India, for providing the iNOS-/- mice (B6.129P2-Nos2tm1Lau/J, Jackson Laboratory; Stock No. 002609) used in the study. We thank the IISER-Kolkata animal facility for providing the necessary support. We thank DBT for supporting and funding the Flow cytometry facility.

NMR based Metabolomics of Mild and Repetitive Brain injury in a realistic rat model

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Abstract

Introduction:
Mild and repetitive mild head injuries are often unreported, and usually undetected byconventional neuroimaging modalities. Although, such injuries are consistently diagnosed by a bunch of behavioral symptoms, such as headache, anxiety, cognitive decline, disorientation, and overall personality changes. The immense heterogeneity of behavioral symptoms and absence of objective markers mostly lead to sub-optimal diagnosis and disease management.
Metabolomics is one of the emerging omics of the new millennia. In the present study, we employed 1H NMR-based metabolomics of urine from a control, mild traumatic brain injury (mTBI) group and a repetitive mTBI (rmTBI) group. We found significant alterations in the urine metabolomics on day 21, day 60, and Day90 post-injury in both the mTBI and rmTBI groups concerning control. The significant urinary metabolic alterations at the later time pointsuggest enhanced metabolic alterations at the systemic level.

Material and Methods:
Adult Wistar rats (N=30) were equally and randomly distributed in three groups, viz. control, mild traumatic brain injury, and repetitive mild traumatic brain injury. The mild head injury method was adapted from Kane et al.2012 (Kane, Angoa-Pérez, et al. 2012) and further improved for adult rats. Adult rats were firstly anesthetized with a mild dose of ketamine and xylazine and placed on a platform. A metal impactor was dropped from 60 cm above the rat head. Immediately, after the impact, the rat rotated 180 degrees and fall on a sponge cushion below the platform. Repetitive mild TBI impacts were given on Day 1, Day 3, and Day5. mTBIgroup had just one impact. Urine samples were collected longitudinally on day21, Day 60, andDay 90 and stored at -800C for further analysis.
Urine samples were prepared for NMR data acquisition according to our previous literature (Khan, Rana, et al. 2011). Urine samples were recorded at the 800 MHz NMR spectrometer (Bruker, Germany), using the CPMGPR1D sequence. Metabolites were manually integrated concerning an external reference compound viz. Tri methyl silyl propionic acid sodium salt (TSP) (0.5mM). The area under the peak was utilized for further statistical analysis. All experimental procedures were approved and followed the institutional animal ethical committee recommendations.
Results: Urine Metabolomics of mild and repetitive mild TBI rat model show significant alterations inurinary metabolites, such as Creatinine and Trans Aconitate significantly altered after 21 Daysof mild and repetitive mTBI. While on Day 60 Creatinine was significantly increased while Hippurate, Taurine, Trans- aconitate, and Acetate were significantly decreased. On day 90 Nicotinate, Hippurate and taurine were significantly decreased only in repetitive mild TBI. The score plots based on the metabolic integrals show clear differentiation of 3 groups at day 90. VIP (Variable Importance in Projection) scores on day 21 and day 60 show Taurine and Creatinine, while on Day 90 Di methyl glycine and Taurine show high VIP scores.

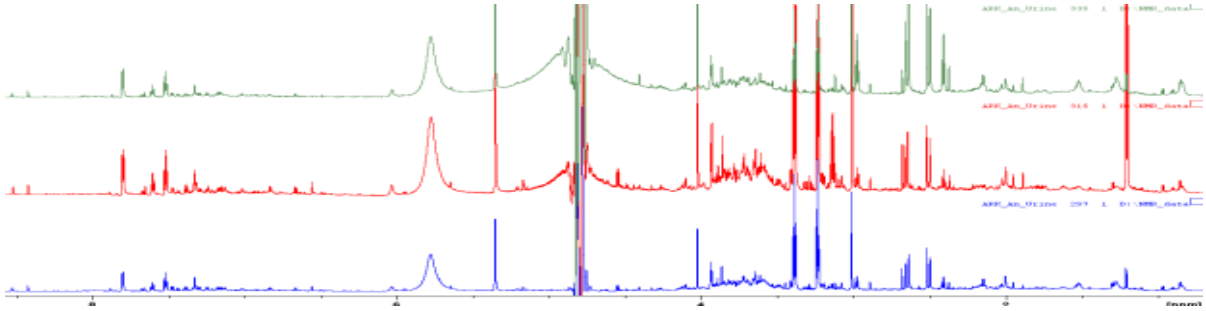


Figure 1: The representative NMR Spectra of urine from rats from control (Blue), mTBI (green), and rmTBI (Red).

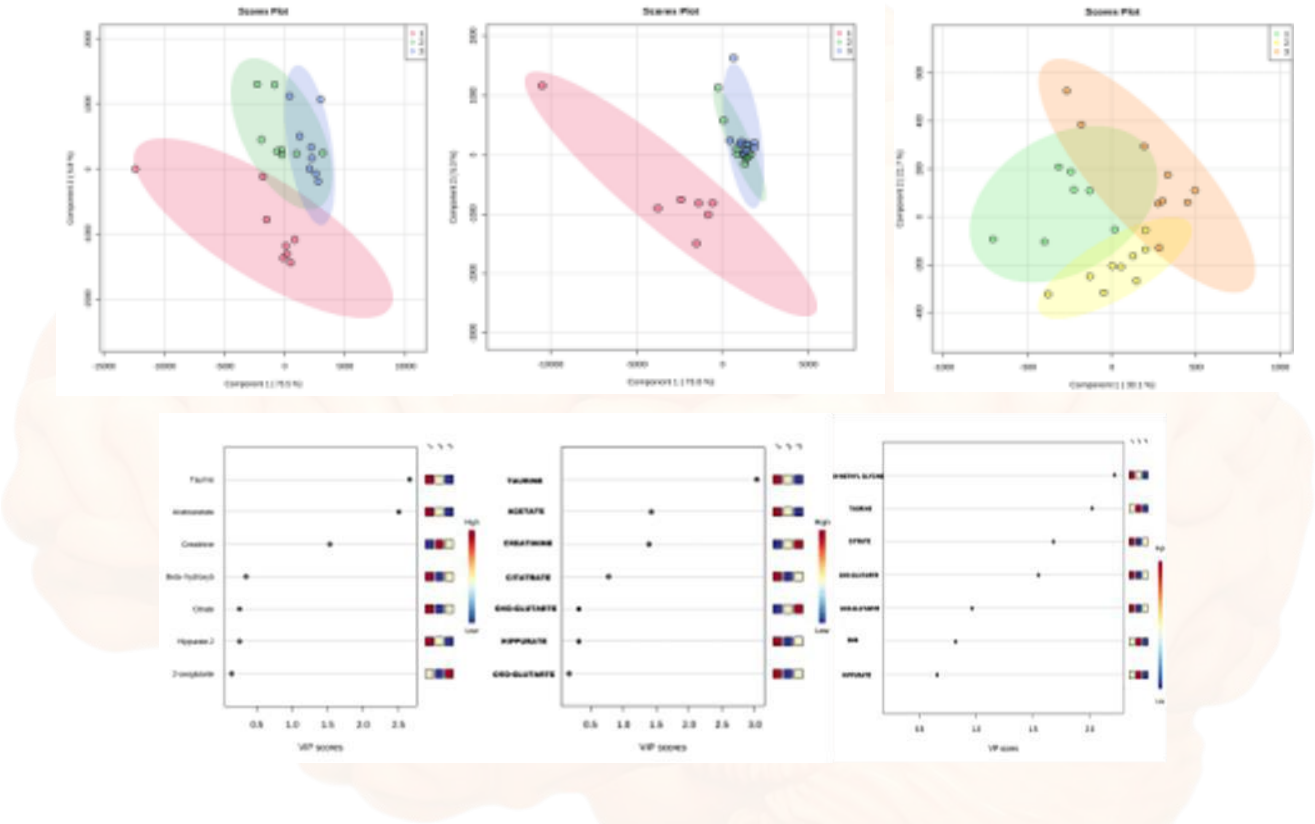


Figure 2: PCA plot at Day 21, Day 60, and Day 90 (L-R). PCA shows complete differentiationon Day 90. VIP score on Day 21, Day 60, and Day 90 (L-R).

Discussion:

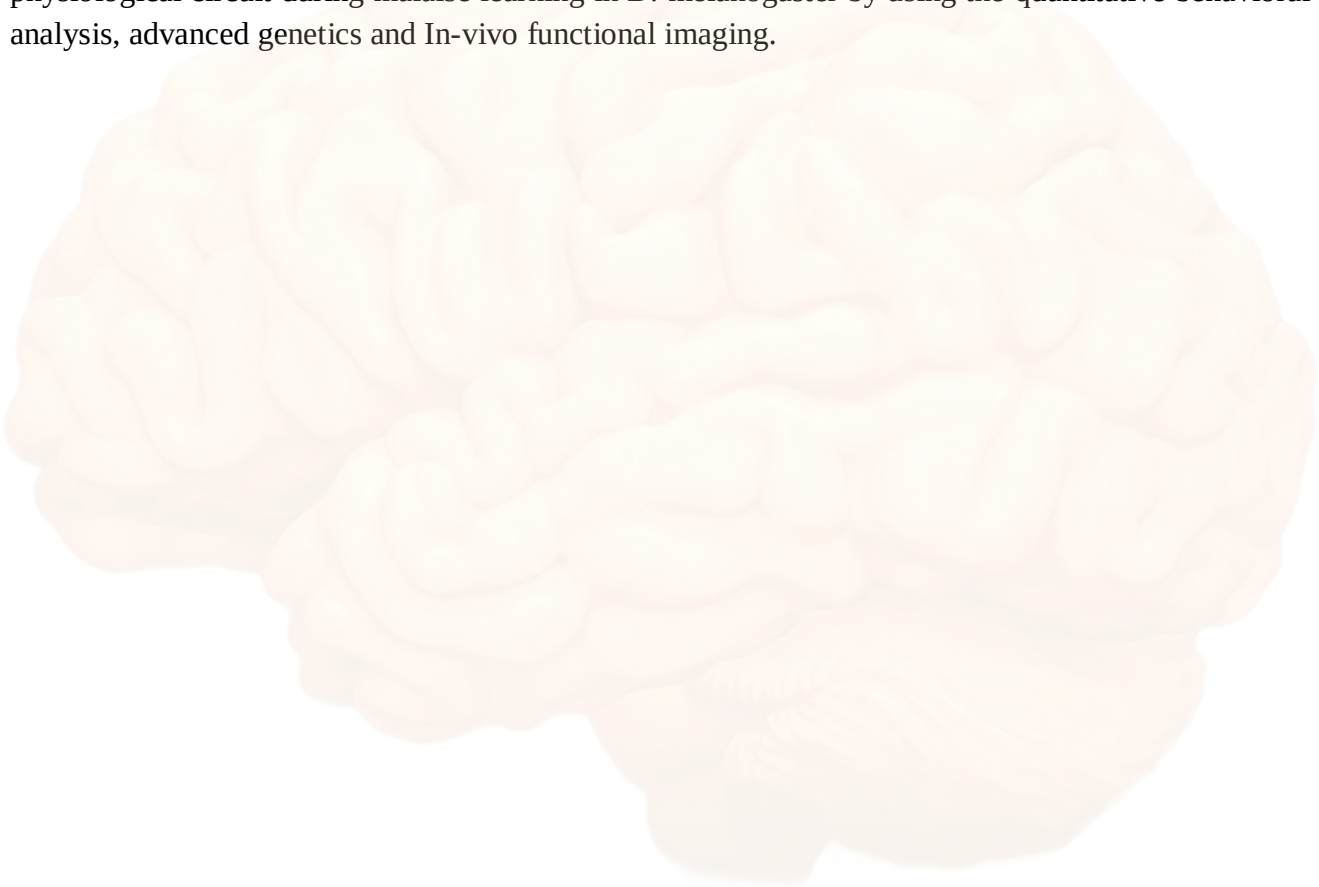
Metabolic alterations at Day 21 in comparison to control, suggest abnormality in energy metabolism. While on Day 60 and Day 90 suggest temporal alterations of systemic pathophysiology of mild and repetitive mild TBI group.

References:

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In many animals, including humans, pathogens or toxin that enter the digestive system via food can trigger malaise resulting in damage to internal organs. However, the mechanisms that allow ingested toxin to be recognized by the animal and how the ingested toxin the ingested toxins trigger malaise remain to be determined. A key element of these decisions is to avoid consuming food containing toxins. Therefore, animals must weigh the potential nutritional benefits of food against the post-ingestion consequences and adapt to their experience accordingly. Learning to avoid toxin-laden food is commonly termed “conditioned taste aversion” (CTA) and heavily studies in rats. Recently progress has been made to use mice and various invertebrates such as C. elegans and D. melanogaster to studyCTA. Yet the molecular and neural mechanism at play remains to be clarified. Moreover, how malaise signal reaches the brain to result in lasting avoidance of the specific taste of food/ odor of the food remains a mystery. Are other internal organs involve in the post- ingestive effects? This project will shed light on the underlying neuronal and inter-organ mediated physiological circuit during malaise learning in D. melanogaster by using the quantitative behavioral analysis, advanced genetics and In-vivo functional imaging.



Comparative Lipid Profiling of Blast and Blunt Induced Traumatic Brain Injury inPreclinical Model

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Abstract

Introduction: Traumatic brain injury (TBI) is defined as a temporary or permanent alteration in brain function, mainly caused by an external force due to road accidents, violence, sports injuries and military blast exposures. Brain injury can be focal (Specific area) or diffusive (widespread) in nature which causes damage to the brain tissue or biological membranes. Lipids are the most abundant constituent of biological membranes and any perturbation to the membrane will result in alteration of lipidome, hence blood lipid levels are expected to reflect brain pathophysiology very well and are likely to translate Successful TBI biomarkers than proteins, as lipophilic nature of Blood-Brain Barrier (BBB) lining cells allow lipids to cross more easily than proteins.
Therefore, Comparative analysis of focal and diffuse injury could provide some useful information to understand the role of lipid molecules as a potent marker of brain injuryirrespective of injury type.

Method: In the present study, we have developed a mild TBI (mTBI) model of Blast and Controlled Cortical Impact (CCI) injury. C57BL/6J male mice (10-12 weeks) were randomly divided into groups of 3 as (1) Control, (2) Blast injury, and (3) CCI injury. Animals were exposed to Blast over-pressure of 100 ±10 kPa in a shock tube. For blunt injury model, injury of -1.5mm impact depth was induced in exposed dura on a stereotactic frame. Serum samples were collected on day1 and day7, followed by biphasic extraction using MTBE/Methanol/Water. Prepared samples were chromatographically separated on Charged Surface Hybrid (CSH) C18 column and acquired on UHPLC-MS with in-house optimized parameters using Electrospray ionization. MS peak list was generated using Markerview^{TM} Software followed by statistical data analysis through Metaboanalyst and SPSS.

Result and discussion: Untargeted lipid profiling generates extensive data features, which were annotated based on m/z and fragment pattern of the molecule using LIPID MAPS® and LipidBlast respectively. In total 360 features were annotated in both modes of ionization. The multivariate analysis clearly segregated the injury groups from controls. Amongst various significantly altered lipid molecules, Glycerophospholipids {PC 30:2, PE O-33:3, PG 28:3; O3 and PS 36:1} fatty acyls {CAR 20:4, NAE 20:5} and Glycerolipids {TG 64:11} were significantly altered in both Blast and CCI group to controls at both day 1 and day 7 post-injury. In addition, some lipid molecules namely cardiolipin and sphingomyelin were uniquely significantly altered in the blast TBI group only. Similar changes have also been reported in a recent study on blast TBI. Sphingolipids are an

important constituent of the myelin sheath and alteration in sphingolipids could be an indirect indication of white matter damage. Pathway analysis by BioPAN has also shown hampered synthesis of Glycerolipids and Glycerophospholipids, which coincides with earlier reports. In support of this data, a set of continuous sequence of behavioral paradigms, Neurological SeverityScore (NSS-R) for rodents performed on Blast and CCI injury groups for evaluation of balance, motor coordination as well as righting reflex in mice, showed significantly altered behavior of injury groups in respect of controls at day1 of Blast and CCI injury. However, NSS continued to reduce till day 7 in blast group indicating persistent changes post-blast exposure. This study demonstrates the potential of lipidomics in the identification of lipid biomarkers for brain injury irrespective of injury type (diffusive or focal).

Conclusion: This work demonstrates the potential of combined blast and blunt injuries for robust identification and validation of lipid biomarkers for TBI. The blast TBI group showed more significant features at both time points than blunt (CCI) group. NSS-R data and altered levels of Cardiolipins and sphingomyelins support the significant change in blast group. Still lot of studies are required to carry out for validation.

Keywords: TBI, Blast, CCI, CSH, LipidBlast, LIPID MAPS®, NSS-R.

Identification of disease-relevant roles of Kalrn locus long non-coding RNAs in the mammalian brain

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Abstract

The mammalian Kalrn gene locus is implicated in several neurodevelopmental and neuropsychiatric disorders like autism and schizophrenia. It spans hundreds of kilobases and encodes several protein-coding isoforms and non-coding transcripts. The protein-coding isoforms are involved in dendrite remodelling and axonal growth and in keeping with the developmental stage, their expression pattern changes dynamically. Although it is understood that the dynamic changes in the expression patterns of the protein isoforms are critical for normal brain development the mechanism of their Spatio-temporal regulation is not clear. Previously, our laboratory discovered a novel brain-specific long noncoding RNA (lncRNA) durga, arising from the 5' end of the kalrna gene in the zebrafish genome. Ectopic overexpression of durga in zebrafish embryos induced expression of kalrna mRNA and altered neuritogenesis. In search of the mammalian equivalent, here we have characterized the lncRNAs arising from mouse Kalrn locus. The mammalian Kalrn locus gives rise to several non-coding transcripts which we have named Kalnc1 to Kalnc7. We characterized their expression profile in various parts of the adult and developing mouse brain. We showed that certain lncRNAs from the Kalrn locus are enriched in the brain and closely associated with the chromatin. Interestingly, the temporal expression profile of Kalnc2 was similar to some of the major protein-coding isoforms. We also extended this study to human neuronal cells and show that lncRNA arising from this syntenic locus in humans exhibit apparent similarities in expression patterns and chromatin association. In agreement with our observation in mice, this putative human KALNC2 lncRNA is reduced as progenitors attain neuronal fate. Kalnc2 in mice and KALNC2 in humans are putatively syntenically conserved with durga in zebrafish. We also extended this study to human neuronal cells and show that lncRNA arising from the syntenic locus in humans exhibit apparent similarities in expression in pattern and chromatin association. Similar to our observation in mice, this putative human KALNC2 lncRNA is reduced as progenitors attain neuronal fate. Our findings indicate, that Kalnc2 may be involved in the regulation of the Kalrn locus thereby controlling brain developmental processes. Besides its direct role at this locus, we are also exploring its effect on other genes in trans.

An in-vitro study on the role of Oligodendroglia in sporadic Amyotrophic Lateral Sclerosis

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Abstract

Amyotrophic Lateral Sclerosis (ALS) is one of the most common forms of motor neuron disorder with multifactorial etiopathogenesis. Despite undeniable evidences in the advancement of the molecular mechanisms, there is no definite cure to halt the progression of the disease. Glial cells, particularly astrocytes and microglia are reported to be disrupting the functions of motor neurons through neuroinflammatory processes. However, the involvement of oligodendroglia is least studied in ALS. Moreover, studies focus on the less prominent familial form than the sporadic form of the disease (SALS) which is represented by 90% of the cases with unknown etiology. Our laboratory focuses on SALS using cerebrospinal fluid of SALS patients (ALS-CSF). Toxicity of ALS-CSF has been demonstrated in both, in-vitro and in-vivo rodent models developed in the laboratory. ALS-CSF induces deleterious effects on motor neurons and affects the astrocytes as well as microglia. However, its effect on oligodendroglia still remains unknown.

In this study, we investigated the role of oligodendroglia in SALS by exposing MO3.13, a human oligodendroglial cell line to ALS-CSF (10% v/v; 48 hrs.). ALS-CSF affected the viability of MO3.13 cells and also reduced the expression of oligodendroglial markers namely, CNPase and Olig2. Surprisingly, when these cells were co-cultured with NSC-34 motor neuronal cells and exposed to ALS-CSF, no degenerative changes such as clumping/dedifferentiation of the cells, cytoplasmic vacuolation or beading of neurites were seen in the motor neurons. Instead, the neuronal cells differentiated and survived well with increased viability and decreased caspase-3 expression when either co-cultured or supplemented with spent medium/conditioned medium of MO3.13 cells that were previously exposed to ALS-CSF. Further, our findings of an enhanced expression of oligodendroglia specific metabolic transporter viz. Monocarboxylate Transporter 1 (MCT1) and lactate levels in MO3.13 cell lysate exposed to ALS-CSF, points towards its neuroprotective role via metabolic support. Additionally, unaltered expression of neurotrophic factors viz., BDNF and GDNF upon exposure to ALS-CSF hints its possible neuroprotective role via trophic support too. Unlike the other glial cells which turn detrimental to motor neurons in such a toxic milieu, the current study demonstrates a neuroprotective role of oligodendroglia opening a new avenue to delve deeper into its molecular mechanisms for better understanding of this devastating neurodegenerative disorder of motor neurons.

Keywords: sporadic ALS, ALS-CSF, MO3.13 Human Oligodendroglial cell line, NSC-34 motor neuronal cell line, BDNF, GDNF, Caspase 3

Plasma metabolic profiling based altered metabolic signatures and pathways in blast-related Mild TBI

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Abstract:

Blast injuries are the growing challenge in both military and civilian populations. Blast injury is a complex form of injury that involves interwoven mechanism of systemic and cerebral response. Blast-related injuries may produce diagnostic, and management challenges to emergency care providers. Extensive research is being carried out around the globe to identify blood-based biomarkers for detection of blunt TBI and some of them have been successfullytranslated to point of care method. However, detection of blast TBI related biomarkers still remains a question of interest.

Present study thus aims to identify promising blood-based markers for blast induced mild TBI using metabolomics. The study further aims to elucidate potential changes associated with proteins and metabolic pathways in the development of acute blast induced injuries. Rats (n =8, SD rats, male) were exposed to a single blast exposure of blast over pressure of 130 □10KPa at blast simulation facility of INMAS in the 9-inch square cross section shock tube and plasma samples were collected at 4hr, day-1 and day-7 of injury. Untargeted metabolic profiling of plasma samples was performed using UHPLC-Q-TOF-MS. A total of 3463 features in positive and 3432 features in negative mode were detected. PCA and PLS-DA score plots revealed clear distinct clusters of injury groups and controls. A total of 58 metabolites were identified and annotated based on analysis showing distinct clustering.

Changes in metabolite levels started appearing at 4 hrs post exposure. However, maximum changes were observed at day-7 with 28 metabolites including, BCAA, alpha amino acid, hydroxy fatty acids, alkaloids and other amino acids being alterted. Trigonelline, 2- Furoglycine, Pipecolic acid and 2-Ethyl-2-Hydroxybutyric acid were consistently significant atall the time points. To obtain information on pathway analysis, these classifier molecules were than employed in pathway and enrichment analysis. Phenylalanine, tyrosine and tryptophan biosynthesis pathway and aminoacyl-tRNA biosynthesis pathway were found to be significantly altered at day-7. This indicated alterations in aromatic amino acid pathways related with the transmission of nervous signals, quenching of reactive oxygen species in thebrain. Additionally, changes in valine and other branched chain amino acids in our study highlight the alteration of BCAA metabolism after TBI and may contribute to decreased energy production and neurotransmitter synthesis thus contributing to TBI pathophysiology. Our study highlights that the metabolomic approach may help in bridging the research gaps of mTBI studies leading to comprehensive understanding of its biochemical changes for better diagnostics, prognostics and therapeutics.

Identification of the complex molecular signatures behind the differential vulnerability between ALS-resistant and sensitive motorneurons — a multi-omics approach

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Abstract:

Amyotrophic Lateral Sclerosis (ALS) is an adult-onset fatal neurodegenerative disease without a known cure. Only a small fraction of the ALS cases are familial, and no single-gene cause has been identified. ALS is marked by selective loss of spinal motor neurons and denervation of skeletal muscles, eventually leading to paralysis of lateral organs. In contrast, a subset of cranial motor neurons (oculomotor, trochlear, and abducens motor neurons) are resistant allowing patients to retain eye movement until the late stages of the disease. The inability of the cells to respond appropriately to endoplasmic reticulum (ER) stress is thought to be one of the major reasons for ALS progression. To understand the molecular differences between cranial and spinal motor neurons that underlie ALS-sensitivity, we exploited a unique platform that generates highly pure populations of induced cranial and spinal motor neurons (iCrMN and iSpMN). Exposing both iCrMNs and iSpMNs to proteotoxic stress, we monitored transcriptome and proteome changes over 36 hours and identified significant hundreds of statistically significant differences at either or both the RNA and protein levels from a core set of 8,206 genes with complete data. We found that the superior proteostasis capability of iCrMNs might, in part, be caused by higher activity and abundance of the fully assembled 26S/30S proteasome.

Neural responses of zebra finches to various interpersonalcalls are influenced by social relationships

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Abstract

Introduction: Animal species rely on vocal communication as the main form of social interaction throughout their lives, yet our understanding of the computational mechanisms behind the perception of intra-specific communication signals is still lacking. In avian species,the brain mechanisms behind the ability to distinguish between familiar and unfamiliar vocalizations are not well understood. Previous research has shown that conspecific song hasa greater effect on the activation of neurons of the caudomedial nidopallium (NCM) region among zebra finches as compared to heterospecific songs or artificial stimuli [1, 2]. In this study, we investigated the neural responses of different types of calls (contact and aggressive calls) from familiar and unfamiliar conspecifics in both primary and secondary avian auditory cortex.

Methods: We utilized a dataset that includes recordings of anesthetized zebra finches listening to the whole vocal repertoire of the species from both known and unknown conspecifics. A 16-electrode array was used to record the neuronal activity of the auditory cortical region in both hemispheres. Data was gathered from the primary auditory cortex (L1, L2, and L3) and the secondary auditory cortex in the brain (NCM, CMM, and CML).
In our analysis, template-based spike detection and sorting were implemented to neural recordings where a single neuron's activity was predominant. The level of excitation brought on by a certain stimulus was measured by estimating the length of the call stimulus that significantly increased the spike rate over the baseline. For both familiar and unfamiliar calls, the reaction strength index was determined.

Results: Initial findings from investigations at the cellular level point to the existence of semantic cells. Semantic cells are cells that are either selective or invariant to a particular type of bird call, or whose activity can be decoded to infer the type of bird call employed as the stimulus. The NCM and caudomedial mesopallium (CMM) also seemed to be important regions in our study for neural representations of these calls because single units of these regions were highly discriminant and selective for various calls depending on call familiarity.

Discussion: Our research examines how social relationship affects the auditory cortex functions in the avian brain. As per our preliminary findings, social situations that potentially influence call-based recognition have an impact on the activity of neurons in the secondary auditory cortex.

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representation of communication calls. European Journal of Neuroscience, 41(5), 546–567. doi:10.1111/ejn.12812

Design and development of Ayurvedic nutraceutical-based food formulations for thetreatment of Parkinson's disease

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Abstract

Parkinson's disease (PD) is a progressive neurological disorder characterized by the death of dopaminergic neurons in substantia nigra pars compacta, resulting in loss of striatal dopamine, leading to a myriad of movement dysfunctions. The most consistent risk-factor forPD is ageing. The treatment options are mainly symptomatic, based on replenishing the dopaminergic activity within the nigrostriatal system, and certain other neuro-modulators. The Indian traditional system of medicine, Ayurveda prescribes rejuvenative therapies including Panchakarma, and intake of varied herbal combinations for controlling the behavioural abnormalities in PD. Seeds of Mucuna pruriens (Mp) and Hyoscyamus niger (Hn), and roots of Sida cordifolia (Sc) and Withania somnifera (Ws) in certain proportions are prescribed as per Ayurveda treatise. The present work developed food formulations like biscuits and rotis out of these seeds and roots, and determined the L-3,4-dihydroxy phenylalanine (L-DOPA) and other major constituents (such as hyoscine, withanolide A, and vasicine) of the plants by employing high-performance liquid chromatography and appropriate detections measures. Mp seeds are the natural source of the amino acid L-DOPA, the precursor of the neurotransmitter dopamine, which is mainly used in the treatment of PD. The HPLC data on the L-DOPA and other contents of these food formulations, when compared with the raw material ie.,the seeds and roots revealed these molecules are safely carried over into the final food products. These food preparations could be developed as novel nutritive-pharmaceuticals or neuro-nutraceuticals for the treatment of aged PD patients, who are reluctant to regularly take the Ayurveda-concoctions as per prescriptions.

Acknowledgements: We acknowledge the funding from Department of Science and Technology, Govt. of India (Sanction No : DST/WOS-B/2017/494-HFN(G)) & Department of Higher Education, Govt. of Kerala.

Effect of alaternin on ischemic reperfusion injury

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Abstract

Background: Alaternin exhibit potent peroxynitrite scavenging activity. Alaternin also reduces oxidative damage and inflammatory responses in transient cerebral hypoperfusion condition in mice by inhibiting BCCAO-induced increases in iNOS expression and OX-42 immunoreactivity.

Aim and Objective: To investigate the effect of alaternin in ischemic/reperfusion injury in rats

Methods: Adult male Wistar rats(200-250g) were used for ischemic stroke by MCAO. Alaternin was administered (10mg/kg, 20mg/kg) at 0 hr and (40mg/kg and 80mg/kg) 24 hrs orally, post ischemic reperfusion. To confirm the induction of ischemic stroke in rats, we compared the behavioural parameter (neurological deficit score and beam walk test) and percent cerebral infarction (TTC staining) in sham, control and treatment group.

Result and discussion: No significant change was observed in neurological deficit, beam walk score and on cerebral infarction area at 24hr with 10mg/kg and 20mg/kg dose ascompared to vehicle treated animals. However, alaternin significantly reduced neurological deficit score and improved beam walk score at 0 hr before ischemic injury on 40mg/kg and 80mg/kg dose.

Conclusion: The present study demonstrated the neuroprotective role of alaternin in early hours of I/R injury.

Key Words: Alaternin, ischemic reperfusion injury, iNOS, neuroprotective

ICAM1 reduces amyloid-β induced gliosis and improves synaptic plasticity in 5xFAD mice model of Alzheimer's Disease

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Abstract

Gliosis is one of the key expositions of amyloid-β (Aβ) exposure in Alzheimer's disease (AD). Microglia, the immune cells of CNS, innately respond to Aβ and get contrastingly activated. Here, we interrogated the kinetics of Soluble Intra Cellular Adhesion Molecule (sICAM-1) secreted from Aβ-treated microglia as well as astrocytes and its role in amelioration of different hallmarks of AD. We have found that sICAM1 is one of the major secretory cytokines to be elevated in glial condition medium in response to $A\beta_{1-42}$ oligomer. ICAM1, when incorporated intraperitonially in 5xFAD transgenic mice, reversed the $A\beta_{1-42}$ mediated microglial as well as astrocytic activation, reduced $A\beta_{1-42}$ mediated neuron loss and cleared Aβ plaques as observed by immunostaining and western blotting. ICAM-1 reduced microgliosis and astrogliosis and protects neurons against Aβ in vitro as well. Moreover, it restored synaptic protein expressions and thereby synaptic plasticity. One of the pathways that inhibited by ICAM1 is Aβ-mediated ERK activation which might play an important role in glial activation as well as subsequent inflammation. Thus our work suggests that ICAM-1 plays a pivotal role in regulation of neuroinflammatory meshwork of AD and targeting ICAM-1 or its receptor Lymphocyte Function Associated Antigen 1 (LFA1) could be a good therapeutic strategy.

Acknowledgement: The work was supported in part by one of the 12th Five Year Plan Projects, miND (BSC0115) of CSIR, Govt. of India

Methylcobalamin recovers demyelination-associated decline in neuronal arborization &cognitive functions in the MoHE rat model of neuroexcitotoxicity

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Abstract

The over activation of glutamate-NMDA receptor is considered as the main triggering event of the neuroexcitoxicity, argued accountable for developing a neuropsychiatric syndrome in the pateints with liver cirrhosis. The brain disorder is known as the hepatic encephalopathy (HE). Demyelination of the neurons in the susceptible brain region is considered as one of the main pathogenic events during such excitotoxicity, hence, myelin homeostasis during excitotoxicity deserves a special focus to understand pathogenesis of HE. The present study describes the level of myelination vs neuroarchitectural aberrations in the hippocampus vis a vis pattern of the neurobehavioral alterations in the moderate grade HE (MoHE) rats developed by administering 100mg/kg BW of thioacetamide for 10 days and in MoHE rats treated with methylcobalamin (MeCbl; 500µg/kg BW, i.p.) for 7 days. As compared to the control rats, the hippocampus from the MoHE rats showed significantly reduced level of the major myelin proteins, MBP and MOG; analysed by immunofluorescence intensity and western blotting data. Concordantly, there was declined level of the methionine synthase (MS) activity with the significantly enhanced level of homocysteine in the hippocampus of those MoHE rats thereby suggesting MoHE associated compromise in the biochemical pathway of MBP synthesis. However, all these factors were observed to be normalized due to the treatment of the MoHE rats with MeCbl. This was consistent with the normalization of MoHE associated deranged neuronal arborisation and declined number of synaptic buttons of the CA1 pyramidal neurons vis a vis recovery in the impaired cognitive functions of the MeCobl treated MoHE rats. Thus, the findings infer that MeCbl protects neurons from undergoing demyelination led neuroexcitotoxicity in the hippocampus of the MoHE rats mainly by improving neuronal myelination via promoting transmethylation reactions. The study provides neurochemical and neuroarchitectural basis of the neuroprotective roles of MeCbl in the MoHE model of neuroexcitotoxicity.
Keywords: Hepatic encephalopathy, excitotoxicity, myelination, methylcobalamin.

Ethical Statement: This work was approved by the Institutional animal ethical committee, BHU. **Acknowledgment**: This work was financially supported by a DAE-BRNS project to SKT. CSIR is acknowledged for providing SRF to AR. The instrumentation facilities provided by ICMR, DBT & DST projects in our lab and by BHU-CDC.

Omega-3 fatty acid polarizes microglial cells towardsanti-inflammatory pathway

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Abstract

Alpha linolenic acid, a polyunsaturated fatty acid, which can be derived from various plant oils, flax seeds etc. has a neuroprotective effect on patho-proteins like neurofibrillary tangles of Tau (NFTs). Through reported studies, it was found that ALA could play a role in attenuating ROS conditions, reducing inflammation, and increasing the fluidity of microglial membrane. They would polarize the microglial cells towards the M2 phenotype and lead to better phagocytosis of cell debris, dead cells, patho-proteins and also help to maintain Tau in random coil structure. These modulations of microglial phenotype are readily influenced by Omega-3 fatty acids. Our aim is to examine the effects of ALA on destined aggregates, alongside changes that take place in microglial cells towards M2 phenotype and inhibition of extracellular Tau propagation. Based on our experimental evidence, that aggregates were incubated with ALA of varied concentration resulted in fragmented fibrils of Tau protein and also increased the hydrophobicity of aggregates. At the higher concentration of ALA, Tau is preserved in random coil structure. Hence, the inference of the studies suggests that ALA helps in maintaining Tau in random coil structure and also mediates extracellular Tau-based toxicity.

Anatomical and morphological characterization of neurons responsible for cognition in pigeon (Columba livia)

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Abstract

Detailed understanding of the neuronal basis of cognitive behavior and its evolution requires investigation of model organisms taken from different taxonomic groups. Recent research suggeststhat birds are considered important taxonomic group which can be compared with mammals. The advantages of this comparative studies are emphasized by research on birds. research on avian model systems more recently has begun to provide insights into the functional organization of the brain. Homing pigeons (Columba livia) have been used as a model for the study of the cognitive behavior underlying learning, memory, and choice behavior. Moreover, the vast amount of available behavioral and anatomical data has rendered the pigeon one of the key model species of behavioral and comparative neuroscience. present study revealed some insights obtained from research with pigeons. Cytoarchitectonic and Morphological characterization of neural features in pigeon brain have been executed by Nissl staining and Golgi colonier techniques. A veryspecialized and unique neuroarchitecture in hippocampal complex, nidopallium and a few areas of striatum have been observed. These areas possess thick, long bipolar spindle shaped projection neurons comparable to von-Economo neurons in mammals, pyramidal neurons and fork neurons. Report of such neuronal components in pigeon brain may provide some special clues to understandtheir role in higher level of cognitive functions.

