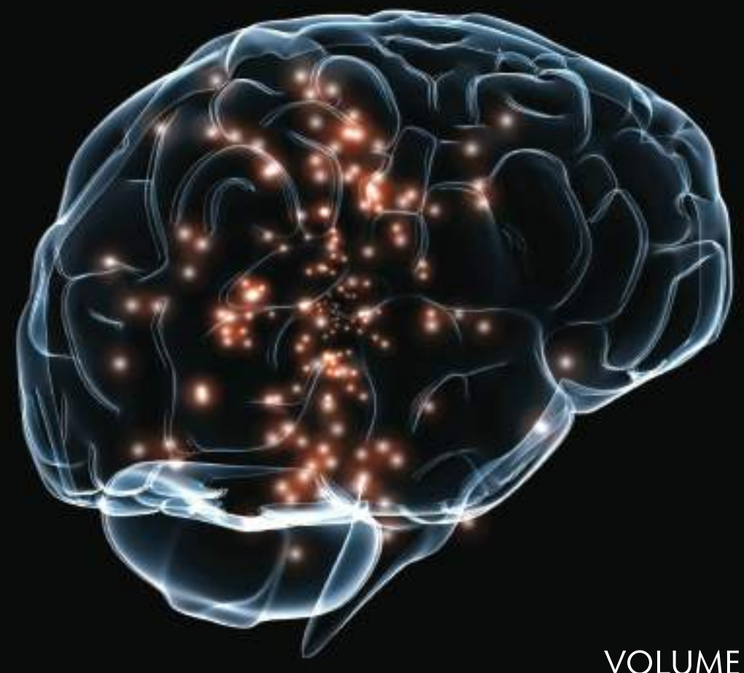
Annals of NEUROSCIENCES

VOLUME 30 ISSUE S1 2023

Annals of NEUROSCIENCES

Abstract Issue: Brain: Chemistry to Cognition
Guest Editors: Ishan Patro, Nisha Patro



VOLUME 30
ISSUE S1
2023

Sage
www.sagepub.com

find this journal **online**
at http://journals.sagepub.com/home/aon
ISSN 0972-7531

ISSN: 0972-7531
Online ISSN: 0976-3260

Annals of Neurosciences is published quarterly — in January, April, July and October by Sage.

Please read the manuscript submission guidelines, then visit the journal's peer-review and submission system [https://peerreview.sagepub.com/aon] to create account/log in to upload your manuscript. Please note that manuscripts not conforming to the guidelines may be returned.

To view the manuscript submission guidelines, please visit journals.sagepub.com/home/aon and click on the 'Submit Paper' tab.

Annual Subscription: Individual rate (print only) ₹3,890; combined institutional rate (print only) ₹6,760, $702, and £380. For orders from Pakistan, Bangladesh, Sri Lanka and the Maldives, SAARC rates apply: individuals £63; combined institutional rate £95. Prices include postage. Print only subscriptions are available for institutions at a discounted rate.

Orders from the Americas should be sent to Sage Publications Inc, 2455 Teller Road, Thousand Oaks, CA 91320, USA (Tel: 00 800 818 7243/E-mail: journals@sagepub.com).

Orders from the UK, Europe, the Middle East, Africa and Australasia should be sent to Sage Publications Ltd, 1 Oliver's Yard, 55 City Road, London, EC1Y 1SP, UK (Tel: +44 (0)20 7324 8500/ E-mail: subscription@sagepub.co.uk).

Inquiries from India/South Asia about single issue rates, availability of back issues, electronic only or print only rates for institutions, advertising and permission requests should be sent to Sage Publications India Pvt. Ltd, Unit No. 323-333, Third Floor, F-Block, International Trade Tower, Nehru Place, New Delhi 110 019, India (Tel: 91-11-40539222/Fax: 91-11-40539234/E-mail: customerservicejournals@sagepub.in). Inquiries from the Americas should be sent to the California address (above), while those from the UK, Europe, the Middle East, Africa and Australasia should be sent to the London address (above).

Claims: Claims for undelivered copies may be made no later than three months following the month of publication. The publisher will supply replacement issues when losses have been sustained in transit and when reserve stocks permit.

Abstracting and Indexing: Please visit http://journals.sagepub.com/home/aon and click on the 'More' button (under 'About this journal'), then click on the Abstracting/Indexing tab to view a full list of databases in which this journal is indexed.

Change of Address: Four weeks' advance notice must be given when notifying change of address. Please send the old address label to ensure proper identification. Please specify the name of the journal and send change of address notification to the Sage office through which you subscribe to the journal.

Printed and published by Sonia Kumar on behalf of Indian Academy of Neurosciences (IAN) at Sage Publications India Pvt. Ltd, Unit No. 323-333, Third Floor, F-Block, International Trade Tower, Nehru Place, New Delhi 110 019, India. Printed at Repro Books Limited, Khasra no. 13/19, 22, 17/2, 9/1/1, Dharuhera, Village Malpura, Haryana 123110, India.

Editor-in-Chief: Dr Akshay Anand.

C O P E COMMITTEE ON PUBLICATION ETHICS

Annals of Neurosciences

Aims and Scope

Annals of Neurosciences is an open access, multi-disciplinary, peer-reviewed publication of the Indian Academy of Neurosciences that aims to cover new advances in Neurosciences, increase our understanding of the neurosciences, and encourage the development of better diagnostic tools and effective treatments for neurological disorders. It provides a platform for papers that range from computational and experimental work in the neurosciences to those that fit the interface between experiments and clinic. The Journal accepts papers from neurologists, neuroscientists and other physicians/students in the neurological sciences. Papers include research articles, reviews, commentaries, book reviews, molecular images, reports, student's perspectives on published reports in the form of journal clubs, and views. It also includes editorials on Policy which may include Intellectual property, Technology commercialization and interdisciplinary issues. Journal is committed to the rapid publication of original findings that increase our understanding of the molecular structure, genetics, function, behavior, physiology, toxicology and development of the nervous system.

Manuscript Submission Guidelines

To view the manuscript submission guidelines, please visit the 'Submit Paper' link at journals.sagepub.com/home/aon

XLI Annual Meeting of the

Indian Academy of Neurosciences

&

International Conference on

BRAIN: CHEMISTRY TO COGNITION

October 4-6, 2023

With Pre-Conference Activities on October 03, 2023

Jiwaji University, Gwalior, India

Abstracts

Guest Editors:
Ishan Patro
Nisha Patro

Annals of Neurosciences

EDITORIAL BOARD

Foreword

I take the opportunity to congratulate the Academy for choosing such an important, currently relevant subject for the International Conference. I deeply regret my inability to be personality participating in this academic feast. However, I wish to share with you some historical vignettes on the subject through this message.

The use of drugs - Chemical or plant derived- to affect conscious state in humans goes back almost to the origin of humanity. The pollens of eight medicinal plants were deposited in a 60,000 years old tomb in Iraq. Opium poppies and cannabis were mentioned in prehistoric documents. Alcohol use has been mentioned in both the old and new testament. It was used by Bacchus community in ancient Greece.

In respect to India, as far as the recorded history goes, the earliest instances of rational medical knowledge are found in the *Rigveda and Atharvaveda*, both of the second millennium B.C. Archaeological excavations of the third century. These indicate a high level of knowledge of physical and chemical sciences, likely to be matched by a similar knowledge of medicinal plants and drugs derived thereof.

Coming to more recent times it was not till 1897, when Sherrington described the synapse that the role of chemicals in the functioning of the nervous system stimulated research in this field. It was John Langley, a contemporary of Sherrington who provided evidence that at most synapses signaling between neurons was chemical in nature. However, Langley's studies were restricted to peripheral and autonomic nervous system. Around the same time Adrian, Eccles and others were investigating the role of electrical activity at the synapses.

The intense debate about the role of chemical or electrical activity in inter-neuronal transmission continued till 1920 when experiments carried out by Otto Loewi and Henry Dale established the primary role of chemical transmission as against the proposed electrical theory. This was further confirmed a few years later by the work of Julius Axelrod and Raymond Ahlquist.

With advances in research methodologies like intracellular recording, microiontophoresis on single cells, fluorometric techniques for measuring the neurotransmitters, Arvid Carlsson a pharmacologist from Sweden, established the role of chemical neurotransmitters in the central nervous systems around 1950s. Interestingly he and his colleagues used reserpine to study its effect on cerebral catecholamines. As you know reserpine a derivative of Rauwolfia Serpentina has been the subject of Pioneering studies by Col. RN Chopra, Prof. BB Bhatia and a host of their pharmacological colleagues and Dr. Rustom JL Vakil in India established its therapeutic use as an antihypertensive and a sedative the first such drug for treatment of these two clinical conditions. The work on Serpasil in USA and Sweden was triggered by these Indians studies (Tandon 2021). After persistent efforts Carlsson along with a number of his Swedish Colleagues - Chemists and pharmacologist - established the methodology to localize dopamine, nor epinephrine and serotonin in the brain. This ultimately led to the use of L-DOPA as a treatment for Parkinson's disease and laid the foundation of the role of chemicals in cognitive activity disorders.

The last couple of decades following the advent of non-invasive neuroimaging and other investigations have witnessed an explosion of development of the cognitive science. This is further enhanced by study of cognitive functions in healthy volunteers.

I am sure the multifaceted contribution of the participants of this International Conference would add to the development of this field.

I once again congratulate the organizers of this conference, specially its President Prof. Ishan Patro and his team to collect such distinguished investigators.

P.N. TANDON
National Research Professor

Reading Material Suggested

- A concise History of science in India second Edition, (Eds) DN Bose, S.N. Sen and B.V. Subbarayappa. Indian National Science Academy, 2009
- Daedalus, Spring 1998: The Brain, https://www.jstor.org/stable/i20027486
- Neurological Foundation of Cognitive Neuroscience. (Ed) Mark D. Esposito MIT Press (2003)
- Evolution of Neurosciences: A Historical Review with Brief Bio graphics of its Selected Pioneers. (Eds) P.N. Tandon and P. Sarat Chandra. Neurology India Vol 70 (Suppl 1) July-August 2022
- Indian Rauwolfia Research led to the evolution of neuropsychopharmacology and the 2000 Nobel Prize (Part I &II) Indian J Med Res 154, 163-168&169-174, 2021

Contents

BK Bachhawat Life Time Achievement Award

Epidemic of misdiagnosis vitamin B12 deficiency: Time to act

UK Misra
TSM Medical College, Director Neuroscience Apollo Medics Super Specialty Hospital & Consultant Vivekanand Polyclinic & Institute of Medical Sciences, Lucknow, India

The history of vitamin B12 "Nature's most beneficial cofactor" is a saga of clinical research in which ironically the treatment preceded the understanding of pathogenesis and is credited by two Nobel prizes. Vitamin B12 deficiency (VBD) is often undiagnosed or blindly treated. Somatosensory evoked potentials are most frequently abnormal (87%) compared to visual (63%) and motor (57%), suggesting the vulnerability of somatosensory pathways to vitamin B12. In VBD patients with and without parietal cell antibodies there was no difference in the presentation, severity or outcome probably to final common pathway. Diverse neuropsychiatric symptoms (anxiety, depression, delirium, psychosis, schizophreniform psychosis, dementia) are associated with VBD, which overshadow the typical symptoms. The neuropsychiatric evaluation in 32 patients with VBD suggested the involvement of fronto-temporal cortex which was supported by SPECT studies. The cognitive evoked potential (P300) was prolonged and imported following treatment. In 30% hospitalized patients with VBD, micturition disturbance was noted and urodynamic study revealed detrusor areflexia and neurogenic over activity with high pressure voiding Optic nerve involvement VBD revealed asymptomatic prolongation of P100 of visual evoked potential without any visual impairment. There is a controversy about presence peripheral neuropathy in B12 deficiency. A nerve conductions study in 68 patients revealed mixed sensory motor changes which improved following treatment. Sural nerve biopsy revealed axonal breakdown, myelin loss and remyelination Rarely VBD can result in acute discriminated encephalomyelitis like picture, seizure and status epilepticus. Vitamin B12 deficiency is associated with venous sinus thrombosis and stroke with possibility of prevention by vitamin B12. In children the clinical picture is very different from adults leading to physical and mental retardation, seizure, movement disorders. The underlying pathology in VBD is myelin dysfunction and glial dysfunction as evidenced by a Nitrous oxide model. Vitamin B12 deficiency is easy to diagnose and treat. More work is needed regarding genetic susceptibility and mechanism of CNS damage.

Key-note address

Serotonin and brainstem dysfunctions in neuropsychiatric and sensory disorders

Harry W.M. Steinbusch
Dept. Translational Neuroscience, Faculty of Health, Medicine and Life Sciences, Maastricht University Medical Centre +, Maastricht, The Netherlands

Despite the fundamental role of the brainstem in regulating vital functional abilities such as arousal, breathing, autonomic nervous system activity as well as regulating all higher cerebral functions via neurotransmitter projections systems originating in the brainstem, the role of the brainstem has received relatively little attention in most neuropsychiatric disorders. Besides the dorsal and median raphe nuclei complex comprising mainly serotonin-producing neurons, the brainstem also contains noradrenalin, dopamine and histamine-producing nuclei, i.e., resp. the locus coeruleus, the substantia nigra and the mamillary bodies. The brainstem is furthermore the relay station of afferent and efferent projections between the autonomic nervous system in the peripheral body and higher cerebral brain regions. The current presentation aims to review the neuroanatomy of the brainstem as well as the current status on findings, derived from a wide range of studies using molecular, cellular and imaging technologies, of brainstem involvement in neurodevelopmental (i.e., autism, schizophrenia) and neurodegenerative disorders (Alzheimer's and Parkinson's disease).
Over the past decades, the incidence of age-related, neurological and psychiatric disorders such as Alzheimer's disease (AD), Parkinson's disease (PD), but also depression has considerably increased. Mood

disorders are strongly related to the exposure to stress. The hippocampus and other forebrain structures are the apex of the stress hormone control mechanism and damage to them may be one way in which stress hormone secretion escapes from inhibitory control in depression. In turn, stress, probably through toxic effects of glucocorticoids, decreases neurogenesis and cell survival while antidepressants enhance these processes in experimental animals. Therefore, since treatment strategies are not yet available, primary prevention in these age-related and stress related neurological disorders is of importance. As mentioned before most of the focus on neurobiological questions on above mentioned disease are related to forebrain structures since they are often associated with cognitive dysfunction. The brainstem is a highly neglected brain area in neurodegenerative diseases, including Alzheimer's (AD) and Parkinson's (PD) disease and frontotemporal lobar degeneration. Likewise, despite a long-standing recognition of brainstem involvement, relatively few studies have addressed the exact mechanisms that underlie brainstem autonomic dysfunction. Improved insight in the cellular and molecular characteristics of brainstem function is pivotal to study the developmental origins. As brainstem dysfunction also poses health issues in several other, neurodegenerative, disorders (like AD and PD), progress in these neurological fields will benefit from scientific advancement in the current proposal as well. In the area of depression, sseveral observations have been made in relation to changes in one particular brain structure: the Dorsal Raphe Nucleus (DRN). In addition, dysfunction of the cerebellum is also observed in AD and associated with pulmonary deregulation. The DRN is also related in the circuit of stress regulated processes and cognitive events.
In order to gain more information about the underlying mechanisms that may govern the neurodegeneration, e.g., amyloid plaques, neurofibrillary tangles, and impaired synaptic transmission in AD, a rat dissociation culture model was established that allows mimicking certain aspects of our autopsy findings. We observed a similar phenomenon in brains from patients suffering from neurodegenerative disease since this also related to changes in BDNF levels. The ascending projections and multitransmitter nature of the DRN in particular and the brainstem in general stress its role as a key target for AD/PD research and autonomic dysfunction. It also points towards the increased importance and focus of the brainstem as key area in various neurodevelopmental and age-related diseases.

Distinguished Lectures

DL.1: Contextual influences on visual processing

Thomas Albright
Salk Institute of Biological Studies, La Jolla, USA

DL.2: RNA in neuroscience

Timothy W. Bredy
UQ Centre for RNA in Neuroscience, Queensland Brain Institute, The University of Queensland Building 79, Upland Rd., St. Lucia, QLD 4072

RNA, once thought to simply represent an intermediate step in the transition from the DNA code to the proteome, has increasingly been recognised as a critical feature of information processing in the brain. This is due, in part, to the discovery that the majority of our genes do not code for protein but instead generate a diverse population of regulatory RNAs that function in a cell-type and state-dependent manner. In addition, dysregulated RNA metabolism is associated with a variety of neuropsychiatric conditions, including depression, phobia, PTSD and the addictions as well as age-related neurodegenerative disorders. RNA therefore represents a new frontier in the quest to design new treatment approaches for brain disorders. This talk will focus on my labs journey through the world of RNA in neuroscience over the a past 15 years, highlighting new avenues for exploration.

K T Shetty Oration

Novel neuromodulatory approaches for functional recovery in spinal cord injury

Suman Jain
Department of Physiology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India

Traumatic spinal cord injury (SCI) is a debilitating condition that initiates a cascade of biochemical, vascular, metabolic and immune alterations, leading to progressive neurodegeneration and partial or complete loss of motor, sensory and autonomic functions. Decompression or fusion surgeries induce minimal recovery, leaving patient completely dependent on others for daily living, implying the need for new neural tissue activity modulatory strategies that can repair, regenerate and restore the structure and function. We explored and compared the potential of two most recent advanced techniques for amelioration of SCI etiology: 1, transcranial magnetic stimulation (MF) and 2, magnetic nanoparticles. In both complete and contusion injury rats, we observed a significant improvement in locomotor behavior, reduction in lesion volume, abolition of glial scar and increase in the expression of GAP-43, indicating axonal regeneration. Notably, magnetic nanoparticles significantly augmented the beneficial effects of MF, suggesting it's therapeutic potential in SCI. We have been able to move our research work from bench to bedside and initiated first phase of clinical trials in complete SCI patients. Intermittent theta burst stimulation have been given to 16 complete SCI patients (ASIA A score) on the leg area of the primary motor cortex. An improvement in SCI independence measure score, walking index, pain, depression and anxiety and cortical excitability is evident. We conclude that magnetic nanoparticles as well as transcranial magnetic stimulation have the potential to modulate neural tissue activity and promote functional recovery providing hope for SCI patients who currently have limited therapeutic options. However, further research and larger-scale clinical trials is required to confirm the safety and efficacy of these techniques in human patients over the long term.

S S Parmar Oration

Targeting epigenetics and epitranscriptomics in stroke therapy

Raghu Vemuganti
Department of Neurological Surgery, University of Wisconsin-Madison and
William S. Middleton Veterans Administration Hospital, Madison, WI, USA

In mammals, DNA and RNA undergo several chemical modifications that modulate the fitness, functionality and the diversity of the cells. These are also sensitive to external and internal stimuli and their dysfunction promotes pathologic states. Importantly, dynamics of 5-methylcytosine (5mC) and 5-hydroxymethylcytosine (5hmC) on DNA is a major epigenetic modification in the CNS that decides the neuronal fate. Our studies show that the levels of 5hmC and TET3 (enzyme that catalyzes its formation) significantly elevate in the peri-infarct cortex after stroke in rodents of both sexes. While TET3 knockdown exacerbated the post-stroke brain damage, its induction by ascorbate was neuroprotective. Importantly, many of the genes that were hydroxymethylated after stroke are neuroprotective that control oxidative stress, inflammation, DNA damage, apoptosis and angiogenesis. In addition, our studies show that scaffolding by specific long noncoding RNAs with TET3 is important for the 5hmC-mediated neuroprotection after stroke. Coding and noncoding RNAs undergo >175 epitranscriptomic modifications that increase the functionality of RNAome. Our studies showed significant induction of methylation of adenosine (N^6-methyladenosine; m^6A) after stroke in the peri-infarct cortex. We observed that shut-down of FTO that mediates m^6A demethylation. Many of the m^6A hypermethylated transcripts in the post-ischemic brain are those that promotes apoptosis and inflammation. Reversing m^6A methylation by restoring FTO with an AAV9 reduced ischemic brain damage and promoted functional recovery in mice of both sexes. We further report that activating FTO by NADPH administration decreases post-stroke grey and white matter damage and improves motor, cognitive and neuropsychiatric recovery after stroke. In addition, induction of m^6A reader YTHDF1 also modulates ischemic brain damage. YTHDF1 knockout mice showed better motor function recovery smaller secondary brain damage after stroke. Thus, we propose epigenetic and epitranscriptomic modifications as novel stroke therapeutic targets.

P N Tandon Oration

Situational awareness to create a platform for translational research for neurosciences

P Sarat Chandra
All India Institute of Medical Sciences, New Delhi

Translational research is challenging, and creating a practically useful paradigm for utility in clinical practice is even more. Team research is the foundation for creating such programs. Having all verticals of research with the clinicians and researchers being able to talk on a common platform and interact every day is the only manner in which clinically useful research may be produced.
The author has spent over 25 years in clinical and basic science research and has published over 600 papers during his academic career and operative experience over 25,000 cases. He would be presenting briefly his journey, challenges, difficulties and some of ecstasies in conducting research in a busy clinical scenario.

P K Seth Memorial Lecture

Virokines hit hard to the brain microvascular endothelial cells

Sunit K. Singh
Dr. B. R. Ambedkar Center for Biomedical Research (ACBR)
University of Delhi (North Campus), New Delhi-110007, India

Viral virulence is encoded in the viral genome and expressed through their structural and non-structural proteins. Viruses utilise multiple routes to affect cellular functions through virus-encoded virokines by altering the cell signal transduction pathways and gene expression. Virokines are virally encoded proteins secreted from the productively infected host cell and proved to be quite toxic for the brain microvascular endothelial cells. These proteins are capable enough to modulate different aspects of the cellular homeostasis. Virokines are also known to affect expression pattern of non-coding RNAs especially microRNAs. MicroRNAs are small non-coding RNAs which play an important role in gene regulation as fine gene tuners. Given the importance of microRNAs in cellular homeostasis, viruses have evolved to take advantage of these cellular microRNA pathways. Viruses have been reported to affect the key proteins of the different cell signalling pathways by exploiting the cellular microRNAs through virokines to get their immediate gains such as viral immune evasion or cellular invasion. Overall virokines play an important role in such practices for the virus during viral infections. Furthermore, virokines can exert a profound impact on the cellular functions, and affect the functionality of Blood brain barrier adversely.

Plenary Lectures

PL.1: How to make a hippocampus

Shubha Tole
Tata Institute of Fundamental Research, Mumbai

Abstract not available

PL.2: Studying the neural basis of real-world vision and cognition in freely moving monkeys

S.P. Arun
Center for Brain Research, Indian Institute of Science, Bengaluru

Most visual tasks involve searching for specific visual features, like the face of a friend or your cycle keys. But we also often perform generic tasks where we look for specific property, such as finding an odd item, deciding if two items are same, or if an object has symmetry. These tasks have no defining visual feature to look for but rather a property in the image that we seem to effortlessly find. How does our brain solve such tasks?
Using simple neural rules, we show that displays with repeating elements can be distinguished from heterogeneous displays using a property we define as visual homogeneity. In behavior, visual homogeneity predicted response times on visual search and symmetry tasks. Brain imaging during these tasks revealed that visual homogeneity in both tasks is localized to a region in the object-selective cortex. I will also present some ongoing work in which we are exploiting the versatility of this task to answer a variety of questions about visual perception.

PL.3: Phosphoregulation of Intracellular Transport in the Axon and Cilium

Krishanu Ray
National Brain Research Centre, Manesar and the Department of Biological Sciences, Tata Institute of Fundamental Research, Mumbai 400005, India

Imagine a city run by autonomous vehicles that can continuously recognize the needs of different parts of the city and adjust the supply and pickup accordingly. Now, zoom into a cell - a neuron in particular - where the supply to synapse at the end of a long axon, the dendrites, or the cilia are precisely timed and balanced with the right amount of resources like specific types of proteins, lipids, and other organelles. A significant part of this logistics is powered by microtubule-dependent motors that can apparently pick the correct type of cargo and move them to appropriate destinations to mitigate the metabolic, physiological, and environmental demands. A cell consists of multiple kinesins, kinases, and phosphatases which compounds the complexity of the problem. How are these logistics managed in real-time? I will discuss this question by describing the roles of kinases and phosphatases that orchestrate the microtubule-dependent movements of kinesins and their interactions with cargoes inside a cell.

Symposia Lectures

Symposium-1: Recent advances in neuropsychiatric and neurodegenerative disorders

S1.1. Emerging role of microglia in synaptic plasticity

S.T. Dheen, G. Saw, D. Kandilya, S. Wong, J. Polepalli
National University of Singapore, Department of Anatomy, Singapore, Singapore

Background: Several lines of studies have reported that microglia are involved in modification of neuronal synapses, and synaptic pruning. We have performed a high throughput miRNA microarray analysis and shown a database of differentially expressed miRNAs in activated rat primary microglia. This study revealed that microglial miR-21-5p targets PI3K which regulates synaptic plasticity by modulating BDNF involved in learning and memory. Understanding the mechanisms of microglial PI3K-BDNF signalling pathway that contributes to neuronal LTP is clinically relevant, since microglia in the aging brain undergo cellular senescence and dystrophic changes which may be associated with age-related dementia and neurodegeneration such as such as Alzheimer's disease. This study explores the role of miR-21-5p in regulation of synaptic plasticity by modulating PI3K/AKT signalling in microglia.
Material and methods: Microglia were exposed to amyloid β and subjected to miRNA microarray analysis. Subsequently, selected miRNA was validated using qPCR, western blot, and luciferase assays. Electrophysiological recording of long-term potentiation (LTP) in pyramidal neurons of rat CA1 hippocampus was performed.
Results: The expression level of miR-21-5p predicted to target PI3K (as revealed by luciferase assay) was elevated in microglia exposed to amyloid β. Moreover, miR-21-5p inhibition upregulated PI3K and its downstream targets including phosphorylation of Akt and CREB as well as BDN in microglia, while its overexpression downregulated the PI3K pathway. Next, impaired LTP that was recorded in hippocampal slices after ablation of microglia, was restored by addition of PI3K or BDNF
Discussion and conclusion: Microglial miR-21-5p targets PI3K, which subsequently regulates BDNF expression and synaptic plasticity. This study also revealed that amyloid β elevates microglial miR-21-5p, leading to down regulation of PI3K-BDNF pathway, resulting in impaired LTP. Understanding the mechanisms by which microglial PI3K is regulated may provide insights into the ways by which microglia-neuronal interactions leading to cognitive decline can be modulated, especially in the case of neurodegenerative diseases.
Acknowledgements: This study was funded by NUS Strategic Research Grant (Memory Networks in Rodent and Primate) DPRT/944/09/14 (R185-000-271-646) and HLCA20Jan-0095 (R-181-000-194-213).

S1.2. Synaptic architecture of remote memory recall

Louise Goh & **Jai Polepalli**
Department of Anatomy; CeLS Neurobiology Program; Healthy Longevity Translational Research Program, National University of Singapore, Singapore

Background: The prefrontal cortex (PFC) is involved in the formation and retrieval of memories. The PFC circuits exhibit diversity in synaptic properties, enabling them to perform precise computations in a fool-proof manner that result in normal behavioural output. Neurexins and neurexin interacting proteins, including cerebellins play crucial role in determining synapse specificity.
Results: One member of the Cerebellin family, Cerebellin-4 (Cbln4) is enriched in the PFC. We show that Cbln4 in the PFC mediates long-term storage of memories. Deletion of Cbln4 in the PFC diminishes recall of remote contextual memory but not recall of recently formed memories. At the synapses, loss of Cbln4 leads to reduced numbers of GABAergic and glutamatergic synapses.
Discussion and Conclusions: Mutations in cerebellins and the complex formed by cerebellins are penetrant in a multitude of diseases. Our recent findings highlight the importance of defining the molecular architecture

of circuits that are responsible for behavioral abnormalities caused by manipulations of proteins that are genetically associated with brain disorders.
Acknowledgement: This research is being funded by NUSMed Startup grant, MOE Tier 2 grant to Jai Polepalli.

S1.3. Mitochondrial control of microglial function in Alzheimer's disease

Lai Kei Onn, Jia Hui Wong, Lauren H. Fairley, Wei Jing Chong, **Anna M. Barron**
Neurobiology of Aging and Disease Laboratory, Lee Kong Chian School of Medicine, Nanyang Technological University Singapore, Singapore, 308232.

Background: Mitochondria are emerging as the command centres of innate immune responses, controlling inflammatory responses via metabolic programming. Here we investigated the neuroimmune function of the mitochondrial translocator protein (TSPO), which is a PET-visible inflammatory biomarker and potential immunotherapeutic target in Alzheimer's disease (AD).
Materials and methods: Unbiased omics approaches were used to identify functional pathways and downstream molecular effectors of TSPO. Findings were validated using pharmacological and genetic loss of function studies in cultured mouse microglia and models of AD.
Results: We show that TSPO and the key glycolytic enzyme, hexokinase-II (HK), play critical roles in the coordination of microglial respiratory-glycolytic metabolism and phagocytosis, an important protective function in AD. Microglia lacking TSPO resembled dysfunctional microglia observed in aging and AD. In the absence of TSPO, HK is recruited to the mitochondria, inducing glycolysis and contributing to phagocytic dysfunction. Based on these findings we developed an optogenetic tool to control microglial glycolytic metabolism.
DISCUSSION and CONCLUSIONS: We propose that mitochondrial TSPO and HK together are a key mitochondrial hub regulating glycolytic-respiratory balance and phagocytosis of microglia, and are promising targets for the development of novel immunotherapeutics in AD.
Acknowledgements: This project was funded by the Nanyang Assistant Professorship Award from Nanyang Technological University Singapore (A.M.B.) and the Ministry of Education, Singapore, under its Academic Research Fund Tier 1 (Project ID RG23/21; A.M.B.).

S1.4. Gut Microbiome: A Source of Diagnostics or Therapeutics for neuropsychiatric disorders

Joyappa Nikhil[a], Chinnasamy Thirumoorthy[a], Sandhya Narasimhan[a], Shivarama Varambally[b] **Kuppan Gokulakrishnan[a]**
[a] Department of Neurochemistry; [b] Department of Psychiatry National Institute of Mental Health and Neuro Sciences (NIMHANS), Hosur Road, Bengaluru, Karnataka, 560029, India

Background: Recently, there has been a growing interest in research on the relationship between gut-microbiota and neurological disorders. The link between intestinal permeability, the gut microbiota, and the aetiology of schizophrenia (SCZ) is not well understood. We studied how zonulin, lipopolysaccharide-binding protein (LBP), and gut microbiota profile differed between drug-naive (DN SCZ) and risperidone-treated SCZ patients (RISP SCZ) compared to healthy controls (HCs).
Materials and Methods: We recruited a total of 60 participants, from the clinical services of a large neuropsychiatric hospital, which included DN SCZ, RISP SCZ and HCs (n=20 each). Plasma levels of zonulin, and LBP were quantified by enzyme-linked immunosorbent assay. Fecal samples were analyzed using 16s rRNA sequencing in this cross-sectional study.
Results: Plasma levels of both LBP and zonulin were higher ($p<0.05$) in patients with SCZ compared to healthy controls and also associated with neutrophil-to-lymphocyte ratio (NLR) - a marker of systemic inflammation. No significant differences were found in taxa richness (alpha diversity) but microbial composition differed between SCZ patients and HCs (PERMANOVA, $p=0.02$). A specific genus-level microbial panel of *Ruminococcus, UCG005, Clostridium_sensu_stricto_1* and *Bifidobacterium* could discriminate SCZ patients from HCs, RISP SCZ vs HCs with the best sensitivity and specificity.
Discussion and Conclusions: Our study identified distinct microbial signatures that could aid in the differentiation of DN SCZ, RISP SCZ, and HCs, and demonstrates an association of zonulin, LBP, in SCZ

patients. Our findings contribute to a better understanding of the role of the gut microbiome/intestinal permeability in SCZ pathophysiology and to identify high risk individuals using gut microbiome signatures. Further research in this area has potential for the development of novel neuropyschobiotic-based therapeutics to treat neuropsychiatric diseases.
Acknowledgements: This work is supported by research grants from NIMHANS and DHR, Govt. of India. JN was supported by fellowship from ICMR.

S1.5. Self-propagating neurotoxicity of APP-C31 drives key pathogenic pathways implicated in Alzheimer's disease

Pawan Kumar and **Gavin S. Dawe**
Healthy Longevity Translational Research Programme, Yong Loo Lin School of Medicine; Department of Pharmacology, Yong Loo Lin School of Medicine; and Neurobiology Programme, Life Sciences Institute, National University of Singapore, Singapore

Background: The amyloid-β precursor protein (APP) undergoes caspase cleavage, resulting in the formation of the cytotoxic APP-C31 fragment. APP-C31 potentially plays a crucial role in Alzheimer's Disease (AD) progression. However, our understanding of this neurotoxin is still limited, particularly concerning the mechanisms that trigger its generation and continued production.
Materials and methods: We investigated caspase cleavage of APP in post-mortem brain and dermal fibroblasts from AD patients. We studied effects of APP-C31 on phosphorylation of APP and activity of caspase 3 in SH-SY5Y neuronal cells, and explored interferon-γ mediated neurotoxic effects in BV2 microglial and SH-SY5Y cell cultures.
Results: We found an association of caspase-cleaved APP with AD in human subjects. In cellular models, we identified that APP-C31 could enhance its own neurotoxicity by increasing the availability of a competent substrate, the phosphorylated form of APP, and the activity of the catalytic enzyme, caspase 3. We also found potential neuron-glia interactions whereby APP-C31 can raise interferon-γ levels and stimulate the Stat1 inflammatory pathway in microglia, which in turn compromises neuronal health.
Discussion and conclusions: Our findings indicate that APP-C31 may sustain its own neurotoxicity, potentially contributing cumulatively to the progression of underlying pathology in AD. Therefore, developing therapeutic strategies to target the APP-C31 neurotoxin could potentially mitigate the pathophysiology associated with AD.
Acknowledgements: This research was supported by the Ministry of Education, Singapore, under its MOE AcRF Tier 3 Award MOE2017-T3-1-002.

Symposium-2: Deciphering neural functions in health and diseases: emerging fronts

S2.1. A *Drosophila* genetic model to study the molecular and physiological pathways of epileptic disorder

Shamprasad Varija Raghu
Division of Neuroscience, Yenepoya Research Centre (YRC), Yenepoya (Deemed to University), Deralakatte, Mangalore, Karnataka 575018

Epilepsy is a chronic neurological disorder that affects more than 70 million people worldwide with a considerable social and economic burden. Relapses and unprovoked spontaneous seizures characterize the disorder. The most common antiepileptic treatments are pharmaceutical. However, in most epilepsy patients, drug therapy cannot control seizures. Despite different alternative treatments such as dietary control, nerve stimulation, and surgery, some patients still do not improve. Therefore, there is an urgent need to develop more effective protocols for the diagnosis and treatment of epilepsy. The genetically amenable model *Drosophila melanogaster* offers several genetic tools to mimic different human neuronal disorders,

including epilepsy. We are using the *Drosophila* genetic model to study the molecular and physiological pathways of epileptic disorders by applying different behavioural and molecular analyses.

S2.2. The role of NMDA receptor subtypes and synaptic plasticity in the epileptic brain

Pradeep Punnakkal
Department of Biophysics, Postgraduate Institute of Medical Education and Research Chandigarh, 160012, India.

Epilepsy is a common neurological disorder, affecting about 1% of India's population. The main reason behind epilepsy is the change in the ratio of excitatory to inhibitory neurotransmission. It is commonly observed that patients with epilepsy suffer memory-related problems. Hippocampus is the region in the brain, which is mainly associated with learning and memory. Long term potentiation (LTP) and long-term depression (LTD) are the two main models to study memory at the cellular level. LTP has been studied extensively in animal models and patients, but very little is known about LTD in epilepsy. Here, we studied the effect of epileptic activity in LTD by studying the Schaffer collateral pathway in the rat brain hippocampal slices. LTD was induced 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 epileptic activity in the hippocampal slices and then applied the LTD protocol induced 20% LTP instead of LTD. The change in the direction of synaptic plasticity was NMDA receptor subtype dependent. We also studied the excitatory and inhibitory ratio in control and epileptic slices by performing whole-cell patch clamp experiments in CA1 pyramidal neurons. We found that there was no change in excitatory current amplitude and inter-event interval, but epileptic activity reduced the GABA A current amplitude and interevent interval significantly when compared with control slices. The change in GABA A currents and loss of LTD in epileptic slices may explain the learning and memory impairments in patients with epilepsy.

S2.3. Mitochondrial disorders - Diagnostic approach using clinical, biochemical and genetic aspects

Christhunesa S Christudass, Sanjith Aaron, Ajith Sivadasan, Maya Thomas, Sangeetha Yoganathan, Poornima Sivamani
Department of Neurological Sciences, Christian Medical College – Vellore, Ranipet Campus, Kilminnal – 632517, Tamilnadu

Mitochondrial disorders are a clinically heterogeneous group of disorders and may present at any age. As the mitochondrial respiratory chain (MRC) is the essential for aerobic metabolism, tissues and organs which are highly dependent on aerobic metabolism are chiefly involved in mitochondrial disorders. Apart from common clinical features like proximal myopathy, exercise intolerance, etc., the central nervous system features include encephalopathy, seizures, dementia, migraine, stroke-like episodes, ataxia, and spasticity. The term 'mitochondrial disorder' generally refers to primary mitochondrial disorders, which are genetic and arise as a result of dysfunction of the MRC, affecting oxidative phosphorylation. Apart from them, many genetic and non-genetic disorders manifesting mitochondrial dysfunction as a secondary feature.
Clinical, biochemical and genetic tests play a vital role in the diagnosis of mitochondrial diseases. When the clinical picture is highly suggestive, we usually start with plasma or CSF lactate, plasma acylcarnitines, and urinary organic acids. Neuroimaging and neurophysiologic studies are warranted in individuals with suspected CNS involvement. Conventionally, the diagnosis of mitochondrial disorders involves the demonstration of mitochondrial dysfunction in a relevant tissue biopsy followed by targeted molecular testing of specific mtDNA and/or nuclear genes. But the recent advent of next generation sequencing has been changing the diagnostic approach drastically. Blood may not be ideal as many mtDNA pathogenic variants are heteroplasmic and large-scale deletions. If molecular genetic testing does not yield or confirm a diagnosis, further investigations with muscle biopsy or skin fibroblast culture will be needed. This lecture presents a comprehensive approach to the diagnosis of mitochondrial disorders.

S2.4. Data management in neuroscience using AI techniques

Arun Anirudhan
Sree Chitra Tirunal Institute, Trivandrum

Frequently, bedside monitors in neurocritical care gather persistent, abundant brain signals of considerable volume and frequency, including intracranial pressure (ICP) and electroencephalographic (EEG) waveforms. Although these signals frequently contain initial indications of neurological decline, effectively identifying these indications in real-time using conventional data processing techniques, primarily tailored for retrospective examination, has proven to be exceedingly difficult. These techniques are ill-equipped to manage the substantial quantities of waveform data generated by bedside monitors. Consistently, the system receives electrocardiographic and intracranial pressure (ICP) signals, examining the morphology of ICP pulses for any irregularities from a stable condition. To facilitate thorough examination of neurosurgical anesthesia, specialized software is necessary to amalgamate and assess information from various patient monitors. This undertaking explored the potential of creating such software to assist in conducting meaningful analysis of neurosurgical anesthesia. Additionally, we are in the process of creating a web interface that can promptly exhibit the outcomes of this analysis within a web browser in real time. Through this interface, medical professionals can conveniently monitor their patients' conditions and directly comprehend and interpret the patients' current states as they evolve. AI techniques are employed to forecast the potential outcomes. The software also facilitates the digital capture of data, prepared for subsequent manual or batch analysis. It allows for the generation of virtual signals, such as critical closing pressure and cerebral compliance, and the assessment of how they correlate with primary modalities. An amassed repository of cases and signals establishes a potent reference resource for delving into and comprehending the intricate pathophysiology.

S2.5. Genetic dissection of a novel molecular player in obesity?

Shobi Veleri and Anjusha Bhasker
Drug Safety Division, ICMR-National Institute of Nutrition**,** Department of Health Research**,** Ministry of Health & Family Welfare, Govt. of India**,** Jamai - Osmania P.O. Hyderabad, India. PIN - 500 007

Obesity is a health menace and is a major risk factor for non-communicable diseases that account for >70% of early deaths in the world (WHO, 2017; Bluehr, 2019). Obesity has multifactorial aetiology. Hence the treatment for obesity remains a challenge. The disruption of leptin signaling pathway is largely implicated in obesity; mutations in *leptin* and its receptor is central to obesity phenotype. However, the search for genetic causes of obesity shown that without mutations in leptin signaling pathway obesity exists in animals and humans (Davenport *et al.*, 2007; Klar *et al.*, 2005). This indicates role of additional molecular players in the onset of obesity, and they remain elusive. We have a mutant obese rat (Giridharan, 2018) with an unknown mutation. Previous analysis suggested a putative genetic locus 4.43 cM region flanking D5Rat256 and D5Wox37 on chromosome 5, which is upstream of Leptin receptor (Rao *et al.*, 2013). We have used Whole Genome sequencing method to identify the elusive mutation. We have pre-screened more 12 mutant genes (SNPs) and excluded chromosome 5. We are applying transcriptomic and histo-pathological analyses to characterize the mutant gene. Our preliminary data indicate the role of a novel gene in the onset of obesity in Wistar rat. This finding may open new avenues for devising novel treatment for obesity in human.

Symposium-3: Stress, aging and neurodegeneration- Building basic and interventional understanding through cell culture and mouse models

S3.1.Basic and interventional understanding of stress, ageing and neurodifferentiation: lessons from cell culture studies

Renu Wadhwa[1], Anissa Nofita Sari[1], Yoshiyuki Ishida[2], Keiji Terao[2], Sunil C. Kaul[1]
[1]AIST-INDIA DAILAB, National Institute of Advanced Industrial Science & Technology (AIST), Tsukuba-305 8565, Japan; [2]CycloChem Bio Co., Ltd., 7-4-5 Minatojima-minamimachi, Kobe-650 0047, Japan

Chronic stress has been linked to a variety of diseases, including brain dysfunction and cancer. The response of cultured cells to stress, which induces adaptations in their biochemical and metabolic pathways, forms the basis for their use in basic and interventional studies. Normal and stressed cells can be easily identified by their morphology, and adaptations in their molecular signalling pathways, determined by upregulation/downregulation of gene expression, extend their use in disease models and drug development. In cell culture systems, stressed cells have been shown to age prematurely and prolonged stress has been shown to induce carcinogenesis. Such a link between stress, ageing and cancer is well documented by molecular studies of CARF (Collaborator of ARF) in our group. While CARF-compromised cells undergo apoptosis, CARF overexpression and superexpression lead to premature senescence and malignant transformation, respectively. In addition, cell-based screens and molecular analyses have led to the identification of some natural anti-stress compounds (e.g., bioactive compounds from honey bee propolis - caffeic acid phenethyl ester, CAPE, and Ashwagandha - withaferin A, Wi-A, and triethylene glycol, TEG) that have been shown to promote neurodifferentiation *in vitro* and memory and brain function in *in vivo* stress/disease models. More recently, under the premise of COVID-19 pandemic, an extreme stress situation, by combining computational and cell culture assays, we reported the anti-COVID-19 potential of Ashwagandha and propolis-derived bioactive compounds, which is beginning to be supported in the clinic.

S3.2. Role of computational biology in basic and interventional understanding of stress, aging and neurodegeneration

Durai Sundar
Indian Institute of Technology Delhi (IIT-Delhi)

Cancer is a disease marked by genetic instability and thus specific inhibition of individual proteins or signaling pathways holds a great potential for subversion of this genetic plasticity of cancers. Many active compounds from traditional medicinal sources could serve as good scaffolds for rational drug design. Combinatorial chemistry approaches based on natural product scaffolds are being used to create screening libraries that closely resemble drug-like compounds. Most of these compounds are part of routinely used traditional medicines and hence their tolerance and safety are relatively better known than any other chemical entities that are new for human use. Thus, traditional medicine-based bio-prospecting offers unmatched structural variety as promising new leads. Recent surge towards usage of high-specificity drugs having reduced side effect profile is urging explorations with naturally occurring herbal drug candidates. Computational tools can be used to elucidate the interactions between the drug and its target molecules and to identify the stability of such interactions. The understanding obtained from these studies will help in developing future approaches towards cure of these nefarious cancerous diseases. This talk will describe the progress in computational approaches for drug discovery and its potential application in biomedicine.

S3.3. Narcolepsy- sleep stress and Orexin: Towards development of new therapies

Mahesh K. Kaushik
International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba,1-1-1 Tennodai, Tsukuba, Ibaraki 305-8575 Japan

Orexins/hypocretins are hypothalamic neuropeptides secreted from orexinergic neurons located in the lateral hypothalamus. Orexins orchestrate their action by activating two G-protein coupled receptors, orexin receptor type-1 (OX1R) and type-2 (OX2R). Narcolepsy/cataplexy, a neurological disorder is caused by the loss of orexin-producing neurons. While orexin effectively mitigated narcolepsy in rodents through ICV delivery, its application in humans is hindered by its inability to penetrate the blood-brain barrier. Hence, we showed that orexin delivered via the intrathecal route at the lumbar level inhibited narcolepsy symptoms and improved sleep-in narcolepsy model mice. Since orexin signaling is crucial for brain physiology and pathology, it became the potential drug target to treat neurological disorders such as insomnia, hypersomnia, narcolepsy, PTSD, AD, etc. One such successful example is the approval of orexin receptor antagonists to treat primary insomnia in human patients. We reported that the orexin receptor antagonist, suvorexant executes its actions in two ways; 1). inhibiting the orexin receptors and thus downstream signaling, 2). decreasing the orexin peptide synthesis. Further, under certain conditions, a high dose of orexin receptor antagonist can induce narcolepsy due to its dual actions. Since enhanced orexin signaling is observed in several neurological disorders and orexin receptor antagonists downregulate orexin signaling, orexin-based therapies could improve neurological pathologies in aging brains. However, our data suggested a cautious use of such therapies for patients with co-morbid neurological diseases.

S3.4. Fears to fierce-tracking the molecular path of post traumatic aggressive behaviour

Arpita Konar
Institute of Health Sciences, Presidency University, Kolkata, India

Traumatic experiences of fear, abuse and neglect leaves lasting impact on higher order brain functions and behaviour posing risk for psychopathy, though molecular culprits are not understood well. In particular, trauma surrounding puberty comprising of childhood and adolescence has been linked with adulthood pathological aggressive behaviour, indicative of violence and anti-social personality. We demonstrated that predator fear (fox odor) and height (elevated platform) exposures around puberty leads to escalated aggression in adult male mice and the hyper-aggressive phenotype was perpetuated in male progenies of subsequent generations. Interestingly, females that showed early life fear responses did not show any signs of later aggression. MAOA, considered crucial for aggression was altered in peripubertal stress induced aggressive males. Further, brain region (prefrontal cortex and hypothalamus) and sex specific transcriptome analysis revealed a number of differentially expressed protein coding genes and long-non coding RNAs. Functional analyses of top-ranking genes by brain region targeted manipulations suggested potential contribution of brain thyroid hormone availability irrespective of circulating hormone states in post-traumatic aggression and its inheritance. We also characterized the novel lncRNAs of our DEG list and based on preliminary observations hypothesize that non-coding RNA mediated long-term epigenetic programming of genes including brain thyroid hormone pathway could underlie lasting impact of traumatic stress on abnormal aggressive behavior and related psychopathologies.

S3.5. Link between hypoxia and neurodifferentiation signaling: experimental and computational perspectives

Jaspreet Kaur Dhanjal[1], Renu Wadhwa[2], Sunil C. Kaul[2]
[1]Department of Computational Biology, Indraprastha Institute of Information Technology Delhi, Okhla Industrial Estate, Phase III, New Delhi 110020, India
[2]AIST-INDIA DAILAB, National Institute of Advanced Industrial Science & Technology (AIST), Central 5-41, Tsukuba 305-8565, Japan

Oxygen is one of the critical requirements for most of the eukaryotic organisms as it ensures the healthy state of the cells by removing harmful electrons and hydrogen. Reduced availability of oxygen, often termed as hypoxia, activates a cascade of gene transcription as a protective measure. However, if the hypoxic condition prevails for long, it may cause physiological or pathological disorders. Hypoxia has been associated with various disorders like cancer, chronic heart and kidney diseases, reproductive diseases and metabolic disorders. Hypoxia has also been shown to be detrimental to the brain and is implicated in the pathogenesis of neurodegenerative diseases. Therefore, identification of pro-hypoxic compounds as preventative and prognostic therapeutic agents holds immense potential. In line with this, we have previously reported caffeic acid phenethyl ester (CAPE) as an effective pro-hypoxia and anti-stress molecule. CAPE has also been studied for its effective anti-cancer and neurodifferentiation properties. We have now identified other naturally occurring small molecules like Withaferin-A and Tectorigenin with pro-hypoxic potential that also possess anti-cancer and neurodifferentiation properties, respectively. In conclusion, nature is a repertoire of therapeutic compounds that offers solution for most of the prevailing health related challenges, and warrant extended exploration.

S3.6. Response of iron-induced experimental epilepsy to anti-peroxidant treatment

Shanuja Beri[1] and Rameshwar Singh[2]
[1]Kalindi College University of Delhi; [2] School of Life Sciences, Jawaharlal Nehru University

Iron released from extravasated hemoglobin catalyses the formation of oxygen-derived free radicals which in turn cause lipid peroxidation of the neuronal membranes and mediate clinical post traumatic epilepsy confirmed by epileptic electrophysiological activity. As lipid peroxidation is the cause, use of antioxidants was studied by us to counter the effect and resultant progression of epileptic activity. Iron induced post-traumatic epilepsy experimental animal model was used to study the effects of antioxidants on the progression of iron-induced epileptic activity in the rat brain cortex. Intracortical injection of $FeCl_3$ in the animals were followed by administration of antioxidant drugs at different intervals. In the present study, the development and occurrence of epileptic activity was monitored electrocorticographically, biochemically as well as was supported by electron micrography of the focal point. The result showed significant attenuation of the electrographic seizures in the ipsilateral epileptogenic focus. Our data provides experimental evidence in support of the view that treatment of post traumatic epilepsy by antioxidants is therapeutically rational. Previous experimental studies concerning the anti-peroxidant prevention of iron epilepsy dealt with only whether pretreatment with an antioxidant could prevent the development of epileptic activity. It was however of more interest to determine whether anti-peroxidant treatment could prevent the progression of epileptic activity after it has developed.

S3.7. Acute and chronic stress differentially affect hippocampal coding

Anupratap Tomar
University of Bristol, UK

Chronic exposure to uncontrollable stress caused by physical or psychological stressors induces anxiety, depression, and cognitive impairments. Notably, deficits in cognitive functions, particularly in learning and memory, are often attributed to compromised functionality of the hippocampus—an integral brain region responsible for encoding names, places, routes, and contextual information. Acute stress is thought to have facilitatory effect on hippocampal information processing. However, it remains unclear if and how the facilitatory effects of acute stress on hippocampal information coding are disrupted as the stress becomes chronic. To examine this, we compared the impact of acute and chronic stress on neural activity in the CA1 subregion of male mice subjected to a chronic immobilization stress (CIS) paradigm. We observed that following first exposure to stress (acute stress), the spatial information encoded in the hippocampus sharpened. However, following repeated exposure to the same stress (chronic stress), spatial tuning was poorer. In addition, gamma oscillations in the local field potential (LFP) were affected. Specifically, the power of both the slow-gamma (30–50 Hz) and fast-gamma (55–90 Hz) oscillations, which correlate with excitatory inputs into the region, decreased. These results support the idea that acute and chronic stress differentially affect neural computations carried out by hippocampal circuits and suggest that acute stress ‘may’ improve cognitive processing.

Symposium-4: The social and emotional brain: A game changer for education and learning

S4.1. Introduction to social and emotional learning – why might it be a game changer for education ?

Nandini Chatterjee Singh
UNESCO MGIEP, New Delhi

The existing design of education systems focuses on academic skills and cognition development in order to build human capital for economic growth. Accumulating research indicates this sole focus on economic growth has led to increasing anxiety, depression and poor mental health in addition to poor learning outcomes. Building on recent research from the neurosciences that demonstrates that learning is a cognitive social emotional process, we postulate that education systems must include training in social and emotional learning (SEL). SEL is the process of developing competencies and attitudes necessary to recognize and control emotions, develop caring and concern for others, form positive relationships, make responsible decisions, and deal with challenging situations. Explicit training in SEL enables deep learning but also trains learners to experience positive emotions, exhibit prosocial behavior and cultivate brain networks for mental well-being. I will discuss the impact of SEL training on both teachers and school children.

S4.2. Decision-making: A social & emotional brain's perspective

K M Sharika
Dept. of Cognitive Science, Indian Institute of Technology, Kanpur

According to the social brain hypothesis, primate brains evolved in size to adapt to the increasing demands of navigating a complex social network. Recent evidence has corroborated this by demonstrating how social interactions (or its lack of) can have measurable consequences on an organism's biological fitness. However, the neural mechanisms underlying our everyday decisions in a social context are still not well-understood. In this talk, I will briefly introduce some aspects of social cognition research with a special focus on the role of valence in decision-making. This is particularly relevant, not only given the common tendency among us to overweigh negative stimuli over that of positive valence across multiple domains of behavior (a phenomenon known as negativity bias), but also because of the crucial role that negative valence plays in empathy research. I will highlight some of our own attempts to investigate this in a modified version of the standard cue association learning task and share some evidence for the role of acetaminophen, an active ingredient in the common painkiller, paracetamol, in valence-based social decision-making. We hope that these preliminary findings will, in the long run, help elucidate the behavioral and neural processes at play and pave the way for the development of optimal strategies for improved health and life outcomes.

S4.3. Social emotional learning and self-regulation: efficacy of a video-game based intervention for prosocial behaviour

Bhoomika R. Kar and Renuguha D.
Centre of Behavioural and Cognitive Sciences, University of Allahabad, Prayagraj

Social and emotional learning (SEL) is the process of gradually acquiring and effectively applying knowledge and skills required to recognize and manage emotions; developing care and concern for others; making responsible decisions; establishing and maintaining positive relationships and handling tough situations with confidence and resilience. It helps to foster regulation of one's thoughts, emotions, and behaviour. The development of prosocial behaviours is important during early years to develop social and emotional competence. The movement known as "Positive Technology" was born out of a growing interest in how digital technologies may help people, organizations, and Interaction partners grow positively (Gaggioli et al., 2019). Research on SEL needs more objective measures such as experiment-based research

that enables comparison among studies and can supplement self-reports, teacher reports, and indirect measures of social and emotional skills. The current study focused on prosociality as an important component of the SEL programs. *Sky: Children of Light* will be presented. A video game based intervention for prosocial behaviour and trust was used and an experimental approach was applied to validate *Sky: Children of light* as an intervention to build prosocial behavior. Performance of adolescents on two allocation paradigms, a resource allocation task to assess prosociality and a trust task, was examined. The resource allocation game examined prosocial behavior in the form of giving and sharing in social interactions including friends, antagonists, neutral and anonymous peers, highlighting the role of social context in the development of prosociality. The trust game was used to assess reciprocity and trust in social interactions. The Prosociality scale showed normative variations in prosocial behaviour among children in the age range of 12 to 15 years. Results based on post intervention assessment suggest improvements in prosocial behavior in terms of fair considerations for the antagonist, neutral, and anonymous peers in the prosocial game. The significance of digital game based SEL programs, their empirical validation and challenges will be discussed in the presentation.

Symposium- 5: Neurocognitive mechanisms underlying working memory

S5.1. Neural substrates of working memory deficits in addictive disorder

Simran Kaur
Stress and Cognitive Electroimaging Lab, Department of Physiology, All India Institute of Medical Sciences, New Delhi

Working memory is an indispensable cognitive domain that enables encoding, updating, maintenance and manipulation of information to ensure successful task execution. Inherent defect in working memory in the subjects with addictive disorder can lead to impairment in volition and irrational heights to attain the substance of abuse despite being well aware of the ominous consequences it brings with it. Even though such studies on cognitive deficits in individuals with addictive disorders exist, a considerable lacuna in the existing studies is about the underlying neural substrates during working memory related performance.128 channel Quantitative EEG was acquired, pre-processed and was further analysed for sLORETA-based source and Cartool-based pre-stimulus microstate analyses in subjects with addictive disorder (alcohol and opioid) compared to matched healthy controls. Network specific cortical source analysis revealed failure of deactivation of default mode network areas and reduced activity in executive function areas, which led to working memory deficit in these patients. Further, novel EEG microstate analysis also substantiated aberrant activity in default mode and fronto-parietal attentional network, as revealed by lower mean duration of microstate maps (Map 2 and 3) in subjects with addictive disorder compared to controls. Thus, inability to suppress default mode network areas, inhibits reallocation of neural resources to executive areas as reflected by pre-stimulus EEG microstate and source analysis, may potentially form the basis of functional impairments in the subjects with addictive disorders.

S5.2. Distractors in working memory: Mechanisms and Models

Sridharan Devarajan
Indian Institute of Science, Bangalore

Working memory is our ability to momentarily store and recall items or events, even when these have vanished from our immediate environment. In everyday life, working memory must function dependably even in noisy, distracting environments. How are the contents of working memory protected from interference by distractors? In this talk, I will show that a salient, unpredictable distractor can bias the contents of working memory at the neural level. The extent of such interference depends on where the distractor occurs in space, its timing and the extent of its gating. I will also present a computational model that parsimoniously explains the experimental findings. This research could help better understand how working memory can be protected or enhanced, even in noisy environments

S5.3. Visuospatial working memory: An endophenotypic marker in Schizophrenia

Ratna Sharma
Dept of Physiology, All India Institute of Medical Sciences, New Delhi

The process of linking brain function and behaviour is an important aspect of pathophysiological states. The novel visuospatial working memory task, simulating day-to-day activities was administered in patients with schizophrenia, their first-degree relatives and healthy controls. Patients committed higher number of errors than controls in higher loads and total errors. Errors in higher loads were significantly higher than in lower load for all groups. Using EEG microstates, neural correlates of visuospatial working memory were assessed. Patients deactivated DMN, RSN, auditory cortex more compared to controls during search period to perform VSWM task. Relatives showed altered activation of right medial and inferior frontal gyri during different events and loads of task in lower frequencies compared to controls. Relatives also showed hyperactivity in right cingulate and parahippocampal gyri compared to controls. This is suggestive of genetic predisposition in schizophrenia and could act as vulnerability markers, further strengthened by no significant differences between patients and relatives. Altered processing of simultaneous ongoing events in patients and relatives can serve as state and trait-specific features of schizophrenia. To conclude, the findings of the study can serve as state markers and trait markers of schizophrenia which in turn will provide objectivity to the diagnosis of schizophrenia.

S5.4. Clinical assessment and therapeutic interventions for working memory deficits in addictive disorders and dual disorders

Yatan Pal Singh Balhara
NDDTC and Department of Psychiatry, All India Institute of Medical Sciences, New Delhi

Working memory deficits among persons with addictive disorders and dual disorders have a significant impact on the daily functioning and worsen the quality of life among these individuals. These also play a crucial role in continuation of the substance use, the addictive behaviour and the cooccurring mental disorder. Hence it is imperative that these deficits are systematically evaluated. The impact of these deficits on the course and outcome of addictive disorders also warrants that the interventions plan should also target these. This presentation shall focus on the approach to clinical assessment of working memory deficits in addictive disorders and dual disorders. Also, the available interventions, their impact and limitations shall also be discussed. The presentation shall also offer an overview of the ongoing research in this area.

Symposium-6: Yogic interventions for tackling mental health issues: A desideratum for contemporary issues

S6.1. The role of pre-natal yoga protocol in managing pregnancy: mechanistic insights for memory enhancement

Akshay Anand
Postgraduate Institute of Medical Education and Research, Chandigarh

Our study aimed to investigate the impact of prenatal Yoga on pregnancy outcomes and the potency of umbilical cord blood (UCB) derived lineage negative (Lin-ve) stem cells. We examined pregnant women aged 18 to 35 who practiced Yoga from the 16th to 18th week of pregnancy until delivery. The study also involved an animal model of brain injury induced by Amyloid beta (Aβ) administration in mice. After Yoga intervention, UCB was collected from the participants, and Lin-ve stem cells were analyzed. Flow cytometry revealed an increased number of CD34+ve cells in the Lin-ve population in Yoga group participants,

indicating enhanced stemness. For the animal model, Lin-ve stem cells from Yoga practitioner mothers and usual care group mothers were injected into mice with Aβ-induced memory loss. Neurobehavioral tests showed improved memory in both transplantation groups, with the Yoga group showing greater improvement. mRNA expression of BDNF, Nestin, and CREB was marginally increased in the Yoga group. Protein expression of BDNF was significantly higher in the braon of mice who received stem cells from Yoga group as confirmed by IHC. These results suggest that Yoga during pregnancy can impact stem cells at a cellular level, potentially enhancing the efficacy of UCB-derived stem cells. Embracing Yoga as a lifestyle during pregnancy may lead to improved outcomes, and Lin-ve SCs derived from Yoga practitioners could be

S6.2. Yoga: mental health and well being

Krishan K
Postgraduate Institute of Medical Education and Research, Chandigarh

Yoga is a vast subject to discuss and number of experiments has been done by using various kind of yoga to cure mental health issues. However, the practice of yoga is now as common as used as a part of healthy life style for all the age group both in western countries as well as in India. Yoga is the one of the most powerful and time-tested spiritual technique to go beyond the body, consciousness and experience subconscious and later on the superconscious states of the self. A positive feature of yoga interventions may in fact be very supportive for the execution and maintenance of a lifestyle changes due to the experience of well-being and the changes in mind and body awareness that occur over time with continued yoga practice. It also supports a desire to adopt and maintain healthy behaviours. Yoga may have potential to be implemented as a beneficial supportive/adjunct treatment that is relatively cost effective and can be practiced at least in part as a self-care behavioural treatment as it provides a life-long behavioural skill, enhances self-efficacy and self-confidence. Yoga interventions are curative treatments remains to be determined and safe to suggest, because of low risk for side effects and potential for actual positive side effects. Nevertheless, there is currently insufficient data on contraindications or side effects related to yoga practices in patients with psychological disorders. Thus, Larger-scale and more rigorous research is highly encouraged for further studies in which patients may benefit from the interventions and which aspects of the yoga interventions (i.e., physical activity and/or meditation and subsequent life style modification) or which specific yoga styles were more effective than others.

S6.3. Spectrum of yogic relaxation techniques

Jyoti Dvivedi
Himalayan Institute of Medical Sciences, Dehradun

Yoga is a holistic science that is relevant to all systems of human physiology. Yoga provides a sound framework to understand and deal with stress. It is a useful technique to look at the unconscious parts of the mind to understand the habits and patterns leading to stress. The guided technique of yogic relaxation practices helps to improve insomnia, ameliorate stress, decrease depression and anxiety and thus lower tendency for cardiovascular diseases. Interestingly, the relaxation response, a meditative technique described by Herbert Benson, has been found to reduce the symptoms of AIDS, cancer and other diseases in scientific studies. The relaxation response seems opposite to the fight-or-flight response observed under perceived threatful situation. With the relaxation technique the heart rate, blood pressure, respiratory rate, and metabolism decreases. Besides this, the ancient yogic literature speaks volumns of ‘shavasana’ popularly refered to as the relaxation technique by the western world. The other relaxation technique is ‘Shavyatra’, which is well established technique of Hatha yoga for the body and mind. Further there are many modified relaxation techniques for the ease to understand by a modern man, one of them being the 61-point relaxation exercise. It should be practiced for about 20 minutes per day in isolation. It does not require specialized equipment. Regular practice helps to elicit the relaxation response easily.

S6.4. Yogic intervention in occupational stress: Trends and Advances

Pramod Avti[1,2], Akshay Anand[2,3], Saurabh Kumar[2], Prashant Verma[2], Kanu Priya[3], Monica Gautam[2], Hosakote S Vadiraja[4], Rao M Raghavendra[4]
[1]Department of Biophysics, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh; [2]CCRYN-Collaborative Centre for Mind Body Intervention through Yoga, PGIMER, Chandigarh; [3]Neuroscience Research Lab, Department of Neurology, PGIMER, Chandigarh; [4]Central Council for Research in Yoga & Naturopathy (CCRYN), New Delhi, India

Stress arising in the public-professional systems due to their fulfilling occupational duties is emerging to a greater extent. This has adverse effects not only on the physiological, physical and mental responses but also drastically impacts the mind-body co-ordination. The overall effects lead to poor quality-of-life and performance to discharge their professional duties. Various trials undertaken on providing regular and systematic yoga training, though the yoga protocols followed are different, for specific defined time scales have shown ameliorating effects at different molecular, amperometric, physiological, and neuropsychological levels. The use of common yoga protocol (CYP) based studies seem to be emerging. In the present talk the use of CYP in the public-professional systems will be presented to evaluate the mechanistic approaches in understanding the ameliorating benefits from the molecular to neuropsychological approaches involved in improving the overall quality-of-life of the professional employees.

S6.5. Physiological insights to yogic interventions

Seema Singh
Era's Lucknow Medical College, Lucknow, Uttar Pradesh

Yoga, an ancient Principle, is now considered a tool for comprehensive health benefits. The world "Yoga" originates from a Sanskrit word "Yu" that relates to uniting or joining. It involves directing and concentrating one's attention. Yoga is considered reliable curative therapy for various physical, mental and biochemical disorders affecting the body although it takes time for the beneficial effects. Yoga helps as an adjunct to routine medical treatment by: Reducing the symptoms, improving energy levels, calming the mind, giving hope and motivation, improving the regenerative processes. Yoga helps in improving the performance in: Sports, competitive exams and in various skills.
The yogic interventions affect the body functions and the physiological effects of various yogic exercises have been investigated and reported in the literature. In this talk the physiological insight to yogic interventions will be discussed.

S6.6. Quantitative EEG application in assessing effects of Kriya yoga on brain

Pooja Ojha[1], Naresh Nebhinani[1], Ambika Chandani[2]
[1]All India Institute of Medical Sciences, Jodhpur, Rajasthan
[2] Indra Yoga Sansthan, Jodhpur, Rajasthan

Our current lifestyle exposes us to physical and mental exhaustion and stressful situation. It brings to fore the need to take up a lifestyle intervention with a positive impact on mental health. Kriya yoga combines several techniques like mantra chanting, breath modulation, pranayam, and asana holding. It can be easily learned and practiced. The participants enrolled in the study were taught the yoga by a trained yoga practitioner and were required to practice it for six weeks. The effects of this technique were investigation on brain waves through the electroencephalogram (EEG). EEG is chosen as it is a non-invasive tool with high temporal resolution. The quantitative EEG comprise digital encoding of the raw data and its subsequent statistical analysis. The EEG signals were acquired before and after six weeks of Kriya Yoga practice. The data were analyzed quantitatively for brain wave powers over several regions of the brain. The results revealed the benefits of Kriya yoga practice and will be discussed in the presentation.

Symposium- 7: Long-term sequel of neuro-COVID: Ghosts of a bygone pandemic

S7.1. Epidemiological aspects of long-term neuro-COVID

Adil Asghar
Department of Anatomy, All India Institute of Medical Sciences-Patna, Patna, India

Background: Several studies have reported prolonged symptoms especially neurological symptoms following acute infection in patients with COVID-19, known as long COVID-19. There are only few studies investigating this population and relatively less known, including nervous system involvement. A systematic review and meta-analysis of these studies are required to understanding the prevalence of persistent neurological manifestations after COVID-19.
Objective: To conduct a systematic review and meta-analysis on the persistent neurological manifestations in COVID-19 survivors.
Methods: Authors conducted a literature search through all major databases till June 2023 according to PRISMA guideline. Furthermore, the authors added additional sources by re- viewing related references. Studies presenting the neurologic features of long COVID-19 patients in their data were included. Case reports and case series also included in this review. The quality of the studies was assessed based on the Oxford Centre for Evidence-Based Medicine guidelines. Selected studies were included in the meta-analysis of proportion and heterogeneity test.
Findings: Most of the included studies had mean duration of follow-up after COVID-19 onset of less than 6 months. Fatigue was the most common (52.8%, 95%CI 19.9 – 84.4) symptoms of long COVID, followed by cognitive disorder (35.4%, 95%CI 2.1 – 81.7); paresthesia (33.3%, 95%CI 2.7 – 76.6); sleep disorder (32.9%, 95%CI 6.5 – 67.4); musculoskeletal pain (27.8%, 95%CI 12.7 – 46); and dizziness (26.4%, 95%CI 4.6 – 57.9).
Conclusion: Neurological manifestations are prevalent and persisting in patients with long COVID. The duration of the symptoms are vary among literatures. However, the frequency are mostly observed during the first six months after the illness onset.

S7.2. Evidence Favouring Viral Injury of Brain Cells as a Pathogenetic Mechanism of Long-Term Neuropsychiatric Illness in COVID-19

Ishani Bora
Department of Virology, PGIMER Chandigarh

SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus-2) causes coronavirus disease 2019 (COVID-19) and associated medical complications. This virus has both neurotropic as well as neuro-invasive properties and has a potentiality to cause injury to the central nervous system (CNS). There has been evidence that viral injuries to brain cells may serve as a plausible pathogenic mechanism underlying long-term neuropsychiatric illnesses in individuals affected by COVID-19. There has also been a possible link associated in neuropathological changes in the brain with neuropsychiatric symptoms, behavioral disturbances and also cognitive dysfunction. The potential biological mechanisms encompass direct micro-invasion of neurons, disruptions within the neuro-immuno-endocrine system, and potential modifications to neuronal excitability. It has been shown that, SARS-CoV-2 utilizes the angiotensin-converting enzyme 2 (ACE2) receptor as a means of cellular entry. This discovery prompts an inquiry into the expression of ACE2 within neurological tissues, as well as an exploration of the potential implications of neurological tissue damage on overall morbidity and mortality caused by COVID-19. Recent indications propose that individuals affected by COVID-19 may experience neurological manifestations including symptoms like headaches, changes in consciousness, and sensations of paresthesia. Autopsies have revealed instances of cerebral edema and limited neurodegeneration in brain tissue. Furthermore, there are indications suggesting the virus's capacity to induce harm to the nervous system. These collective observations imply a potential link between the virus and the emergence of immediate psychiatric symptoms and persistent neuropsychiatric consequences stemming from COVID-19. Consequently, the neurological complications linked to COVID-

19 infection may exert enduring effects on cognitive functions and understanding these mechanisms is crucial for the development of targeted interventions and therapies to alleviate the burden of long-term neuropsychiatric consequences in COVID-19 survivors.

S7.3. Pathogenesis mechanisms for long-term neuro-COVID

Sujeet Kumar
Centre for Proteomics & Drug Discovery, Amity University Maharashtra, Mumbai

The emergence of COVID-19 pandemic by the novel coronavirus SARS-CoV-2 and its sub-variants have imposed long-term health implications. The SARS-CoV-2 virus, primarily thought to infect lungs through the internalization mediated by the host-cell entry mediators angiotensin-converting enzyme 2 (ACE2) and transmembrane protease, serine 2 (TMPRSS2), has later been observed to infect multiple organs lacking these mediators. The involvement of organs other than the lungs often involved a non-ACE2 dependent mechanism and the studies have suggested that an alternative host cell entry receptor, neuropilin-1 (NRP1), can mediate the entry of furin-cleaved SARS-CoV-2 spike proteins into host-cells. The protein expressions of NRP1 and furin are observable in the brain tissue's neuronal cells, neuropil, and glial cells. The pathological involvement of the nervous system in COVID-19 patients poses a long-term risk of developing a neuropsychiatric illness in survivors that may persist for years. Although mental health conditions such as anxiety and depression return to normalcy over time, but the increased risks of cognitive impairment (brain fog), seizures, dementia, psychosis and other neurocognitive conditions persist for at least 2 years. Possible mechanisms for these neuropathologies include neuroinflammation, damage to blood vessels by coagulopathy and endothelial dysfunction, and injury to neurons. Although the current findings are critical to understanding long COVID, to prioritize & strengthen long-term neuro-COVID research, the future studies must engage patients meaningfully throughout the research process and be inclusive of marginalized populations.

S7.4. Long-term risks of neurodegenerative diseases in recovered COVID-19 patients

Ashok K. Datusalia
Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research (NIPER) Raebareli, Lucknow

In the recent years, the mankind has faced the pandemic caused by the severe acute respiratory syndrome 2 coronavirus (COVID-19), which caused around 10 million deaths and approximately 700 million positive infections with survival worldwide. Although COVID-19 mainly affects the respiratory tract level, there are several evidence, indicating that other organs such as the heart, kidney, pancreas, and brain are badly affected in individuals on infection. A characteristic observed in blood serum samples of patients suffering COVID-19 disease in moderate and severe stages, is a significant increase in proinflammatory cytokines such as interferon-α, interleukin-1β, interleukin-2, interleukin-6 and interleukin-18, as well as the presence of autoantibodies against interferon-α and interferon-λ. Interestingly, it has been described that the chronic cytokinemia is related to alterations of blood-brain barrier permeability and induction of neurotoxicity. Similarly, Evidence also indicates accelerating the Parkinson's disease Alzheimer's disease phenotype in surviving individuals after Covid infections. Furthermore, the generation of virus specific antibodies and autoantibodies alter the processes of neurogenesis, neuronal repair, myelination, and the optimal astrocytes-microglia axis. These observations indicate that COVID-19 subjects may show neurological sequelae and neuropsychiatric disorders on short and long term after survival.

S7.5. G6PD deficiency mediated dysregulation of redox equilibrium contributing to Covid-19 mediated neuroinflammation

Abir Mondal[1], Subrata Munan[2], Isha Saxena[1], Soumyadeep Mukherjee[1], Prince Upadhyay[1], Waseem Dar[1], Nutan Gupta[3], Animesh Samanta[2], Shailja Singh[3] and **Soumya Pati[1]**
[1]Department of Life Sciences, School of Natural Sciences, Shiv Nadar Institution of Eminence, Delhi-NCR, India; [2]Department of Chemistry, School of Natural Sciences, Shiv Nadar Institution of Eminence, Delhi-NCR, India; [3]Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi, India.

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 the regulation of redox equilibrium and nucleotide biosynthesis. Additionally, G6PD-derived NADPH can follow pro-oxidative and anti-oxidative pathways 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 a very common enzymatic disorder that affects more than 1 million individuals per year in India and worldwide. Besides, several clinical reports suggested that G6PD deficient patient shows aggravated Covid-19 response and severe neuroinflammation.
Aim: The mechanism of G6PD deficiency-mediated Covid-19 responses is still ambiguous. In this study, we are investigating the functional dichotomy of G6PD in Covid-19 mediated neuroinflammation.
Methods: We generated a CRISPR-mediated G6PD deficient *in-vitro* model to study the response of human microglia under foreign pathogenic stimulus. To study covid-19 mediated neuroinflammation, we used *in-vitro* translatable 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 a 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 a reduction of ROS and Nitric oxide production *in-vitro*. Surprisingly, we also observed a decrease in lysosomal acidification in G6PD deficient cells which could possibly be due to the reduction of cellular NADPH which affects the acidification of lysosomes by altering the function of the proton pump.
Conclusion: G6PD is the most crucial enzyme for restricting SARS-CoV-2-mediated neuroinflammation. A 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 a detailed understanding of neuroinflammation.

Symposium- 8: Cellular and molecular insights into CNS disorders: Possible therapeutic approach

S8.1. Regulation of glioblastoma through mitochondrial quality control

Pransu Srivastava[1], Sabya Abbas[1], Ved Prakash Maurya[2], Meenakshi Tiwari[3] and **Lokendra Kumar Sharma[1]**
[1]Department of Molecular Medicine and Biotechnology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Rae Bareli Road Lucknow, (U.P.) 226014, India; [2]Department of Neurosurgery, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Rae Bareli Road Lucknow, (U.P.) 226014, India; [3] Department of Biochemistry, All India Institute of Medical Sciences, Patna, Bihar-801507, India

Glioblastoma Multiforme (GBM) is the most challenging type of High-Grade Glioma (HGG) with high recurrence and chemotherapeutic resistance contributing to its poor survival rate. Studies have shown that a small population of cells commonly referred as glioblastoma-initiating cells (GICs) is thought to cause tumor relapse and therapeutic resistance. However, mechanism of GICs survival during carcinogenic insult and/or therapeutic stress remains unclear. Although increased glycolysis is a hallmark of cancer (Warburg effect), reprogramming of mitochondria is now recognized as an important event in the adaptation of cancer cell for survival and proliferation. Mitochondrial functions are regulated through its quality control such as biogenesis, dynamics (fusion and fission) and clearance (mitophagy). Although, changes in mitochondrial functions have been reported in GBM; mitochondrial contribution to GICs survival and therapeutic resistance is not known. We utilized three dimensional (3D) spheroids as a GICs model derived from human GBM cells lines or from primary cultures and investigated their mitochondrial functions and quality control pathways. We found that GICs display stemness potential and differ in mitochondrial functions compared to their monolayer counterparts. In addition, these GICs show significant alterations in mitochondrial dynamics and

autophagic clearance pathways, contributing to their survival. Our results also indicated that pharmacological agents targeting specific mitochondrial pathways (alone or in combination with GBM therapeutics) could effectively sensitize GICs population and inhibit their growth potential. Altogether, alteration in mitochondrial pathways contributes to GICS survival and therapeutic targeting of specific mitochondrial quality control pathway could be useful to combine with existing therapeutics for effective GBM treatment.

S8.2. Critical role of mitochondrial metabolism in drug resistance of Glioblastoma Multiforme.

Ashutosh Shrivastava, Manendra Singh Tomar
Center for Advance Research, Faculty of Medicine, King George's Medical University, Lucknow, Uttar Pradesh, India

Background: Glioblastoma Multiforme (GBM) is the primary brain neoplasm with a low median survival of ~15 months after the initial diagnosis. Temozolomide (TMZ) is a first-choice alkylating agent inducted as a standard therapy for GBM. However, efficacy of TMZ is limited due to development of intrinsic and extrinsic drug resistance.
Material and Methods: We established a model of acquired TMZ-resistance in GBM. We performed cell cytotoxicity assay to find out IC-50 of sensitive and resistant U-87 and LN-229 GBM cells. We used Gene expression. Flow cytometry and Metabolomics to understand the mechanism of TMZ resistance in GBM.
Results: The IC-50 of sensitive U-87MG and LN-229 was ~60µM and ~10µM respectively compared to 365.5µM of U-87MG and 135.3 for the LN-229 resistant cells. The mitochondrial copy numbers were significantly decreased while membrane potential was significantly higher in the resistant cell lines compared to sensitive cells. There was a decrease in the expression of TFAM and PGC –α gene in the resistant cells. We also found elevated level of ROS in sensitive cell lines on TMZ treatment but no significant change in ROS levels in the resistant cells. We subsequently performed Metabolomics and found TCA cycle, Warburg effect, Pentose Phosphate Pathway, glutathione metabolism and nucleotide metabolism to be upregulated in the resistant GBM.
Discussion and Conclusion: Based on these preliminary findings, it can be concluded that TMZ resistant cell lines have decreased mitochondrial DNA number. On the other hand upregulated TCA cycle and Warburg effect for energy production provide these cells with survival advantage.

S8.3. Exploring the role of autophagy in temozolomide-induced glioma cancer stem cells population

Meenakshi Tiwari[a], Suraj Kumar Singh[a], Sabiya Abbas, Pransu Srivastava, Lokendra Kumar Sharma[b]
[a] Department of Biochemistry, All India Institute of Medical Sciences-Patna, Bihar, India; [b] Department of Molecular Medicine & Biotechnology, Sanjay Gandhi Post Graduate Institute of Medical Sciences-Lucknow, (U.P.) India.

Glioblastomas (GBM) are highly recurrent and aggressive tumors that are associated with poor prognosis. The existence of glioma stem cell (GSC) populations has been identified in these tumors that are associated with aggressiveness and recurrence of the tumors. These GSCs possess properties of stem cells that include self-renewability, proliferation, and therapeutic resistance, contributing to the poor clinical outcome. Thus, targeting these stem cells in tumors offers a reliable and potential target to improve treatment outcomes in glioblastoma. Our laboratory focuses on understanding the role of autophagy in the existence of cancer stem cells (CSCs) in tumors, specifically in high grade gliomas. We have identified the role of autophagy in the maintenance of GSCs as well as Temozolomide (TMZ)-induced therapeutic response, the most commonly used treatment against GBM. Using primary and well-established cell lines of human origin, we have demonstrated the role of autophagy in maintaining the glioma stem cell population. Further, our experimental data suggested that autophagy provides a survival advantage to glioblastoma cells in response to chemotherapy. More interestingly, we have identified that TMZ treatment significantly increases the population of GSCs that is associated with upregulation of autophagy. Our findings implicate that, inhibition of autophagy prevented TMZ-induced increased GSC population, suggesting a critical role for autophagy in therapy-induced generation of the GSC pool. Currently, we are generating some exciting data that suggests

the important role of autophagy in GSCs and the use of various autophagy modulators as combinational agents to overcome chemoresistance in these GSCs. CSC is a relatively unexplored field with high potential, and the present study is providing some important data that may form the basis for defining the mode of therapy in the future.

S8.4. Neurotoxins therapeutics: Small molecule inhibitor a ray of hope

Nandita Saxena
Defence Research and Development Establishment, Jhansi Road, Gwalior (MP)

Neurotoxins are synthetic or naturally occurring substances that destroy, or impair the functioning of the central and/or peripheral nervous system. Botulinum toxin is one of the neurotoxins (BoNTs) that target motor neurons and block acetylcholine neurotransmitter release. This action results in the life-threatening flaccid paralysis that defines the disease botulism. Current therapeutic options are of a predominantly prophylactic nature and cannot be used in mass population, new strategies and ultimately potential treatments are desperately needed to combat any widespread release of these neurotoxins. Small molecule, non-peptidic inhibitors offer the best opportunity for the development of post-exposure therapeutics. Small molecule inhibitors, are potent, effective, safe, and possess suitable absorption, distribution, metabolism, excretion, and toxicity (ADMET). Our laboratory is trying to identify the small molecule inhibitor against the neurotoxin and other toxin which may cause neurotoxicity. Targeting catalytic domain of BONT is specific approach and hold promise for selective therapy. Studies were performed to screen inhibitors *in silico* followed by high throughput screening via in house developed Fluorescence Based Thermal Shift Assay (FTSA) and in vitro assays. Interaction of small molecules with toxin is confirmed via SPR. Endopeptidase assay and cell free translation assay is also done to validate functionality of the molecules. Shortlisted molecules were finally evaluated in *in vivo* to confirm their efficacy. Amide based derivative and quinol molecules were found to be lead compound and may be considered for further development as post exposure therapeutics.

S8.5. Restoration of nerve demyelination by methylcobalamin in an excitotoxic brain disorder model

Surendra Kumar Trigun, Anima Roy, Anamika, Debashmit Mallick, Archita Khanna Biochemistry Section, Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi-221005

Nerve demyelination is considered a common neuronal aberration of all neurodegenerative brain disorders. Methylcobalamin (MeCobl) is a widely used supplement for the patients with neurological complications. However, the mechanism by which MeCobl does so remains largely unexplored. We have studied the effect of MeCobl on the neurochemical, neuroarchitectural and neurobehavioral aspects using moderate grade hepatic encephalopathy (MoHE) model of neuroexcitotoxicity. The nurobehaviorily characterized MoHE was induced in rats by administration of 100 mg/kg b.w of thioacetamide i.p. for 10 days. In experimental group, MoHE rats were post treated with 500 mg/Kg. b.w. MeCobl, i.p.. Followed by neurochemical, neuroarchitectural and neurobehavioral studies. In comparison to the control rats, a significant decline in the level of the myelin basic protein (MBP) vs enhanced level of neurodegenerative changes could be observed in the MoHE rats. This was consistent with the similar changes in the methyl group transfer enzymes, immunochemically detected deranged myelination of the hippocampus neurons and a compromise in the dendritic arborization and number of synaptic knobs in the CA1 pyramidal neurons of those MoHE rats. However, when these MoHE rats were treated with MeCobl, all these aberrations could be normalized back resulting into recovery in the neurobehavioral deficits observed with the MoHE pathogenesis. Taking together, it is evident that MeCobl treatment recovers MoHE associated neuronal derangements by modulating MeCobl utilizing neurochemistry vs re-myelination of the hippocampus neurons.
Ethical Statement: The animal study 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 A DAE-BRNS project to SKT and award of CSIR SRF to AR.

S8.6. Neuro acoustic methodologies for diagnosis and treatment of various neuropsychiatric disorders at early stage

Shahzad Aasim, Rakesh Banal, Sanjeev rana, Ranjeet Kumar, Hilal Ahmad, Suhail Ahmad

Dementia and Alzheimer's being an irreversible neurodegenerative disease that impairs memory and cognitive development of brain. It is estimated that more than 25 million people around the world have been affected by Dementia and Alzheimer's disease (AD). It is also estimated that every year new 5 million are added and total cases get doubled every 20 years. Having such an enormous impact on the health of mostly old age people has promoted researcher around the world to go for an innovative therapeutic approach for curbing this menace. These approaches are mostly symptomatic, regenerative and disease modifying in nature.

We are proposing a non-invasive novel therapeutic interventional approach using Neuro Acoustic stimulation for the early diagnosis, prognosis and treatment of Dementia and AD. This can aid in the reduction of pathology and symptoms of Dementia and AD. The proposed therapeutic methodology will be focussing on stimulating brain waves that are falling in a certain narrow range of principle frequencies and are classified as alpha, beta, theta, delta and gamma. The intervention stages will involve identification of the specific and selective acoustic loops/ sub frequencies among the huge set of available principal frequencies. It will also involve stimulation of these selective frequencies for analysing the effect and impact on the brain wave patterns. These interventions will be analysed using ML and DL algorithms. This can also be followed by the correlation with various bio-chemical parameters that will be analysed with regards to the changes effected by these interventions.

Variables: ***Independent variable:*** The independent variable is the use of specific neuro acoustic loops as non-invasive therapeutic intervention. ***Dependent variables:*** Acoustic Loop effect: Impact of specific therapeutic acoustic loop/s on subject patient with recorded response. Memory Record and Retention: This involves storing of long and short-term memories. Memory Retrieval: These involves accessing and retrieval of these short and long-term memories. Memory Transition Specificity: Involves enabling of episodic memories. Excepted Outcome: The identification and intervention of these specific acoustic loop stimulations will aid in treatment of Dementia and AD. It will also aid in slowing down the cognitive declination of the subjects/patients. It may aid in slowing down the cholinergic neuro degeneration process by reducing the levels of amyloid-beta and phosphorylated tau proteins and also stimulating the neuro transmitters like acetylcholine and dopamine.

Symposium-9: Drug-resistant epilepsy: Mischievous networks- From bench to bedside

S9.1. Surgical strategies to tackle the networks in drug resistant epilepsy

P Sarat Chandra[2], Ramesh Doddamani, Madhavi Tripathi[1], CS Bal[1], S Gaikwad[2], Manjari Tripathi[3]
[1]Department of Neurosurgery[2], Neurology[3], Nuclear Medicine and Neuroradiology[1], All India Institute of Medical Sciences and MEG resource facility, New Delhi

India has an estimated 20 million persons with Epilepsy and over 5 million are likely to have drug resistant epilepsy (DRE). The only definitive treatment for DRE is surgery as of now. Surgery involves localizing the abnormal networks and either disconnecting or removing them. Likewise, the surgical strategies could be evolved on 2 basic techniques, disconnective or resective surgeries. Localization of abnormal networks is done by both pre-operative investigations i.e., MRI as per epilepsy protocol, video EEG, ictal SPECT, PET and magnetoencephalography. A third strategy includes neuromodulation i.e., a mechanism to modify the abnormal networks. Stereoencephalography is a technique whereby very thin caliber electrodes are implanted into brain using a robotic guidance. They provide excellent recordings, whereby network localization may be provided which allows creating a good hypothesis for a surgical strategy even if other investigations may be negative. The following lecture provides a brief overview, demonstrating the role of various surgical

strategies based on a center's experience of over 3000 cases over 25 years with over 400 publications on this subject.

S9.2. Evaluation of mischievous aberrant networks in epilepsy

Manjari Tripathi and P Sarat Chandra
Dept of Neurology, All India Institute of Medical Sciences, New Delhi

It is important for the neurologist to clearly define whether the patient really has drug resistant epilepsy. It is not un-common to find "pseudo refractory epilepsy". The common causes of this include, pseudo seizures, poor drug compliance, poor drug combination for polytherapy, selection of wrong first drug e.g. carbamazepine for juvenile myoclonic epilepsy (JME), sub-optimal dosage of drug, non-epileptic conditions mimicking epilepsy e.g. syncope, etc.
At our center, we start working up the patient for a possible epilepsy surgery when the seizures are not controlled with 2 drugs. This is done as soon as the patient referred to our center. Children require a more expeditious work up as they are prone to epileptic encephalopathy. The following investigations are performed to localize the networks. These include video EEG. In a cohort of over 200 patients with drug resistance in our center, we found that presence of structural lesion (Odds ratio 20.4), on-response to first drug (OR 19), mental retardation (OR 9) and high initial seizure frequency (OR 6) had the highest predictors for drug resistance. An MRI as per epilepsy protocol, which includes 0.5 mm thin perpendicular slices to hippocampus. In addition, advanced investigations like ictal SPECT, PET and Magnetoencephalography. Intra-operative mapping techniques includes electrocorticography and stereo encephalography. Multi modal imaging in recent times has become a key strategy for better localization of networks. A study of ours studying the concordance between the PET and ictal SPECT demonstrated a good cinical outcome especially for extra temporal epilepsies if both the modalities were concordant with each other and with video EEG and MRI.
The presentation will include a brief overview of the techniques of localizing the abnormal networks based on the author's experience of over 25 years and with an extensive research experience of over 400 publications.

S9.3. Drug-resistant temporal lobe epilepsy (TLE): Cellular basis of abnormal neuronal networks

Jyotirmoy Banerjee[1], Vivek Dubey[1], Aparna Dixit[2], Manjari Tripathi[3], M C Sharma[4], Ramesh Doddamani[5], P Sarat Chandra[5]
[1]Department of Biophysics, All India Institute of Medical Sciences, New Delhi; [2]Dr. B. R. Ambedkar Center for Biomedical Research, University of Delhi, Delhi; [3]Department of Neurology, All India Institute of Medical Sciences, New Delhi; [4]Department of Neuropathology, All India Institute of Medical Sciences, New Delhi; [5]Department of Neurosurgery, All India Institute of Medical Sciences, New Delhi

Temporal lobe epilepsy (TLE), commonest DRE pathology, is associated with large-scale network abnormalities involving hippocampal and extra-hippocampal structures. The underlying cellular mechanisms responsible for generation of abnormal neuronal networks is poorly understood. We utilized cellular and molecular strategies to determine the configuration of the synaptic networks, particularly to ascertain the presence of more than one abnormal network in different brain structures. We investigated the abnormal neuronal networks in resected brain samples obtained from patients with TLE as well as from animal model of TLE. Whole cell patch-clamp technique was used to record excitatory postsynaptic currents (EPSCs) from pyramidal neurons in slice preparations of brain samples. Frequency and amplitude of spontaneous EPSCs was higher in both the TLE samples compared to non-seizure controls. The magnitude of contribution of the action potential-dependent excitatory activity to hyper excitability in anterior temporal lobe (ATL) samples was higher than that in the case of the hippocampal samples. Similar results were also observed in animal model of TLE. This was the first direct evidence at cellular level that two epileptogenic networks are present in TLE, one emanating from the hippocampus and the other from ATL. This indicated that the reinforced glutamatergic synaptic connectivity to form a network in the hippocampus was different from that in the ATL in TLE. mRNA and protein expression of glutamate receptor subunits were checked by qPCR and western blot. We demonstrated region-specific differential alterations of glutamate receptor subunits in TLE, both in patients' samples as well as in animal model, suggesting independent cellular mechanisms contributing to generation of independent epileptogenic networks in different temporal lobe structures. Further we found that

neuroanatomical changes and alterations in dendritogenesis contribute to development of independent networks in the hippocampus, ATL and frontal neocortex of TLE rats. Large-scale networks exist even at the cellular level in TLE, further confirming the conjecture that TLE is a distributed network disorder and not a focal disorder. He will also discuss the clinical relevance of these findings with respect to resective surgery being performed on patients with TLE. The surgical procedures used for the treatment of TLE include standard anterior temporal lobectomy, combined with amygdalo-hippocampectomy and selective amygdalo-hippocampectomy. Thus, an anterior temporal lobectomy along with amygdalo-hippocampectomy is likely to have a better outcome than selective amygdalo-hippocampectomy, which spares the anterior temporal lobe.

9.4. Altered lipid profiles in brain tissues resected from patients with focal cortical dysplasia (FCD): with a potential role in defining the epileptogenic zone during surgery

Aparna Dixit, Krishan Kumar[2], Nitin Yadav[1], Jyotirmoy Banerjee[3], Manjari Tripathi[2], M C Sharma[4], Sanjeev, Lalwani[5], Fouzia Siraj[6], P Sarat Chandra[7], Shantanu Sengupta[8]
[1]Dr. B. R. Ambedkar Center for Biomedical Research (ACBR), University of Delhi, Delhi; [2]Department of Neurology, All India Institute of Medical Sciences (AIIMS), New Delhi; [3]Department of Biophysics, AIIMS, New Delhi; [4]Department of Neuropathology, AIIMS, New Delhi; [5]Department of Forensic Medicine and Toxicology, AIIMS, New Delhi, India; [6]Department of Forensic Medicine and Toxicology, AIIMS, New Delhi, India; [7]Department of Neurosurgery, AIIMS, New Delhi; [8]CSIR-Institute of Genomics and Integrative Biology, New Delhi

FCD, being one of the most common pathologies of drug-resistant epilepsy (DRE), accounts for one-third of the cases referred to surgery. Failure to precisely localize the epileptogenic zone (EZs) is a major reason for poor surgical outcomes in FCD. Currently, no molecular or cellular biomarkers are available to aid in defining EZs. Dr Dixit used liquid chromatography coupled high-resolution tandem mass spectrometry to identify altered lipid profiles in the resected tissues from FCD patients obtained during electrocorticographically (ECoG)-guided surgery compared to autopsy. Lipids were extracted from frozen brain tissues using a modified Bligh & Dyer method and separated on an ExionLC™ system with a Waters AQUITY UPLC BEH HILIC column. A SCIEX QTRAP® 6500+ LC-MS/MS system with polarity switching, Turbo V™ source, and electrospray ionization probe was used. For identification and relative quantification of all the lipid species, theoretical multiple reaction monitoring (MRM) library was generated using LIPIDMAPS. Lipids were quantified by MultiQuant™ 3.0.2 quantitation software. The intensity values (mz/rt) were normalized with spiked internal standards. MetaboAnalyst software (v5) was used for missing values imputation. Mass spectral profiles of a total of 1224 lipids with 607 in positive mode and 617 in negative mode were detected. A total of 13 lipids (8 upregulated and 5 downregulated) were altered in FCD compared to autopsy ($p<0.05$ and fold-change ≥ 2). The upregulated lipids in FCD comprised neutral triacylglycerols (TAGs) and downregulated lipids included phosphatidylcholine (PC) and phosphatidylethanolamine (PE). Dr Dixit will discuss distinct lipid mass spectra of TAGs, DAGs, PC, and PE which were observed in FCD tissue in comparison to controls. As a proof-of-concept the lipid library might prove to be useful in defining the epileptogenic zone and aid in iKnife strategy. Further research on understanding the TAG and DAG metabolism in FCD may prove to be insightful in understanding the role of lipid metabolic pathways and enzymes in the process of epileptogenesis in FCD.

Symposium- 10: Learning and memory in invertebrate systems

S10.1. Learning from visceral maliase in Drosophila

Gaurav Das
NCCS, Pune, India
Learning to avoid experiences that cause visceral malaise/sickness is an adaptive behavior that promotes survival. However, malaise-reinforced learning can also be maladaptive. The exact neural circuitry that mediates this kind of aversive anticipatory learning are poorly understood in any species. Our ongoing work

shows that flies show signs of distress and vomiting upon ingestion of toxins (CuSO4, nicotine). They also learn to associate an odor with toxin ingestion and its consequences. Later, re-exposure to the same odor induces learned emesis even in the absence of the toxin. I am going to talk about what we have found out about the underlying gut-brain connections.

S10.2. Miles to go before I sleep: the neuroethology of colour vision in bees

Hema Somanathan
Indian Institute of Science Education & Research, Thiruvananthapuram, India

Bees are well-known for their role in human nutrition and for the pollination services they render. Colour is a primary visual cue by which bees detect and remember flowers, and flower colour is adaptive to colour vision of bees and other pollinators. Bees are primarily day-active and have apposition compound eyes, the typical eye design of diurnal insects. Most bees are trichromats with photoreceptors sensitive in the UV, blue and green. While diurnal colour vision was established a century ago in bees, it was accepted that bees were colour-blind in dim light. Here, I present the first evidence of nocturnal colour vision in two bees – the solitary Indian carpenter bee *Xylocopa tranquebarica* which is obligately nocturnal, and more recently, the Asian Giant honeybee *Apis dorsata,* a facultatively nocturnal bee. These findings indicate remarkable visual adaptations because the insensitive apposition eyes were thought incapable of supporting nocturnal colour vision. Exactly how nocturnal colour vision is achieved in apposition eyes remains to be understood, but increasing experimental and theoretical evidence suggests that neural summation mechanisms are likely to be necessary.

S10.3. Interplay of temporal patterning and oscillations in olfactory learning in honeybees

Joby Joseph
University of Hyderabad, India

Temporal patterning and oscillations are two features of the conditioned stimulus (CS) in olfactory pathway. PER conditioning is a classical conditioning paradigm where olfactory stimulus as CS is associated with sugar reward (US). We manipulate the CS sequencing, CS-US intervals and the inter stimulus interval of the PER conditioning paradigm to get at the interplay of these phenomena and its consequences in learning and memory, and discrimination ability. We use modelling and simulations to arrive at sufficient mechanisms to explain these observations.

S10.4. Bidirectional long-distance transport of organelles during synapse formation, maintenance and plasticity

Sathya Puthanveettil
UF Scripps Biomedical Research, USA

Despite the decades of research on the mechanisms of synapse formation, we still do not know how the communication between neuronal soma and its terminals results in proper formation of synapses, and the maintenance of appropriate synaptic connections. Organelles such as mitochondria help provide energy to the cell, and lysosomes assist in the recycling and degrading macromolecules. However, whether and how the availability of these biologically essential organelles is modulated for synapse function remain elusive. To address this question, we explored the advantages of the well described pre- and post-synaptic neurons of *Aplysia* gill withdrawal reflex to perform quantitative live imaging and assess the flux and velocities of anterograde and retrograde transport of mitochondria and lysosome related organelles (LROs). These experiments show that in the presynaptic sensory neurons of the *Aplysia* gill withdrawal reflex, the formation of functional synapses leads to a bidirectional progressive enhancement in mitochondrial flux whereas retrograde transport of LROs were significantly reduced following synapse formation and induction of long-term plasticity. Gene expression and systematic characterization of signaling pathways suggest that cAMP-PKA and signaling from Golgi bodies modulate the retrograde transport of LROs. Taken together, our results

suggest a new mechanism for the synapse formation, maintenance and plasticity. Specifically, the long-distance bidirectional transport of organelles is selectively and temporally modulated for dynamic changes at the synapse.

S10.5. Understanding memory formation using *C. elegans*; the old, the new and the strange

Kavita Babu
Indian Institute of Science, Bangalore, India

I will present a model for studying long term memory in *Caenorhabditis elegans*
and how we are using this model to study aspects of communication between animals during the process of memory formation. Our assay has allowed us to study long-term associative memory in *C. elegans* using pairing of a positive stimulus (Isoamyl alcohol odor) with an aversive stimulus (heat). These two stimuli are paired and the animals are treated to this airing through a training protocol. Twenty to twenty-two hours after this training the animals that would in the naïve condition be attracted to Isoamyl alcohol, now show no response or aversion to the chemical. In this talk I will discuss this paradigm and the mechanistic basis of this behaviour is *C. elegans*.

Symposium-11: Novel mechanisms and therapies to mitigate secondary brain damage

S11.1. Epitranscriptomic modulation as a novel therapy to mitigate secondary brain damage

Vijay Arruri, Anil K Chokkalla[1], Suresh L Mehta[1] and **Raghu Vemuganti[1,2]**
[1]Department of Neurological Surgery, University of Wisconsin, Madison, WI; [2]William S. Middleton Veterans Administration Hospital, Madison, WI

Mammalian RNAs undergo >175 chemical modifications that are collectively known as epitranscriptomic modifications. These increases the diversity and functionality of RNAome. The major RNA modification seen in CNS is addition of the methyl group to form N^6-methyladenosine (m^6A). Our studies show that experimental stroke in rodents significantly increased m^6A methylation in the peri-infarct cerebral cortex. We further observed that downregulation of m^6A writer FTO is responsible for increased RNA methylation after stroke. Many of the m^6A hypermethylated transcripts in the post-ischemic brain are those that promotes apoptosis and inflammation. Furthermore, reversing post-stroke m^6A methylation by restoring FTO with an AAV9 ameliorated the ischemic brain damage and promoted functional recovery in mice of both sexes. As we observed that the nicotinamide adenine dinucleotide phosphate (NADPH) is a potent activator of FTO, we tested its efficacy in adult male and female C57BL/6J mice subjected to focal ischemia. Intravenous administration of NADPH at 2h of reperfusion following transient middle cerebral artery occlusion induced cerebral FTO expression. NADPH treatment also significantly decreased post-stroke grey and white matter damage and improved the recovery of motor function, cognition and lowered depression in mice of both sexes. Furthermore, stroke led to upregulation of m^6A reader YTHDF1 in the ischemic cortex. When YTHDF1 knockout male mice were subjected to focal ischemia, post-ischemic motor recovery (evaluated by rotarod test and beam walk test) was lower and the infarct volume was bigger compared with the wild-type mice. We currently targeting these proteins to modulate RNA methylation to protect the post-stroke brain.

S11.2. Brain microvascular energetics: Impact of sex, aging, and stroke

Venkata Sure, Siva Sakamuri, Lokanatha Oruganti, and **Prasad Katakam**
Department of Pharmacology, Tulane University School of Medicine, New Orleans, Louisiana, USA.