Ethical statement: Protocol has been used accordance of the animal ethics.

Differential role of autophagy in dry and wet age-related macular degeneration

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Abstract

Background: Age-related macular degeneration (AMD) is an eye disease that leads to blindness in individuals who are ≥50 years of age. In AMD, the retinal pigment epithelium (RPE) cells and photoreceptor degenerates due to the accumulation of toxic materials, eventually causing blindness in the elderly. Autophagy plays a crucial role in clearing of the accumulations, which needs to be inveatigated. There are two forms of AMD, namely, dry AMD and wet AMD. Same treatment is unable to provide similar effects in dry and wet AMD. Hence, it is critical to develop a specific treatment for dry and wet AMD. The present study targets autophagy and is designed to identify and investigate novel risk markers.

Methods: This is a case-control observational study conducted in 150 controls and 150 AMD patients. In the present study, differential expression of 8 genes and proteins ofmacroautophagy i.e. MTOR, ULK1, BECN1, PIK3C3, CDK5, SH3GLB1, LC3 and ATG16L1 will be investigated to decipher whether different or same genes are active/inactive in the two forms. Genetic and physiological basis of dry and wet AMD will be evaluated to identify the risk markers and understand the pathophysiology by RT-PCR, FACS, ELISA and SNP genotyping. Socio-demographic factors, clinical and biochemical parameters, and genetic variants will be correlated to estimate true interaction.

Result: We have collected samples from 34 participants, 27 controls and 7 AMD patients. The control samples have an average age of 63.32±7.08 years with 68% males and 32% females. Cataract was present and operated in 28% of the participants. No memory loss was reported among the participants. Comorbidities were present in 48% of participants in the form of hypertension (32%) and diabetes (28%). FACS of lymphocytes has yielded sufficientnumber of viable cells for detecting mTOR.

Conclusion: The predictive power of risk assessment enhances when genetic information of multiple genes is considered in combination with epidemiologic and environmental factors. The present study will establish a risk pathway defining the susceptibility of AMD, probably specific to dry and/or wet AMD.

Caveolin-1 Over Expression Mitigates Glutamate Mediated Excitotoxicity by Modulating Ionotropic Glutamate Receptor Function:

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Abstract

Background: Excitotoxicity, known to be a root cause of various neurological disorders where excessive release of glutamate in the extra synaptic space upshots stimulation of ionotropic glutamate receptors and leads to a rise in intra cellular concentration of Na^+ and Ca^{2+} ions followed by a cascade of intracellular events, such as delayed calcium deregulation (DCD), impaired calcium extrusion mechanism, inhibition of mitochondrial electrophoretic calcium uptake, membrane permeability collapse, subsequent generation of reactive oxygen species which eventually leads to neuronal cell death. Caveolins, a family of integral membrane proteins and scaffolding protein of membrane lipid rafts (MLRs) interacts with other signaling molecules and involve in cell signaling. The impairment of Cav-1 expression is reported in Alzheimer's disease, aging, cancers, Huntington's disease, Amyotrophic lateral sclerosis (ALS) schizophrenia and cerebral ischemia. The role of Cav-1 in glutamatergic excitotoxic signaling in hippocampal neurons is not known.

Objective: To understand the impact of Cav-1 OE on excitotoxicity.

Methods: 10 days in vitro (DIV) primary rat hippocampal neurons were transfected with Cav-1 m Cherry and plane m Cherry plasmids. Transfected neurons on 13-14 DIV were used for studying intracellular calcium [Ca^{2+}] i, reactive oxygen species generation (ROS), and mitochondrial functions using live cell fluorescence imaging.

Results: Glutamate (100µM) caused a biphasic [Ca^{2+}]i peak in hippocampal neurons and the peak was diminished by 65% in Cav-1 OE neurons (0.2272 ± 0.06, n=13) in comparison to control (0.912 ± 0.06, n =15). Also Cav-1 OE neurons showed a faster recovery without a secondary peak of [Ca^{2+}]i after glutamate challenge than the controls. Likewise, OE of Cav-1 declined glutamate induced ROS formation by 3–fold (0.5390 ± 0.07, n= 12) compared to the controls (1.6246 ± 0.19, n=16). Further glutamate stimulation caused decreased mitochondrial depolarization in Cav-1OE (0.1931 ± 0.02, n=18) pertaining to the controls (0.5016 ± 0.02, n= 23). Apart from this, mitochondrial uncoupler CCCP also caused significant decrease in Rh123 fluorescence in Cav-1 OE neurons (1.4524 ± 0.06) with respect to control (2.099 ± 0.04). However, in the absence of extra cellular Ca^{2+} glutamate did not affect[Ca^{2+}] i, $\Delta\Psi m$ and ROS generation. Our results demonstrate NMDA and non NMDA antagonist caused decreased [Ca^{2+} i peak and ROS generation in hippocampal neuron, in which Cav-1 OE neurons could attenuate AMPA and KA receptor mediated calcium influx and ROS generation than that of NMDA receptors.

Conclusion: Over expression of Cav-1 offsets excitotoxic glutamate mediated calcium overload,

ROS generation and loss of mitochondrial function by modulating ionotropic glutamate receptors function.

Ethics: Approved by NIMHANS IAEC. **Funding:** SERB-DST Extramural for YSM, UGC fellowship for SKK

Conflict of interest: None

Efficacy of Mind- Body practice in maintaining good psychological healthamong pregnant women.

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Abstract

Introduction & Objective- - Pregnancy is phase where pregnant women face psychological imbalance and compromised quality of life which may lead to pregnancyrelated complications. The present study is aimed at examining the effect of prenatal Yoga- YOGESTA (Gestational Yoga) on neuropsychology and quality of life of the pregnant women.

Method- Pregnant women who were in the second and the third trimesters of their gestation period, underwent a 16-week online Prenatal Yoga intervention. We allocatedone hundred pregnant women aged 18 – 35 into two groups, Yoga and Usual Care Groups. Sixty pregnant women completed the pre- and post- intervention survey (26 inthe Yoga group and 34 in the control group) measuring Perceived stress, Depression, Anxiety, Stress and quality of life.

Results- We found significant changes in scores of almost every parameter we measured after intervention. A significant decrease was observed in perceived stress, depression, psychological stress and improvement in the psychological and environment domain of Quality of Life-BREF scale noticed in Study group (Yoga Group), on the other hand, in the usual care group, perceived stress and anxiety increased significantly. Between-group analysis showed no difference at baseline but significantly reduced scores of perceived stress, depression, anxiety, psychological stress, and significant improvement in the psychological well-being and quality of life Yoga group was noticed in the study group at the follow-up after intervention.

Conclusion-Prenatal Yoga protocol, if adapted during pregnancy as an adjuvant with conventional usual care, can act as a cost-effective and safe intervention among healthy pregnant women to maintain psychological health by reducing the instances of stress, anxiety, depression. It helps sustaining the quality of life, and prevents the developmentof stress during pregnancy.

Fear conditioning leads to enduring alteration in RNA transcripts in hippocampalneuropil that is dependent on EphB2 forward signaling

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Abstract

Background: Alterations in the RNA transcriptome have been associated with changes in brain functions. Here we aimed to unveil whether fear conditioning leads to long-lasting alteration in mRNA levels in the basolateral amygdala (BLA) and hippocampus, using RNA-Seq in combination with laser microdissection microscopy. We further aimed to unveil whether these mRNA changes are involved in memory formation by monitoring their levels in EphB2$^{lacZ/lacZ}$ micethat can form short-term, but not, long-term fear conditioning memory.
Results: First, we found mRNA transcriptome signatures that comprise specific cellular pathways unique to each brain region. Next, we revealed that fear conditioning leads to alterations in mRNA levels 24 hours aftertraining in hippocampal neuropil, but not hippocampal cell layers or BLA. The two main groups of altered mRNAs encode proteins involved in neuronal transmission and neuronal morphogenesisand development and the vast majority are known to be enriched in neurons. None of these mRNAlevels were altered by fear conditioning in EphB2$^{lacZ/lacZ}$ mice that were also impaired in long-termfear memory.
Conclusion: Fear conditioning leads to enduring alteration in mRNA levels in hippocampal neuropil that is dependent on processes mediated by EphB2 needed for long-term memory formation.

Fluorescence Lifetime imaging by stochastic labelling using fluorogen activated FAST tags

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Abstract

Evaluation of protein -protein interactions in living neurons is one of the most challenging because of the developmental changes as well as due to changes in heterogeneity in sub cellular environment. The development and characterization of novel fluorescent probes are thus important to understanding the microenvironment of biomolecules in living cells. Fluorescence-Activating and absorption-Shifting Tag (FAST) is a new class of genetically encoded optical highlighters based on stochastic labelling which is half the size of a classical green fluorescent protein. FAST:fluorogen complexes absorb and emit fluorescence in the range of conventional fluorescent tags used for light microscopy. The switching of FAST from a bright to dark state can be manipulated by depleting the available fluorogen from the media. Another striking feature of FAST is the possibility to generate fluorogen probes with different photophysical and photochemical properties enabling multiplexed protein detection. The application of FAST in cell biology is under explored and this is in part due to the lack of characterization of these probes for quantitative bioimaging in combination with live cell microscopy. Towards this end, we evaluated the suitability of FAST for fluorescence lifetime imaging (FLIM) and its suitability as an acceptor with conventional genetically encoded fluorescence proteins. First, we observed the nanosecond fluorescence lifetime of FAST when expressed as a volume marker in Neuro 2A cells. We identified a concentration window for fluorogen complexes that would result in generating lifetime images in live cells. The intensity decays recorded by the single photon counting detector fit as mono exponential models. We also verified the suitability of FAST as a tool for sensing subcellular environments by tagging them to organelles of interest. As expected some of the FAST:fluorogen complexes behaved distinctly in different organelles indeed indicating it as an interesting tool to report changes in the microenvironment in living cells. Next, we used it as an acceptor with monomeric enhanced green fluorescent protein as a donor. In contrast to classical donor-acceptor pairs, the ability of FAST allowed us to reduce the sample sizes required for such experiments. Since we can utilize the labelling of FAST when needed, FAST as an acceptor can be used for high throughput screening where we can reduce the sample size to one third of what is required when compared to conventional paradigms. These observations highlight the flexibility and adaptability of FAST in microspectroscopic studies. Thus, we show that the stochastic origin of fluorescence from FAST is a promising probe for quantifying the variability of lifetimes in subcellular compartments and can be used in different cellular environments. In short, here we use genetic targeting combined with the switching on or off the fluorescence for fluorescence lifetime imaging and resonance energy transfer. The applicability of this technique reduces the number of samples required to be used in microspectroscopic measurements paving way for high through measurements to study in vivo protein-protein interactions. We believe this will open novel observation strategies and ease nanoscale observation of cellular organization in living cells and primary cultured neurons.

Keyword: Fluorescence-Activating and absorption-Shifting Tag (FAST), fluorogen, Fluorescence lifetime imaging

Insulin like growth factor-1 with dopamine is neuroprotective against proliferative diabetic retinopathy

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Abstract

Background: Diabetic retinopathy (DR) involves neurodegeneration accompanied with vascular damage leading to vision loss. Angiogenesis characterizes the disease progression from the Non Proliferative Diabetic Retinopathy (NPDR) into the advanced stage known as Proliferative Diabetic Retinopathty (PDR). Dopamine (DA) deficiency in addition to low levels of insulin like growth factor (IGF-1) marks the NPDR stage and increasing IGF-1 manifests into PDR. Although IGF-1 proved to be proangiogenic manifesting neovascularization in the PDR stage but regulation of IGF-1 levels with adequate DA may delay the onset of angiogenesis.

Materials and Method :A group of 40 Wistar rats were maintained for a period of 8, 12 and 16 weeks after induction of diabetes with streptozotocin (STZ) and subsequently treated with DA and DA with IGF-1 in combination. The cytotoxicity of the combination is tested in retinal pigment epithelium(ARPE-19) cell line . The retinae from treated animals were assessed for morphological changes through H & E staining and TEM, DA level analyzed by HPLC, antiangiogenic mechanism of action confirmed through tube formation assay in HUVEC cell line and protein expression patterns of Akt, pAkt, Erk and pErk , recceptor levels by RT-PCR and immunofluorescence.

Results :Improved retinal morphology were observed in response to 10mg/kg body weight of rats , DA as well as combination of DA and 2µl /eye of IGF-1. DA levels were significantly low in 16 weeks as compared to 12 weeks in retina and these levels were supported by DA levels in serum. The levels of angiogenic markers VEGFR1 and VEGFR2 were enhanced in 16 weeks compared to 12 weeks which was supported by tube formation assay in HUVEC cells .Consequently Dopamine receptors DR1, DR2,DR4 and insulin growth factor -1 receptor, IGF-1R were also decreased in these time points which could be augmented by administration of DA in combination with IGF-1.Increased expression of pAkt and pErk indicates involvement of phosphoinositol pathway. The synergistic antiangiogenic effect of DA and IGF-1 was also established in an alternate CAM model Inhibition of angiogenic factors causing vascular proliferation needs to be well timed in order to prevent the progression of NPDR to PDR stage.

Conclusion : L-DOPA at concentrations of 10mg/kg body was able to attenuate IGF-1 induced hypervascularization as visible through H & E staining and TEM. The symptoms of PDR like onset of neovascularization due to disruptions in dopaminergic neurons and increased IGF-1 levels could be prevented by combination of DA and IGF-1.This allowed to restrict the associated pathologies to the less-invasive NPDR stage. An effective formulation of DA and IGF-1 if applied as topical drops can prevent onset of angiogenesis and vision loss.

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In-vitro characterization of EIF4EBP2 using CRISPR-Cas9 mediated knock out and lentiviral mediated knockdown in HEK 293T and SHSY5Y cell lines.

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Abstract

Background: Eukaryotic translational Initiation Factor-4E Binding Protein-2 (EIF4EBP-2) is a member of a family of translation repressor protein and well-known substrate of mTOR signaling pathway. 4EBP2 is enriched inthe brain and acts as a key regulator of synapse activity and neuronal stem cell renewal via its ability to repress translation initiation. 4EBP2 mediates the regulation of protein translation that signals through MAP kinase and mTORC1 pathway which are essential for cell growth and metabolism. With this background, we want to assess the differential expression and also pleiotropic effects of 4EBP-2 in in- vitro condition in HEK 293T and neuroblast cell lines (SH-SY5Y). This might provide relevant information on the control of protein metabolism and cellular homeostasis in neurodegenerative and metabolic disorders.

Methods: CRISPR- Cas9 mediated transfection; - HEK 293T and SH-SY5Y cells are cultured and subjected to transfection using gene editing via CRISPR/Cas9 technology. The knockout of 4EBP2 is validated using genomic cleavage detection strategy. Confirmed knock out cells are serially diluted and single clonal population is isolated. 4EBP2 null background was further confirmed using western blot and qPCR as compared to control cells.
LENTIVIRAL mediated stable cell line generation: - 4EBP2 shRNA and scrambled shRNA lentivirus was generated. HEK293T and SH-SY5Y cells were transduced with 4EBP2 shRNA and scrambled shRNA. Post transduction cells were selected via Puromycin pressure. Single cells were clonally expanded for further downstream experiments.
Results: -We were able to knock out 4EBP2 gene in HEK 293T cells. Knock down of 4EBP2 gene expression using lentiviral shRNA in HEK293T cells is currently ongoing. Further downstream experiments will be performed once both the 4EBP2 knock out and knock down cell lines are obtained.
Key words: - CRISPR Cas9, Transfection, Transduction, Knock out cells, EIF4EP2.

Predicting White Matter abnormalities in Children Bipolardisorder

Abstract

Background: PediatricBipolar disorder (PBD) is a mental illness that has a stronger genetic connection and is associated with abnormalities in the brain's white matter (WM), the reason behind that is not exactly found. Some studies have examined the changes in the neuroanatomy of bipolar disorder both in adults and children. The neuropathogenesis of BPD pediatric remains poorly described due to the complexity of this disorder, as well as the very limited number of studies available in the literature. Euthymic phase clinical symptoms are not entirely absent but are diminished to a degree that mood and daily behavior are not affected. The understanding of human and non-human microstructural brain alterations in the course of neurodegenerative diseases has substantially improved by the non-invasive magnetic resonance imaging (MRI) technique of diffusion tensor imaging (DTI).

Methods: Diffusion magnetic resonance imaging data were obtained from 20 prospectively confirmed euthymic pediatric bipolar disorder (age 7–18) and 20 healthy control (age 7–18) were reori outpatients of King George Medical College (KGMC). We examined longitudinal change in Fractional Anisotropy (FA), (AD), and (MD), using tract-based spatial statistics (TBSS), and Information was collected on a 3T Siemens MagnetomSkyra scanner at the Centre of Biomedical Magnetic Research.

Results: Compared to the healthy control group, PBDeuthymicsubjects'FA, AD, and MD values were found to be higher in the thalamus, precentral, Corticospinal tract, and Superior Longitudinal Fasciculus. The control group, on the other hand, saw an increase in the Body of corpus callosum, Inferior Fronto- occipital fasciculus, and Middle Cerebella Penuncle.

Conclusions: This study presents evidence of a typical white matter development in a crucial limbic tract involved in emotion regulation. The Superior Longitudinal Fasciculus exhibits microstructural white matter changes early in the course of illness, and the form of these changes may serve as a biomarker of resistance to mood disorders, according to our findings.

SRF-deficient reactive astrocytes are neuroprotective in the aging mouse brain

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Abstract

The aging brain manifests cognitive deficits and becomes more vulnerable to neurodegeneration. Astrocytes play several critical roles in the brain, including maintenance of homeostasis, regulating synapse formation and function, and behaviour. Astrocytes respondto injury and pathological stimuli through an evolutionarily conserved phenomenon termed astrocyte reactivity or reactive astrogliosis, characterized by a multitude of molecular, cellular, and functional changes. Astrocyte reactivity is beneficial for neural repair and restoring homeostasis but can become detrimental depending on the nature and duration of the stimuli. Astrocytes during aging have been shown to exhibit a neuroinflammatory phenotype and this may predispose the brain to neurodegeneration. Our lab recently showed that astrocyte- specific deletion of the stimulus-dependent transcription factor, SRF ($Srf^{GFAP}CKO$ and $Srf^{GFAP\text{-}ER}CKO$) in the mouse brain resulted in widespread and persistent reactive astrocytes, without affecting normal brain architecture and functions. Interestingly, these reactive astrocytes conferred significant neuroprotection following kainic acid-induced excitotoxicity and 6-hydroxydopamine administration. In a mouse model of Alzheimer's disease, the SRF mutant mice exhibited a significant reduction in β-amyloid plaques in the brain. Given these observations, we hypothesized that the "SRF-deficient reactive astrocytes can alleviate aging-associated changes in the brain." We found that in 24-month-old $Srf^{GFAP\text{-}ER}CKO$ mice, there was significantly less aging-associated loss of cerebellar Purkinje neurons and ventral tegmental area dopaminergic neurons, higher synapse numbers and dendritic arborization in the neocortex and hippocampus, more oligodendrocytes and reduced myelin loss. RNA- sequencing of control and mutant astrocytes followed by KEGG pathway, Gene Ontology anddifferential gene expression analyses revealed that pathways related neuronal and synapse functions, and behaviour were upregulated, whereas pathways implicated in synapse elimination, aging, Alzheimer’s disease, Parkinson’s disease, and Huntington’s disease were downregulated. Together, these findings establish that unlike control astrocytes, the SRF- deficient reactive astrocytes are not detrimental in any discernible way to the brain and can protect the brain from aging-associated cellular changes.

Development of a chronic kindling model of adult zebrafish with clinical correlation

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Abstract

Epilepsy is a life-threatening disorder of central nervous system that affects around 5 million people every year in the world. Generally, antiepileptic drugs (AEDs) are used as the first line of treatment for epilepsy, however, 30% of patients remain unresponsive towards the AEDs. Therefore, there is a pressing need of developing new AEDs which greatly depends on the better screening tools and advanced animal models. Nowadays, zebrafish has become an immensely important research model for imitating the various neuropathologicalconditions. In case of epilepsy, it has been employed as a potential acute model of convulsions for the screening of antiepileptic agents as it offers many advantages over traditional rodent models. Though, the chronic animal models of epilepsy have enhanced similitude with the clinical epilepsy, therefore in the current study, an attempt to develop and validate a chronic epilepsy model and associated comorbidities in the adult zebrafish was made. Briefly, a sub- convulsive concentration of pentylenetetrazole (PTZ) was daily administered to the adult zebrafish until the appearance of tonic-clonic seizures. A number of fish showing tonic-clonic seizure for three consecutive days were titled as kindled group. Whereas, a fish group following similar exposure time in system water only was also simultaneously continued till the other group reached kindled stage.Thereafter, the fish groups were employed to carry out behavioral tests for the presence of epilepsy associated comorbid conditions. At the end, fish groups weresacrificed and brains were isolated for neurotransmitter and gene expression studies. A significant increase in the Glutamate/GABA, dopamine, and serotoninlevels was observed in the kindled group. Additionally, a significant effect on theexpression levels of specific genes in accordance to the behavioral tests and neurotransmitter levels was also found in the kindled group.

Comparative Study of Low-Dose Antibiotics in MPTP-Induced Parkinson's Disease: Pre- clinical Study

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Abstract

Parkinson's disease (PD) is a neurodegenerative condition which is complex, chronic and progressive disease. Mitochondrial dysfunction, inflammation-derived oxidative damage and cytokine-induced toxicity thatplays a significant role in PD. In the 21st century, the role of the antibiotic has emerged at the forefront of medicine in health and human illness. Theastonishing effects of antibiotics and their neuroprotective properties against neurodegenerative and neuroinflammatory diseases would be phenomenal for the development of effective therapy against PD. The present study was designed with the aims to have a comparative study ofefficacy of the low dose of antibiotics in MPTP induced mice model of PD. In-silico study was designed to establish the tested drug interactions with well-known targets of PD. Behavioral studies, biochemical estimations and histopathological examinations were designed for comparative study.The in-vivo experimental protocol IAEC/2019/II-R21 was approved by the Institutional Animal Ethics Committee (IAEC) of the University (Registration No.- 215/GO/ReBi/S/2000/CPCSEA).

After 7 days of MPTP.HCL (four doses of 23.4 mg/kg, s.c.) treatments, the tested low dose of Minocycline, Rifampicin, and Azithromycin treatment (each 50 mg/kg, p.o.) phase started on the daily basis and L-Dopa (10 mg/kg) as standard drug treated group. During the treatment phase behavioral studies were performed (i.e. on day-0, day-1, day-3, day-5 and last 7th day of treatment). Body weight, resting tremor, muscle coordination in rotarod, locomotor index in actophotometer and hole boardtest parameters were recorded. On 7th day of treatment, additional behavior tests viz. hot plate test, tail flick test, tail suspension test was done. After behavior tests, mice were sacrificed for brain tissue, kidney, spleen isolation. Brain tissue supernatants was used for assay total protein content, neurotransmitters level, cytokines level (IL-1α, IL-6, TNF-α) and total antioxidant capacity. One representative whole brain, kidneyand spleen from each group were used for histopathology with H&E stained slides. GraphPad Prism-5 software was used for statistical analysis. The p value $p<0.05$ was always considered as statistically significant.

Molecular docking study revealed that Minocycline and Rifampicin might be better potential drug candidate for PD in term of better docking score with human Parkin protein DJ-1 and human alpha-synuclein respectivelyand compared to third antibiotics Azithromycin studied in the present work. In-vivo study with MPTP induced PD demonstrated better efficacy of Minocycline than Rifampicin and Azithromycin studied in the present study in term of normalized behavioral tests parameters associated with PD, modulation of neurotransmitters (DA, 5HT and NE) level and suppression of cytokines storm (by decreasing level of IL-1α, IL-6 and TNF-α) in brain striatum. Histological examinations also demonstrated better efficacy in term of recovery of morphological parameter in

brain, spleen and kidney. Overall neuroprotective efficacies were in the order of Minocycline >Rifampicin >Azithromycin and somewhat better that the standard drug which are currently used pharmacotherapy of PD. Therefore, Minocycline might be better therapeutic drug which can be repurposed for the treatment of PD. However, further molecular studies are warranted for Minocycline to be considered as potential pharmacotherapy for the treatment of Parkinson's disease in clinical setup.

Sweep Screening of Working Professionals using parametric MMSE domains

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Abstract

Background: Prevalence of dementia and Alzheimer increases exponential by age for individuals aged 60 years and over. Less is known about trajectories of cognitive functioning in middle-age or according to education level, cognitive reserves, excessive screen-time, and anthropometric characteristics particularly how these attributes influence the six distinct parametric cognitive domains.

Objective: This study investigated cognitive performance according to age, body-mass-index (BMI), domain-expertise, excessive screen-time, and professional/role responsibilities among middle-aged (21-60 years) healthy adults.
Method: A long-established 30-point Mini-Mental State examination (MMSE) digitized screening tool is developed to assess cognition in 92 healthy working professionals (Scientist (n=21), PhD/Research Scholars (n=23), and others (n=48)). A widely accepted tool provides support to screen for dementia, determination of severity and progression of cognitive impairments. The association of six distinct parametric domains is analyzed based on includedattributes using Kruskal-Wallis Test ($p<0.05$). Moreover, for multiple comparison significancevalue have been adjusted by the Bonferroni correction. The data normality is determined usingShapiro-Wilk test ($p>0.05$).
Results: The MMSE domain recall (immediate and delayed) is associated significantly and shows a decline with aging ($p<0.0001$), and education level ($p<0.05$). The language sub- domain of cognition is significantly different to age, BMI, and education level ($p<0.05$). However, attention and orientation are seemingly related to professional responsibilities ($p\leq0.01$). Thus, education level is expected to have substantial effect on crystallized abilities better reflected in domain-expertise and professional qualities. Executive functioning not significantly associated but illustrates decreasing trend with aging and BMI. Excessive screen- time had resulted in affecting chronic sensory stimulation during brain developmental stages in early adulthood.

Conclusion: This research demonstrated potential sub-domains that are better indicative of cognitive decline at various life-stages. So, primary reflections can support for early preventive measures as better physical and structural brain development accounts for improved cognition in later life. It can also be used as a preliminary screening tool for distribution of organizational work load matched to one's expertise and role handling capabilities increasing productivity.
Significance: The impairments in explicit MMSE domains identifies cognitive dysfunction probably indicating cortex areas contrived by neurodegeneration, and defacements in others imitate lack of acquisition of relevant capabilities.

Neuropeptide S facilitates fear extinction learning and memory by enhancing the activity of mesolimbic dopaminergic circuitry

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Abstract

Background: The impaired ability to extinguish learned fear is one of the important risk factors in the development posttraumatic stress disorder. However, little is known about the neurobiology underlying the extinction of fear. The role of ventral tegmental area (VTA) dopaminergic system projecting to nucleus accumbens shell (AcbSh) has been suggested in the fear extinction. However, the neurotransmitter/ neuropeptide system regulating the activity of dopmainergic circuitry in the fear extinction is not known.
Objective: To test the importance of endogenous neuropeptide S (NPS) system in the VTA-AcbSh circuit in the regulation of fear extinction learning and memory.
Materials and methods: Pavlovian fear conditioning paradigm was used to assess the effect of NPS or NPSreceptor antagonist (SHA-68) on fear extinction learning and memory.
Results: While NPS-containing neurons of the pericoerulear (periLC) area project to the VTA, the tyrosine hydroxylase (marker of dopamine) containing neurons in the VTA co-express NPS receptors. NPS administration in the VTA, prior to fear extinction training facilitated, while NPS receptors antagonist (SHA-68) impaired the fear extinction learning and memory. Intra-VTA NPS injection in the fear conditioned rats increased the dopamine concentration and cFOS immunoreactivity within AcbSh area comparedwith aCSF-control.
Conclusion: It suggests that NPS in the VTA might facilitate fear extinction learning and memory through the activation of mesolimbic dopaminergic circuitry.

Activation of Kappa Opioid Receptor epigenetically regulates BDNF expression in the prefrontal cortex

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Abstract

Current antidepressants require weeks to months of treatment before achieving clinical efficacy on depressed mood, and that too without any effect on suicidal thoughts or cognitive impairment. Moreover, about 40% of major depression patients are unresponsive to currently available antidepressants. We have previously shown that increased kappa opioid receptor (KOR) signaling induces a treatment-resistant depression (TRD)-like phenotype and decreases brain-derived neurotrophic factor (BDNF) expression in mice (Dogra et al., 2016). Given the importance of BDNF and its epigenetic regulation in mood disorders, in this study we investigated the epigenetic mechanisms of KOR-mediated BDNF expression inhibition in the prefrontal cortex (PFC). To investigate this, we performed series of experiments on C57BL6j mice treated with a selective KOR agonist, U50488 (5 mg/kg, 21 days), and observed decreased expression of BDNF transcripts II and IV in the prefrontal cortex (PFC). In addition, we observed a significant decrease in the acetylation of histone H3 at Lysine 9 (H3K9ac) in the PFC of U50488-treated mice compared to saline-treated mice. Tofurther investigate the mechanisms of KOR-induced suppression of BDNF expression in the PFC, we performed chromatin immunoprecipitation (ChIP) analysis with an antibody specific to H3K9ac and profiled the histone acetylation at different BDNF promoters. Excitingly, we discovered a decrease in H3K9ac levels in the PFC of mice treated with U50488. Since histone deacetylases (HDAC) and Sirtuins (NAD-dependent protein deacetylase) modulate BDNF expression (Boulle et al., 2012), we profiled HDACs and the SIRT family of proteins in the PFC of mice treated with U50488. Intriguingly, we discovered a selective increase in the expression of only HDAC5 in the prefrontal cortex (PFC) of U50488 treated mice, suggesting the role of deacetylation of histone H3 and subsequent suppression of BDNF transcription (BDNF-2 and BDNF-4).This result is supported by a ChIP data establishing the link between HDAC5 and BDNF expression. These results demonstrate for the first time an epigenetic link between KOR and depression and strengthen the hypothesis of targeting KOR selectively asa possible treatment for TRD.

Behavioral and Pharmacological Validation of New Clinically Mimickable Model of Chemotherapy-induced Neuropathic Pain

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Abstract

Chemotherapy-induced neuropathic pain (CINP) is among the most common side effects with the use of anti-cancer drugs but till date, there is no effective treatment isavailable for the management of the same. One of the reasons for this could be the unavailability of preclinical animal models which can best represent the clinical situation. Chemotherapeutics agents are generally prescribed in the combination of two or three drugs and based on this observation, in this study we have used a cocktail of chemotherapy (paclitaxel, cisplatin, and vincristine) for the development ofnovel model of CIPN and compared with a conventional paclitaxel model using rats. Results revealed that rats administered with a cocktail of chemotherapy have significantly increased the pain sensitivity which persisted up to the 8^{th} week however,the paclitaxel-treated rats showed pain up to the 5^{th} week. Next, we found an upregulation of mRNA expression of different receptors such as TRPA1, TRPV1, TRPM8, NR2B, and neuro-peptides including substance P and CGRP in the DRG and spinal cord of the cocktail treated rats as compared to both PTX and vehicle- treated rats on day 35. The levels of neuro-inflammatory markers such as TNF-α and IL-1β and nitrosative stress was also increased in cocktail-treated rats compared to both PTX and vehicle-treated group. Further, using the pharmacological tools we observed that on the 14^{th} day both cocktail and PTX treated rats showed significant pain sensitivity which was significantly attenuated by gabapentin 40 mg/kg i.p. The treatment with gabapentin also reversed the molecular and biochemical alterations inthe DRG, spinal cord, and sciatic nerve of both cocktail and PTX treated rats as compared to the vehicle administered group. The novel cocktail-treated animal model for CINP successfully demonstrated the face, predictive and constructive validity and therefore it could be utilized as an additional resource for unraveling the mechanismresponsible for the development of pain and screening of pharmacological agents against CINP.

Keywords: Peripheral Neuropathy; Cocktail Chemotherapy; Chronic pain: Novel animal model; TRP Channels.

Proteomic landscape: novel insights into pathogenesis and toward biomarker discovery for Alzheimer's disease

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Abstract

Alzheimer's disease (AD) is a neurodegenerative disease, the most common cause of dementia in elderly persons. Accumulation of amyloid plaques in the brain is a characteristic of AD. The requirements for a biomarker include the ability to measure a pathologic process, predict outcome, distinguish disease or measure a pharmacological response to a drug treatment or therapeutic intervention. However, there are no reliable biomarkers for AD. Based on amyloid cascade and tau hypotheses, protein biomarkers of different Aβ and tau species in cerebrospinal fluid (CSF) and blood/plasma/serum have been examined to correlate with brain pathology. Recently, unbiased proteomic profiling of these human samples has been initiated to identify many novel AD biomarker candidates, but it is challenging to define reliable candidates for subsequent large-scale validation. We present a comprehensive strategy to identify biomarker candidates of high confidence by integrating multiple proteomes in AD, including cortex, CSF, and serum. The proteomes were analyzed by the multiplexed tandem-mass-tag (TMT) method, extensive liquid chromatography (LC) fractionation and high-resolution tandem mass spectrometry (MS/MS) for ultra- deep coverage. Finally, candidate biomarkers identified by the MS discovery were validated by the enzyme-linked immunosorbent (ELISA) and TOMAHAQ targeted MS assays. We quantified 13,833, 5941, and 4826 proteins from human cortex, CSF and serum, respectively. Compared to other studies, we analyzed a total of 10 proteomic datasets, covering 17,541 proteins (13,216 genes) in 365 AD, mild cognitive impairment (MCI) and control cases. In summary, 37 proteins emerged as potential AD signatures across cortex, CSF and serum, and strikingly, 59% of these were mitochondria proteins, emphasizing mitochondrial dysfunction in AD. Finally, we prioritized the most promising AD signature proteins including SMOC1, TAU, GFAP, SUCLG2, PRDX3, and NTN1 by integrating all proteomic datasets. Our results demonstrate that novel AD biomarker candidates are identified and confirmed by proteomic studies of brain tissue and biofluids, providing a rich resource for large-scale biomarker validation for the AD community.

Transcriptional Control of Mammalian Axon Regeneration - Role of Nuclear Receptors (NR) family of Transcription factors

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Abstract

Axons are cables in the Nervous System that are enclosed within the Spinal Cord and relay critical signals between the Brain and the Body. When injured, embryonic neurons respond via activation of regenerative transcriptional networks resulting in full repair and recovery. However, in a dramatic switch, a week after birth, this regenerative capacity is lost irreversibly. Our lab is interested in understanding the molecular basis of the developmental loss of regenerative ability. In this project, we are focusing on exploring the role of Nuclear receptor family of transcription factors in modulating mammalian axon regeneration. Previously, we have shown that a combination of Klf6/ Nuclear receptors Nr5a2 and Rarb partially recover the regenerative loss in injured adult neurons. There are about 40 nuclear receptor transcription factors that are highly expressed in the mammalian cortex in multiple cell types **only** during periods of axon growth. We have identified that ~15% of these factors are bound to and regulate critical axon growth genes during development, making it highly likely that they are involved in the regulation of axon regeneration. We propose to simultaneously test the relevance of these select NR factors in promoting regeneration following injury across a spectrum of supraspinal neurons. Using a combination of in vivo mouse models of Spinal Injuries, Single-cell assays of gene expression and chromatin accessibility, we are systematically profiling the transcriptional, epigenetic and regenerative responses of NR receptors across multiple cell types and developmental ages. Overall, this research is expected to clarify fundamental overlap in molecular mechanisms that regulate axon growth during development and regeneration. This work also has the potential to identify novel therapeutic targets to improve regenerative outcomes following Spinal Cord Injury.