Background: Bioenergetics play an important role in cellular responses to pathophysiological processes and cerebral microvasculature display functional impairments during aging and following stroke. The objective of the study was to study the sex and aging-related alteration of bioenergetics in brain microvessels (BMVs).
Methods: BMVs were isolated from young (3-4 months) and aged (18-20 months) C57Bl/6 mice by subjecting the brain homogenates to a combination of gradient centrifugation and filtration. Extracellular acidification rate and oxygen consumption rate were measured utilizing Agilent Seahorse XF^{e}24 analyzer.
Results: Realtime ATP rate assay observed reduced total ATP production rate in female BMVs versus male BMVs. Compared with males, female BMVs showed reduced ATP derived from both glycolysis and %oxidative phosphorylation (OxPhos) despite a significant increase in contribution of %glycolysis to overall energy production relative to % OxPhos. Mito Stress test in female BMVs showed reduced basal and maximal respiration that was accompanied by reduced spare respiratory capacity and proton leak versus male BMVs. Similarly, glycolytic rate assay observed diminished basal and compensatory glycolysis compared to male BMVs. Paradoxically, old female BMVs displayed greater total ATP production rate with increased ATP generation from mitochondria and reduced contribution to energy production from %glycolysis.
Conclusions: BMVs rely on mitochondria/OxPhos for energy contrary to existing claims. Aging induces an energy deficient phenotype in mouse BMVs. Female microvasculature displayed sex and age dependent paradoxically diminished mitochondrial respiration and glycolysis in contrast to small arteries which display increased mitochondrial respiratory parameters. Reduced spare respiratory capacity and compensatory glycolysis in female BMVs compared to males indicate an inability to meet the excess energy demands consistent with the evidence of stroke-related microvascular vulnerability in women.
Acknowledgement: This work was supported by funding from National Institute of Health (AG074489 and NS114286).

S11.3. Targeting neutrophil integrin α9 improves long-term functional outcomes after stroke in mice with obesity-induced hyperglycemia

Anil K. Chauhan
Department of Internal Medicine, Division of Hematology/Oncology, University of Iowa, Iowa City, Iowa, USA.

Background: Obesity-induced hyperglycemia is a significant risk factor for stroke. Integrin α9β1 is expressed on neutrophils and stabilizes adhesion to the endothelium via ligands, including fibronectin containing extra domain A (Fn-EDA) and tenascin C. Following ischemic stroke, both Fn-EDA and tenascin C, are elevated in the circulation. While myeloid deletion of α9 reduces susceptibility to ischemic stroke, it is unclear whether this is mediated by neutrophil-derived α9. The role of α9 in neutrophil extracellular traps (NETs) formation is also unclear. We determined the mechanistic role of neutrophil-specific α9 in NETosis and stroke in a mice model with obesity-induced hyperglycemia.
Methods: $\alpha9^{Neu\text{-}KO}$ ($\alpha9^{fl/fl}$MRP8Cre$^+$) and littermate control $\alpha9^{WT}$ ($\alpha9^{fl/fl}$MRP8 Cre$^-$) mice were fed on a 60% high-fat diet for 20 weeks to induce obesity-induced hyperglycemia. Functional outcomes were evaluated up to 28 days after stroke onset in mice of both sexes using a transient (30 min) middle cerebral artery ischemia. Infarct volume (MRI) and post-reperfusion thrombo-inflammation (thrombi, fibrin, neutrophil, p-NFκB, TNFα, and IL1β levels, markers of NETs) were measured post 6 or 48 h of reperfusion. Functional outcomes (mNSS, rotarod, corner, and wire-hanging test) were measured for up to 4 weeks.
Results: Stroke upregulated neutrophil α9 expression more in obese mice ($P<0.05$ vs. lean mice). Irrespective of sex, deletion of neutrophil α9 improved functional outcomes up to 4 weeks, concomitant with reduced infarct, improved cerebral blood flow, decreased post-reperfusion thrombo-inflammation, and NETosis ($P<0.05$ vs. $\alpha9^{WT}$ obese mice). Obese $\alpha9^{Neu\text{-}KO}$mice were less susceptible to thrombosis in $FeCl_3$ injury-induced carotid thrombosis model. Mechanistically, we found that α9/cellular fibronectin axis contributes to NETosis via ERK and PAD4, and neutrophil α9 worsens stroke outcomes via Fn-EDA but not tenascin C. Obese wild-type mice infused with anti-integrin α9 exhibited improved functional outcomes up to 4 weeks ($P<0.05$ vs. vehicle).
Conclusion: We identified neutrophil-specific α9β1 as a novel regulator of NETosis and thrombo-inflammation in the stroke setting. As a translational potential, we found that targeting α9 with a blocking antibody improves long-term functional outcomes in a mice model with obesity-induced hyperglycemia.

S11.4. Sex-dependent mechanisms underlying cognitive deficits following repeated mild TBI in adolescent rats

Ramesh Raghupathi, Taylor McCorkle, Laura Giacometti
Program in Neuroscience and Department of Neurobiology and Anatomy, Drexel University College of Medicine, Philadelphia PA

Sports-related concussions (SRC, a subset of mild traumatic brain injury, TBI) affect approximately 1.5 million adolescents annually in the United States. Post-traumatic deficits in prefrontal cortex-dependent working memory as well as hippocampal-dependent learning and memory are frequently reported short- and long-term impairments. Whereas dopamine is implicated in working memory, acetylcholine regulates hippocampal-dependent cognition. Following a single mild TBI, female rats exhibited a deficit in novel object recognition (NOR) memory at 3 days ($p<0.01$), but not at 8 days, whereas male brain-injured rats did not exhibit deficits at either time point. This deficit was associated with an increase in the area of hypocretin (HCRT, a neuropeptide implicated in NOR memory) immunoreactivity within the prelimbic cortex at 3 days post-injury. A HCRT receptor 1 antagonist administered immediately following injury and subsequently on days 1 and 2 reversed NOR memory deficits. In addition, systemic administration of a D1 receptor antagonist at the time of behavioral testing completely reversed the injury-induced NOR memory deficits. These data suggest that alterations in HCRT expression and activation of the dopamine D1 receptor may be involved in mild TBI-induced acute working memory deficits. When adolescent male and female rats were subjected to repeated mild TBI, we observed that male brain-injured animals exhibit early and sustained spatial learning deficits whereas female brain-injured animals show a delayed onset of impairment; these deficits were associated with decreased choline acetyltransferase (ChAT) expression in the medial septum (MS) and decreased activity of nicotinic acetylcholine receptors (nAChR) in the dorsal hippocampus. Infusion of a corticotrophin releasing factor receptor 1 antagonist into the MS reduced spatial learning deficits and restored ChAT immunoreactivity in female but not male animals. In contrast, systemic administration of a nAChR antagonist reversed the learning deficits in both sexes. Together, these data underscore the complex relationship between sex and neurotransmission in the cognitive deficits following mild TBI.

S11.5. Regulatory RNAs as therapeutic targets to mitigate brain damage

Sarra Limam[1], Ankit Patel[1], Sandeep Miryala[1], Maria Sara Cueto[1] and **Ashutosh Dharap[1,2]**
[1]Department of Molecular Medicine, University of South Florida, Tampa, FL 33613; [2]Byrd Alzheimer's Center and Research Institute, University of South Florida, Tampa, FL 33613

Background: Enhancer RNAs (eRNAs) are a novel class of regulatory noncoding RNAs that are transcribed by enhancer elements in a stimulus-dependent manner. The eRNAs are known to play roles in enhancer-mediated gene regulation and phenotypic outcomes, but their expression and functions in stroke are largely unknown.
Methods: Adult C57BL/6 mice underwent a 1h middle cerebral artery occlusion and 6h of reperfusion. Ipsilateral cortices were used for genome-wide H3K27ac ChIP-seq, high- throughput RNA-seq, and Hi-C (n=3/group) to map active enhancers, transcribed eRNAs, and higher order chromatin interactions, respectively. The cellular localization of the eRNAs was mapped using single-molecule FISH.
Results: We identified 77 eRNAs that were significantly upregulated in the cortex in response to stroke versus sham controls. Of these, 55 eRNAs were exclusively expressed during stroke. We pinpointed direct, stroke-responsive DNA looping between the enhancers and distal genes facilitated by higher-order chromatin reorganization in 3D genomic space, indicating potential gene regulatory relationships. We mapped the cell-type and subcellular localization of the eRNAs and found that the majority of the activated enhancers/eRNAs were in neurons.
Conclusions and Discussion: This study presents the first report identifying stroke- responsive eRNA expression, stroke-dependent enhancer-gene looping across the 3D genome, and eRNA cell-type and subcellular localization that together may comprise an immediate-early, cell-type-specific gene regulatory response that drives the subsequent post- stroke pathophysiology. The findings of this study will drive future investigations into the cell- type-specific functions and effects of the eRNAs with the overarching goal of identifying specific RNAs for targeted therapeutic manipulation.

Acknowledgements: This work was supported by the National Institute Of Neurological Disorders And Stroke of the National Institutes of Health under Award Number R01NS115835

Symposium-12: RNA and brain disorder

S12.1. Synapse-enriched lncRNA: Implications in memory during early life stress

Sourav Banerjee
National Brain Research Centre, Manesar

Long non-coding RNA (lncRNA) is emerging as a key regulatory RNA in the nervous system. However, physiological relevance of this regulatory RNA in sculpting neural circuits and governing input-specific cognitive functions *via* spatial resolution of gene expression control remains elusive. We have performed a genome-wide transcriptomics analysis using total RNA purified from synaptodendritic compartment from hippocampus to identify synapse-enriched lncRNAs. We have highlighted a hitherto unknown regulatory function of lncRNAs that operates at spatial scale to regulate excitatory synapse development and memory. Furthermore, our study defined highlighted the importance in memory deficits due to early life stress.

S12.2. FMRP determines the epitranscriptome of ribosomes through which it may regulate the development

Ravi Muddashetty
CBR, Indian Institute of Science, Bangalore

FMRP is an RNA-binding protein the absence of which significantly impacts neuronal development and causes Fragile X syndrome (FXS). The function of FMRP is primarily studied in neurons, particularly at the synaptic connections. We recently identified a novel interaction of FMRP with a class of small nucleolar RNA (C/D box snoRNAs) in human embryonic stem cells (hESCs). Through this interaction, FMRP determines the 2'O methylation marks on ribosomal RNA which is a major epitrascriptome modification on ribosomes. 2'O methylation on rRNA is critical for ribosome biogenesis, turnover and to generate ribosome heterogeneity. Ribosome heterogeneity is thought to be essential for specialized ribosomes which may regulate the differentiation and cell fate determination from embryonic stem cells. FMRP controls the 2'O methylation of rRNA and thus influences the neuronal differentiation process. This FMRP-mediated regulation of ribosome epitranscriptome predominantly happens in embryonic stem cells and significantly reduces with lineage specificity. This finding indicates a very exciting possibility that FMRP has a critical role in the very early stages of neuronal differentiation and also the role of epitrascriptome modification in development.

S12.3. Towards understanding molecular mechanisms of memory

Amitava Majumdar
National Centre for Cell Science, Pune

How proteins with a limited half-life can help in maintaining memory over a lifetime is one of the central questions in understanding the molecular mechanism of memory. Previously a protein synthesis regulator CPEB was implicated in this process. CPEB behaves like a functional prion and was shown to be essential for the maintenance of long-term facilitation in Aplysia. It was further suggested this prion-like behavior helps CPEB to maintain the altered state of synapse and long-term memory. The Drosophila homolog of CPEB, Orb2 was found to exhibit prion-like properties, and blocking its prion-like oligomerization interfered with the persistence of memory. Orb2 is one of the first identified physiologically beneficial functional prions. Since this prion-like oligomerization of Orb2 is the key to regulating the persistence of

memory, it is very important to understand how this oligomerization is regulated in the brain. In my talk, I will discuss our findings on this question.

S12.4. Nuclear FMRP: Implications in Fragile-X-Syndrome

Carole Gwizdek
CNRS, Paris, France

Dysfunction of Fragile-X-Mental Retardation protein (FMRP), a key RNA binding protein in the brain, leads to the neurodevelopmental disorder known as Fragile-X-Syndrome. Established functions of FMRP characterized so far are attributed to its cytoplasmic fractions. However, emerging studies have identified specific regulatory functions of FMRP restricted in nucleus. Mutations of FMRP affecting the nuclear function have also been reported. However, our understanding of nuclear FMRP function and its importance in the Fragile-X-Syndrome are limited. The presentation will highlight how distinct function of nuclear FMRP is regulated via its interacting partner and how nucleus specific functions of FMRP influences neuronal development and plasticity.

Symposium- 13: Development of nervous system

S13.1. Understanding critical molecular signals in oligodendrocyte development: from the perspective of treating neonatal neurodegenerative disorders like cerebral palsy

Tyagi S[1], Shrivastava V[1], Dey D[1], Rani S[1], Sharma JB[2], Palanichamy JK[1], Sinha S[1], Seth P[3], **Sen S**[1]
[1]Department of Biochemistry and [2]Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi; [3]Department of Cellular and Molecular Neuroscience, National Brain Research Centre, Manesar, Haryana.

Background: Understanding oligodendrocyte (OL) maturation and development is a critical aspect of understanding and eventually treating the molecular events in cerebral palsy (CP). Understanding the mechanistic pathways of OL development is a prerequisite to developing therapeutic strategies to overcome OL maturation arrest commonly seen in CP. **Materials and methods**: Analyzing RNA-seq data generated from human fetal neural stem cells (FNSC) differentiating into primary OL cells, revealed the unique involvement of the JAK-STAT cell signaling pathway in terminal OL maturation. To validate our findings, we used the Mo3.13 cell line resembling premyelinating OL, which can be differentiated into mature OL over 7 days, using phorbol 12-myristate 13-acetate (PMA). **Results and Discussion**: Morphological changes, along with changes in the expression of mature-OL marker MBP and premyelinating OL markers NG2 and O4 confirmed the differentiation of Mo3.13 into mature OL (n=5). Flow cytometry (MBP) also confirmed this OL differentiation (n=3). Upregulation of critical players of the JAK-STAT pathway (IL-6 and STAT3), validated its involvement during OL maturation in Mo3.13 cells (n=3). Increased phosphorylated STAT3 (pY705) levels during Mo3.13 differentiation (western blotting) reinforced our findings (n=3). Flow cytometry demonstrated a decrease in MBP-positive cells (when treated with STAT3-specific inhibitor) thus confirming the involvement of the JAK-STAT pathway in terminal OL maturation (n=3). **Conclusion**: These novel findings underline the involvement of the JAK-STAT pathway in OL maturation and may have potential therapeutic options in demyelinating disorders like cerebral palsy.

S13.2. Establishment of neural circuits in the developing human auditory cortex

Soumya Iyengar
National Brain Research Centre, Manesar

A detailed knowledge of the sensitive periods of plasticity in the human auditory cortex is important for planning interventions such as cochlear implants for deaf children and understanding the neural basis for the

ability to learn multiple languages. We had earlier demonstrated that excitatory thalamocortical and cortico-cortical synapses were established during prenatal development in the human auditory cortex. Whereas cortico-cortical synapses underwent pruning by ~7 postnatal years, which correlates with the sensitive period for learning speech, thalamocortical synapses underwent pruning between adolescence and adulthood. Our recent findings suggest that changes in the density of excitatory synapses are accompanied by a significant increase in the density of inhibitory synapses in the human auditory cortex between the fetal period and childhood in the supragranular layers (2 and 3) and Layer 4 of the primary auditory cortex. This is followed by pruning and a significant decrease in their density between childhood and adolescence, which coincides with the changes observed in excitatory cortico-cortical connections. Besides studying inhibitory synapses, we also demonstrated changes in the patterns of distribution and structure of somatostatin-positive (SOM) interneurons across development in the human auditory cortex. Our results demonstrate that there were significant increases in the density of these interneurons in the human auditory cortex between the third trimester and childhood, followed by a significant decrease in this measure between childhood and adolescence. Furthermore, there was a significant decrease in the complexity of their neurites between the fetal period and adulthood. Taken together, our results suggest that the density of both excitatory and inhibitory synapses undergoes significant changes in the auditory cortex during the sensitive period for learning speech and language.

S13.3. Modelling a spectrum of early-onset human neurodevelopmental disorders – timing and mechanisms

Achira Roy
Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bengaluru, India

Background: The PI3K-AKT-MTOR and RAS-MAPK pathways are crucial for cell growth and metabolism. Mutations in these pathways cause cancers and early-onset developmental brain malformations including cortical dysplasia, developmental hydrocephalus, epilepsy, and autism. Many such patients are unresponsive to conventional medications. Understanding mutation-specific pathophysiology is thus critical for developing molecularly targeted therapies.
Materials and methods: We use genetic mouse models of clinically relevant mutations to recapitulate the key pathological features. Using these models and different *cre* lines, we sought to determine cellular mechanisms underlying cortical malformations, using histology and immunohistochemistry. Specific pathway inhibitors were administered to preclinically study their potential therapeutic actions on these anomalies.
Results: We identified that mutations in PI3K-AKT-MTOR and RAS-MAPK pathways affect the size of brain, cortical lamination, and lateral ventricles, only when acquired during embryogenesis. We also found some having complicated motor dysfunction, the reason behind which is yet to be elucidated. By repurposing inhibitors of signalling pathways originally developed to treat cancer, we were able to attenuate both ventriculomegaly and epilepsy preclinically.
Discussion and Conclusions: Our findings indicate a distinct mechanistic milieu underlying certain developmental hydrocephalus and intractable epilepsy and promise potential precision therapeutics towards their treatment. We also identified differential critical developmental periods behind a spectrum of early-onset human neurodevelopmental disorders using conditional mouse models. In my talk, I will highlight some of these studies that establish a platform to our lab's future goals of finding convergent mechanisms across the range of developmental brain disorders.
Acknowledgements: We thank Suzanne J. Baker, Jean J Zhao, Kathleen J Millen, Jackson Laboratories, USA and BLiSC Animal Care and Resource Center (ACRC), India, for gifting mouse lines. We thank the animal facility of JNCASR for the maintenance of mouse lines. This work was funded by the Ramalingaswami Re-entry Fellowship from the Department of Biotechnology (DBT), India (AR), a research donation from M-CM Foundation, USA (AR) and the intramural funding from the Jawaharlal Nehru Centre for Advanced Scientific Research, India (AR).
Acknowledgment: We are grateful to DBT (Govt. of India) for research funding.

S13.4. Regeneration of spinal cord connectivity by endogenous forces in zebrafish

Subhra Prakash Hui and Samudra Gupta
S. N. Pradhan Centre for Neurosciences, University of Calcutta, 35 Ballygunge Circular Road, Kolkata

Background: Unlike mammals, teleost zebrafish, possess a remarkable capacity for spinal cord regeneration, providing a model to understand how axonal regeneration in spinal cord might be induced in human. Advantages in available genetic techniques has been established zebrafish as a unique model for studying natural mechanisms of spinal cord regeneration.
Materials and methods: Here, we have used novel genetic tools of zebrafish along with standard cellular, molecular and behavioural assays to study the functional role of immune cell and epigenetic modifier in spinal cord regeneration.
Results: In this study, we investigated the potential role of the immune cells and epigenetic modifiers in regulating spinal cord regeneration in zebrafish. By characterizing the immune cell types and epigenetic modifiers in the regenerating zebrafish spinal cord and identified their key contribution in development of pro-regenerative niche after injury. The functional role of the identified immune cell population and the epigenetic modifier during the regeneration of the spinal cord will be discussed in the meeting.
Discussion and conclusions: Our results reveal a novel pro-regenerative role of immune cell and necessary epigenetic modification during spinal cord regeneration in adult vertebrates, a finding that may have a significant therapeutic implication for future regenerative medicine.
Acknowledgements: Our research supported by SERB (CRG/2022/001663), Govt. of India; Australian Research Council, NHMRC, Australia; DBT and CSIR, Govt. of India as Ramalingaswami Fellowship award and Junior Research Fellowship award to SPH and SG respectively.

Symposium-14: Understanding cognitive tuning through lens of sleep process

S14.1. Multivariate brain dynamics in EEG during sleep

Arun Sasidharan[1], Vrinda Marigowda[2], Ravindra PN[1], Bindu M Kutty[1]
[1]Centre for Consciousness Studies, Department of Neurophysiology,
NIMHANS, Bengaluru, Karnataka, India; [2]Axxonet Brain Research Laboratory, Axxonet System Technologies Pvt. Ltd., Bengaluru, Karnataka, India

Background: Conventionally, sleep is studied as repeated transitions of distinctive stages (N1, N2, N3 and REM) lasting at least 30s, with characteristic EEG features (like spindles). But recent studies using multivariate EEG data-driven approaches show that neural state transitions during sleep are much more dynamic and warrants further exploration.
Materials and methods: We relooked our existing full-night sleep EEG data across illness-to-wellness spectrum (Vipasana meditators, controls and patients with Schizophrenia patients; n=15 each). From 4s EEG epochs of 3 channels (Fz, Cz and Pz), >50 features (spectral and non-linear) were used to compare the dynamics of EEG multifeatured- clusters across stages and groups.
Results: We find that EEG multifeatured-clusters show different transition dynamics within 30s epochs, with some sequences more often observed in certain sleep stages. The duration and proportion of the EEG multifeatured-clusters also showed distinct differences between meditators, patients and controls. We also observed increased contribution from non-linear features in the sleep clusters.
Discussion and conclusions: As in recent studies, we could replicate the increased dynamics in sleep EEG using a multifeatured-based clustering approach. We also demonstrated the applicability of such 'sleep EEG microstate dynamics' in capturing unique differences between meditators, general population, and patients with mental disorders. Overall, these add further support for brain dynamics occurring within the 30s scoring duration and studying such approaches in individuals across the illness-to-wellness would help better understand sleep neurophysiology (beyond conventional hypnograms).

Acknowledgements (must include funding sources): The primary research works of all the above sleep datasets were done at Department of Neurophysiology, NIMHANS, Bengaluru, India. We thank the other authors of the primary work that includes: Sulekha S., Nirmala Maruthai, Gulshan Kumar, Rahul Venugopal, Pranay, Sunil Kumar, Ajay Kumar Nair, Ammu Lukose, Sumit Sharma, Chetan Mukundan and John P. John. We also thank interns/JRFs (Adla Zubair, Sruthi S Kuriakose and Deepankan) whose preliminary work helped conduct the above exploration. The funding for the primary works were partially supported by Indian Council for Medical Research (ICMR), Government of India (Senior Research Fellowship; Ref. No.: 3/1/3/37/Neuro/2013-NCD-I) and Department of Science and Technology (DST, SATYAM), Government of India (Grant No. Ref. No – SR/SATYAM/18/2015).

S14.2. ERPs during wake and sleep to tap maladaptive emotion processing in patients with chronic pain

Vrinda Marigowda[1] Arun Sasidharan[2] Bindu M kutty[2] Geetha Desai[3]
[1]Axxonet Brain Research Laboratory (ABRL), Axxonet System Technologies Pvt. Ltd., Bengaluru, India; [2]Centre for Consciousness Studies (CCS), Department of Neurophysiology, NIMHANS; [3]Department of Psychiatry, NIMHANS, Bengaluru, India

Background: Chronic pain (CP) is associated with unpleasant sensory and emotional experiences. The acute to chronic pain transition involve numerous aberrant plasticity changes, resulting in maladaptive emotional processing. We used event related potential (ERP) to understand this among CP subjects during wake and then also conducted a pilot study during sleep.
Materials and methods: For awake emotion-ERP assessment, sixteen CP subjects and age-matched controls of both genders participated, and data captured using a 64-channel EEG system during Emo-ANGEL paradigm. For the pilot sleep emotion-ERP assessment, short auditory clips primed with emotional videos were used during sleep in two participants.
Results: Two ERP components were assessed from the wake ERP paradigm, EPN (Early Posterior Negativity) and LPP (Late Positive Potentials). Both groups exhibited higher EPN and LPP for negative emotional images. However, compared to the control, CP subjects showed a significant reduction in LPP for negative images, whereas EPN was comparable. In pilot study, CP subject showed a differences in sleep-ERP components (P200,N550,P900) to negative- primed auditory stimuli compared to neutral-primed, in both NREM and REM stages.
Discussion and conclusion: Reduced LPP in CP group suggests lesser perturbation of brain processing by negative valenced stimuli, compared to controls. This could mean reduced emotional engagement for waking task and higher allocation of attention away to bodily sensations. Interestingly, during sleep, negative-primed auditory stimuli evoked greater perturbation in CP subject. This could mean greater emotional engagement was possible during sleep and hence overreaction to negative emotion. This warrants further studies on ERPs during wake and sleep.
Acknowledgements: I would like to express my sincere gratitude to DST-CSRI for their financial support, NIMHANS for providing the lab facility that enable this research study. I would also like to acknowledge all the participants of the study and Axxonet Brain Research Laboratory, Axxonet System Technologies Pvt Ltd, Bengaluru, India.

S14.3. Circadian rhythm manipulations help to reverse sleep abnormalities in ventral subicular lesioned rats

Bindu M. Kutty
Centre for Consciousness Studies (CCS), Dept. of Neurophysiology, NIMHANS, Bangalore 560029

The phenomenon of dreams is always an enigma as we need to elucidate much about the phenomenon. Dreams and dream recall are associated with distinct electrophysiological characteristics. Moreover, the electrophysiological features of dreams differ across different stages of sleep, contributing to the occurrence of dreaming. In this presentation, we try to explain the phenomenon of dreaming through the lens of electrophysiological features as the mechanisms underlying dream recall remain unclear, motivating the

present study to identify specific features of dream recall during both REM and NREM sleep. Building on previous research, it was hypothesized that the electrophysiological factors influencing dream recall differ between NREM and REM sleep due to their distinct physiological and neurobiological underpinnings. Additionally, the study explores whether learned events could be integrated into dream experiences.

We have studied 25 participants, both male and females, aged 20-35 recruited from NIMHANS campus and polysomnography was conducted for three consecutive nights. On the first night, all participants underwent whole night polysomnography with 64 electrodes in place for EEG recordings. This is to get the baseline sleep architecture. During the second night, participants were randomly awakened during the second half of the night through a serial awakening paradigm to study about the dream reports. On the third night, before sleep, participants were taught specific audio-visual task to look at the impact of sensory cues on dreams.

The results from the second night demonstrated the electrophysiological correlates of dreams. We found that REM sleep dream recall was associated with increased beta activity in the frontal region, whereas NREM dream recall was linked to decreased delta activity at the temporo-parietal region. The study revealed that dream reports occurred in 59.6 percent of awakenings from N2 sleep and 78.7 percent of awakenings from REM sleep. Furthermore, during the third night, 11.5 percent of audio cue presentations led to the incorporation of video content into dreams.

The study highlights that cortical EEG activity plays a role in successful dream recall, and the electrophysiological characteristics could potentially predict dream recall experiences during sleep. Conscious experience recall during sleep may be correlated with beta activity during REM sleep and delta activity during NREM sleep. Moreover, the study suggests that newly learned experiences can be integrated into dreams, potentially altering the dreaming experience. These findings offer promising avenues for addressing conditions such as PTSD or nightmares during sleep. However, further investigations are warranted to explore methods for incorporating positive events into dreams to modify the dreaming experience concerning negative experiences.

S14.4. Sleep structure and brain morphometry in older adults

Nasreen Akhtar
Department of Physiology, All India Institute of Medical Sciences, New Delhi

Sleep plays a crucial role in synaptic plasticity, information processing, and the execution of various functions. When left untreated, sleep disturbances and disorders can have detrimental effects on physical, psychological, social, and economic well-being. Among the various factors influencing sleep patterns (duration and frequency), aging has been consistently identified as the most significant and influential factor. The most pronounced alterations due to age are observed in non-rapid eye movement (NREM) sleep characteristics, with reduced density and amplitude of slow waves, K-complexes, and sleep spindles. Age-related changes also impact the phase-locked synchrony between slow waves and sleep spindles. Additionally, primary sleep disorders such as insomnia, restless leg syndrome, REM behavior disorder, and sleep-disordered breathing are more prevalent in older adults. The findings of some studies suggest that good sleepers with larger right hippocampal volumes are more likely to generate spindles during sleep, which may support better memory consolidation. These results highlight the importance of adequate and high-quality sleep for memory processing, as well as the role of the hippocampus in this process. This relationship is lost in poor sleepers, emphasizing the importance of good quality sleep in memory consolidation. Sleep spindles have been observed to be coupled with hippocampal sharp wave ripples in rodents. Understanding the relationship between sleep quality and cognitive/brain health in older adults is imperative, particularly considering the increasing global prevalence of dementia.

Symposium- 15: Unmasking the puzzle: Novel insights into neurodegenerative disorders and therapeutic targets

S15.1. Genomic architecture of Alzheimer's disease: lessons from human and mouse models of the disease

Emily Miyoshi[1,2,†], Samuel Morabito[2,3,4,†], Caden M. Henningfield [1,2], Negin Rahimzadeh[2,3,4], Sepideh Kiani Shabestari[1,5], Sudeshna Das [1,2], Neethu Michael [1,2], Fairlie Reese[4,6], Zechuan Shi[1,2], Zhenkun Cao[1], Vanessa Scarfone[5], Miguel A. Arreola[1,2], Jackie Lu[1], Sierra Wright [2], Justine Silva[2], Kelsey Leavy[2], Ira T. Lott[7], Eric Doran[7], William H. Yong[8], Saba Shahin[1,2], Mari Perez-Rosendahl[2,8], Elizabeth Head[2,8], Kim N. Green[1,2], Arshi Shahin[1,2,4] and **Vivek Swarup[1,2,4]**
[1]Department of Neurobiology and Behavior, University of California Irvine, Irvine, CA, USA; [2]Institute for Memory Impairments and Neurological Disorders (MIND), University of California Irvine, Irvine, CA, USA; [3]Mathematical, Computational, and Systems Biology (MCSB) Program, University of California Irvine, Irvine, CA, USA; [4]Center for Complex Biological Systems (CCBS), University of California Irvine, Irvine, CA, USA; [5]Sue and Bill Gross Stem Cell Research Center, University of California Irvine, Irvine, CA, USA; [6]Department of Developmental and Cell Biology, University of California Irvine, Irvine, CA, USA; [7]Department of Paediatrics, University of California Irvine School of Medicine, Orange, CA, USA; [8]Department of Pathology and Laboratory Medicine, University of California Irvine, Irvine, CA, USA [†]These authors contributed equally

The pathogenesis of Alzheimer's disease (AD) is influenced by environmental and heritable factors, exhibiting differences at the molecular level between individuals. We conducted a transcriptomic survey using spatial transcriptomics (ST) and single-nucleus RNA-seq in cortical samples from early-stage AD, late-stage AD, and AD in Down Syndrome (DS-AD) donors. Studying DS-AD offers a unique perspective on the AD transcriptome, potentially connecting genetic mouse models to sporadic AD.
Our analysis uncovered spatial and cell-type specific alterations in the disease, with similarities between sporadic AD and DS-AD. Further ST experiments were performed in 5xFAD and wildtype mice for cross-species comparisons. Additionally, amyloid plaque and fibril imaging in the same samples used for ST allowed direct correlation between gene expression changes and pathology accumulation.
The findings of this study reveal essential connections between genetic expression, disease stages, and pathology, providing insights that could guide future research and therapeutic development. By integrating advanced techniques and cross-species comparisons, our work contributes to the comprehensive understanding of AD, emphasizing the potential for personalized approaches in diagnosis and treatment. In conclusion, our study provides novel insights into the molecular landscape of AD, highlighting the utility of spatial and single-nucleus transcriptomics in revealing the intricate connections between genetic expression and disease pathology. The results from this study contribute significantly to the evolving understanding of AD and lay the groundwork for more focused and personalized therapeutic strategies.

S15.2. Potential reversal of Alzheimer's disease pathology by antibody TB006 targeting Galectin-3, the root cause of oligomerization of amyloid proteins

Suhail Rasool, Jenny Johansson, Ludmila Volobouéva, Sangmi Lee, Xi Lan, Taufeeq Ahmed & Dongxu Sun
True Binding, Inc. 300 Lincoln Centre Dr, Foster City, CA USA; 94404

Alzheimer's disease (AD) is a chronic progressive neurodegenerative disorder caused by multiple pathogenic factors including Amyloid-β (Aβ), phospho-Tau (pTau), alpha-synuclein, and ApoE4, etc. It is widely accepted that intermediate oligomeric forms**,** rather than monomers or mature fibrils**,** are more neurotoxic. Galectin-3 (Gal-3) was reported to be involved in Aβ oligomerization. In vivo, in three mouse models of AD, cognitive deficits were strongly attenuated after just two weeks of mTB001 treatment. Mechanistically, Gal-3 antibody blocked the initiating events in AD (Aβ aggregates), reduced inflammation and rescued neuronal

damage. Furthermore, microhemorrhages, a potential safety liability seen in clinical stage drugs, were reduced. Here, we show that Gal-3 promotes oligomerization of Aβ and other pathogenic factors, and TB006**,** a monoclonal antibody targeting Gal-3**,** acts as a possible treatment for AD by degrading neurotoxic oligomers. Pre-clinical studies show that TB006 is an efficacious therapeutic entity through degradation of toxic oligomers and blocking or even reversing AD progression. Clinically, TB006 has shown a superior safety profile without any drug-related adverse events in healthy volunteer trial. Promising efficacious data are expected from the ongoing phase II AD trial.

S15.3. Neuroprotective strategies to prevent neuroinflammation and cognitive dysfunction in cranial radiation-induced brain injury

Robert P. Krattli[1,*], An Do[1,*], Sanad El-Khatib[1], Leila Alikhani[1], Mineh Markarian[1], Arya R. Vagadia[1], Manal T. Usmani[1], Shreya Madan[1], Janet E. Baulch[2], Richard J. Clark[3], Trent M. Woodruff[3], Andrea J. Tenner[4], **Munjal M. Acharya[1]**
[1]Department of Anatomy & Neurobiology, University of California Irvine, United States; [2]Department of Radiation Oncology, University of California Irvine, United States; [3]School of Biomedical Sciences, The University of Queensland, St Lucia, Brisbane, Australia; [4]Department of Molecular Biology & Biochemistry, University of California Irvine, United States; *Contributed equally

Cranial radiation therapy (CRT) for brain cancers leads to long-term, irreversible impacts on cognitive function. We have shown that CRT-induced cognitive deficits (RICD) are linked with (i) elevated microgliosis, astrogliosis, (ii) aberrant CNS complement cascade activation, and (iii) excessive synaptic loss. CNS complement system mediates reactive gliosis and regulates synaptic pruning, which is detrimental if dysregulated. Complement components also promote glioma proliferation and invasiveness. Thus, complement cascade inhibition would be beneficial against RICD and glioma. We used gene knockdown and pharmacologic approaches: microglia-selective C1q-KO, C5aR1-KO, and an orally active, BBB-permeable, C5aR1 antagonist (PMX205) to reverse RICD. C1q-KO mice lack C1q expression in the CNS without affecting circulating C1q, thus designed to determine CNS-specific impact of C1q-KO. Adult WT C57 mice received 9 Gy CRT and PMX205 treatment in drinking water for 1-month. Adult C1q-KO and C5aR1-KO mice received CRT. Cognitive function, tissue, and cellular studies were carried out one-month post-CRT. CRT significantly impaired cognitive function compared to the irradiated C1q-KO, C5aR1-KO, or irradiated WT mice+PMX205 on the frontal cortex and hippocampal-dependent behavior tasks. C1q-KO, C5aR1-KO, and PMX205 reduced microglial activation and synaptic loss in the irradiated brains. Importantly, either C1q-KO, C5aR1-KO or PMX205 treatment to the syngeneic, orthotopic astrocytoma and glioblastoma-bearing mice did not interfere with the therapeutic efficacy of CRT in killing tumor in vivo. In summary, inhibition of CNS complement signaling is neuroprotective from toxic, overzealous inflammatory effects of CRT without interfering with the therapeutic efficacy for glioma and thereby supports the translational applicability of this novel approach.

S15.4. Sex-specific locus coeruleus dysfunction expedites disease progression in APP/PS1 mice

Srishti Kushwaha[1†], Rupsa Roy Choudhury[1†], Jyotirmoy Biswal[2], **Smitha Karunakaran[1]**
[1]Centre for Brain Research, [2]Indian Institute of Science, Bangalore.
[†]These authors contributed equally

Background: Alzheimer's disease (AD) is more prevalent in women than men above the age of 65. Early symptoms include sleep disturbances and neuropsychiatric symptoms, and involves a brainstem nucleus called locus coeruleus (LC). However, fundamental biology of LC, and how they may drive the prodromal stages of AD is not known.
Materials and methods: Stereological assessment of LC neurons, and LC terminal density in the hippocampus were evaluated in the APP/PS1 mice using ImageJ. LC was stimulated using environmental enrichment (EE), and structural changes in hippocampus astrocytes were studied using ImageJ. Evans blue tail vein injections were performed to account for blood brain barrier breach.

Results: Our research utilizing an amyloidogenic mouse model, APP/PS1, indicates that the LC is sexually dimorphic. In the presence of amyloid-β oligomers, sex-specific differences were observed in the LC terminals projecting to the hippocampus, with the neuronal numbers remaining intact. Stimulating the dysfunctional LC using EE induced aberrant plastic changes in the hippocampus astrocytes in a sex-dependent manner, culminating in blood brain barrier breach at 9-months-of age.
Discussion and Conclusions: Considering AD disproportionately affects women, the sexual dimorphic nature of the LC could play a role in driving the early stages of AD. Stimulating a dysfunctional LC may cause an increase in NE release, resulting in post-synaptic sensitization, elevated neuronal firing rates, and subsequent cognitive decline. Based on our findings, LC neuroimaging shows promising potential as an early biomarker for diagnosing individuals who are predisposed to conditions like AD.

S15.5. Sex-specific differences in evolution of cognitive decline in Alzheimer's disease

Reddy Peera Kommaddi[1], Aditi Verma[2], Graciela Muniz-Terrera[3,4], Vivek Tiwari[1], Keerthana Chithanathan[2], Latha Diwakar[1], Ruturaj Gowaikar[2], Smitha Karunakaran[2], Palash Kumar Malo[1], Neill R Graff-Radford[5], Gregory S Day[5], Christoph Laske[6,7], Jonathan Vöglein[8, 9], Georg Nübling[8,9], Takeshi Ikeuchi[10], Kensaku Kasuga[10], the Dominantly Inherited Alzheimer Network (DIAN)[11,#] and Vijayalakshmi Ravindranath[1,2]
[1]Centre for Brain Research, Indian Institute of Science, Bangalore-560012, India; [2]Centre for Neuroscience, Indian Institute of Science, Bangalore-560012, India; [3]Centre for Clinical Brain Sciences, The University of Edinburgh, Edinburgh, Scotland, UK; [4]The Department of Social Medicine, Ohio University, Athens, OH45701, USA; [5]Department of Neurology, Mayo Clinic Florida, Mayo Clinic College of Medicine and Science, 4500 San Pablo Road, Jacksonville, FL 32224, USA.; [6]German Center for Neurodegenerative Diseases, Munich, Germany; [7]Section for Dementia Research, Department of Cellular Neurology, Hertie Institute for Clinical Brain Research, Department of Psychiatry and Psychotherapy, University of Tübingen, Tübingen, Germany; [8]Department of Neurology, Ludwig-Maximilians-Universität München, Munich, Germany; [9]German Center for Neurodegenerative Diseases (DZNE), Munich, Germany; [10]Department of Molecular Genetics, Center for Bioresources, Brain Research Institute, Niigata University, 1-757 Asahimachi-dori, Chuo-ku, Niigata City, Niigata 951-8585, Japan; [11]Charles F. and Joanne Knight Alzheimer Disease Research Center, Department of Neurology, Washington University School of Medicine, St. Louis, MO, USA

Abstract not available

S15.6. N-Acetylcysteine amide protects neurons form degeneration in In-Vitro STZ-model of Alzheimer's Disease

Muddanna S Rao and Smitha S
Department of Anatomy, College of Medicine, Kuwait University Kuwait

Introduction: Initiation of Alzheimer's disease is claimed to be through oxidative stress (OS). Antioxidant therapy to alleviate the neurodegeneration in AD is most explored research area recently. N-Acetylcysteine amide (NACA), an antioxidant substance proved to be effective in neuroprotection in several neural injury models including AD. Recent findings suggest AD is an insulin resistant brain's state. Streptozotocin (STZ) is a glucosamine-nitrosourea compound commonly used to induce type-1 diabetes in rodents. Administration of STZ into rodent's cerebral ventricles or into neural culture has been shown to produce pathophysiological changes such as neuroinflammation, oxidative stress and biochemical changes as in AD. Hence, STZ-model of AD is one of the established animal models of AD. Neuroprotective effects of NACA in the in-vitro Aβ1-42 model of AD is well established but not in STZ-induced in-vitro model. **Objectives:** The present study was aimed to evaluate the neuroprotective effects of NACA against STZ-induced AD-like pathology in an in-vitro model. **Methods:** Primary culture of cerebral cortical tissue from E18 day fetus was done in advanced DMEM media containing 10% fetal calf serum, and 100 IU antibiotics. Cultures were grown for six days in a CO2 incubator maintained at 37^{o}C, with 5% CO2. Cultures were then divided into Control, STZ-10μM, STZ-10μM + NACA-10μM, STZ-10μM+NACA-20μM groups and treated with 10μM STZ, 10 and 20μM NACA either for 24-hours or 72-hours duration. For all dose and duration triplicate culture were maintained. After treatment period, all cultures were fixed with 2% paraformaldehyde and immunostained with Tuj1 to

stain the neurons and with GFAP to stain Astrocytes, Iba1 to stain the microglia. Number of neurons, their processes, number of astrocytes and number of microglia were quantified. Results were analyzed with One-way ANOVA, followed by Bonferroni's multiple comparison test. **Results:** STZ-decreased the neuronal size, number of processes, and neurite length compared to control group. STZ astrogliosis and enhanced reactive microglial cells. Treatment with NACA prevented neurons from degeneration at both doses, however effect was significant at 20µM concentration for 72hrs treatment. NACA also reduced the astrogliosis and microgliosis in STZ treated culture. **Conclusions:** This study demonstrates the neuroprotective effects of NACA in the in-vitro STZ model of AD. This model may be used to study AD-pathology in in-vitro.

Symposium-16: Neuromodulation strategies in health and disease

S16.1. Application of low intensity electromagnetic fields in ameliorating cognitive dysfunction and synaptic pruning in streptozotocin induced sporadic Alzheimer's disease rat model

Suman Jain[1], Avishek Roy[1], Jyotirmoy Banerjee [2] and Soumya Iyengar [3]
[1]Department of Physiology, [2] Department of Biophysics, All India Institute of Medical Sciences, New Delhi, India; [3]National Brain Research Centre, Manesar, Haryana, India

Background: Electromagnetic field stimulation (EMF) is a neuromodulation procedure that alters the activity of neural tissue to repair, regenerate and restore the structure and function. In the present study, we investigated the therapeutic efficacy and mechanism of action of EMF in i.c.v. streptozotocin induced rat model of AD.
Materials and Methods: A group of rats were exposed to EMF (17.96µT, 50Hz, 2hr/day), 24h after STZ injection (3mg/kg bwt, bilaterally, single bolus) for 60 days in a customized MF chamber. A battery of behavioural tests followed by Golgi Cox staining and assessment of oxidative stress was done at the end of study.
Results: A statistically significant improvement in spatial and recognition memory upon exposure to EMF was observed, which was associated with increase in GSH content and catalase activity in hippocampus. 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 EMF treatment to AD rats.
Discussion: The present study provides scientific evidence for the 1, development of Alzheimer's disease rat model by injecting streptozotocin (3mg/kg bwt) intra-cerebroventricularly; 2, therapeutic potential of electromagnetic field stimulation in Alzheimer's disease; and 3, amelioration of cognitive impairment in AD rats by EMF is through enhancement of synaptic plasticity and attenuation of oxidative stress.
Acknowledgement: We acknowledge Indian Council of Medical Research, Delhi for providing Senior Research fellowship and funds to carry out this research work.

S16.2. Utility of neuromodulation in mood and movement disorders

Kaviraja Udupa
Departments of Neurophysiology, NIMHANS, Bengaluru, India

Background: There is growing interest in utilizing various brain stimulation techniques such as non-invasive brain stimulation (NIBS): repetitive transcranial magnetic stimulation TMS and transcranial direct current stimulation (tDCS), transcranial alternating brain stimulation (tACS) and transcutaneous auricular vagal nerve stimulation (taVNS). TMS is shown to be non-invasive, safe and effective mode of investigation to explore the physiology of cortical circuits in health and disease. 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 mood and movement disorders.

Materials and Methods: 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. 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 discussing these neurophysiologic perspectives of brain stimulation, possible combination of various modes of brain stimulation and mechanistic basis of these stimulation protocols.

Results, Discussion and Conclusions: Although rTMS treatment has been successfully considered as add-on in management of clinical depression and various other neuropsychiatric disorders, we are still lacking the clear understanding of their mechanisms of action in neurodegenerative conditions. 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 on the 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 mood and movement disorders.

S16.3. Probing functional brain networks using transcranial brain stimulation

Nivethida Thirugnanasambandam
Department of Biosciences & Bioengineering, Indian Institute of Technology Bombay, Mumbai, India

Our brain is functionally organized into specialized networks comprised of multiple interconnected regions. Emerging evidence indicates that synchronized interaction of brain regions within and across these functional networks plays a crucial role in shaping behaviour. Functional brain networks can be identified using advanced non-invasive imaging methods such as functional MRI and magneto-/electro encephalography at different spatial and temporal resolutions. Several such networks have been identified and implicated in specific cognitive functions. Notably, disruptions in the activity of these networks have been linked to neuropsychiatric disorders such as Parkinson's disease, Alzheimer's disease, ADHD and schizophrenia. Thus, it is conceivable that modulating these networks could potentially restore abnormal function associated with these disorders. Transcranial brain stimulation has recently emerged as an effective and safe tool for non-invasive neuromodulation. In this talk, I will review the different non-invasive brain stimulation techniques with specific focus on their effects on functional brain networks and their implications on behavioural/clinical outcomes. I will also highlight the importance of a multimodal approach in investigating the causal role of brain networks in health and disease.

S16.4. Brain state-specific regulation of neural activity in dementia

Anuraag Chetty[1], Justin Joseph[1], Harsha Bhardwaj[1], Aswin Sekhar C S[1], **Chinnakkaruppan Adaikkan[1]**
[1]Centre for Brain Research (CBR), Indian Institute of Science (IISc), Bangalore 560 012

There has been a growing interest in identifying early biomarkers of Alzheimer's disease (AD). They include biofluid-based (e.g., amyloid levels in blood plasma) and also brain signal-based (e.g., EEG) biomarkers. In the EEG-based approach, various features of EEG are examined to correlate with cognitive function, including mini-mental state examination score (MMSE). Although the latter approach provided promising results, progress in this area is hampered by the lack of resources and tools for neurologists to examine these EEG-based features as they require specialized training and experts. Therefore, we investigate the relationship between brain rhythm features and memory/dementia using a neural EEG collected non-invasively from the scalp of human subjects. We developed a software package to examine the EEG signal complexity and randomness. Forty meticulously crafted temporal, spectral, and spectro-temporal complexity features in EEG are extracted and regressed these EEG features with MMSE. We find feature-specific and

region-specific EEG features correlating with MMSE scores, suggesting that EEG-based biomarkers could be explored for AD diagnosis.

S16.5. Modulation of motor neuron excitability and muscle contractile properties in complete spinal cord injured rats by electromagnetic field stimulation

Arpita Chakraborty[1,3], Mehar Chand Sharma[2], Suman Jain[3]
[1]Department of Neurology, Institute of Neurosciences Kolkata, Kolkata 700017, India
[2]Department of Pathology and [3]Physiology, All India Institute of Medical Sciences, New Delhi, India

Background: Spinal cord injury (SCI) is a catastrophic condition associated with significant neurological deficit with loss of muscle mass, strength and activity. Aim of our study was to investigate the motor neuron excitability and muscle contractile properties after electromagnetic field stimulation.
Materials and Methods: Adult male rats were subjected to spinal cord transection at T13 level and 24h thereafter exposed to EMF for 7 and 14 days (2h/day,17.96μT). On terminal days, electrophysiological recording of Hoffman reflex and contractility (twitch force, tetanic force) of soleus muscle was performed in Sham, SCI and EMF groups (n=6). 10μm thick sections of snap-frozen soleus muscle were taken to perform immunohistochemistry.
Results: Hyper-reflexia, muscle atrophy, reduction in twitch and tetanic force with earlier onset of fatigue was evident in the SCI group. EMF stimulation showed significant improvement in H/M ratio, muscle twitch, tetanic force, fusion frequency and fatigability as compared to SCI group. EMF stimulation significantly increased peak force generation in progressive manner at both time points at each stimulus frequency (5-50Hz). A significant increase in regenerating myofibers (eMHC positive) and decreased type IIA following EMF was evident.
Discussion and conclusions: The results suggest significant neuroprotective effects of early and chronic administration of EMF stimulation on reflex, muscle spasticity, contractile properties, fiber type transformation and muscle regeneration. Our study shows the potential of electromagnetic field stimulation to modulate the excitability of motor neurons and muscle by activity-dependent mechanisms that facilitate neuronal and muscle plasticity for better functional recovery.
Acknowledgement: This original research work was funded by Institution (AIIMS, New Delhi) and ICMR.

Symposium- 17: Glia in health and disease

S17.1. The glee'a: Do glia make us happy?

Swananda Marathe
Indian Institute of Technology, Dharwad

Mood and anxiety disorders, including depression, are the most common psychiatric disorders across cultures, geographies and genetic backgrounds. These disorders lead to profound adverse effects on patients' wellbeing, and they can be life threatening, mainly because of the heightened risk of suicides. Despite several decades of research, we do not understand the pathophysiology underlying depression. As a result, currently prescribed medications are highly inadequate, owing to their low efficacy, delayed onset of action, side effects and high frequency of relapse.
One of the most common features seen in suicide victims of depression is massive degeneration of glia, across various brain regions. Interestingly, selective ablation of glial cells from the medial prefrontal cortex induces the behavioral symptoms of depression in rats, suggesting a possible causal link between glial degeneration and the behavioral symptoms of depression.
Despite the mounting evidence showing glial involvement in the pathophysiology of depression, we don't understand the underlying mechanisms. Furthermore, we don't know if glia might be involved in the behavioral effects of antidepressant therapies, and whether their functions can be harnessed for novel therapeutic approaches.

Our lab has discovered a novel form of structural plasticity in astrocytes induced by antidepressant therapies. I will also discuss how we may be able to exploit this plasticity to produce antidepressant-like behavioral effects.

S17.2. Reactive astrocytes in aging, neuronal injury and neurodegenerative diseases

Narendra Kumar Ramanan
Indian Institute of Science, Bangalore

Astrocytes, the major cell type in CNS, play several critical functions including ion homeostasis, synapse formation and synaptic plasticity. Astrocytic dysfunction is central in several CNS disorders including epilepsy, amyotrophic lateral sclerosis, Parkinson's, and Alzheimer's disease. In response to CNS injuries and pathologies, astrocytes undergo a spectrum of molecular, physiological and structural changes, in a process termed reactive astrogliosis. Reactive astrogliosis can be beneficial or detrimental to normal brain functions and there is increasing interest in unravelling the molecular mechanisms that regulate astrogliosis as these might provide valuable therapeutic targets to improve neuronal survival and promote CNS repair and recovery. We have identified the transcription factor, serum response factor (SRF) as important for the maintenance of astrocytes in a non-reactive state. We have found that deletion of SRF in astrocytes in the mouse brain results in widespread and persistent reactive-like astrocytes. These SRF-deficient astrocytes do not affect neuron survival, synapse numbers, synaptic plasticity or learning and memory. However, the brains of Srf knockout mice exhibited neuroprotection against kainic-acid induced excitotoxic cell death. Relevant to human neurodegenerative diseases, SRF-deficient reactive astrocytes abrogate nigral dopaminergic neuron death and reduce β-amyloid plaques in mouse models of Parkinson's and Alzheimer's disease, respectively. Interestingly, the brains of aged SRF knockout mice showed attenuated cell loss and myelination in several brain regions along with better motor coordination compared to the age-matched control mice. Collectively, these findings establish SRF as a key molecular switch for the generation of neuroprotective astrocytes in the mammalian brain.

S17.3. ALA augment Tau phagocytosis and endosomal degradation in microglia

Subashchandrabose Chinnathambi
National Institute of Mental Health and Neurosciences, Bengaluru

Physiologically, microglia in resting state inspects the brain environment with their long extensions for the extracellular targets. Omega-3 fatty acids has neuroprotective properties and plays an important role in development and differentiation of neuronal cells. Docosahexaenoic acid (DHA-22:6n-3), Eicosapentaenoic acid (EPA-20:5n-3) and α- Linolenic acid (ALA 18 3n:3) are the most important long-chain fatty acids found in the brain and constitute to majority of the cell membrane. These fatty acids are incorporated in the cell membrane as long chains of phospholipids. Omega-3 fatty acids are the vital factors to decide the polarity of microglia cells as M1 or M2. DHA tends to increase the M2 phenotype of microglia by changing the cell membrane composition and influencing the production of lipid mediators. Omega-3 fatty acids also increase the phagocytosis of myelin debris, clears extracellular Aβ peptide in the AD brain environment, which is the major causes of neuroinflammation. In this study, we aim to understand the effect of α-Linolenic acid, a precursor of DHA and EPA, on actin remodeling related to phagocytosis and migration. In Tauopathies, extracellular Tau seeds tend to activate microglia to induce inflammatory activation. However, the study involves understanding the effect of ALA on phagocytosis and related actin-remodeling in microglia in the presence of extracellular Tau seeds. Phosphatidylinositols are the product of different phosphatidylinositol kinases and the state of phosphorylation at D3, D4, and D5 positions of inositol ring. PI 3,4,5-P3 involves in phagocytic cup formation and cell polarization. PI4,5-P2-mediates phagosome formation and further fusion with early endosome and relates actin remodeling.

S17.4. To grow or not to grow: Hyperglycaemia induced alterations in neurite outgrowth

Vasudharani Devanathan, Sapna Sharma, Harshini Chakravarthy, Gowthaman Suresh
Department of Biology, Indian Institute of Science Education and Research, Tirupati

Background: Primary cultures utilize foetal rodent neurons, but very rarely adult neurons from larger mammals. We established hyperglycemia model in retinal neurons from Goat. We explored role of cell adhesion molecules in hyperglycemia implicating to Diabetic Retinopathy. Further study demonstrated that metabolic environment markedly affects neurite outgrowth and transcriptional regulation of CAMs in adult retinal neurons.
Materials and Methods: Retinal neurons were successfully cultured and maintained *in-vitro* for 10 days. We confirmed the cellular sub type by Immunofluorescence and neurite length in altered metabolic conditions were measured. Furthermore, using biochemical methods, we also showed transcriptional regulation of Cell adhesion molecules involved in neurite outgrowth regulation.
Results: Immunofluorescence staining revealed that the cellular population was heterogenous composed of neurons and glial cells. These cells were maintained *in vitro* for 10 days and were supplemented with high glucose concentration to induce hyperglycaemia. The neurite outgrowth was measured using ImageJ and the length of neurons increased in hyperglycaemia condition. Using this model, we have identified novel molecular markers that regulate neurite outgrowth in cultured Retinal neurons.
Discussion and Conclusions: Retinal neurons have the advantage of being the most accessible cells of the CNS, and serves as a reliable mirror to the brain. Higher mammals such as pigs have similar retinal structures as humans, while dogs develop morphological lesions most similar to diabetic human retina. Our results obtained from Goat retinal cells show role of hyperglycemia in regulating cell adhesion molecules governing neurite elongation. These cell adhesion molecules of the neuron may act as early molecular markers or as therapeutic targets for Diabetic retinopathy.
Acknowledgements: We thank IISER Tirupati for constant support. The project was funded by IISER Tirupati, VD is a recipient of Early Career Research Award from SERB, Department of Science and Technology (Grant Number: ECR/2016/001124/LS). HC is a recipient of Women Scientist Scheme-A (WOS-A), Department of Science and Technology (Grant Number: SR/WOS-A/LS-327/2018). VD would like to thank DST, Government of India and IISER Tirupati for research support. GS and SS thank UGC, DAAD and IISER Tirupati for their research fellowships.

S17.5. Retro-Engineering brain tumours: Uncovering inflammation, immunity and tumour biology

Sushmita Jha
Department of Bioscience and Bioengineering, Indian Institute of Technology, Jodhpur

Malignant gliomas, the most common primary brain tumours that arise from glial cells within the central nervous system (CNS), are among the most fatal human cancers. With a median survival of only 14.6 months, even after aggressive therapy with surgery, radiation, and chemotherapy, most patients succumb to their disease within two years of the initial diagnosis. Taking into consideration the paradigm shifts from traditional surgical resection to precision medicine, we use a multi-pronged approach taking into account the cellular heterogeneity of gliomas, their microenvironment and 3-dimensional cell-cell interactions to identify the role of innate immunity and inflammasome signalling pathways in gliomas. This could potentially provide a novel link between innate immunity and glioma pathophysiology with widespread therapeutic implications for delaying glioma progression and/or sensitizing gliomas to other treatment modalities.
We first established the importance of innate immune pathways in cell lines and used the cancer genome atlas (TCGA) data, with funding from SERB (Young Scientist Award grant). We next set up a tripartite MoU between IIT Jodhpur, Tata Memorial Hospital and ACTREC & AIIMS Jodhpur to understand the cellular and molecular landscape of gliomas for the identification of novel therapeutic targets, especially in the context of the Indian subcontinent, funded by the Department of Biotechnology. These studies resulted in the identification of a novel prognostic marker for glioblastomas (*Sci Rep* **9,** 8480 (2019)). We have also developed a portable hypoxia chamber that will provide a platform to study the role of hypoxia in several diseases including gliomas. This chamber design is under patent (Patent Application No. 201811017208).

We are now in the process of translating this technology with the help of industry partners. Additionally, we recently discovered Dopamine-induced microglia extracellular traps. Dopamine plays a central role in our brain's pleasure and reward systems, movement and cognition, but its role in regulating innate immunity is unclear. Our research showed for the first time that dopamine can induce DNA-based extracellular traps in microglia cell lines and primary human microglia. These extracellular traps are formed independently of reactive oxygen species, actin polymerization and cell death. The traps are functional and capture *Escherichia coli* even when reactive oxygen species or actin polymerization is inhibited. Interestingly, we found microglia extracellular traps within the *Glioblastoma multiforme* microenvironment. This is crucial because these tumours are known to secrete dopamine, but the mechanistic insights to this were largely undiscovered. Our results demonstrate that dopamine plays a significant role in neuro-inflammation by inducing microglia extracellular traps paving the way for targeting dysregulated neuroinflammation. It would be interesting to explore how these extracellular traps play a role in other neurodegenerative and cognitive diseases where dopamine is central to pathophysiology.

With funding from the Ministry of Electronics and Information Technology (MEITY) for the development of an interdisciplinary research platform for dissecting complex cellular interactions using patient-derived normal and tumour organoids, computational biology and artificial intelligence-based approaches. We have successfully created a protocol for matrix-free patient-derived glioblastoma organoids (Indian Patent application No: 202311002108). These organoids can serve as a personalized medicine framework to allow for pre-clinical drug development, biomarker analysis, drug-testing model, and basic cancer research.

Our research at IITJ has been published in leading international journals, including Nature Reviews Immunology, The Journal of Experimental Medicine (JEM), Scientific Reports, iScience, Journal of Immunology(JI), Journal of Visualized Experiments (JoVE), STAR Protocols, Cellular and Molecular Lifesciences etc. (https://www.sushmitajhalab.com/publications). Importantly, our research aims to create a deeper understanding of glioma pathophysiology from the Indian subcontinent and develop technologies for precision medicine.

S17.6. Inflammation and Neuroprotection in Mouse Brain: Role of HMGB1

K.P. Mishra
DRDO Defence Institute of Physiology and Allied Sciences, Delhi-110054

The damage associated molecular pattern HMGB1 is an endogenous alarmin that causes inflammation, neurodegeneration and cognitive decline. In the present study, we have delineated the potential inhibitory effect of a novel receptor of HMGB1-CXCL12 complex known as atypical chemokine receptor 3 (CXCR7) on HMGB1 induced glial phenotype switching, neuroinflammation and subsequent memory loss. Upregulation of CXCR7 inhibits HMGB1-CXCL12 complex induced peripheral inflammatory cells infiltration to the brain. Whereas, ablation aggravates inflammatory responses in hippocampus region and immune cell infiltration to the brain tissues by breached blood brain barrier. This study also indicates the important role of CXCR7 in maintaining CNS homeostasis, by balancing M1/M2 microglia and A1/A2 astrocytes, which ameliorates HMGB1 induced neurodegeneration and memory loss in mice. Overall, the study summarizes several significant protective functions of CXCR7 against HMGB1 induced neuroinflammation, neurodegeneration and memory loss and thereby provides a new paradigm for novel therapeutics development against stress induced neurodegenerative diseases.

Symposium- 18: Neurochemical basis of neurotoxicity

S18.1. Trolox aids Coenzyme Q10 in protection of neural retina in NMDA induced glutamate excitotoxic damage via upregulation of VEGF in rat model

Shikha Upreti and **Madhumita P. Ghosh**
Amity Institute of Biotechnology, Amity University, AUUP Noida

Background : Glutamate receptors play an important role of regulating extracellular glutamate concentrations to maintain signalling processes in the eye. Elevated levels of glutamate in the vicinity of

retinal ganglion layer perturbs N-methyl-D-aspartate (NMDA) receptors present on retinal ganglion cells (RGCs) leading to cell death. Here we put forth the role of trolox in enhancing neuroavailability of COQ10 and recover the glutamate concentrations in a rat model of NMDA induced degeneration.
Materials and Method : Wistar rats were administered with NMDA intravitreally and subsequently treated with coenzyme Q10 and Trolox. After 7 days of incubation, animals sacrificed, eyes enucleated and subjected to H& E staining, measuring ROS, mitochondrial membrane potential, mRNA expression of VEGF and NMDA receptors and protein expressions of VEGF and p VEGF.
Results : The release of ROS and oxidative stress, nitric oxide is decreased on treatment with CoQ10 and Trolox. The mitochondrial membrane potential challenged due to damage of NMDA receptors recover in response to the combination of Trolox with COQ10.The mRNA expressions of VEGFR2 increases on the treatment and that of NMDA receptors, Nrd 2A increases and that of Nrd2B decreases in COQ10 and Trolox mediated neuroprotection. The proteins VEGFR2 and ERK signalling are enhanced.
Discussion : As there have been many reports about α- tocopherol enhancing neuroprotection when used with CoQ10, this is the first report in our knowledge to demonstrate the efficacy of trolox with COQ10, which will help to devise ways to maintain VEGF levels that are lowered in ocular diseases due to NMDA related toxicities.
Acknowledgement : The work is funded by Indian Council of Medical Research.

S18.2. Suppression of bisphenol-A induced oxidative stress and mitochondrial dysfunction by taurine promotes neuroprotection and restores aggressive behaviour in adult zebrafish *(Danio rerio)*

Lilesh Kumar Pradhan[a,b] and Saroj Kumar Das[a,c]
[a]Neurobiology Laboratory, Centre for Biotechnology, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar, India; [b]Centre of Excellence, Natural Products and Therapeutics Laboratory, Department of Biotechnology and Bioinformatics, Sambalpur University, Odisha, India; [c]P.G. Department of Life Sciences Sri Krushna Chandra Gajapati (Autonomous) College, Paralakhemundi, Odisha, India

Background: Bisphenol A (BPA), a prevalent industrial chemical, raises concerns for its neurodegenerative potential, causing neuronal damage, oxidative stress, inflammation, and neurotransmitter imbalances. Taurine, with its antioxidative, anti-inflammatory, and neuromodulatory properties, offers promise in combating oxidative stress.
Material and methods: The current experimental design spanned 56 days to investigate taurine's neuroprotective effectiveness against BPA-triggered neurotoxicity in zebrafish through waterborne exposure. Neurobehavioral assessments utilized the mirror biting test. Furthermore, biochemical assays for oxidative stress indices, gene and protein expression studies associated with mitochondrial dysfunction were performed on adult zebrafish brain.
Results: BPA-induced neurotoxic effects result in a reduction in the levels of BDNF. Additionally, exposure to BPA leads to a decrease in the expression of tyrosine hydroxylase protein. The heightened expression of JNK protein corresponds to modifications in the mRNA expression of genes associated with apoptosis. Furthermore, taurine effectively countered the neurobehavioral, biochemical, and neuromorphological alterations within the zebrafish brain. Notably, taurine supplementation reversed the distorted protein and mRNA expressions induced by BPA.
Discussion and conclusions: In a nutshell, the findings of our study shows the neuroprotective efficacy of taurine against BPA-induced oxidative damages, neurobehavioral alterations and mitochondrial dysfunction.
Acknowledgement: The authors acknowledge the Centre for Biotechnology, SOA (Deemed to be University) for providing the infrastructure facility and financial support.

S18.3. Dietary *Lactobacillus rhamnosus* GG (LGG) attenuates the toxic effects of benzo[a]pyrene and ethanol on zebrafish (Danio rerio) via gut microbiota modulation

Manorama Patri
Neurobiology Laboratory, Department of Zoology, School of Life Sciences, Ravenshaw University, Odisha, India

Background: Endogenous gut microbiota can greatly sway down all aspects of host's physiology including gut–brain communication, brain function and even behavior. Recently, probiotics have come into limelight as a novel for safely keeping a healthy intestinal microbiota, and thus having impact on the gut–brain function.
Materials and methods: Our present study aimed of taking zebrafish as a model organism to investigate the effect of *Lactobacillus rhamnosus* GG (LGG) along with Benzo[a]pyrene (B[a]P) and Ethanol which causes neurochemical alterations in the central nervous system leading to modulation of behavior. Wild-type zebrafish were designated as Naive; Vehicle Control (DMSO); Probiotic, fed with feed supplemented with LGG; B[a]P (at a conc. of 0.4µg/ml); B[a]P+ Probiotic group; Ethanol (0.1% v/v); and co-treatment of Probiotic & Ethanol group. **Results:** After chronic exposure of these pollutants the novel tank test and light/dark test was used to evaluate fish behavior, which was analyzed using ANY-Maze video-tracking system. LGG alone didn't alter any behavioral pattern rather kept the histo-architectural structure intact. Histopathological changes of following H&E staining of zebrafish intestine revealed that the intestinal epithelial cells, lumen, villi and intestinal folding were varied significantly ($P<0.05$) in B[a]P and ethanol exposed groups in comparison to naive and control groups.
Discussion: In B[a]P and ethanol treated groups it showed reversal in scototaxis (anxiety-like) behavior which was restored by co-supplementation of LGG. Similarly, Cresyl violet staining of the zebrafish brain's section showed significant increase in pyknotic cell counts following waterborne exposure to B[a]P and ethanol as compared to naive and control. However, co-supplementation of LGG leads to behavioral restoration and reduction of pyknotic cells in B[a]P+LGG & Ethanol+ LGG groups as compared to B[a]P and Ethanol groups.
Conclusion: This study provides clues that probiotic strain can modulate gut commensal bacteria influencing behavior and histology of brain in adult zebrafish.

S18.4. Neuroprotective properties of GC-MS-identified phytoconstituents in Persicaria hydropiper (L.) Delarbre methanolic leaf extract: An in silico and in vivo study

Meenakshi Bawari, Linda B Hrangkhol
Department of Life Science and Bioinformatics , Assam University, Silchar , Assam

Background: Neurological disorders pose significant challenges to global healthcare systems, necessitating the exploration of novel therapeutic strategies. This study focuses on Persicaria hydropiper (L.) Delarbre, a medicinal plant used in treating various ailments, and aims to investigate the neuroprotective properties of phytoconstituents present in its methanolic leaf extract.
Materials and methods: GC-MS analysis identified phytoconstituents in Persicaria hydropiper methanolic leaf extract. Swiss ADME's in silico approach was used to determine phytoconstituents pharmacological properties. Molecular docking simulations were performed to assess binding interactions with key targets including serotonin, GABA, NMDA and potassium channel receptor. An in vivo study was conducted to validate neuroprotection.
Results: GC-MS analysis of Persicaria hydropiper methanolic leaf extract revealed several bioactive compounds with high binding affinities and favourable pharmacological properties. An in silico study exhibited that these compounds modulate target protein activity for rendering neuroprotection. BIOVIA Discovery Studio software's advanced visualisation features revealed detailed binding interactions of the ligands and target proteins. In the in vivo study, neuroprotective effects were observed in mice treated with the low dose of this plant extract.
Discussion and Conclusion: GC-MS analysis substantiates the rich diversity of the phytoconstituents in Persicaria hydropiper methanolic leaf extract, potentially responsible for promoting neuroprotection. In silico pharmacological and molecular docking results provided insights into the plausible mechanisms underlying the neuroprotective effects. The in vivo study indicated that the plant extract has neuroprotective benefits in a dose-dependent pattern. In silico predictions and in vivo results support further exploration of this plant source as a therapeutic intervention for neurological disease.
Acknowledgement: Funding Source : NIL; GCMS analysis – AIRF , JNU, New Delhi

Symposium- 19: Therapeutics and neurodegeneration

S19.1. Criticality of gender in the treatment of neuropsychiatric disorders

Sumana Chakravarty
Applied Biology, CSIR- Indian Institute of Chemical Technology (IICT), Hyderabad.

Introduction: Neuropsychiatric disorders account for a major burden among the global non-communicable diseases. Despite ongoing research efforts, our understanding of the etiopathology of depression remains limited. Furthermore, most of the preclinical research uses only male models though sex difference is evident in the incidence of many neuropsychiatric disorders. We are trying to fill the void by uncovering gender difference in the underlying molecular etiopathology.
Materials and Methods: Chronic Variable Mild Stress (CVMS) paradigm was used to induce depression and related mood disorder phenotype in male and female C57Bl/J mice, assessed by a battery of behavioral tests; The affected brain neurogenic area (Dentate Gyrus, DG) from both sexes were subjected to transcriptomic study by RNA-Seq. The validation of differentially expressed genes (DEGs) was done using RT-qPCR.
Results: The CVMS resulted in mood disorder phenotype in both the sexes; however, no remarkable cognitive disorder phenotype was observed across the sexes except mild cognitive impairment in spatial memory of stressed females. RNA-Seq results suggest sex difference in the differential molecular regulation for apparently similar depressive phenotype. The molecular analysis of the whole hippocampus revealed a definite sex difference in the expression of transcriptionally repressive epigenetic marks H3K9 and K27me2, following CVMS. Additionally, the onset of depressive behaviors also showed sex-specific difference.
Discussion and Conclusion: A total of 2230 DEGs was identified in male DG subjected to CVMS and the preliminary analysis of the top pathways affected is synaptogenesis signalling, axon guidance, Siruins, etc. The RNA-Seq data from female DG had variations due to difference in stages of the estrous cycle the animals were at the CVMS paradigm. Overall findings suggest that molecular mechanisms underlying the depressive disorder differ across the sexes despite sharing similar phenotype. Further research to validate and find novel, sex-specific molecular targets for depression in underway.
Acknowledgement: We wish to thank CSIR and SERB for the support to conduct this study. This project was mainly supported by **SERB-POWER Fellowship** to SC [SPF/2021/000045].

S19.2 Taupathies and neurodegeneration

T C Yasha
Department of Neuropathology, National Institute of Mental Health and Neurosciences, Bangalore-560029, India

The microtubule associated protein, tau, forms insoluble cellular aggregates in a heterogeneous group of neurodegenerative diseases, termed tauopathies. They are characterised as primary/secondary, depending on whether additional protein aggregates/inclusions are involved; or 3R/4R/both based on the accumulated tau-isoform. The clinical manifestations of tauopathies are chiefly determined by the neuroanatomical sites involved, and the neurons, oligodendroglia and less frequently astroglia show a spectrum of morphological inclusions from pretangles, neurofibrillary tangles, coiled bodies, globular bodies, Pick bodies, neurites and others. In Alzheimer's disease, the neurofibrillary tangles (tau) and neuritic plaques (tau and beta-amyloid) contain both 3R and 4R tau. Pick's disease has 3R tau containing Pick bodies, while several of the other frontotemporal lobar degeneration related tauopathies (FTLD-T), like corticobasal degeneration (CBD), progressive supranuclear palsy (PSP), argyrophilic grain disease (AGD), and globular glial tauopathy (GGT) contain 4R. Additionally Multiple system tauopathy with Dementia (MSTD), caused by several pathogenic variants of the *Tau* gene, result in both 3R and 4R tau tauopathy. Diagnosis is by clinical features, radiological findings, and biomarker studies. Understanding the neuropathology, the pathogenesis, the selective cellular vulnerability, and the stereotypical spread of tau pathology in a prion-like manner, provides a scope for developing more accurate biomarkers for correlation with neuropathology, early detection, diagnosis, monitoring and assessing therapy outcomes in clinical trials and developing newer molecules for therapeutic targeting.

S19.3. Fyn kinase-Tau protein interaction and its implication on Alzheimer's disease pathology and N-methyl daspartate receptor function

Sivaraman Padavattan, Sneha Jos, Roshni Poulose, Archanalakshmi Kambaru, Hemanga Gogoi, Bhupesh Mehta
Department of Biophysics, National Institute of Mental Health and Neurosciences, Bangalore-560029, India

Fyn kinase SH3 domain interaction with PXXP motif in the Tau protein is implicated in Alzheimer's disease (AD) pathology and is central to N-methyl D-aspartate receptor **(**NMDAR) function. Nevertheless, a structural understanding of how the Fyn-SH3 domain interacts with the Tau PXXP motifs at a molecular level is not available. Likewise, hyperphosphorylation of Tau is considered a key pathological feature and a primary driver behind fibrillar deposits in several tauopathies, including AD. So far studies have shown how hyperphosphorylation at the Tau microtubule-binding domain reduces binding affinity for its primary ligand tubulin. However, the consequence of AD-specific phosphorylation encompassing PXXP motifs' interaction with the SH3 domain needs to be studied. Here we combined structural and biophysical approaches to determine Fyn-SH3 domain -Tau (207-221) peptide consisting of 5^{th} and 6^{th} tandem PXXP motifs and studied the effect of AD-specific phosphorylation in the above interaction. Subsequently, we investigated whether the above Tau peptide has any role in remodeling NMDAR current using whole-cell patch clamp electrophysiology.
Funding: Non-funded project

S19.4. TNT-Mediated protein transmission: Implications for neurodegenerative disease spread in the brain

Srinivasa Subramaniam
Department of Neuroscience, The Wertheim UF Scripps Biomedical Research and Innovation, The Scripps Research Institute Member, Norman Fixel Institute for Neurological Diseases 130 Scripps Way, C323, Florida, Jupiter, 33458

The CAG/CAA expansion encoding polyQ huntingtin (mutant huntingtin [mHTT]) causes Huntington disease (HD), which is characterized by atrophy and loss of striatal medium spiny neurons (MSNs), which are preceded by neuropathological alterations in the cortex. Previous studies have shown that mHTT can spread in the brain, but the mechanisms involved in the stereotyped degeneration and dysfunction of the neurons from the striatum to the cortex remain unclear. In this study, we found that the mHTT expression initially restricted in the striatum later spread to the cortical regions in mouse brains. Such transmission was diminished in mice that lacked the striatal-enriched protein Ras-homolog enriched in the striatum (Rhes). Rhes restricted to MSNs was also found in the cortical layers of the brain, indicating a new transmission route for the Rhes protein to the brain. Mechanistically, Rhes promotes such transmission via a direct cell-to-cell contact mediated by tunneling nanotubes (TNTs), the membranous protrusions that enable the transfer of mHTT, Rhes, and other vesicular cargoes. These transmission patterns suggest that Rhes and mHTT are likely co-transported in the brain using TNT-like cell-to-cell contacts. On the basis of these new results, a perspective is presented in this seminar: Rhes may ignite the mHTT transmission from the striatum that may coincide with HD onset and disease progression through an anatomically connected striato-cortical retrograde route.

S19.5. Astroglia proliferate upon clearance of α-synuclein-induced toxicities through tunneling- nanotubes

Abinaya Raghavan[1], Rachana Kashayap[1+], Sreedevi P[2+], Sneha Jos[3] , Suchana Chatterjee[1], Ann Alex[1], Michelle Ninochka D'Souza[4], Mridhula Giridharan[2], Ravi Muddashetty[4], Ravi Manjithaya[2], Sivaraman Padavattan[3], **Sangeeta Nath[1]**
[1]Manipal Institute of Regenerative Medicine, Bengaluru, Manipal Academy of Higher Education, Manipal, India, [2]Autophagy Laboratory, Molecular Biology and Genetics Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Bengaluru, India, [3]Department of Biophysics, National Institute of Mental Health and

Neurosciences, Bengaluru, India; [4]Centre for Brain Research, Indian Institute of Science, CV Raman Avenue, Bengaluru, India.

Astrocytic cells are a subtype of glial cells that engulf pathogenic aggregates derived from degenerative neurons to facilitate its degradation. Here, we show that exposure to α-SYN protofibrils caused a transient increase in biogenesis of tunneling nanotubes (TNTs) in primary astrocytes and astrocyte-origin cancer cell-lines (U-87 MG and U251). Biogenesis of these nascent TNTs corresponds to α-SYN protofibril-induced organelle toxicities, increased reactive oxygen species (ROS), and oxidative stress-induced premature cellular senescence. These TNTs-mediated cell-to-cell transfer not only accelerated degradation of α-SYN protofibrils, but helped cells to eliminate toxic dysfunctional mitochondria and curb ROS levels, that aid in reversal of cellular senescence, cell survival and increased proliferation. We observe internalization of α-SYN results in transient localization of focal adhesion kinase (FAK) to nucleus, resulting in biogenesis of TNTs probably *via* modulation of FAK mediated ROCK (Rho-associated kinases) signalling pathway. Eventually, the TNT-mediated rescued cells proliferate through ROCK regulated upregulation of ERK1/2, NF-κB. Our study emphasizes that TNT- mediated cell-to-cell transfer rescues α-SYN protofibrils-induced toxicities and stress-induced senescence, which leads to enhanced proliferation in the post-recovered astroglia cells.

S19.6. Mechanistic insights and therapeutic implication of astrocyte secreted cytokines in Alzheimer's disease

Subhas Chandra Biswas
Neurodegenerative Disease Research Laboratory, Cell Biology & Physiology Division, CSIR-Indian Institute of Chemical Biology, Kolkatta

The multi-factorial aetiology of Alzheimer's disease (AD) strongly suggests an integrated role of neurons and glia in pathobiology of the disease. Astrocytes, the most abundant of the glial cells, undergo morphological, biochemical, molecular, and functional changes during the pathogenesis of neurodegenerative diseases including AD termed as reactive astrogliosis. Reactive astrocytes are rich reservoirs of cytokines which may exert both beneficial and detrimental impacts on neuronal health. Our studies identified intercellular adhesion molecule-1 (ICAM-1) and tissue inhibitor of matrix metalloproteinase-1 (TIMP-1) as major neuroprotective candidates of glia origin that protect neurons and ameliorate cognitive deficits in AD models. Interestingly, we found strikingly diminished levels of TIMP-1 in the brain of six-month-old 5xFAD mice (a transgenic model of AD) concomitant with high levels of Amyloid-β (Aβ), versus wild-type mice. Intracerebroventricular injection of TIMP-1 in 5xFAD mice ameliorated their cognitive functions. TIMP-1 not only ensured neuronal viability against apoptosis and aberrant autophagy in the AD model, but also conferred synapse–specific effects. Synaptosomal analysis revealed that TIMP-1 elevates dendritic spine size and protein levels. Electrophysiology study revealed that it promotes post-synaptic long-term potentiation in hippocampus, independent of pre-synaptic activity. ICAM-1 protected neurons and improved cognitive behaviours in 5xFAD mice by NF-kB signaling. Therefore, we identify TIMP-1 and ICAM-1 as multifunctional cytokines with strong protective mechanisms-of-action on neurons with long-term benefits and propose them as promising therapeutic candidates in AD.

Symposium- 20: Parkinson's Disease-Perspectives from cells to clinic

S20.1. Epigenetics: A game changer in understanding the disease biology of neuropsychiatric disorders

Arvind Kumar
[1]CSIR-Centre for Cellular and Molecular Biology (CCMB), Hyderabad, India; [2]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, U.P., India

Background: The molecular etiopathology most neuropsychiatric disorders including Major Depressive Disorder (MDD) is still elusive, and so is efficacious therapeutics. Epigenetic dysregulation of transcription appears to be involved in etiology. Most of the epigenetic studies involve histone lysine methylation, in mediating chronic stress induced perturbations on the reward circuitry. Here, we report the role of histone arginine (R) methylation, another abundant epigenetic modification that is least studied.
Materials And Methods: Chronic Social Defeat Stress (CSDS) model was used to induce depression-like phenotype in C57bl/6 Ncrl mice, as assessed by a battery of behavioural assays. RT-qPCR was used to map changes in transcription of Protein Arginine Methyltransferase (PRMT) family members in hippocampus & its neurogenic region DG. This was followed by uncovering the genomic targets of PRMT5 involved in altered DG neurogenesis and remodelled hippocampal circuitry using ChIP-Seq and ChIP-qPCR.
Results & Discussion: We uncovered dysregulation of some PRMTs including PRMT5 in hippocampus and DG in etiology of MDD-like phenotype following CSDS, and also in Alcohol Use Disorder (AUD) phenotype using mouse models. ChIP-Seq on the proliferating and differentiated DG neural progenitor cells (NPCs) obtained from post-natal day 2 (PND2) mouse pups using antibody against PRMT5, led us to identify genomic targets of PRMT5 involved in hippocampal neurogenesis. The overlap in ChIP-Seq data on PRMT5 enrichment, its epigenetic target histone H4 arginine dimethylation (H4R3me2) enrichment on target promoters and transcriptomics (RNA-Seq) data on the same pups' DG samples, revealed hundreds of target genes through which PRMT5 might mediate its effects on neurogenesis and remodelled hippocampal circuitry.
Acknowledgements: We wish to thank DBT Glia projects in health and disease Phase I & II, for the support to conduct this study.

S20.2. Pax6 regulated putative biomarkers in brain of MPTP-treated mouse model of Parkinson's disease

Nidhi Ghosh and **Rajnikant Mishra**
Biochemistry and Molecular Biology Lab, Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi- 221005, India,

Introduction: Identification and evaluation of the transcription factors to serve as diagnostic markers and therapeutic targets are of current scientific concern. This report describes evaluation of Pax6 regulated putative biomarkers because patients having mutation of PAX6 show microcephaly, autism, mental retardation, aniridia, glucose intolerance and aging associated disorders.
Methods: Brain of mouse model of Parkinson's disease, developed by injecting MPTP (1mg/kg) intraperitoneal for 21 days in adult mice of AKR strain and equal volume of saline in vehicle control group, was used. Integrated-omics study was performed using whole brain transcriptomes, proteomes, ChIP and ChIP-sequencing. Anti-Pax6 was used for immunoprecipitation.
Results: Whole brain transcriptomics and proteomics reveal significant alterations of Cytokines, growth factors and neurotrophic factors. Pax6 binds to promoter sequences, UTR, distal Intergenic and Introns regions of several genes associated with synaptic functions, cell junction assembly and inflammatory processes.
Conclusion: Pax6 may serve as a transcription factor-based biomarker for differential diagnosis and better management of Parkinson's disease because Integrated-omics evaluation provide insights on Pax6 dependent regulation of cytokines, growth factors, neurotrophic factors involved in motor and non-motor functions of Parkinson's disease.
Acknowledgements: Financial support from the DBT, BT/PR28908/MED/122/174/2018 Dt 10/02/2020, India is gratefully acknowledged.

S20.3. Neuronal determinants of autophagy flux

Ravi Manjithaya
Molecular Biology and Genetics Unit; Neuroscience Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore 560 064 India

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. Genetic manipulation of the autophagy pathway in motor neurons by blocking the initiation complex also revealed behavioural and synaptic defects, revealing the tight coupling of synaptic function with presynaptic autophagy. Our work aims to understand how modulation of the autophagy pathway can rescue defects associated with synaptopathies *in vivo*.

S20.4. Parkinson's Disease in India: Unanswered puzzle

Prashanth LK
Consultant Neurologist and Movement Disorders Specialist, Parkinson's Disease and Movement Disorders Clinic, Bangalore, India. Manipal Hospital Miller's Road, Bangalore, India.
www.movementdisordersclinic.com

Parkinson's Disease is a chronic neurodegenerative disorder that affects a significant number of individuals in India. The exact prevalence of Parkinson's Disease in India varies across different regions, but it is estimated to affect approximately 1% of the population over the age of 60. As India's population is aging, the number of individuals living with Parkinson's Disease is expected to increase dramatically over the next decades. Diagnosis and awareness of Parkinson's Disease have improved in India over the years, but there is still a lack of awareness, especially in rural areas. Many cases go undiagnosed or are misdiagnosed as other conditions due to the lack of specialized healthcare facilities and neurologists in some regions. Access to quality healthcare and specialized treatment for Parkinson's Disease can be challenging, especially for individuals in rural and underserved areas. In urban centers, there are specialized clinics and neurologists who can provide better care, including medications and therapies to manage the disease's symptoms. However, the cost of some of these treatments can be a barrier for many patients. India has made progress in Parkinson's Disease research, with several institutions and hospitals conducting studies to better understand the condition with collaborative efforts. The current works of Parkinson Research Alliance of India (PRAI) working on the Young Onset Parkinson's Disease cohort genetics (GOPI-YOPD) and the Michael J Fox Foundation funding through the global Parkinson Genetic program (GP2) has made significant strides in collaborative Indian works to answer the missing puzzle pieces of Parkinson's from India. The Indian government has taken steps to address neurological disorders like Parkinson's Disease. Public health initiatives have been launched to create awareness about neurological disorders, including Parkinson's. However, more efforts are needed to improve access to care and support for patients. Several challenges persist in the management of Parkinson's Disease in India, including: Limited Access to Specialized Care: Many patients do not have access to neurologists and movement disorder specialists, resulting in delayed diagnosis and suboptimal treatment. Stigma and Awareness: There is a stigma associated with neurological disorders in some parts of India, which can lead to social isolation for patients and their families.
Cost of Medications: The cost of Parkinson's medications can be high, and insurance coverage may not always be adequate.
Future Prospects: To improve the status of Parkinson's Disease in India, efforts should focus on increasing awareness, improving access to specialized care, and reducing the cost of medications. Collaborative research initiatives and public-private partnerships can also contribute to better understanding and management of the disease.

S20.5. Organellar hierarchy in Parkinson's disease: Investigations using experimental models

Bidisha Bhaduri[1], Rashmi Santhosh Kumar[2], Dwarakanath Srinivas[3], Pramod Kumar[4] Pal, Ravi Yadav[4], **Phalguni Anand Alladi[1]**
[1]Department of Clinical Psychopharmacology and Neurotoxicology, National Institute of Mental Health and Neurosciences; [2]Department of Neuropathology, National Institute of Mental Health and Neurosciences; [3]Department of Neurosurgery, National Institute of Mental Health and Neurosciences; [4]Department of Neurology, National Institute of Mental Health and Neurosciences MH Marigowda Road, Bangalore 560029

Background: Higher prevalence of PD in Caucasians compared to Asian-Indians and 5-times lower prevalence in Anglo-Indians; the admixed F1-generation of these two ethnicities, is well demonstrated. Very similar to this; C57BL/6J, CD-1, and their F1X2 crossbred mice exhibit variable response to the neurotoxin MPTP; where C57BL/6J mice with fewer nigral DA neurons are more vulnerable. Although sub-cellular organellar dysfunction is commonplace during neurodegeneration, rare reports describe the chronology of degeneration of major organelles in response to PD mimetics.
Materials And Methods: Here, we aimed to evaluate the possible temporal hierarchy of sub-cellular organellar degeneration in experimental models of Parkinson's disease (PD), using MPTP/MPP^+. Our study traced organellar degeneration in the striatal and nigral areas of control and MPTP-injected C57BL/6J, CD-1 and F1X2 mice, subjected to semi-quantitative analysis of organelle associated proteins and electron microscopy (EM). Separately, SH-SY5Y cells were exposed to MPP^+ and mitochondria-ER tracker dyes followed by live imaging, mitochondrial respiration analysis and EM in a temporal pattern. Human skin biopsies were evaluated by EM.
Results & Discussion: Altered expression of calnexin, TGN-38 as well as ultrastructure hinted that most organelles were severely impaired in the nigro-striatum of C57BL/6J. Live cell imaging revealed a gradual loss of ER and mitochondria tags, though initial loss was prominent in ER. In patient skin biopsies, decompacted myelin and an increase in intermediate filaments were noted. Mild induction of autophagy and mitochondrial biogenesis may be the coping strategies of neurons. Similarities in C57BL/6J and patient skin suggest parallels in pathogenesis and a reliable replication in the model. The chronology of degeneration seen in SHSY5Y cells may be critical determinants of PD and useful in designing therapeutics.
Acknowledgements: NIMHANS Intramural funds to PAA and Fellowship to BB.

Symposium- 21: Pathology of brain disorders

S21.1. Novel insights into molecular events following virus induced neurodegeneration

Guneet Kaur, Himali Arora, Bindu, and **Pankaj Seth**
National Brain Research Centre, NH-8, Nainwal Road, Manesar (Gurgaon)-122052, India

Background: Neurotropic viruses adopt various strategies to circumvent the innate and adaptive immunity and to breach blood brain barrier (BBB) for infecting brain cells. Zika virus (ZIKV) infects human neural stem cells (hNSCs) in developing fetal brain tissue by breaching the blood placental barrier via infection of trophoblast cells. ZIKV and its proteins affect the pool of hNSCs by altering their proliferation and stemness, however the details of mechanisms are not well understood.
Material and Methods: We studied effect of structural and non-structural proteins of ZIKV on blood brain barrier cells as well as hNSCs to gain novel insights into molecular mechanisms of ZIKV neuropathogenesis in infants and adults. For this study, we used a two cell model of BBB comprising primary cultures of human brain microvasculature endothelial cells (hBMECs) and human astrocytes.
Results: We observed that ZIKV envelope (ZIKV-E) protein altered BBB integrity by altering trans endothelial electrical resistance, affected properties of both hBMECs and astrocytes and tight junctional proteins. Furthermore, ZIKV E protein also altered hNSCs proliferation (as seen with alterations in SOX-2, brdU, Ki67 levels) and resulted in immature differentiation (alterations in DCX levels) as indicated by mRNA and protein expression studies. We also identified role of some long non coding RNAs in ZIKV-E protein induced neuropathogenesis.
Discussion and Conclusions: Our study has helped to gain insights into the underlying molecular mechanisms by which ZIKV-E protein alters hNSCs proliferation. The findings have significant clinical implications in understanding the ZIKV induced microcephaly. **Acknowledgements:** Authors acknowledge the financial support from NBRC Core funds.

S21.2. Curcumin protects age induced neurodegeneration: Desynchronisation of interplay between clock, immune and microglia resting genes

Anita Jagota
Neurobiology and Molecular Chronobiology Laboratory, Department of Animal Biology, School of Life Sciences, University of Hyderabad, 500046, India

Background: Aging is associated with changes in several basic parameters of circadian timing system (CTS) in mammals leading to circadian dysfunction. Circadian clock in Microglia have been known to regulate the several age-associated pathologies like PD, AD etc. In young brain microglia has several beneficial roles, however, with aging the primed microglia are hypothesized to be detrimental in their functions. As curcumin is a pleiotropic molecule which has various properties such as anti-oxidant, anti-inflammatory, anti-carcinogenic, anti-microbial, anti-aging etc. was investigated for its therapeutic influences on microglia.
Material and Methods: Male Wistar rats of three age groups: 3,12 and 24 months were used. They were maintained individually in standard polypropylene cages with temperature at 23 ± 1 °C, relative humidity 55 ± 6 %; under light-dark cycle (LD) 12:12 for 2 weeks prior to experiments. Microglia were isolated at various time points Zeitgeber time (ZT) 0/24, 6,12 and 18 using density gradient method. Curcumin was administered orally 100 mg/ml in 0.5 % carboxy methyl cellulose. Various clock and immune genes were studied using qRT-PCR. Data was analysed using R-program Pearson correlation and one way ANOVA.
Results: Our studies demonstrated that clock and immune genes show temporal expression pattern in microglia in young age. With aging, *rPer2* and *rCd172* in microglia showed differential alterations in expression pattern. Interestingly, curcumin showed restoration of daily rhythms of *rNf-κb1*, *rTnfα* and *rIl6* in microglia. Curcumin also restored the altered mean levels of *rCry2*, *rCx3cr1* and *rCd45* in microglia. Correlations between the clock and immune genes were altered with aging.
Discussion and Conclusions: Overall, this study helps in paving a new path for the development of new therapeutic strategies using the pleiotropic molecule curcumin to address several age related chrono-immune attritions. In addition, our study gave an insight into the cross-talk between clock and immune systems to underpin the molecular mechanisms involved in chrono-immunological pathologies
Acknowledgements: The financial support from ICMR is acknowledged

S21.3. Temporal lobe Epilepsy – from biochemistry to biology

Anita Mahadevan, Shwetha SD, Srinivas Bharat MM[1], Arivazhagan A[2], Sanjib Sinha[3]
Departments of Neuropathology, Clinical Pharmacology & Neurotoxicology[1], Neurosurgery[2] and Neurology[3], National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru

Background and objective: Studies in animal models of temporal lobe epilepsy suggest a pathogenetic role for mitochondrial dysfunction, although validation studies in humans are scarce. We chose to evaluate the mitochondrial status in the hippocampus resected from patients with mesial temporal lobe epilepsy (MTLE) through proteomic approaches.
Materials and Method: Crude mitochondrial preparations from human hippocampus samples, resected from patients with MTLE, who underwent amygdalohippocampectomy (Early-onset <10years of age, n=9 and late-onset ≥11years of age, n=9), compared with age matched normal controls (n = 9) were subjected to quantitative proteomics using high-resolution mass spectrometry (MS). MS data was validated by mitochondrial respiratory chain complex assays (CI- CIV).
Results: The MS identified 7,961 proteins among which, 183 proteins and 61 mitochondrial proteins differentially expressed in early and late onset respectively ($p \leq 0.05$). Proteins associated with biological processes such as mitochondrial electron transport chain, mitochondrial translation and branched-chain amino acid catabolic process were differentially overexpressed in cases with early onset MTLE, suggesting a pathogenetic role. Mitochondrial respiratory complex I activity was higher in early onset compared to late onset MTLE and controls, validating the proteomics data. The activities of mitochondrial complexes II-IV remained unaltered. Proteomics of astrocyte enriched fraction showed only few mitochondrial proteins, with down regulation of Complexes I, IV, V, and VDAC2 in both early-onset and late-onset HS, differing from total proteomics data suggesting that astrocytes do not contribute to the mitochondrial dysfunction in HS
Conclusions and clinical relevance: Mitochondrial dysfunction in hippocampus appears to have a role in the pathogenesis of early onset MTLE, in particular, mitochondrial complex I subunits. Evidence for role of mitochondrial dysfunction may aid in development of novel therapeutic strategies for treatment of MTLE.

S21.4. Exploring brain energy metabolism in Amyotrophic Lateral Sclerosis

Anant Bahadur Patel
CSIR-Centre for Cellular and Molecular Biology, Uppal Road, Hyderabad-500007, India; Academy of Scientific & Innovative Research, Ghaziabad-201002, India

Amyotrophic Lateral Sclerosis (ALS) is the most common adult-onset progressive motor neurodegenerative disease that causes skeletal muscle atrophy. Only 5-10% of ALS cases are inherited, out of which 20% of patients have a mutation in the Cu/Zn superoxide dismutase (*SOD1*) gene. Moreover, ~0.4-4% of ALS cases involve mutations in Optineurin (*Optn*), a multifunctional adaptor protein that regulates autophagy, chronic inflammation, and necroptosis. We are using $SOD1^{G37R}$ and $Optn^{-/-}$ mice to understand the pathophysiology of ALS. The objective of the current study was to evaluate the impact of stress on ALS phenotype and energy metabolism in *Optn* KO mice. An approach of ^{1}H-[^{13}C]-NMR spectroscopy together with an intravenous administration of [1,6-$^{13}C_2$] glucose or [2-^{13}C] acetate was to evaluate the neuronal and astroglial metabolic activity. Our analysis in $SOD1^{G37R}$ mice indicated a reduction in NAAG level while an elevation in myo-inositol in the spinal cord of female and male mice. The male ALS mice exhibited increased acetate oxidation in the spinal cord and cerebral cortex suggesting astrocytic involvement in the pathogenesis of ALS. The rates of glucose oxidation were increased in the cerebral cortex of male and female ALS mice. $Optn^{-/-}$ mice did not exhibit motor impairment, but progressive impairment in neuromuscular strength and motor coordination was observed in $Optn^{-/-}$ stressed mice after 30 days of chronic stress. Moreover, there was a significant reduction in the rate of neuronal glucose oxidation in the cerebral cortex and spinal cord $Optn^{-/-}$ stressed mice. In contrast, astroglial metabolic activity was increased in the cerebral cortex. Molecular studies using quantitative polymerase chain reaction have revealed a decrease in expression of CTIP2 and OLIG2 with a concomitant increase in S100β and TMEM119 in the motor cortex of $Optn^{-/-}$ stressed. In this presentation, I will be discussing these findings in detail

Acknowledgments: The study was supported by funding from the Department of Science and Technology (DST/CSRI/2017/258) and CSIR-CCMB.

S21.5. Can cell therapy bring mitochondrial resilience following ischemic stroke?

Deepaneeta Sarmah, Aishika Datta, Nikita Rana, Bijoyani Ghosh, **Pallab Bhattacharya**
Department of Pharmacology and Toxicology NIPER-Ahmedabad, Gandhinagar, Gujarat

Background: Stroke is a medical condition that has a profound impact on patient's quality of life. Mitochondria are highly vulnerable to damage following stroke,hence, the need of the hour is to search for agents that can limit the stroke outcomes. Stem cell therapy for stroke is promising as both preclinical and clinical studies have shown beneficial outcomes.

Materials and methods: We aim to investigate the involvement of sirtuin 1 (SIRT1) in modulating the mitochondrial functions and bringing resilience following endovascular delivery of stem cells in animal model. Ovariectomized Sprague Dawley rats were intraarterially (IA) infused with $1*10^5$ Mesenchymal stem cells (MSCs) at 6 h post-MCAo. Following 24 h of MCAo, animals were evaluated for functional and behavioral outcomes. Brains were harvested for molecular studies and mitochondrial studies.

Results: Significant improvement in functional and behavioral outcomes and a decrease in infarct size were observed following infusion of stem cells post-stroke. An increase in average neuronal length and viability were also observed. Increase in SIRT1, mitochondrial fusion, biogenesis, and tunneling nanotube protein markers were observed while reduction in mitochondrial fission protein markers were seen in the brain regions following IA MSCs treatment. Improvement in mitochondrial bioenergetics was also observed post-MSCs infusion.

Discussion and conclusions: Results from the study demonstrate the role of SIRT1 in modulating mitochondrial functionality post-IA MSCs therapy in a rodent model of ischemic stroke. The IA approach for administering MSCs is highly relevant in the present clinical scenario.

Acknowledgements: Department of Pharmaceuticals, GoI. Indian Council of Medical Research (ICMR)

S21.6. Somatostatin-releasing inhibitory interneurons of the olfactory bulb mediate perceptual learning deficits in an early life stress mouse model

Nixon M. Abraham
Laboratory of Neural Circuits and Behaviour (LNCB), Department of Biology, Indian Institute of Science Education and Research (IISER), Pune, Maharashtra, 411008, India

Unraveling neural circuits responsible for sensory and cognitive dysfunctions is one of the major challenges in Clinical Neuroscience. The critical step towards this is undertaking a multi-pronged experimental approach in order to confirm the causality between circuits and behavior. Despite many reports on somatostatin-releasing GABAergic interneurons (SOM-INs) in the olfactory bulb (OB), their involvement in mediating perceptual learning deficits under early life stressed (ELS) conditions, and their contribution to inhibitory interactions and neuronal computations in the OB remain elusive. To address these questions, it is essential to untangle the intricate interplay of molecules, synaptic circuits, and behavioral actions. Our results demonstrate olfactory perceptual learning and memory deficits in ELS mice using a well-established go/no-go odor discrimination paradigm. Lowered c-Fos activity in the external plexiform layer and a reduction in the number of dendritic processes of SOM-INs in the ELS mice led us to hypothesize the underlying neuronal circuit. We recorded reduced synaptic inhibitory feedback on mitral/tufted (M/T) cells, in the OB slices from ELS mice, explaining the learning deficiency caused by compromised refinement of OB output. To study the role of SOM-INs in modulating olfactory perception, we performed in vivo opto-physiological recordings using GCaMP6f expression in these neurons. Our results proved learning-dependent refinement of Ca2+ dynamics in SOM-INs during odor discrimination. To investigate the causal role of SOM-INs involving circuitry, we carried out optogenetic bi-directional modulation of SOM-INs while animals were learning to discriminate different odor pairs. Photo-activation of these neurons rescued the learning deficits in ELS mice. Conversely, optical inhibition of SOM-INs in control animals mimicked the ELS- induced learning deficiency, while it completely abolished the learning in ELS mice. These results confirm the role of inhibitory circuits formed by SOM-INs in mediating learning deficits we observed in ELS mice.

Invited Lectures

IL1.1. Role of dopamine on iron homeostasis in astroglial cells

Chinmay K. Mukhopadhyay, Som Dev, Reshmi Mukherjee, Pratibha Singh, Somya Asthana
Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi-110067

Background: Astroglia plays crucial role in maintaining neuronal iron homeostasis. Iron is an essential component for biosynthesis of catecholamine neurotransmitters including dopamine (DA). Iron deposition in substantia nigra and affected DA synthesis are commonly reported in Parkinson's disease (PD). However, role of DA on astroglial iron homeostasis is little understood so far.
Materials and Methods: C6, U87MG and primary astrocytes were used. Expressions of iron homeostasis components were detected by Western blot and RT-qPCR analysis. Protein degradation was determined by chase assay and methods involving autophagy. siRNAs were used for gene silencing. Protein-protein interaction was determined by Co-IP and immunoblots.
Results: Here we report that DA promotes astroglilal ferritin degradation by a lysosomal mechanism. NCOA4 acts as a specific cytosolic cargo to carry ferritin to lysosome. DA promotes ferritin degradation by chaperon mediated autophagy. We further reveal that DA induces cathepsin B expression to degrade ferritin and suppress iron release components to elevate iron content in mitochondria.
Discussion and conclusions: Our results established a direct role of DA on astroglial iron metabolism. DA could induce ferritin degradation and affect iron release components resulting elevation of iron in mitochondria. These results implicate a role of DA in astroglial mitochondrial iron homeostasis that may be relevant in understanding mitochondrial dysfunction reported in PD.
Acknowledgement: CKM acknowledges financial support received from SERB. SD and PS were supported by fellowships from CSIR and ICMR respectively.