Fear conditioning leads to enduring alteration in RNA transcripts in hippocampal neuropil that is dependent on EphB2 forward signaling

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Abstract

Background: Alterations in the RNA transcriptome have been associated with changes in brain functions. Here we aimed to unveil whether fear conditioning leads to long-lasting alteration in mRNA levels in the basolateral amygdala (BLA) and hippocampus, using RNA-Seq in combination with laser microdissection microscopy. We further aimed to unveil whether these mRNA changes are involved in memory formation by monitoring their levels in EphB2$^{lacZ/lacZ}$ micethat can form short-term, but not, long-term fear conditioning memory.
Results: First, we found mRNA transcriptome signatures that comprise specific cellular pathways unique to each brain region. Next, we revealed that fear conditioning leads to alterations in mRNA levels 24 hours aftertraining in hippocampal neuropil, but not hippocampal cell layers or BLA. The two main groups of altered mRNAs encode proteins involved in neuronal transmission and neuronal morphogenesisand development and the vast majority are known to be enriched in neurons. None of these mRNAlevels were altered by fear conditioning in EphB2$^{lacZ/lacZ}$ mice that were also impaired in long-termfear memory.
Conclusion: Fear conditioning leads to enduring alteration in mRNA levels in hippocampal neuropil that is dependent on processes mediated by EphB2 needed for long-term memory formation.

Study on the ameliorative potential of Methyl cinnamate in Alzheimer's disease model of Drosophila melanogaster.

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Abstract

Alzheimer's disease is an age-related disorder characterized by loss of neurons in the hippocampal and cortical region of the brain. The disease is known to cause permanent atrophy of the related areas causing an decrease in the quality of lifestyle and disabilities in the learning and memory functions of. This disease is featured by Amyloid Beta and neurofibrillary tangles' aggregation in the brain region, leading to dementia and neuronal cell death/neurodegeneration. Amyloid beta is a sequence of amino acids formed due to the faulty cleavage of a transmembrane protein called Amyloid Precursor Protein (APP) by beta secretases and gamma secretases. On the other hand neurofibrillary tangles are formed due to the hyperphosphorylation of TAU proteins. The Amyloid Beta deposition and neurofibrillary accumulation in the brain leads to ROS aggregation and increase in oxidative stress. Oxidative stress portrays to be a causative agent for neurodegeneration. Several compounds are proven to reduce ROS accumulation and oxidative stress. One such compound called 'Methyl cinnamate' (MC)— a methyl ester derivative of cinnamic acid has proven to show antioxidant properties. Therefore, making it a potential agent for the current study. In the study we use the Drosophila melanogaster GMR-ABeta42. The study is aimed to demonstrate the anti-inflammatory and antioxidant properties of MC in the Drosophila melanogaster model of Alzheimer's disease. The study also aims to report thebehavioral and biochemical changes occurring in the Drosophila model; upon MC induction.

Curcumin activates selective autophagy through p62-mediated Nrf2-Keap1 pathway in Parkinson's disease

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Abstract

Background: Parkinson's disease (PD), a motor disease, is caused due to aggregation of abnormally misfolded alpha-synuclein protein in cytoplasm of dopaminergic neurons. These aggregated proteins are cleared by a process called autophagy which degrades long-lived and damaged proteins and organelles from the cell. Curcumin, a polyphenol, is known to be a potent autophagy inducer.

Objective: To study the effect of curcumin on autophagy and Nrf2-Keap1 pathway as a potential treatment therapy in Parkinson's disease.

Methodology: The mice were divided into four groups, Control group; Rotenone group; Rotenone + Curcumin group and; Curcumin alone group. The mice were subcutaneously injected with rotenone (2.5mg/kg bw) and co-treated with oral administration of curcumin (80mg/kg bw) for 35 days.

Results: The results revealed the downregulation of Nrf2 in the rotenone-intoxicated mice along with decrease in tyrosine hydroxylase (TH) level. However, the level of both Nrf2 and TH were significantly restored on the treatment with curcumin. Autophagy was evaluated by the change in expression of autophagic markers, p62 and LC3-II. Increased p62 expression and decreased LC3 expression in the rotenone mouse model of PD confirmed the compromised autophagy pathway, consequently increasing the aggregation of misfolded protein α-syn. Whereas, curcumin treatment showed a significant decrease in the expression of autophagy substrate p62 along with down-regulation of α-syn expression and increased level of LC3-II.

Conclusion: The findings reveal the neuroprotective role of curcumin in rotenone-intoxicated mice by activating p62-dependent Keap1-Nrf2 autophagy pathway.

Assessing The Therapeutic Potential Of Methyl Cinnamate On park^{13} Mutants, aParkinson's Disease Model Of Drosophila melanogaster.

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Abstract

Progressive neurodegenerative conditions result in permanent neuronal atrophy, which greatly lowers quality of life and causes severe disabilities. After Alzheimer's, Parkinson's disease (PD) is the most prevalent neurological condition worldwide.

Approximately 60,000 new cases are reported annually, and its manifestations include tremors, bradykinesia, muscle rigidity, poor posture and balance, and loss of autonomic movement. It has impacted almost 10 million individuals worldwide. In this, the substantia nigra's dopaminergic neurons degenerate, causing debilitating motor and non-motor symptoms. Parkin is a key member of a family of genes that can lead to Parkinson's disease (PD) and is typically involved in fission-fusion dynamics, biogenesis, and mitochondrial quality control. Any imbalance in these elements can harm neurons by raising the amounts of Reactive Oxygen Species (ROS). L-Dopa replacement therapy is the current standard of care for PD, but its effectiveness wanes with time. Organic compounds such as Cinnamic acid and its derivatives like Methyl Cinnamate are known to show high levels of anti-inflammatory and anti-oxidant properties, which can be utilised for treatment of PDsince they act by sequestering the ROS.

This study assess the effects of Methyl cinnamate using a fly model of PD; parkin null mutant, park^{13}. Three behavioural tests, including climbing, larval crawling, and puff-tethered flight experiments, were used to evaluate motor activity. Antioxidant enzyme levels, specifically those of catalase and Mn-SOD, were measured as part of biochemical assays for oxidative stress. DCFDA staining was performed to check forROS levels in the fly brain.

When compared to wild type CsBz flies, the parkin mutants show significantly more impaired motor behaviour. According to preliminary data, the majority of the mutant population exhibits climbing defects, with the majority of them not being climbers. As a result of wing muscle wasting, park flies tyre out during flight far more quickly than control flies do. Administration of the therapeutic is hypothesised to provide rescue by down regulating the levels of ROS downstream of parkin and hence show promise as a novel treatment for PD that needs to be further investigated.

Evaluation of Anti-Parkinson's activity of Silver herbomineral (Rajat bhasma) on MPTP induced Parkinson's disease in C57BL/6 mice

Abstract

Background: The study was designed to validate the claims in Ayurveda regarding the efficacy of Ayurvedic drugs in neurodegenerative disorders. It was decided to conduct an efficacy study of a herbomineral drug (Rajat bhasma) on Parkinson's disease induced in C57BL/6 mice. Parkinson's disease has symptom descriptions in Ayurveda and modern medicine. The latter offers only the symptomatic therapy by replacing dopamine, the neurotransmitter involved, but does not slowdown or reverse the loss of dopaminergic neurons.

Method: 8 weeks old male C57BL/6 mice were used for the study. Parkinsons disease was induced by MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine). The dose selected for inducing Parkinsons disease was 20 mg/kg, i.p., twice a day at an interval of 12 hours for four consecutive days. The positive control used was l-Dopa. The test drug used was a herbomineral (Rajat bhasma). The groups in the study were- Healthy normal group, Disease group, Positive control group and Test drug group. The model was for a period of 15 daysand MPTP was injected between 07^{th} day to 11^{th} day. L-Dopa and test dug were fed on all 15 days. The disease group was fed with saline. Behaviour tests- Rotarod test, Photoactometer, Paw stride length and Open field test was carried on the 16^{th} day. After carrying out the tests, the mice were sacrificed and striatum was dissected out. One set of striatum were used for Neurotransmitter (Dopamine) and its metabolites (Homovanillic acid and 3,4-Dihydroxyphenylacetic acid) and the other set were used for Immunohistochemistry of Tyrosine hydroxylase neurons.

Result: Bahaviour studies showed that the test group had a significant improvement in Rotarod test, Open field test, Paw stride length and Open field test. Neurotrasmitter (Dopamine) and its metabolites (Homovanillic acid and 3,4-Dihydroxyphenylacetic acid) levels were improved in the test drug when compared to the disease group. Immunohistochemistry of Tyrosine hydroxylase neurons in Striatum showed a significant protection of neurons in the group fed with the test drug.

Conclusion: The drug (Rajat bhasma) was found to be effective in reducing the inflammation in the brain of the mice indicating its anti-inflammatory properties. There was asignificant improvement in the neurotransmitter levels and immunohistochemistry suggestingthat the drug plays a protective role against the MPTP agent.

A metagenomic approach to investigate the alterations in the gut microbiome of patients with Parkinson disease compared to Healthy controls

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Abstract

Parkinson's disease (PD) is a progressive neurodegenerative disease characterized by the loss of dopaminergic neurons in the substantia nigra. Recent research suggests that gut bacteria hold the potential to modulate neurodegenerative diseases via gut microbiota-brain axis (GMBA). There have been no attempts to characterize the alterations in the composition of gut flora occurring in PD in the South Indian population.

The present clinical study focuses to distinguish the microbial community structure between the gut microbiome of Parkinson's patients and healthy controls in the South Indian population. The study included 45 PD patients (mean age=58.8 ± 13.24, M: F=14.24) and age-matched 45 healthy controls (HCs, mean age:57.84 ±11.1, M: F=22:23)). All study participants had similar physical activity and dietary profiles. The 16s amplicon is performed on Illumina MiSeq system and Bioinformatic analysis was done using QIIME2 module plugin integrated with R package. Acrossall 90 participants, bacteria was the major constituent of the microbiota in every sample. The QIIME 2-based 16S rRNA sequence analysis showed the presence of bacteria belonging to 32 phyla, 78 classes, 168 orders, 247 families, and 437 genera. The fecal microbial distribution of the PD group was found distinctively different from controls at the phylum level. The dominant phyla were found to be Firmicutes followed by Proteobacteria, Actinobacteriota and Acidobacteriota. However, the total count in phyla Proteobacteria, Actinobacteriota and Acidobacteriota were found significantly high in patients compared to controls. The Kruskal- wallis rank sum test analysis showed phylum Actinobacteriota, Bacteroidotes, Bdellovibrionota, Euryarchaeota and Verrucomicrobia are significantly increased in PD and Cyanobacteria and Elusimicrobiota were found more in HCs. Lachnospireceae was the most abundant family in both control and patients followed by Ruminococcaceae, Helicobactereaceae, Christensenllaceae and Bifidobactereaceae. Faecalibacterium was the abundant genus found in all subjects and it was found significantly decreased in patients. F/B ratio is generally used to assess gut health, we calculated F/B ratio in PD patients and healthy participants, compared using Mann-Whitney test (Mann-Whitney; U = 738, p = 0.0265), this shows that F/B ratio differs significantly between thegroups.

The study demonstrates the occurrence of potential variations in the bacterial community structure in the PD gut compared to HCs which is expected to contribute to the microbial product-mediated PD pathogenesis via GMBA.

Keywords: Gut Microbiota, Gut-Brain-Axis, Metagenome, Parkinson's Disease, Relative abundance

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CSPG upregulation causes impaired dendritogenesis and spinogenesis, leading to synaptic dysregulation and inhibition of plasticity in a double-hit rat model of protein malnutrition (PMN) and bacterial infection (LPS)

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Abstract

Introduction: The extracellular matrix (ECM) plays a vital role in growth, guidance and survival of neurons in the central nervous system (CNS). The chondroitin sulphate proteoglycans (CSPGs), a typeof ECM proteins are crucial for CNS homeostasis. The major goal of this study was to uncover the effects of astroglial activation and associated CSPG upregulation on dendritic complexity and spine density of cerebellar Purkinje neurons as well as on synaptic activity and plasticity following synergistic exposure of maternal protein malnutrition (PMN) and bacterial infection.

Methodology: Female Wistar albino rats (3 month old) were switched to control (20% protein) or low protein (LP, 8% protein) diet for 15 days followed by breeding. A set of pups born to control/LP mothers and maintained on respective diets throughout the experimental period constituted the control and LP groups. A separate set of both control and LP group pups were exposed to bacterial infection by a single intraperitoneal injection of lipopolysaccharide(LPS) (0.3mg/ kg body weight) on postnatal day 9 (P-9) and constituted control+LPS and LP+LPS groups respectively. Standard immunohistochemical procedures were performed to measure the relative fluorescence intensities and number of cells expressing CSPG, Arc, Egr and PSD-95 at P-21, 3 and 6 months of age. Sholl analysis performed on camera lucida traced Golgi images revealed dendritic arborisation and spine count in Purkinje neurons.

Results: The results revealed astrogliosis and associated CSPG upregulation in LP+LPS animals resulting in morphologically deteriorated Purkinje neurons and impaired PSD-95 expression. Moreover, reduced Purkinje neuron dendritic arborisation and spine density as well as alteration in plasticity proteins (Arc and Egr) were also observed in double hit group. Thus, it is suggested that these alterations may contribute to synaptic dysregulation and inhibition of plasticity both during development and adulthood, potentially contributing to the emergence of schizophrenic-like phenotypes.

Conclusions: The study indicates that PMN and bacterial infection either singularly or synergistically exerts their effects possibly via CSPG upregulation. Thus, modification of CSPG expression seems to be an attractive therapeutic approach for restoring CNS function following PMN and bacterial infection, while there are still many questions which need to be answered.

Evaluation of the protective effect of fisetin nanoformulation in an experimental model of Alzheimer's disease

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Abstract

Alzheimer's disease (AD), the most common neurodegenerative disease worldwide, is characterized by a decline in memory and cognition but has no proper cure to date. Fisetin, a flavonol, possesses anti-oxidant, anti-inflammatory, and anti-apoptotic properties and has shown its potent neuroprotective effect against AD in several preclinical studies. However, the clinical application is limited owing to low oral bioavailability. In our study, we aimed to evaluate the protective effects of fisetin nanoformulation in an experimental model of AD.

For induction of AD, Aβ1-42 was administered intracerebroventricularly in the mice. Further, the animals were treated with fisetin and fisetin nanoformulation (5 mg/kg/day; p.o.) for 28 days. The effect of different treatments on memory impairment, spontaneous locomotor activity, motor coordination, and depression-like behavior was analyzed. The cortex and hippocampus were estimated for various oxidative stress markers and proinflammatory cytokine levels.

Treatment with fisetin nanoformulation resulted in significant improvement in Aβ1-42- induced neurobehavioral alterations in mice. Treatment with fisetin did not show substantial protective effects on neurobehavioral impairments. Further biochemical analysis suggested improved cortical and hippocampal oxidative stress, nitrosative stress, and proinflammatory cytokine levels with fisetin nanoformulation treatment.

Thus, the study's outcome suggested that the nanoformulation approach improved the pharmacodynamic effects of fisetin in the experimental AD model, possibly via improvement in its pharmacokinetic variables.

EVALUATION OF FISETIN NANOFORMULATION IN EXPERIMENTAL MODELOF TEMPORAL LOBE EPILEPSY

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Abstract

An abnormal electrical disturbance characterizes epilepsy in the brain that causes psychological, neurological, and social consequences. Inflammation, apoptosis cascade activation, and ROS generation are the central neurological sequelae during epileptic conditions. Fisetin is one of the most commonly used bioactive flavonoids with an anti- inflammatory, ROS inhibitory effect. However, its clinical translation is limited due to its poor bioavailability. Therefore, this study is envisaged.

The status epilepticus was induced using pilocarpine in male BALB/C mice. Fisetin and fisetin nanoformulation was administered (5 mg/kg/day; p.o.) for 28 days. The effect on neurobehavioral impairments was analyzed by monitoring spontaneous locomotor activity, motor coordination, memory impairment, and depression-like behavior. After behavioral assessments, the animals were sacrificed, and different brain regions were isolated for the evaluation of oxidative stress markers and proinflammatory cytokines.

Behavioral assessments suggested improving pilocarpine-induced behavioral deficits only with the fisetin nanoformulation treatment. These behavioral outcomes were supported by the reduction in oxidative stress and proinflammatory cytokines in the cortex and hippocampal region.

Therefore, the outcome of the study suggested that the nanoformulation approach improved the antiepileptic effect of fisetin, possibly via improving its pharmacokinetic variables.

Protective effect of fisetin on arsenic and fluoride induced neurotoxicity

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Abstract

Arsenic and fluoride are groundwater's inorganic contaminants, and their chronic exposure caninduce neurotoxicity. Both these elements affect the hippocampus and cortex region causing impairment of short-term and long-term memory, gliosis, neurodegenerative lesions, and decrease in glutamate level. In neuronal cells, arsenic and fluoride co-exposure accumulation enhances excessive ROS production. An extreme level of ROS initiates the caspase-mediated apoptosis pathway and NF-kB-mediated inflammatory pathway. Fisetin is a hydrophobic polyphenolic flavonoid having both antioxidant and anti-inflammatory properties. Fisetin reduces the level of ROS by scavenging the free radicals and ultimately inhibits the NF-kB inflammatory pathway and neuronal apoptosis. Thirty Balb/c mice were taken for this study and divided into six groups. Group I served as the normal control group and received no treatment, group II served as the arsenic-fluoride exposed group and administered arsenic (as NaAsO2, 70 mg/L) as well as fluoride (as NaF, 120 mg/L), group III served as fisetin per se group, which received only fisetin (20 mg/ kg/day; per os), group IV served as low dose fisetintreated group which received fisetin (5 mg/kg/day; per os) and arsenic-fluoride containing drinking water, group V served as medium dose fisetin treated group which received fisetin (10 mg/kg/day; per os) along with arsenic-fluoride containing drinking water, and group VI served as high dose fisetin treated group which received fisetin (20 mg/kg/day; per os) along with arsenic-fluoride containing drinking water. After four weeks of continued exposure and treatment, neurobehavioral tests were performed to evaluate the spontaneous locomotor activity, memory impairment, motor coordination, and sensory-motor activities. Apart from the neurobehavioral tests, colonoscopy was performed to assess the gut wall damage due to arsenic and fluoride co-exposure. Then, all mice were sacrificed, and collected the brain and blood for biochemical estimation. This study aims to evaluate the protective effect of fisetin onarsenic and fluoride-induced neurotoxicity.

American ginseng attenuates astrocytopathy in cell culture study

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Abstract

Astrocytopathy is considered one of the cardinal features in the pathophysiology of demyelination. In the in vitro models of astrocytopathy, cytokines are considered one of the most acceptable inducers for astrocytopathy. In our previous study, we report the neuroprotective activity of American Ginseng (Panax quinquefolius; AG) in ethidium bromide-induced demyelination in the experimental rodent model. However, the effect of AG on the extent of astrocytopathy remains to be elusive. Therefore, the present study investigates the therapeutic activity of AG against cytokine-induced astrocytopathy in cell culture study. In the study, astrocytopathy was induced in the human U87Mg cell line after its transformation by db-cAMP, by a mixture of cytokines (TNF-alpha, IL-1alpha, and C1q at a concentration of 1.7 nM, 1.7 pM, and 597 pM respectively). AG (25, 50, and 100 µg/ml) significantly attenuated the mixture of cytokines-induced cytotoxicity in astrocyte cultures in the MTT assay. Further, AG (100 µg/ml) significantly ameliorated the mixture of cytokines-induced increase in the level of mRNA expression of GFAP, and C3 markers for reactive astrocytes, in RT-PCR study. In addition, AG (100 µg/ml) significantly ameliorated the mixture of cytokines-induced increase in the level of expression of GFAP in immunohistochemistry study and the level of ROS for reactive astrocytes. These observations indicate the fact that AG can mitigate cytokines-induced astrocytopathy. However, its plausible therapeutic mechanism against astrocytopathy is yet to be established. In conclusion, AG could be a potential therapeutic alternative in the management of demyelination.

American Ginseng exhibits anti-neuroinflammatory activity in LPS-stimulated microglia inan in-vitro study

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Abstract

Neuroinflammation is the main cause of many neurodegenerative diseases. It has been suggested that microgliosis is considered one of the events in the pathophysiology of neuroinflammation. Microgliosis could be a potential therapeutic target in the management of neuroinflammation. Several anti-neuroinflammatory drugs have been reported in clinical and animal studies. However, these drugs possess several potential side effects. Further, there are few anti-neuroinflammatory drugs that possess significant therapeutic effects against microgliosis. Hence, there is a need to investigate an alternative anti-neuroinflammatory agent with potent therapeutic potential against microgliosis. Literature review suggests that American ginseng (AG) possesses a significant beneficial effect against microgliosis in ischemia reperfusion-induced neurotoxicity in animal studies. However, there is no report of AG on microgliosis in vitro studies. Therefore, the present study investigated the therapeutic potential of AG (25, 50, and 100 µg/ml) against lipopolysaccharide (LPS)-induced microgliosis in the cell culture study. Results suggest that AG (25, 50, and 100 µg/ml) per se did not exhibit any cytotoxicity in BV2 cell lines. Further, AG (100 µg/ml) significantly promoted cytotoxicity in LPS-challenged BV2 cell lines. Moreover, AG (100 µg/ml) significantly attenuated LPS-induced increase in intracellular ROS, level of gene expression of tumor necrosis factor-alpha, interleukin-12, and Interferon-gamma in BV2 cell lines. Hence, it can be postulated that AG could be a potential therapeutic agent to attenuate microgliosis. However, the plausible anti-microgliosis mechanism is yet to be established in future studies.

Activation of cholinergic REM-ON neurons in PPT projecting to VTA increases REMS in rats: implications with intermittent appearance of REMS

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Abstract

Rapid eye movement (REM) sleep (REMS) is characterized by de-synchronized EEG, muscle atonia and rapid eye movements. Most dreams, particularly those we remember, appear during REMS. Disturbed REMS and hallucinations are observed in REMS behavior disorder and several psychiatric disorders like depression and schizophrenia in which role of dopaminergic (DA-ergic) neurons in ventral tegmental area (VTA) has been implicated. Often similarity has been drawn between hallucinations during waking with dreams appearing during REMS; however, the neural mechanism(s) of action for their appearance are yet unknown. The VTA possesses DA-ergic neurons receiving projections from pedunculopontine tegmentum (PPT), the site containing cholinergic REM- ON neurons. Hence, we proposed that during REMS, intermittently some of the REM-ON neurons in PPT might beactivating DA neurons in VTA resulting in prolonging or increased REMS and appearance of dreams during REMS. Further, malfunctioning of this circuitry during waking might be at least among the causes ofhallucinations.

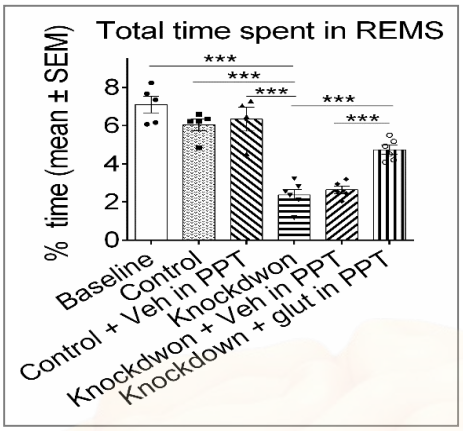
. Under surgical anesthesia guide cannulae targeting 2 mm above VTA (AP= -6.0 mm; ML= ±0.5 mm; DV= -8.4 mm) and PPT (AP= -7.8
mm; ML= ±1.8 mm; DV= -7.4 mm) as well as EEG, EMG, and EOG electrodes were implanted bilaterally in 250-275gm male Wistar rats. Post-surgical recovery, sleep-waking (S-W) was recorded in chronically prepared rats for 8 h between 10 AM-6 PM with or without microinjection of either scopolamine (SCOP) in VTA or glutamate (GLUT) into PPT alone or both simultaneously. In another set of experiments, tyrosine hydroxylase
(TH) was downregulated by microinjecting TH-shRNA into VTA and PPT stimulated by glutamate. At the end of the experiments, under overdose of anesthesia, the brains were extracted for histological confirmation of the microinjection sites. TH-knockdown was confirmed by immunohistochemistry and by western blotting of punched out tissue. The sleep-waking data was scored offline using SleepSign software; total sleep-wake, REMS frequency, and duration/episode were calculated.

We observed that upon SCOP injection into the VTA, the REMS was decreased, which was prevented by simultaneous stimulation of PPT with GLUT. Compared to baseline and control-shRNA into VTA, REMS was reduced in TH-shRNA induced TH-knockdown rats. However, REMS was comparable to control-shRNA injected and baseline groups stimulation of PPT in VTA-TH knockdown rats.

We propose that some phasic REM-ON neurons activate VTA neurons for intermittent appearance of dreams during REMS. Thus, the findings of this study support our contention, which however, need to be confirmed, preferably in humans.

Acknowledgement: Funding to BNM under SERB JC Bose Fellowship; UGC; DST-PURSE and ICMR fellowshipto DR

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Proinflammatory and anti-inflammatory mediators regulate the host response to viral infection by altering the connexin 43 mediated gap junctional communication

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Abstract

Background and rationale: Mouse hepatitis virus (MHV), a murine β-CoV induced neuroinflammation, provides an excellent cause-effect platform to understand the viral-induced acute neuroinflammation and chronic progressive demyelination, which are the characteristic hallmarks of the human neurological disease Multiple Sclerosis. During β-CoV infection, the host cell proteins regulate the host response to viral replication. One such host protein is connexin 43 (Cx43), a transmembrane protein belonging to the gap junction family. In the mouse brain, Cx43 is predominantly expressed on astrocytes. Previous studies have shown that at day five post- infection (p.i), the Cx43 expression is significantly downregulated in the mouse brain. This downregulation of Cx43 coincides with the peak of viral titer and neuroinflammation. After Day 10 p.i, as the viral titre reduces and neuroinflammation resolves, the Cx43 expression returns to its normal basal levels. However, it is yet to be understood weather it is the viral replication or neuroinflammatory mediators that affect Cx43 expression. The current study investigates this nexus between neuroinflammatory mediators and the alteration of Cx43 expression.

Methods: Four-week-old, MHV-free, C57BL/6 mice were inoculated intracranially with a 50%LD50 dose of RSA59 (20,000 PFU). The transcriptional regulation of different inflammatory cytokines in the alteration of Cx43 expression on different days p.i was investigated.

Results: On day 5 p.i when the neuroinflammation is at its peak, the inflammatory milieu is skewed towards the direction of proinflammatory cytokines with TNF-α, IL-6, and IL-1β significantly upregulated, which co-indices with downregulation of Cx43. However, by Day 10 p.i, the inflammatory milieu shifts towards the direction of anti-inflammatory cytokines with the expression of IL-10 and TGF-β significantly upregulated, and the Cx43 expression is brought back to its basal levels. This re-establishment of intercellular communication may be essential to restoring homeostasis in the inflamed brain.

Conclusion and Discussion: The antiviral role of Cx43 mediated gap junction in regulating viral spread has already been established. This study sheds light on the importance of balance between proinflammatory cytokines and the anti-inflammatory mediators in regulating the host response to counteract the viral infection by altering the gap junctional communication.

Ethics statement: All experimental procedures and animal care and use were strictly regulated and reviewed as per animal ethics approved by the Institutional Animal Care and Use Committee at the Indian Institute of Science Education and Research Kolkata (AUP no. IISERK/IAEC/AP/2019/28.01). Experiments were performed following the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), India.

Acknowledgment: This work is supported by a research grant from Council for Scientific and Industrial Research (CSIR), India (27(0356)/19-EMR-II) to JDS and research funds from IISER-K. GK was supported by Junior Research Fellowship by CSIR.

Comprehending the molecular cascade promoting motor neuron degeneration in a stemcell model of Amyotrophic Lateral Sclerosis

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Abstract

Introduction and background of the study: Amyotrophic lateral sclerosis (ALS) is an adult-onset prototypical neurodegenerative disease specifically targeting the motor neurons of the brain and spinal cord. Despite the wealth of studies undertaken globally to understand glutamate excitotoxicity, mitochondrial dysfunction, and oxidative stress, the pathogenetic mechanisms are still ambiguous. The lack of biomarkers and undecipherable genetic complexity calls for the need for potential cellular models to understand the molecular etiologyof the disease. Stem cell-based models offer a prodigious avenue for disease modeling as they enable researchers to understand disease development and identify therapeutic targets for precision medicine. The non-canonical Wnt/Ca2+ pathway is known to regulate intrinsic electrophysiological properties and mobilize calcium ions to maintain neuronal integrity. In this study, we attempted to establish a stem cell-based model of ALS using amniotic membrane-derived mesenchymal stem cells (AMMSCs) to comprehend the interplay between Wnt/Ca2+ pathway, mitochondria, and its molecular events leading to motor neuron degeneration in ALS.

Methodology: Motor neuron differentiation, overexpression of SOD1 G93A, assays such as ROS, FURA-2 AM, TMRE, and ATP, CYTO-ID autophagy detection kit, gene expression analysis, Western blotting, and immunocytochemistry.

Results: We hereby interpret that the hyperactivated Wnt/Ca2+ pathway leads to the over- influx of calcium ions into mitochondria resulting in the build-up of oxidative stress. The mitochondrial biogenesis markers and quality control mechanism which regulate the mitochondrial integrity were found to be dysregulated. These events further worsen the disease status, leading to the over-accumulation of fragmented as well as dysfunctional mitochondria, inevitably resulting in deregulated autophagic pathways leading to apoptosis, eventually prompting the demise of motor neurons.

Conclusion: Our study led us to understand the possible interplay of the Wnt/Ca2+ pathway with mitochondrial dysfunction, disrupted autophagic machinery and a series of other molecular events which possibly contributed to motor neuron degeneration. Further studies on Wnt/Ca2+ pathway modulators could prove to be a novel therapeutic approach to restore neurodegeneration.

Dream Detector: Decoding Multivariate EEG pattern between dream recall and no recall from High-density PSG data

Adla Zubair[1,#], Gulshan Kumar[2,#]



Abstract:

Ethical Statement:

Acknowledgement:

Personality or hunger states: What determines rationality in zebrafish (Danio rerio)?

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Abstract

Consistency in choices between any two options regardless of further options included in the choice set is crucial to upholding economic rationality. Animals are widely known to violate such normative principles of rational decision-making, suggesting a relative rather than absolute valuation mechanism of options. Interindividual differences in performing such cognitive tasks also suggest some variation in the valuation mechanism within individuals of aspecies, and these also provide an opportunity to investigate the neural and developmental mechanisms mediating these kinds of decisions. Here we use zebrafish, a model system amenable to the use of behavioral, neurobiological, genetic, and pharmacological tools, to test the normative principle of independence of irrelevant alternatives with respect to interindividual differences. We test the hypothesis that personality types categorized based ona battery of behavioral tests and movement parameters can predict the measure of rationality irrespective of hunger states. We infer shoaling preferences from the spatial trajectories of freely swimming zebrafish individual zebrafish in an arena where they could observe and engage in shoaling behavior near conspecific zebrafish in nearby display tanks in binary and ternary choice sets.

Keywords: Rationality, Decision-making, Personality

Single-dimensional multi-alternative shoal choice decoy space map of zebrafish (Danio rerio)

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Abstract

Normative principles of economic rationality assume that a rational individual makes consistent choices that maximize utility. The principle of independence of irrelevant alternatives (IIA) proposes the invariance of preference order between two options, regardless of the inclusion of other alternatives, or decoys, in the choice set. Organisms ranging from slime molds to human beings are reported to have violated IIA in various tasks, mostly with respect to combinations of two or more choice attributes. Here we investigate the decoy effect in zebrafish across a single dimension of shoal size, exploring decoy space using various combinations of dichotomous and trichotomous shoal size choices. A single focal fish freely moved in an arena with only visual information from shoaling conspecifics placed in display tanks surrounding the arena, with the randomized placement of various fish shoal sizes in the display tanks. The shoal choice preference was inferred from time spent in the respective sectors facing the display tanks, using the focal fish's trajectory data. The study is a novel attempt to model the multi-alternative decision-making space along a single attribute dimension in any non-human animal system.

Keywords: Rationality, Decision-making, Independence of Irrelevant Alternatives

The neuroinflammatory markers in the frontal cortex are correlated with some memory impairments in intracerebroventricular streptozotocin injected rats in a time dependentstudy.

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Keywords: Alzheimer's disease, memory impairment, COX2, PGE2, TNFα, IL-1β
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Abstract

Back ground: Intracerebroventricular (ICV) administration of streptozotocin (STZ) is a well-established and widely accepted animal model to study sporadic AD. Different investigators reported neuroinflammation in hippocampus and memory impairments in ICV STZ injected rats (ICV-STZ-IR) at various doses and at different time points. The optimum dose of STZ (3mg/kg body wt) has been reported to produce neuroinflammation in hippocampus and memory impairments at 3 weeks of post-injection. The inflammatory markers in the frontal cortex in ICV-STZ-IR may also change which may affect the memory parameters.

Aims and objectives: To study the changes of neuroinflammatory markers in the frontal cortex and memory parameters after ICV injection of STZ at optimum dose (3mg kg body wt) at three different time points (24^{th} hour, 7^{th} day and 21^{st} day) of post-injection, and to investigate any correlation between increased inflammatory markers in frontal cortex and memory impairments in ICV-STZ-IR in this time dependent study. Working memory errors (WME), reference memory errors (RME), latency to enter first baited arm (L1B) and latency to enter four baited arms (L4B) were measured in a Radial Arm Maze (RAM) along with the concomitant levels of COX2, PGE2 and TNF α, IL-1β in frontal cortexat 24^{th} hour, 7^{th} day and 21^{st} day after ICV STZ injection in rats, and the results were compared with that of sham-operated (ICV artificial CSF injection, aCSF) and control rats (without any injection). The memory parameters were analysed for any correlation with the increased levels of inflammatory markers in ICV-STZ-IR in this time dependent study.

Results: WME and RME were increased in ICV-STZ-IR at 24^{th} hour, 7^{th} day and 21^{st} day and WME, RME andL4B were elevated progressively from 6th day to 21st day after ICV STZ injection in 21-day study. The neuroinflammatory markers in the frontal cortex (TNF α, IL-1β, COX 2 and PGE 2) were also increased at all the time points and showed graded increase with time after ICV STZ injection.

Discussion and conclusion: The increased errors in memory (WME and RME) in ICV-STZ-IR were correlated significantly with the increased levels of the observed neuroinflammatory markers in the

frontal cortex in this study; but L1B and L4B were not correlated with these markers. It appears from the results of these three time duration studies that the neuroinflammation in frontal cortex and memory impairments in ICV-STZ- IR are probably linked.

Acknowledgement: This research work has been funded DST, CSRI, Govt. Of India [RefernceNo.SR/CSRI/353/2016(G) dt.24.4.2017]

Neurosteroid basis of molecular mechanism of Chronic Immobilization Stress: Systematic literature analysis

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Abstract

Immobilization stress is known to induce both psychological and physical strain.
Alteration in brain Cholesterol & Neurosteroids (synthesized de novo in the brain from the precursor molecule cholesterol) are contributing factors to neuroendocrine dysfunction and cognitive behavioural changes. Therefore, it is important to comprehend chronic immobilization stress (CIS) induced specificchanges in brain cholesterol metabolism & neurosteroids.

The microarray dataset (GSE2870) of gene expression profiles in the Cerebral cortex of chronic immobilization stress (CIS) (3 hours/day for consecutive 14 days) induced rats (n=15) and control rats(n=15) were collected from the NCBI GEO database.
Microarray data was processed in R language using basic packages of the Bioconductor project to finddifferentially expressed genes (DEGs) with the criteria of adjusted p-value < 0.05 and log2FC > 0.4.
Eight genes and 12 biomolecules that are vital for brain cholesterol metabolism were selected from PubMed search. 340 DEGs along with eight genes had been incorporated on the STRING 11.0 database. 340 DEGs along with eight genes and twelve biomolecules had been incorporated on the STITCH 5.0 database. CPI network (developed in STITCH) and PPI network (developed in STRING) were importedin Cytoscape 3.8.0 software and merged.
CentiScaPe 2.2, MCODE and CytoCtrlAnalyser plugins were used to identify Hub-bottleneck nodes, major sub-network and driver nodes respectively from the PPI-CPI network.
Hub-bottleneck and driver genes found in the top sub-network were submitted to Enrichr webtool platform for the enrichment analysis of functional annotations gene ontology (biological processes, cellular component, molecular functions), KEGG pathways and Jensen Disease. Functional annotations were ranked based on the levels of combined scores with adjusted p-values < 0.05. Relevant genes related to our topic of interest selected from top 10 terms.