IL1.2. Sedation with Midazolam in the NICU: A Double-Edged Sword

Nghi M. Nguyen[1,2], Adrian Flores[1,3], Jina Yi[1,2], Pranavi Athota[1], Daniel Meyer[1], Sowmya Yelamanchili[1,2,5], and **Gurudutt Pendyala[1,2,4,5]**
[1]Department of Anesthesiology, University of Nebraska Medical Center (UNMC), Omaha, NE;
[2]Department of Genetics, Cellular Biology, and Anatomy, UNMC, Omaha, NE, [3]Department of Cellular and Integrative Physiology, UNMC, Omaha, NE; [4]Child Health Research Institute, Omaha, NE; [5]National Strategic Research Institute, Omaha, NE

Background: Premature neonates frequently receive sedatives and anesthesia due to surgeries and ventilation. While these agents help manage agitation, their repeated use early in life might cause cognitive issues. Our research examines how the common neonatal sedative, **midazolam** (MDZ), affects neurodevelopment from infancy to adulthood using a rodent model.
Methods: We established a dose-escalation regimen from postnatal day (P) 3 pups until P21 to mimic long-term MDZ exposure at a very early age to meticulously analyze how prolonged MDZ exposure during early development influences neurodevelopment across phenotypic, molecular, and behavioral dimensions.
Results: Our findings demonstrated that long-term MDZ exposure during the neonatal period negatively affects physical attributes in early childhood. Surprisingly, while adult bodyweights between control and MDZ-exposed rats remain comparable, the MDZ rats exhibited accelerated and robust weight gain. Notably, during adulthood, the dopamine release in MDZ-exposed rats was markedly reduced, suggesting a potential for developing binge eating behavior. We also observed elevated levels of pro-inflammatory cytokines and growth factors during adulthood, hinting at a shift in development due to early MDZ exposure. Furthermore, we observed trends of heightened anxiety-like behavior, nociception, and reduced social interaction during early adolescence compared to other stages.
Discussion: Our study presents for the first time a comprehensive assessment of how long-term MDZ exposure during neonatal stages impacts outcomes throughout life. These insights serve as a foundation for unravelling mechanisms that could contribute to overcoming neurodevelopmental complications associated with long-term MDZ use in neonates.

Acknowledgements: This work is supported by the National Institutes of Health R01DA042379, (SVY), DA049577 (G.P.), Lieberman Endowment (G.P), Nebraska Collaborative Research Initiative (S.V.Y & G.P.) and Startup funds from the Department of Anesthesiology, UNMC (G.P. and S.V.Y).

IL1.3. Tale of a Tailed Neuron: Insights from the TRPV1 Channel

Luna Samanta
Redox Biology and Proteomics Laboratory, Department of Zoology, Ravenshaw University, Cuttack – 753003, India

Multiple lines of evidence suggest significant similarities between the human brain and testis, sparking interest within the scientific community. This connection is underscored by observed associations between intelligence and certain semen quality parameters, as well as apparent links between brain dysfunctions and testicular issues. When examining these tissues, numerous shared molecular features and a substantial number of common proteins become evident. Functionally, human neurons and sperm exhibit similarities, such as reliance on the exocytotic process and the presence of comparable receptors and signaling pathways. The common proteins primarily participate in exocytosis, tissue development, and processes associated with neurons/ brain-associated biological processes. Neurons are excitable cells known for their diverse ion channels, such as voltage-gated Ca^{2+} and Na^{+} channels, and ligand-gated receptor channels. These channels play a role in rapid membrane potential changes and electrical signaling. Surprisingly, sperm cells also possess many of these channels. This similarity has led to the idea that any cell with a combination of such channels can be considered excitable. Thus, spermatozoa can be viewed as excitable cells. Albeit, this area remains relatively unexplored, and warrants further investigation to establish a clearer connection between these cells, few recent studies have ventured into establishing the association of these receptors with sperm function. The role of transient receptor potential vanilloid 1 (TRPV1) in this regard cannot be undermined, particularly for sperms produced in testis with 2^0C lower scrotal temperature to their maturation and field of action at normal body temperature. Our laboratory the first time demonstrated the Ca^{2+}-sensitive TRPV1 channel to be under-expressed in spermatozoa of subfertile men, idiopathic infertile men, and normozoospermic infertile males with high ROS (idiopathic infertility and unilateral varicocele). To investigate the role of TRPV1 in fertility, its expression in spermatozoa from men achieving pregnancy through natural conception (NC+, n = 10), IVF (IVF+, n = 23), or ICSI (ICSI +, n = 9), and those with failed pregnancies NC- (n = 7), IVF- (n = 23), or ICSI- (n = 10), were compared by both immunocytochemistry and flow cytometry. Reduced TRPV1 expression in IVF+/- and ICSI+/- groups in comparison to NC+ suggests its role in successful fertilization. Conversely, underexpression in NC-/IVF-/ICSI- sperm implies its importance in conception and pregnancy maintenance. Since reactive oxygen species (ROS) is regarded as one of the major contributors to both neurological disorders and sperm dysfunction, we also explored TRPV1 as a redox sensor due to its link with sperm dysfunction and ROS generation in neurons. H_2O_2 treatment increased acrosomal reaction and calcium influx, which were modulated by TRPV1 agonists resiniferatoxin (RTX) and antagonists iodoresiniferatoxin (iRTX), indicating TRPV1's role in H_2O_2 response. *In silico* analysis of the crosstalk between TRPV1 with fertility candidate proteins (reported to influence IVF outcome) revealed cell death and survival, cellular compromise, and embryonic development to be the primary networks affected by anomalous TRPV1 expression. Therefore, it is postulated that TRPV1 can act as a redox sensor, and its expression in spermatozoa may serve as a fertility marker. Such research could enhance our understanding of the dysfunctions affecting both the brain and testis, ultimately leading to the development of more effective therapeutic strategies.

Acknowledgements: Financial support from Centre of Excellence in Environment and Public Health by Higher Education Department, Government of Odisha (Grant No.: 26913/HED/HE-PTC-WB-02-17) is duly acknowledged.

IL1.4. Altered Subcortical-Cortical Dynamic Network Reconfigurations in Focal-to-Bilateral Tonic-Clonic Seizures

Shilpi Modi[1,2], A. Ankeeta[1], Walter Hinds[1], Michael Sperling[1], Joseph Tracy[1]; [1]Department of Neurology, Thomas Jefferson University, Philadelphia, Pennsylvania; [2]Institute of Nuclear Medicine and Allied Sciences (INMAS), Delhi

Background: Temporal lobe epilepsy (TLE) is the most common focal epilepsy syndrome in adults, with focal to bilateral tonic-clonic seizures (FBTCS+) its most severe form. In this project, we pursued a comprehensive characterization of resting state (RS) dynamic functional connectivity (dFC) in FBTCS+, examining four distinct set of subcortico-cortico communication/propagation pathways.
Materials and Methods: Left TLE (n=55) patients (FBTCS-; FBTCS+current; FBTCS+remote) and age-matched controls (n=56) underwent an 8 min RS-fMRI scan. After pre-processing (fMRIPrep), dFC measures- *recruitment*, *integration* and *flexibility* were computed (sliding-window approach) for Schaefer 7-cortical and 4 subcortical (mesial-temporal/striatum/thalamus/cerebellum) network combinations. MANOVAs on the deviation scores of the *dFC* measures were run.
Results: An increased recruitment was obtained in anterior thalamus, DAN and limbic system in FBTCS+current group. Left-right VAN showed an increased integration with both caudate and cereb-5 in FBTCS+current (versus FBTCS-) group. As compared to FBTCS+remote, FBTCS+current showed greater integration between caudate/ left control and cereb-5/left DMN systems. Random Forest classification models with MANOVA findings as predictor variables further suggest that the functional connectivity within and between certain networks cohere differently based on the FBTCS status.
Discussion and Conclusions: Anterior thalamus has been shown to be recruited early before the clinical manifestation of seizures in TLE. The heightened recruitment of the DAN and limbic systems appears to be an adaptive feature of network dynamics in FBTCS. A complex set of increased subcortio-cortico integration/synchronization might serve as seizure propagation pathways in FBTCS. Our analyses are the first to capture altered RS dynamic network reconfigurations in subcortico-cortico intrinsic systems in the setting of FBTCS.

IL1.5. Morphological changes in the mice central nervous system in a L-arginine induced model of chronic pancreatitis

Punit Kumar[a], Manish Kumar Sharma[b], Intizaar Mehdi[c], Kumari Priyam[a], Tara Sankar Roy[d], **Tony George Jacob[a]**
[a] Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India; [b] Department of Anatomy, Maulana Azad Medical College, New Delhi, India; [c] SOS in Neuroscience, Jiwaji University, Gwalior, Madhya Pradesh, India; [d] Department of Anatomy, North DMC Medical College & Hindu Rao Hospital, Delhi, India

Background: Studies on magnetic resonance imaging reveal that there is structural reorganization in the brain areas involved in visceral pain processing. Here, we used repetitive injections of L-arginine to induce chronic pancreatitis (CP) in mice and report behavioural, morphometric, and molecular changes related to chronic visceral pain of pancreatic origin.
Materials and Methods: CP was induced in adult male Swiss albino mice by injecting L- Arginine intraperitoneally for six-weeks. We assessed pain by von-Frey filaments. Stereological methods were used to estimate the number of neurons in thalamus and sensory cortex. The expression of NeuN, VGlut1 and GAD67 in brain was compared by immunoblotting.
Results: Mice with CP showed significantly decreased pain threshold (0.008g) and increase in total percentage of responses in von-Frey test indicating progressive mechanical allodynia. The number of neurons were decreased in L-Arginine treated mice as compared to saline treated groups. The expression of NeuN decreased but the expression of VGlut1 and GAD67 were equivocal.
Discussion and Conclusion: The L-arginine model of CP induces chronic visceral pain as shown by allodynia and hyperalgesia. Decrease in the number of neurons reported by unbiased stereology and its validation by decrease in the expression of NeuN by immunoblotting indicates that viability of neurons in the brain were affected by CP.
Acknowledgement: The authors are grateful to Indian Council of Medical Research, New Delhi for funding this study (51/6/2019/ANA/BMS).

IL1.6. Mitochondrial dysfunctions induced reactive oxygen species in Parkinson's disease rodent model

Jitendra Narain Singh, Bhupesh Vaidya,Mahesh Polepalli, Shyam Sunder Sharma
Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research, S.A.S. Nagar, Punjab- 160062

Parkinson's disease is a neurodegenerative disease in which considerable mitochondrial dysfunction and cell death localised to the substantia nigra pars compacta is observed for which novel therapeutic advancements are urgently required. An increasingly appealing and accepted theory advanced the notion that such bioenergetical dysfunction may be the cause, or perhaps the consequence of pathological ROS accumulation within the mitochondria and the propensity for these messengers to stimulate the amplification of their effects throughout the cell in a process termed 'ROS-induced ROS release.
In this study, the effect of 2-aminoethoxydiphenyl borate (2-APB), a TRP channel blocker was investigated in the context of mitochondrial dysfunctions in 1-methyl-4-phenylpyridinium (MPP+)-treated SH-SY5Y cells and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-administered Sprague Dawley rats.
MPP+-treated SH-SY5Y cells exhibited reductions in cell viability, generation of reactive oxygen species (ROS) and loss of mitochondrial membrane potential. Co-treatment with 2-APB led to an increase in cell viability, reduction in intracellular and mitochondrial ROS and improvement in mitochondrial membrane potential compared to MPP+-treated SH-SY5Y cells. In addition, intranigral administration of MPTP led to a significant reduction in motor function in the rats. Fourteen days of 2-APB (i.p.) treatment improved behavioural parameters. MPTP-induced decrease in complex I activity and mitochondrial potential were also blocked by 2-APB in the mitochondria isolated from the brain regions i.e., midbrain and striatum. MPTP-induced decrease in tyrosine hydroxylase levels were also restored by 2-APB.
Moreover, MPTP-induced reduction in proteins involved in mitochondrial biogenesis, viz. peroxisome proliferator-activated-receptor-gamma coactivator and mitochondrial transcription factor-A were increased after 2-APB treatment in vivo. In summary, 2-APB has a promising neuroprotective role in the MPP+/MPTP models of PD via targeting mitochondrial dysfunctions and biogenesis.

IL1.7. Traumatic brain injury alters the limbic system of both rats and humans leading to impaired memory function

Richa Trivedi, Palkin Arora, Megha Kumari, Maria M D'souza, Kailash Manda, Poonam Ra
Radiological, Nuclear and Imaging Sciences (RNAIS), Institute of Nuclear Medicine and Allied Sciences (INMAS), DRDO, Delhi 110054, India

Background: Traumatic or stressful event to the brain initiates a sequalae of structural and functional alterations. Trauma can lead to activation of the limbic system as an adaptive response of the body. Alterations in the limbic system can be associated with TBI induced neuropsychiatric disorders and PTSD. Therefore, the present study involved assessment of microstructural changes in the limbic system along with functional outcome in rats and human subjects.
Materials and methods
Results: TBI showed altered microstructure in rats and humans. The DTI scalars including apparent diffusion coefficient (ADC), fractional anisotropy (FA), radial diffusivity (RD) and axial diffusivity (AD) were computed in both rats and human subjects. A decrease in ADC with decreasing RD values were observed in the limbic regions. The rat brain also showed astrocytic proliferation in the limbic structures with the presence of neurite plaques distinctive of axonal injury. Behavioral tests in the rats indicated decreased short-term memory with increased anxiety like behavior. On the other hand, human TBI subjects had a similar alteration in the limbic microstructure with impaired memory function.
Discussion and conclusions: The microstructural changes observed using diffusion MRI in the limbic system of both rats and humans gives an insight into the altered tissue composition with cellular changes after TBI. These structural changes are accompanied by impaired memory and cognitive functions in rats and humans. Therefore, this study highlights an important role of limbic circuitry in the development of neuropsychiatric disorders including, PTSD after TBI.
Acknowledgements: This work was supported by the DRDO, Ministry of Defence, India (INM-324).

IL1.8. Development of natural inspired novel therapeutic, and diagnostic agents for Alzheimer's disease

Gyan Modi[1], Saroj Kumar[2], Saripella Srikrishna[3], Sarika Gupta[4], Geeta Rai[5], Vegi GM Naidu[6], Gauri Shankar[1], Himanshu Rai[1], Gourav Singh[1]

[1]Department of Pharmaceutical Engineering & Technology, Indian Institute of Technology (Banaras Hindu University), Varanasi, 221005, India; [2]Department of Biophysics, All India Institute of Medical Sciences, New Delhi-110029, India; [3]Department of Biochemistry, Banaras Hindu University, Varanasi-201005, India; [4]National Institute of Immunology, New Delhi-110029, India; [5]Department of Molecular and human genetics, Institute of Sciences, Banaras Hindu University, Varanasi-201005, India; [6]Department of Pharmacology & Toxicology, National Institute of Pharmaceutical Education and Research (NIPER)-Guwahati-781032, India

Background: Alzheimer's disease (AD) is a multifactorial progressive neurodegenerative disorder characterized by gradual memory impairment. Natural products have gained enormous interest in preventing or diagnosis of AD. To address the issues associated with natural products, we developed ferulic acid (FA) and rivastigmine analogs.
Material and methods: The novel molecules were designed, synthesized and characterized following the art of medicinal chemistry. The enzyme inhibition studies were carried out with modified Ellman method. SHSY5Y cells were utilized to evaluate the neuroprotection ability of the lead molecules. The in-vivo studies were carried out in various AD mice models and in AD autopsy samples.
Results: The lead molecules were potent inhibitors of AChE/BChE (IC_{50}= 2.09±0.1, and 3.9±0.8 nM for AChE and BChE, respectively). The lead molecules exhibited promising antioxidant, $A\beta_{1-42}$ and tau aggregation modulation, NLRP3 inhibition, and metal chelation property. Further, the lead molecules were efficacious in the AD drosophila model, *in-vivo* and ex-vivo in scopolamine-induced AD models. The lead probe molecules have shown promising and selective Aβ aggregation detection ability in different AD models.
Discussion and conclusion: The promising anti-AD properties in various in-vitro and in-vivo AD models of the developed molecules may be attributed to their structural modification. The efficient brain permeability and favorable brain kinetics in live murine models, along with distinctive ocular imaging pattern in the AD Drosophila model, strongly suggest that probes holds promise as a dependable indicator for rapid, noninvasive assessment of new therapeutic modulators or inhibitors in AD.
Acknowledgment: GM is thankful to the Indian Council of Medical Research (ICMR/ EMR/2021-10363), the Science and Engineering Research Board under Core Research Grant (SERB-CRG/2018/003490), and the Indian Institute of Technology (BHU) (SM/2016 – 17/1198/L). GM also thanks Dr. Anita Mahadevan, Coordinator, Human Brain Bank (NIMHANS), for providing the autopsy tissue samples from clinically diagnosed AD patients.

IL2.1. Vulnerability of Müller glial cells in aging human retina: impact on photoreceptor cell survival

Tapas C Nag
Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India

Background: Müller cells (MC), a type of radial glia that span the entire retina, maintain homeostasis via extrasynaptic removal of neurotransmitters and providing trophic support to retinal neurons, like astrocytes perform metabolic support for neurons in the CNS. As oxidative stress is intensified with normal aging, it would be of significance to investigate how MC alter with aging and respond to oxidative stress to support the aging retinal neurons.
Materials and methods: This study examined aging changes in MC of donor human retina (age: 35-98 years; N=18 donors), via approval from Institute human ethics committee. Retinal samples were fixed and processed for TEM analysis. Immunohistochemistry was performed to localise the expression of MC markers (GFAP, vimentin, glutamine synthetase and aquaporin 4) and oxidative stress (4-hydroxy 2-nonenal and nitrotyrosine) with aging.
Results: MC undergo gliosis, lipid peroxidation and edematous changes with advanced aging (>80 years). Photoreceptor cells also undergo oxidative-nitrosative stress with aging, and their synapses also show osmotic swelling. Oxidative stress response by MC is mediated by proliferation of smooth endoplasmic reticulum and upregulation of aquaporin-4 in endfeet and outer retina. In advanced aged retinas (81-98 years), they show mitochondrial disorganisation, accumulation of lipids and autophagosomes, lipofuscin granules and axonal debris in their inner processes, suggesting a reduced phagocytotic potential in them with aging. Glutamine synthetase immunoreactivity upregulates in endfeet and Henle fiber layer only advanced aged retinas.
Discussion and conclusion: It is evident that MC are vulnerable with aging and this could be a reason for photoreceptor cell abnormalities and loss reported with aging of the human retina.
Acknowledgements: This study was supported by funds from ICMR, New Delhi (51/5/2019-BMS/ANA).

IL2.2. Unlocking the neural symphony: A study on learning and memory in Vedic Sanskrit scholars

Uttam Kumar
Center of Biomedical Research, Lucknow, India

Background: The exceptional memorization skills of Vedic Sanskrit experts have sparked scientific intrigue. This study probed the neuroanatomical substrates underpinning these abilities, focusing on white matter tract differences related to learning and memory.
Materials and methods: 25 Vedic Sanskrit experts and 25 non-experts were analyzed using Diffusion Tensor Imaging (DTI) and functional Magnetic Resonance Imaging (fMRI). Fractional Anisotropy (FA) values and Seed-Based Connectivity (SBC) analysis, targeting the caudate, cingulate, hippocampus, and thalamus, were employed.
Results: The analysis revealed a statistically significant augmentation in Fractional Anisotropy (FA) values within the pre-post central, mid, posterior cingulate caudate, and orbitofrontal regions among Vedic Sanskrit experts. These variations indicate enhanced white matter integrity, likely associated with specialized learning and memory functions. Furthermore, Seed-Based Connectivity (SBC) analysis unveiled distinctive and complex connectivity patterns within selected seed regions, illustrating the unique neural circuits engaged in the memorization processes intrinsic to Vedic Sanskrit expertise.
Discussion and conclusions: The study elucidates a complex interplay of neural substrates underlying the advanced learning and memory capabilities of Vedic Sanskrit experts. With a marked increase in FA values and distinctive connectivity patterns, these findings offer compelling evidence of specialized neural adaptations. The results underscore a novel insight into cognitive neuroscience and provide a foundation for further investigation into cognitive augmentation strategies and the neurobiology of expert-level language processing.
Acknowledgements (Intramural funding): This work was supported by intramural funding.

IL2.3. Influence of neuroactive steroids and mozart effect on neuronal oscillations and cognition: An EEG Study

Afreen Begum H Itagi
All India Institute of Medical Sciences, Mangalagiri (A.P)

Introduction and Objectives: Neuroactive steroids (NAS) interact with neurotransmitter receptors and alter the excitability and synaptic transmission to modulate learning and cognitive processes. Focusing on subtle changes in Electroencephalogram (EEG) by spectral analysis, the synchronous neocortical oscillations reflecting brain circuits can be predicted. Listening to music serves to strengthen the neuronal pathways subsequently leading to the execution of cognitive tasks. This research aims to evaluate the effect of Neuroactive steroids on exposure to Mozart music involved in directed attention during cognitive task performance along with Correlation of EEG Changes reflecting highly specific Neuronal oscillations.
Materials and Methodology: This cross-sectional Analytical study was undertaken in 30 healthy individuals above 18 years at EEG Laboratory, AIIMS Mangalagiri. The temporal and frequency properties of EEG: Power/ERSP of EEG bands were recorded at rest, followed by exposure to soft music of Mozart with eyes open and close for 3 minutes each. An event was marked in the continuous EEG data to see the effect of music on EEG bands. Blood sample was collected for measurement of Neuroactive steroids: cortisol and DHEA-S before and after exposure to music. Participants also performed cognitive tasks like Stroop Test, Trial Making Test and Mini Mental State Examination, after which the event related potential (ERP) data was processed using P300. Standard auditory "oddball paradigm" on computerized evoked potential recorder (RMS EMG MK-2) using 10/20 system was used to know the engagement of attention.
Results: Exposure to MOZART MUSIC lead to changes in Power/ERSP of EEG bands and alteration of NAS: Cortisol and DHEA-S. The accuracies and latencies showed improvement in cognitive task performance by increased directed attention due to MOZART EFFECT. Participants with higher levels of DHEA-S performed better in-terms of higher percentage accuracy and reaction time. Lower P300 latencies reflects faster reaction time with better response accuracies resulting better cognitive performances. Cortisol/DHEA- S ratio was significantly increased in individuals with poorer attention and performance.

Conclusion: Alteration of NAS: Cortisol and DHEA-S leads 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 cognition.

IL2.4. Understanding the pathophysiology and virulence determinants of *Burkholderia pseudomallei* strains causing neuro-melioidosis

Somasish Ghosh Dastidar
Centre for Molecular Neurosciences, Kasturba Medical College, Manipal Academy of Higher Education, Manipal

Background: Neuromelioidosis is an emerging but neglected infectious disease caused by a gram-negative, saprophytic bacteria *Burkholderia pseudomallei which is a Risk-GroupIII organism.* This disease mimics Guillain-Barre syndrome, aseptic meningitis, or brain-stem encephalitis with a 25% mortality rate. The pathogenesis, host-pathogen relationship, virulence determinants, and genetic variability of Neuromelioidosis-causing strains are unknown.
Methods: *Burkholderia pseudomallei* strains were isolated from patient samples with and without CNS involvement. Phenotypic, microbiological 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 infected 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 was observed in Neuromelioidosis cases. *Burkholderia pseudomallei* strains were isolated from blood, body fluid and CSF samples. Differences in phenotypic and genotypic characterization were observed in the Indian strains. Different mutations, presence of genomic islands and virulent factors was noted in the Indian strains. *In-vitro* infection led to neuronal cytotoxicity and difference in lipid droplet formation.
Conclusion: Functionally novel virulent genes *sugC, LPS-rfb,* and *cysC1* were identified in our strain. We observe the presence of genomic islands, indicative of horizontal gene transfer, harboring two virulent genes, *gmhA* and *gmhB2*, associated with pathogenesis. The current lack of diagnostic kit for early detection and lack of commercial vaccine for *B. pseudomallei* urgently demands an in-depth multidisciplinary approach to decipher the molecular heterogeneity in *B. pseudomallei,* phylogeny, virulome, and the host-pathogen interactions.
Acknowledgement: We would like to thank KMC, MAHE for providing financial and instrumental support to pursue this research work.

IL2.5. Longitudinal MR evaluation of yoga-induced changes in brain in post-stroke recovery

Dushyant Kumar[1], Chahat[1], MV Padma Srivastava[2], Rama Jayasundar[1]
Departments of [1]NMR, [2]Neuroradiology, [3]Neurology, All India Institute of Medical Sciences, New Delhi

Background: Stroke is a leading cause of disability worldwide, affecting countries both in terms of economy and work productivity. Although physiotherapy is used conventionally in post-stroke recovery, there is growing attention on the therapeutic use of yoga. In this study on ischemic stroke patients, the effects of yoga on post-stroke rehabilitation have been evaluated for the first time using Magnetic Resonance (MR) techniques.
Methods: Thirteen first-ever left hemisphere stroke patients (18-60 years) were enrolled for the study after approval from the Institute Ethical Committee. All had motor deficits with NIHSS score < 15 for left and < 10 for right hemispheres. The patients practiced yoga for six months (one hour everyday) under the supervision of certified yoga trainers. All assessments were carried out pre- and post-(3, 6 months) intervention. NIHSS, mRS and Barthel Index scores, and pro-inflammatory (IL-1β, IL-6 and TNF-α) and anti-inflammatory (IL-10) cytokines were evaluated. The fMRI studies were carried out in 3T MR scanner: with motor task (hand fist open and close). For the latter, time series data from precentral gyrus region were extracted and the results presented as frequency distribution for each patient.
Results: Longitudinal changes in NIHSS showed significant ($p < 0.05$) clinical improvement. The frequency distribution of the BOLD activity from patients showed significant clinical improvement. The peak

corresponding to the zero-time point signifies that the activity was nearly absent (most of the activity was very close to the mean). The 2nd and 3rd time points indicated increase in bold activity.
Conclusion: The current MR study has shown for the first-time yoga-induced clinical and functional changes (improvement) in brain in post-stroke recovery patients. Further in-depth analysis is under way.

Il2.6. Contribution of glial gap junctions towards neuropathic pain in rats

Kaler Jhajhria S, Kumar A, Ray SB
All India Institute of Medical Sciences, New Delhi

Background: Gap junctions are made up of a pair of hemichannels. The hemichannels and glial cells have a role in neuropathic pain, but their exact mechanism is not fully understood in neuropathic pain. The study aimed to understand the mechanistic role of gap junctions in neuropathic pain.
Materials and Methods: Male Sprague Dawley rats underwent partial sciatic nerve ligation. Baseline behavioral studies were done and followed at different intervals (7th, 14th, 21st and 28th days). On the 28th day, the spinal cord (L2-L4) was procured after sacrificing rats. Expression was quantified by immunohistochemistry, immunofluorescence and western blot.
Results: Behavioral studies showed persistent neuropathic pain between days 7th-28th and maximum pain was observed on day 14. Immunostaining revealed increased expression of Iba-1 and GFAP markers for microglia and astrocytes, respectively, on the same side of the dorsal horn of the spinal cord in the experimental rats as compared to the control. Immunofluorescence also revealed microglial activation on the ipsilateral side in neuropathic pain-induced rats. Western blot shows an active Cx-43 gap junction.
Discussion and Conclusion: Microglia, the gatekeepers of CNS immunology, are involved in various neurogenerative diseases. Gap junctions connect glial cells. Connexin-43 is the most abundant gap junction, and it has a role in glial cell activation. This study concludes the role of microglia and astrocytes in neuropathic pain. Further studies are required on agents that can suppress glial cell activation and can be used as potential analgesics for neuropathic pain through these gap junctions.
Acknowledgement: The work was supported by SERB, DST Grant. No conflict of interest.

IL2.7. Neuronal and epigenetic underpinnings of social isolation stress in *Drosophila*

Pavan Agrawal
Centre for Molecular Neurosciences, Kasturba Medical College, Manipal; Manipal Academy of Higher Education, Udupi-576104, Karnataka, India

Background: Social isolation (SI) causes deleterious changes to mental health and behaviors as observed during the recent CoVID19 induced global lockdowns. SI disrupts behaviors across animal kingdom including sleep and aggression. My group is using *Drosophila melanogaster* which, similar to mammals shows disruption in sleep and increased aggression due to SI.
Materials & methods: Our earlier work using cell type specific genomics and behaviors has identified role of dopaminergic neurons and peptidergic neurons in regulating SI induced sleep disruptions and aggression. We used targeted optogenetic and thermogenetic manipulation of different dopaminergic subsets and investigated effects on behaviors using high-throughout, machine vision based behavioral assays.
Results: Our experiments reveal a small cluster of dopaminergic neurons that reverse sleep disruptions caused by social isolation and also mediate aggressive and social behaviors. Targeted RNAi knockdown experiments further revealed specific epigenetic modulators and transcription factors that are involved in regulating sleep disruptions in these neuronal subsets.
Conclusion: These results reveal neuronal clusters responsible for encoding effects of social isolation at unprecedented resolution. We also identified specific transcriptional and epigenetic mechanisms in these neurons to elucidate causal relationship between epigenetic changes and altered behaviors.
Acknowledgements: DBT, extra mural research grant; DBT, Ramalingaswami Fellowship; SERB, Core Research Grant; Manipal Academy of Higher Education for intramural support.

IL2.8. Advanced neuroimaging and artificial intelligence in understanding human brain health and diseases: Sneaking into gliomas and aging brain

Vivek Tiwari
Department of Biological Sciences, Indian Institute of Science Education and Research (IISER), Berhampur

Understanding the clinically relevant molecular underpinning of brain disorders is complicated, given the challenges associated with surgical interventions in brain to obtain the tissue biopsies for genetic and epigenetic investigations. Therefore, my group is employing advanced neuroimaging and artificial intelligence to investigate clinically relevant hard-to-detect structural, vascular and biochemical events signifying the brain health, especially in aging associated disorders and gliomas to bypass the need of invasive procedures. We are employing 'Advanced neuroimaging, RadioGenomics and RadioMetabolomics' approaches to understand aging, dementia and glioma associated 'Quantitative signatures' for improved clinical management.

In 2016, WHO revised the glioma classification and introduced for the first-time molecular basis of glioma classification as IDH mutant and wild type. Irrespective of the histologic grade, the gliomas harboring somatic mutations in isocitrate dehydrogenase (IDH) confers better prognosis and improved survival compared to the IDH wildtype. The structural and geometric heterogeneities across gliomas are potentially a phenotypic manifestation of tumor relevant genetic and epigenetic events. Identification of mutational and epigenetic status requires tissue biopsy/surgical interventions. Given the complexity of surgical interventions in the brain, clinical management of gliomas and other brain tumor patients is challenging. Establishing the genome-phenome relationship by unravelling the tumor substructural geometry; viz enhancing, non-enhancing, necrosis and edema components across gliomas harboring distinct molecular background, is likely to establish a non-invasive method of structural geometry as an indicator of molecular status and associated clinical outcomes for prior treatment planning and improved clinical management. To investigate the structural and molecular basis of genotypic status in gliomas, we have performed glioma segmentation and fractal dimension measurements using MR images. The fractal dimensions serve as a metric for quantifying the complexity and irregularity exhibited by various shapes and structures. Fractal dimensions vary for IDH mutant tumors compared to IDH wild type tumors. A combined approach of fractality and lacunarity of tumor subcomponents is predictive of IDH mutational status and MGMT methylation. In addition to structural remodelling, my recent findings elucidate the alterations in pool and kinetics of 'Glycine' and '2-Hydroxyglutarate' as indicator of glioma aggressiveness and its role in patient survival. Biochemical heterogeneity of gliomas is predictive of patient survival.

In a parallel study on aging and dementia, we observe that a subset of the aging population maintains the cognitive abilities with minimal structural changes with aging while another subset of population transforms to mild cognitive impairment and dementia with manifold structural variations. Most importantly is heterogeneity of white matter lesions arising because of small vessel infarcts. With the application of advanced neuroimaging and AI methods in aging and dementia patients, we establish that the **'Brain Age'** pattern is distinct from that of Chronological age. For the first time we shoe that Only Three MRI features are that includes quantity of small vessel pathologies are definitive of Brain age and Cognitive status.

IL2.9. Glutamate receptor trafficking: Ins and Outs

Samarjit Bhattacharyya
Department of Biological Science, Indian Institute of Science Education and Research (IISER), Mohali

In the brain, a variety of neurotransmitters and neuromodulators act on target receptors to activate cellular signaling events which transfer information from one cell to the next. Normal signaling depends on accurate localization of such receptors in specific regions of the cell, and the process of receptor trafficking plays a critical role in controlling this localization. In addition, in case of most G-protein-coupled receptors (GPCRs), receptor trafficking also plays crucial roles in the regulation of the receptor. Despite the obvious significance of this process, we still know very little about the molecular mechanisms that mediate trafficking of neurotransmitter receptors in the brain. Our labs specific interest lies in studying the cellular and molecular mechanisms that regulate the trafficking of glutamate receptors in the central nervous system. These trafficking events are thought to be critical for virtually all forms of experience-dependent plasticity, including learning and memory and are believed to play crucial role in various neuropsychiatric disorders. The talk will be focused on the trafficking of glutamate receptors in neurons and implications of these processes in the brain.

Oral Sessions

OR1.1. Complexity of a Mendelian disease: can variants in *ATP7B* and modifier loci regulate cognitive decline and other neurological phenotypes in Wilson disease?

Arpan Saha[1], Shubhrajit Roy[2], Rittika Dutta[1], Samragni De[1], Bratati Dutta[1], Tithi Dutta[1], Arnab Gupta[3], Shaswata Mukherjee[4], Jharna Ray[5], Arkaprava Chakroborty[6], S.K. Das[6], Ashish Bavdekar[7], Prasanta K Gangopadhay[8], AtanuBiswas[6], Kunal Ray[9], Mainak Sengupta[1].
[1]Department of Genetics, University of Calcutta,[2]Johns Hopkins university, [3]Indian Institute of Science Education & Research Kolkata, [4] Kalyani Mahavidyalaya,[5] S.N. Pradhan Centre for Neurosciences,[6] Bangur institute of Neurosciences, Kolkata, [7]KEM hospital, Pune,[8] KPC Medical College & Hospital,[9]Ramakrishna Mission Vivekananda Educational and Research Institute.

Background: Wilson Disease (WD), caused by mutations in *ATP7B*, is a rare autosomal recessive disorder of copper metabolism, characterised by a wide-range of neurological symptoms including cognitive decline. This study aims screening variants in *ATP7B* and other modifier loci in an attempt to correlate them with phenotypic differences in WD patients.
Materials and methods: The neurological symptoms of the patients were evaluated by expert neurologists; cognitive decline assessed through ACEIII, VLT and FAB; genotyping was done through PCR/RFLP/sequencing approach followed by statistical analysis to correlate the genotype with the phenotype.
Results: Analysis of the 85 *ATP7B* mutations and genotype data of 12 potential modifier polymorphisms of *APOE*, *PRNP*, *BDNF, DRD2* and *HFE* revealed ***ATP7B*** p. Ala1241Val to be associated with risk of dysarthria; ***APOE*** rs429358 CC-CC/CTwith cognitive impairment and dystonia, ***BDNF*** rs6265 AA/AG with tremor, cognitive impairment and drooling, and ***BDNF*** rs56164415 CT/TT genotypes as protective to dysarthria. ***DBH*** rs1108580 AG, ***HFE*** rs2071303 CC and ***DBH*** rs1611115 TT genotypes were associated with severity in cognitive decline.
DISCUSSION and CONCLUSIONS: Analysis of *ATP7B* mutations alone have not been able to provide effective genotype to phenotype correlation in WD. Clinical heterogeneity in neurological phenotypes including cognitive decline among the patients may be attributed to the presence of different modifier genes implicated in copper metabolism and various neurological diseases having overlapping symptoms with WD. Concordant to our finding, variations in ***DBH***, ***BDNF*** and ***APOE*** have been associated with cognitive dysfunction in different neurological disorders.
Acknowledgement: This study is supported by DST-CSRI, G.O.I and Presenting author is supported by UGC-SRFship, From G.O.I.

OR1.2. Unraveling hippocampal proteome dynamics in hepatic encephalopathy rat model through label-free LC-MS/MS profiling

Papia Acharjee[1], Vishal Vikram Singh[1], Shambhu Kumar Prasad[1], Arup Acharjee[2]
[1]Department of Zoology, Banaras Hindu University, Varanasi-221005; [2]Department of Zoology, Faculty of Science, Allahabad University, Prayagraj-211002

Background: Hepatic Encephalopathy, a metabolic brain disorder results in cognitive and motor deficits. Hyperammonemia led increased glutamate-NMDAR overstimulation is the key pathogenic factor in HE pathogenesis. However, targeting NMDAR for therapy is unfeasible due to its vital role in brain function. To uncover alternative non-NMDAR therapeutic option, proteomic profiling of MoHE rat's hippocampal proteome were conducted using high-resolution accurate mass spectrometry.
Materials & Methods: Adult male rats were divided into control and MoHE group. MoHE was induced by thioacetamide (100mg/kg bw, i.p) treatment while the control group received normal saline for 10 days once daily. Hippocampal proteins were extracted from both groups and analyzed using label-free based LC-MS/MS. MetaboAnalyst was used to perform various statistical analysis. Network and enrichment analysis performed by STRING and Metascape.

Results: We identified 2175 proteins, 47 of which exhibited significant alterations at threshold of 1.25-fold change and p≤0.05 in the HE hippocampus. Out of 47differentialy expressed, 42 were upregulated and 5 were downregulated.
Discussion: Several key proteins stood out among the top upregulated proteins, including Homer-2, Y-box-binding protein 3, Autophagy-related protein 9A, Focal adhesion kinase 1, Tetraspanin 2, and CD9. Validation of these findings was performed through various methods including qPCR, western blotting, and immunofluorescence. Focal adhesion kinase 1, Tetraspanin 2, and CD9 showed increased expression in the hippocampus of MoHE compared to controls rats. STRING analysis showed the interaction pattern among significantly altered proteins. Pathway enrichment analysis using Metascape revealed enriched biological processes in the central nervous system (CNS) that may be disrupted during MoHE. These processes include gliogenesis, astrocyte differentiation, myelination regulation, and protein phosphorylation.
Acknowledgments: Financial assistance: DST-SERB Grant (ECR/2017/001018), IOE BHU grant ((IoE Dev. Scheme-6031) to PA, Project assistant fellowship and ICMR SRF to SKP, UGC-SRF TO VVS.
Facilities: Prof SK Trigun Lab (Department of Zoology, BHU), CDC BHU, DBT-ISLS, BHU and Prof Sanjeeva Srivastava, BSBE, IIT Bombay for MASSFIITB facility (BT/PR13114/INF/22/206/2015).

OR1.3. Age-related qualitative morphological changes in the human stria vascularis

Silka Agarwal[1], Charanjeet Kaur[2], Tara Sankar Roy[3], Daya Nand Bhardwaj[4], Tony George Jacob[1]
[1]Department of Anatomy, All India Institute of Medical Sciences (AIIMS), New Delhi; [2]Department of Otolaryngology-Head and Neck Surgery, Massachusetts Eye and Ear, Boston, Massachusetts, USA; [3]Department of Anatomy, North DMC Medical College & Hindu Rao Hospital, New Delhi, India; [4]Department of Forensic Medicine and Toxicology, AIIMS, New Delhi

Background: Stria vascularis (SV) is a vascular epithelium in the cochlea that secretes endolymph. Melanosomes are brown-coloured pigments that maintain the ionic concentration of endolymph through ATP-pumps. They also help in the formation of blood-strial barrier and reducing oxidative stress. Here, we studied qualitative, age-related changes in human strial melanosomes.
Materials and methods: Ten human cochleae, from deceased persons aged 13 to 74 years were fixed, decalcified, dehydrated and embedded in celloidin. Transverse sections were cut and stained with hematoxylin and eosin. These sections were studied under a microscope.
Results: The SV was seen as stratified cuboidal epithelium with three types of cells- basal, intermediate and marginal (from peripheral to luminal). More melanosomes were seen in the intermediate layer. The number of melanosomes appeared to increase with advancing age of the deceased. The blood vessels, strial ligament, organ of Corti did not display any overt morphological changes.
Discussion and Conclusion: The number of melanosomes increased with increasing age, probably to compensate for the increasing oxidative damage associated with ageing. This may be a useful morphological indicator of the age-related loss of hair cells and spiral ganglion neurons due to oxidative and excitotoxic damage that results in presbycusis i.e., age-related hearing loss. We would like to further quantitate any relationship between the number of melanosomes and the number of hair cells in the organ of Corti.
Acknowledgments: This study was undertaken as part of the dissertation work for the MD degree of Dr. Silka Agarwal and was thus funded by the Department of Anatomy, AIIMS, New Delhi.

OR1.4. Network pharmacology: Integrating system biology with computer aided drug design for dealing with neurological disorders

Prachi Srivastava
Amity Institute of Biotechnology, Amity University Uttar Pradesh, Lucknow, 226028

The human nervous system is a complex of several genes and proteins. Diseases of the brain are multifactorial that get triggered by several proteins. Management and treatment of such neurodevelopmental, neuropsychic, and neurodegenerative diseases require a holistic approach. Thus, the traditional approach of one-drug, one-target for the management of diseases has faced some serious challenges in the past. Recent studies have now demonstrated network pharmacology as the more promising approach for dealing with neurological disorders. Network pharmacology is a new discipline that uses networks and systems to identify key targets in a disease. This has revolutionized the classic concept of computer aided drug designing by emphasizing

on targeting multiple genes with a single drug. This is a more practical approach since biological components are involved extensively in intricate and complex relationships, thus it becomes more essential to use network biology concepts when learning about biology. Network biology works on the principle that drugs can effectively combat multifactorial diseases with the help of the novel strategic approach. System biology methods help look at the disease as a whole and target multiple proteins associated with the disease directly or indirectly. The system biology-based drug targets aid in focusing on the vital biological pathways that contribute to the development and progression of the disease. Network pharmacology is now being extensively used for several disorders like attention deficit hyperactivity disorder, autism, intellectual disability, and epilepsy. Therefore, by using multiple system biology approaches more effective and precise drugs can be formulated for dealing with several neurological disorders.

OR1.5. Non-permitted food colorants induced neurotoxicity in rats: A behavioral, neurochemical and histological study

Rajesh Singh Yadav[1] and Pronit Biswas[2]
[1]School of Forensic Science, National Forensic Sciences University (An Institution of National Importance), Bhopal – 462036 (MP), India; [2]Department of Forensic Science, School of Basic and Applied Sciences, ADAMAS University, Kolkata, India

Background: Non-permitted Food Colorants (NPFCs) are prohibited due to health concerns, but it is still claimed that they are injudiciously used, particularly in the developing countries. Continuous use raises concerns about adverse health effects in exposed individuals.
Material and Methods: The present study designed to investigate the effects of 3 NPFCs (metanil yellow - MY, malachite green - MG, and sudan III - SIII) on neurobehavioral, neurochemicals, mitochondrial dysfunction, oxidative stress and histological changes in brain regions of rats. **Results:** Rats were treated with MY (430 mg/kg), MG (13.75 mg/kg), SIII (250 mg/kg) and mixture (YGR) (MY 143.33 + MG 4.52 + SIII 83.33 mg/kg) p.o. for 60 days showed a significant decrease in grip strength, motor activity, learning and memory impairments as compared to controls. A significant increase in the lipid peroxidation and decrease in the level of reduced glutathione, activity of catalase and superoxide dismutase were observed in corpus striatum, hippocampus and cerebellum in these rats. A significant decrease in the activity of acetylcholinesterase (AChE), monoamine oxidase - B (MAO-B), mitochondrial complex I and II were also observed in NPFCs treated groups.
Discussion and Conclusions: Further, the histological damages to the neurons in the brain regions evident for the toxic effects of NPFCs resulted into the behavioral dysfunctions in rats linked with other biochemical and neurochemical alterations. The findings of the present work suggested that chronic exposure of NPFCs caused neurotoxicity involving behavioral impairments, biochemical and neurochemical alterations, mitochondrial dysfunction and neuronal cell damages in rat brain.

OR1.6. Assessment of short-term memory loss in recovered COVID-19 patients: Indications from a two-year follow-up study

R. K. JHA, G. Kumar[1], P. Dwivedy[1], A. Asghar[1], R. K. Narayan[7], S. K. Ghosh[1], R. Kirti[2], D. Rai [3], L. Tiwari[4], A. Banerjee[5], A. Sarfaraz[6]; A. Kumar[1]
[1]Dept. of Anat., [2]Dept. of Med., [3]Dept. of Pulmonary Med., [4]Dept. of Pediatrics, [5]Dept. of Biochem. [6]Dept. of Microbiology, All India Inst. of Med. Sciences-Patna,Patna, India; [7]Dept. of Anat., ESIC-MCH, Bihta, India

Background: Short-term memory loss as a persistent symptom reported in recovered COVID-19 patients. We assessed post discharge persistence of this symptom in hospitalized patients.
Methods: A total of 209 hospitalized patients of COVID-19 followed up for two years post discharge. Patients were verbally interviewed through a telephonic call and asked about the presence of the symptoms confirming the loss of short- term memory, such as increased forgetfulness or a problem with retaining a piece of recent information.
Results: The loss of short-term memory was present in ~ 11% (24/207) of the patients. At the end of one year: the symptom persisted in ~ 87.5% (21/24) of patients. At the end of second year: 25% (6/24) completely recovered, ~ 21% (5/24) reported improvement, and in 42% (10/24) symptom was persistent. One patient

died during study and two did not respond to the interview call.
Conclusion: There is significant improvement or remission in short term memory loss in the long COVID patients after two years of hospital discharge**.**
Acknowledgements: Funding for this study received from All India Institute of Medical Sciences-Patna.

OR2.1. Expression of Pax3 in human neural tube defects

Swati Tiwari[1], Sabita Mishra[2]
[1]Dept of Anatomy, Maulana Azad Medical College, New Delhi; [2]Dept of Anatomy, Maulana Azad Medical College, New Delhi
Background: The mechanisms encompassing neural tube formation have not been completely understood. Studies in mice suggest role of Pax3 gene which is expressed in early neurogenesis in dorsal half of neural rube. This gene regulates neuroepihelial proliferation. There is limited literature on the role of Pax3 in human neural tube defects.
Materials and methods: Aborted fetuses with neural tube defects and age matched controls were obtained from Department of obstetrics and gynaecology at Lok Nayak Hospital, New Delhi, after obtaining consent and ethical approval from institutional ethical committee. The spinal cord was processed for immunohistochemistry and the expression of Pax 3 in the fetuses with neural tube defects was compared with the expression in normal fetuses.
Results: The expression of Pax 3 was visibly more in normal fetuses in comparison to the fetuses with neural tube defects. The difference in expression was marked especially in the dorsal aspect of the proliferating neural epithelium.
Discussion and conclusions: Pax3 functions to maintain the neuroepithelium in a proliferative, undifferentiated state, allowing neurulation to proceed as suggested by several studies in mice. Reduced expression in the fetuses with neural tube defects indicates that it has an important role in neurulation in humans as well.
Acknowledgements: We are grateful to the Govt. of NCT of Delhi for providing us with the funds for our project under the scheme “Strengthening of research at MAMC”.

OR2.2. Association Between the Minutes Spent on Smart Mobile Phone Before Falling Asleep and Sleep Quality

Pasang Tshering Dukpa[1], Smita Sahu[2], Afreen Begum H. Itagi[3]
[1]Department Of Physiology, A.B.N.Seal College, Cooch Behar, [2]District Hospital, Baloda Bazar, Chhattisgarh, [3]Department of Physiology, All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh[2]

Background: examine the association between mobile phone usage before falling asleep and: (i) sleep duration, (ii) subjective sleep quality; and (iii) excessive daytime sleepiness in a sample from RIMS , Raipur
Material and method: Study was carried out in RIMS , Raipur, during the months of July – August’ 2018. A total of 100 participants were recruited in this study. Sleep quality was assessed with the help of the Pittsburgh Sleep Quality Index questionnaire. Chi square test was used for comparing demographic characters. Correlations between mobile phone usage before falling asleep and sleep variables were computed using bivariate Pearson correlation analyses.
Result: Of the 100 participants, 51 (51 %) had PSQI ≥5, reflecting poor sleep quality. A higher use of mobile phone before falling asleep was significantly associated with a poor sleep quality as a component of PSQI questionnaire (P=0.01) The minutes spent on smart mobile device before a falling asleep had a significant positive correlation with the Latency period ($p<0.05$) and daytime dysfunction ($p<0.01$) and sleep disturbance ($p<0.05$).
Discussion and conclusions: This study revealed the evidence of the impact or effects of smart mobile devices on sleep quality. Day time dysfunction was significantly related to sleep disturbance. Since health trainees are required to be alert & attentive during learning period so that they acquire professional level knowledge & skills of patient care, day time dysfunction and bad sleep quality may lead to significant stress and mental health problem.
Acknowledgement: This work was supported by the Indian Council of Medical Research (ref no. 2018-01706)

OR2.3. Mechanisms underlying the development of the axonal actin-spectrin Membrane Periodic Skeleton

Shivani Bodas[1], Ashish Mishra[2], Prof. Pramod Pullarkat[2], Prof. Aurnab Ghose[1]
[1]Indian Institute of Science, Education and Research (IISER-Pune), Biology, Pune, India; [2]Raman Research Institute, Bangalore, India

Background: The advent of super-resolution microscopy has revealed the presence of a membrane-associated periodic actin-spectrin cytoskeleton (MPS) precisely located beneath the axonal plasma membrane, repeating every ~190 nm (Xu et al., 2013). This periodic arrangement, bound to the plasma membrane, is observed to respond to extracellular stimuli by recruiting and colocalizing G protein-coupled receptors (GPCRs), receptor tyrosine kinases (RTKs), and cell adhesion molecules (CAMs) to the membrane.
Method, Results & Discussion: Our previous work highlighted the importance of the Actin-spectrin Membrane Periodic Skeleton (MPS) to be crucial for buffering axonal rest tension(Dubey *et al*;2020) .However, the mechanisms underlying MPS formation and remodelling during neuronal development remain unclear. To investigate the mechanism of MPS development, we measured spectrin dynamics using FRAP. Interestingly, very little recovery was observed for spectrin even at DIV 1, when MPS was not prevalent. This suggests the recruitment of spectrin to a stable structure before the establishment of the MPS. Lat-A-treated axons revealed a faster initial recovery phase. The mobile fraction in early-stage axons (DIV1-2) was higher than that in the controls, although this was not the case for late-stage axons (DIV4). These experiments suggest the recruitment of spectrin to a stable network via a combination of actin and membrane binding which is later elaborated to form the MPS. This hypothesis is being tested using specific deletion constructs in spectrin knockout cells and is expected to reveal the sequence of interactions resulting in the development of the MPS. We have shown that MPS prevalence in chick DRG axons increases with the developmental stage (DIV 1-4; days in vitro). This increase in prevalence over time correlates with an increase in axonal rest tension. Perturbation of actin and microtubule dynamics affects MPS prevalence and stability and reveals the role of microtubule stability in MPS formation and maintenance.
Acknowledgements: Project fund -SERB, Fellowship-IISER-Pune; IISER-Pune microscopy facility, RRI, Bangalore

OR2.4. Proteomic profiling of the aging rat hippocampus: Insights from machine learning and High-Resolution Mass Spectrometry

Arup Acharjee[1], Vishal Vikram Singh[2], Shambhu Kumar Prasad[2], Papia Acharjee[2]
[1]Department of Zoology, Faculty of Science, Allahabad University, Prayagraj-211002; [2]Department of Zoology, Banaras Hindu University, Varanasi-221005

Background: Biological aging is associated with an exponential risk of cognitive decline and neurodegenerative disorders. Therefore, obtaining deeper insights into the healthy aging process in the brain and exploring novel strategies to achieve healthy brain aging and prevent neurodegenerative diseases are urgently needed. Thus, we intend to understand the hippocampal proteome dynamics in aging rats by High-Resolution Accurate Mass Spectrometry (HRAMS).
Materials and Methods: Young and old male, Charles Foster rats were taken for the experiment. Each group contained 6 rats. Hippocampal protein was extracted and processed for LC-MS/MS study followed by protein identification. The obtained protein dataset was analyzed using a Machine learning approach and statistical analysis by Metaboanalyst, and functional analysis by Metascape.
Results: A total of 1021 proteins were processed for machine learning and statistical analysis. Some important features identified by random forest are Neuronal cell adhesion molecule 1, 14-3-3 protein gamma, MICOS complex subunit Mic60, and 14-3-3 protein zeta/delta. Statistical analysis identified a total of 278 age-associated dysregulated proteins (log2 fold change and the p-value threshold of 0.05), among which 123 were upregulated and 155 were downregulated proteins. Few examples: ERC protein 2, Protein piccolo, Plectin-1 were upregulated and Septin-5, Mitogen-activated protein 1, and 14-3-3 protein were downregulated in aging rats.

Discussion: Our findings highlight critical proteins as essential players in the age-associated hippocampal proteome dynamics. Through network analysis tools, upregulated proteins are involved in modulation of chemical synaptic transmission, synapse organization, monoatomic ion transmembrane transport, with neuron projection development being most significant. Pathways that were uniquely identified in the 155 downregulated proteins are cellular detoxification, response to reactive oxygen species, intracellular protein transport, and metabolism of nitric oxide. The comprehensive analysis of all 278 proteins dysregulated in the aging rats identified neutrophil dysregulation, cellular response to stress, aerobic respiration, and Signalling by Rho GTPase to be highly significant.

Acknowledgments: Financial assistance: DST-SERB Grant (ECR/2017/001018), IOE BHU grant ((IoE Dev. Scheme-6031) to PA, ICMR SRF to SKP, UGC-SRF TO VVS.
Facilities: Prof SK Trigun Lab (Department of Zoology, BHU), CDC BHU, DBT-ISLS, BHU and Prof Sanjeeva Srivastava, BSBE, IIT Bombay for MASSFIITB facility (BT/PR13114/INF/22/206/2015).

OR2.5. Disease-modifying effect of quercetin in iron-induced experimental model of post-traumatic epilepsy

Chandra Prakash, Shyam Sunder Rabidas, Shweta Saran, Deepak Sharma
School of Life Sciences, Jawaharlal Nehru University, New Delhi-110067

Background: Epilepsy is one of the most common neurological disorders afflicting people all over the world. The traditional antiepileptic medications are known to cause drug toxicity and cognitive impairment. Thus, the present study was intended explore the disease-modifying effect of quercetin, a flavonoid in the rat model of post-traumatic epilepsy.
Materials and methods: Male Wistar rats were given an intracortical injection of $FeCl_3$ (5 µl of 100 mM solution). After 15 days, quercetin was administered orally for 15 consecutive days. Electrophysiology, Morris water maze test, open field test, histopathology and immunofluorescence analysis were employed to evaluate the disease-modifying potential of quercetin.
Results: The results showed that quercetin treatment distinctly reduced occurrence seizures and cognitive impairment in epileptic rats. Histopathological examinations depicted recovery of degenerating neurons and cell death in the cortical and hippocampal regions of epileptic rats by quercetin treatment. Furthermore, immunofluorescence analysis revealed attenuation of neuronal loss and glial activation both in the cortex and hippocampus regions.
Discussion: Overall, our observations suggest that quercetin possesses substantial neuroprotective effect in the epileptic brain. Quercetin may have decreased the number of neurodegenerating neurons and cell death. Furthermore, the flavonoid may have escorted an anti-seizure effect by ameliorating neuronal loss and glial activation in experimental model of post-traumatic epilepsy.
Acknowledgement: The work was supported by the Indian Council of Medical Research, New Delhi in the form of Research Associate (RA) Fellowship (3/1/3/123/Neuro/2019-NCD-I) to C.P.

OR2.6. Impact of quercetin on endothelial cells of retinal capillaries in diabetic rats

P. Kumar[a], J.Kumari[a], Ankita[a], B.P Sinha[a], B. Sharma[b] ,L. K. Arya[a], , M. Kumar[c], T.C Nag[b], M. Nath[d], T Velpandian[d]
[a]Regional Institute of Ophthalmology, Indira Gandhi Institute of Medical sciences, Patna; [b]Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India; [c]Central Animal House, Indira Gandhi Institute of Medical sciences, Patna; [d]Department of Ocular pharmacology, Dr. Rajendra Prasad Center for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

Background: Diabetic Retinopathy(DR)is one of the leading causes of blindness caused due to hyperglycemia. Uncontrolled hyperglycemia causes oxidative stress to retina leading to leaking of blood vessels. ROS overproduction causes pro-inflammatory cytokines to elevate, endothelial cells degeneration and pericyte death. Quercetin being an anti-oxidant, possess ROS scavenging property, holds potentiality to take care of the oxidative damage caused due to hyperglycemia.

Materials and methods: Diabetes was considered to exist in streptozotocin(45mgKg^{-1}BW)-induced rats with blood glucose levels of 300mgdL^{-1}. Once diabetes was maintained, quercetin was administered once a week for 16 weeks (50mgKg^{-1}BW). To observe morphological changes in the retina, fundoscopy was performed. Following the histopathological evaluations, TEM was performed to look for ultrastructural alterations. To measure the levels of TNF- and IL-1, ELISA was performed.
Results: ELISA findings of retinal homogenate showed significant increase inIL-1β($p \leq 0.001$) and TNF-α($p \leq 0.01$) levels in diabetic retina as compared to control and quercetin treated. Histopathological findings revealed significant cell degeneration in INL of diabetic retina in comparison to control and qctn treated (DR & Control $p \leq 0.01$) (DR & DR+ Qctn $p \leq 0.001$). TEM studies of retinal capillaries showed significant degeneration of endothelial cell degeneration and pericyte death in diabetic retina as compared to control and quercetin treated ($p \leq 0.001$).
Discussion and conclusions: Considering the above findings Microaneurysms, Dot and Blot hemorrhages observed in diabetic retina are results of endothelial cells degeneration and pericyte death in the retinal capillaries. Increased levels of IL-1β and TNF-αadds on to the cascading of oxidative stress damage further worsening the DR progression. Quercetin treated retina showed significant reduction in DR symptoms and appeared similar to control group, leading to improved vision. Hence quercetin appear to improve DR. Other markers of endothelial cell degeneration yet to be explored.
Acknowledgements: Funding agency- SERB, New Delhi (project code:- SRG/2021/000913), TEM work done at SAIF, AIIMS, New Delhi.

OR2.7. The Neuroprotective effects of *Withania somnifera* on age-related cognitive decline-A study of oxidative stress and memory function in mice brain

Manju Lata and A. Jain
Department of Zoology, MSJ College, Bharatpur (Raj)

Background: Aging is a natural process that affects all living organisms. In humans, it is associated with a decline in cognitive function, including memory loss, learning difficulties, and impaired attention. These age-related cognitive impairments are caused by various factors, including oxidative stress, and decreased neurogenesis. *Withania somnifera*, commonly known as ashwagandha, has been used for centuries in traditional Ayurvedic medicine to treat various ailments, including cognitive decline. In this study, we investigate the neuroprotective effects of Withania somnifera on age-related cognitive decline in mice.
Material and method: Male Swiss albino mice aged 8 months were used in this study. The mice were divided into three groups: control, aging, and aging+*Withania somnifera*. The aging+*Withania somnifera* group received *Withania somnifera* extract (200 mg/kg body weight/day) for six weeks. Behavioral tests were conducted, and oxidative stress markers were measured in the brain tissue of the mice.
Result: The aging+*Withania somnifera* group showed a significant decrease in escape latency and swimming distance compared to the aging group. The aging+*Withania somnifera* group also showed a significant increase in SOD and CAT levels and a significant decrease in MDA levels compared to the aging group. The aging+*Withania somnifera* group also showed a significant increase in ACh and ChAT levels compared to the aging group.
Discussion and Conclusion: The results of this study suggest that *Withania somnifera* extract has neuroprotective effects against age-related cognitive decline. This suggests that *W. somnifera* can ameliorate oxidative stress-related changes in behavior and that by doing so they might promote healthy aging in humans.
Acknowledgement: Thanks to UGC, New Delhi, (UGC Project **IDRA-2016-18-GE-RAJ-7281)**

OR2.8. Olfml3 could act as a central molecule in the regulation of microglia-mediated brain immunity

Himanshi Yadav[1], Jaldhi[1], Shweta[1], Amrita Bakshi[2], Anamika[2], **Shashank Kumar Maurya[1]** [1]Biochemistry and Molecular Biology Laboratory, Department of Zoology, Faculty of Science, University of Delhi, Delhi; [2]Department of Zoology, Ramjas College, University of Delhi, Delhi

Background: Olfml3 belongs to a family of olfactomedin domain-containing proteins. The expression of Olfml3 is confined to microglia in the brain. However, the role and importance of Olfml3 in the brain are still elusive. Therefore, the present study evaluates the possible involvement of Olfml3 in the regulation of microglia-mediated brain immunity.
Materials and Methods: Neuroinflammation was induced by intraperitoneal injection of LPS (500 μg/kg) for 7 days in adult male BALB/c mice. An equal volume of saline was given to the control group. The qPCR and western blotting were done to check expression, IHC for co- localization and in silico analysis for Olfml3 interacting protein.
Results: The expression of Olfml3 was found to be increased on induction of neuroinflammation. Olfml3 was found to co-localize with Tmem119 and Iba1. Tmem119, Sall1, Iba1, P2ry12, Siglec-h, Csfr1, Trem2, Cx3cr1, Gpr34, Bmp1, Sparc identified as putative interactors of Olfml3. Based on its interacting partners, Olfml3 has been analyzed to be possibly involved in the regulation of major biological functions in the brain including neuroinflammation, neurogenesis and synaptogenesis in the brain of mice.
Discussion and Conclusion: The expression levels of Bdnf, Tgf-β1, and Tnf-α were assessed to confirm inflammation in the brain following LPS treatment in mice. Further, the levels of Olfml3 and Iba1 were found to increase while Tmem119 expression decreased in the brain by LPS treatment. By interacting with proteins of microglia, neurotropic factors, and inflammatory response genes, Olfml3 could act as a central molecule in the regulation of microglia-mediated brain immunity.
Acknowledgements: Financial support from the Institution of Eminence (IoE), University of Delhi is gratefully acknowledged.

OR2.9. Gasdermin D inhibition confers protection from neuroinflammation and anxiogenic behavior in a rodent model of anxiety disorder

Soni Tiwari[1,2], Santi Ranjan Atta[3], Zaidan Mohammed[3], Shweta Kaushik[1], Amla Chopra[2], Itender Singh[1], **Simantini Ghosh[3]**
[1]Ambedkar Centre for Biomedical Research, Delhi University, Delhi; [2]Department of Zoology, Dayalbagh Educational Institute, Agra; [3]Department of Psychology, Ashoka University, Rai

Stress and anxiety disorders are complex and leading mental health problems. Stress and anxiety disorders are associated with a chronic increase in pro-inflammatory mediators such as interleukin- 1beta and NLRP3 inflammasome in brain. The present study investigated the mechanism underlying induction of interleukin-1beta and inflammasome pathway in a rodent model of anxiety disorder.
Materials and Methods: The experimental rodents were subjected to physical restraint and underwater trauma to induce anxiety disorder. Gasdermin D was inhibited with necrosulfonamide and disulfiram, and thereafter animals were assessed for anxious behavior using open field test, light–dark test, elevated plus maze test and fear conditioning and social interaction.
Results: We found the induction of caspase 11 and cleavage of gasdermin D, the downstream mediators of inflammasome pathway, in the brains of rodents with anxiety disorder. We found that inhibition of gasdermin D with disulfiram as well as necrosulfonamide ameliorated the stress induced anxiogenic behavior. Further, disulfiram inhibited the release of interleukin-1beta in the brain. A combinational treatment with Ibrutinib, a BTK-inhibitor and disulfiram enhanced the protection from stress-induced anxiogenic behavior.
Discussion and Conclusions: Cleaved gasdermin D forms membrane pores, leading to cytokine release and enhancement of inflammatory cell signaling in the brain. Our study have identified gasdermin D as an essential element for enhanced and prolonged sustenance of IL1β signalling following stress induced anxiety. Further studies are required to explore the potential of inhibition of gasdermin D, especially disulfiram, a FDA approved drug for addiction, as novel targets for the treatment of PTSD and anxiety disorders.
Acknowledgement: This study was supported by intramural research grant from Ashoka University to S.G; Brain Aneurysm Foundation and Ramalingaswamy Fellowship to I.S., and a graduate student fellowship from Ashoka University to Z.M.

OR2.10. Outcome of EP2 antagonist treatment to a two-hit mouse model of Alzheimer's disease depends on the mouse strain and the sex

Avijit Banik[1,2], Radhika Amaradhi[1], Michael Sau[1], Raymond Dingledine[1], Thota Ganesh[1]
[1]Department of Pharmacology and Chemical Biology, School of Medicine, Emory University. Atlanta, GA 30322; [2]Department of Biotechnology, GITAM School of Science, GITAM deemed to be University, Visakhapatnam, AP 530045

Background: Alzheimer's disease (AD) is the largest spectrum of dementia, and is a chronic condition that severely impairs memory, thinking, and social abilities, negatively impacting the daily life of the Prostaglandin-E2 (PGE2) receptor EP2, which is activated downstream of cyclooxygenase-2 (COX-2) signaling, emerged as a neuroinflammatory target in several neurodegenerative diseases including AD.
Materials and Methods: Here we investigated the effect of a selective EP2 antagonist on behavioral deficits in 5xFAD transgenic mice subjected to mild, systemic inflammation by lipopolysaccharide (LPS). We have exposed a cohort of 5xFAD mice in C57BL/6 and B6SJL backgrounds with once-a-week intraperitoneal injection of LPS (0.5 mg/kg or 1 mg/kg) and treated with either vehicle or EP2 antagonist TG11-77. HCl (100 mg/kg/day) for 12 weeks in drinking water.
Results: Complete blood count (CBC) analysis was performed to demonstrate that LPS induced an anemia of inflammation, and induction of inflammatory gene expression (mRNA) in these mice brains. TG11-77.HCl improves memory retention both in single hit – environmental and two hit mice. Further, TG11-77.HCl ameliorates mRNA expression of many proinflammatory chemokines and cytokines in two-hit male cortex in B6SJL backgrounds while females showed significant improvement in C57BL/6 strains. This was corroborated by attenuated amyloid pathology in two-hit B6SJL male brain, but no alteration was found in female brains in C57BL/6 mice.
Discussion and Conclusion: This study reveals that EP2 antagonism is a prudent therapeutic strategy in reducing brain inflammation and behavioral deficits in Alzheimer's brain when it is subjected to an external secondary hit of neuroinflammation. But these outcomes are strain and sex specific.
Acknowledgements: This study was supported by the NIH funds NIA Grant: U01AG052460 (T.G.) and NINDS Grant: R21/R33 NS101167 (T.G.).

Young Scientist Colloquium-1

YS1.1. SIRT3 activation by honokiol restores mitochondrial dysfunction and cognitive impairmentduring MoHE led excitotoxicity

Anamika[1,2] and Surendra K Trigun[1]
[1]Biochemistry section, Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi-221005; [2]Department of Zoology, Ramjas College, University of Delhi, Delhi-110007

Background: Excessive glutamate receptor stimulation results in calcium overload and mitochondrial dysfunction. Which in turn results in neuronal aberration; key to several neurodegenerative disorders. Therefore, we attempted to seek neuroprotection by re-establishing the mitochondrial stature and function by targeting a conserved mitochondrial deacetylase, SIRT3.
Material and Method: The studies were undertaken in the hippocampus of the neurobehavioral characterized model for ammonia neuroexcitotoxicity induced moderate grade HE (MoHE; induced by 100 mg/Kg bw TAA for 10days) rats, post treated with SIRT3 activator Honokiol (HKL) (10 mg/Kg b.w.) for 7 days. Samples obtained were processed for biochemical and histological studies.
Results: The results suggested that honokiol treatment ensued restoration of SIRT3 expression and activity which were consistent with recovery of mitochondrial dysfunction by modulating Ca^{2+} influx and the factors involved in maintenance of mitochondrial integrity and bioenergetics. Direct evidence of SIRT3 activation led prevention of neurodegeneration is evident from the normalization of neuroarchitectural parameters of the CA1 pyramidal neurons and neurobehavioral impairments in MoHE rats.
Discussion and conclusion: Mitochondrial SIRT3 is a highly conserved bonafide metabolic sensor which plays crucial roles in maintaining mitochondrial structure and function. Our findings indicate that SIRT3 activation could recover the deranged mitochondrial integrity mainly by modulating critical transcription factors FoxO3a and PGC1α. This is consistent with recovery in the damaged neuronal structures and neurobehavioral impairments. In is evident that SIRT3 could be a potent pharmacological target in protecting mitochondrial integrity during MoHE pathogenesis.

Acknowledgement: This work was financially supported by a DST project to SKT and award ofCSIR-SRF fellowship to Anamika. The instrumentation facilities provided by CAS and DST FISTgrants to Zoology and DBT-BHU ISLS unit and BHU CDC facilities are also acknowledged.

YS1.2. Social and emotional behavioral alterations in mouse models lacking presynaptic Bassoon in GABAergic interneurons

Anil Annamneedi
Department of Biotechnology, School of Bioengineering, SRM Institute of Science and Technology, Kattankulathur, Tamilnadu, India

Background: A central organizer protein Bassoon at the presynaptic active zone sites is involved in important functions including homeostatic synaptic plasticity, proteasomal degradation, autophagy, CA3 mossy fiber synapse development. Excitatory specific conditional knockout mice for Bassoon (Bsn^{Emx1}cKO; $Bsn2^{lx/lx}$ X $Emx1^{Cre/+}$) display immature DGphenotype and enhanced learning.
Materials and methods: Bassoon role in inhibitory synaptic terminals has not been addressedso far. To answer this, we have generated conditional KO of Bassoon in GABAergic interneurons($Bsn^{Dlx5/6}$cKO; $Bsn2^{lx/lx}$ X $Dlx5/6^{Cre/+}$) and in Parvalbumin (PV) interneuronal subtype (Bsn^{PV}cKO; $Bsn2^{lx/lx}$ X $PV^{Cre/+}$) and compared to littermate controls.
Results: Both the $Bsn^{Dlx5/6}$cKO and Bsn^{PV}cKO mice display strong social recognition deficits in 3-chambered test, increased stereotype behavior such as rearing and grooming behaviors andincreased anxiety. Further, $Bsn^{Dlx5/6}$cKO mice display deficits in nest building behavior in the home cage and a reduced approach towards females in estrus or their urine and a lack of ultrasonic vocalizations. Both the $Bsn^{Dlx5/6}$cKO and the Bsn^{PV}cKO mice display altered numbers of PV positive (PV+) interneurons in hippocampus.

Discussion and Conclusions: Human *BSN* gene mutations have been associated with Landau-Kleffner syndrome (an early childhood epilepsy), intellectual disability, schizophrenia. Together, these results suggest a disturbed GABAergic function, resulting from selective lossof Bassoon in GABAergic interneurons including PV sub-type in mice. The pronounced emotional and social behavioral changes are reminiscent of autism spectrum disorders,arguing that these models might be helpful to determine the critical synaptic and network activity changes involved under such neuropathological conditions.
Acknowledgement: Sincere thanks to DFG-CRC779 (Neurobiology of Motivated Behavior); Center for Behavioral Brain Sciences (CBBS) funded by Saxony-Anhalt and European Funds forRegional Development (EFRD) (ZS/2016/04/78113); CBBS Science Campus funded by the Leibniz Association (SAS-2015-LIN-LWC) for the financial support; Prof. Eckart D. Gundelfinger,Prof. Oliver Stork, Dr. Gürsel Caliskan and Dr. Carolina Montenegro-Venegas (Germany) for their constant scientific support and collaboration and Department of Biotechnology, Schoolof Bioengineering, SRM IST for providing new platform to continue the work in India.

YS1.3. Astaxanthin protection against neuronal excitotoxicity via glutamate receptor inhibition and improvement of mitochondrial function

Swapna K. K, Madhura Milind Nimonkar, SuraviSasmita Dash, Bhupesh Mehta, Yogananda S. Markandeya
Department of Biophysics, National Institute of Mental Health & Neurosciences (NIMHANS), Bengaluru, 5600029, INDIA

Background: Excitotoxicity, a well-known cause of neurodegenerative diseases is characterized by excessive release of glutamate, over activation of glutamate receptors, calcium overload, mitochondrial dysfunction, and excessive reactive oxygen species (ROS) formation. Astaxanthin (AST), a carotenoid antioxidant protects neurons from excitotoxic injuries. However, the mechanism of AST in neuroprotection is not clear.
Objective: To understand the role of AST in neuroprotection from excitotoxicity.
Materials and Methods: Cortical neuronal cultures were prepared from postnatal day-1Wistar rat pups. Fluorescence imaging was performed to study the intracellular calcium ($[Ca^{2+}]i$), ROS, mitochondrial membrane potential, and cell viability by using Fura AM, Dihydro ethidium, Rhodamine-123, and Calcein-AM & Ethidium homodimer. NMDA, AMPA, and KA receptor expressions were evaluated by Western blot.
Results: The AST-pretreated neurons showed increased cell viability (53%) upon glutamate exposure compared to controls (34%), and a significant reduction in $[Ca^{2+}]i$, mitochondrial calcium, ROS and mitochondrial depolarization. AST-treated neurons upon NMDA stimulation showed a 51%reduction in $[Ca^{2+}]i$, AMPA stimulation showed an inhibition by 20%;KA showed a reduction by 43%. AST significantly reduced the protein expression of NMDAR, and AMPAR by 63% and67% respectively, with no significant change in Kainate receptor expression.
Summary and Conclusion: AST alleviates glutamate-mediated excessive elevation in $[Ca^{2+}]I$ and secondary sustained calcium response. AST modulates Ca^{2+} influx through the ionotropic glutamate receptors as well as the protein expression of NMDA and AMPA, however, no change in KA receptors expression. Inhibition of abnormal ROS formation, mitochondrial membrane potential, and mitochondrial calcium accumulation by AST indicate its neuroprotective role. In conclusion, AST protects neurons from excitotoxicity by regulating cytosolic secondary calcium rise and mitochondrial calcium.
Ethics: Approved by NIMHANS IAEC.
Funding: SERB-DST Extramural for YSM, UGC fellowship for SKK.

YS1.4. NOX2 activation and alteration in mitochondrial dynamics involved in muscle damage following Japanese Encephalitis virus infection

Alok Kumar[1], Gajendra Singh[1], Kulwant Singh[2].
[1]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Department of Molecular Medicine and Biotechnology, Lucknow-226014, U.P., India; [2]Stem Cell Research Center, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, 226014, (UP), India

Background: Skeletal muscle wasting is a clinically proven pathology associated with Japanese Encephalitis Virus (JEV) infection; however, underlying factors for muscle damage are yet to be established. Here, we characterized the skeletal muscle from JEV-infected mice through histological, biochemical, and molecular

analysis.
Materials and methods: 3-weeks-old suckling BALB/c mice were intracranially infected with the JEV (GP78) strain with 3×10^6 plaque-forming units (PFU) by stereotaxic intracerebral injection. 7-days post-infection, tibialis anterior (TA) and extensor digitorum longus (EDL) muscles were isolated and processed for JE viral copy number, histological, biochemical, and molecular analysis.
Results: Histological analysis of TA and EDL muscles identified collagen deposition,decreased total nuclei count, and increased JE viral copy number, suggesting JE virus infection causes muscle death and fibrosis. Further, it is noted damage to skeletal muscle occurs through NOX2-mediated generation of reactive oxygen species, activation of apoptosis, and autophagy. The mitochondria dynamics (fusion/fission) have been found altered, resulting in a decrease in total mitochondria copy number.
Discussion and Conclusions: This is the first demonstration showing JE virus directlyinfects skeletal muscle and induces muscle cell death by activating the NOX2-mediated oxidative stress pathway. JE virus infection led to alterations in mitochondrial dynamics; however, the crosstalk mechanism between the NOX2 pathway and mitochondrial dynamics needs to be elucidated further.
Acknowledgements: This study is supported by the Ramalingaswami re-entry fellowship (BT/RLF/Re-entry/13/2014) from the Department of Biotechnology, Ministry of Science and Technology, Government of India, and Grant-in-aid Scheme of the Department of Health Research (DHR-GIA; R.11013/66/2021-GIA/HR) to Alok Kumar.

YS1.5. Pearls in the lake: Unique histomorphic features of psammoma bodies in human Choroid Plexus

Rajesh Kumar[1], Ravi K Narayan[2], Banshi Nath[1], Rakesh K Jha[2], Adil Asghar[1], Ashok Kumar Rastogi[3], Ashutosh Kumar[1]
[1]Department of Anatomy, All India Institute of Medical Sciences, Patna; [2]Department of Anatomy, ESIC Medical College, Bihta, Patna; [3]Department of Forensic Medicine and Toxicology, All India Institute of Medical Sciences, Patna

Background: The choroid plexus (ChP) is an indispensable component for brain homeostasis by regulating the secretion of the cerebrospinal fluid (CSF) and forming blood-CSF barrier. Naturally occurring changes with ageing within ChP have been noted but data regarding morphological characterisation of Psammoma bodies (PBs) within ChP is lacking.
Materials and Methods: A preliminary observational study was done for characterisation of histomorphic features of Psammoma bodies within ChP by various stains namely haematoxylin and eosin, Masson's trichrome (MT) and periodic acid Schiff (PAS). Samples were obtained from bilateral inferior horn of lateral ventricle of 7 postmortem human brains after proper consent.
Result: Middle-aged and older individuals exhibited a significant number of psammoma bodies within ChP. It is characterised by acellular, laminar structures in the connective tissue. Central heterogeneous calcification area surrounded by concentric acellular fibrous lamellae with an outermost cellular layer containing fibroblasts. Fibrous lamellae in blue and fibroblasts nuclei in black colour were clearly seen by MT staining. Epithelial basement membranes in pink with blue nuclei of fibroblasts were clearly appreciated by PAS staining.
Discussion and Conclusion: Because of the increase in the number of the elderly in the world's population, much attention is given to the study of ageing and age-related diseases, including neurodegenerative disorders. The nature and the mechanism of occurrence of PBs are not fully elucidated, but it is generally accepted that they represent dystrophic calcifications. Morphological appearance and characterisation by different staining techniques would help to differentiate age-related changes from the abnormalities that imply any pathological process.
Acknowledgement: We acknowledge the tissue donor and their family for greatest gesture towards scientific community. No funding was needed for this work.

YS1.6. A freshwater zooplankton, *Daphnia sinensis* as a disease model system in the study of motor symptoms in Parkinson's disease

Neethumol O P, Prabha Mariam Jacob, Khurana S, Vignesh O, Mullasseril R, Remya VR, Usha R, Pramod K, Chandra G, Mohanakumar KP

Inter University Centre for Biomedical Research & Super Speciality Hospital, Mahatma Gandhi University Campus at Thalappady, Rubber Board P.O., Kottayam, Kerala - 686009

Background: Animal models of neurological diseases are very crucial for understanding the disease processes, the discovery of biological targets for diagnosis, and the development of treatment strategies. Parkinson's disease (PD) pathophysiology can be characterized well the best animal model is MPTP-treated non-human primates that replicate all the behavioral syndromes. Lab-bred rodents, fishes, and lower animals such as *D. melanogaster*, *C. elegans* have been used in PD research. In view of the fact that idiopathic PD forms more than 90% of the population, and all forms of this disease have heterogenic aetiology and pathology, all types of animal models are very relevant for understanding PD aetiology and pathogenesis. Lower animals in research have several advantages such as low cost of maintenance, very swift reproductive cycle, well-defined neuropathology and behaviours, ease of genetic manipulation, and globally absent animal ethical issues for research use.
Materials and methods: Here we have identified a zooplankton crustacean *Daphnia sinensis* for characterizing PD biology in terms of behaviour and pathology. Initially we formed a colony of these animals from a single parent, and these cloned animals were characterized for their genetic uniqueness and identification by determining the mitochondrial genes, Cox I, and small subunit ribosomal RNA gene.
Results: We effectively used the phototactic behaviour of *Daphnia* to characterize the movement-pathophysiology of PD in them. The PD-neurotoxin MPP^+ dose-dependently (1-100 nM) reduced phototactic movement and speed, which correlated well with diminishing dopamine levels and its metabolism.
Discussion: We propose here that *D. sinensis* could be employed as a useful, valuable, and effective model organism in PD research. The advantages are such studies require inexpensive instruments, laboratory space and facilities, and ease of time.
Acknowledgement: The presenter is financially supported by UGC JRF, Mahatma Gandhi University and IUCBR & SSH

YS1.7. Study of early-stage Parkinson's illness EEG activity using wavelet techniques

Angana Saikia[1], Sudip Paul[2]
[1]Amity University Uttar Pradesh, Noida, India; [2]North-Eastern Hill University, Shillong, India

Background: Electroencephalography (EEG) is an effective tool for diagnosing neurodegenerative disorders like Parkinson's. PD is an age-related degenerative brain condition where the level of dopamine decreases. EEG captured by sensors is affected by artifacts. Wavelet analysis is a valuable tool for processing and analysis of EEG for disease detection.
Material and methods: EEG was acquired using dual channel Electrodes (AD instruments) from the frontal and temporal brain lobes. PD patients recruited were suffering from an early illness (Stage 1, 1.5). The mean age group of all the recruited participants (PD and Non-PD) was 60±10 years. The signal analysis was done in MATLAB.
Results: Using different wavelets: Daubechies, Haar, symlet, Coiflet, and EEG for various subjects were examined, and it was found that normal subjects showed a higher value than PD using Daubechies wavelet.
Discussion and Conclusions: Daubechies wavelet was most efficient at detecting various changes in Parkinson's Disease as Daubechies sequence has higher scalability and flexibility for weighting boundary problems. Daubechies wavelet showed a higher value in the case of the typical subject compared to Parkinson's disease patients for all the extracted features. This indicates an imbalance in the transmission of neuronal signals from the brain to the muscle in the case of a Parkinson's disease patient.
Acknowledgements: We want to acknowledge the doctors and technical staff of North Eastern Indira Gandhi Regional Institute of Health & Medical Science, Shillong, and North-Eastern Hill University, Shillong, for providing the required participants and laboratory space for our study.

YS1.8. Reviving mobility: Investigating the therapeutic potential of intermittent theta burst stimulation (iTBS) in spinal cord injured rats

Sharma G[1], Hariprasad G[2] Kochhar K P[1], Kumar N [3], Jain S[1]
[1]Department of Physiology, All India Institute of Medical Sciences, Delhi; [2]Department of Biophysics, All India Institute of Medical Sciences, Delhi; [3]Department of Psychiatry, All India Institute of Medical Sciences, Delhi

Background: SCI leads to severe neurological deficits, including paralysis and loss of sensory function. Intermittent theta burst stimulation (iTBS), a form of repetitive transcranial magnetic stimulation (rTMS), has been shown to induce long-term potentiation (LTP) and enhance synaptic plasticity in CNS. This study examines whether iTBS can elicit functional recovery in complete SCI rats.
Materials & Methods: Rats were randomly divided into five groups control, sham SCI, SCI, SCI+iTBS & SCI+sham stimulation. SCI surgery was performed at T13 spinal segment. iTBS was administered on primary motor cortex (50Hz, 2 sessions/day X 5days). Motor threshold (MT), motor evoked potential (MEP), BBB scoring, and urinary bladder function were recorded before and after the intervention. Rats were euthanized, and spinal cord tissues were collected for histological analysis.
Results: Preliminary results demonstrated that rats subjected to iTBS exhibited improved locomotor function compared to the SCI group. Electrophysiological recordings indicated increased cortical excitability, decreased MT in the iTBS treatment group, and increased MEPs amplitude in the treated groups. There was no significant improvement in urinary bladder function in SCI + iTBS treated group over SCI and sham stimulation groups. Histological analysis showed enhanced axonal sprouting and reduced glial scar formation in the iTBS group.
Discussion &Conclusion: The alterations in the MT and MEPs that were recorded from forepaw suggest cortical reorganization after the spinal cord injury. iTBS exposure also lead to reduction of lesion area, glial scar suggesting decrease in secondary damage. The results suggest that iTBS can potentially revitalize neural circuits and promote functional recovery in rats with complete spinal cord injury. The investigation has implications for developing novel iTBS paradigms to improve functional outcomes in individuals with SCI.
Acknowledgement: This work was supported by Department of Science & Technology (DST), Government of India and we would like to thanks CSIR/UGC for providing fellowship.

YS1.9. The Neural correlates of deception

PrashansaTripathi[1], Meghna Shekar[1], Sumit Sharma[1], Arun Sasidharan[2], Vrinda Marigowda[1]
[1]Axxonet Brain Research Laboratory (ABRL), Axxonet System Technologies Pvt. Ltd., Bengaluru, India; [2]Center of Consciousness Studies (CCS), Department of Neurophysiology, National Institute of Mental Health and Neurosciences, Bengaluru, India

Background: Deceiving is a complex cognitive act that involves interaction between different brain regions, especially in the prefrontal cortex. These interactions can help us gain a comprehensive understanding of the cognitive processes involved in deception. This study explores the change in EEG connectivity during lying in the CQT (Control Question Test) paradigm.
Materials and Methods: The study was conducted on 10 healthy-participants. EEG data was acquired with a 32-channel system (BESS) using saline-based cap at 1000Hz sampling rate. Using Brainstorm software, filtered and eye-blink removed 2s epochs were analyzed for Phase Transfer Entropy based connectivity.
Results: After multiple-comparison correction, we found stronger delta-band connection from TP8 to FP1inthe lying condition compared to the truth condition. No other frequency bands showed statistically significant connectivity differences
Discussion and Conclusion: Our finding shows that the right temporo-parietal (TP8) and frontal (FP1) brain regions were more synchronized when participants were lying than when telling the truth. This is in line with previous studies on the important role of frontoparietal networks in deception. Delta band is highly associated with attention and memory updating processes. So, the increased synchronization in delta band could indicate stronger attention to lie stimuli and more processing load of working memory during lying.
Acknowledgements: The authors would like to express their gratitude towards Munna RS, Varsha Vijayan, and other members of Axxonet for their contribution to this study. The authors would also like to thank all the participants of this study. This research work is supported by Axxonet Brain Research Laboratory, Axxonet System Technologies Pvt. Ltd., Bengaluru.

Young Scientist Colloquium-2

YS2.1 Closed head injury leads to bi-directional crosstalk between the brain and systemic physiology

PalkinArora[1,2], Megha Kumari[1,3], Kavita Singh[1], Poonam Rana[1], Maria MDsouza[1], Rajat Sandhir[2], Richa Trivedi[1]
[1]Radiological, Nuclear and Imaging Sciences (RNAIS), Institute of Nuclear Medicine and Allied Sciences (INMAS), DRDO, Delhi 110054, India; [2]Department of Biochemistry, Panjab University, Chandigarh,160014, India; [3]Department of Biotechnology, Delhi Technological University (DTU), Delhi 110042, India

Background: TBI is a stressful impact to the brain which can lead to progression of structural and functional deficits. Physiologically, a stressful event or trauma to the body leads to activation of the HPA axis as an adaptive response leading to release of glucocorticoids which can regulate the inflammation and metabolism in the system. Therefore, the study was aimed to evaluate HPA axis along with assessment of neuronal and systemic changes after closed head injury (CHI).
Materials and methods: To study CHI induced HPA axis dysfunction, brain microstructure was assessed using diffusion tensor imaging (DTI). Cellular and morphological alterations were observed in microglial and astrocytic population using immunohistochemistry. Serum corticosterone and ACTH levels were quantified using ELISA along with quantification of serum metabolitelevelsusing^{1}H-NMR. Systemic inflammatory markers (TNF-α,IL-1β andIL-10) levels were quantified. The gut microbiome composition was studied using 16S rRNA sequencing.
Results: TBI leads to structural changes in the brain as observed by decreased diffusivity parameters (Apparent diffusion coefficient) in the hypothalamus and hippocampus of the injured rats. The altered DTI scalars were accompanied by glial pathology and amyloid plaque deposition. The structural changes in the brain led to changes in the HPA axis with decreased serum ACTH and increased serum CORT levels. In addition, the serum pro- inflammatory cytokines were upregulated after injury. The serum metabolic profile showed increased lactate:pyruvate ratio and decreased amino acids after injury. Hyperactive HPA axis, inflammation and neurological alterations were accompanied by changes in the gut microbiome composition.
Discussion and conclusions: The neuronal structural changes are accompanied by glial pathology and axonal injury leading to hyperactive HPA axis with altered metabolism, inflammation and gut dysbiosis. CHI is a forceful impact to the brain that can lead neurological alterations as well as systemic perturbations. HPA axis, an important adaptive stress response system of the body gets dysregulated post injury and acts as a major mediator of bi-directional brain and systemic changes after injury.
Acknowledgements: This work was supported by the DRDO, Ministry of Defence, India (INM-324). Palkin Arora is supported by DRDO fellowship (EST/3009/JRF/2020). The authors would like to acknowledge Nucleome Informatics Private Limited for the fecal 16S rRNA sequencing.

YS2.2. A novel, non-toxic polymeric nanoparticle for neuronalmitochondria targeting

Nishad Keethedeth, Goutam Chandra, K P Mohanakumar, Rajesh A Shenoi
Inter University Centre for Biomedical Research & Super Specialty Hospital, Mahatma Gandhi University Campus at Thalappady, Rubber Board P O, Kottayam-686009, Kerala

Background: Mitochondrial dysfunction is implicated in several neurodegenerative diseases. Efficient and selective delivery of drugs to mitochondria requires design of safe nanocarriers. Here, we report a safe, neutral, and versatile polymeric nanocarrier system based on multivalent presentation of triphenylphosphonium (TPP) on dendritic polyglycerol (PG) for targeting drugs to neuronal mitochondria.
Materials and Methods: PG nanoparticles were synthesized by anionic ring-opening polymerization and reacted with TPP to generate PG-TPP conjugates. Mitochondrial localization of FITC-labelled conjugates was achieved in SH-SY5Y neurons by fluorescence imaging. Neurotoxicity of the conjugates was investigated by assessment of cell viability, mitochondrial membrane integrity, and ROS generation.
Results: Neurotoxicity and mitochondrial localization of the PG-TPP conjugates were dependent on molecular weight and the density of TPP groups. All the conjugates were non-toxic to neurons up to 100 μM.

This displayed efficient mitochondrial localization, with PG-4 kDa-15TPP showing the highest (98%) intra-mitochondrial localization, without altering the mitochondrial membrane potential at 100 µM. This conjugate exhibited excellent mitochondrial localization when incubated with MPP^+- treated cells without altering mitochondrial membrane potential and with reduced ROS generation.

Discussion and Conclusion: The present study revealed that molecular weight and TPP density of the nanocarrieraffect mitochondrial localization and neurotoxicity., Apparently, optimizing these parameters is critical in designing mitochondrial drug delivery systems. This is the first report of selective mitochondrial localization of a dendritic polymer nanoparticlein neurons. These dendritic polymer nanoparticles exhibited improved safety profiles when compared to dendrimers, designating them as a potential nanodrug delivery system for mitochondrial targeting.

Acknowledgment: This research was funded by Core Research Grant (CRG/2019/006028) fromScience and Engineering Research Board, Government of India. Financial supports from Higher Education and Health & Family WelfareDepartments, Government of Kerala are acknowledged.

YS2.3. CREB-binding protein (CBP) plays an essential role in the regulation of cocaine and amphetamine-regulated transcript peptide (CARTp) during operant conditioning for intracranial self-stimulation

Namrata Pawar[1], Biru Dudhabhate[2], Dipak Sahare[2], Dadasaheb Kokare[2], AmulSakharkar[1]
[1]Department of Biotechnology, Savitribai Phule Pune University, Pune, Maharashtra, India411007
[2]Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, Maharashtra, India 440033

Intracranial self-stimulation (ICSS) in lateral hypothalamus-medial forebrain bundle (LH- MFB) is widely employed to unravel the molecular underpinnings of reward and reinforcement. Cocaine- and amphetamine-regulated transcript peptide (CARTp) in LH-MFBis induced by both, natural stimuli and addictive drugs. However, the role of experience- dependent chromatin remodelling in the CARTp regulation remains elusive. The current study probes the involvement of CREB-binding protein (CBP), a transcription factor with intrinsic histone acetyltransferase activity in the CART expression during ICSS. The male Wistar rats (n=6) were stereotaxically implanted with the bipolar electrode targeted at the right LH-MFB. Animals were trained to press the lever to seek electrical self-stimulation for reward stimuli. ICSS conditioning increased the CART mRNA levels in LH. Immunohistochemistry showed the heightened levels of CART and pCREB post conditioning. Further, ICSS also induced CBP binding and histone acetylation (H3K9) levelson the CART promoter as measured by chromatin immunoprecipitation assay. CBP siRNA (2µg/µl) infusion in LH not only attenuated self-stimulatory activity but also reduced CART mRNA levels in the LH. In addition, CBP binding and H3K9 acetylation levels on CART promoters were lowered reflecting the crucial role of CBP-mediated histone acetylation in CART gene regulation. Interestingly, CBP siRNA-mediated reduction in self-stimulation wasalso rescued by co-infusion of CART peptide. Hence, these results strongly implicate the CBP-induced CART expression within the framework of LH in the reward and reinforcement.

Acknowledgement for funding support from: SERB-DBT, UGC (Govt. of India)

YS2.4. Identifying emotions par formats: EPN and LPP during emotion recognition in human faces, emoji faces, and stick figures

Munna R. Shainy[a], Meghna Shekar[a], Sumit Sharma[a], Arun Sasidharan[b], Vrinda Marigowda[a]
[a]Axxonet Brain Research Laboratory (ABRL), Axxonet System Technologies Pvt. Ltd., Bengaluru, India; [b]Centre for Consciousness Studies (CCS), Department of Neurophysiology, National Institute of Mental Healthand Neurosciences, Bengaluru, India

Background: Evidence suggests humans recognize emotions, not just in other human beings but also in inanimate objects. In today's world of digital-mediated communication, where emotions are depicted using 2D or 3D counterpart formats, this study aims to demarcate if human faces, emoji faces, and stick figures are differently processed cortically.

Materials and Methods: Eight young healthy-adults attempted a visual search paradigm-based experiment in which they recognized positive, negative, and neutral emotions shown in three formats. Simultaneously,

32-channel EEG recordings were acquired to study the event-related potentials: early posterior negativity (EPN) and late positive potential (LPP) in the posterior areas of the brain.

Results: Irrespective of image format, the area under the curve (AUC) of EPN was most negative during recognizing neutral emotions, while that of positive emotions was the least. On the other hand, LPP was higher during negative emotion recognition and least during neutral emotion recognition. Considering image format, posteriorLPP was elicited more during emotion recognition in human faces, followed by stick figures and emoji faces, while posterior EPN showed the opposite trend.

Discussion & Conclusion: The current results of the inquiry are consistent with existing literature indicating typical sustained deeper processing but weaker rapid initial emotion processing of human facial features. Notably, this study unveiled stick figures elicit relatively intermediate posterior EPN and LPP, plausibly signifying a distinct pattern of neural processing mechanism while perceiving embodied emotions in body postures. Overall, current findings suggest neural responses to emotion recognition in stick figures are more similar to humans than emoji faces.

Acknowledgments: The authors would like to extend their sincere gratitude to Axxonet System Technologies, Bengaluru, for funding this research project and to the participants of the study, Prashansa Tripathi, Varsha Vijayan, and other staff members of Axxonet System Technologies, Bengaluru, for their contributions towards this research. We also want to acknowledge Dr. Nim Tottenham (Development Affective Neuroscience Lab, Columbia University, USA) for granting the NimStim Set of Facial Expressions material required for this project.

YS2.5. Medial-Septal GABAergic neurons are essential for social memory in mice

Apoorva Bettagere Shivakumar, Sonam Fathima Mehak, and Gireesh Gangadharan
Department of Cell and Molecular Biology, Manipal School of Life Sciences, Manipal Academy of Higher Education (MAHE), Manipal-576104, Karnataka, India

Social memory, the ability to recognize and remember familiar conspecifics, critically relies on the hippocampal region. Interestingly, it has been described that the medial septum (MS), which constitutes a heterogeneous population of neurons provides rhythmic drive to the hippocampus and control diverse behaviors. In particular, the innervation of hippocampal inhibitory interneurons by septal GABAergic neurons modulates hippocampal function and information processing. However, the role of septal GABAergic neurons in social memory remains elusive. We examined this issue using a novel immunotoxin, anti-vGAT-SAP (vesicular GABA transporters-saporin), to selectively lesion GABAergic neurons in the MS. Here, our findings show that lesions of MS GABAergic neurons in mice resulted in impaired social memory, while sociability and social novelty preference remained intact. Moreover, these lesions led to disrupted theta rhythm in the dorsal CA2 (dCA2) region of the hippocampus, a crucial area for social memory. Additionally, we observed altered expression of arginine vasopressin (AVP) and oxytocin (OXT), key mediators of social behaviors, in the dCA2 area of the hippocampus. Together, our results indicate that septo-hippocampal GABAergic neuronal circuit is an important component of social memory. Importantly, these results support the notion that inhibition/excitation imbalance in the hippocampus contributes to social deficits reminiscent of neuropsychiatric/neurodevelopmental disorders.

Acknowledgement: This work was supported by Ramalingaswami Re-entry Fellowship, Department of Biotechnology, Government of India (No. BT/RLF/Re-entry/49/2018) and Science and Engineering Research Board (SERB), Government of India (No. CRG/2020/004205) to GG. ABS was supported by Innovation in Science Pursuit for Inspired Research (INSPIRE) fellowship, Department of Science and Technology, Government of India (IF190783). The authors thank the DBT-Builder grant, Manipal School of Life Sciences, Manipal Academy of Higher Education (MAHE), Manipal, Karnataka for the infrastructure and support.

YS2.6. ICAM-1 reduces Amyloid β mediated neuroinflammation and cognitive impairment by potentiating microglial phagocytosis

Soumita Goswami, Subhas C Biswas
Cell Biology and Physiology Division, CSIR-Indian Institute of Chemical Biology, 4 Raja S. C. Mullick Road, Kolkata 700 032, India

Background: Alzheimer's Disease (AD), the most prevalent neurodegenerative disorder currently affects almost 70% of total dementia patients worldwide. Neuroinflammation plays major role in development of AD pathologies like neuronal loss, synaptic degeneration and ultimately cognition and memory impairment. However, identifying molecules to target inflammation associated disease manifestation is yet to be discovered.
Results: Here we have found that, Aβ causes induction of inflammation in microglia cells by activating ERK MAPK pathway. Microglia secreted ICAM-1 is found to potentiate microglial phagocytosis of Aβ, thus reducing Aβ induced ERK phosphorylation which leads to reduced inflammation in microglia. Not only that, intra peritoneal administration of ICAM-1 also reverts Aβ associated cognitive and memory deficits by restoring synaptic protein expressions in 5xFAD TG mice. Lastly we have seen inhibition of interaction between ICAM-1and its receptor LFA-1 renders ICAM-1 mediated cognitive improvement
Discussion: So far, these data suggest that ICAM-1 plays a pivotal role in regulation of neuroinflammatory meshwork of AD by inducing phagocytosis of Aβ and restores memory and cognition by improving synaptic health. Thus, targeting this interaction could be a good therapeutic strategy to reduce neuroinflammation and associated AD hallmarks.
Materials &methods: To assess the effect of ICAM-1 *in vitro,* we performed Western blot and immune cytochemistry and to assess *in vivo* we did immunohistochemistry, western blot, behavioral assays like novel object recognition, open field test and cue dependent fear conditioning tests.
Acknowledgement: The work was supported in part by one of the 12th Five Year Plan Projects, miND (BSC0115) of CSIR, Govt. of India.

YS2.7. Diet restriction-induced reward sensitization: A role for chromatin remodeling in dopaminergic neurocircuit

Vaishnavi Borade, Smruti Sahoo, Amul Sakharkar

Department of Biotechnology, Savitribai Phule Pune University, Pune 41100

The dopaminergic neurocircuit between ventral tegmental area (VTA)-nucleus accumbens (NAc) serves as an epicenter of reward. It is highly sensitive to dietary patterns, feeding habits and energy valence. Diet restriction increases dopamine (DA) release and reinforcing properties of rewarding stimuli. However, the precise mechanisms of diet-restriction-induced reward sensitization are largely elusive. Adult male Wistar rats were subjected to diet restriction for 48 hours followed by food *ad libitum*. After diet restriction and feeding, behavioural sensitization for reward was investigated by using nose-poke operant conditioning. Interestingly, diet restriction dramatically enhanced nose-poke activity to seek sweet pellets. This effect persisted for a duration of three days, highlighting a state of heightened sensitivity to rewards. On fifth day, the number of nose-pokes reduced to normal levels. Diet restriction heightened the expression of dopamine receptor1 (DRD1) and transporters (DAT) in the NAc. Moreover, tyrosine hydroxylase (TH) levels in the VTA were also improved after diet restriction. The increased neuronal activity in NAc is further supported by elevated levels of *cFos* and *Bdnf*. Diet restriction caused chromatin remodeling by altering histone methylation (H3K4me2 and H3K9me2) at the promoter of *Drd*1, which was likely modulated by two distinct histone methyltransferases, MLL1andG9a. These results implicated MLL1 and G9a in the formation of open chromatin to induce the *Drd*1 expression in response to diet restriction. Insum, the present study underscores the causal role for chromatin remodelling in diet restriction-induced reward sensitization by undertaking neuroadaptations in the dopaminergic neural circuit.
Acknowledgment for funding support from: SERB-DBT, UGC (Govt. of India)

Posters

P1: G6PD-Nitric oxide axis: a fundamental regulator of neuroinflammation and phagocytotic clearance of SARs-CoV2 Spike protein

Abir Mondal[1], Subrata Munan[2], Isha Saxena[1], Soumyadeep Mukherjee[1], Prince Upadhyay[1], Waseem Dar[1], Nutan Gupta[3], Animesh Samanta[2], Shailja Singh[3] and Soumya Pati[1]
[1]Department of Life Sciences, School of Natural Sciences, Shiv Nadar Institution of Eminence, Delhi-NCR, India; [2]Department of Chemistry, School of Natural Sciences, Shiv Nadar Institution of Eminence, Delhi-NCR, India; [3]Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi, India.