A total of 3 hub bottleneck (COL1A1, LPL, GAD1) and 3 driver genes (CYP1B1, CYP26B1, CRHBP) were identified whose expression altered significantly in response to CIS. These genes are crucial for regulation of brain cholesterol & neurosteroid metabolism in response to CIS.

Correlative effects of distressed-body image scores on metastatic markers and depressionin Indian women with breast cancer

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Abstract

Background and Rationale: Metastatic tumor progression depends on stress-associated factors triggered by psychosocial factors such as distressed body image and depression in patients with breast cancer. Prevalence of psychosocial stress across treatment paradigms and disease stage, warrants studies to understand associated neuroendocrine alterations in the progression of the disease.
Methods: Indian women with breast cancer were recruited for the study (n=190), and their psychosocial and functional wellbeing was assessed using psychometry tools such as Body Image scale, Montgomery-Åsberg Depression Rating Scale (MADRS), and Social and Occupational Functioning Assessment Scale (SOFAS). The staging of the disease was categorised using TNM classification. Serumsamples were collected for measuring stress hormone (Cortisol), markers of liver metastasis (ALT, AST) and bone metastasis (ALP). Plasma samples were collected for measuring norepinephrine.
Results: Serum metastatic markers such as ALT, AST and ALP were significantly higher in patients experiencing moderate and high distressed-body image as compared to patients with low distressed-body image. Similarly, the norepinephrine and cortisol levels were significantly elevated in patients showing high distressed-body image as compared to patients with low distressed-body image. Interestingly, the distressed-body image was significantly lower in stage 3 and 4 breast cancer patients as compared to stage 1 patients. The depression and distressed-body image were positively correlated, whereas SOFAS were negatively correlated.
Conclusion: Taken together, the role of psychosocial stress is crucial to understanding cancer metastasis and patient care.
Ethics Statement: All studies were conducted with the approval of Institutional Ethics Committee, and volunteers were recruited with informed consent.
Funding: This research is funded by Department of Science and Technology, India-Inspire Scheme (DST/IFA-15/LSBM-154; Principal Investigator: Dr. Hannah P. Priyanka).

CB1 receptor in the catecholaminergic neurons: A “brake” for exaggerated stress response

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Abstract

A stressful situation triggers a cascade of stress responses that activate the sympathoadrenomedullary system and catecholaminergic neurons in the central nervous system. Stress exposure leads to changes in several neurobehavioral processes such as depression, anxiety, memory, pain sensitivity, and addiction. Catecholamine synthesizing neurons are mainly located in the locus ceruleus, nucleus tractus solitarius, and ventrolateral medulla region of the brain. In addition, catecholamine synthesizing cells can be found in sympathetic post-ganglionic neurons and the adrenal medulla. The endocannabinoid system (eCB) consists of cannabinoid receptor type 1 (CB1) and type 2 (CB2), and two main endogenous ligands anandamide and 2-arachidonyl glycerol (2-AG). The CB1 receptor is widely expressed in the nervous system and coupled to $G_{i/o}$ proteins. The CB1 receptor is primarily localized to axon terminals therefore deletion of these receptors promotes the release of neurotransmitter release into the synapses. The genetic deletion of the CB1 receptor by using the Cre-LoxP system specifically from catecholaminergic neurons provides valuable information about the role of the CB1 receptor in regulating basal and stress-induced neurobehavioral and neuroendocrine changes. Our studies suggest that the genetic deletion of CB1 receptor from catecholaminergic neurons renders mice sensitive to the physiological stress-induced rise in corticosterone levels however psychological stress does not yield an appreciable increase in corticosterone level. Catecholaminergic neuron-specific deletion of CB1 receptor leads to increased anxiety, and depression-like behavior as confirmed by an open field, light-dark, elevated plus maze, and forced swim test. In summary, the CB1 receptor in catecholaminergic neurons protects from stress-induced neurobehavioral disorder and provides resilience to stress.

Keywords: CB1 receptor, Stress, catecholaminergic neurons, anxiety, depression,

Funding: We kindly acknowledge the support from DST SERB (CRG/2021/01717) and DBT-RLF

Monoaminergic and neuropeptide interaction in mammalian brain cerebral cortex duringimmobilization stress: Systematic literature analysis.

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Abstract

Immobilization stress is one of the most widely used methods to induce physiological responses to stress where the source of stress is not physical pain but psychological in nature.
Alterations in brain monoamines levels as well as monoaminergic and neuropeptide metabolic dysfunction is associated with various neurodegenerative conditions, therefore the present study was carried out to elucidate the association between chronic immobilization stress and bioaminergic metabolic dysfunction, utilisng bioinformatics tools.
Microarray dataset (GSE2870) of gene expression profiles in the Cerebral cortex of chronic immobilization stress (CIS) (3 hours per day for 14 days) induced rats (n=15) as well as control rats (n=15) was obtained from NCBI-GEO database. Bioconductor package was utilised to find DifferentiallyExpressed Genes (DEGs) (adjusted p-value < 0.05, $\log_2$FC > 0.4) using R language.
Certain genes (10 nos) and biomolecules (16 nos) associated with immobilization stress (IS) were identified by PUBMED search. These genes and biomolecules along with DEGs (340 nos) were analysed using STRING and STITCH database to create the protein-protein interaction (PPI) and chemo-protein interaction (CPI) networks which were subsequently merged in Cytoscape software (ver. 3.8.0) wherein MCODE plugin was used to identify the sub-networks and CentiScaPe 2.2 and CytoCtrlAnalyser plugins were utilised to identify the Hub-bottleneck (HB) (32nos) and Driver (D) (64 nos) nodes respectively.
Furthermore 3 top ranked (MCODE score ≥ 4) sub-networks were identified and HB (28 nos) and D nodes among these networks were taken for enrichment analysis using ENRICHR web tool wherein the top 10 terms each (combined score value, adjusted p-value <0.05) of 5 functional annotations (Biological process, Cellular component, Molecular function, KEGG pathway and Jensen disease) were highlighted. The genes associated with these top ranked terms were further analysed and certain genes relevant to our research interest were identified as potential targeted host proteinsassociated with bioamines metabolism as compensatory response to CIS-induced damage in cerebralcortex.

Population encoding of meaning in the avian auditory cortex

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Abstract

Introduction: Birds use a rich repertoire of vocalizations for communication. As a few examples, they use songs to attract mates, alarm calls to alert other birds to danger, and distance calls to contact partners when they aren't in sight. Despite the crucial importance of vocal communication to birds, little is known about how sounds are processed in the avian brain.
Previous studies [2, 3] have analyzed neural populations by looking at the activity of individual neurons one at a time. Recent advancements in computational neuroscience point towards a population doctrine, wherein information is encoded not in the activity of individual neurons, but in the joint activity of a population of neurons [1].
We hypothesize that semantic information exists at the population level in the avian auditorycortex.

Methods: We use a dataset of single neurons (n=914 single units) recorded in anesthetized zebra finches (4 males and 2 females) listening to the entire repertoire of vocalizations used by the species. The birds were recorded using an electrode array of 16 electrodes. Brain regions from which data was collected include the primary auditory cortex (L1, L2, and L3) and the secondary auditory cortex (NCM, CMM, and CML).
In our analysis pipeline, the discrete spike-train data is first converted to continuous firing- rates by convolving with a boxcar window. Then, PCA is used to extract population activitycomponents from the firing rates. These population components are analyzed for selectivity, invariance, and discrimination properties. These properties are then compared with their counterparts in single cells.

Results: Initial results from cell-level analyses indicate the presence of semantic cells. Semantic cellsare those cells that are either selective or invariant to a bird-call type; or whose activity can be decoded to infer the type of bird call used as the stimulus. We find that about half of all recorded cells contain at least some type of semantic information. Similarly, initial results from population-level analyses indicate the presence of semantic components.

Discussion: Our study investigates auditory processing in birds. To our knowledge, this is the first use ofpopulation analyses to study the avian brain. Initial results suggest that population activity does indeed contain semantic information. Further analyses will compare this population- level information content to that at the single neuron level.

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Single-dimensional multi-alternative shoal choice decoy space map of zebrafish (Danio rerio)

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Abstract

Normative principles of economic rationality assume that a rational individual makes consistent choices that maximize utility. The principle of independence of irrelevant alternatives (IIA) proposes the invariance of preference order between two options, regardless of the inclusion of other alternatives, or decoys, in the choice set. Organisms ranging from slime molds to human beings are reported to have violated IIA in various tasks, mostly with respect to combinations of two or more choice attributes. Here we investigate the decoy effect in zebrafish across a single dimension of shoal size, exploring decoy space using various combinations of dichotomous and trichotomous shoal size choices. A single focal fish freely moved in an arena with only visual information from shoaling conspecifics placed in display tanks surrounding the arena, with the randomized placement of various fish shoal sizes in the display tanks. The shoal choice preference was inferred from time spent in the respective sectors facing the display tanks, using the focal fish's trajectory data. The study is a novel attempt to model the multi-alternative decision-making space along a single attribute dimension in any non-human animal system.

Keywords: Rationality, Decision-making, Independence of Irrelevant Alternatives

Metabolic and behavioral assessment of moderate blunt TBI at sub-acute time point.

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Abstract

Traumatic brain injury (TBI) is one of the leading reasons of accidental death and disability worldwide. For the young population, increased use of motorized vehicle, and popularity of contact sports are common causes of tbi while fall is most common reason of tbi for elderly population. It induces hypo or hyper metabolic responses, neurodegeneration, altered cerebral blood flow, membrane permeability, altered energy metabolism and other responses. TBI also affects the memory, motor coordination and cognitive behavior. The present study demonstrates the effect of TBI on animal behavior and metabolic harmony at sub-acute time point. Here, 15 rats were divided into three groups: control, day3 and day7 post injury (PI) and, then, they were subjected to moderate blunt TBI. After 3rd and 7th day of injury, hippocampus and frontal cortex were collected and stored at – 80^0C. For NMR metabolomics, metabolites were extracted using acetonitrile: water (1:1) and then lyophilized. For NMR spectra acquisition lyophilized sample were re-suspended into 600µl D2O+0.5mM TSP mixture. NMR spectra were acquired using the water suppression NOESYPR1d pulse program. Each spectrum was processed manually and thenstatistical analysis was done. Novel Object Recognition Test (NORT) and Open field test (OFT) were done to assess the behavioral change due to TBI at 7 day post injury. Statistical analysis showed a clear difference between injury and control rats. We found a significant change in the level of energy metabolites, membrane metabolites and neurotransmitter. Behavioral changes were also observed. This study gives an overview of metabolic changes induced by blunt TBI and its behavioral outcome. This may help in the management and mitigation of TBI patients.

The effect and mechanism of CXCL10 modulation of neuroinflammation and its consequences on synapticplasticity and cognition

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Abstract

Chemokines are 8 to 14 kda small secreted proteins which chemo attract and activate immune and non- immune cells both in vivo and in vitro. Chemokine receptors belong to GPCR family, and multiple line of emerging evidence suggests that several chemokines are elevated in brain of neurodegenerative disorders. We also confirmed significantly increased CXCL10 expression in old mice (18 month) as compared to adult mice (2 month old). This lead to hypothesize that CXCL10 being a component of SASPs may aggravate/perpetuate the brain ageing process and finally neurodegenerative diseases. To test this hypothesis, we treated the primary cortical neuron (DIV-7-9) and found increased expression of senescent protein P16 and REST/NRSF with CXCL10 treatment. Using genetic autophagy biosensor mRFP-GFP-LC3, we also observed that CXCL10 decreased the autophagic flux in primary cortical neurons. Further, we show that CXCL10 also increased the lipid droplets and β-gal staining in primary microglial cells. So, overall our observation supports the hypothesis that CXCL10, an agonist of CXCR3 facilitate the brain ageing and could be targeted for the management of ageing associated CNS disorders.

Achievement motivation during adolescence:a case study on siddi children

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Abstract

Background: Achievement Motivation is the energizing behaviour in pursuit of a goal and it essential for all deliberative behaviours which involve an individual's striving to accomplish something. Human adolescence is the developmental phase where there is an increased reward-seeking, sensation seeking and heightened risk taking. Achievement motivation is crucial at this phase.
Siddi are Indians with African origin and features. They live in Gujarat, Andhra Pradesh, Maharastra, Goa and Karnataka and often employed by land lords as daily wage labourers forhard manual labour. Siddi adolescents who go to school are often perceived as showing low motivation, lack of determination and perseverance, under-performing in academics, negativeself-esteem etc. They also get discriminated based on their academic performance, skincolour and odour.

Purpose: In humans, adolescence, an age period of 12-18 years is the developmental phase where there are widespread neurobiological changes such as shifts in brain grey and white matter composition, enhanced neural plasticity, modifications of neural synchrony, increased hormonal influence and alterations in neurochemical circuitries. It is a period marked by changes in motivational and cognitive brain systems. Social discrimination is a well- established environmental risk factor for mental health disorders, including depression, anxiety, and post-traumatic stress disorder. Prolonged experience of social discrimination has negative ramifications for neuro-behavioural development that includes a sense of self and social identity with internalization of stereotypes. It may manifest itself in aggression, low motivation, lack of interest etc. Thus, the present study examined the differences in achievement motivation of Siddi and non-Siddi adolescents. It also examined the differences in the perceived social discrimination between the experimental subjects and age- and sex-matched controls.

Methods: Data was collected vide questionnaire. The subjects were administered the Deo-Mohan Achievement Motivation (n-Ach) Scale and Everyday Discrimination Scale by Williams. One-way ANOVA followed by appropriate post tests, T test and Pearson's correlation were run for the scores obtained using IBM SPSS Statistics 28.0.1. The study was carried out after due ethical clearance from the Institutional Human Ethical Committee.

Results: The findings revealed that there are significant differences in achievement motivation scores between the Siddi and non-Siddi adolescents. The achievement motivation scores among Siddi adolescents were significantly lower as compared to age- and sex-matched non-Siddi adolescents. Overall, females had higher achievement motivation scores than their males. Siddi adolescents also experienced more social discrimination as compared to non-Siddis. However,

results demonstrate no co-relation between perceived social discrimination scores and achievement motivation scores.

Conclusion: The results indicate that there is motivational deficit in Siddi adolescents, and they also experience a greater discrimination as compared to non-Siddi adolescents. This provides cause to implement changes in pedagogy and life-affirming interventions particularly in educational institutions with Siddi adolescents.

Key words: Achievement motivation, adolescence, discrimination index.

Toxicological effects on serotonergic system and its neuro-behaviouralchanges on chronic triclosan exposure in adult zebrafish

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Abstract

Background: Triclosan (TCS) is an antibacterial agent widely used in consumer products such as personal care products, household items etc. Studies have shown that TCS is an endocrine disrupting chemical and its increased use on a regular basis has led to an impact on the central nervous system causing changes in neuronal cell activity, resulting in visual loss and behavioural abnormalities.
Aim: The serotonergic system governs a variety of physiological processes and behaviours. The aim of this research work is to examine the toxicological effects due to chronic TCS exposure on the serotonergic system by assessing the neurobehavioral parameters and the cognitive functions thereby analysing its impact on the serotonergic system and the HPA axis. **Methods**: Wild type zebrafish were divided into five groups- control, solvent control (0.01% ethanol), $1/100^{th}$ of LC50 concentration, $1/1000^{th}$ of LC50 concentration and $1/10000^{th}$ of LC50 concentration of TCS. The exposure was renewed every 24 hours for a period of 30 days.
Neurobehavioral tests and quantification of serotonin, cortisol and acetylcholinesterase (AChE) activity were done.
Results and Conclusion: This study showed that chronic exposure to TCS decreased locomotive function, AChE activity and cortisol while it increased levels of serotonin and anxiety in zebrafish. Impaired memory and learning function were also observed in the exposed zebrafish. The lower concentrations of TCS exposure showed greater effects on femalezebrafish. On the other hand, males showed greater effects when exposed to higher concentrations of TCS. Overall, the sexually dimorphic effect of TCS on the serotonergic system and neurobehavior was observed.

Keywords: Triclosan, Neurobehavior, Serotonin, Endocrine Disrupting Chemical, HPA Axis

Apelin-13 alleviates post-stroke depression via regulating BDNF mediated phosphorylation of forkhead box O 3A protein in rat model of ischemic stroke

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Abstract

Background and Aim: Post-stroke depression (PSD) is a significant complication of stroke patients resulting in greater disability and mortality. It has been recognized by the clinicians many years ago, however lack of systematic clinical studies are the main limitation to develop specific therapeutic modalities. PSD includes psychiatric disorders such as imbalance between depression and anxiety; apathy, cognitive disorder, mania, psychosis, pathological affective display, catastrophic reactions, fatigue, and anosognosia. Earlier reports suggest thatthe cumulative percentage of patients developing depression within first five years of stroke ranges from 39%-52% and there is an association of low-level serum brain derived neurotrophic factor (BDNF) within hours of stroke that may increase the susceptibility to develop PSD. Currently, treatment of PSD utilizes conventional drugs that are used to treat non stroke related mood disorders. However, substantial success rate of these drugs has led researchers to investigate novel therapeutic strategies that can specifically treat PSD. Apelin-13 is an adipocytokine that has been reported to exhibit beneficial effects in stroke as well as depression. Therefore, the present study aims to explore the role of Apelin-13 in alleviating PSD via regulation of BDNF mediated phosphorylation of forkhead box O 3A protein (FOXO3A) in rodent model of ischemic stroke.

Methods: Apelin-13 in an optimized dose and time was administered to male SD rats post transient middle cerebral artery occlusion (tMCAo) and acute depression induction. Rats were evaluated for neurodeficit score and motor coordination at 24 h of reperfusion. Brains were harvested for infarct size estimation, biochemical assays, comparative histology as well as molecular studies.

Results: Apelin-13 administration in PSD rats rendered neuroprotection and alleviated depressive like behavior as evident by the reduction in infarct size, neurodeficit score, improved motor co-ordination and behavioral co-ordination. Normalization of biochemical parameters were achieved in Apelin-13 treated group. Reduction of FOXO3A phosphorylation with relation to BDNF expression was evident by relevant protein expressions.

Conclusion: This study provides a preliminary evidence of Apelin-13 therapy in ameliorating PSD which can further provide a promising rationale to explore novel mechanism as well as specific treatment approach of PSD.

In silico analysis of two novel variants of the voltage-gated sodium channel encodinggene SCN1A involved in epilepsy

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Abstract

Background: Epilepsy is a general term for a spectrum of neurological disorders characterised by spontaneous and recurrent seizures resulting from neuronal misfiring. Majority of genes linked to genetic epilepsy disorders are voltage-gated ion channels. Pathogenic variations in these genes bring about structural and functional alterations in the polypeptide domains of the ion channels, significantly impairing the channel kinetics, thereby leading to neuronal hyperexcitability. One such gene with over 1200 documented pathogenic mutations is SCN1A,which encodes Nav1.1, a subunit of the voltage-gated sodium channel family. The type and severity of epileptic syndrome depends largely on the location of these pathogenic variants. Understanding the association between the nature of the mutation and the resulting functionalalteration is crucial given the genetic heterogeneity in these epileptic disorders. We report 2 novel missense variants of the gene SCN1A - Ile1214Lys and Glu1032Lys paired with in silico analysis of their structure to understand and predict the possible pathomechanism.

Methods: The SCN1A gene sequence was obtained from the UniProt database. Several in silicotools were employed to study the sequence alignments, structural altercations and consequences of these missense mutations.

Result: The missense variant NM_001165963.4(SCN1A):c.3094G>A (p.Glu1032Lys) is novel (not in any individuals) in 1kG All as well as in gnomAD. There is a small physicochemical difference between glutamic acid and lysine, which is not likely to impact secondary protein structure as these residues share similar properties. The gene SCN1A has a low rate of benign missense variation as indicated by a high missense variants Z-Score of 5.23. The gene SCN1A contains 542 pathogenic missense variants, indicating that missense variantsare a common mechanism of disease in this gene. For these reasons, this variant has been classified as Uncertain Significance.

The missense variant NM_001165963.4(SCN1A):c.680T>C (p.Ile227Thr) causes the same amino acid change as a previously established pathogenic variant. The p.Ile227Thr variant is novel (not in any individuals) in 1kG All as well as in gnomAD. There is a moderate physicochemical difference between isoleucine and threonine. The gene SCN1A has a low rateof benign missense variation as indicated by a high missense variants Z-Score of 5.23. The gene SCN1A contains 656 pathogenic missense variants, indicating that missense variants are a common mechanism of disease in this gene. 12 variants within 6 amino acid positions of the variant I227T have been shown to be pathogenic, while none have been shown to be benign. This variant is predicted to be damaging by both SIFT and PolyPhen2. The isoleucine residueat codon 227 of SCN1A is conserved in all mammalian species. The nucleotide c.680 in SCN1A is predicted conserved by GERP++ and PhyloP across 100 vertebrates. For these reasons, thisvariant has been classified as Pathogenic.

Conclusion: The voltage-gated sodium channel subunit $Na_V1.1$ is highly conserved across species at

the residues 1214 and 1032. Furthermore, the variant I227T was found to be pathogenic whereas E1032K was found to be of uncertain significance.

Ethics: Approved by NIMHANS Institutional Ethics Committee, Institutional Committee for Stemcell Research.

Conflict of interest: None

Poor regulation of mitochondrial dynamics exacerbates stroke outcome in rodent model of chronic kidney disease-stroke complex

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Abstract

Background and Aim- Stroke is cerebrovascular disease which is a major leading cause of death and disability worldwide. Following stroke, mitochondria becomes vulnerable due to its direct involvement in adenosine tri-phosphate (ATP) generation. Ischemia can also lead to impairment of mitochondrial dynamics, and biogenesis leading to poor mitochondrial health. In clinical setting, different comorbid factors such as persistent chronic kidney disease (CKD) has reported to worsen stroke outcome. To date, cerebro-renal interaction has been reported as important factor to exacerbate CKD-stroke outcome. However, none of them could decipher the mechanism associated with exacerbated stroke outcome. Hence, the present study aims to investigate the dysregulation of mitochondrial dynamics in aggravating stroke outcomein rodent models of CKD-stroke complex.

Methodology- Male Sprague Dawley rats were fed adenine rich diet, followed by middle cerebral artery occlusion (MCAo) to induce CKD-stroke complex. Rats were evaluated for neurodeficit and motor in -coordination and were sacrificed at 24 h following MCAo. Brains were harvested for infarct size estimation, mitochondrial, biochemical and molecular studies

Result- CKD-stroke complex animals showed enhanced neurodeficit as well as motor co-ordination impairment than CKD or stroke animals. Infarct size, oxidative stress, mitochondrial impairment, as well as apoptosis were increased as evident by molecular studies.

Conclusion- This study reports a preliminary evidence of involvement of mitochondrial impairment to exacerbate stroke outcomes in CKD. Therefore, the findings can pave a way to explore newer therapeutic modalities to reduce stroke severity in patients predisposed with CKD.

Stroke in pregnancy: An exploration towards altered epigenetic regulation in offspring

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Abstract

Introduction: Stroke occurs due to sudden reduction of blood flow in brain due to blockage or rupture of a vessel carrying blood to brain. It results in consequent decrease of oxygen, and nutrients to the brain tissue, therefore, cells begin to die within seconds. Loss of oxygen hampers adenosine triphosphate (ATP) production in mitochondria as well asreduction in neuronal membrane potential, resulting in anoxic depolarization, calcium and glutamate excitotoxicity, excessive reactive oxygen species (ROS) production, and cumulative alteration in the normal function of subcellular organelles leading to cell death. In pregnant women estrogen functions as a neuroprotective, however, recent clinical reports demonstrate an increased stroke occurrence with severe outcome in pregnant women in their third trimester. Various studies suggest that an increase in clotting factors may be an important risk factor to this, however, the exact mechanism of pregnancy associated stroke severity is yet to be explored. In addition, genetic and epigenetic modifications play an important role towards stroke susceptibility. Earlier studies have reported a direct co-relation with mitochondria and endoplasmic reticulum (ER) health alteration following stroke. Therefore, the current study aims to decipher the possible role of altered mitochondrial and ER dynamics towards exacerbating stroke outcome in rat model of pregnancy associated stroke as well as epigenetic modulation in the offspring.

Methodology: Focal ischemic stroke model will be induced by middle cerebral artery occlusion (MCAo) in pregnant rats. Following stroke induction, neurodeficit scoring and behavioral studies were performed. Dams and pups were sacrificed, and brain was harvested for further biochemical and molecular studies. Protein expressions related to mitochondria and ER dynamics, as well as histone modification were assessed by Western Blotting.

Result: Alteration in mitochondrial and ER dynamics were evident in relevant molecular studies. Modification of different epigenetic markers, oxidative stress levels and tissue morphology were noticed by subsequent molecular studies as well as comparative histological study.

Conclusion: This study reports preliminary evidence to decipher the mechanism how altered mitochondria and ER functionality as well as epigenetic modification can exacerbate the stroke outcome in pregnancy. This study is clinically relevant and can explore better therapeutic modality to manage the global burden of pregnancy associated stroke.

Endoplasmic Reticulum Stress exacerbates Stroke Outcome in Rodent Model of Chronic Kidney Disease

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Abstract

Background: Stroke is one of the leading causes of morbidity and mortality worldwide. The pathophysiology of stroke is multifaceted that involves various excitotoxicity and dysfunction of subcellular organelles. Once stroke occurs, individuals with persistent comorbid factors such as chronic kidney disease (CKD) has been reported to exhibit exacerbated outcome. Therefore, a co-relation between CKD and stroke can be explored. The association of stroke and endoplasmic reticulum stress (ER stress) is well reported. Excessive ER stress can result in enhanced apoptosis and subsequent poor stroke outcome. Therefore, the present study aims to decipher the role of ER stress in exacerbating stroke outcome in rat model of CKD-stroke complex.

Methodology: CKD-stroke complex has been induced by middle cerebral artery occlusion (MCAo) in male Sprague Dawley rats fed with adenine rich diet. At 24h of reperfusion, neurodeficit scoring and behavioural outcomes were assessed. Further, the animals were sacrificed, and brains were harvested to determine infarct size and perform biochemical assays, molecular studies, and histopathological studies.

Result: Increased infarct, higher neuro-deficit score, and severe motor co-ordination deficits were observed in CKD-stroke complex animals than CKD and stroke animals per se. Enhanced ER stress, oxidative stress and associated apoptosis were also observed in the CKD-stroke complex animals.

Conclusion: ER stress can attribute to an exacerbated deleterious outcome post stroke in CKD-stroke complex animals. This study will help to explore new treatment strategy in future that may alleviate stroke outcome in patients with persistent CKD.

Post-stroke inosine therapy alleviates inflammasome activation and modulates microglial polarization in rodent model of ischemic stroke

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Abstract

Introduction: Microglia are resident macrophages which are a part of innate immune system in the central nervous system (CNS). They are involved in defence mechanism and also involved in neuroinflammation. Following ischemia, microglial polarization via NLRP3 inflammasome pathway to its pro-inflammatory (M1) form is well reported. Inosine, a purine nucleoside, is a metabolite of adenosine, which has been reported as neuroprotective in stress condition as well as in stroke. It has been reported that inosine can activate purine sensitive kinase and results in enhanced axonal rewiring in ischemic condition. Therefore, the present study aims to explore the effect of inosine on inflammasome mediated microglial polarization post-stroke in a rat model of focal ischemia.

Methodology: Inosine was administered via intraperitoneal route at an optimized dose in male Sprague Dawley rats following induction of ischemic stroke via middle cerebral artery occlusion. Further, animals were assessed for neurodeficit score, motor coordination as well as behavioural impairment. At 24 h of reperfusion, animals were sacrificed, and brains were harvested to determine infarct size and neuronal survival. Further, biochemical assays and molecular studies were performed. Long-term neuroprotection was evaluated by comparative behavioural and histopathological studies at 7 days of reperfusion.

Result: Post-stroke inosine treatment was found to normalize oxidative stress, reduce the gene and protein expression of various inflammatory and cell death markers. Comparative histopathological study shows long-term neuroprotection and improved motor-behavioral co-ordination following stoke.

Conclusion: The current study reports the beneficial role of post-stroke inosine therapy in modulating microglial polarization through regulating inflammasome signaling leading to neuroprotection

HDAC6 promotes podosome-mediated migration in neurons

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Abstract

Alzheimer's disease is a progressive disease affecting memory in the aged population. Memory loss encompasses the disruption of synaptic connections and the cytoskeleton. In this study, we present anovel role for the HDAC6 ZnF UBP (Histone Deacetylase Zinc Finger Ubiquitin Binding Protein) domain in the restructuring of neuronal cytoskeletal. This has been demonstrated in actin-rich podosomes through immunofluorescence colocalization and various biochemical studies. We further studied the potential of this domain in facilitating podosome-mediated in neurons. We have established that HDAC6 ZnF UBP is able to increase the localization of proteins, involved in the actin remodelling, within the podosomes, thereby improving the migration capacity in neurons. We propose that this study could help build an efficient therapeutic strategy for the betterment of neuronal health.

Role of Statin in Regulating Endoplasmic Reticulum Stress in Stroke

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Abstract:

Introduction: Currently approved US Food and Drug Administration (FDA) treatment for stroke including tissue plasminogen activators (tPAs) and mechanical thrombectomy, have amajor drawback of narrow therapeutic window. This drawback impedes the positive outcome in the stroke patients. Drug repurposing has emerged as a novel approach widening the treatment options for stroke. A majority of the clinical reports have reported the positive outcome of long-term statin therapy in patients with history of ischemic stroke. The cholesterol-lowering drugs that inhibits the β-Hydroxy β- methylglutaryl CoenzymeA reductase (Statins), have shown effective results as an adjunctive therapy for stroke based on its pleiotropic actions. To explore further its pleiotropic properties, a study was designed to understand how statin can regulate thestroke induced endoplasmic reticulum (ER) stress. During stroke, hindered blood flowcauses oxygen and glucose deprivation, which leads to glutamate excitotoxicity. This excitotoxicity causes up-regulated calcium release. This enhanced intracellular calcium level triggers the misfolding of proteins (ER stress), although it is counteractedby the unfolded protein response (UPR) but a prolonged activation of this response leads to apoptotic and autophagic pathway within the cell. Autophagy allows the cellsto annul the effect of stress while apoptosis is a pre-defined cell death mechanism. Thus, this study is designed to explore how statin modulates the autophagic pathwayin post-stroke condition and help in achieving a better outcome in stroke Sprague Dawley (SD) male rats.

Methodology: The Middle cerebral artery occlusion (MCAO) model was induced in Sprague Dawleymale rats. Simvastatin was administered at optimized time points, both prophylactic and post-stroke induction. Neurological changes were analysed by staining techniques and behavioural experiments. Alteration in the post-stroke oxidative stressand following the treatment, was assessed using biochemical assays. Changes in theproteins expression were evaluated by western blotting and immunohistochemistry and mRNA expression was evaluated by RT-PCR.

Result: The infract region was significantly reduced after the administration of Simvastatin while the neuronal viability was also seen to be improved by the staining techniques. Improved neurological function was observed after the treatment, based on motor function evaluation and neurodeficit scoring. Increased level of glutathione and catalase whereas decreased level of malondialdehyde and nitrite by biochemical assay, concluded that Simvastatin ameliorates the post-stroke oxidative stress. ER stress markers' protein expression was observed to be significantly altered by the treatment. Expression of the autophagy proteins were significantly reduced after the administration of simvastatin.

Conclusion: Simvastatin showed effective improvement in the outcome in stroke induced SD rats. It was also observed to significantly modulate the autophagic pathway that is involved during post-stroke ER stress. These results open up the scope for exploration of statins to be established as an effective post-stroke adjunctive treatment strategy. Further exploration into the role of statins in regulating the cellular dynamics shall assist in developing a proper treatment strategy to curb the post-stroke effects.

Neuroprotective potential of Tinospora cordifolia in attenuating hippocampal CA3 neuronal damage induced by prenatal stress and maternal separation

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Abstract

Background: Prenatal stress has been shown to have detrimental effects on cognition, behavior, and psychosocial characteristics. Tinospora cordifolia (TC) is believed to possess antistress and learning and memory enhancing properties. However, there is no experimental data in the literature to suggest its efficacy against prenatal vibratory stress and maternal separation. Therefore, we aimed to evaluate the neuroprotective potential of TC in rat neonates subjected to prenatal vibratory stress and maternal separation.

Materials and Methods: Pregnant Wistar rats were divided into normal control (NC_M), vehicle control (VC_M), 3 hour / day vibratory stress (VS_M) groups and TC treated group which received 6 mg/kg body weight of TC extract orally before subjecting them to vibratory stress (VS+TC_M). The neonates born to mothers of control groups were allocated into NC_N and VC_N groups. The neonates born to VS_M group were further categorised into prenatally stressed control (VS_N control) and prenatally stressed and postnatal maternal separation (VS+MS_N) group and prenatally stressed with postnatal TC treated group (VS+PNTC_N). Neonates born to VS+TC_M were divided into VS+TC_N control, maternal separation (VS+TC+MS_N) and maternal separation followed by postnatal TC treatment (VS+TC+MS+PNTC_N) groups. After the treatment period [at postnatal day 45], animal brains were dissected and processed for Golgi cox staining to study the hippocampal CA3 neuronal arborization.

Results: Hippocampal CA3 neuronal apical dendritic branching points were significantly ($p<0.001$) increased in 20µ to 60µ concentric zones whereas increase in basal dendritic branching points was observed in 20µ to 100µ concentric zones in VS+TC_M compared to VS_M group. The apical and basal dendritic intersections were significantly ($p<0.01$) increased in TC treated mothers compared to stressed mothers. Neonates of VS_N Control and VS+MS_N had lesser apical and basal dendritic branching points compared to that of normal control and prenatal and postnatal TC treated neonates. A significant ($p<0.001$) increase in number of apical dendritic intersections were observed in TC treated neonates at 60µ to 100µ concentric circles whereas basal dendritic intersections were in inner concentric circles close to the soma.

Conclusion: Treatment with TC extract attenuates hippocampal CA3 neuronal dendritic damage induced by prenatal vibratory stress and maternal separation.

Key words: Prenatal stress, herbal extract, maternal separation, hippocampus

Major visual processing centres of Hieroglyphus banian

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Abstract

Visual systems of insects have been studied in many species. They have been well studied in the order diptera (flies) and to a much lesser extent in other species. Optic lobes (OL) of diptera contain lamina, medulla, accessory medulla, lobula and lobula plate as identifiable neuropils. In orthopterans like Schistocerca gregaria, S.americana and Locusta migratoria, visual systems are well studied. Optic lobes of orthoptera contain identifiable neuropils, lamina, medulla, accessory medulla and lobula complex, but no identified lobula plate. Here I present characterisation of the major visual processing centres of the grasshopper Hieroglyphus banian (HB). Hieroglyphus banian is a grasshopper species endemic to south east asia, also called rice grasshopper. I identify all the neuropils of the optic lobe and subcompartments of the lobula using immunohistochemistry, tract tracing and intracellular fills. I also present the visual processing centres in the central brain anterior optic tubercle (AOTu), posterior optic tubercle (POTu) and lateral accessory lobe (LAL) and the tracts linking the compartments of the OL to them. Simultaneous electroretinogram (ERG) and local field potential (LFP) recordings from these visual processing centres of the brain revealed spectral sensitivity and their gross responseproperties.

Evaluation of Cortical Vision with Next Generation Optogenetic Tools

Abstract

Vision is a dominant sensory modality on which humans depend for providing information about environment. Loss in vision has a greater impact on daily life such as not being able to recognize faces, read and find objects. Patients suffering from inherited and age-related macular degeneration undergo loss of light sensitive retinal photoreceptors such as rods and cones. While the photoreceptor cells die the second and third order downstream retinal neurons remain intact and are able to send information to the brain. These neurons have become potential targets for optogenetic therapy to turn them into functional photoreceptors and restore vision. Recent studies using ion channel and G protein coupled receptors as optogenetic effectors have shown restored light responses in vitro from retinal ganglion cells. Further these studies resort to local field potential (LFP) measurements or optical imaging from visual cortex to assess recovery of vision beyond the retina. Since the neural responses in primary visual cortex(V1) correlates to visual perception it is important to decipher how the neurons in V1 interpret the signals carried by optogenetically restored visual neurons.

For this blind mice (C3H/HeOuJ) were injected with a vector carrying the transgene **e**Opto-mGluR6-IRES-TurboFP635 targeted to retinal ON-bipolar cells. To assess whether the injected construct mediated retinal photo responses were transmitted to the visual cortex, visual evoked potentials were recorded from all layers of the V1 using LED stimulus. Responses were recorded from 40-50 stimuli. The injected construct was able to reliably and reproducibly mediate responses to light pulses similar to normal seeing mice. The maximal responses were observed from the middle layers of the cortex. These findings imply that the treated retina is able to regain its natural signaling pattern and transmit signals to downstream visual centers.

The role of p21 activated kinase in the repair of oligomeric amyloid-β induced plasma membrane damage and its implication in pathology spreading in Alzheimer's disease

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Abstract

Progressive development of pathology is the major characteristic feature of neurodegenerative diseases. Alzheimer disease (AD) is the most prevalent among them. The oligomers of amyloid-β (oAβ) are attracting the greatest attention as they regarded as potentially neurotoxic species and their progressive penetration through the anatomically connected brain areas may explain the possibility of direct neuron-to-neuron spreading in AD. However, the mechanism of direct transfer is not revealed yet. Exosomes and the recently revealed tunneling nanotubes (TNTs), the actin membrane conduit between cells were proposed as a long-range intercellular transfer mechanism. We have shown in differentiated and partially differentiated SH-SY5Y cells shows, the consequences of oAβ induced membrane damage and its repair via lysosomal exocytosis instigatethe formation of TNTs and cell-to-cell transfer of oAβ. Plasma membrane (PM) damage was followed by propidium iodide influx in the absence of extracellular Ca^{2+} using flow cytometry and microscopy. Fluorescence imaging was performed to observe increased localizations of LAMP 1 in the PM upon oAβ treatments. oAβ induced PM repair process causes activation of Phospho- p21 activated kinase 1 (phospho-PAK1), which mediates long-stretched membrane F-actin conduits between cells. IPA-3, a highly cell-permeable, and a selective non-ATP competitive inhibitor of PAK1. IPA-3 inhibits PAK1 dependent internalization of oAβ, PM repair and formation of TNTs between cells. Furthermore, we have observed that repair of oAβ induced PM damage occurs via Rab3 dependent vesicle fusion/exocytosis. Several studies have shown Rab3 and PAK1 involve in AD. The study could reveal the role of Rab3 and PAK1 in oAβ induced membrane damage and repair, to intercellular propagation of pathology in AD.

Evaluation of lipid composition at various stages of neurodevelopment

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Abstract

The principle structural component in the human brain is lipid. However, very limited information is available regarding the lipid composition at various stages of neurodevelopment. Since developmental human brain is inaccessible for analysis, we have used human pluripotent stem cells to derive specific neurodevelopmental stages using directed differentiation protocols. In this study, we conducted a comprehensive mass spectrometry based untargeted lipidomic analysis at different neurodevelopmental stages from pluripotent stem cells to mature neurons. Our preliminary results show that, at the pluripotent stage, lipid classes such as MG, DG, TG, PG, PC, PS, PE, PI are enriched. However, upon development into multipotent neural stem cell stage, lipid species such as DG and PE were significantly altered. Further studies are underway to identify lipid composition in human neurons. Also, studies are underway to uncover the influence of external supplements during the early stages of neurodevelopment. In conclusion, the lipidomic analysis will allow us to improve our understanding of the composition of specific lipid species during stages of neurodevelopment.

Identification of PPAR modulators as therapeutic targets in Alzheimer's Disease

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Abstract

Neurodegenerative diseases (NDDs) affect millions of people worldwide. Alzheimer's Disease(AD) is the most common form of dementia. Presently, scarce treatment options are available for AD. Peroxisome Proliferator Activated Receptors (PPARs) are ligand activated transcription factors which bind to enhancers of their target genes to regulate their expression. Fatty acids and eicosanoids can activate PPARs, which further, triggers the lipid and fat metabolism in the liver. Imbalance in PPAR activation disrupts numerous pathways and consequently leads to disorders like AD and Metabolic Syndrome. The beneficial effects PPAR activation are via multiple pathways and it was hypothesized that selective PPAR modulators may help in alleviating neurodegenerative symptoms. The present study was designed for virtually screening the binding affinities of 5,000 synthetic ligands of PPARs and manually curated library of 300 natural compounds against PPARs using molecular docking and ADMET analysis. Top 10 natural and synthetic compounds with most stable binding affinities were selected for ADMET analysis and their interactions with protein structure were investigated. The results showed that all selected compounds bind PPARs in the cavity of the binding pocket with strong hydrogen and hydrophobic bonds. The ADMET results indicate good drug-like properties in selected lead compounds. Selected natural compounds were deemed to be better therapeutic options than synthetic ligands owing to their blood-brain- barrier permeability, bioavailability and potentially minimal side effects. The selected compounds may be investigated further in in vitro and in vivo experiments as potential therapeutic targets for prevention and treatment of AD.

Identification of non-steroidal LXR modulators as a key regulator of cholesterol homeostasis against Alzheimer's diseases

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Abstract

Liver X Receptors (LXRs) are members of the nuclear receptor superfamily that regulate cholesterol metabolism. LXRs have been suggested as promising targets against Alzheimer's disease (AD). The present study was aimed to identify novel non-steroidal molecules that maypotentially modulate LXR activity. The structure-based virtual screening (SBVS) was used to search for suitable compounds from the Asinex library. The top hits were selected and filtered based on their binding affinity for LXR α and β isoforms. Based on molecular docking and scoring results, 24 compounds were selected that had binding energy in the range of − 13.9 to
− 12 for LXRα and − 12.5 to − 11 for LXRβ, which were higher than the reference ligands (GW3965 and TO901317). Further, the five hits referred to as model 29, 64, 202, 250, 313 were selected by virtue of their binding interactions with amino acid residues at the active site of LXRs. The selected hits were then subjected to absorption, distribution, metabolism, excretion, and toxicity (ADMET) analysis and blood-brain permeability prediction. It was observed that the selected hits had better pharmacokinetic properties with no toxicity and could cross blood-brain barrier. Further, the selected hits were analysed for dynamic evolution of the system with LXRs by molecular dynamics (MD) simulation at 100 ns using GROMACS. The MD simulation results validated that selected hit possess a remarkable amount of flexibility, stability, compactness, binding energy and exhibited limited conformational modification. The root mean square deviation (RMSD) values of the top-scoring hits complexed with LXRα and LXRβ were 0.05–0.6 nm and 0.05–0.45 nm respectively, which is greater than the protein itself. Altogether the study identified potential non-steroidal LXR modulators that appear to be effective against AD involving perturbed cholesterol and lipid homeostasis.

Advanced Neuroimaging and Event Based Modeling of Brain Structures and Microstructures: Development of Imaging based artificial intelligence platform predictive of Cognitive status and Dementia

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Abstract

Aging is one of the major risks for dementia. Changes in brain health with aging involve a series of brain structure, vascular and functional changes over the period. The events of brain health changes during normal aging need to be precisely delineated from the alterations that identify with manifestation of mild cognitive impairment and dementia as early, intermediate and late events. We believe that when the kinetics of structural atrophy of a definitive brain feature undergo pathological changes beyond a threshold, it would result in aging cognitive impairment and dementia. Brain MRI provides a noninvasive method to sneak into brain anatomic changes. Unfortunately, we have yet not been successful in identifying a series of events determined from MRI investigations that can predict the trajectory of aging: towards normal aging or pathological aging. Here, we have employed comprehensive MRI morphometry and artificial intelligence on brain MRI measurements of small vessel disease pathologies and neuroanatomic volumes, resting state and tractography to develop an event-based model predictive of cognitive status of aging subjects.

Method: Brain segmentation was performed on 3D MPRAGE, T2-FLAIR and diffusion imaging to determine neuroanatomic-volume and White matter hyperintensity (WMH) load from an aging cohort (N=1871) from National Alzheimer's Coordinating Center with total of 2646 longitudinal- MRI scans. The Supervised Machine Learning model was trained to optimize a series of MRI events that can predict cognitive status of subjects with high accuracy. An ensemble of neuroanatomic volume was generated using ML modeling to pick up the most optimal combination of neuroanatomic and vascular change predictive of subjects as cognitively normal, mild cognitive impaired or dementia.

Result: A series of Neuroanatomic changes such as progressive loss in gray matter volume, reduction in cortical thickness of parahippocampal gyrus, reduction in hippocampal volume together with accruing of periventricular and deep white matter pathologies identify with MCI and Dementia compared to cognitively normal subjects. A serial combination of 8-MRI events provided the highly precise and sensitive identification of subjects as Alzheimer's disease, cognitively impaired and cognitively normal subjects. This study provides MRI identified optimal number of brain structure and microstructure changes associated with pathological aging.

Conclusion: Here we show that a combination of artificial intelligence and advanced neuroimaging measurements provide a definitive quantitative series of events diagnostic of aging, MCI and Alzheimer's disease.

Role of bisphenol A in exaggerating the oxidative stress in the brain of obese femalerats

Anuradha Mangla, Sheikh Raisuddin

Abstract

Introduction: Bisphenol A, an endocrine disrupting chemical as well as a known obesogen. Females are more susceptible to its endocrine disrupting effects. This chemical is known for deteriorating endocrine signaling, but its role in declining neurological functioning has not been widely explored. Oxidative stress contributes as a major factor that affects almost all systemic functioning including neurological and metabolic functions. So, in this study, we have put an effort to explore the effect of Bisphenol A on the neurological and metabolic functioning of obese female rats with oxidative stress.

Aim and Objectives: To study the effect of Bisphenol A in exaggerating the oxidative stress in the brain of obese female rats.

Material and methods: Female Wistar rats were procured from the institution Central AnimalHouse Facility. A total of four groups were taken, Group 1 (control), Group2 (High-fat diet (HFD)), Group 3 (HFD+BPA) and Group 4 (BPA). Initially, a high-fat diet (60%) was given to the group 2 and group 3 rats for 2 months and then after the confirmation of obesity made through physiological parameters and glucose tolerance test. Followed this BPA was administered via the oral route(drinking water (10ppm)) for the next 4 months in Group 3 & 4. After almost 6 months, rats were sacrificed and brains were dissected to observe morphological changes through histological techniques and to perform biochemical tests to study parameters related to oxidative stress.

Results: Lipid peroxidation level was significantly found to be higher in HFD and BPA group as compared to the HFD or BPA group. Also, the level of reduced glutathione (GSH), an antioxidant has been downregulated in the experimental groups as compared to the control group. Experimental groups have shown significant downregulation in the enzymatic activities of Glutathione S Transferase & Catalase. BPA also led to the neuronal death and apoptosis in the brain tissue of treated groups. Structural changes and deposition of lipid droplets in the treated group were established by Hematoxylin & eosin and Oil red O staining.

Conclusion: It is concluded that Bisphenol A besides having endocrine disrupting effectshas the potential to induce oxidative stress and thus can further complicate the functioning at the cellular level in obeserats and can lead to the development of neurological diseases.

Role of actin signalling pathways in α-synuclein induced tunneling nanotubes mediatedtransformation of neuroglial cells into cancer stem-like cells

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Abstract

Parkinson's disease (PD) pathology develops with the toxic burden of α-synuclein (α-SYN) aggregates in the brain. A recent study has shown that in addition to the conventional cellular clearance mechanisms, microglia facilitates clearance of α-SYN protofibrils by establishing cell-to-cell network of open-ended membrane actin channels or tunneling nanotubes (TNTs) in response to load of toxic burdens.

We observe that upon exposure to α-SYN protofibrils, cancerous glial cells (human glioblastoma-astrocytoma cell line, U-87 MG) transform to senescent like stressed cells and transfer toxic organelles (lysosomes and mitochondria) through transiently formed membrane nanotubes or tunneling nanotubes (TNTs) and acquire stem-like properties that aid in survival and proliferation. Probably, inherent properties of cancer cells to delay apoptosis resulted in cells to adapt to alternate TNT-mediated rescue mechanism to rid of toxic burden resulting in enhanced proliferation and ultimately leading to formation of a CSCs population. CSCs have great importance and are consideredas promising therapeutic target that can eliminate drug resistance population.

TNTs are structurally open-ended membrane actin conduits. Thereby, it is obvious that modulation of membrane and cytoskeleton will play a major role in their biogenesis. Studies have shown that proteotoxicity, oxidative stress and downstream signalling pathways of RhoGTPases play significant role in the biogenesis of TNTs. However, exact mechanism of TNT biogenesis is not known. We screen inhibitors in the actin signalling pathways to unfold molecular events behind the α-SYN toxicity induced actin regulatory pathways that modulate biogenesis of TNTs and consequently transformation of neuroglial cells to CSCs. The study could open up new target/s to develop potential therapeutics to overcome conventional treatment-resistant cancer cell population.

Role of genistein in cognitive impairment through SOD and CAT manifested in behavioral test of stressed mice

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Abstract

The unpredictable stress (US) condition may cause cognitive decline by lowering antioxidative defence. Genistein (GEN) is abundantly found in soya beans and soy products. It acts through estrogen receptor (ER) and performs wide range of brain functions. GEN may exert neuroprotective effect through superoxide dismutase (SOD) and catalase (CAT) and modulating behavioural changes. Hence, the present study aims to evaluate neuroprotective effect of GEN against US condition. Briefly, ten Swiss albino 25weeks male mice (30g) were placed into four groups; Group I (Control), group II (US), group III (US+Vehicle) and group IV (US+GEN). Briefly, stressors such as wet bedding, cage tilt, sleep deprivation, tail pinch, tail suspension, light/dark cycle alterations, physical restraint and food deprivation were imposed unpredictably to mice for preparing US model . Thereafter, GEN dissolved in sesame oil was dosed orally (1 mg/kg/day) and vehicle group received sesame oil only. To assess effect of GEN on anxiety, and learning and memory open field test (OFT) and novel object recognition test (NOR) were performed. Moreover, SOD and CAT levels were measured in the brain. In OFT, no significant changes were observed in the exploratory activity, and anxiety in GEN treated mice as compared to US, vehicle and control group. In NOR, control mice showed high frequency of entry towards novel object than US and US+Vehicle group, whereas entry toward novel objects was higher in GEN treated than US and US+Vehicle and closer to control group. SOD was observed to increase in US+GEN in comparison to US and US+Vehicle group, whereas its activity decreased in US, US+Vehicle and US+GEN group than control group. Further, a significant increase in CAT in US+GEN as compared to other groups were observed. Such studies suggest that GEN treatment may restored cognitive function as indicated in NOR of stressed mice through SOD and CAT.

Keywords: Genistein, OFT, NOR, Superoxide Dismutase, Catalase, Stress

Repurposed drug exerts neuroprotective effect in sub arachnoid hemorrhage via restroring mitochondrial dysfunction

Abstract

Subarachnoid hemorhhage (SAH) is a subtype of stroke characterized by pooling of blood in the subarachnoid space (SAS) existing where cerebrospinal fluid (CSF) is present between the arachnoid membrane and pia matar. Oxidative stress and neuronal apoptosis have been demonstrated to be key features in early brain injury (EBI) after subarachnoid hemorrhage (SAH).Pathophysiologic mechanisms of EBI include blood-brain barrier breakdown, brain tissue hypoxia, neuroinflammation, and excitotoxicity leading to brain edema and metabolic derangement. In the current study we repurposed an anticonvulsant drug for EBI following SAH. SAH was induced by endovascular puncture surgery with minor modifications in our laboratory.Male Wistar rats (220-250g), were used.The experimental animals were randomly divided into 4 groups : sham , SAH, SAH + 125mg/kg ETX and SAH + 250mg/kg ETX .Rats in the sham group underwent a similar surgical procedure except perforation in the MCA; rats in the SAH group underwent SAH without any treatment; and SAH
+ ETX group underwent treatment.Dosages were calculated on the basis of previous studies. . A panel of neurological tests, Subarachnoid hemorrhage Grade Scoring, biochemical, histological and western blotting was performed after 24 hours of surgery. Evaluation of neuronal damage was performed with the help of hematoxyline and eosine staining and western blotting. Ethosuximide showed significant improvement in neurobehavioral impairment, reduce the infract volume in Endovascular Puncture model of Subarachnoid hemorrhage and inhibit the neuronal cell damage. ETX inhibit the release of CytochromeC from mitochondria to cytosol and also down regulate the Bax expression. These studies showed that ETX has neuroprotective properties to protect the neuronal cell in Endovascular Puncture model of Subarachnoid hemorrhage.

Amelioration of cognitive deficit by atorvastatin in Aβ1-42 induced Alzheimer's disease ina rat model

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Abstract

Alzheimer's disease (AD) has been well associated with the progression of synaptic failure, neuronal cell death, and mitochondrial dysfunctions. The proposed study is aiming at repurposing a selected drug Atorvastatin (ATOR) based on the docking score. ATOR is an FDA-approved and cost-effective drug and works by reducing the amount of cholesterol madeby the liver. We have investigated the neuroprotective potency of ATOR against Amyloid beta(Aβ) dysfunction. In vivo Aβ model was established by intracerebroventricular (i.c.v) administration. The rats were treated once daily with ATOR (5mg/kg;10 mg/kg, p.o) and Donepezil (0.1mg/kg, p.o) for 21 days after 7 days of i.c.v surgery. Our data also showed that ATOR significantly reduced the accumulation of intracellular ROS in a dose-dependentmanner against DCFH2-DA (2′,7′-dichlorofluorescein diacetate) probes when compared to theAβ group. SOD and LPO activity were significantly reduced in the Aβ group when comparedto the control group and also showed significantly increased levels in ATOR groups with different concentrations. ATOR prevented the Aβ-induced high expression of apoptotic factorsBax but the expression of Bcl 2 was restored, which confirms the anti-apoptotic property against Aβ. ATOR can also increase the nuclear translocation of Nrf2 expression against Aβ and control groups. These results suggest that ATOR conspicuously inhibited the Aβ damage to the hippocampus. Activation of the Nrf2 signaling pathway will be a promising factor withtranslational value in AD. The potential molecular mechanism mediated by ATOR has been the focus of extensive research in the future.

Keywords: Alzheimer's disease (AD), Atorvastatin, Mitochondrial dysfunctions, Neuroprotection and Signaling pathway

Brain tumor segmentation using multimodal neuroimaging techniques: a deep convolutional neural network approach

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Abstract

Introduction: Glioma is the most prevalent malignant primary brain tumour, and more than 50% of these tumours are grade IV glioblastomas. This calls for an early detection and segmentation to decide treatment/therapy. Various techniques for forecasting and segmenting gliomas have been developed, which have limitations such as requirement for specialised assistance, the lengthy run-time, and the selection of an appropriate feature extractor.
We propose a convolutional neural network-based method for segmenting gliomas from multimodal structural magnetic resonance data in order to get over these challenges (T1w, FLAIR and Post contrast T1w).

Methods: This study made use of the mpMRI Brain Tumour Segmentation (BRATS 2021) dataset. Three classes—Enhancing Tumour, Peritumoral Edematous Tissue, and Necrotic Tumour Core - were included in the scan annotation for each image. In order to create the tumour segmentation masks, our method was created by training deep neural networks utilising just three modalities: T1w, FLAIR, and Post contrast T1w.

Results: Using 1251 mpMRI images for training and validation, we were able to attain a mean dice score coefficient (DSC) of 0.89 in this study. We have validated the model algorithmically by separating data into training and validation sets. Additionally, we have also generated tumor masks manually for data never seen by model and had them evaluated by an expert radiologist, and compared the results to those generated by our algorithm. This yielded a mean DSC of 0.88 and a tumour core DSC of 0.92.

Discussion: We have been able to generate a CNN based model to segment gliomas from only three modalities (T1w, FLAIR, and post-contrast T1w scans) as opposed to most studies which make of four modalities (T1w, T2w, FLAIR, and post-contrast T1w scans).

Future implications: This study demonstrates that deep convolutional neural networks can accurately and quickly separate distinct subregions of a tumour, which has important therapeutic implications in brain tumour detection, prognosis, therapy, and presurgical planning.
Additionally, it can be useful in understanding how tumours affect tractography and network mapping.Utilizing these segmentation masks to account for a general shift in the brain's tissues and improve the precision in capturing functions of the brains, in turn making a better Eloquent cortex mapping.

Transient receptor potential vanilloid 2 (TRPV2) in the rat brain: role in modulation of the nigrostriatal dopaminergic pathway

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Abstract

TRPV-subfamily of cationic channels are abundantly expressed in the brain and emerged as novel regulators of neuronal function and behaviour. Among the thermosensitive TRPVs, TRPV2 is activated beyond noxious threshold temperature, expressed in the brain, but its significance in neural regulation is poorly understood. The midbrain dopamine (DA)-ergic neurons in rodents are thermosensitive and in a pilot study on rats, we observed TRPV2 neurons in the substantia nigra pars compacta (SNc). We have therefore hypothesized that TRPV2 in SNc regulate nigrostriatal DA-ergic pathway. Immunofluorescence using anti- TRPV2 specific antisera on the rat brain sections showed TRPV2-ir neurons widely distributed in the brain. We observed TRPV2-mRNA expression in midbrain tissue, and TRPV2-ir neurons in the ventral tegmental area (VTA) and SNc. While TH neurons in VTA as well as SNc co-expressed TRPV2, SNc TH neurons were more TRPV2 enriched than those in VTA. Retrograde neuronal tracer iontophoresed in the dorsal striatum accumulated in TH/TRPV2 SNc neurons. Intra-SNc TRPV2-agonist, Probenecid increased DA release in dorsal striatum and locomotor activity, whereas prior intra-dorsal striatal administration of DA-D2 receptor antagonist reduced Probenecid-induced response. In ex vivo midbrain slice superfusion, compared to control, Probenecid treatment increased TH-ir in SNc neurons. Parkinson (PD)-like condition was induced by 6-Hydroxy dopamine (6-OHDA, intra-SNc). Compared to controls, intraperitoneal (i.p.) apomorphine injection produced contralateral rotations in 6-OHDA-treated rats. Intra-SNc Probenecid prior to apomorphine injection further enhanced contralateral movements in PD-like condition. The results suggest that the widely expressed TRPV2 in brain regions regulate a range of physiological functions. TRPV2 in SNc may serve as novel regulator of nigrostriatal DAergic pathway and a potentialdrug target for Parkinson's disease.

Elucidating the anti-inflammatory role of SCFA in JEV mediated neuroinflammation in mice

Abstract

Short chain fatty acids (SCFAs), majorly, acetate, propionate and butyrate are metabolites generated by anaerobic fermentation of indigestible complex carbohydrates by the bacteria in the gastrointestinal tract, predominantly consisting the Bacteroidetes and Firmicutes phyla. Japanese encephalitis virus (JEV), a neurotropic flavivirus accounts for approximately 70,000 reported cases annually with a 30% mortality rate. The viral infection of the brain causes severe neuro-inflammation and neuronal death leading to various neurological symptoms and eventually death. Emerging evidence suggests anti-inflammatory nature of SCFAs in multiple neurodegenerative disorders. In thisstudy we aim to elucidate the possible role of SCFAs in JEV induced neuro-inflammation.

Post-natal day 10 BALB/c mice were randomly assigned to groups. Each group was intraperitoneally injected either with SCFA mixture (Acetate:propionate:butyrate = 35mM:15mM:10mM) or PBS for a period of 7 days, followed by JEV infection. All mice were observed for onset and progression of symptoms. Upon reaching terminal illness, mice were sacrificed by transcardial perfusion and the brain tissue was collected for further analysis. Protein was analysed by cytokine bead array, immunohistochemical techniques and RNA was analysed by qRT-PCR.

SCFA treated mice showed delayed onset of symptoms (piloerection, inability to move, paralysis) upon infection as opposed to the PBS treated animal, thereby increasing the survival by 3 days. Cytokine bead array revealed significant downregulation of inflammatory cytokines TNF-α, MCP-1, IL-6, IFN-Y in SCFA treated group relative to JEV infected control group. Corroborating results were obtained in RNA analysis. Tissue section analysis revealed reduced microglial activation in SCFA treated animals with respect to the JEV animals. However, despite the reduction in cytokine storm and microgliosis, the viral gene levels were consistently increased in SCFA-JEV animals. Through our study, we establish SCFA as a possible supplementary intervention in attenuating JEV mediated neuro-inflammation.

Mitophagy in retinal cells after experimental iron accumulation in rats

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Abstract

Introduction: Mitochondrial quality control and maintenance of cellular homeostasis are achieved via mitophagy. Degenerated organelles are degraded via autophagy induced by inactivation of mammaliantarget of rapamycin complex 1 (mTORC1). mTORC1 controls mitochondrial biogenesis, cellular proliferation, and autophagy. Dysregulation of mTORC1 can induce pathological states, including metabolic and neurological disorders.

Aim: The aim of this study was to examine the pattern of expression of various markers involved in mitophagy in iron-accumulated retina.

Material & Methods: Male Wistar rats (2-month-old) were reared and treated with ferrous sulphate dissolved in water by oral gavage (500 mg/kg body weight/week; iron availability: 20% of the amount fed), until 6 months of age. The control animals received water as vehicle. The animals were sacrificed, their eyes enucleated and fixed in 4% paraformaldehyde. Immunohistochemistry for retinal localizationof mTORC1, P62, LC3 II (markers for autophagy) and transferrin receptor-1 (involved in iron transport), and transmission electron microscopy (TEM) was performed to find changes in the retina bystandard method.

Result: Serum and retinal iron levels of control and experimental animals were compared and accumulation of iron in the retina was found in experimental group by the end of six month of age. Mitochondrial damage was evident in retinal ganglion cells after iron accumulation. Upregulation of P62 and LC3-II immunoreactivity was observed in inner retinal cell layers, suggestive of link between iron accumulation and autophagy. There were changes in the protein levels of mTORC1 in iron- accumulated retina, indicating mitophagy follows after iron accumulation in the retina. Ganglion cells showed mTORC1 IR in experimental animals.

Conclusions: These results suggest that mTORC1-regulated mitophagy is common after iron accumulation in the retinal ganglion cells.

Morphometric analysis of anterolateral triangle of cavernous sinus with its clinical significance – a cadaveric study

Ariyanachi Kaliappan, Rohini Motwani, Mrudula Chandrupatla

Abstract

Introduction: Modern neurosurgery is moving towards endovascular and radiosurgery because of their high degree of safety and faster recovery times. However, certain individuals still require invasive surgery by a neurosurgeon as in cases of tumours like pituitary adenoma, schwannoma, meningioma and chondroid tumour. An essential anatomical reference for the skull base surgery is the anterolateral triangle, one of the ten surgical triangles of the cavernous sinus. It serves as a corridor for infraorbital, maxillary, and pterygoid tumours.

Methodology and results: A total of 9 cadaveric skull base (18 sides) available for undergraduate dissection at AIIMS Bibinagar were dissected. The anterior, posterior, and lateral margins of the triangle were identified and measured. The mean lengths and standard deviations of the anterior, posterior, and lateral borders were statistically analysed.

Conclusion: Evaluating and designing surgical strategies to the middle cranial fossa and cavernous sinus are made easier by using the anterolateral triangle. To better access the pathologic alterations inside and surrounding this region, it is therefore necessary to first identify the typical anatomic relations and proportions of the anterolateral triangle.

Reduced cortical activation and functional connectivity in Attention deficit hyperactivitydisorder during working memory task: A QEEG study

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Abstract

Introduction: Attention deficit hyperactivity disorder is the most common neurodevelopmental disorder. Impairments in working memory can lead to poor academic and social outcomes. The disruption in the underlying neural circuitry implicated for working memory impairments needs to be investigated. Thus, the current study is planned to understand the cortical sources and its connectivity in subjects with ADHD as compared to age matched controls during working memorytask.

Aims and Objectives: To study the cortical sources and its connectivity in ADHD subjects compared to matched healthy controls using Quantitative EEG.

Materials and methods: After obtaining the ethical clearance (IECPG-137/23.04.2020), 42 ADHD (12.09 ± 2.6 yrs.; 34:8 (Male: Female), and 44 age-matched controls (12.60 ± 3.2 yrs.; 20:24(Male: Female) performed 20 trials of n back working memory task, designed using EPrime V2. Simultaneously EEG data was acquired using 128 channel dense array and data was pre-processed.500 ms pre-response data was segmented for all the 86 subjects and analysed for cortical sources and connectivity using sLORETA software.

Results: In ADHD subjects, lower cortical activity was seen in superior frontal gyrus, inferior frontal gyrus, superior parietal lobule, precentral gyrus, postcentral gyrus, superior temporal gyrus,transverse temporal gyrus and precuneus (exceedance proportion test (<0.05, t=2.366) compared to matched controls. Lagged linear coherence was computed band-wise in eight regions of interests(ROIs) for the functional brain connectivity, wherein significantly (p=<0.05, t=2.973) lower coherence was seen in upper alpha between precuneus and superior temporal gyrus in ADHD as compared to controls.

Discussion: Lower activity of superior frontal gyrus, inferior frontal gyrus, precentral and postcentral gyrus can lead to working memory deficits by alteration in the goal-oriented behaviour. Delayed maturation of temporal cortex in ADHD children can cause age-inappropriate deficit of attentional control in working memory task, this may attribute to lower activity of superior temporal gyrus and transverse temporal gyrus. Lower activity of superior parietal lobule can leadto the deficits in tasks requiring visual and spatial information, as used in working memory n backtask. Precuneus is

known to be involved in performance monitoring and attention reallocation, thus decreased activity can lead to attentional deficits. Lower source connectivity betweenprecuneus and superior temporal gyrus, can be the basis of attentional lapses in ADHD.

Conclusion: Dysfunctional cortical sources and connectivity can be the neural basis of working memory impairment in ADHD subjects.

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Measuring Behavior in Neuroscience Research: ANY-maze Software is more than just another video tracking system

Richard Mills
Company: Stoelting Co. & ANY-maze, a division of Stoelting Co.
Vice-President of Global Marketing and Sales & Chief Scientific Officer

Abstract

The use of video tracking software combined with a computer and camera allows for automated and manual scoring of various behaviors in animals, particularly rats and mice. The ANY-maze software is used worldwide for video tracking behavior in mice and rats in laboratories all over the world. In addition, the ANY-maze software can now connect and coordinate video tracking with other instruments critical for neuroscience research. The ANY-maze input/output (I/O) interfaces are available for independent control of other devices by the ANY-maze software for the synchronization of behavior and applications such as optogenetics, electrophysiology, and operant conditioning. Currently, the ANY- maze software functions as the proprietary software for controlling such behavioral equipment as the Orofacial Pain Assessment Device (OPAD), the Ugo Basile Fear Condition System, Ugo Basile Thermal Gradient Ring, and the latest is the Med Associates Inc. Operant Conditioning Testing System.

The impact of social rank on vulnerability to stress

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Abstract

In most socially living species, dominance hierarchy is established to gain access to resources, such as food, space, reproductive success etc. Studies in human and other species show that social rank can have broad effects on the physiology, behaviour, and health of individuals (Sapolsky 2005; Adler et al., 1994). Despite growing evidence for individual differences in vulnerability to stress, how social hierarchy affects an animal's ability to cope with stress remains less explored. Hence, we examined how hierarchical status of an animal (i.e., dominant vs. subordinate) influences its response to stress, and how stress exposure alters pre-existing social hierarchy. To this end, we subjected male Sprague Dawley rats (55-60 days old), to the social dominance tube test. Once the hierarchical rank within a cage was determined, rats were subjected to either acute immobilisation stress (2h) or chronic immobilisation stress (2 h/day for 10 days). Next, to assess the impact on stress on pre-established social hierarchy, cage-mates were compared in the tube test one day after acute and chronic stress. Surprisingly, pre-determined hierarchical rank amongst rats housed in the same cage was unaffected one day after either acute or chronic stress. However, the same acute stress had a significant impact on social rank when stressed rats competed with stranger rats from a different cage. Specifically, subordinate rats, but not dominant rats, that were subjected to stress avoided conflicts regardless of the social status of the novel conspecifics. These findings underscore the importance of considering the sub-group structures that exist within cages while assessing social behaviours in stress-related psychiatric disorders.

Psychological stress exacerbates neurological deficits in experimental model of Irritable bowel syndrome

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Abstract

Irritable bowel syndrome (IBS) is a disabling functional gastro-intestinal disorder (FGID) characterised by altered bowel habits, bloating, visceral hypersensitivity. Despite the high clinical prevalence, there are limited models to mimic the disease. Clinical studies suggest the importance of stress on the development and progression of IBS. The present study was designed to analyse the impact of different psychological chronic stresses on severity of IBS. Wrap restrain stress (WRS) and water avoidance stress (WAS) were used to induce psychological stress in mice. Dextran sulfate sodium (DSS) was administered to induce IBS and was assessed in terms of macroscopic scoring based on colon length, weight and disease activity index. The results showed significant neurobehavioral alterations in terms of cognition, spatial memory, CNS integrity, and anxiety analysed by elevated plus maze, Y maze, pole test and open field tests respectively. In addition, changes in colon length and weight were observed on exposure. Further, mucosal morphology of the gut evaluated by H&E staining was found to be altered. Biochemical analysis in terms of oxidative stress and intestinal permeability were affected in the animals that were exposed to combined stress. Taken together, these findings suggest that this combined psychological stress exacerbates changes in gut and brain following IBS model is relevant for understanding gut-brain associated manifestations in IBS.

Astaxanthin Regulates Ionotropic Glutamate Receptors and Mitochondrial Calcium Uptake in Cortical Neurons

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Abstract

Background: Excitotoxicity is known to associate with neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, Huntington's disease, as well as aging, stroke, trauma, ischemia and epilepsy. Excessive release of glutamate, overactivation of glutamate receptors, calcium overload, mitochondrial dysfunction and excessive reactive oxygen species (ROS) formation are a few of the suggested key mechanisms. Astaxanthin (AST), a carotenoid, is known to act as an antioxidant and protect neurons from excitotoxic injuries. However, the exact molecular mechanism of AST neuroprotection is not clear.

Objective: To investigate the role of AST in neuroprotection in excitotoxicity

Methods: Cortical neuronal cultures were prepared from post-natal day -1 Wistar rat pups. 100 µM glutamate +10 µM glycine was used in all our experiments while using glutamate stimulation, unless stated otherwise. Intracellular calcium was measured using calcium sensitive dye Fura-2 AM and neurons were depolarised with 60mM KCl stimulation. Neurons were exposed for 25 minutes with the ionotropic glutamate receptor agonists, and imaged for 15 minutes after agonist application to identify the effect of AST on Ca2+ influx in cortical neurons upon ionotropic glutamate receptor stimulation. Dihydroethidium (5 µM), a fluorescent ROS dye was used to determine the impact of AST on glutamate-mediated ROS formation. Rh123 dye(5µM) and Rhod5N were used to measure the mitochondrial membrane potential ($\Delta\Psi m$) and mitochondrial calcium ($[Ca^{2+}]m$) accumulation respectively.

Result: AST pretreated neurons significantly increased viability (53%, N=3) upon glutamate exposure when compared to the AST non -treated cultures (34% N=3). Our results also demonstrate that AST; (1) alleviates primary and irreversible secondary sustained $[Ca^{2+}]i$ response, by showing a significant reduction in the primary Ca^{2+} influx (0.6304 ± 0.05, n=19) upon glutamate application (Control- 0.8890 ± 0.06, n=23) (2) regulates the permeability of NMDA, AMPA, KA receptors. (3) inhibits mitochondrial calcium accumulation (234 ± 2.3, n =49) in comparison to the control (1550.4 ±2.4, n = 36) (4) inhibits abnormal $\Delta\Psi m$ (Control- 1.92 ± 0.07, n = 36; AST-0.25 ± 0.01, n = 35) and diminished (55%) ROS formation upon glutamate stimulation (Control- 1.2331± 0.05; AST- 0.4027 ± 0.04).

Conclusion: AST regulates influx of calcium through glutamate receptors at the plasma membrane, as well as improving mitochondrial function by reducing calcium uptake, thereby protecting the neurons from excitotoxicity.