Background: Glucose 6 Phosphate dehydrogenase (G6PD)-derived NADPH can follow pro-oxidative and anti-oxidative pathways for the generation and removal of ROS respectively in a tissue-specific manner. Therefore, the deficiency of G6PD leads to the dysregulation of microglial defense mechanisms which can facilitate SARs-CoV2 pathogenesis and may
cause several neurological disorders.
Materials and Methods: Human microglia activation was confirmed by qPCR. The production of Nitric oxide (NO) and phagocytosis were evaluated by confocal microscopy. SARs-CoV2 responses were evaluated by using spike protein. Additionally, the CRISPR-mediated G6PD deficient microglia model was used to identify the role of the G6PD-Nitric oxide axis in neuroinflammation and phagocytic clearance.
Results: Our data indicated that G6PD-derived NADPH is essential for NO production in human microglia. NO plays a crucial role in the phagocytic clearance of foreign particles. The G6PD deficiency causes a 70% reduction in NADPH level which further affects NO production and ROS regulation in human microglia. As a result, G6PD deficiency and dysregulation of NO signaling aggravate SARs-CoV2 pathophysiology.
Discussion and conclusion: G6PD is the most crucial enzyme for restricting SARS-CoV-2-mediated neuroinflammation. A deficiency of G6PD leads to a reduction in NO production and an alteration of redox equilibrium which further aggravated Covid-19 responses. However, we are also generating clinically relevant G6PD variants to study its responses in neuro-glia interaction for a detailed understanding of neuroinflammation.

P2: Relationship between levels of Vitamin D and cognitive functioning in an urban Indian ageing cohort: An explorative study

Aishwarya Ghosh, Palash Kumar Malo, TLSA Study Team, Thomas Gregor Issac
Centre for Brain Research (CBR), IISc. Bangalore

Background: Vitamin D regulates the calcium and phosphate balance in the human body andhas implications in brain health and cognitive functioning. Studies suggest that low levels of Vitamin D are associated with impaired cognitive functioning. This study aimed to investigate the relationship between Vitamin D and cognition.
Materials and Methods: 999 healthy individuals were recruited from the baseline data of theCBR-Tata Longitudinal Study for Aging (TLSA). Addenbrooke's Cognitive Examination-III (ACE-III) and Hindi Mental Status Examination (HMSE) scores were considered to measure cognitive functioning and Vitamin D levels were obtained. Data was analysed using IBM SPSS software.
Results: Participants were divided into age-groups of 45-54, 55-64 and >65 years. Globalstandards of Vitamin D levels of <20ng/ml (high risk), 20-40ng/ml (insufficient) and>40ng/ml (normal) were considered. Shapiro-Wilk test was used to check for normality. Kruskal-Wallis's H-test indicated no significant difference ($p > 0.05$) in cognitive functioningbetween participants with different levels of Vitamin D across the age groups.
Discussion and Conclusions: The results suggest that there was no relationship between thelevels of Vitamin D and cognitive functioning in the cohort as opposed to the current body ofliterature. Hence, these results provide scope for further investigation and subsequently a potential for developing new standards of Vitamin D levels for the Indian population.
Acknowledgements: I would like to acknowledge all the members of the CBR-TLSA for helping us with the collection of data. I would thank the participants for their participation and kind cooperation. I also extend my gratitude to Tata Trusts and Centre for Brain Researchfor their financial support.

P3: Expression of Neurotrophins (BDNF and NT-3) and their Receptors in Adult Human Cochleae

Akanksha Mishra[a], Dr Abhishek Yadav[b], Dr T.C. Nag[a] Dr T.S. Roy[c], Dr Tony George Jacob[a]
[a] Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India; [b] Department of Forensic Medicine and Toxicology, All India Institute of Medical Sciences, New Delhi, India; [c] Department of Anatomy, North DMC Medical College & Hindu Rao Hospital, New Delhi, India

Background: Sensorineural hearing loss's definitive management is cochlear implantation, contingent on presence of SGNs, hair-cells. Their age-related degeneration is a limiting factor in cochlear implant efficacy. Neurotrophins are keystones for development, differentiation of SGNs and synapses. They're expressed in mice, rat, chick cochleae: experimental absence leading to deafness; delivery, SGN survival. Neurotrophin expression in human cochleae remains unexplored.
Methods: Twelve human temporal bones containing cochlea were derived within 24 hours of death. Bones fixed in 4% paraformaldehyde, decalcified with 10% EDTA for twelve weeks, cryoprotected, mounted, sectioned at 40µm on a cryotome to obtain coronal sections of cochlea. Immunohistochemistry was used for studying expression of BDNF, NT-3, and receptors.
Results: BDNF and NT-3 expressed in SGNs and neuropil, showing membranous and cytoplasmic positivity. Apical layer of stria vascularis (SV) expressed distinct positivity among three layers. SGNs expressed bipolar positivity for TrkB, TrkC. Entire SV stained positive for receptor proteins.
Conclusion: It can be extrapolated that apical layer of SV produces neurotrophins which act on cells expressing TrkB/TrkC. This information extrapolated across ages can provide insight for future therapeutic intervention. Age-related changes will be concluded with including more age-groups in this qualitative observational study.
Acknowledgements: ICMR Project No. 51/1/2018-ANA/BMS

P4: Iron overload and unfolded protein response (UPR): Induction of UPR after iron accumulation in the retina of male Wistar rat

Akanksha Singh, Tapas C Nag
Department of Anatomy, All India Institute of Medical Sciences, New Delhi 110029

Background: Unfolded protein response (UPR) combats the endoplasmic reticulum (ER) stress caused by increase in unfolded proteins and maintains protein homeostasis. It acts via upregulation of ER chaperones such as GRP78, attenuation of protein translation mediated by the phosphorylation of eIF2α by PERK and degradation of misfolded proteins via ER associated degradation. Mechanisms of iron accumulation in the retina, leading to ER stress and modulating UPR are unclear. This study was aimed to see if retinal cells develop ER stress after iron accumulation and how ER stress influences UPR in iron-accumulated retina.
Material and methods: Male Wistar rats (aged 2 months) were treated with ferrous sulphate dissolved in water by oral gavage (500 mg/kg body weight/week). The control animals received water as vehicle. Animals were euthanised, killed after 6 and 8 months of chronological age, their eyes enucleated and fixed in 4% paraformaldehyde. Histochemical staining with Perls Prussian blue (iron deposition), and immunohistochemical localisation of the markers of iron homeostasis (Transferrin, ferroportin), GRP78 and UPR markers (CHOP, p-PERK) were performed.
Results: Mild positive Perls staining was seen in the retina of experimental rats. Increased expression of iron regulators was found in experimental groups. Upregulation in the immunoreactivity of GRP78 was seen in cell layers of the retina in six- and eight-month group. As compared to control group, increased immune expression of CHOP and phosphorylated PERK was seen in retinal cell layers of experimental groups.
Discussion and conclusions: These data suggest iron accumulation-induced ER stress causes activation of unfolded protein response in the retina.
Acknowledgements: Supported by funds from ICMR, New Delhi (51/4/2000-ANA/BMS).

P5: The neuronal NOS activates SC-VTA circuitry during reversal learningbehaviour impaired in schizophrenic like condition in rats

Akash M. Waghade[1], Ashwini A. Patil[1], Dipak K. Sahare[1], Sanjay N. Awathale[1], Nishikant K.Subhedar[2], Dadasaheb M. Kokare[1]
[1]Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University,Nagpur- 440 033, Maharashtra, India; [2]Indian Institute of Science Education and Research, Dr Homi Bhabha Road, Pune-411 008, Maharashtra,India

Background: The change in environment causes superior colliculus (SC) to regulate reversal performance, whereas the ventral tegmental area (VTA) conserves reward processing. In schizophrenic illness reversal learning gets disrupted. The neuronal NOS has abundantly present in SuG layer of SC. However, the role of neuronal NOS in SC-VTA circuitry for reversal learning behavior impaired in schizophrenic illness is not established yet.
Materials and Methods: Reversal learning was assessed in adult male Wistar rats in operant chamber. MK801 treatment (ip) was given to impair reversal learning. Open field test was used to assess locomotion activity. The 7-nitroindazole (7-NI; nNOS inhibitor) and L-arginine (nitric oxide precursor) treatment was given via intra-SuG. Additionally, combination treatments like MK801+L-arginine and MK801+aCSF was employed. The neuronal NOS and TH immunohistochemistry (IHC) was performed. DiI retrograde tracer was given in VTA to track projection from SC to VTA.
Results: MK801 treated rats decreased lever press activity and showed hyper-locomotion during reversal learning than the saline treated group. In combination group, MK801+L-arginine showed significantly elevated lever pressings and switching behavior, and decreased hyper-locomotion compared to MK801+aCSF. While 7-NI significantly increased lever pressings and switching behavior, L-arginine had no effect on both the parameters. The IHC study revealed that NOS and THcells were increased in reversal trained group. The retrograde tracing has revealed the NOS positive cells of the SC were projected to the VTA.
Discussion and conclusion: The prior treatment of L-arginine has improved reversal learning impaired by MK801 treatment. The 7-NI and/or L-arginine treatment has enhanced reversal learningbehavior in rats. It suggests that neuronal NOS of SC has prominent role in reversal learning impaired in MK801treated rats. Additionally, we observed neuronal NOS positive cells in SC and TH cells in VTA. Furthermore, we found that NOS cells were projected in VTA. Herein, the presentresearch work demonstrated that the neuronal NOS in SC might regulate reversal learning behavior via SC-VTA circuitry, and could be helpful for improving schizophrenic illness.
Acknowledgement: This work was supported by the grants from (DST-SERB) (CRG/2020/004971), Govt. of India, New Delhi, India and Mahatma Jyotiba Phule Research & Training Institute (MAHAJYOTI) fellowship, (An Autonomous Institute of The Other BackwardClass Bahujan Welfare Department, Govt. of Maharashtra).

P6: Impact of gender on the progression of Alzheimer's disease in AβPP-ps1mouse model: a behavioral and metabolic analysis

Akila Ramesh[1, 2], Anant Bahadur Patel[1, 2]
[1]NMR Microimaging and Spectroscopy, CSIR-Centre for Cellular and Molecular Biology, Habsiguda, Uppal Road, Hyderabad 500007, India; [2]Academy of Scientific and InnovativeResearch, Ghaziabad 201 002, India

Background: Alzheimer's disease (AD), an age-related neurodegenerative disorderwith progressive loss of memory, is the most common form of dementia that accounts for about 60-70% of the cases.Epidemiological studies suggests that two-thirds of AD subjectsare women. However; it is not clear whether the higher prevalence of AD in women is due to longer life expectancy or increased susceptibility.
Materials and methods: Transgenic AβPP-PS1 male and female mice (6 months) were used for the study. The learning and memory of the mice were assessed using Y- maze and Morris Water Maze (MWM) test. Proton observed Carbon-13 edited NMRspectroscopy together with an administration of [1,6-$^{13}C_2$] glucose was used to monitor the metabolic activity of neurons.
Results: Male AβPP-PS1 and WT mice recorded an escape latency of 70.8±23.8 s and 61.6±29.8 s, respectively, in MWM test. Female AβPP PS1 reached the platform at 59±26.2s while WT mice reached at

59.1±27.6 s on an average. In Y maze, the spontaneous alternation of male AβPP-PS1 was 54.5±11.7 % while that of WT was 58.5±1.0 %. Similarly,the female AβPP-PS1 showed 65.2±7.6 % alternation while WT mice had 63.4±10.5 %. Theevaluation of neurometabolites homeostasis and the cerebral metabolic rates of glucose oxidation are in progress.

Discussion and conclusion: Memory assessment through Y-maze and MWM test revealed that memory was intact in male and female AβPP-PS1 mice at 6 months of age. Since molecular/metabolic changes precede phenotypic changes, we anticipate perturbation in neurometabolic activity in transgenic AβPP-PS1 mice in a region-specific manner. This will be identified in metabolic measures.

Acknowledgements: This study was supported by Council of Scientific and IndustrialResearch (CSIR-CCMB: NCP/MLP0139).

P7: Sertad1 depletion using lentivirus ameliorates behavioural deficits by autophagy modulation in models of Alzheimer's disease

Naqiya Ambareen, Subhas C Biswas
Cell Biology and Physiology Division, CSIR-Indian Institute ofChemical Biology, 4, Raja S.C. Mullick Road, Jadavpur, Kolkata- 700032 and Academy of Scientific and Innovative Research (AcSIR), Sector 19, Kamla Nehru Nagar, Ghaziabad, Uttar Pradesh- 201 002

Background: Dysfunctional autophagy, marked by abnormal accumulation of autophagosomes is a prominent characteristic of the Alzheimer's brain. Sertad1, a transcriptional coregulator is upregulatedin response to Aβ toxicity and aids in neurodegeneration. This study explores the role of Sertad1 in autophagy modulation in cell and animal models of Alzheimer's disease.

Materials and Methods: To study autophagy dysfunction in AD, lysates from cortex and hippocampusof 5xFAD mice were prepared and subjected to Western blotting. For mechanistic studies, Sertad1 wasdepleted using shRNA followed by Western blotting and immunocytochemistry experiments to check for its effect on autophagy modulation. Lentivirus containing shSertad1 was injected by bilateral stereotactic surgery in 5xFAD mice brain and behavioral studies were carried out to check for cognitiverecovery. Golgi staining was done to determine number of dendritic spines.

Results: Autophagy markers are robustly induced with disease progression in 5xFAD mice at differentages. Sertad1 is also upregulated in 5xFAD mice brain. shSertad1 confers neuroprotection in primary neurons by lowering autophagy markers, LC3 and p62. Sertad1 depletion increased P-FoxO3a levels at Ser 253 responsible for its cytosolic retention due to Akt activation. Further, 5xFAD mice infused withshSertad1 containing lentivirus performed better in fear based cognitive learning and spatial memory tasks. These animals also showed better synaptic health and lower autophagy levels.

Discussion and Conclusions Impaired autophagy results in a failure of autophagosome clearance fromthe brain. Sertad1, a transcriptional coregulator is upregulated in Alzheimer's disease. Sertad1 depletionprotects neurons against Aβ induced toxicity by autophagy modulation. FoxO3a, translocates to the nucleus to activate autophagy and apoptosis genes. Depletion of Sertad1 blocks FoxO3a nuclear translocation and this is regulated by Akt activation. 5xFAD mice that were infused with lentivirus expressing shSertad1 performed remarkable well in locomotor activity, fear conditioning and spatial learning tasks and showed synaptic recovery. Overall, this study shows that Sertad1 depletion can modulate autophagy flux and provide behavioral benefits to 5xFAD mice and is an excellent target fortherapeutic intervention.

Acknowledgements: This work was supported in part by Council of Scientific and Innovative Research (CSIR), Govt. of India and Academy of Scientific and Innovative Research (AcSIR)

P8: Investigation on agmatinergic pathway in attention deficit hyperactivity disorder using exposure of 6-ohda in mice

Amit Shiwal, Apeksha Tambe, Nitu Wankhede, Mayur Kale, Brijesh Taksande, Milind Umekar
Division of Neuroscience, Department of Pharmacology, Smt. Kishoritai Bhoyar College of Pharmacy, Kamptee Nagpur, Maharashtra, India – 441002.

Background: Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that affects both children and adults and is characterized bypersistent patterns of inattention and impulsivity that

significantly impact daily functioning and quality of life. During adolescence, the prefrontal cortex develops connectivity with other brain regions to engage executive functions and impulsive behavior

Materials and methods: Swiss albino mice (SAM) exposed to 6-OHDA hydrobromide on PND 5 underwent assessment: Hyperactivity (open field), Attention/Impulsivity (Object-based task), Memory (Elevated plus maze), Anxiety (Marble Burying Test), Depression (Sucrose preference), and Anti-social behavior (Social interaction task). Oxidative stress markers, Neurotransmitter levels were also analyzed.

Results: In the present study, 6-OHDA-induced ADHD-like behavior was significantly attenuated by agmatine (20, 40, and 80 mg/kg, i.p.), L-Arginine (60 mg/kg,i.p.), Aminoguanidine (50 mg/kg, i.p.), Arcaine (30 mg/kg, i.p.). Since ADHD is associated with increased oxidative stress and inflammation as well as alterations in neurotransmitter levels, we have also monitored the nitrite, lipid peroxidation, reduced glutathione, and superoxide dismutase, as well as Dopamine and GABA levels in 6- OHDA-mice.

Discussion and conclusions: Injection of 6-OHDA induced dopaminergic neuron lesions, mimicking ADHD-like human pathophysiology. Agmatine and its modulators mitigated ADHD-associated hyperactivity, anxiety, depression, anti-social tendencies, inattention, and memory deficits. Additionally, agmatine notably elevated dopamine levels and, in combination with its modulators, effectively curtailed oxidativestress linked to 6-OHDA-induced ADHD-like behavior in mice. Overall, these results propose agmatine as a potential therapeutic avenue for addressing behavioral alterationslinked to ADHD, warranting further investigation for clinical application.

Acknowledgements: Not Declared.

P9: Identification of common biological pathways between Alzheimer's disease (AD) and metabolic disorders (MD)

Ananya Shukla, Neha Singla, Rajat Sandhir
Department of Biochemistry, Panjab University, Chandigarh- 160014

Background: Alzheimer's Disease (AD) is an age-related neurodegenerative disorder. People afflicted with metabolic disorders like Diabetes and Obesity have a higher chance of developing AD. As number of individuals affected by metabolic disorders increases, the patients impacted by ADwill also exponentially grow. However, the exact mechanism responsible for this association is not fully understood**.**

Materials and Methods: Firstly, transcriptomic analysis was conducted using Illumina Base Space Correlation Engine (BSCE) to discover Differentially Expressed Genes (degs) followed by pathway enrichment.These results were validated in female Wistar rats through biochemical tests, HPLC, ELISA and molecular biology assays like Western blot and RT-PCR to determine the prominent changes induced by the three diseases among the ascertained pathways.

Results: The *in-silico* study helped delineate 11 common genes between the datasets: TNFAIP6, HIGD1A, RPS15A, GNG11, DPH3, CARD16, ATP5F1C, NGDN, AIM2, TNFSF10, RPL9**.**The pathway enrichment of the degs focused on biological processes primarily related to neurotransmission (like gabaergic pathway), Immune system and Oxidative Phosphorylation. The pathways ascertained from computational analysis were found to be significantly dys-regulated in rat brain due to the three disorders. Neuroinflammation and glutamate excitotoxicity were found to be increased in rat brain. The levels of neurotransmitterswere also observed to be disturbed in Wistar rats**.**

Discussion and Conclusion: The results clearly suggest role of metabolism in development of neurodegenerative phenotype in animal model. Apart from the delineated pathways, neurodegenerative markers and inflammatory conditions were also increased in rat brain. These are prominent indicators of neurodegeneration. Further, the pathways determined from *in-silico* analysis help understand the mechanisms through which a dysfunctional metabolism might lead to neurodegeneration. This study has aided in identification of novel cellular and molecular mechanisms that might link AD progression with metabolic disorders and will further aid in formulating new treatmentregimens.

Acknowledgement: The fellowship provided by University Grants Commission (UGC), New Delhi (referencenumber: 559\CSIR-UGC NET JUNE 2019) is acknowledged.

P10: Stripe Factors for targeted epigenetic remodeling for nervous system regeneration

Anisha S Menon, Dhruva Kesireddy, Manoj Kumar Kumaran, Sneha Manjunath, Shaik Shafiulla, and Ishwariya Venkatesh
Laboratory of Axon Growth and Regeneration, CSIR-CCMB, Hyderabad

Background- The bundle of Axons which ferry the signal back and forth between the Brain and Body is critical for normal nervous system function. When injured, this disrupts the communication vital for the nervous system's function. Axonal injury necessitates precise transcriptional control to initiate a regenerative response which is coordinated by master proteins called Transcription factors (TFs). These factors then re-activate genes supportive of growth (pro- growth genes). Although transcription factors are crucial for gene activation, a prerequisite for their function is the availability of relaxed chromatin around pro-growth genes. Therefore, epigenetic factors are higher up in the regulatory cascade and gate accessibility to TFs to activate genes. DNA methylation patterns and histone modifications are altered, influencing accessibility and the expression of pro-growth without modifying the underlying DNA sequences. Understanding the nature and pattern of self-imposed epigenetic constraints in injured neurons is a vital component in achieving neural repair.
Materials and Methods- We are using an integrated approach starting with *in vitro* assays of growth, *in vivo* models of injury, and functional epigenomics.
Results- Previously, we have shown that in adult neurons, the chromatin is entirely restricted around pro-growth genes, preventing TF access. However, broad remodelling genome-wide is ineffective in chromatin relaxation and thereby increasing the expression of the gene. To override the lack of targeting with broad remodelers, we are now focusing on achieving targeted remodelling. To this end, we are exploring a novel set of proteins, called stripe factors to enable targeted remodeling. Our preliminary data suggests that the extent of chromatin restriction around pro-growth gene loci is more severe than previously demonstrated and that stripe factors may be playing an essential role in chromatin remodelling during development.
Discussion and Conclusion- Currently, we are testing the effects of stripe factors such as Patz1, Sp2, Klf6, etc. for their ability to induce precise chromatin relaxation around pro-growth genes and ensuing gene expression and regeneration. This research will clarify novel fundamental molecular mechanisms that control nervous system development and regeneration. In the future, our findings could help in designing targeted therapeutic strategies to achieve neural repair.
Acknowledgment- Council for Industry and Scientific Research (CSIR).

P11: Exploring the links between serum uric acid levels and cognition – A study conducted in an Urban Cohort, Southern India

Anjana J Menon, Ashvin V, Shubham Jain & TLSA Study teams, Thomas Gregor Issac
Centre for Brain Research, Indian Institute of Science, Bangalore

Background: There is an intricate relationship between uric acid and cognition. The antioxidant property of uric acid confers neuroprotective effect. Nevertheless, increased uric acid levels can have detrimental effects on cognition. Therefore, this study tries to understand the relationship between uric acid levels and cognition among urban-dwelling individuals in Southern India.
Methodology: 156 participants, aged ≥ 45 years, enrolled in CBR- Tata Longitudinal Study of Aging (TLSA). HMSE (Hindi Mental State Examination) and CDR (Clinical Dementia Rating) used to classify into healthy and cognitively impaired. Logistic regression performed after adjusting covariates like age, education, diabetes, hypertension, dyslipidemia.
Results: Out of 156 participants, 139 (89.1%) were cognitively healthy and 17 (10.9%) with mild cognitive impairment (MCI). Prevalence of hypouricemia was more in MCI (17.65%) than in cognitively healthy participants (3.60%) and hypouricemia was found to be significantly associated with MCI ($p=0.05$). Both years of education and hypouricemia were statistically significant ($p<0.01$) independent variables. Logistic regression showed that the odds of developing cognitive impairment in hypouricemic participants was 5.98 times compared to normouricemic participants.
Discussions and Conclusion: Hypouricemia was found to be associated with increased odds of developing MCI. The results of our study suggest that hypouricemia can contribute to decreased cognition. Decreased uric acid levels are often linked to poor nutrition. Given that hypouricemia is a modifiable risk factor, it may

be worthwhile to address this in the future. Therefore, dietary changes such as the intake of food items rich in protein can be advocated to ensure normal uric acid levels.
Acknowledgments: I would like to acknowledge the staff of CBR-TLSA (Tata Longitudinal Study of Aging) for carrying out the clinical and cognitive assessments. I also thank our study participants for their participation and kind cooperation. The study is funded by Tata Trusts through the Centre for Brain Research, Indian Institute of Science, Bangalore.

P12: Caffeic acid a therapeutic natural medicine against cyclophosphamide induced acute neuronal toxicity in rats

Ankita Mukherjee and Monika Bhadauria
Toxicology and Pharmacology, Department of Zoology Guru Ghasidas University, Bilaspur (C.G.)

Background: Chemotherapy of cyclophosphamide (CP) is prescribed to treat various types of cancer, including leukaemia, sarcoma, breast cancer, and neuroblastoma, that also possesses wide range of side effects. In present investigation, caffeic acid was used to reduce CP induced toxic effect in brain.
Materials and Method: Thirty-six male albino rats of *Wistar* strain (150±10g) were allocated to six equal groups. Group 1 served as control. Group 3-6 received different doses of caffeic acid (10, 20, 30 and 40mg/kg) for six days. Group 2-6 received CP (200mg/kg) on 7th day. And group 2 considered as experimental control.
Results: Administration of CP increased level of lipid peroxidation and cholesterol in neuronal tissues, and decreased level of GSH and activities of SOD, catalase and GST. Therapy of CA reversed the toxic effect of CP in these biochemical parameters significantly. CA reduced lipid peroxidation and cholesterol whereas, increased the level of GSH and activities of SOD, catalase and GST in a dose dependent manner indicating its antioxidant nature.
Discussion and Conclusion: CP induced oxidative stress and diminished antioxidant system is evident by increased LPO and decreased level of the GSH, SOD, catalase and GST. Different doses of CA therapy-maintained homeostasis in the brain. CA at 40mg/kg of dose was observed to be the most effective dose against CP induced toxicological reactions observed in rats. These results indicate that caffeic acid can be suggested as an ameliorative natural compound against CP induced toxicity in rat brain.
Acknowledgement: VRET non-NET fellowship awarded from Guru Ghasidas University is acknowledged. Department of Zoology for providing laboratory facility.

P13: Unravel the impact of TUDCA on Iba-1 immuno-positive microglial cells and DR progression

Ankita J. Kumari[a], B.P Sinha[a], N. Mohan[a], B. Sharma[b] ,L. K. Arya[a], , M. Kumar[c], T.C Nag[b], M. Nath[d], A. Kumari[a], A.K. Jha[e], T Velpandian[d], R.V. Azad[d], P. Kumar[a]
[a] Regional Institute of Ophthalmology, Indira Gandhi Institute of Medical sciences, Patna; [b]Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India; [c]Central Animal House, Indira Gandhi Institute of Medical sciences, Patna; [d]Department of Ocular pharmacology, Dr. Rajendra Prasad Center for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India; [e]The University of Tennesse Health Science Center, Memphis TN 38163, USA.

Background: Diabetic Retinopathy (DR) is one of the leading causes of vision loss globally. One of the major complications of DR involves swelling. Tracing the chemistry behind, literature suggests that there is activation of microglia, oxidative stress and inflammation due to prolonged episode of hyperglycemia causing retinal neurodegeneration. TUDCA has shown to possess neuro-protective behavior, hence could be capable of tackling the above-mentioned complications.
Materials and methods: Streptozotocin (45mgKg^{-1}BW) induced rats showing blood glucose level of 300mgdL^{-1} were contemplated as diabetic. Once diabetes was sustained TUDCA administration was done weekly(500mgKg^{-1}BW) for 16 weeks. Fundoscopy was done to see morphological changes in retina. Rat retina was put to IHC study to observe Iba-1 levels in retina. ELISA was performed to quantify TNF-α and IL-1β levels.

Results: IHC study of retinal section showed, microglia was dispersed throughout retina layers and showing significant increase in number of activated microglia in diabetic rats when compared to control and TUDCA treated group (Control & DR $p \leq 0.01$) and (DR&DR+TUDCA $p \leq 0.001$). INL showed mild swelling in diabetic group in contrast with control and TUDCA treated which appeared alike to each other. TNF-α ($p \leq 0.01$) and IL-1β ($p \leq 0.001$) levels were significantly increased in diabetic group in comparison with control and TUDCA treated.

Discussion and conclusions: The above finding suggests that the swelling observed in DR could be attributed to activation of microglia. These activated microglia in turn increases the level of inflammatory cytokines which further worsens the DR progression, while as observed in TUDCA treated group where all the parameters kept in consideration appeared similar to the control group. Considering all the above findings TUDCA appears to reduce the number of activated microglia in retina which further leads to reduced swelling.

Acknowledgements: Funding agency- ICMR, New Delhi (project code: - 5/4/6/6/OPH/2020-NCD-II), TEM work done at SAIF, AIIMS, New Delhi.

P14: Investigation of hypothalamic 5HT2C receptor signalling in obesity & metabolic ageing

Annu Yadav[1,2] Shajia Parveen[2] Atul Goel[2], and Prem N Yadav
[1]Division of Neuroscience and Ageing Biology, [2]Division of Medicinal and Process Chemistry, CSIR-CDRI Lucknow, India. [2]Academy of Scientific and Innovative Research Ghaziabad, Uttar Pradesh- 201002

Serotonin (5-HT, 5-Hydroxy Tryptamine), is essential for maintaining energy balance in all vertebrate and invertebrate species. In animals, the central nervous system (CNS)-produced 5-HT governs several essential physiological functions, such as libido, mood, and hunger. The adult central nervous system (CNS) contains resident neural stem cells (NSCs) that are capable of self-renewal and proliferation to produce new neurons, as well as oligodendrocytes. These NSCs are found in niches such as the dentate gyrus and hypothalamus. Emerging evidence shows that physiological aging and obesity contribute to a deterioration in NSC self-renewal and regeneration abilities, which in turn results in several chronic CNS and metabolic diseases. It is now commonly accepted that maintaining a healthy NCS pool is essential for the best possible metabolic and mental performance. In this study, we screened many chemical series that were focused and rationally designed, and discovered a selective and specific 5-HT2C positive allosteric modulator (PAM), CDRI-0327. This compound does not stimulate this receptor activity on its own but significantly potentiates the effect of endogenous agonist serotonin this receptor. We also examined the effects of CDRI-0327 and LRC (Lorcaserin, 5-HT2C agonist on the proliferation of hypothalamic NSCs and discovered that activating the 5-HT2C receptor via PAM induces the proliferation of neuronal stem cells. Further *in vivo* studies with genetically obese *Db/Db* mice, we observed that CDRI-0327 restores learning and memory deficits. Further studies are in progress to elucidate the mechanisms of 5-HT2C PAM to induce NSC homeostasis.

P15: An advanced diffusion magnetic resonance imaging tractography study in Euthymic Pediatric Bipolar Disorder

Anshita Singh[1,2]; Raj Shree[2]
[1]Centre of Bio-Medical Research, Sanjay Gandhi Postgraduate Institute of Medical Sciences Campus, Lucknow, Uttar Pradesh 226014, India; [2]Department of Information Technology, Babasaheb Bhimrao Ambedkar University, Lucknow, India

Background: Pediatric Bipolar disorder (PBD) is a complex mental disorder associated with episodes of mood swings ranging from depressive lows to manic highs. Multiple factors such as combination of genetics, environment and altered brain structure may play a crucial role in this disorder. Some recent brain imaging studies have strongly linked it with the white matter (WM) abnormalities. To further explore the white matter association with this disorder we perform non-invasive magnetic resonance imaging (MRI) technique of diffusion tensor imaging (DTI) to establish the association of white matter interaction. For this purpose, we selected children with bipolar children under euthymic phase and compared with typically developing children. In euthymic phase clinical symptoms are not entirely absent, but are subdued enough, so that mood and normal activity are not affected.

Methods: For this study we recruited 20 PBD patients from Department of Psychiatry King George Medical University Lucknow and 20 typically developing children from nearby locality for comparison. All participants were aged between 7to 18years. All the DTI data was collected at in housed 3T-MRI at Center of Biomedical Research, Lucknow. The tract-based spatial statistics (TBSS) analysis of DTI data was performed to locate alteration in Fractional Anisotropy (FA), Mode of anisotropy (MO), and Coordinates of linearity (CL), Coordinates of planarity (CP).
Results: Compared to the Typically Developing children, euthymic children with bipolar disorder shows alteration in FA, CL, CP and MO values at multiple regions that include thalamus, precentral, corticospinal tract, superior longitudinal fasciculus, corpus callosum, inferior fronto-occipital fasciculus and middle cerebella peduncle.
Conclusions: The outcome of this study suggests a strong association of white abnormalities in euthymic children with bipolar disorder involving multiple neural regions. Our findings further suggest that bipolar disorders have underlying WM pathology on DTI. Measuring WM pathology using DTI is emerging as a useful tool for identifying individuals with various psychopathologies and may lead to early diagnosis and treatment.

P16: Molecular docking and simulation studies indicate immunomodulatory role of seaweed metabolites by interacting with microglia-specific proteins

Anurag Thapliyal, Shashank Kumar Maurya
Biochemistry and Molecular Biology Laboratory, Department of Zoology, Faculty of Science, University of Delhi, Delhi-110007

Background: Seaweed metabolites are novel compounds with great therapeutic potential but with little known effects on microglia during neuroinflammation. Microglia have been shown to display marked upregulation of certain proteins, which are directly involved in aggravation of neuroinflammation. Targeting these proteins might prove beneficial in alleviating gravity of neurodegenerative disorders.
Methodology: 1072 seaweed metabolites were screened for their physicochemical properties and pharmacodynamics. The ligand binding sites on IBA1, CD40L, CSFR1 and P2Y12R protein 3D structure were detected. Molecular docking (MD) and molecular dynamics simulation of drug-like compounds with each protein was evaluated.
Results: 106 seaweed metabolites showed positive physicochemical properties and pharmacodynamics to be considered as therapeutic/drug-like in nature. Following MD, 32 compounds interacted successfully with the selected microglia-specific proteins with significant binding affinities, inhibition constants and hydrogen bonds. 5 compounds bind to IBA1, 15 compounds interact with kinase domain of CSF1R, 4 compounds prevented CD40-CD40L interaction by blocking binding site of CD40L and 8 compounds interacted antagonistically with P2Y12R. The results were further validated with MDS.
Discussion and Conclusion: Targeting of microglial proteins can mitigate neuroinflammation. However, the effects of their inhibition or activation are poorly understood. Secondary metabolites provide a novel set of compounds that can interact with the microglia-specific proteins leading to identification of novel compounds which can be translated to the level of therapeutic drugs in neurodegenerative disorders. The results indicate a great potential of these compounds to be involved in regulation of microglial activity during neuro-inflammation.
Acknowledgements: Financial support of Institution of Eminence, University of Delhi (IoE, DU) is gratefully acknowledged.

P17: Understanding the role of PIWIL 1, 2 and 4 in depressive disorder using Chronic Social Defeat Stress mouse model

Arpan Mukhoti[1,3], Nitin Khandelwal[1], Ashutosh Kumar[1], Devika Mahimkar[1,3] , Bhanu Pranav N.[1,3], Annapoorna P K[1,3] , Pratishtha Wanderkar[1,3] , Sumana Chakaravarty[2,3], Arvind Kumar[1,3],
[1]CSIR- Centre for Cellular and Molecular Biology (CCMB), Hyderabad; [2]Applied Biology Division, CSIR-Indian Institute of Chemical Technology (IICT), Hyderabad; [3]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, U.P.

Background: Major depressive disorder is a debilitating psychiatric disorder. Variable response to chronic stress suggests an important role of the underlying epigenetic factors. Differential levels of expression of

retro-elements have been observed in psychiatric disorders in post mortem brain samples. This work focuses on PIWIL proteins and piRNAs that are involved in the regulation of retrotransposons.
Materials and Methods: Chronic Social Defeat Stress (CSDS) Paradigm of 10 days and PSDS (Progressive SDS) paradigm of 1-5 days were used to induce stress by social aggression for depression-like phenotype. Behavioral tests were used for evaluating the signs of depression-like conditions such as Anhedonia, helplessness, etc. RT-qPCR and Immunoblotting was used for estimating the levels of change in gene/protein expression.
Results: Behavioral data show an advent of symptoms of Depressive disorder after 5-day defeat. PSDS induced depressive disorder was associated with the progressive advent of the behavioral markers relative to the number of stress instances. qPCR estimation shows dysregulation of PIWIL family genes in different brain regions by CSDS. PSDS resulted in interesting pattern of dysregulation where the levels of PIWIL 1 & 2 spikes at the 3rd stress instance.
Discussion & Conclusion: Social Defeat Stress results in a depression-like phenotype in mice, and the intensity of the behavior phenotype is dependent on the number of stress events. Molecular studies show a change in PIWIL genes in different brain regions in response to stress and a varying level of change is found depending on the number of stress events. The results suggest that PIWIL genes appear to be involved in the epigenetic mechanism underlying CSDS & PSDS induced depressive disorder phenotype.
Acknowledgements: We wish to thank CSIR-CCMB and AcSIR for the support. We would also like to acknowledge CSIR fellowship to AM, and DBT grant to AK on Glia research in health & disease.

P18: Computational elucidation of selected kinase inhibitors as potential PINK1 activators crucial for Parkinson's disease through molecular docking, simulation and scaffold analysis

Arpita Soreng[1], Achyutananada Samal[1], Pabitra Mohan Behera[2] and Manorama Patri[1]
[1]Neurobiology Laboratory, Department of Zoology, Ravenshaw University, Cuttack, Odisha, [2]Redox Biology and Proteomics Group, Center of Excellence in Environment & Public Health, Department of Zoology, Ravenshaw Univarsity, Cuttack, Odisha, Pin-753003, India

Background: The human PTEN-induced kinase 1 (PINK1) protein is characterized by its critical role in mitochondrial function and quality control. Mutations in the PINK1 gene are the main cause of mitochondrial dysfunction and leads to early onset of Parkinson's disease. Here we report selected kinase inhibitors as potential PINK1 activators crucial for Parkinson's disease.
Materials and methods: The UniProtKB database was searched for selection of human PINK1 protein canonical and four natural variants characterized by point mutations A168P (rs768091663), G309D (rs74315355), T313M (rs74315359) and L347P (rs28940285). The PubChem database was searched for downloading of twenty-two kinase inhibitors currently used for different disease conditions as reported in literature.
Results: The homology models of PINK1 canonical and four natural variants designed with the template structure (PDB ID: 7MP9) have more than 90% residues in the allowed regions of the Ramachandran plots. The molecular dynamics simulation of the designed models suggested their stability and further use. The docking studies of selected kinase inhibitors were associated with some reasonable docking score (-7 to -9 kcal/mol) and hydrogen bond interactions with some important amino acid residues lining the selected binding site.
Discussion and conclusions: In the absence of human PINK1 protein crystal structure we were able to model the canonical and four natural variants crucial for the onset of Parkinson's disease. The comparative molecular dynamics studies of the models revealed their stability. The selected kinase inhibitors accommodated themselves in the defined binding site and the fetching of potential scaffolds from them may be crucial for the design of new chemical entities as PINK1 activators crucial for PINK1 mutation onset Parkinson's disease.
Acknowledgements: National Fellowship for Scheduled Tribe Students (NFST), Arpita Soreng with award number(202223-NFST-ODI-01547).

P19: Early detection of Parkinson's disease by using artificial intelligence and analysis of clinico-genetic correlates

Arvind Kumar Das[1], Gyaneshwar Chaubey[2], Kaushal Kishor Shukla[3], Vijaya NathMishra[1]
[1]Department of Neurology, Institute of Medical Sciences, Banaras Hindu University,Varanasi
[2] Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi; [3] Department of Computer Science, Indian Institute of Technology, Banaras HinduUniversity, Varanasi

Background: Parkinson's disease, a complicated neurodegenerative disorder, affects millionsof people worldwide. It influenced by hereditary variables such single nucleotide polymorphisms (SNPs), which has a negative impact on quality of life. An artificial intelligence-driven methodologies aid in identifying SNPs, discovering novel player biomarkers, and creating prediction models for disease risk assessment.
Material and Methods: Videos and blood sample of PD patients were collected from S.S.L. Hospital, IMS, BHU, Varanasi. The AI technique was used to screening and feature selection for PD using Machine and Deep Learning, such as KNN, SVM, NB, DT, and RF. Further genetic analysis is performed to find out the SNPs.
Result: AI tools has identified the pattern of disease (motor and non-motor function) and checkthe accuracy rate and performance. Exome sequencing retrieved the SNPs in certain gene suchas: SNCA, PARKN, DJ1, and LRRK2 that could potentially be used as biomarkers for the earlydiagnosis of PD. AI-driven genetic dataset analysis uncovers genetic changes related to Parkinson's subtypes and symptoms severity.
Discussion and Conclusion: AI is still in its infancy, its integration into PD research has greatpromise for accelerating the development of novel therapies, improving patient outcomes, andultimately advancing our understanding of the disease's core causes. In conclusion, the AI couldbe helpful in examining if any person having any of these symptoms is a Patient of Parkinson's
by machine learning which can detect the changes in expression and movement of the patientand their correlation with SNPs.
Acknowledgement: The authors kindly acknowledge Department of Computer Sciences, IIT, BHU for providing software and the computational facilities for AI analysis, and Department of Zoology, Instituteof Science, BHU for providing plate form for genomic experiment. We are highly grateful to the Department of Neurology, IMS, BHU for extending laboratory facilities.

P20: Identification of a novel Hv_1 proton channel inhibitor to ameliorate neuroinflammation

Ashutosh Sharma[1], Suchitra Gupta[2], Atul Goel[2] & Aravind Singh Kshatri[1] [1]Neuroscience and Ageing Biology Division, [2]Medicinal and Process Chemistry DivisionCSIR- Central Drug Research Institute, Lucknow, India

Voltage-gated proton channels (Hv1) are specifically expressed in the microglia of mammalian nervous systems and are associated with neuroinflammation. Emerging data from various preclinical animal models demonstrate that persistent activation of these channels significantly contribute to chronic neuroinflammation and subsequentlyneurodegeneration. Despite the potential clinical significance, no high throughput assay Hv1 inhibitors with a reasonable affinity and selectivity currently exist to target these channels. To address these research gaps, we aimed to identify new classes ofpotent and selective inhibitors of this channel using a novel fluorescent based HTS methodology. The *in vitro* efficacy of the identified hit compounds was done using RT-PCR technique and docking studies were also performed to identify their binding sitesin the Hv1 channel. After screening of an in-house library of heterocyclic compounds, we have identified a benzothiazole derivative, BTZ-26 as a potent inhibitor of Hv1 channels (IC_{50}=0.3μM). Subsequently, our specificity studies established that it does not alter the activity of other ion channels belonging to Na_V and TRP families. Cell toxicity experiments revealed that BTZ-26 is non-toxic (up to 10μM) for BV-2 microglialcells. Our preliminary data also indicated that BTZ-26 largely abrogated inflammatoryneurotoxicity by reprogramming LPS-activated microglia. Molecular docking data indicated that BTZ-26 binds to the extracellular region of Hv1 channel and makes contact with hydrophobic amino acids. The predicted binding region of BTZ-26 is completely different than that of the existing modest Hv1 channel blocker (2GBI) which binds in the intracellular end of the channel. Although our hit appears to be Hv1 selective, a through functional

characterization is required using patch clamp electrophysiology technique. Similarly, future studies should focus on target validationexperiments using the gene knock down techniques. Ultimately, in vivo efficacy of BTZ-26 remains to be established in preclinical rodent models of neuroinflammation to evaluate its translational value. Together our data highlight that BTZ-26 is a potent,selective inhibitor of $Hv1$ channels that has a potential to treat neuroinflammation.

Acknowledgements: This work was supported by CSIR-CDRI and UGC-JRF Fellowship to Ashutosh Sharma

P21: Root of *Argyreia speciosa* attenuate post-stroke biochemical defects and histopathological alterations in rats

Bhagat Singh Jaiswal and Mukul Tailang
School of Studies in Pharmaceutical Sciences, Jiwaji University, Gwalior, M.P., India

Background: The plant *Argyreia speciosa* Linn. f. is commonly known as Vridhadaraka (anti-aging) in Sanskrit. In Ayurvedic system of medicine, its root part is used as the nervine tonic and prescribed for the various neurological medication in Ayurvedic formulations such as Ajmodadi Churna (hemiplegia), Maharasnadi Kashayam (cerebellar ataxia) and Ashtanga Ghrita (cerebral palsy).
Materials and methods: Global cerebral ischemic reperfusion injury (GCIRI) induced by occlusion of bilateral common carotid arteries for 30 min followed by 24 h of reperfusion period. Rats were pretreated with *Argyreia speciosa* (100, 200 and 400 mg/kg). Stroke was measured by area of cerebral infraction and brain oxidative stress markers malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px) were assessed. Lastly, histopathological changes in the cortex, hippocampus and striatum of brain were studied.
Results: GCIRI significantly increases cerebral infraction area, increased the brain MDA content while decreased SOD, CAT and GSH-Px activity. Additionally, GCIRI rats brain tissue exhibited disturbed histoarchitecture when compared with Sham control rats. Pretreatment with *Argyreia speciosa* significantly reduced the cerebral infraction area and improved the all above changes to normal level in a dose-dependent ($p< 0.05$ - $p < 0.001$) way when compared to GCIRI rats.
Discussion and Conclusion: Pretreatment with *Argyreia speciosa* has shown the significant protective effect which may be due to a reduction in oxidative stress. The neuroprotection offered by *Argyreia speciosa* against GCIRI induced stroke was confirmed by the histopathological investigations. In conclusion, the root of *Argyreia speciosa* exhibited a beneficial effect on global cerebral ischemia-reperfusion injury and validates its traditional Ayurvedic use in the treatment of stroke or the related disorder.
Acknowledgements: The authors are grateful to the Head, Department of SOS in Pharmaceutical Sciences Jiwaji University, Gwalior for providing necessary facilities for the research work and Dr. DP Nagar, Scientist (Pharmacology & Toxicology division), DRDE, Gwalior for extending a helping hand in histopathological study.

P22: Immunocompetent cells and their possible role in age-related choroidal capillary changes in rat eye

Bhaskar Sharma, Tapas C Nag
Neurobiology Laboratory, Department of Anatomy, All India Institute of Medical Sciences, New Delhi 110029

Background: Aging and age-related ocular diseases are associated with a significant loss of choroidal capillaries. Owing to a lack of nutrients and oxygen to the outer retina, this capillary loss results in geographic atrophy characterized by loss of photoreceptors and retinal pigment epithelium. This study aimed to examine the phenotypes of microglia and other immunocompetent cells in choroidal capillary changes associated with ageing.
Material and methods: Male Wistar rats were reared until they were 12 months of age. Their eyes were enucleated, the choroid removed and ELISA and Western blotting performed to measure the levels of different cytokines. Histochemistry and immunohistochemistry were used to examine the distribution of

different immunocompetent cells in the choroid. Capillary changes in the choroid of young and aged animals were evaluated using TEM.
Results: The control rats showed fenestrated capillaries with a mean luminal diameter of 12±2.5 μm, whereas in experimental rats, they were larger in size (mean diameter: 16.7-19.4 μm). In controls, the endothelium and pericyte in most vessels were intact, whereas the endothelium was vacuolated and the pericyte layer was electron-dense in aged rats. The level of proinflammatory cytokine markers in the choroidal homogenates of aged rats was significantly higher than that of young rats. Whole-mount choroid revealed mast cells were oriented along the capillaries. The quantity of Iba-1 positive microglia increased in older rats compared to younger rats. These findings suggest that both mast cells and microglia contribute to capillary injury.
Discussion and conclusion: These findings suggest that immunocompetent cells play a role in choroidal capillary changes with ageing.
Acknowledgements: Supported by funds from ICMR, New Delhi (51/4/2000-ANA/BMS, TCN).

P23: In-house natural product library screening identifies a resveratrol oligomer as Monoamine oxidase inhibitor in brain: therapeutic implications against Parkinson's disease

Chayan Banerjee[a, b], Raju Barman[c], Priya Darshani[c], Meghana Pillai[a], Sanchi Ahuja[a],Rupsha Mondal[a, b], VS Pragadheesh[d], Joy Chakraborty[a, b], Deepak Kumar[b, c]
[a]Cell Biology and Physiology Division, CSIR- Indian Institute of Chemical Biology, Kolkata- 700032, India; [b]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad- 201002, India; [c]Organic and Medicinal Chemistry Division, CSIR-Indian Institute of Chemical Biology, Kolkata- 700032, India; [d]CSIR-Central Institute of Medicinal and Aromatic Plants, Research Centre, Bengaluru, 560065, India

Background: Due to progressive loss of dopaminergic (DAergic) neurons at substantia nigra, Parkinson's disease (PD) patients experience DA shortage at striatum. As Monoamineoxidase (MAO) metabolizes DA, managing its activity is instrumental to preserve DA levels. Though plant-derived compounds are well-utilized in therapeutics, identificationof promising MAO inhibitors is still insufficient.
Material and methods: Based on current literature, we choose 39 compounds of different classes and screenedfor their MAO inhibitory properties and the appropriate molecule was evaluated for preliminary *in-vitro* and *in-vivo* toxicity studies. Finally, therapeutic implication of the molecule was evaluated in a toxin-induced sporadic mouse model of PD.
Results: CB1 (a resveratrol oligomer; Mol. formula $C_{42}H_{30}O_9$) offers highest level of MAO inhibition among all compounds and exhibits no effect on cell viability, cellular reactiveoxygen species (ROS) levels and mitochondrial morphology *in-vitro*. Preliminary *in- vivo* toxicity study in *Drosophila* does not show any alteration as well. The compoundcould not protect against toxin induced DAergic neuronal loss in sporadic PD model, however, PD-associated akinesia and catalepsy are mitigated via elevated levels of striatal DA.
Discussion and conclusions: We propose to consider CB1 as an adjuvant therapeutic agent for PD associated behavioral improvements or in conditions where MAO inhibition may offer therapeuticamelioration.
Acknowledgement: The authors are thankful to the director of CSIR-IICB for providing necessary support and funding. RM, CB, PD and RB are recipient of research fellowships from CSIR, UGC, NIPER-K and CSIR (MLP-138) respectively.

P24: p38MAPK inhibitor SB202190 regulates iron storage component ferritin inglioma cells

Poonam Gupta, **Chayanika Banerjee,** Avijit Paul, Chinmay K. Mukhopadhyay
Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi 110067

Background: High iron availability is required for enhanced growth and proliferation for any cancer cell including glioma. We recently reported that endogenous phosphoinositol-3-kinaseactivity could suppress translation of iron storage component ferritin to avail higher iron pool for proliferation in glioma cells. However, role of any other kinase remains unexplored.
Methods: Glioma cells were treated with p38MAPK inhibitor SB202190 and ferritin subunitswere detected

at protein and mRNA levels. Ferritin regulation was verified at transcriptional and translational level. Cell proliferation and intracellular reactive oxygen species (ROS) were also measured.
Results: Significant increase in ferritin subunits was detected by SB202190 at protein and mRNA levels but not by p42/44 MAPK inhibitor. Regulation was at transcriptional level as detected by ferritin-H promoter assay but no effect was found on translation as detected by IRE-IRP interaction. SB202190 treatment also blocked cell proliferation and decreased intracellular ROS generation.
Discussions and conclusions: Our results show that p38MAPK inhibitor SB202190 can promote transcription to elevate ferritin synthesis in glioma cells. Simultaneous blocking of cell proliferation suggests that elevated level of ferritin may store higher iron from labile poolto reduce the availability of iron required for cell proliferation and ROS generation.
Acknowledgement: AP acknowledges support of D.S. Kothari post-doctoral fellowship.