Ethics: Approved by NIMHANS IAEC
Conflict of interest: None

Wristband for Position Tracking of Alzheimer's Patients with Health Condition Monitoring

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Abstract

Dementia is a symptom of Alzheimer's. It is a progressive neurological disorder due to death of the brain cell. Memory loss is the main symptoms of that disease. Approximately 50 million people all over the world suffering with dementia among them 75 years age group are affected with Alzheimer's diseases. India has 2nd world largest population in the world. Probability of India has more Alzheimer's patients because maximum people staying in poor economic condition. The patients who are suffering with Alzheimer's some time not able to reach their destination due to forgot the address. Wristband with GPS tracking system may help the guardian/caretaker to track the person location to pick up them. The role of GSM modems to continuous track the patient location in the form of latitude and longitude. The wristband attached with body temperature monitoring device and pressure sensor and heart rate monitor that continually monitoring physical condition of the patient. All the data of the sensor has been communicated via GPS to microcontroller GSM interface and help of that patient location also displayed in controlled room monitor. Wristband device is very light weight easy to carry like armband. This device may help the people of India to adopting a policy for the old age person's to proper heath care and movements.

Keywords: Wristband, GPS, GSM, Position Tracker, Society, Alzheimer

The Calsyntenin orthologue, CASY-1, affects neuromodulation to regulate sensorimotor output in *C. elegans*.

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Abstract

A remarkable feature of the nervous system is to regulate inter-neuronal communication that senses the environment and generates the behavioral output. Interestingly, there is a complex network of neuronal circuits, responsible for maintaining the excitation-inhibition (E-I) balance at neuromuscular junction (NMJ). Several cell adhesion molecules (CAMs) have been found to act as dynamic regulators of this sensorimotor circuit function [1]. CASY-1, is one such CAM present in the neurons of nematode *Caenorhabditis elegans* (*C. elegans)*, known to coordinate motor output by maintaining E-I balance at NMJ. It has been demonstrated that the *casy-1* mutants display accelerated motor activity and paralysis in response to Aldicarb (acetylcholinesterase inhibitor), suggesting higher cholinergic signaling. However, the exact mechanism by which the CASY-1 present at the sensory level acts to regulate cholinergic signaling in the motor neurons is poorly understood. Numerous studies report the role of neuropeptides in modulating E-I balance in the locomotory circuit [2]. Also, neuropeptide processing *egl-3* and *egl-21* mutants are found to suppress the Aldicarb hypersensitivity of *casy-1* mutants. Moreover, Preliminary experiments have indicated the genetic interactions between *casy-1* and the neuropeptide *flp-21*, based on Aldicarb and locomotion assays. This led us to hypothesize that CASY-1 possibly acts through neuropeptidergic signaling to regulate sensory-evoked motor output. In order to understand the intricate neuromodulatory mechanisms operating in the sensorimotor circuit, *C. elegans* is employed as a model system since its neural connectome has been studied in detail. Hence, we aim to establish the neuropeptidergic circuit, responsible for CASY-1 mediated regulation of motor circuit dynamics and associated locomotory behavior.

Keywords: Sensorimotor circuit, Neuropeptides, CASY-1

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Functional connectivity disturbances in psychogenic non-epileptic seizures: A machine learning study using Resting-State fMRI

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Abstract

Background: Psychogenic non-epileptic seizures (PNES) are epilepsy-like paroxysmal behaviors that resemble seizures, but lack the biological mechanism underlying the epileptiform brain activity.

Objective: To identify changes in brain networks in PNES and provide markers for automatic classification from healthy controls (HC) based on graph theory and machine learning approaches.

Method: In this study, 25 patients with PNES and 25 HC were prospectively recruited to evaluate the brain networks by resting-state functional MRI. All participants were instructed to keep their eyes open while being scanned. The pre-processed was used to construct the functional connectivity matrix following the parcellation of the whole brain into 116 regions. Graph theory measures of clustering coefficient (CC), betweenness centrality (BC), nodal efficiency (NE), local efficiency (LC), assortivity, small-worldness, and path length (PL) were used for classification.

Results: In comparison with HC, PL (p-0.033) and assortivity ($p<0.01$) were decreased in PNES. On node-wise comparison, PNES showed decreased segregation, decreased efficiency, and higher centrality in the motor, executive, auditory and visual networks. PNES also showed denser connectivity in select DMN regions (lateral parietal). Best classification performance was observed with random forest and K-nearest neighbor of 90% (AUC-80.0%) and 80 % (AUC-82%) respectively.

Conclusion: PNES patients displayed abnormalities in several well-known resting networks. The results of this study demonstrated network measures as potential biomarkers which may help in the diagnosis of PNES in a clinical setting.

Comparison of ACE III scores between amnestic and non-amnestic MCI

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Abstract

Background

Mild Cognitive Impairment (MCI) is a transition state of cognitive decline from healthy brain todementia. Based on whether memory is affected or not, MCI can be classified as amnestic (aMCI) and non-amnestic (naMCI). In aMCI, memory is significantly impaired and in naMCI, memory remains intact while one or more other cognitive abilities are significantly impaired.

ACE III (Addenbrooke's Cognitive Examination III) is a neuropsychological test which assesses attention, memory, fluency, language and visuospatial skills to test for cognitive impairment.

While MCI and dementia can be differentiated based on ACE III score, it is unknown if it can differentiate between aMCI and naMCI.

Aim

To classify a large cohort of ageing participants based on their Clinical Dementia Rating (CDR)scores into aMCI and naMCI and compare their ACE III scores.

Methodology

For this study, 40 participants with MCI were selected from Tata Longitudinal Study of Aging (TLSA), an urban cohort study. The criteria for MCI were considered to be a CDR score of 0.5.Based on the scores of memory domain of CDR, the participants were classified as aMCI (CDRMemory = 0.5) and naMCI (CDR Memory = 0). Since normality could not be established for the ACE scores by Lilliefors test, Mann-Whitney U test was performed to compare the median ACEscores of the two MCI subtypes.

Results

Among the 40 participants with MCI, 35 participants were with aMCI while 5 were with naMCI. The median ACE score and standard deviation of the amnestic subgroup was 89.5±9.59 and for non-amnestic MCI subgroup, the median ACE score and standard deviation was 94±6.62. There was a significant difference between the aMCI and naMCI ACE scores (U=97; p=0.012).

Conclusion

The ACE scores of aMCI was significantly lower than that of naMCI. This result suggests that ACE III score may differentiate between aMCI and naMCI.

Short duration, early exposure to low intensity magnetic field stimulation amelioratescognitive deficits and restores delta power in Alzheimer's disease rat model

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Abstract

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disease and begins long before any symptoms become apparent. It is an irreversible brain disorder slowly compromising learning and memory skills. AD is an approaching public health crisis which presently lacks an effective treatment. Non-invasive, magnetic field stimulation therapy proposes a promising alternative approach to traditional pharmacological interventions for AD.

Materials and Methods: Adult male Wistar rats were taken as study model and divided into three groups: Sham, AD and AD+MF. For development of AD, STZ was injected intra- cerebro ventricularly, at a dose of 3mg/kg body weight using stereotaxic apparatus. AD+MF animals were exposed to low intensity magnetic fields from 8th day of STZ treatment till 15th day. Behavioral recordings of passive avoidance task and novel object recognition task for cognitive assessment were performed at day 15. To study the extent of damage, cresyl violet staining was performed. Electrocortical recordings from frontal and occipital lobes.

Pb and β-amyloid peptide induced toxicity leads to the mitochondrial alterations in the mitophagy and apoptosis in the human neuronal cells

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Abstract

Lead (Pb), an environmental contaminant, has a strong link to the onset of neurodegenerative diseases due to impaired mitochondrial function. Defective mitochondrial accumulation could be one of the factors that contribute to Alzheimer's Disease (AD) progression. Studies have been directed at the mechanisms that lead to the altered mitochondrial homeostasis in AD. Mitophagy is required for the mitochondrial pool to remain healthy. Here, we provide evidence that Pb causes human neuronal cells to undergo defective mitophagy. By assessing particular marker proteins of mitophagy like parkin and PINK1 in human neuronal cells, we explored the PINK1/parkin dependent pathway to learn more about its function in Pb-induced AD. Our findings showed that cells exposed to β-amyloid peptides (Aβ (25-35) and Aβ (1-40)) and Pb separately and in various combinations, had significantly lower levels of parkin and PINK1, which resulted in impaired mitophagy. The study also reveals the mitochondrial oxidative stress, condition of the mitochondrial membrane potential (MMP) and permeability transition pore (MPTP) in cells exposed to Aβ peptides and Pb. The exposed groups showed increased mitochondrial oxidative stress, improved MPTP pore formation, decreased mitochondrial mass and a lowering of membrane potential. We also found that β–amyloid peptides and Pb are able to cause apoptosis induction by increasing specific apoptotic marker proteins like BAK, AIF (apoptosis inducing factor), caspase-3 and cytochrome c. According to the aforementioned studies, Pb-induced neurotoxicity could be caused by processes such as mitochondria-mediated apoptosis and defective PINK1/parkin-mediated mitophagy.

PLGA-based *Centella asiatica* nanoformulation: *In vitro* preclinical findings on its effects against Parkinson's disease pathogenesis

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Parkinson's disease (PD) is the second most common neurodegenerative disease characterized by the progressive loss of dopaminergic neurons in substantia nigra pars compacta that results in striatal dopamine loss and motor dysfunctions. Most of the currently available therapies have failed in slowing the rate of neuronal loss and provide only symptomatic relief, but with associated side effects. Hence there is an urgent and unmet clinical need to develop alternative, safe, non-toxic and disease-modifying therapies for PD. The use of herbal drugs with multiple active constituents has been considered as a promising approach for drug development and these active constituents may act on multiple targets in the brain involved in a multifaceted disease such as PD. However, one of the major limitations in the use of herbal drugs for an indication is their poor bioavailability. A holistic approach through integration of whole plant extracts into nanoparticles would be an attractive approach to overcome this issue. We hypothesize that encapsulation of whole plant extracts and active molecules into nanoparticles would help these to cross blood brain barrier, resulting in better bioavailability and improved therapeutic effect at lower dosages. In order to test this hypothesis, a single herb *Centella asiatica*, and its active constituent, asiatic acid, both of which are known to have neuroprotective effect were selected for the present study. Nanoformulations of *C. asiatica* extract and asiatic acid were prepared by double emulsion polymerization using polylactide-co-glycolide (PLGA) nanoparticles and characterized for their size and Zeta potential using dynamic light scattering. Targeted nanoformulations were also prepared using lactoferrin as the targeting ligand. The nanoformulations were optimized for their size, encapsulation efficiency and drug loading efficiency. The *in vitro* toxicity and neuroprotective effect of the nanoformulations were evaluated in MPP^+-induced Parkinsonism in differentiated SH-SY5Y neurons. The nanoformulations of the extract and asiatic acid exhibited reduced toxicity when compared to the unformulated drugs. Both the extract and asiatic acid showed neuroprotective effect in MPP^+-induced cell model of PD.

Key words: Parkinson's disease, nanoformulations, *Centella asiatica*, PLGA

Acknowledgements

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Identification of Novel miRNA-protein regulatory modules and their implications inarsenic-induced neurodegeneration

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Abstract

Introduction

The acquisition of neurodegeneration hallmarks entails an extremely dynamic and interactive system of multiple layers of molecular markers. Arsenic exposure represents a major public health threat for populations worldwidewith special reference to developing countries. Long-term intake of arsenic causes a wide range of neurological complications by involving pathogenic mechanisms that are extremely complex and likely multifactorial. Due tothe lack of straight dependency between miRNA and protein, focusing on one approach-either microRNAome or proteomic may result in only a partial explanation or even misinterpretation of the biological response. For reliable outcomes, omics integration is an ideal approach. Therefore, the present study aimed to identify potent regulatory modules between miRNAs and proteins that might uncover pathophysiological mechanisms underlying arsenic-induced neuronal death.

Principle and Methods:

Integrated Open array-based miRNA profiling and unlabelled LC-MS/MS global protein profiling were carried out in differentiated human neuroblastoma SH-SY5Y cells with/without arsenic exposure. Various *in-silico* tools such as mirPath (DIANA TOOL v.3), Target Scan, String, and DAVID were employed to identify potential targets and for pathway analysis. Transient transfection studies were carried out using mimics and inhibitors of miR-29b via RT-PCR assay.

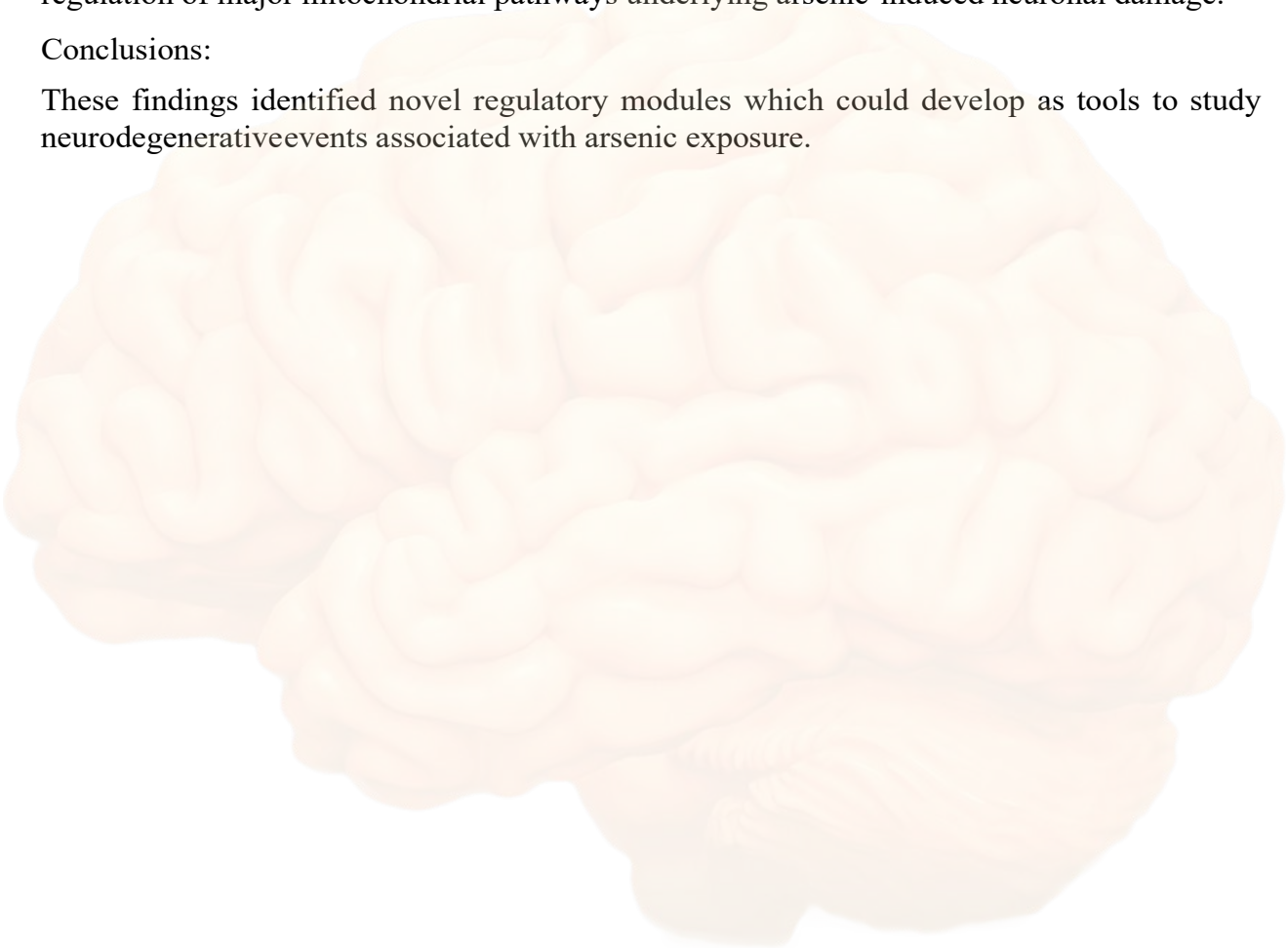
Results:

Arsenic exposure to SH-SY5Y cells dramatically increased the expression of mmu-miR-153, hsa-miR-29b, hsa-miR-221, hsa-miR-199a, hsa-miR-503, hsa-miR-543, hsa-miR-505, hsa-miR-490, while hsa-miR-126, hsa-miR-138, and hsa-miR-664 have shown maximum downregulation. The proteomics analysis revealed that proteins involved in oxidative stress,

mitochondrial function, oxidative phosphorylation, glycolytic process, mitophagy, metabolic processes, cell cycle regulation, DNA replication, protein folding, autophagy, apoptosis were found to be significantly deregulated in the proteome profile of SH-SY5Y cells receiving the toxic insult of arsenic. Furthermore, transcriptional analysis revealed that YY1 regulated gene PGC-1α as well as its associated genes *viz.*, MFN-1, OPA-1, FIS-1, and DNM-1L, which are major mitochondrial dynamics regulatory genes were also found to be deregulated following arsenic exposure. Integration of multi-omics data sets discovered potent regulatory modules between miRNAs and proteins, with miR-29b as a potential regulator of key targets involved in cellular and molecular mechanisms of mitochondrial functions in neuronal cells. Transient transfection studies confirmed the involvement of miR-29b in the regulation of major mitochondrial pathways underlying arsenic-induced neuronal damage.

Conclusions:

These findings identified novel regulatory modules which could develop as tools to study neurodegenerativeevents associated with arsenic exposure.



Expression of miR-29b regulates Sirtuin-1-mediated apoptosis and cellular bioenergetics in Parkinson's disease

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Abstract

Introduction

Parkinson's disease (PD) is an aging-related degenerative disorder caused by the loss of dopaminergic neurons in the substantia nigra. Accumulating evidence revealed that the expression of miRNAs mediates various processes involved in PD pathogenesis via controlling the expression of sirtuins. Despite an abundance of potential and budding options, the precise mechanism driving the selective death of dopamineneurons in PD remains enigmatic. The present study aimed to carry out miRNA profiling employing Open Array technology in the rotenone-induced PD model and explore the role of identified miRNA in sirtuins- mediated apoptotic cell death and rotenone-induced mitochondrial dysfunction in neuronal cells.

Materials and Methods

We have carried out miRNA expression profiling to identify miRNAs deregulated upon rotenone exposure in terminally differentiated SH-SY5Y neuronal model system. Identification of potential targets of miRNAsand functional enrichment analysis was carried out employing various *in-silico* tools such as mirPath (DIANA TOOL v.3), Target Scan, and Cytoscape. The effect of induction and inhibition of miR-29b was studied on genes involved in apoptotic pathway in SH-SY5Y cells employing mimics and inhibitors of miR- 29b via RT-PCR assay. Real-time bioenergetics analysis of neuronal cells in response to rotenone alone, andin combination with inhibitors of miR-29b was done using Seahorse XFp metabolic flux analyzer.

Results

Our miRNA profiling results have identified a significant increase in the expression of hsa-miR-29b, hsa- miR-490, mmu-miR-499, hsa-miR-543, hsa-miR-494 while significant downregulation was observed in hsa- miR-331-5p, hsa-miR-182, and bta-miR-139. miR-29b, which was the most upregulated miRNA following rotenone exposure in SH-SY5Y cells, has also been shown to be deregulated in a variety of neurological disorders, including PD. Comprehensive *in-silico* analysis

revealed sirtuin-1(SIRT-1) to be the potential target of miR-29b. Gain and loss of function studies were conducted to explore the role of miR-29b in SIRT- 1 mediated caspase-dependent apoptotic pathway. Mimics and inhibitors studies revealed miR-29b as a direct regulator of SIRT-1 mediated caspase-dependent neuronal death via regulating the expression of SIRT-1, PARP-1, CYT-C, BCL-2, CAS-3, and CAS-9. Transcriptional analysis has also revealed deregulation of mitochondrial function governing genes and activation of SIRT-1-dependent apoptotic pathway following rotenone exposure in neuronal cells. Real-time bioenergetics analysis of neuronal cells in response to rotenone exposure showed that rotenone caused a reduction in Oxygen consumption rate (OCR), Basal respiration, Maximal respiration, and Non-mitochondrial respiration relative to the control group. However, inhibition of miR-29b resulted in the slight restoration of respiration parameters.

Conclusion

Our results revealed that miR-29 is a direct modulator of the SIRT-1 mediated apoptotic pathway and mitochondrial bioenergetics in the cellular model of PD. Thus, miR-29b could develop as an exciting noveltarget for potential therapeutic interventions in PD.

Secretagogin, a calcium binding protein in the brain of Indian wall lizard *Hemidactylus leschenaultti*

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Abstract

The calcium binding proteins (CBPs) are equipped with Ca^{2+} binding sites and serve as buffersto regulate the free cytoplasmic Ca^{2+} in neurons. The evolutionarily conserved CBP, secretagogin (scgn) is an hexa EF-hand protein. It is highly enriched in neuroendocrine cells, serves as a Ca^{2+} sensor, modulate regulated exocytosis, and regulates Ca^{2+} homeostasis in neurons and the neuroendocrine system. The expression, neuroanatomical organization, and significance of scgn have been studied in the brain of mammals, birds, and teleosts. The relevant information in the reptilian brain is not available. Using a specific anti-scgn antiserumand immunofluorescence, we studied the scgn-expressing elements in the brain of the Indian wall lizard, *Hemidactylus leschenaultti*. The characterization of *scgn* mRNA revealed an openreading frame (ORF) of 819 bp which encoded 273 putative amino acid protein, both shared high similarity with other lizards, amphibians, aves, fishes and mammals. Further, homology modelling of the scgn protein from *H. leschenaultti* predicted the presence of six conserved and functional EF-hands motifs for Ca^{2+} binding. Western blot analysis of the whole brain of
H. leschenaultti using a polyclonal anti-scgn antiserum showed the presence of a single scgn- ir band of ~32 kDa, equivalent to the known molecular weight of scgn. Using immunofluorescence, the scgn-ir cells and fibres were observed in distinct regions of the pallium, subpallium, and preoptic area. In the hypothalamus, scgn-ir was observed in the neurons of the lateral hypothalamic area, supraoptic, paraventricular (PVN), and inferior hypothalamic (IH) nuclei. Scgn-ir was observed in the dorsomedial thalamic nucleus, substantia nigra, lateral superior reticular nucleus, parabrachial area, nucleus interpeduncularis, and the raphe nucleus. Double immunofluorescence was employed to determine the

neurochemical phenotype of scgn-expressing neurons. While scgn neurons in PVN co-expressed cocaine-and amphetamine regulated transcript (CART), those in the IH

expressed neuropeptide Y (NPY). The wide distribution of scgn in the brain of *H. leschenaultti* suggest role of this CBP in a range of physiological functions including neuroendocrine regulation and behaviour.

NADPH oxidase inhibitor apocynin attenuates Paraquat-induced motor deficits in therat model of Parkinsonism.

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Abstract

Background: Parkinson's disease (PD) is the second most common progressive neurodegenerative disease after Alzheimer's disease characterized by the presence of intra- cytoplasmic inclusion bodies known as Lewy bodies having α- synuclein aggregate and the loss of dopaminergic neurons in the substantia nigra regions of the brain. The exact cause of dopaminergic neuronal loss in PD remains unknown for a long time; however, recent studies report that oxidative stress plays a crucial role in the pathogenesis of PD. Paraquat (PQ), a widely used herbicide, is an oxidative stress inducer that has been implicated as a potential risk factor for the development of PD. To date, no complete cure is available for the disease. Pharmacological approaches targeting antioxidant machinery may have therapeutic value against PD. Flavonoids are naturally occurring polyphenolic compounds that display a variety of therapeutic properties against oxidative stress. Apocynin (4-hydroxy-3- methoxyacetophenone) is a natural flavonoid obtained from the medicinal plant *Picrorhiza kurroa* that exhibits neuroprotection against PD-related pathology. However, studies on its neuroprotective role and the underlying mechanisms are scarce.

Aim: The proposed study will explore the effect of Apocynin on Paraquat-induced motor deficits in the rat model of Parkinsonism.

Methods: As a part of preliminary study, we have developed PQ-induced Parkinsonism model in adult Wistar rats. We performed motor coordination-related behavioral experiments and immunohistochemistry to validate the establishment of PQ-induced Parkinsonism. Then we determined the effect of Apocynin on motor function in the PQ-induced rat model of *Parkinsonism.*

Results: Paraquat-induced nigro-striatal dopaminergic neurodegeneration in the rat model of Parkinsonism. Apocynin improved motor deficits in the PQ-induced rat model of Parkinsonism.

Conclusion: Apocynin treatment alleviates PQ-induced motor deficits in the rat model of

Parkinsonism. In the future, we will be assessing the neuroprotective effect of Apocynin in the developed model of Parkinsonism.

Keywords: Parkinson's disease, paraquat, neuroprotection, Apocynin, neurodegeneration.

Understanding the role of Sertad1 in autophagy dysfunction in Alzheimer's disease

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Abstract

Alzheimer's disease (AD) is often considered a proteinopathic disorder due to failed clearance of misfolded protein aggregates by the autophagy-lysosome machinery. Despite robust induction, autophagosomes accumulate in the AD brain due to impaired autophagy flux. Autophagy defects occur at later stages where faulty lysosomal acidification causes failure in proteolysis within the lysosome. To monitor autophagy progression with age, we prepared cortical and hippocampal lysates of 5xFAD mice of different age groups andperformed Western blot. We found a significant increase in autophagosome and lysosome markers with increasing age in AD, suggesting robust autophagy induction. Similar results were found in amyloid-β (Aβ) treated PC12 cells and primary cortical neurons suggesting high levels of autophagosome synthesis. Sertad1, a cell-cycle protein, which aids apoptosis, isupregulated upon Aβ treatment. An intricate cross-talk between autophagy and apoptosis led us to explore the role of this protein in autophagy dysfunction in AD. Sertad1 is upregulated in our AD model. Upon depleting Sertad1 using shRNA, we found that neurons are able to cope better with Aβ mediated neurotoxicity as shown by cell survival assay. Remarkably, shRNA against Sertad1 reduced levels of LC3 and p62 in our cellular models and also reduced FoxO3A translocation inside the nucleus suggesting a possible role of Sertad1 in autophagy modulation through FoxO3A. Sertad1, being a transcriptional coregulator might mediate its regulatory effects through interaction with other transcription factors. Usinggenetic manipulation in 5xFAD mice, we will explore the role of Sertad1 in autophagy flux modulation and AD pathogenesis. We propose that targeting later stages of autophagy could be a useful strategy for therapeutic intervention in AD.

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Intracranial self stimulation of LH-MFB ameliorate impaired reversallearning in schizophrenic like condition in rat: role of neuronal nitric oxide synthase

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Abstract

Background: The intracranial self stimulation (ICSS) reversal learning paradigm offers rewarding current to the lateral hypothalamus-medial forebrain bundle (LH-MFB) to assess the behavioral manifestation in animals. The neuronal nitric oxide synthase (nNOS) in distinct neural substrates has been recognized for various neurobiological activities. However, the role of nNOS for reversal learning behaviour has been less understood. The rewarding current to the LH-MFB activates the nNOS in the LH and superior colliculus (SC), critically involved in reversal learning has not been documented.

Aim and Objectives: The aim of present study was to investigate the role of nNOS of SCand LH-MFB in reversal learning impaired during schizophrenia like condition via ICSS paradigm.

Methods: Reversal learning behavior was assessed in adult male Wistar rats using ICSS paradigm and lever press activity was counted. Two groups of rats were treated with chronic intraperitoneal administration of saline (0.9% W/V) and MK801 (Glutamatergic NMDA receptorantagonist) for 6 consecutive days, and reversal learning behavior was monitored. To test the involvement of nNOS in ICSS reversal learning, cohort of rats were administered with 7- nitroindazole (7-NI; selective nNOS inhibitor) in superficial grey layer (SuG) of SC and intra- LH-MFB, and lever pressings were measured. The SC and LH-MFB area of trained rats were processed for nNOS immunohistochemical profile. Moreover, to track the nitrergic (nNOS) pathway from LH-MFB to SC, DiI retrograde tracer was given in SC, and DiI cells were co-labeled with nNOS cells in LH-MFB area.

Results and Discussion: The MK801 treated rats showed significant decrease in lever press activity as compared to saline treated group. It suggests that chronic treatment of MK801 produce

impairment in reversal learning is one of the core symptoms of schizophrenic like condition. The intra-SuG and intra-LH treatment of 7-NI showed significant increased in lever pressings, which imply the role of nNOS in reversal learning. The nNOS immunoreactive cells in the SC and LH-MFB were significantly increased in trained rats as compared to the control.

This data suggest that nNOS of the LH-MFB and SC are prominently involved in the regulationof reversal learning. The retrograde study revealed that nNOS positive cells of the LH-MFB were projected to the SC and modulates the reversal learning behavior impaired during schizophrenic like condition.

Conclusion: The present research work demonstrated the role of nNOS of the SC and LH- MFB in the regulation of reversal learning behavior which impaired in schizophrenic like condition. These findings might be useful for the neuroscientist in near future for the preclinicalevaluation of drug and develop treatment strategy against schizophrenia like neuropsychiatric disorders.

Key Words: Superior colliculus, Neuronal nitric oxide synthase, lateral hypothalamus-medial forebrain bundle, reversal learning, Intracranial self stimulation.

A natural small molecule inhibits alpha-synuclein aggregation, maintains native monomeric structure and prevents neuronal degeneration.

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Abstract

Neurodegenerative diseases are characterized by the accumulation of pathological proteins and progressive loss of neurons. Parkinson's disease (PD) is the second most common neurodegenerative disease. PD is characterized by degeneration of dopaminergic neurons in the *substantia nigra pars compacta* and accumulation of misfolded α-synuclein (α-syn) as intracellular inclusions called Lewy bodies. Over a decade, a large number of plant-based small molecules have been studied extensively as a therapeutic strategy to treat disease pathogenesis. While only a few are reported as neuro-protectants because of their ability to prevent pathogenic protein aggregation. Majority of small molecules exhibiting antibacterial, antiviral, and anti-cancerous activities also possess anti-aggregation properties. In the present study, we investigated shikonin (SHK), a natural plant-based naphthoquinone, known for potent anti-microbial activities for its anti-aggregation activity against α-syn. We studied the α-syn aggregation kinetics in the presence of SHK and found that SHK has a potency to prevent α-syn aggregation. This SHK-mediated inhibition of α-syn aggregation was further confirmed by circular dichroism spectrum and transmission electron microscopy. 1D NMR and simulation and docking showed that SHK binds to the C-terminus, near the NAC region of α-syn. The binding of SHK to α-syn maintains α-helical and disordered secondary structures of α-syn by reducing its beta-sheet content. These results depicted SHK as a potent aggregation inhibitor, that significantly reduces the seeded and non-seeded aggregation of α-syn at sub-stoichiometric concentrations by increasing the lag phase and stabilizing its α-helical and disordered form. This anti-aggregation propensity of SHK was further validated in *Caenorhabditis elegans* PD models, where it prevented dopaminergic (DA) neuronal degeneration.

The Purinergic receptor P2Y12 in Tau aggregate clearance by endocytosis and degradation in microglia

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Abstract

Microglia are the resident immune cells of the central nervous system, which are in constant surveillance of the brain microenvironment to maintain tissue homeostasis. Microglia play significant role both in the physiological and pathological conditions of the brain. Our earlier studies elucidated the role of P2Y12R in direct interaction with toxic Tau species; P2Y12R mediated full-length Tau oligomer internalization through actin remodeling followed by endocytosis, accumulation, and degradation. In this study, we are focused on elucidating the fate of toxic Tau aggregate upon P2Y12R interaction. Based on the immunofluorescence analysis, we observed that Tau aggregate are actively colocalizing with P2Y12R in a time-dependent manner, signifying receptor-mediated endocytosis. Upon internalization, Tau aggregate enters endocytic pathway as it colocalizes with Rab5A, which is an early endosomal marker. The degradation mechanism and receptor desensitization pathway underlying P2Y12R mediated Tau aggregates are the future directions of this study. Further, we are interested in exploring the signaling mechanism underlying P2Y12R and Tau aggregate interaction that could lead to aberrant activation of Rab5 in AD pathology.

Animal models with behavioural distinctions in full blown and prodromal Alzheimer's disease

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Abstract

Alzheimer's disease (AD) is the most prevalent form of dementia, for which no disease modifying therapy is available. The development of successful treatments for AD can be facilitated by developing animal models that recapitulate key phenotypes found in the human disease. Being a highly complex progressive mental disorder, modelling neurobehavioral phenotypes of different stages of AD in mice is challenging. Although a number of toxicants induced and transgenic mouse models are available, none of these models accurately recapitulate all key features of AD phenotypes. We compared a number of crucial neurobehavioral alterations including spatial and reference memory deficit, and exploratory and anxiety related behaviour of streptozotocin (STZ)-induced and amyloid β-42 (Aβ-42)-induced AD mouse models. Behavioural phenotyping at 7, 14 and 28 days after STZ (intracerebroventricular injection of 3mg/kg of STZ) or Aβ-42 (100µM Aβ-42 oligomers infused into the dentate gyrus of the hippocampus) administration in three months old male C57BL/6 mice were done followed by neuropathological characterization. We found that STZ induces mild cognitive dysfunction in these mice, while Aβ-42 oligomers hippocampus causes a progressive and substantial memory decline akin to AD. This is accompanied by a more severe neuronal loss in the hippocampus of Aβ-42 treated mice than the STZ treated animals. Our data suggest that STZ model may be useful to study mild cognitive impairment, which represents prodromal AD, while Aβ-42-induced model may recapitulate more advanced and aggressive form of AD.

Rule-Based Categorization of Tactile Textures Using Linguistic Labels

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Abstract

Categorical perception is the tendency to perceive a continuum of sensory input as discrete entities. This involves the formation of an arbitrary 'boundary' through enlargement of differences between two points on the spectrum of sensory input. The formed categories can be divided into dense and sparse, based on high and low statistical density respectively, which is defined as the ratio of category-relevant features to total variance among category members. Dense, or naturalistic categories, are predicted by perceptual similarity of their collective physical attributes whereas sparse categories are identified by abstract rules. Linguistic tags can act as category-inclusion rules when the relationship between category members is not explicit. Language has been associated with improved abstraction since verbalization of the semantic relation in sparse categories increases its salience and highlights the relevant dimensions through modulation of attention processes and symbolic juxtaposition. In the visual domain, linguistic training with verbal labels shifts the category boundaries in favor of a semantic rule and inhibits the perceptual similarities amongst category members. In this study, we sought to determine the effect of pseudoword labels on rule-based categorization of tactiletextured stimuli with and without perceptual similarities. We also tested whether supervision leads to better performance in categorization tasks, as explicit explanation of the category- inclusion rule allows for discovery of the semantic relation in sparse categories. In the presentexperiment, we created two sets of textures by 3D printing and asked the participants to categorize the stimuli freely in the pre-test condition. After that, we formed two sparse categories artificially using the same textures, and associated two pseudowords with each of them respectively, but there was no perceptual rule underlying the new sets. To demonstrate the learning of verbal association, we then conducted a post-test under supervised and unsupervised conditions. We found that after training, the named categories predicted the category response significantly in the supervised condition, whereas in the unsupervised condition, the perceptual categories remained the significant predictor, similar to the pre-test. This suggests that when the semantic relation is explicit, naming can act as a rule for categorization of dissimilar items in tactile texture categories. These findings have implications for the neuroscience research that shows a dichotomy between the neural substrates of perceptual similarity and rule-based judgements, connecting it to recent neuroimaging studies that reveal a dissociation between the functional pathways of perceptual color categorization and color naming.

Keywords: categorical perception, rule-based, tactile textures, verbal labels, supervision

Effect of medial forebrain bundle deep brain stimulation on affected reward motivation due to chronic stress model of depression

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Abstract

Background: Loss of motivation appears to be a hallmark of multiple psychiatric and neurological disorders, including major depressive behavior. In humans, the dysfunction of reward circuit invariably results in loss of motivation and/or hedonic response. To successfully treat the motivational deficits in psychiatric disorders, we need to understand the neurobiological and molecular substrates underlying different aspects of motivational behavior. Recently, deep brain stimulation (DBS) targeted at lateral hypothalamus-medial forebrain bundle (LH-MFB) showing maximum antidepressant response in the patient of treatment-resistant depression; but the underlying molecular mechanism is still unknown.

Aim and Objectives: To study the effect of deep brain stimulation of LH-MFB in the chronic unpredictable mild stress (CUMS) induced reward deficit using operant conditioning and participation of CARTergic system.

Methods: Different unpredictable stressors were applied to Adult male Wistar rats for 6 weeks. The rats were implanted with bipolar electrodes and divided into different groups (control, CUMS, DBS and CUMS + DBS). DBS treatment was given to the CUMS animals for 4h/day for 14 days and assessed for depressive behavior. Subsequently, the rats behaviors were assessed with the forced swim test (FST), sucrose preference test (SPT), open field test (OFT) and motivation test (operant test/progressive ratio test).

Results: The DBS of LH-MFB elicit rapid antidepressant effects and improved the affected reward motivation due to depression in CUMS animals. Additionally, it has reversed the anhedonia, behavioral dispairs, reduced locomotor counts and weight, and the decreased CART immunoreactivity in the CeA, DG, DRN, LH and VTA region of depressed rats.

Conclusion: The treatment of DBS targeted at LH-MFB opens up a new avenue to treat motivational deficit in depression and suggested the involvement of CARTergic system in its mechanism.

Pax6 and CTCF are inversely regulated in brain of Streptozotocin–treated hyperglycemic mice

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Abstract

Background: The Pax6, a transcriptional regulator, has been critical for development and maintenance of functional anatomy of central nervous system, eyes, pancreatic islets, and pituitary. Pax6-haploinsufficient rats have reduced proliferation of neural stem/progenitor cells and subsequent production of neurons inside the hippocampus. Patients having anomalies with PAX6 have reduced cortical brain thickness, impaired glucose tolerance and impaired memory. Pancreatic β-TC-1-6 cell line exposed to high glucose concentrations showed decreased Pax6 and increased expression of CTCF (An evolutionary maintained zinc-finger protein). CTCF interacts with a repressor element of Pax6 in corneal epithelial cells. CTCF knock down in the HTCE cells shows decreased Pax6 mRNA levels suggesting. However, CTCF-mediated Pax6 regulation in brain is unknown. Therefore, it has been intended to evaluate association CTCF, Pax6 and co-expressed genes in brain of STZ-induced hyperglycaemic mice.

Materials and Methods: The hyperglycaemic mouse model was developed by intraperitoneal injection of 50 mg/kg body weight of Streptozotocin for five consecutive days. Streptozotocin dissolved in 0.1M citrate buffer (pH-4.5) was injected in mice (n=6) for five days. The blood glucose levels were measured using Accu-Check Active until Blood glucose level reached >200mg/dl (considered as hyperglycaemic). The brains of control and hyperglycaemic mice were used for comparative study. The expression of genes and proteins (Pax6, Ctcf, Creb, Arc, Ncam, Tgf-β, Irs1, Vegf, Sod, Ldh, Catalase, Erk ½, Ras, iNOS, eNOS, Tnf-α, Ifn-γ were evaluated by qPCR and western blotting. Protein-protein interaction (immunoprecipitated with anti-CTCF and anti- Pax6 followed by western blotting with anti-Pax6, -Vegf, -Tgf-β, -Bdnf, -Creb, -NCAM, -Irs1). The co-expression and co-localization of Pax6 and CTCF positive cells were evaluated by immunohistochemistry. Pax6-binding sites were explored by eukaryotic promoter database and STRING (http://string-db.org).

Results: At the transcript and protein levels, expression of Pax6, Irs1, Tgf-β, Erk1/2, Sod and iNos decreased, however, Ctcf, Sod, LDH, Cat, ERK1/2, eNos, Tgf-β, Vegf, Ras, NCAM, Arc, Irs1, Tnf-α, Ifn-γ, Bdnf, and Creb increased in STZ treated mice compared to control mice. The Pax6 and Ctcf interact as observed in anti-Pax6 and anti-CTCF pulled brain proteins followed by western blotting.

Conclusion: There is inverse association between Pax6 and Ctcf in brain of Streptozotocin–treated hyperglycemic mice. Since Ctcf, Sod, LDH, Cat, ERK1/2, eNos, Tgf-β, Vegf, Ras, NCAM, Arc, Irs1, Tnf-α, Ifn-γ, Bdnf, and Creb increased in STZ treated mice, Pax6 may be serving as their negative regulators and Ctcf as their positive regulators. Since Pax6 and Ctcf interact, there may be direct or indirect autoregulation in neuronal cells during the hyperglycaemic condition. Normal level of Pax6 seems critical for Vegf-mediated angiogenesis.

Keywords: Pax6, CTCF, hyperglycaemia, localization, Brain, Protein-Protein interaction

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Mind body techniques-based amelioration of stress through neurogenic molecular mechanism

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Conflict of Interest: Kanupriya Sharma: None, Akshay Anand: None, Sonu Goel: None

Abstract

Background and Objective: Sedentariness is a cause of various lifestyle disorders, including atherosclerosis, diabetes, hypertension, and cardiovascular diseases (CVDs). Lifestyle modification by the inclusion of Yoga and similar activities has shown beneficial effects in disease prevention and psychological management. Through this exploratory controlled study, we wanted to understand the molecular mechanism through which Mind Body technique-based yoga protocol helps in amelioration of lifestyle-based disorders.

Methodology: As a non-randomized controlled study, N=60 healthy adults between the age of 18-55 years were given 3 months of Common Yoga Protocol intervention for 5 days/week and for control group N=45 healthy adults were recruited (no intervention was given). For comparison of short term and long term of yoga practice N=70 yoga trainer's were recruited for this study. Blood samples of Yoga intervention group and control group was collected at baseline, after 1 month and after 3 months and in case of Yoga trainer's blood sample was taken at one time point. Blood samples were assessed for lipid profile, and also serum assessment of BDNF, VEGF and Angiogenin was done. Yoga intervention and control group were assessed for psychological tests (, Digit Span test (DST), Trail Making Test (TMT A & TMT B) and Digit Symbol Substitution Test (DSST), General Health Questionnaire (GHQ) and stress and anxiety through STAI questionnaire at baseline and after 3 months.

Results: After 3 months, Yoga intervention group showed a significant increasing trend in BDNF, VEGF and Angiogenin with time, however control group didn't show any change with time. Yoga intervention group also showed an overall improvement in general health and a

decline in stress and anxiety score. Yoga intervention group also showed an improved executive function by showing reduced TMT B score. Also, Yoga trainer's had a significantly lower Triglycerides in comparison to Yoga intervention and control group.

Conclusion: These results show that Yoga practice in daily lifestyle can help maintain a stress-free life with improved cognition.

MCC950 modulates the SIRT3-NLRP3 inflammasome dynamics in oxygen glucose deprived stem cells

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Abstract

Stroke is the second largest cause of mortality and a significant contributor to disability globally. Stem cell treatment for ischemic stroke significantly improves functional outcomes. However, the fate of these pathways following transplantation is mostly unknown. By utilizing the NLRP3 inflammasome, the current work investigates the impact of oxidative and inflammatory pathological events related to experimental ischemic stroke (*in vitro*) on human dental pulp stem cells. Using oxygen-glucose deprivation settings, we investigated the fate of the aforementioned stem cells in the stressed micro-environment and the capacity of MCC950 to reverse the magnitudes. In hDPSC treated with OGD, we observed an increase in the expression of NLRP3, ASC, cleaved caspase1, active IL-1β, and active IL-18. Interestingly, the MCC950 dramatically decreased the activity of the NLRP3 inflammasome in OGD-treated hDPSC. In OGD group cells, oxidative stress was observed to be increased, which was successfully reversed by MCC950 supplementation. It is interesting to note that SIRT3 was reduced in the OGD treated cell while an increase in NLRP3 expression was observed, implying that these two processes are intertwined. In brief, we discovered that MCC950 inhibits NLRP3-mediated inflammation by up-regulating SIRT3.

Keywords: oxygen-glucose deprivation; human dental pulp stem cell; NLRP3 Inflammasome; SIRT3; MCC950.

Naringenin modulates oxidative stress and promotes mitochondrial perturbation in paraquat-induced parkinsonism in rats

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Abstract

Parkinson's disease (PD) is a second most neurodegenerative disease after. It ischaracterized by the progressive loss of dopaminergic neurons in the substantia nigra. Mitochondria is a prime source for generation of energy as well as free radicals and these free radicals can lead to mitochondrial damage. Mitochondrial oxidative stress and mitochondrial dysfunction has been implicated in the pathogenesis of PD. Therefore, present study determined the neuroprotective effect of NAR in alleviating the mitochondrial oxidative stress and mitochondrial dysfunction in Wistar rats. Mitochondrial oxidative stress was determined by measuring lipid peroxidation and protein carbonyl content which was found to be significantly elevated. Mitochondrial complexes were also modulated from the exposure to NAR. Our results demonstrated the remedial role of NAR in ameliorating mitochondrial dysfunctions that are modulated PQ intoxicated rats and provided support for mitochondrial-mediated neuroprotection as a putative therapeutic agent.

Keywords: Oxidative stress, Mitochondria dysfunction.

A Neural Mechanism of Malaise learning in Fruit Fly

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Abstract

In many animals, including humans, pathogens or toxin that enter the digestive system via food can trigger malaise resulting in damage to internal organs. However, the mechanisms that allow ingested toxin to be recognized by the animal and how the ingested toxin the ingested toxins trigger malaise remain to be determined. A key element of these decisions is to avoid consuming food containing toxins. Therefore, animals must weigh the potential nutritional benefits of food against the post-ingestion consequences and adapt to their experience accordingly. Learning to avoid toxin-laden food is commonly termed "conditioned taste aversion" (CTA) and heavily studies in rats. Recently progress has been made to use mice and various invertebrates such as *C. elegans* and *D. melanogaster* to study CTA. Yet the molecular and neural mechanism at play remains to be clarified. Moreover, how malaise signal reaches the brain to result in lasting avoidance of the specific taste of food/ odor of the food remains a mystery. Are other internal organs involve in the post-ingestive effects? This project will shed light on the underlying neuronal and inter-organ mediated physiological circuit during malaise learning in *D. melanogaster* by using the quantitative behavioral analysis, advanced genetics and *In-vivo* functional imaging.

The epigenetic effect of Cardiac Yoga Protocol on coronary artery disease patients and its impact on neuropsychological and molecular profile of CAD Patients

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Abstract

Background: The present study is aimed at examining the effect of Cardiac Yoga protocol in neuropsychology and molecular profile of CAD patients.

Method: This study is a randomized control trial and will be conducted at Department of Cardiology, PGIMER Chandigarh, India. Coronary artery disease (CAD) patients who will undergo coronary intervention will be recruited for the study and the control group will get usual care. Patients undergoing percutaneous coronary intervention (PCI) for CAD are eligible for the study. Cardiac patients will undergo yogic intervention (Cardiac Yoga Protocol). Total 150 participants will be recruited as for in control and intervention group. For the study Physical Yoga intervention for first 10 days will be given at PGIMER followed by online classes for 3 months and follow-up will be done till 6 months. Neuropsychological questionnaires will be administered to study participants at baseline, 3 and 6 months such as Patient Health Questionnaire-9, Generalized anxiety disorder-7, scale Social Support Questionnaire, WHO quality of life. ELISA or calorimetric assay kits will be used to estimate biochemical parameters, which are E- selectin, P-selectin, Nf-KB, V-CAM, and Aldosterone.

Outcome/Result: Yoga has been said to be associated with improvement in general health, cardiovascular risk factor prevention and other non-communicable diseases. Yoga has shown improvement in BMI, blood pressure, lipid profile, lesion progression in CAD. However, the biomolecules through which Yoga acts on body in unclear in CAD. Thus, this study investigates different risk factors of CAD. The study will aid in revealing the biomolecule that brings about the positive health effect in Yoga practitioners.

Conclusion: This study aims to identify difference at biochemical and neuropsychological levels when patients practice Yoga. The study also aimed to evaluate various biomarkers; this will aid in identification of plausible mechanism of action of Yoga in CAD. Yogic intervention will help in improving symptoms of CAD with low mortality rate. Yoga can be low cost replacement for cardiac rehabilitation.

Deciphering if Senataxin, a gene whose mutation leads to Amyotrophic lateral Sclerosis 4, may act as a genetic modifier for sporadic Amyotrophic Lateral Sclerosis and familial Amyotrophic Lateral Sclerosis.

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Abstract

Senataxin (SETX) is a large 303-kD protein that is thought to be important for RNA homeostasis and neurodegenerative disease. The functions best ascribed to SETX may be its role in 'R-Loop resolution' and in directing nascent RNA to the exosome for degradation when RNA pol II (RNAP II) collides with the DNA replication machinery. *SETX* gene mutations lead to two distinct neurological disorders that separate along clear lines of genotype–phenotype correlation. Relatively common recessive mutations of *SETX* lead to Ataxia with Oculomotor Apraxia type 2 (AOA2, OMIM: 606002). Rare, dominant mutations of *SETX* lead to Amyotrophic Lateral Sclerosis type 4 (ALS4, OMIM: 602433). ALS4 is a moderate, not fatal, juvenile-onset, familial ALS (fALS). In ALS4, the L389S and R2136H SETX mutation is of key significance. Thus, SETX joins a group of key RNA binding proteins that when mutated, cause MND, including: *TDP-43, FUS*, *SMN* and *C9orf72*. C9orf72 is unique in that the disease-associated repeat expansion is the most common cause of fALS, and toxic dipeptide repeats (DPR) are generated by RAN-translation. DPR's that contain arginine are thought to be the more toxic peptides, and possibly acting via aberrant RNA binding.

We have recently reported on the characterization of ALS4 murine models, based upon gene-targeted expression of the L389S mutation. These mice show motor deficits and characteristic TDP-43 mislocalization in MN's. In this study we seek to investigate the role of SETX as a genetic modifier in ALS as *SETX* point mutations have been identified in several sALS screens. To investigate this possibility, we have are using *SETX* transgenic (Tg) models in Drosophila that are more amenable to genetic interaction testing, *in vitro* based molecular biology approaches and transgenic mice models of ALS. Our preliminary data indicates that SETX can be a modifier of DPR toxicity of C9orf72.

Keywords: Amyotrophic Lateral Sclerosis, Sentaxin, dipeptide repeats, C9orf72, FUS, neurodegeneration.

SIRT1 activation dependent transcriptional regulation of NMDAR subunits (NR2A and NR2B)by HIPK2 in animal model of major depressive disorder

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Abstract

NMDAR is a tetrameric protein complex comprising of seven subunits having one obligatory subunit NR1, and varying numbers of a family of NR2 (NR2A-D) or NR3 (NR3A-B) subunits, with binding sites for glutamate, polyamine and glycine. One striking characteristics of NMDAR is its dynamic changes in the subunit composition, contributing to synaptic plasticity, maturation and diversity. Although it is well established that the composition of NMDAR subunit undergoes a switch from NR2A to NR2B or vice versa under different physiological condition, the molecular mechanism regulating this switch remains poorly understood. Some studies have shown the involvement of certain transcription factors like HIPK2 (Shang *et al*, 2018) and NRF1/ NRF2 (Priya *et al*, 2013) in NMDAR subunit alteration. In addition, a few findings suggest the role of acetylation and deacetylation of HIPK2 like transcription factors (Imamura *et al*, 2016; Park *et al*, 2014) and thereby advocating a significant role of SIRTUIN family deacetylases in this process.

SIRT1 is the most aploused sirtuin family NAD+ dependent histone deacetylase member. It performs cytoprotective function by mediating deacetylation of certain histones and non histones. Homeodomain-interacting protein kinase 2 (HIPK2) is a serine/threonine kinase which regulates tumorigenesis, DNA damage, tissue fibrosis and neural development. Recently, it has been reported that HIPK2-JNK-c Jun signaling pathway regulates the subunit composition of NMDAR subunit GluN2B to GluN2A in post natal brain by transcriptional control of *Grin2a* and *Grin2c* genes. Besides, HIPK2 mediated increase in NR2A via ERK-CREB activation is also considered responsible for prosurvival mechanism. Importantly, it is suggested that SIRT1 deacetylates HIPK2 which promotes survival and proteasomal degradation of HIPK2 in HEK293 cells (Hwang *et al*, 2013). Thus, there appears to be a molecular association between SIRT1-HIPK2-downstream signalling pathways

Major depressive disorder (MDD) is a chronic and life threatening mental disorder which increases the risk of cardiac dysfunction, cerebrovascular disease or could be lethal due to possibility of suicide. It produces greatest decrement in health when compared to diseases like diabetes and arthritis and in spite of the availability of a number of antidepressant medication and psychotherapy; it suffers a huge treatment gap worldwide. Some reports have suggested the involvement of NMDAR signaling in the pathophysiology of MDD. Thus, molecular mechanisms involving NMDAR system could be used as a promising therapeutic target for development of more effective therapies for MDD. In this regard, as SIRT1 activation is considered neuroprotective, it could also serve as a therapeutic target in case of depression as well, however, cellular and molecular basis of this effect needs to be understood in suitable

depression models.

Keywords: SIRT1, NMDAR, HIPK2, Resveratrol, Depression.

Acknowledgement: This work was financially supported by CSIR RA award to Dr. Archita Khanna.

Understanding the proteomic signature responsible for the Vitamin D3-mediatedrestoration of spatial memory in a mouse model of Huntington's disease.

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Abstract

Huntington's Disease (HD) is an autosomal dominant neurodegenerative disorder characterized by the presence of expanded polyglutamine (CAG repeat) sequence in the huntingtin protein. HD exhibits unique phenotypes, including motor coordination dysfunction, movement impairment, cognitive decline, and behavioral deficits. The selective vulnerability of the medium spiny neurons in the striatum brain region in HD is mainly responsible for motor deficits and slowly targets the cortical neurons atrophy, causing cognitive and memory decline. In spite of the widespread expression of mutatedhuntingtin, HD has long been considered primarily a disease of the striatum. In this regard, Vitamin D3 (VD) administration is documented recently by Manjari *et al*., 2022 to rescuethe advent of motor symptoms in 3-nitropropionic acid induces (3-NP) induced mouse model of HD. Other behavioral tests have also confirmed the rescue effect of HD symptoms. Here, we want to elucidate the downstream molecular repertoire responsiblefor the improvement in the motor activity and spatial memory dysfunction observed in ourstudy. The spectrum of pathophysiological symptoms in HD indicates underlying complex signaling events. To understand its underlying mechanism, quantitive proteomics using different brain regions, namely the striatum, cortex, and hippocampus will be implemented which will enable us to identify modifier proteins controlling HD-related pathophysiology.

Neuroprotective role of daidzein, a phytoestrogen in rotenone-induced Parkinson's Disease

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Abstract

Objective: A task as simple as picking up a glass of water to quench your thirst can become an arduous one to a person plagued with Parkinson's disease (PD). A progressive degeneration of dopaminergic neurons within the substantia nigra (SN) that causes one to lose control over their voluntary and involuntary movements, describes this disease. Current pharmacological treatments for this debilitating disorder focus on improving dopamine availability despite the side effects of long-term usage. Over the last decade, oxidative stress mediated pathways leading to neurodegeneration have been associated with its pathophysiology. Natural plant antioxidants have been shown to mediate the oxidative stress-induced effects in PD, which has gained considerable attention in both in vitro and in vivo studies. Daidzein (DZ), a naturally occurring isoflavone, is found in a large spectrum of foods, and can be specifically derived fromplants like soy and dietary-based supplements. This phytoestrogen is a non-steroidal compound that exerts antioxidant, immunomodulatory roles as well as shows effect in cardiovascular disorders, osteoporosis, and ischemic stroke by promoting neuronal regeneration. In this study, the neuroprotective potential of DZ was assessed against rotenone-induced pathophysiological alterations. Rotenone, an environmental neurotoxin,is a risk factor in PD.

Materials and Methods: In this study, rats were subjected to stereotaxic bilateral injection of rotenone (12µg/µl) within the substantia nigra, n=10 followed by oral treatment with DZ (5, 10, 20 mg/kg) for 30 days.During the study, neurobehavioural studies including Rota-rod, Open field test, and Barnes maze test (BMT) were conducted. At the end of 30 days, the midbrain tissue samples were used for biochemical analysis including antioxidant (Reduced glutathione, superoxide dismutase, catalase, and lipid peroxidation) and inflammatory (TNF-α) parameters; immunohistochemistry for TH positive neurons and Glial Fibrillary Acidic Protein (GFAP), and analysis of mitochondrial complex I activity observing Mitochondrially Encoded Cytochrome C Oxidase I (MtCO1/COX1) gene expression.

Results: A significant amelioration in the motor deficits by DZ was observed that can be attributed to the protection of TH positive neurons from degenerating. Biochemically, the oxidative stress and inflammation triggered by rotenone was significantly diminished by DZ. Also, DZ prevented the inhibition of Complex I as evident by a significant increase in the complex I activity and upregulation of MtCO1/COX1 gene expression as compared to diseased group.

Conclusion & future scope: The preliminary results thus firmly advocate the neuroprotective potential of DZ to prevent rotenone-induced neurotoxicity in rats. This phytoestrogen can be formulated and developed into an effective supplement and/or drug for the management of PD by enhancing its biodistribution in thebrain.

Keywords: Daidzein, Rotenone, Parkinson's Disease, Neuroprotection, Barnes Maze Test

Peripheral neuropathy in alcohol use disorder patients: Exploring the role of oxidativeand nitrosative stress pathway.

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Abstract

Background: Alcohol, a commonest psychoactive substance consumed across the globe is known to enhance the risk of developing a number of neurological complications. Of these, peripheral neuropathy is the most common neurological complication of alcohol use disorder (AUD). However, the underlying mechanisms leading to peripheral neuropathy in AUD are inadequately understood.

Aims: To examine the role of oxidative and nitrosative stress (O&NS) pathway in causing peripheral neuropathy in patients with AUD.

Methods: In this prospective study, 57 patients fulfilling the Diagnostic and Statistical Manual of Mental Disorders (5th edition) criteria for AUDs were recruited. Approximately 10 ml. of peripheral blood was collected to separate the plasma, sera and peripheral blood mononuclear cells (PBMCs). RNA was isolated from PBMCs (QiaAmp Blood Mini RNA isolation kit) and converted to cDNA (TAKARA Prime Script cDNA kit). Sera of the recruited study participants were used for estimation of lipid peroxidation [TBARS kit (Thiobarbituric Acid Reactive Substances)], catalase (CAT) activity, superoxide dismutase (SOD) activity, total nitrate metabolites (TNM) and total antioxidant (AO) content. Plasma was used to assay glutathione peroxidase activity (GPX). In addition, quantification of lymphocyte expression of *Sod1, Sod2, Cat* and *Gpx* genes was carried out. The results were compared with that of 21 healthy subjects. Non parametric analysis using the Wilcoxon signed rank test was performed to compare the median group differences, pairwise, of redox markers such as TBARS, AO, CAT, GPX, SOD and TNM among the groups.

Results: All the recruited subjects were males. In the AUD group, 29 participants had neuropathy (AUD-NP, mean age=44.14±7.7 years), and 28 participants did not have evidence of neuropathy (AUD-NNP, mean age=37.53±8.03 years). They were matched for age with the healthy controls (mean age=37.47±8.97 years). There was no statistically significant difference observed between the group medians. However, non-parametric pairwise analysis revealed

significant group differences for the lipid peroxidation levels in serum between the AUD-NP and AUD-NNP groups where the median of AUD-NNP (11.13) was significantly higher than AUD-NP (7.90) (Z= -0.64, p=0.004). Besides this, the contents of AO, CAT, and GPX appeared to be lower in the AUD-NP group as compared to the AUD-NNP group, while the TNM levels were higher in the AUD-NP than that of AUD-NNP. Additionally, the CAT gene expression in AUD-NNP (1.06) was reduced as compared to the healthy control group (1.02) (Z= -1.82, p=0.06). Pairwise comparison between healthy controls and AUD-NP groups revealed a significant difference in the gene expression pattern of SOD2, with the median values being significantly reduced in the AUD-NP (0.87) as compared to the healthy control group (0.94) (Z= -2.68, p=0.007).

Conclusion: The present study provides evidence towards a defective antioxidant defence mechanism in AUD subjects who develop peripheral neuropathy. The elements of O&NS pathway might serve as important signatures for identifying AUD patients, likely to develop peripheral neuropathy.

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A Comparative Study of VEMP and vHIT IN Vestibular Migraine and Other Variants of Migraine

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Abstract

Introduction: Vestibular migraine is considered to be the second most common cause of vertigo and the most common cause of spontaneous episodic vertigo, presenting to physician, neurologist and otolaryngologist. The pathophysiology is not fully understood.

Objective: To analyse the results of Vestibular Evoke Myogenic Potential (VEMP) and Video Head Impulse Test (vHIT) in patients with vestibular migraine [VM] versus other variants of migraine [M] in comparison to normal controls [N].

Methodology: A case control study of 8 months duration (December 2021- July 2022) was performed in 30 individuals. VEMP and vHIT was performed in 30 individuals (n=30; 10 patients with VM, 10 subjects with M and 10 control subjects [N]). oVEMP and cVEMP was performed at 95 dB Nhl for clicks and tone burst ;latency of P1 and N1 waves were recorded and P1-N1(peak to peak) amplitude was analysed. vHIT was similarly performed in the above groups and the gain values for laterals, RALP and LARP were compared among the groups.

Results: In oVEMP (95 dBnHL/click) the mean latency for P1 and N1 waves was 18.33±3.14 msec (VM group), 17.47±3.57 msec (M group) and 15.85 ±3.27msec (N group) respectively, showing significant difference ($p<0.05$) between VM and N. No significant difference was found for latency of P1 and N1 waves (TB) and P1-N1 amplitude (95 dBnHL/ click and tone burst) between the groups in oVEMP.

In cVEMP, no significant difference was found between the groups, considering the mean latency of P1 and N1 peaks, both for click and tone burst ($p>0.05$). ANOVA showed a significant difference in latency between all the groups with respect to the stimulus (click/tone burst) and the ears. But for P1-N1(95 dBnHL/click and tone burst) amplitude significant difference was found between VM and N (22.90±8.07µv versus 36.55±26.05µv for click) and (29.42±13.19µv versus 40.56±19.27µv tone burst). No significant difference was found between the VM and migraine group.

In vHIT, the mean VOR gain for VM group mean gain in RA is significantly greater in VM than N group (1.05±0.19 and 0.95 ±0.11 respectively, $p<0.05$), but not with M group.

Conclusion: We conclude that both the saccule and utricle are affected in vestibular migraine as well as those suffering from other variants of migraine. Though VEMP result was significantly different between VM and normal control, no differences was found between the VM and migraine group. Abnormal results of VEMP study in both VM and migraineurs

shows involvement of the vestibulo-collic pathway. vHIT does not seem to contribute in diagnosing or differentiating VM from M. The study will be continued to ascertain whether increased vHIT gain in one canal can be a marker of vestibular migraine. The results from this study would help in clinical diagnosis of Vestibular migraine and its differentiation with Migraine and help the clinicians in analysing the extended effect of CSD on the vestibular system and its different pathways. The limitations of the study were small number of participants which might represent the effects of pathophysiological symptoms clinically but might not be able to represent it statistically.

Effect of cardiovascular risks on Brain Structure Volumetry with Aging in Cognitively Normal, Mild Cognitive Impairment and Dementia Patients : Advanced Neuroimaging Investigations in ADNI Cohort

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Abstract

The human brain undergoes inevitable structure and functional changes with aging. The subtle brain structure changes during the course of normal aging overlap to a large extent to the brain volumetric and surface changes associated with cognitive impairment and dementia. Aging associated brain health changes may get altered manifold with comorbid cardiovascular risks such as diabetes and hypertension. Here, we have investigated effects of diabetes and hypertension on brain structure morphometry and brain functional connectivity, and cognition in cognitively normal, impaired and dementia cohorts of Alzheimer's Disease Neuroimaging Initiative (ADNI) study.

Brain segmentation was performed on T1, T2, T2-FLAIR MR images to determine the volume of brain structures and White matter hyperintensity (WMH) load using Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort with a total of 5102 longitudinal-MRI scans. Changes in the different brain structure volumes with age were investigated across Cognitively normal (CN), Mild Cognitively Impaired (MCI), and Dementia(AD) groups. Multivariate analysis using inhouse developed methods in R and Python were performed to understand the association of change in structural volumetry and cerebrovascular risk factors in different cognitive groups.

Subjects with hypertension showed a significant increase in the WMH load with age compared to normotensive subjects across all three groups i.e CN, MCI and DM. The rate of increase of WMH load with age is significantly higher in CI and AD subjects compared to CN. However, subjects with only diabetes had similar kinetics associated with brain volumetric changes with aging across CN, MCI, and dementia cohorts compared with non diabetic and normotensive subjects. However, diabetes and hypertension have additive effects on increase in cerebrospinal fluid volume(CSF) and loss in white matter with age.

Concurrent occurrence of diabetes and hypertension has a profound effect on WMH increase and ventricular hypertrophy with aging than isolated events of hypertension or diabetes.

Keywords: White Matter Hyperintensity, Aging, Cognition, Cerebrospinal fluid, Diabetes, Hypertension

Traumatic brain injury leads to acute changes in systemic metabolism in rats

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Abstract

Traumatic brain injury (TBI) leads to neurological disability with neuro-endocrine response and altered systemic physiology. A bi-directional brain-systemic interaction helps in maintaining physiological function while stressors or trauma can lead to relocation of metabolic substrates to aid in increased energy demands and stress adaptation. Therefore, the study involved assessment of serum and urine metabolomics in the injured rats along with serum corticosterone levels. Rats were subjected to weight-drop injury using modified Marmarou's weight drop injury model to induce both mild and moderate injuries. The samples including serum and urine were collected post injury 4 hours. Serum and urine metabolomics was performed using NMR spectroscopy. The serum and urine metabolites showed classifying metabolites that helped distinguished control rats from the injured rats. Finally, the study indicates that TBI leads to systemic metabolic dysregulation with altered serum and urine metabolic fingerprint of the injured rats. The TBI associated alteration further strengthens the knowledge of diagnostic markers and help distinguish injury related outcomes after TBI.

Neuronal Correlates of effects of Sleep deprivation induced Neuroinflammation on Fear Extinction Memory Consolidation

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Abstract

Sleep deprivation is biological stress that leads to a cascade of neuroinflammatory responses. It is still unclear how sleep deprivation induced immune dysregulation leads to chronic inflammatory conditions eventuating in immunological, metabolic, endocrine, and psychiatric disorders. We hypothesized that total sleep deprivation (TSD) for 48 hours will induce microglial mediated neuroinflammation via TLR4 receptor and antagonism of Adenosine A1 receptor may rescue neuroinflammation induced impairments on Cued fear extinction memory recall.

Animals were randomized into 3 groups; Cage Controls (CC), TSD+Vehicle (20% Dimethyl Sulfoxide), and TSD+ 8-Cyclopentyltheophylline (8-CPT; Adenosine A1 Receptor Antagonist, 10mg/kg, twice daily - morning and evening). We used our lab- custom-designed automated rodent sleep deprivation system to deprive male Sprague Dawley rats (n=5, 8 to 10 weeks old) of total sleep for 48 hours after the Cued fear extinction training on day 2 (74.37±2.43, $p<0.001$) of cued fear conditioning paradigm. Statistical analysis of data was done using appropriate ANOVA measures and Tukey's and Bartlett's multiple comparison tests were used for post-hoc analysis.

It was observed that 48h TSD impaired extinction memory recall (100.3±2.43, $p<0.001$) whereas, 8-CPT administration ameliorated the cued fear extinction recall (69.23±2.37, $p<0.01$). This implied that 8-CPT improved TSD induced impairment of memory recall. Immunohistochemical analysis showed increased co-expression of TLR4 (22.08±2.35, $p<0.03$) with Iba1 (no.of. activated microglia) (11.14±1.76, $p<0.04$) and increased expression of neuroinflammatory markers like IL1β (16.05±2.18, $p<0.01$), phospho-NFκB (15.84±2.04, $p<0.03$), TNFα (10.86±1.72, $p<0.01$) in the dorsal hippocampus of TSD animals as compared to CC. Decrements in expression were found in synaptic plasticity markers like PSD-95 (20.84±2.94, $p<0.02$) and synaptophysin(21.27±1.98, $p<0.001$) in TSD animals as compared to CC. These results correlate with the detrimental effect of TSD on extinction memory recall. Sleep recordings showed that NREM and REM sleep was reduced in TSD+8-CPT animals as compared to CC and TSD. However, we scored rat sleep EEG differentiating N1 and N2 stages of sleep. We found that the N1 sleep stage (delta waves less than 50% of 10s epoch) significantly increased post 8-CPT administration compared to SD treatment.

In conclusion, we present data on microglial mediated neuroinflammation triggered by TSD. Our findings enable a better understanding of receptor biology of neuroinflammation induced by TSD in rodents Antagonism of Adenosine A1 receptor rescues neuroinflammation and synaptic plasticity. Our study recognizes Adenosine A1 receptor as a therapeutic target for pathological conditions of memory recall impairments.

Keywords: Total Sleep Deprivation- Neuroinflammation – Fear Memory – Synaptic Plasticity – Adenosine A1 Receptor

Effect of methyl paraben on serotonin levels governing autistic behavior in zebrafish larvae.

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Abstract

Autism Spectrum Disorder (ASD) develops during childhood and persists throughout adulthood and causes complicated neurodevelopmental disorder. Serotonin has an important role in brain development. The altered serotonin levels were found in the ASD patients, which indicates that the serotonergic system plays a role in phenotypes related to autism. Though serotonin is recognized for its role as a neurotransmitter, it is produced mostly in the gastrointestinal tract which accounts for > 90% of serotonin level in the body.Autism spectrum disorder (ASD) disturbs communication and behavior during development. The symptoms normally appear in the first two years of life and can be diagnosed at any age. People with ASD have difficulties with communication and social behavior, constricted interests, and symptoms that harm the person's capability function properly in his/her life. Although genetics plays a crucial role, evidence suggests that environmental chemicals increase the risk of ASD. Endocrine Disrupting Chemicals (EDCs) disrupt homeostasis by altering the endogenous hormone activity during early stages of development leading to neurological abnormalities. It causes significant effects on public health which was observed from human clinical observations, results from animal models and epidemiological studies. The direct exposure of the offspring after birth or hatching to EDCs cause risk to the developing organism. When the mother is exposed to chemical at any time in her life before giving birth to offspring the chemicals get accumulated in body fat, which gets transferred to offspring during pregnancy and lactation, which is known as transgenerational exposure. Neurobehavioral toxicity of EDCs was determined from thyroid hormones serving as a key factor for behavioral outcomes. One such EDC is methyl paraben.Being highly social organisms, for studying neuropharmacology with increasing applications in understanding of brain syndromes and in finding new treatments. Since zebrafish offer numerous logistical and economic advantages over mammalian models, it has been used as a model for a variety of shortfalls related to ASD and other neurological disorders.. In this proposed work, zebrafish embryos were exposed to sub-lethal

concentrations of Methyl Paraben and behavioral changes such as anxiety and depression were observed. Overexpression of several genes such as SHANK3, PTENA, NRXN1a and NLGN3a were also found in the exposed groups. It was concluded that dysregulation of genes involved in brain morphogenesis reduces the levels of ACHE and serotonin activity inducing autistic spectrum behavior.

Keywords: Autism Spectrum Disorder, methyl paraben, EDC, Zebrafish Embryo.

Acute Dexamethasone Exposure Induces Developmental Toxicity and Alters Antioxidant Enzyme Activity in Zebrafish Embryo

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Abstract

Dexamethasone is a glucocorticoid molecule that possesses anti-inflammatory and immunosuppressive properties and is often employed in the therapeutic care of neurological illness but it may cause adverse effects in the developing foetus. Vitamin C that has antioxidant and neuroprotective properties may help attenuate the adverse effects of dexamethasone. The primary objectives are to check for developmental toxicity and track changes in antioxidant enzyme activity in dexamethasone exposed zebrafish embryos while simultaneously studying the attenuated effects of vitamin C. Zebrafish embryos were exposed to Dexamethasone (Dex) and Vitamin C (VC) in concentrations: 2µM Dex, 2µM Dex + 100µM VC, 2µM Dex + 200µM VC, 4µM Dex, 4µM Dex + 100µM VC and 4µM Dex + 200µM VC for 96 hours post fertilization (hpf). During exposure, hatching rates, heart rates and body malformations along with body length and head size were determined, followed by evaluation of apoptotic activity, neurobehaviour, and antioxidant activity. Statistical analysis was done using GraphPad Prism software. Dexamethasone exposure showed delayed hatching, heart rate and developmental deformities like pericardial edema, bent spine and revealed anxiety-like behaviour as well as stress, which was confirmed by suppression of Acetylcholinesterase (AChE) activity. Increase in apoptosis, alterations in antioxidant enzyme activity were observed which were restored by Vitamin C. In this study, Dexamethasone showed delayed hatching, decreased heart rate compared to control along with body deformities. The exposed larvae developed elevated levels of anxiety and stress, as well as impairment in memory and recognition. The Alcian blue staining results demonstrate that exposed larvae have signs of microcephaly, which leads to cognitive impairment, and the Acridine orange staining results exhibits increased apoptotic activity in the head region of exposed larvae. The result of acetylcholinesterase assay indicates

that the enzyme activity was significantly reduced in the exposed groups indicating dysregulation in the cholinergic system due to accumulation of acetylcholine in the synapse. The reduced acetylcholinesterase activity supports the results of behavioral endpoints observed in zebrafish. The antioxidant enzyme activity of SOD, CAT, GST and GPx was reduced after exposure to dexamethasone, whereas lipid peroxidation was increased, indicating the increase in oxidative stress. It demonstrates that Dexamethasone causes oxidative stress, and that Vitamin C, which has antioxidant characteristics, has restorative qualities.With the help of the various assays performed, we believe that zebrafish larvae exposed to Dexamethasone at the early stage, suffer from severe developmental toxicity, neurobehavioural abnormalities and antioxidant enzyme activity alterations which can be successfully attenuated with Vitamin C supplementation.

Keywords: Dexamethasone, Vitamin C, Zebrafish embryo, Developmental toxicity, oxidative stress.

Acute Dexamethasone Exposure Induces Developmental Toxicity and Alters Antioxidant Enzyme Activity in Zebrafish Embryo

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Abstract

Dexamethasone is a glucocorticoid molecule that possesses anti-inflammatory and immunosuppressive properties and is often employed in the therapeutic care of neurological illness but it may cause adverse effects in the developing foetus. Vitamin C that has antioxidant and neuroprotective properties may help attenuate the adverse effects of dexamethasone. The primary objectives are to check for developmental toxicity and track changes in antioxidant enzyme activity in dexamethasone exposed zebrafish embryos while simultaneously studying the attenuated effects of vitamin C. Zebrafish embryos were exposed to Dexamethasone (Dex) and Vitamin C (VC) in concentrations: 2µM Dex, 2µM Dex + 100µM VC, 2µM Dex + 200µM VC, 4µM Dex, 4µM Dex + 100µM VC and 4µM Dex + 200µM VC for 96 hours post fertilization (hpf). During exposure, hatching rates, heart rates and body malformations along with body length and head size were determined, followed by evaluation of apoptotic activity, neurobehaviour, and antioxidant activity. Statistical analysis was done using GraphPad Prism software. Dexamethasone exposure showed delayed hatching, heart rate and developmental deformities like pericardial edema, bent spine and revealed anxiety-like behaviour as well as stress, which was confirmed by suppression of Acetylcholinesterase (AChE) activity. Increase in apoptosis, alterations in antioxidant enzyme activity were observed which were restored by Vitamin C. In this study, Dexamethasone showed delayed hatching, decreased heart rate compared to control along with body deformities. The exposed larvae developed elevated levels of anxiety and stress, as well as impairment in memory and recognition. The Alcian blue staining results demonstrate that exposed larvae have signs of microcephaly, which leads to cognitive impairment, and the Acridine orange staining results exhibits increased apoptotic activity in the head region of exposed larvae. The result of acetylcholinesterase assay indicates that the enzyme activity was significantly reduced in the exposed groups indicating dysregulation in the cholinergic system due to accumulation of acetylcholine in the synapse. The reduced acetylcholinesterase activity supports the results of behavioral endpoints observed in zebrafish. The antioxidant enzyme activity of SOD, CAT, GST and GPx was reduced after exposure to dexamethasone, whereas lipid peroxidation was increased, indicating the increase in oxidative stress. It demonstrates that Dexamethasone causes oxidative stress, and that Vitamin C, which has antioxidant characteristics, has restorative qualities.With the help of the various assays performed, we believe that zebrafish larvae exposed to Dexamethasone at the

early stage, suffer from severe developmental toxicity, neurobehavioural abnormalities and antioxidant enzyme activity alterations which can be successfully attenuated with Vitamin C supplementation.

Keywords: Dexamethasone, Vitamin C, Zebrafish embryo, Developmental toxicity, oxidative stress.

Human Brain Detects and Responds Against the Filarial SERPINS; A Way Forward Towards Theragnostic of Neuropathies

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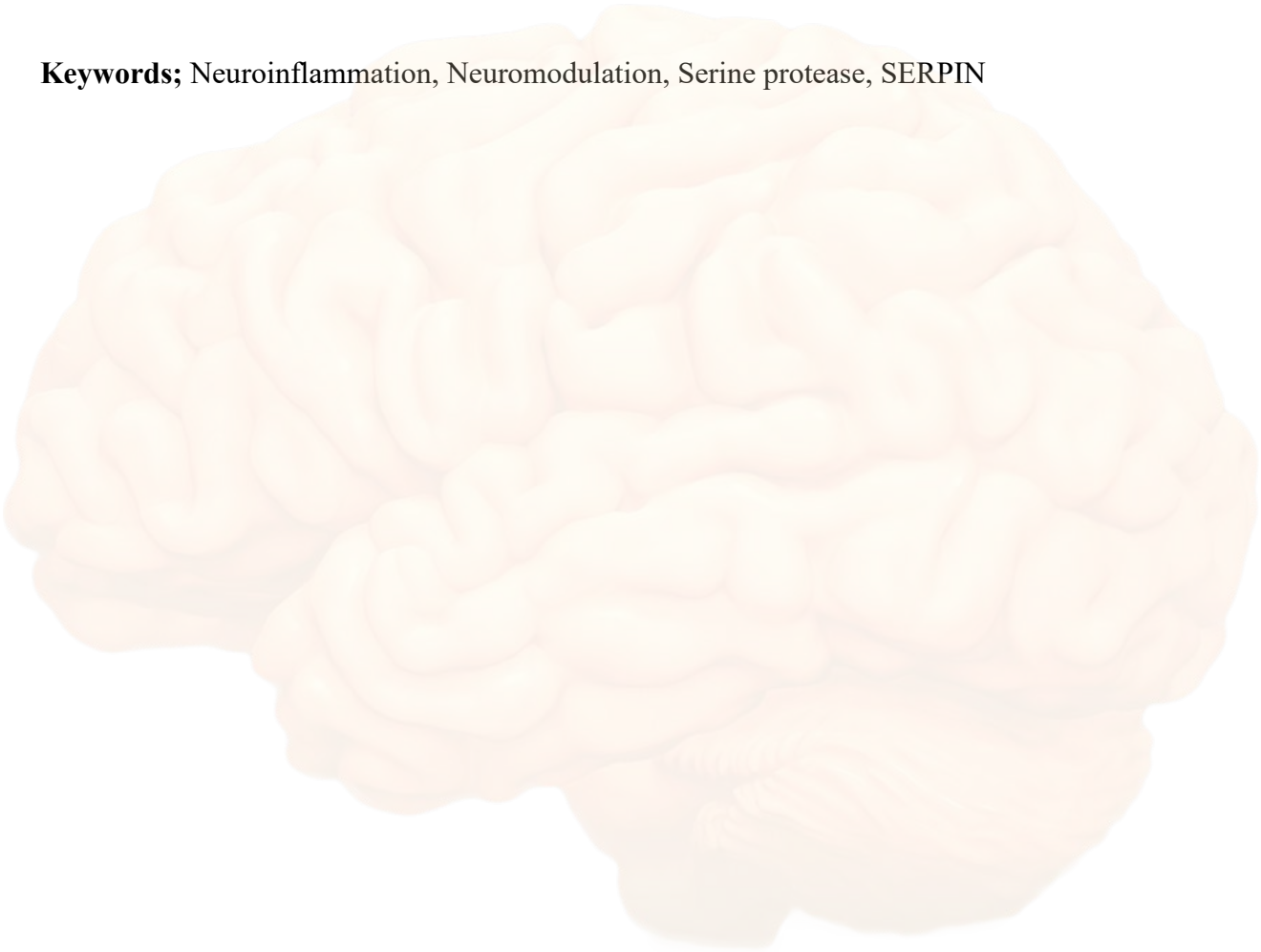
Abstract

Microglia are the resident brain macrophages that exerts both protective and detrimental effects in brain when challenged by various pathogenic stimuli. Their neuroprotective mode includes clearing of apoptotic cells, release of neurotrophic factors and growth hormones, while detrimental efforts include production of large number of proinflammatory cytokines like tumor necrosis factor α (TNF-α), IL-6, and IL-1β, reactive oxygen species (ROS) and excitotoxins, including glutamate depending on the microenvironment characteristics. Notably, the microglial activation and response to any pathogenic insult is often regulated by release of serine proteases thrombin, lactoferrin (LTF), C1r-Like Serine Protease Analog Protein(C1rl) urokinase-type plasminogen activator (uPA), and tissue-type plasminogen activator (tPA), Serine Protease 2 (PRSS2) etc. Thus, these serine proteases are known to play significant roles in microglia-dependent neuro-modulation.

Recent studies on large-scale proteomic analysis to identify the excretory-secretory (ES) products of the L3 stage using cDNA sequence analysis of Wuchereria bancrofti, Brugia malayi, Onchocerca volvulus revealed the presence of immunogens like Wb123 and OV16 which belongs to serine protease inhibitor (SERPIN) family and BM33 which belongs to aspartic protease inhibitor (Aspin) family. However, their exact role in filariasis induced neuroinflammation and neuropathies is still ambiguous. In this study, we investigated the role of these filarial SERPINS in brain invasion and neuroinflammation. Therefore, using in-silico based study, we selected few of serine proteases which are highly expressed in microglia using Allen Brain Atlas and RNA sequencing data from diseased brain. Further, we performed in-silico docking analysis of these filarial SERPINS to specific serine proteases using HADDOCK to identify the critical interactions. Additionally, we have cloned and purified the filarial SERPINs and studied their physical

interaction with microglia-specific serine proteases (MsSPs), including PRSS2 in-vitro using microscale thermophoresis (MST). In parallel experiments, we have also cloned and expressed other MsSPs to investigate their biophysical interaction with filarial SERPINEs. Since PRSS2 is a known neuroprotectant secreted by activated microglial cells, we assume targeting their inhibition in microglia cells by filarial SERPINS may lead to breaching of immunomodulatory responses in vitro. Overall, our study would unravel the one of the possible mechanisms underlying filariasis-induced neuropathologies. As a part of ongoing work, in near future, we are developing novel strategies for utilizing filarial SERPINS for theragnostic of neuropathies.

Keywords; Neuroinflammation, Neuromodulation, Serine protease, SERPIN



Role of lncRNA Gm20559 in flaviviral infection and associated inflammation in microglia

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Abstract

Long non-coding RNA (lncRNA) are a group of RNA molecules which are longer than 200 nucleotides in size. Research has shown that the expression of many lncRNAs is misregulated in case of various diseases. Previous reports from the lab have already shown role of many microRNAs (another class of non-coding RNA) in case of flaviviral infections. We wanted to learn about the lncRNA profile in Japanese Encephalitis infection of microglia, in order to achieve that RNA sequencing of JEV-infected N9 microglial cell sample and uninfected cells was done. Sequencing revealed dysregulated expression of many lncRNAs due to the infection. Gm20559, one such lncRNA showed a considerable amount of fold change in infected cells. Increase in expression of Gm20559 in JEV-infected N9 was also associated with an upregulation of many proinflammatory cytokines (IFN-α, IFN-β, IFN-γ, IL-6, IL-1β, IP-10), chemokines (MCP-1), interferon stimulated genes (ISG) (RIG-1, OAS-2) as well as viral replication as checked by qPCR. Similar results were also obtained in case of West Nile Virus (WNV) infected-N9 cells. Upon inhibiting Gm20559 there was a sharp reduction in the expression of proinflammatory cytokines, chemokines, ISGs and viral replication in both JEV and WNV-infected N9 microglia cells. More experiments are required to decipher the role of Gm20559 in modulating inflammation in case of both JEV and WNV infection. We also have to check the different inflammatory pathways that are involved in Gm20559-mediated infection in both JE and WNV at protein level. Further investigations aimed at deciphering effect of Gm20559-regulated inflammation upon neuronal physiology requires studying neuronal cells treated with N9 secretome (in the context of Gm20559 inhibition) thus shedding insight into microglia-neuronal crosstalk evident during flaviviral infections.

Keywords: lncRNA, inflammation, knockdown, cytokines, viral replication

Post synaptic density 95 (PSD95)–Actin interaction: A critical regulator of synaptic strength and plasticity.

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Abstract

PSD95 serves as a scaffolding protein to several neurotransmitter receptors, signal transduction components, and adhesion molecules. It is a potential regulator of synaptic strength and plasticity by regulating glutamatergic receptor trafficking. PSD95 interacts directly with NMDA receptors while the interactions with AMPA receptors are through an auxiliary subunit TARPs. Actin cytoskeleton is highly enriched at the synapse. However, PSD95-actin interaction at the synapse is remaining unclear. Therefore, we tried to investigate the critical role of PSD-95 association at the synapse with actin, AMPA and NMDA receptors using AD mice. Here, we isolated the synaptosomes and performed immunoprecipitation. PSD95 association is detected with actin in synaptosomes isolated from adolescent and middle aged WT and APP/PS1 mouse brain cortex. We found that PSD95-actin association is significantly decreased in middle aged APP/PS1 mice compared with WT while it remains unaffected in the F-actin fraction of synaptosomes in APP/PS1 mice. We could also found out that the Intrathecal injection of an actin stabilizing agent, Jasplakinolide could rescue the fear memory, restore the reduced association and synaptic F-actin levels in APP/PS1 mice. The association of PSD-95 with both AMPAR and NMDAR subunits were detected and the association with only GluA1 subunit is affected in middle aged APP/PS1 mice. Interestingly, interaction of NMDAR subunits (GluN1 and GluN2B) with PSD-95 is greatly enhanced at adolescent APP/PS1 mice even though these subunit protein levels are significantly diminished. Thus, our results suggest the role of PSD-95 as a crosslink between glutamatergic receptors and actin filaments. We conclude that altered PSD-95 – actin interaction may have critical implications in glutamatergic neurotransmission, synaptic strength and plasticity.

Are claudins involved in synapse function in vertebrate neurons?

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Abstract

Claudins belong to a class of cell adhesion molecules and form major structural components of tight junctions in vertebrates. Conventionally, they are known to play a crucial role in maintaining the permeability of various cellular barriers such as epithelial cells tight junctions, and the blood-brain barrier. They are known to be conserved across phyla. The structure of the claudin proteins allows them to interact with other non-tight junction proteins such as actin cytoskeleton, Ephrins, EpCAM which makes us wonder if they might have other non-canonical roles to play as well. A few recent studies have shed some light on the presence of claudins in neurons as observed by their increased
expression in the brain of Alzheimer's and vascular dementia patients. Recent research has also suggested a link between claudin depletion and several neurological disorders like schizophrenia, ADHD, and autism. Studies on model organisms such as *C. elegans* have provided evidence for their role as a signaling molecule at the synapse. However, their role in neurons is still poorly understood. We have examined the expression of 24 mammalian claudins in primary cortical neuronal cultures by using reverse transcription-PCR and compared the expression at two developmental time points, namely days in- vitro (DIV) 7 and 14. Since spine density and dendritic arborization increase from DIV 6 onward, and the functional GABA switch from excitatory to inhibitory occurs around DIV 14, studying these time points can give us insights into whether claudins play a role in neuronal development and synaptogenesis. We are currently working to knock down specific claudins, and we will be examining how this affects synapse structure and functions. In this presentation, I will try to explain claudin knockdown affects on neurons and synaptic function.

Molecular analysis of the pathophysiology and virulence determinants of *Burkholderia pseudomallei* from Neuromelioidosis patients in Indian setup.

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Abstract

Melioidosis is a potentially life-threatening, emerging infectious disease caused by *Burkholderia pseudomallei. Burkholderia pseudomallei* is a gram-negative saprophytic bacterium typically found in subtropical and tropical environments with approximately 165,000 human Melioidosis cases reported per year worldwide, and 89,000 (54%) of those cases resulting in mortality. Melioidosis can be acute or chronic, bacteremic or non-bacteremic, and localized or disseminated. *Burkholderia pseudomallei* is an opportunistic, facultative intracellular organism, that causes CNS abnormalities that may lead to **Neuromelioidosis** mimicking Guillain-Barre syndrome, aseptic meningitis, or brain-stem encephalitis. Neuromelioidosis currently is reported to be 3-5% of Melioidosis cases with a 25% mortality rate worldwide. The pathogenesis, host-pathogen relationship, virulence determinants, and genetic variability of Neuromelioidosis causing strains are yet unknown.

Methods: *Burkholderia pseudomallei* strains were isolated from patient samples with and without CNS involvement. Phenotypic, microbiological characterization, and genotypic characterization were performed. We analyzed the risk factors, virulence factors, antimicrobial resistance, phylogenetic parameters, genotypic diversity, and population dynamics of these bacterial strains. We plan to perform *in vitro* studies in neuronal cell lines to determine the factors behind the etiology of Neuromelioidosis.

Results: CNS manifestations aided by radiographic/MRI findings and clinical presentations like fever, headache, seizure, cranial nerve palsies, altered sensorium, and limb weakness were considered to differentiate neuromelioidosis strains isolated from blood, body fluid, and CSF. Different strains exhibit different growth traits and biofilm-producing capacities. Whole genome analysis data indicate the novelty of strains specific to the Indian sequence type in terms of the mutation, presence of genomic islands, and virulent factor genes. These findings might lead to further development of diagnostic toolsor vaccine development.

Keywords: Neuromelioidosis, Melioidosis, India, Genome Island, Virulent factors, vaccine candidates, mortality,Bioterrorism.

Characterizing the antidepressant potential of RXFP3 agonists in mice and rats

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Abstract

Depression is a highly prevalent disorder which causes debilitating mental health symptoms, and is also a large burden on healthcare resources within India and the rest of the world. Current antidepressant drugs mostly act on the arousal system by increasing the synaptic levels of the neurotransmitters serotonin and/or noradrenaline. RXFP3 (Relaxin Family Peptide 3 Receptor) is a neurotransmitter receptor expressed within the brain, and is an exciting target for the development of novel antidepressant drugs as Relaxin-3/RXFP3 system acts on the arousal system in a parallel pathway. For example, rodent studies have shown that drugs which active RXFP3 (agonists) reduce anxiety and display other antidepressant-like actions. However, these early versions of RXFP3 agonists have required direct brain injection, as they do not cross the blood brain barrier (BBB). This approach is associated with a range of problems, such as the need for surgical implantation of a guide cannula, and uneven drug distribution within the brain. Therefore, the crucial next step is to develop and characterise an RXFP3 agonist that crosses the BBB, and demonstrate its antidepressant actions following peripheral injection. This project will screen four RXFP3 agonists, and determine which elicits the most promising acute changes in depression-relevant behaviours in mice and rats. The pharmacological specificity of this best performing RXFP3 agonist will be confirmed using RXFP3 knock-out mice, as on-target RXFP3 drug effects will not be present within this strain of mouse. Importantly, we will also determine the therapeutic potential of chronic RXFP3 agonist treatment in a mouse model of depression, and the acute and chronic mechanisms of action will be characterised via whole transcriptome sequencing of key brain regions post treatment.

Keywords: Depression, RXFP3, Blood Brain Barrier, RXFP3 agonist, neurotransmitter.

Computational Markers for Validation of Long-Term Memory Consolidation Utilizing Behavioral Tagging and *In Vivo* Electrophysiology

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Abstract

The day-to-day functioning of brain depends on learning and memory. Based on neurobehavioral experiments in rodents, previous literature has identified a number of memory-related molecular markers as a target for memory formation; however, there is a dearth of research material that could identify the memory formation markers in real time. A powerful technique for investigating the kinetics of memory formation in real time is in vivo rat electrophysiological. The current study uses in vivo electrophysiological data and machine learning technologies to identify and validate the memory formation in rodent brain. 16-channel head stage electrodes were surgically placed in Wistar rats' CA1 hippocampi. Three days of the Novel Objection Recognition Task were conducted on rats using Behavioral Tagging paradigm. During the behavioural challenge, local field potentials and brain spike signals were captured. Following the acquisition of the bio-signals, MATLAB machinelearning methods were used to identify the computational markers of memory formation. Theidentified computational indicators were further confirmed through the estimation of established memory-related biological markers and the examination of behavioural data. The findings demonstrated that neural signals change during the neurobehavioral activity and that aspects of neural signals are typical of the memory created during the training task. Together, these findings show that memory creation does not always correspond to behavioural data, but that computational markers might shed light on the dynamics of memory consolidation mechanisms without relying on behavioural research.

Keywords: Learning; Long-Term Memory; Machine Learning; Bio-signal Processing; Behavioral Tagging

Alterations in the Expression of PNPO, FOXO3, and GABRA Affect the Electro-Behavioral and Spatial Learning in $FeCl_3$-Induced Epileptic Rats

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Abstract

Background: Epilepsy is a neurological disorder characterized by episodes of recurrent seizures. The prevalence and onset of epilepsy is multifactorial and contributed by alterations in the expression of multiple vital genes. Several animal models used in studying the mechanism of epileptogenesis are limited to pathophysiological and structural changes. The role of multiple genes associated with epilepsy in patients still remained to be studied in animal models, to explore the onset and progression of epileptogenesis which opens the window for therapy. Hence, in our study, we evaluated the expression pattern of PNPO, FOXO, GABRA genes, and electro-behavioral alterations in $FeCl_3$-induced epilepsy.

Methods: Male Wistar rats (~300gms) were injected with 5µl of 100mM $FeCl_3$ intracortically to induce epilepsy. Epileptiform seizures were confirmed by electroencephalographic and multiple unit activity (MUA) in the cortex and hippocampus of the brain, post 25 days of injection. Electro-behavioral assessment was carried out by using the Racine scale. Morris water maze (MWT) test was performed to investigate spatial learning in epileptic rats. The mRNA expression of PNPO, FOXO3, and GABRA wasanalyzed using real time-PCR.

Results: Our results demonstrated the occurrence of discrete epileptiform episodes concurrent with MUA counts in the cortex and hippocampus. Increased MUA counts in both cortex and hippocampus suggested epilepsy in iron-induced rats. It was further confirmed by the electro-behavioral analysis. Decreased spatial learning was observed in epileptic rats. The expression of PNPO, FOXO3, and GABRA was seen to be down-regulated in both cortex and hippocampus of $FeCl_3$ Induced Epileptic Rats

Conclusion: The product of these three genes FOXO3, PNPO, and GABRA could be involved in the altered electro-behavioral expression affecting spatial learning andcollectively inducing epilepsy in $FeCl_3$- injected rats. Hence, this model can be further explored to get an insight into the gene expression patterns, observed in human epileptic conditions.

Ethics statement: Ethical clearance for use of animals was duly approved by the Institutional Ethical committee of JNU, New Delhi.

Acknowledgment: Financial assistance for the present study was provided by ICMR, New Delhi, India.

Identification of novel genes regulating social isolation induced behaviors in *Drosophila.*

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Abstract

Animal behaviors are influenced by numerous internal and external stimuli. Social isolation is a form of passive stressor that profoundly alters animal behaviors. Social isolation increases aggression and disrupts sleep across the animal kingdom, including humans, rodents and fruit flies. Our earlier work, using the fruit fly *Drosophilamelanogaster*, identified ~90 differentially expressed genes in the heads of socially isolated and enriched flies including a neuropeptide *Dsk*.

Here, we are using high-throughput screening to identify causal relationships of several of these genes with social isolation induced behaviors including aggression and sleep. We will present our findings which sheds light on the causal mechanistic interactions of responsible genes in specific cell types of the brain. Our study is also investigating role of neuropeptide and interactions with candidate genes to drive isolation induced behaviors.

Keywords: Social isolation, *Drosophila melanogaster*, Aggression, Sleep, Neuropeptide.

Evaluation of gut microbiota diversity in Amyotrophic Lateral Sclerosis

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Abstract

Motor Neurodegenerative Disease (MND) known as Amyotrophic Lateral Sclerosis (ALS) is fatal and has complicated pathogenesis. Riluzole and Edaravone, two medications that the Food and Drug Administration (FDA) has approved, extend life by two to three months. The likelihood of finding a cure for the condition is reduced by the absence of a clear cause and pathogenesis. The gut microbiota has received a lot of attention as a solution to these issues since it is seen as a hub of possible ALS and other neurodegenerative diseases (NDD). To establish a potential link between ALS and bacteria, a study is being conducted to examine the gut microbiota of ALS patients as well as to compare it to that of their spouse, healthy controls (HC), and other NDD. To carry out the aforementioned, culture-dependent as well as culture-independent methods will be used to detect and isolate gut bacteria in ALS patients. Pathogenic bacteria or clinical strains that may be involved in the course of the disease can be identified by differences in the population of gut microbes. The findings will lay the groundwork for establishing a connection between the gut and ALS, and if one is established, faecal matter transplantation (FMT) or washed matter transplantation (WMT) may offer an additional therapeutic option for modifying the intestinal flora.

Keywords: Amyotrophic Lateral Sclerosis (ALS), Gut microbiota, Culture-dependent, and Culture-independent methods

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Neurotoxicity Assessment of Fenpropathrin in Drosophila Melanogaster

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Abstract

Fenpropathrin is a synthetic insecticide that is used widely to control the agricultural pest. Concerns about exposure to this pesticide are now mainly related to their neurotoxicity and nigrostriatal dopaminergic neurodegeneration. The main neurotoxic mechanisms include oxidative stress, inflammation, neuronal cell loss, and mitochondrial dysfunction. However, other receptors, enzymes, and several signalling pathways can also participate in disorders induced by fenpropathrin. Signalling pathways such as Nrf2 , keap1 and oxidative enzymes like SOD, GST etc have a potential, but the effects of their agonists against fenpropathrin- induced neurotoxicity have not yet been investigated. Invertebrate animal model Drosophila melanogaster have several powerful attributes for toxicological studies including a high degree of genetic conservation of fundamental signalling and structural protein networks and an extensive array of molecular genetic tools . The aim of this work is to elucidate the main mechanisms involved in neurotoxicity caused by Fenpropathrin on Drosophila melanogaster animal model Study divided in two parts - neurobehavioral analysis and molecular analysis of particular targets including apoptosis, Nrf2-keap1. To explore the effect of fenpropathrin on survival and climbing and jumping behaviour of Drosophila melanogaster . Neurobehavioral assays such as the locomotor behavior assay (also known as the forced climbing assay), jumping assay, larval crawling assay were performed after five days of fenpropathrin exposure (CantonS) with concentrations 3 mg/L and 5 mg/L and 10 mg/L.

In development timing assay 10 mg/L hampered prepupa to fly development where as 5 , 3 mg/L showed developmental delay . In longevity assay (survival assay) observed declined survival in 10 mg/L. Fenpropathrin at a concentration of 10 mg/L significantly hampered the development cycle, survival rates, locomotor, jumping and crawling ability of the C 5 B Z (CantonS) fruit flies. We investigate common targets and pathways of neurogenerative disease therapy, including Nrf2, keap1 . How they are affected by exposure to Fenpropathrin. The aim of this work is to clarify the involvement in neurotoxicity induced by Fenpropathrin and propose the course of future investigations to improve our understanding of the problems at hand and protection against Fenpropathrin induced neurotoxicity. We conclude with possibilities to be addressed by future research of novel methods of protection against neurological disorders caused by pesticides that may also find their use in the management/treatment of neurodegenerative disease.

G6PD deficiency mediated dysregulation of redox equilibrium contributing to Covid-19-mediated neuroinflammation

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Abstract

Background: Glucose 6 Phosphate dehydrogenase (G6PD) is located in the X- chromosome and it is a key enzyme for the pentose phosphate pathways which contributes 70% of total cellular reduced nicotinamide adenine dinucleotide phosphate (NADPH) production. This NADPH plays a critical role in regulation of redox equilibrium and nucleotide biosynthesis. Additionally, G6PD-derived NADPH can follow pro-oxidative and anti-oxidative pathway for the generation and removal of ROS respectively in a tissue-specific manner. Therefore the deficiency of G6PD leads to alteration of fundamental metabolic and regulatory pathways which causes several neurological and metabolic disorders. G6PD deficiency is considered as a very common enzymatic disorder which affects more than 1 million individuals per year in India and worldwide. Besides, several clinical report suggested that G6PD deficient patient shows aggravated Covid-19 response and severe neuroinflammation.

Aim: Mechanism of G6PD deficiency mediated Covid-19 responses are still ambiguous. In this study, we are investigating functional dichotomy of G6PD in Covid-19 mediated neuroinflammation.

Methods: We generated CRISPR-mediated G6PD deficient *in-vitro* model to study response of human microglia under foreign pathogenic stimulus. To study covid-19 mediated neuroinflammation, we used *in-vitro* transcribable Covid-19 RNA. Transfection of Covid-19 RNA and its downstream expression of viral protein triggers inflammatory responses in human microglia which were characterized by PCR using inflammatory markers. Further, nitric oxide and ROS production and their localization were characterized by confocal microscopy using specific probes.

Results: Our data indicated that G6PD-derived NADPH followed pro-oxidative pathway by generating ROS and NO in human microglia which may further promote the destruction of Covid-19. On the contrary, G6PD deficiency causes reduction of ROS and Nitric oxide production *in-vitro*. Surprisingly, we also observed the decrease in lysosomal acidification in G6PD deficient cells that could possibly be due to reduction of cellular NADPH which affects acidification of lysosome by altering the function of proton pump.

Conclusion: G6PD is the most crucial enzyme for restricting SARS-CoV-2 mediated neuroinflammation. Deficiency of G6PD leads to dysregulation redox equilibrium which further causes aggravated Covid-19 responses. However, we are also generating clinically relevant G6PD variants to study its responses in neuro-glia interaction for detailed understanding of neuroinflammation.

The nitrergic projection from SC to VTA plays an essential role in the modulation of cognitive flexibility in rats

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Abstract

Background: Superior colliculus (SC) involve in the conduction of visual message from the environment, whereas ventral tegmental area (VTA) is prominently involve in the reward processing. However, the role of SC-VTA circuitry for cognitive flexibility has not been documented. Additionally, neuronal nitric oxide synthase (nNOS) found in discrete neural regions and produce 90% nitric oxide in the mammalian brain. It is involve in the process of learning and memory, cognitive performance. Though nNOS is involve in cognitive function, yet it activity in SC-VTA circuitry for cognitive flexibility has not been revealed.

Aim and Objectives: The aim of present study was to investigate the role of neuronal nitric oxide synthase (nNOS) in SC-VTA circuitry for cognitive flexibility by using reward reversal learning paradigm.

Methods: Cognitive flexibility was analyzed in adult male Wistar rat using food self administration (reward) reversal learning in operant conditioning chamber and lever press activity was monitored. To assess the involvement of SC in reward reversal learning, trained rats were administered with MK-801 (NMDA receptor antagonist) directly into the superficial grey layer (SuG) of SC and intra-VTA, and lever pressings were measured. To examine the involvement of nNOS with dopamine (DA) of SC, trained rats were administered intra-SuG with 7-nitroindazole (7-NI) and sulpiride (DA2 antagonist) and lever press activity was measured. The SC brain area of trained rats was processed for NOS immunohistochemistry (IHC). Although VTA involved in the reward mechanism is well known, the projection of the NOS of the SC to VTA not yet

documented. Hence, retrograde tracing was performed to confirm the neuronal connection between SC and VTA.

Results and Discussion: Intra-SuG treatment of 7-NI significantly increased the lever press activity, whereas DA2 antagonist treatment decrease the lever press activity indicates the role of nNOS and DA of SC in cognitive flexibility. However, the NOS immunoreactive cells in the SC were significantly reduced in trained rats as compared to the control. This data suggest that NOS of the SC may be responsible for the modulation of cognitive flexibility. The retrograde study revealed that NOS positive cells of the SC were projected to the VTA and modulated the dopaminergic system.

Conclusion: Herein, the present research work demonstrated that the nitrergic system of SC play an important role in the modulation of the cognitive flexibility. Evaluation of nNOS at behavioral and molecular level may be useful for the scientist to develop treatment strategy against the impaired cognitive disorder.

Key Words: Superior colliculus, Neuronal nitric oxide synthase, Reversal learning, Dopamine.

Neuropeptide S facilitates reward by enhancing the activity of CARTergic neurons in lateral hypothalamus

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Abstract

Background: Reward is experienced in response to discrete stimuli, providing enjoyment and arousal, while addiction involves persistent, compulsive, and uncontrolled behaviors that are both maladaptive and destructive. Despite these differences, reward and addiction share common neurobiological underpinnings. The dopaminergic pathway projecting from ventral tegmental area (VTA) to nucleus accumbens shell (AcbSh) serves as major reward circuitry involved in the initiation of addiction. The role of cocaine- and amphetamine-regulated transcript (CART) peptide in modulating the activity of mesolimbic dopaminergic pathway has been well established. However, the neuromodulatory system regulating the activity of lateral hypothalamic (LH) CARTergic system in reward is unknown.

Aim and Objective: To investigate the possible interaction between neuropeptide S (NPS) and LH-CARTergic system in the reward regulation.

Methods: Operant conditioning chamber was employed to study the effect of NPS on reward behaviour.

Results: NPS administration in the LH increased the lever press activity for food reward, however NPS receptors antagonist (SHA-68) showed opposite effect. CART-ab (1:250) treatment in the VTA decreased lever press activity compared to aCSF-control. Pre-treatment of CART-ab (intra-VTA) blocked the reward promoting effect of NPS (intra-LH). NPS treatment in the LH increased the tyrosine hydroxylase immunoreactivity within the AchSh area.

Conclusion: NPS in the LH might modulate the CARTergic inputs to the VTA, which in turn may enhance the activity of mesolimbic dopaminergic neurons and produce reward.

Key Words: Neuropeptide S, CART peptide, lateral hypothalamus, mesolimbic dopaminergic pathway, reward.

XL ANNUAL MEETING OF INDIAN ACADEMY OF NEUROSCIENCES

(DECEMBER 8 - 10, 2022)

PRE-CONFERENCE WORKSHOP: DECEMBER 7, 2022

DEPARTMENT OF BIOMEDICAL ENGINEERING, SCHOOL OF TECHNOLOGY
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Theme: "Neuroscience Research : Current Trends and Future Needs"

Proposed Symposia

Aging and Dementia
Artificial Intelligence and Neuroscience
Brain Injury and Neuroregeneration
Drug Repurposing for Neurological Diseases
Emotion and Cognition
Neurodevelopmental disorders
Neuroglial signaling
Neuroimaging
Neurointerventions and Clinical Challenges
Neurological Disorders and Cell Therapy
Neuroprosthetics and Rehabilitation
Neuroprotection
Trends in Neurotoxicology
...any other relevant symposia also invited

Scientific Programme

Pre-conference workshops
Plenary sessions
Symposia
Invited talks and Special lectures
Young scientist sessions
Poster sessions
Panel discussion



Organizing Secretary

Dr. Sudip Paul
Assistant Professor & Teacher In-Charge
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Deadlines	
SUBMISSION OF PROPOSALS FOR SYMPOSIA & SATELLITE MEETINGS	AUGUST 16, 2022
EARLY BIRD REGISTRATION AND ABSTRACT SUBMISSION	AUGUST 16, 2022
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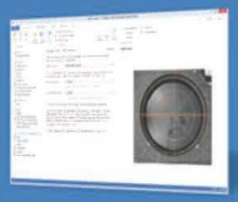
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