P25: Understanding cognition and neuro-metabolism in 5xFAD mouse model of Alzheimer's Disease

Chaynita Dashora[1,2], Akila Ramesh1,2, Anant Bahadur Patel[1,2]
[1]NMR Microimaging and Spectroscopy, CSIR-Centre for Cellular and Molecular Biology, Habsiguda, Uppal Road, Hyderabad 500007, India; [2]Academy of Scientific and Innovative Research, Ghaziabad 201002, India;

Background: Alzheimer's disease (AD) is a neurodegenerative disorder, characterized by memory loss and amyloid-beta plaques accumulation1 . Several studies have reported hypometabolism in the AD brain in mouse models as well as human subjects2,3 . The aim of this study was to understand the alterations in cognition and neurometabolism with the progression of AD.
Materials and methods: Six and twelve months old 5xFAD male mice were used in the study4 . Memory assessment was done using the Y-Maze and Morris Water Maze tests. Neuronal metabolic activity was measured using 1H-[13C]-NMR spectroscopy in brain tissue after intravenous injection of [1,6-13C2]glucose in mice5 .
Results: There was a significant reduction in spontaneous alternation (%) in 6 months old 5xFAD mice (48.57±5.19%, p=0.02), which further reduced at 12 months (47.32±5.65%, p= 0.017).
Discussion: This study aimed to investigate how memory impairment is manifested in neurometabolism with the progression of AD. The significant reduction in working memory in the Y-Maze test suggests deterioration of memory with the progress of age in 5xFAD mice. Moreover, a reduction in the rate of glucose oxidation in glutamatergic neurons points towardsreduced excitatory activity in the 5xFAD model of AD.
Acknowledgement: This study was supported by the Council of Scientific and IndustrialResearch (CSIR-CCMB: NCP/MLP0139). CD would like to thank DBT for SRF

P26: Peripheral and central nervous system immune correlates of early life stress induced aggressive behavior

Chetan Mishra[1,2], Beena Pillai[1,2] and Arpita Konar[3]
[1]CSIR- Institute of Genomics and Integrative Biology, Mathura Road, New Delhi, India; [2]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India; [3] Institute of Health Sciences, Presidency University, Kolkata-700156, West Bengal, India

Brain, a relatively immune-privileged organ, undergoes an aberrant influx of immune cells and cytokines during pathological conditions. Apart from astrocytes and microglia, immune cells entering the brain from circulation also cause inflammation. The cytokines produced by these immune cells not only cause neuroinflammation but are also observed to affect the behavior of anindividual. Traumatic experiences during adolescence often lead to abnormal aggression, though molecular correlates are still elusive. Earlier, we showed that male mice exposed to fear inducing stressors during peripubertal age showed heightened aggression in adulthood. Here, we have investigated the status of circulatory and CNS immune markers during peripubertal stress (PPS) induced long-term aggressive behaviour. We observed that cytokines were altered both in brain regions (prefrontal cortex; hypothalamus) and serum of PPS exposed male mice. Interestingly, circulating and brain region specific levels of cytokines were also modulated in post weaning social isolation (PWSI for 7 weeks) subjected escalated aggressive males, another early life stressinduced

behavioral model system. CNS immune markers including GFAP (astrocyte marker) and IBA1 (pan microglial marker) were also altered in both the experimental regimes. Further studies will help us to understand how the circulatory and brain specific immunity play roles in early lifestress induced aggressive behavior. These findings will eventually help us find potential immune biomarkers related to trauma induced aggression in humans, which might be useful for reducing the aggression phenotype.

Acknowledgements: We would like to thank AcSIR for registration, CSIR for infrastructure and DBT for funding.

P27: Neuropeptide S suppresses pain-related aversion via activation of GABAergic neurons within anterior cingulate cortex

Dadasaheb M. Kokare[1], Harish M. Kawade[1], Utkarsh P. Patil[1], Nishikant K. Subhedar[2]
[1]Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur-440 033, India
[2]Biology Department, Indian Institute of Science Education and Research, Dr. Homi Bhabha Road, Pune-411 008, India

Background: The role of neuropeptide S (NPS) in the sensory pain is extensively studied, however the effect of NPS on affective dimension of pain and underlying mechanisms have not been clarified. The GABAergic neurotransmission in the anterior cingulate cortex (ACC) has been emerged as a key player in the pain-associated emotions.

Materials and methods: Herein, we investigated the involvement of GABAergic interneurons of the ACC in the action of NPS on pain-induced aversion. The adult male Wistar rats were cannulated in the ACC for different drug treatments using stereotaxic apparatus. The formalin injection (intra-plantar) was used to induce conditioned place aversion (F-CPA) in animals.

Results: The intra-ACC NPS infusion (2 nM/rat, ACC) in the formalin-treated rats showed attenuation of pain-related aversion compared to a CSF-injected control. The pre-treatment of GABA-A receptor antagonist, bicuculline (50 ng/rat, ACC) blocks the anti-aversive effect of NPS in formalin-treated rats. NPS administered directly in the ACC showed increase in the cfos (marker of neuronal activity) expression on GAD67-containing (marker of GABA interneurons) neurons within ACC of formalin-treated rats.

Discussion and conclusion: We used F-CPA model which is an operant behavior that involves a learning process, and allows the assessment of supraspinal pathways underlying pain-induced aversion. While NPS (intra-ACC) injection attenuated the pain-related aversion, this effect was blocked by bicuculline treatment. The NPS treatment showed activation of GAD-67-containing neurons (GAD67+cfos colabelling) within ACC. The data suggest that NPS in the ACC attenuate the pain-induced aversion via activation of GABAergic interneurons.

Acknowledgment: We acknowledge the Science and Engineering Research Board (SERB) (File No. CRG/2020/004971), Government of India, New Delhi, India for financial support.

P28: Effect of Citrus odor exposure on the performance in Stroop Task and Salivary Testosterone Levels in healthy individuals

Deep Shikha[a], Pooja Ojha[b], Kamla Kant Shukla[c], Om Lata Bhagat[b], Abhinav Dixit[b]
[a]Department of Physiology, All India Institute of Medical Sciences, New Delhi, India; [b]Department of Physiology, All India Institute of Medical Sciences, Jodhpur, India; [c]Department of Biochemistry, All India Institute of Medical Sciences, Jodhpur, India

Background Olfaction and cognitive functions share a related structural nexus. Olfaction also affects Testosterone secretion and testosterone has been shown to affect cognitive performance. This study investigated the effects of citrus smell on Stroop task, a cognitive task, and salivary testosterone levels.

Material and method: Participants performed two sessions of the computer-based Stroop task at an interval of one hour. Electrodermal activity and photoplethysmography were recorded in both sessions following a baseline recording. A pure citrus essential oil was used as an olfactory intervention in the experimental session during the Stroop task.

Result Paired t-test and Wilcoxon signed-rank test (n=30) revealed that citrus odor significantly improved the reaction time (p=0.000) in the Stroop task. An increasing trend of salivary testosterone level with the cognitive tasks was observed. It was more in the presence of the citrus odor inhalation in experiment session as compared to the control session but the difference was not statistically significant.

Conclusion Olfactory stimulation with citrus odor improves the performance in stroop task and increases the salivary testosterone levels. Citrus odor may be utilized for cognitive enhancement and increasing release of salivary testosterone.

P29: Neuropeptide S alleviate neuropathic pain symptoms via activation of lateral hypothalamic orexinergic system

Deepali M. Pandhare[1], Utkarsh P. Patil[1], Harish M. Kawade[1], Nishikant K. Subhedar[2], Dadasaheb M. Kokare[1]
[1]Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur- 440 033, Maharashtra, India; [2]Indian Institute of Science Education and Research (IISER), Pune, Maharashtra, India

Background*:* Neuropathic pain (NP) develops from the lesions of peripheral and/or central nervous system. The efficacy of available treatment strategies for NP is limited. The orexinergic and neuropeptide S (NPS) systems per se in the brain showed potent antinociceptive effect. Herein, we investigated the interactions of these two systems in regulating symptoms of neuropathic pain.
Materials and methods*:* The chronic constriction injury (CCI) of sciatic nerve was used to induce mechanical allodynia and thermal hyperalgesia in Wistar rats. The cannula was stereotaxically implanted in lateral hypothalamus (LH) and periaqueductal gray (PAG) for drug treatments. The symptoms of the NP were tested by Hargreaves and von Frey filament tests.
Results*:* On third day after the surgery, neuropathic pain-like symptoms were developed in CCI rats. NPS administration (0.2 nM/rat, LH) in CCI rats increased paw withdrawal latency (PWL) and threshold (PWT) compared to aCSF-injected control. The pre-treatment of orexin-1 receptor antagonist, SB-334867 (60 nM/rat, PAG) blocks the antinociceptive effect of NPS. While intra-LH NPS injection showed an increase in orexin immunoreactivity, the decrease was observed in the glial fibrillary acidic protein (GFAP) expression in the PAG.
Discussion and conclusion*:* The pathological conditions following CCI surgery in animals are similar to human neuropathies, hence this model is widely used. While NPS injection (intra-LH) alleviate the neuropathic pain symptoms, this effect was blocked by SB-334867 treatment. In addition to activation of orexinergic system of LH, NPS also reduced GFAP expression in the PAG, indicates anti-inflammatory property of peptide in the brain. The data suggest that NPS produced antinociceptive effect through activation of the LH-PAG orexinergic pathway.
Acknowledgment*:* We acknowledge the Science and Engineering Research Board (SERB) (File No. CRG/2020/004971), Government of India, New Delhi, India for financial support.

P30: Studying olfactory behavior of *park*^{13} mutant, A Parkinson's Disease model of *D. melanogaster*

Deepanjali Ghadge, Mayur Gaikwad
Department of Life Sciences, Sophia College (Autonomous), Bhulabhai Desai Road,
Mumbai 400026

Background: Parkinson's disease is a neurodegenerative disease showing motor symptoms along with non-motor symptoms. This occurs prior to motor symptoms and can be used as potential biomarkers for early PD diagnosis. One such symptom is olfactory dysfunction and this study is conducted using the *park*^{13} model, a *parkin* null mutant**.**
Materials and methods: Larval Olfactory Assay tests olfactory dysfunction in drosophila larvae using odorant iso-amyl acetate and benzaldehyde.

The adult fly olfactory assay is performed using an olfactometer with different age groups of flies to test olfactory dysfunction and its progression as they age using odorant iso-amyl acetate.
Results: Results indicate a significant decrease in olfaction of *park*^{13} larvae compared to wild types when assay was performed using odorant iso-amyl acetate with 10^{-3} dilution.
The same assay was performed with odorant benzaldehyde to test odor non-specific behavior with 10^{-4} dilution. This also shows a significant decrease in olfaction.
These results help to explore the potential of using olfaction as a means of monitoring PD progression and developing new treatments
Discussion and conclusions: In recent studies using the PINK-1 and alpha-synuclein model, olfactory deficit is seen earlier than motor symptoms.
Our study indicates that *park*^{13} shows a juvenile form of PD and thus is an excellent model for investigating olfactory dysfunction. The cause for olfactory deficit is not yet confirmed and is predicted to be associated with impairment in the olfactory system. More studies need to be conducted to establish theformer and hence could be used as a predicting marker for PD.
Acknowledgements: I extend my gratitude to the Principal, Dr. Anagha Patil Tendulkar the Head of the Department of Life Science, Dr. Sree Nair, and my supervisor, Mr. Mayur Gaikwad for giving me invaluable guidance, insights, moral support, and direction to the project. Heartfelt thanks to my faculty of the Department of Life Sciences as well as my lab partner Sonia Joshi for unnerving support.

P31: Role of TGR5 in Neural Stem Cell Homeostasis

Devanshu Kaushik, Prem N. Yadav
Division of Neuroscience & Ageing Biology, CSIR- Central Drug Research Institute, Lucknow, Uttar Pradesh, India, Jawaharlal National University- New Delhi, 110067

G- protein coupled bile acid receptor 1, also known as Takeda G- protein coupled receptor TGR5 is a $G\alpha_s$ Coupled GPCR discovered in 2002 by Maruyama. TGR5 is an endogenous bile acid receptor, which upon activation is known to initiate a number of signaling pathway modulating multiple physiological responses. For example, energy metabolism, bile acid regulation and inflammatory responses. TGR5 mRNA has been detected in many rodent and human brain tissues, including macrophages/monocytes, gallbladder, placenta, intestine, liver and brain. However, the precise role of TGR5 signaling in CNS is still not clear. Given that neural stem cell (NSC) homeostasis is considered paramount in healthy ageing and mood., we investigated the role and mechanism of TGR5 signaling in NSC homeostasis. Furthermore, NSC proliferation and adult neurogenesis has been shown to be significantly reduced during ageing and brain injury. We have found abundant expression of TGR5 in primary cultured neural stem cell from hippocampus, and in dentate gyrus region of mice. We have shown increased proliferation of NSC upon stimulation with TGR5 selective agonist TCG-1005. Although TGR5 agonism has been reported to cause itch upon activation by bile acids, however we found that synthetic agonist TCG-1005 did not induce itch in mice. Furthermore, administration of TGR5 agonist TCG-1005 significantly increased doublecortin (DCX) positive cells (a marker or immature neurons), indicating TGR5 role in NSC homeostasis and adult neurogenesis. More importantly, we also found that TGR5 activation led to increases in the quiescent neural stem cells in cultured NSC. These observations suggest that TGR5 might be a good target to ameliorate perturbed NSC homeostasis in various CNS disorders.

P32: Platelets-Neutrophils and Platelets-Monocyte crosstalk in TBM: A Pilot Study

Devesh Kumar[1], Priya Dev[1], Abhishek Pathak
[1]Department of Neurology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, 221005, India.

Tuberculous meningitis (TBM) is the most serious and fatal type of extrapulmonary tuberculosis (EPTB). Early disease detection and treatment are important for the prevention of death or neurological damage. Mycobacterium tuberculosis cannot be effectively detected in TBM patients using only a single diagnostic technique. A combination of tests including clinical, bacteriological, and neuroimaging may help in early

TBM diagnosis and hence, better treatment options. The current study investigates the mechanistic basis of platelet responsiveness in TBM patients compared with healthy controls (HCs). This was a pilot study that included 20 TBM patients admitted in the Neurology ward, IMS, BHU after using consensus III diagnostic criteria (probable and definite), and another 20 individuals who had no disease were recruited as HCs. Demographic characteristics and clinical profiles of diseased subjects were collected. 20 µL Fresh blood samples from all study participants were collected and were added to a cocktail containing 10 µL each of APC anti-CD41a (platelets specific) and FITC anti-CD14 (leukocyte specific) antibodies within 20 minutes of blood withdrawn, mixed gently, and analyzed by a flow cytometer (FACS Calibur, BD Biosciences). Unequal variance was used for statistical analysis of results using GraphPad Prism, version 9.0. The significance of the test was set at $p<0.05$. Compared to healthy controls, platelets-monocyte, and platelets-neutrophil interactions were elevated in TBM patients, but this elevation is significant only in the case of platelets-neutrophils. Platelets were hyperactive in TBM patients as compared to HCs but we need a large sample size for further confirmation and evaluation of results.

Acknowledgement: Department of Neurology, IMS, BHU.

P33: Delineating the sex-specific role of Forkhead family proteins in anxiety-like phenotype using the prenatal stress mouse model

Devika Mahimkar[1,3], Arpan Mukhoti[1,3], Unis Ahamad Bhat[1], Aaheli Chakrabarty[1], Sumana Chakravarty[2,3], Arvind Kumar[1,3]

[1]CSIR- Centre for Cellular and Molecular Biology (CCMB), Hyderabad; [2]Applied Biology Division, CSIR-Indian Institute of Chemical Technology (IICT), Hyderabad, [3]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, U.P.

Background: Prenatal stress (PNS) appears to have a consequence on the offspring's health in later life and its molecular aetiology is still elusive. Transcriptomic data using the PNS mouse model indicated dysregulation of Forkhead family transcription factors (TFs) in the hippocampus. Here, we strive to understand the role of a few Forkhead proteins in PNS-induced etiopathology.

Materials and methods: PNS by restraint was administered to the pregnant dam. A battery of behaviour tests was performed on the offspring during adolescence and adulthood. Environment Enrichment (EE) for 6 weeks was used for the rescue of the phenotype. RT-qPCR for expression of Forkhead TFs was performed on the hippocampus tissue and the derived dentate gyrus (DG) neural stem cell culture.

Results: The analysis of behaviour data suggests that both male and female offspring developed an anxiety-like phenotype. The phenotype was rescued in male offspring by the EE paradigm; however, the data on the recovery of females appear inconclusive. Our molecular data show some dysregulated Forkhead family TFs in the hippocampus in response to PNS. Additionally, PNS appears to affect the proliferation and differentiation potential of neural stem cells from offspring DG.

Discussion and Conclusions: Male and female offspring subjected to PNS developed anxiety-like phenotypes in the adult stages. However, there seemed to be no significant changes in their object recognition memory and social interaction. Due to the increased activity of the EE group animals, better behaviour tests are required to correctly assess the phenotype. Some Forkhead TFs seem to be involved in the process of neural stem cell differentiation. The underlying mechanism involving the Forkhead family TFs is being investigated in detail.

Acknowledgements: We thank CSIR-CCMB and AcSIR for their support. We would also like to acknowledge the DST-INSPIRE fellowship to DM, and the DBT grant to AK on Glia research in health & disease.

P34: Neurotoxicity of Neonicotinoid Pesticides in early life exposure: A Meta Analysis

Dhanshree Sayangrushi Borkar and Rajesh Singh Yadav

School of Forensic Science, National Forensic Sciences University (An Institution ofNational Importance), Bhopal – 462036 (MP), India

Background: Developing foetus are at high risk of pesticides exposure and resulting adverse consequences due to immature blood brain barrier and detoxification mechanism. The toxicity of neonicotinoids was

formerly thought to be low, but many experimental studies suggested a number of adverse health impacts. In view of thetoxic effect of neonicotinoids, the present work aims to analyze the studies reporting developmental neurotoxicity caused due to neonicotinoid pesticides both in humans andanimals.
Materials and methods: An online literature search was conducted through PubMed, Scopus, Science direct and web of science data bases using the keywords: 'neonicotinoids', 'neurotoxicity', 'developing brain' as well as combinations of these terms.
Results: A total 255 articles were fetched from the data base in which 64 were found duplicate and therefore removed. Out of 191 articles, 152 were found the studies on lower animals, adult age group and in vitro studies and not fit for the inclusion criteriaof the present study. Further, out of 39 selected research articles, 8 were not found in the selected study criteria and therefore excluded from the study. A total 31 relevant articles including 07 clinical and 24 experimental studies were included in the present work.
Discussion: The findings of the present work suggested that the neonicotinoids caused neurobehavioral toxicity in developing children and animals associated with enhanced oxidative stress, neurochemical and molecular alterations. The study will open new vistas for regulatory agencies to draw suitable guide maps for its use, risk assessments and reviews the threshold limit values.

P35: Beyond witnessing: Underlying neurobiological mechanisms of vicarious trauma-mediated development of learned helplessness in male and female mice

Shashikant Patel[1,3], **Dhaygude Sainath Sunil**[1], Roli Kushwaha[1,3], Kalyani Soren[1,3], Arvind Kumar[2,3], Sumana Chakravarty[1,3]
[1]Applied Biology, CSIR-Indian Institute of Chemical Technology, Tarnaka, Uppal Road, Hyderabad 500007, India; [2]CSIR- Centre for Cellular and Molecular Biology, Habsiguda, Uppal Road, Hyderabad 500007, India; [3]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad- 201002, India

Background: Depression is a multifaceted mental disorder manifesting a state of profound despair and helplessness. At its core lies the concept of learned helplessness, where individuals perceive an inability to control adverse circumstances. To illuminate the neurobiological dimensions of depressive-like behaviors, we explore the novel paradigm of vicarious trauma-induced learned helplessness using male and female mice.
Materials and methods: Our study employs meticulous animal procurement and housing to establish controlled conditions for a transformative 7-day investigation. Demonstrator mice are subjected to controlled footshocks in a modified fear conditioning apparatus, while vicarious mice bear witness to these events without direct exposure through an insulated compartment.
Results: Behavioral assessments—including the FST, EPM, and Empathy Test—reveal heightened stress and depressive-like behaviors in both Demonstrator and Vicarious mice. Our results provide insights into the potential transference of learned helplessness and its emotional manifestations in vicarious mice. Subsequent to behavioral analyses, affected brain regions- AD, NAc, PFC, Hippo, Dorsal Striatum, and Hypothalamus were microdissected and assessed. Western blot analyses shed light on intriguing trends, including elevated NGF levels within the amygdala, along with attenuated PSD95 levels indicative of synaptic adaptations.
Discussions and conclusions: This study unveils the intricate dynamics of vicarious trauma-induced learned helplessness, bridging the gap between observational experiences and depressive-like behaviors. The findings provide a deeper understanding of the underlying neurobiological mechanisms and their relevance to stress-related disorders. By elucidating the neural basis of vicarious learned helplessness, this research contributes to a comprehensive comprehension of depression and offers potential avenues for therapeutic exploration.
Acknowledgements: SP and RK acknowledge CSIR for fellowship. DSS acknowledges Ministry of Ayush for fellowship.

P36: Role of central amygdalar dopaminergic system in the generation of anger-like responses in rats

Dipak K. Sahare[1], Biru B. Dudhabhate[1], Nishikant K. Subhedar[2], Dadasaheb M. Kokare[1]
[1]Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur- 440 033, Maharashtra, India; [2]Indian Institute of Science Education and Research, Dr Homi Bhabha Road, Pune-411 008, Maharashtra, India

Background: Anger is a negative emotion that have great impact on daily life and abnormally expressed in various neuropsychiatric disorders like depression, bipolar disorders, etc. Previous reports suggest that amygdala plays an important role in the anger, fear, aggression and emotional responses. However, its neurological underpinning has not been clearly studied.
Materials and Methods: Herein, we sought to investigate the role of central amygdala (CeA) dopaminergic system in the regulation of anger-like behaviour by using novel anger paradigm in rats. We checked *cFos* immunoreactivity profile in different subregions of amygdala. Moreover, dopaminergic D2 receptor modulators [agonist (Quinpirole) and antagonist (Sulpiride)] were administered via intra-CeA.
Results: In present study, we observed that the 48-hours food restricted (48-hFR) (food on display) rats significantly increased anger-like behaviour (number of bites and duration of biting) as compared to fed rats. Moreover, the anger induction also increases the *cFos* immunoreactivity profile, specifically in the CeA region of 48-hFR (food on display) rats as compared to 48-hFR (no food on display). Interestingly, while quinpirole treatment significantly elevated anger-like behaviour, sulpiride attenuated.
Discussion and conclusion: The increased number of bites and duration of biting indicates anger-like behaviour. We observed that the *cFos* immunoreactivity profile revealed the activation of CeA during anger-like behaviour. The finding showed DA D2 receptors agonist and antagonist altered anger-like behaviour. Thus, we conclude that the central amygdalar dopaminergic system is involved in the generation of anger-like behaviours of rats.
Acknowledgement: This work is supported by a grant from the DST-SERB (CRG/2020/004971), Government of India, New Delhi

P37: Disparate unfolded protein response of astrocytes in Alzheimer's disease

Diptesh Roy, Subhas C Biswas
Cell Biology and Physiology Division, CSIR-Indian Institute of Chemical Biology, 4 Raja S. Mullick Road, Kolkata 700 032, India

Astrocyte dysfunction contributes to pathogenesis of neurodegenerative diseases including Alzheimer's disease (AD). Misfolded and aggregated amyloid-beta (Aβ) and hyperphosphorylated tau, the hallmark signatures of AD is accompanied with organelle dysfunction especially mitochondria, endoplasmic reticulum (ER), and lysosomes. Being as a major controller of proteostasis, ER plays a key role to modulate cellular milieu with initiating unfolded protein response (UPR) in such neurodegenerative diseases. Previously it has been reported that neuronal dysfunction has been implicated in AD with metabolic changes due to a moderate dose of Aβ(1-42) treatment in primary neuron culture. In this study, a primary astrocyte culture in serum free conditioned medium has been developed to evaluate the effect of this moderate dose of Aβ(1-42) on metabolic changes particularly on UPR response. This astrocyte culture has been characterized morphologically as well as genetically upon Aβ treatment in different time points. We found that anti-inflammatory molecules were the major entities during early onset of Aβ exposure. However, some pro-inflammatory molecules were also increased upon prolonged Aβ exposure. The effect of this moderate dose of Aβ on ER stress was obscure in primary astrocyte cultures unlike neuron cultures. We found that UPR has been initiated in astrocytes. ER membrane bound stress sensor proteins like PERK and IRE1α have been activated as well as altered significantly in its protein level in a time dependent manner in response to this moderate dose of Aβ administration. But, GRP78, ER resident constitutively expressed hsp70, responded in different manner. Downstream effector proteins of PERK & IREIα i.e. eIF2α and JNK were also activated upon prolong treatment. We have also checked the expression profile of components of UPR response pathway in transgenic AD mice which corroborated the findings of culture system. Thus, astrocytes responded differently compared to neurons upon moderate dose of Aβ treatment and ER stress is limited to UPR.
Acknowledgement: The work was supported by Institutional Projects P07(IP1-SCB/547) of CSIR-IICB, Govt. of India

P38: Protective efficacy of caffeic acid against acrylamide-induced neurotoxicity in rats

Divya Gupta, Sadhana Shrivastava, Sangeeta Shukla
Reproductive Biology and Toxicology Lab Jiwaji University, Gwalior, (M.P.)

Background: The presence of acrylamide (AA) has been reported prominently in starchy food processed at high temperatures (>90℃). AA and its epoxide metabolite glycidamide form protein and DNA adducts

leading to neurodegeneration. Caffeic acid (CA) is an active phytochemical compound found in relatively high levels in herbs and spices. CA acts as an antioxidant and prevents oxidative stress.
Materials and Methods: 18 adult Wistar rats were randomly divided into three groups. These groups were normal saline, AA (19.13 mg/kg) for 28 days, and AA (as in group 2) +CA (20 mg/kg) for 7 days. All animals were euthanized after 24 hours of last treatment. Serum and brain sample was collected for further experiments.
Results: Our result showed all the sign and symptoms of acrylamide toxicity which include reduction in body weight, hind limb splaying, hair loss, and skin irritation. AA intoxication significantly increases LPO and DNA damage, and reduces BuChE, AChE, and GSH cycle enzyme activities when compared with normal. Our biochemical findings were reinforced by our light and electron microscopic observation. Treatment with caffeic acid restored tissue and serological indices accompanying towards normal.
Discussion and conclusion: Our experimental findings demonstrate that histopathological changes in the brain and alteration in biochemical parameters and DNA damage were recovered toward normal after administration of CA. This proves that CA exerts a protective effect against AA-induced toxicity. These ameliorative effects of CA were due to its strong antioxidant properties. This investigation provides a piece of useful information for future deep research on the molecular mechanism of the pharmaceutical potential of CA against AA-induced toxicity.

P39: Understanding the role of phytochemicals and Notch 1 in C6 glioma cells and N2A Neuroblastoma cells: An In silico and in vitro validation

Duhita Jadhav, Geetanjali Ganguli
Department of Life Science, Sophia College (Autonomous), Bhulabhai Desai Road, Mumbai 400026.

Background: Glioblastoma (GBM) is a malignant grade IV astrocytoma. Neuroblastoma is an extracranial solid tumor occurring predominantly in infants. The Notch1 signaling pathway participates in cell proliferation, metastasis. Notch1 acts as a tumor promoter in GBM. In Neuroblastoma Notch1 expression predicts poor outcome. Notch1-antagonizing strategies are important in therapeutics.
Materials and methods: The In-Silico study is conducted using multiple databases. For 3D structures prediction ofphytochemicals and protein the Pubchem and Pdb database software are used respectively. Toxicity is predicted using PROTOX II servers. Molecular docking studies are done using Autodock software, Open Bable and PyMoL.
Results: In silico work both the drugs are following the drug likeliness and toxicity criteria. Molecular docking results show that the lowest binding energy of Azelaic acid with notch protein is -5.10 binding at amino acid residue VAL485, GLU473, PHE474, CYS476 and Limonene with notch protein is -4.31 binding at amino acid residue VAL485, GLN475, PHE474, CYS476. In which both the drugs have low binding energy which shows they have high binding affinity.
Discussion / conclusions: The results of molecular docking generate the binding energy between the protein and ligand which is an essential parameter. The lower the binding energy value, the higher is the binding affinity and docking. The present work indicates the binding energies of the notch protein with phytochemicals as -4.31 and -5.10. Our next aim is to study the role of these phytochemicals and notch 1 on C6 and N2A cell lines in vitro.

P40: The role of gut microbiome and associated metabolome in the regulation of symbiosis and dysbiosis through behavioral alteration protecting neural damage in adult zebrafish

Elora Barik and Manorama Patri
Neurobiology Laboratory, Department of Zoology, School of Life Sciences, Ravenshaw University, Odisha, India

Dysbiosis in the gut are found to be associated with the inflammatory bowel diseases (IBD), irritable bowel syndrome (IBS), diabetes, obesity, cancer, cardiovascular and central nervous system disorders. Benzo[a]pyrene (B[a]P), a polycyclic aromatic hydrocarbon (PAH) is known for its neurotoxic potential causing behavioral alterations in animal models. Thus, the present study was conducted on Zebrafish model to address the potential role of microbes on B[a]P-induced dysbiosis leading to neurodegenerative disease

like phenotype. We investigated the role of probiotic, *Lactobacillus rhamnosus* GG (LGG) in modulating host behavioral responses using Light/Dark Preference Test (LDPT) and Novel Tank Diving Test (NTDT) through the metabolic processes of toxicant and microbes interaction regulating the symbiotic process. Waterborne B[a]P exposure was carried out for a stipulated period of 21 days at a concentration of 20 µg/L. Learning and memory was assessed by T-maze and explorative behavior was assessed by novel tank diving test. The findings of the present study advocated that chronic exposure to B[a]P significantly impaired the reference learning memory in zebrafish. Chronic exposure to B[a]P significantly reduced the distance travelled and velocity in novel tank. To address the possible role of microbes in B[a]P-induced learning and memory impairment showing progressive neurodegenerative phenotypes affecting the balance between symbiosis and dysbiosis. The gram-positive cells, behavioral alteration and neurodegeneration were analysed and results showed significant increase in gram negative cells and pyknotic cell count in brain with locomotor impairment. The study showed remarkable behavioral modulation in presence of LGG in toxicant-microbiota relationship providing a major clue for improving animal and human health. Therefore, the findings of the present study address the potential role of probiotic maintaining symbiosis in B[a]P-induced neurodegenerative phenotypes of adult zebrafish.

P41: Evaluation of neuroprotective effects of *Salvia officinalis* on brain tissues in cerebral ischemia

Harshita Ghanghoriya, Arvind Singh Jadon and Manoj Sharma
School of Studies in Pharmaceutical Sciences, Jiwaji University, Gwalior-474001, MP, India

Background: The brain requires 25% of blood pumped by heart, and any interruption in flow of blood can result in cerebral ischemia and neurological deficits. Cerebral ischemia is one of the leading causes of neuronal damage worldwide. The current study looks at neuroprotective properties of Salvia Officinalis (SO) in cerebral ischemia rats.
Methods: The study involved four rat groups: control, ischemia/reperfusion (I/R), and two groups treated with Salvia officinalis (100 and 200 mg/kg, p.o.) for 15 days prior to I/R. After the study period, all rats were sacrificed, and their brains were analyzed. Various parameters, including malondialdehyde (MDA), nitric oxide (NO), superoxide dismutase (SOD), and glutathione peroxidase (GPX) levels, were assessed to evaluate oxidative stress in brain tissue. Additionally, measurements were taken for cytokines (IL-10 and TNF-α), nuclear factor kappa B p65 (NF-κB), caspase-3, brain ATP levels, and DNA damage using the comet assay in the brains of cerebral ischemic rats.
Results: The study found that Salvia officinalis treatment reduced MDA and NO levels ($p<0.01$) and increased SOD and GPX activity in cerebral ischemic rat brains compared to I/R rats. Additionally, SO treatment raised IL-10 and brain ATP levels and lowered TNF-α, caspase-3, and NF-κB levels in cerebral ischemic rat brains compared to I/R rats. The comet assay showed less DNA damage in SO-treated rat brains compared to ischemic rat brains.
Discussion and Conclusion: The current study concludes that Salvia Officinalis has a neuroprotective effect in cerebral ischemic rats due to its antioxidant, anti-apoptotic and anti-inflammatory activity.

P42: Decoding Sanskrit Effect – Impact of Chanting on the Working Memory of Children

Harshini J Anand[1], Deepti Navaratna[2]
[1]Jiwaji University, Gwalior; [2]National Institute of Advanced Studies, IISc, Bangalore

Practices such as Mantra chanting have long been used traditionally to enhance focus and concentration. This study investigated the effectiveness of incorporating mantra-based interventions into educational settings to improve working memory in children. Thirty children (16 boys), aged between 5 and 7 years, with comparable socio-economic backgrounds and basic intelligence were taught a high metric and syllable-accent complexity chant for 30 minutes daily over a period of 5 weeks. Their baseline phonological awareness, working memory, and mantra acquisition parameters (syllable recognition accuracy, pulse, accent and beat pattern recognition, recall and performance) were recorded prior to the intervention. They were tested for changes in their working memory using assessments like the digit span and other phonological assessment

methods. The results indicate an increase in the digit span capacity and an increased accuracy in the digit span assessments. The children also showed a marked increase in the rhythm and pulse perception scores alluding to increased ability to retain and manipulate information in the phonological loop. Enhancement of pulse perception was driven by the effect of the intervention study on the children's ability to perceive and predict a metronome beat pattern and timing. The findings suggest that regular mantra practice may have a positive impact on the development and of working memory in children. They also highlight the potential of incorporating mantra chanting into the educational curricula as a tool to support cognitive development and increase academic performance in children.

P43: Lateral habenula-deep brain stimulation improves spatial recognition memory in depressed rats

Hemant S Kanhere[1], Biru B Dudhabhate[1], Nishikant K Subhedar[2], Dadasaheb M Kokare[1]
[1]Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur-440033, Maharashtra, India; [2]Indian Institute of Science Education and Research, Dr Homi Bhaba Road, Pune 411008, Maharashtra, India

Background: Lateral habenula (LHb) is an important brain structure plays a critical role in spatial memory and depression. LHb hyperactivity results in depressive phenotype. Evidences suggesting the pharmacological inhibition of LHb in depressed rats alleviates depression-like behavior, but in normal rats it results in spatial working memory impairments.
Material and Methods: Rats were exposed to chronic unpredictable mild stress (CUMS) for 6 weeks, unilaterally (intra-LHb) implanted with electrodes and subjected to 14 days deep brain stimulation (DBS) treatment (1h/day). Thereafter, spatial memory with novel object recognition (NOR), and depression by forced swim test (FST) and sucrose preference test (SPT) were assessed.
Results: The chronic stress exposure for 42-days increased immobility time in FST (behavioral despair) and decreased sucrose consumption in SPT (anhedonia). Moreover, the novel object exploration and discrimination index in the NOR test also decreased in CUMS rats, while LHb-DBS application reversed the depressive phenotype.
Discussion and Conclusion: Our results suggest that application of LHb-DBS to the CUMS rats ameliorates the behavioral despairs and anhedonia, reflecting its robust antidepressant effect. Interestingly, the DBS treatment also improved the recognition memory, which is affected due to chronic stress exposure. It has been suggested that DBS may improve the LHb neuropathology and reversed the memory deficit associated with depression. Further studies need to be performed to explore the involvement of LHb in learning memory.
Acknowledgement: We Acknowledge Department of Science and Technology- Science and Engineering Research Board (DST-SERB) (CRG/2020/004971) and Chhatrapati Shahu Maharaj Research, Training and Human Development Institute (SARTHI Provided Ph. D. research fellowship).

P44: Analysis of Olfml3 for its possible involvement in microglia-mediated brain immunity

Himanshi Yadav, Shashank Kumar Maurya
Biochemistry and Molecular Biology Laboratory, Department of Zoology, Faculty of Science, University of Delhi, Delhi-110007

Background: Neuroinflammation is a hallmark of many neurological disorders characterized by microglia activation and infiltration of blood-borne macrophages. Olfml3, a microglia-specific protein has been reported to be a direct target of TGFβ1/Smad2 and may have a role in the regulation of microglia functions. However, information about the Olfml3 protein and its possible involvement in neuroinflammation is still lacking.
Materials and Methods: Lipopolysaccharide-induced neuroinflammatory mice model was used to study the expression pattern of Olfml3 by qPCR and western blotting. Furthermore, the in-silico analysis was done to predict the physicochemical properties, structure, specific interacting proteins, and signaling pathways.
Results: The expression of Olfml3 at both transcript and protein levels was observed to increase in LPS-induced mice as compared to the control. Olfml3 is predicted to be a stable protein with a high aliphatic index, a large proportion of beta sheets, and novel posttranslational modification sites. It was found to interact with proteins essential for microglia proliferation, activation, and migration, extracellular matrix

organization, immunoregulatory interactions between a lymphoid and a non-lymphoid cell, and integrin cell surface interaction.
Discussion and Conclusion: The results of the present study demonstrated an increase in Olfml3 expression in LPS-treated mice. The Olfml3 instability index was found to be low and the aliphatic index was recorded high indicating thermostability. The coiled-coil domain and olfactomedin-like domain were found to be conserved across mammals. By interacting with proteins of microglia, neurotrophic factors, and inflammatory response mediators, Olfml3 could play an important role in the regulation of brain-specific immunity.
Acknowledgements: Financial support of the Institution of Eminence, University of Delhi (IoE, DU) is gratefully acknowledged.

P45: Unraveling the Auditory Enigma: A Comprehensive Neuroimaging Investigation of White Matter Tracts in Subjective Tinnitus

Himanshi Raj Pandey[1, 2], Neeraj Sinha[1], Uttam Kumar[1]
[1]Centre of Biomedical Research, SGPGIMS Campus, Lucknow; [2]Academy of Scientific & Innovative Research (AcSIR), Ghaziabad, India

Background: Tinnitus, delineated as the phantom perception of sound devoid of corresponding external auditory stimuli, is classified into two distinctive categories: subjective and objective tinnitus. The former, a perceptual anomaly without observable neurological pathology, stands in contrast to the latter, stemming from specific neurological aberrations.
Materials and Methods: In this study, 22 subjective tinnitus patients and 22 controls were analyzed using diffusion tensor imaging data acquired from 3T MRI. The focus was on cerebral white matter tracts implicated in tinnitus, with analysis conducted via DSI Studio software, highlighting specific alterations in auditory processing pathways.
Results: Our investigation revealed marked alterations in fractal anisotropy in the Inferior Fronto- Occipital Fasciculus (IFOF) and Uncinate Fasciculus (UF) in subjective tinnitus patients. These white matter tracts are crucial for connecting auditory and visual association cortices with the prefrontal cortex and are implicated in auditory verbal and declarative memory functions. Intriguingly, these disparities were primarily localized to the right cerebral hemisphere, delineating a unique neuroanatomical pattern when juxtaposed with the control group.
Discussion and Conclusions: Subjective tinnitus, a complex neurological puzzle, involves intricate axonal connections. The Inferior Fronto-Occipital Fasciculus (IFOF) forges connections between auditory domains and visual association cortex, extending to the prefrontal cortex. The Uncinate Fasciculus (UF), comprising motor and sensory fibers, links the orbital and inferior frontal gyri with the anterior temporal lobe. These pathways hint at the multifaceted neuroanatomical underpinnings behind phantom auditory sensations, but their exact roles remain elusive.
Acknowledgements- We acknowledge DST (IF200126) and ACSIR for providing funding and academic support.

P46: Diving into anxiety

Irshikaa Sharma, Navin Chawathe, Dr. Tressa Jacob
Department of Life Sciences, Sophia College (Autonomous), Bhulabhai Desai Road, Mumbai 400026

Background: Anxiety is a common psychological condition characterised by excessive fear in everyday situations. Schreckstoff (German word for fright substance), which is released upon mechanical damage to the fish, induces anxiety in zebrafish. The effects of anxiolytics suchas ethanol have been tested to study the reversal of anxiety caused by Schreckstoff.
Materials and methods: Adult zebrafish (1.5-2 years) were used to collect Schreckstoff and also tested for the behavioural analysis. The novel test tank assay has been modified and used to test for anxietyinduced in zebrafish.
Result: A novel method has been devised wherein the chemical can be extracted from the skin of thezebrafish by simply scrapping the skin. On introducing the fish to Schreckstoff, they show anxious behaviour such as darting movements, freezing bouts and reduced exploration of thetank. We have recently shown that after

treatment with ethanol, the anxious behaviour is reduced. 1% ethanol has proven to be the best suited concentration for anxiety reversal.
Discussion and conclusion: Schreckstoff can be collected from the wounds of the fish skin by injuring it multiple times. The novel method devised by our lab works as an alternative to this method wherein the fish need not be sacrificed after Schreckstoff collection. The effects of anxiolytics such as ethanolhave been tested to study the reversal of anxiety caused by Schreckstoff in zebrafish. Currently, we are addressing the neurotransmitters related to this anxiety process in zebrafish.
Acknowledgements (include fundings): I thank the Principal, Dr. Anagha Patil Tendulkar and the Head of the Department of Life Sciences, Dr. Sree Nair for giving me the opportunity to present my work. I thank the Department of Life Sciences at Sophia College, Mumbai for providing me with the fish facility and the resources required to carry out my project. I would like to Dr. Mahendra Sonawane and his lab members at TIFR, Mumbai for helping me learn the various techniquesrequired for my project. I would also like to thank Dr. Kalidas Kohale and his team of the fishfacility at TIFR, Mumbai for providing me with the wild type strain used in the experiments. Thank you to my supervisor, Dr. Tressa Jacob and all the faculty members at the Department of Life Sciences, Sophia College, Mumbai for giving me their guidance. Thank you to mysenior Navin Chawathe for initiating this project and supporting me.

P47: Deciphering the role of 17β-estradiol in pathogenesis of temporal lobe epilepsy

Jaldhi[1], Sonali Kumar[2], Ozasvi R. Shanker[2], Dr. Jyotirmoy Banerjee[3], Dr. P Sarat Chandra[4], Dr. Manjari Tripathi[5], Dr. Shashank Kumar Maurya[1], Dr. Aparna Dixit[2], Dr. Amrita Bakshi[2,6]
[1]Department of Zoology, University of Delhi, Delhi, India
[2]Dr. B. R. Ambedkar Centre for Biomedical Research, University of Delhi, Delhi, [3]Department of Biophysics, [4]Department of Neurosurgery, [5]Department of Neurology, All India Institute of Medical Sciences, New Delhi, [6]Department of Zoology, Ramjas College, University of Delhi, Delhi, India

Background: Temporal lobe epilepsy (TLE) is one of the most common drug-resistant epilepsy. Although 17β-estradiol affects neuronal excitability, expression of its receptor (ERα, ERβ) is least explored in epilepsy. Therefore, present study is designed to elucidate expression of estrogen receptors (ERα, ERβ) in hippocampus of epileptic rats and correlate with neuroinflammation.
Materials and methods: Adult male rats were administered with pilocarpine to generate acute model of TLE. Western blotting and qPCR of estrogen receptors, neurotrophic factors and neuroinflammatory markers were performed to analyse hippocampal protein and mRNA levels, respectively.
Results: The expression levels of estrogen receptors, neurotrophic factors and neuroinflammatory markers were found to be upregulated in hippocampus of epileptic male rats as compared to the controls.
Discussion and conclusions: Increased expression of ERα and ERβ were seen to positively correlate with the levels of neurotrophic factors and neuroinflammatory markers. A single report in ovariectomized mice demonstrates reduced hippocampal expression of ERβ. Further, deletion of ERβ has shown to elevate the seizure susceptibility which suggests its neuroprotective role in chronic epilepsy. Additional studies are required to validate the role of ERs in neuroinflammation and seizure susceptibility in epilepsy.
Acknowledgement: Department of Health Research (DHR), Ministry of Health and Family Welfare, New Delhi is acknowledged for the financial assistance.

P48: Targeting adult neurogenesis for hippocampal regeneration following neurodegeneration by recruitment of endogenous neural progenitors

Jhilik Dey[1,2,3] and Prem Prakash Tripathi[1,2,3]
[1]Cell Biology and Physiology Division, CSIR-Indian Institute of Chemical Biology (CSIR- IICB), Jadavpur, Kolkata -700032, India; [2]IICB- Translational Research Unit of Excellence (IICB- TRUE), Kolkata- 700091,India; [3]Academy of Scientific and Innovative Research (AcSIR), Gaziabad - 201002, India.

Background: Seizure-induced neurodegeneration in the hippocampus provides a powerful model for investigating adult neurogenesis as a response to injury in an attempt for brain regeneration following neurodegeneration by recruitment of endogenous neural progenitors. Our present study investigates the response of endogenous neural progenitors following injury and their roles in hippocampal regeneration.
Materials and Methods: Kainic Acid was administered once intraperitoneally at a dose of 30mg/kg of animal body weight followed by BrdU injection at various time points to mark the newborn neurons.

Transcardial perfusion was performed; brain samples were fixed and processed by cryosection. Immunofluorescence was performed using a routine procedure.
Result: Seizure-induced selective lesions at the CA1 and CA3 regions of the hippocampus were detected following KA treatment by Nissl staining. Also, TUNEL+ cells were observed at thoseinjury sites (CA3 and CA1). Our result showed that there is massive activation, proliferation and migration of the endogenous neuronal progenitors at injury sites following KA-induced neurodegeneration. Around 45 days of post-KA treatment, the reappearance of pyramidal neurons at injury sites was observed.
Conclusion: In response to neurodegeneration following a seizure, a robust proliferation of endogenous neuronal progenitors in the dentate gyrus of the adult brain has taken place. These newborn neural progenitors may, in turn, have subsequently migrated at the injury sites to generate newneurons there. Thus, the presence of new neural progenitors at injury sites, followed by gradualregeneration of hippocampus pyramidal neurons shows the endogenous repair potential of thebrain to restore brain functions.
Acknowledgement: The authors gratefully acknowledge the financial assistance from SERB, CSIR and UGC-JRFFellowship.

P49: Identifying transcriptional factors involved in non-canonical Hes1activation

Jyothi P Nair[1,2], Rahul Jose[1,3], Budhaditya Basu[1,3], Surya Suresh[1,2], Archana R[1], RiyaAnn Paul[1,2], Parvathy Surendran[1,2], Meera V[1,2] and Jackson James[1]
[1]Neuro Stem cell Biology Laboratory, Regenerative Biology, Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram, Kerala-695014, India; [2]University of Kerala, Thiruvananthapuram, Kerala-695014, India; [3]Regional Centre for Biotechnology (DBT-RCB), Faridabad, Hariyana-121001, India

Background: Hes1 is a crucial transcription factor that plays a fundamental role in stem cell maintenance and differentiation. Conventionally, Hes1 activation has been associated with the canonical Notch signaling pathway involving CBF1. Along with other reports, we found the existence ofCBF1 independent Hes1 activation in mouse neocortex.
Materials and methods: The Reverse Chromatin Immunoprecipitation (Reverse-ChIP) assay was employed with Hes1 promotor using mouse cortical nuclear extract (E14). Utilizing Molecular techniques, Mass spectrometry and Bioinformatics we examined the regulatory elements and signaling pathwaysthat contribute to Hes1 upregulation independent of the canonical Notch pathway**.**
Results: We identified the binding of transcriptional factors (β catenin, Smad, Tead1, Foxg1) involvedin other signaling pathways on Hes1 promoter using mass spectrometry. We found an enrichment of signalling pathways such as Wnt, Hippo, TGFB, FOXO and Hedgehog, amongwhich, Wnt signaling is the most prominent. Our analysis suggests a possible cross talk amongthe signalling pathways. The findings offer significant implications on regulatory mechanismscontrolling gene expression and transcriptional regulation of the Hes1 promoter**.**
Discussion and conclusion: The study contributes to our understanding regarding gene regulation and its impact on corticaldevelopment. The signaling pathways involved in activation of Hes1 non canonically would help us understand how the neural stem cells are maintained in the neocortical niche. The implications of our findings extend beyond the realm of developmental biology, as dysregulation of Hes1 has been linked to various pathologies, including cancer and neurodegenerative disorders**.**
Acknowledgement: Supported by DST SERB (CRS/2021/005847) and Intramural grand from RGCB. Fellowshipto JPN (366288) from UGC RJ (12416) from CSIR

P50: Ex vivo metabolic alterations in a rat model of repetitive brain injury

Jyoti Chaurasia[1], Samiya Zehra[2], AK Baranwal[3], Kamlesh Singh Bhaisora[4], Ahmad Raza Khan[2]
[1] Department of Biochemistry, University of Lucknow, Lucknow, U.P; **[2]**Department of Advanced Spectroscopy and Imaging, Centre of Biomedical Research (CBMR), SGPGI Campus, Raebareli Road, Lucknow, India.; **[3]**Experimental Animal facility, SGPGIMS, Raebareli Road, Lucknow**;** [4]Department of Neurosurgery, SGPGIMS, Raebareli Road, Lucknow

Background: In most instances, mild and repetitive mild head injuries (RmTBI) are unreported, although is a strong risk factor for neurodegenerative diseases. Due to the absence of any objective markers for such injuries, it's crucial to develop effective prevention strategies. Ex-vivo metabolic changes in RmTBI rat models suggesting elevated oxidative stress.

Material and Method: Rats were divided into three groups, viz. control, mTBI and RmTBI. The latter two experiencing single and triple head injuries. Brain tissue metabolites were extracted using perchloric acid extraction method. NMR data were acquired on 800 MHz NMR-Spectrometer and analyzed on Metaboanalyst platform.
Results: The multivariate data analysis was performed on all the 1D ^{1}H CPMG NMR spectra obtained for the injured and control group revealing significant differences between control and mTBI and RmTBI groups through PCA analysis. In post-mortem brain tissue, ^{1}H NMR was utilized to aptly detect total 18 metabolites. Through ANOVA ($p<0.05$), acetate and formate were found significant out of all metabolites profiled in the hippocampus.
Discussion and Conclusion: A systemic change in the metabolites occurs during brain injury. We observed a significant variation in acetate and formate only in the hippocampus region. Acetate indicated energy perturbation in both groups and suggest disturbed energy metabolism. While formate significantly altered only in the mTBI group and suggest neurodegeneration. Metabolic profiling of the motor cortex and cerebellum region did not show any significant metabolic alterations. Therefore, we concluded that the hippocampus is the most sensitive region of the brain.
Acknowledgements: The work is funded by the Department of Biotechnology, Govt of India under the Ramalinga swami Re-entry Fellowship grant 2019. We would also like to thank our host institute, the Centre of Biomedical Research (CBMR), under the Department of Health and Family Welfare, UP Govt. We also thank our collaborators for their support for animal experimentation at SGPGI, Lucknow.

P51: BBPT prevents apoptosis through Caspase-3/BCL-2 expression and suppresses neuro-inflammatory pathway in 6-OHDA induced unilaterally lesion rat model of Parkinson's disease through non-dopaminergic pathway

Jyoti Mishra, Pratibha Mehta Luthra
Neuro-pharmaceutical Chemistry Laboratory, Dr. B. R. Ambedkar Centre for Biomedical Research, North Campus, University of Delhi, Delhi 110007, India.

Background: Parkinson's disease (PD) is neurodegenerative disorder characterized by dopaminergic neuron damage in SNPc which involved in neuro-inflammation, dysregulation in calcium signalling, autophagy and apoptosis. Therapeutic potential BBPT as A_{2A} receptor antagonist investigating the efficacy of BBPT in counteraction of free radical-scavenging and superoxide scavenging activities by 6-OHDA induced PD.
Material and Methodology: Various antioxidant assays DPPH and ABTS assay had done before evaluating the neuro-protecting effect of BBPT. Unilaterally lesion 6-OHDA model in rats was established and validated by behavioural test. Neurochemical protein expression (TH and dopamine level), anti-oxidants MDA, GSH, SOD, catalase, dopamine and glutamate levels were studied in 6-OHDA induced PD.
Results: BBPT showed better antioxidant activity in comparison to ascorbic acid. BBPT reverse significant changes in motor and non-motor symptoms of unilaterally lesioned 6-OHDA induced PD. Neurochemical alteration like TH enzyme, Dopamine, genetic mutation (DJ-1 and parkin level), anti-oxidant enzymes, neuro-inflammatory (TNF-α and IL-6) and apoptotic proteins (Caspase-3 and BCL-2) were restored after BBPT treatment in unilaterally 6-OHDA induced PD in SD rats.
Discussion and Conclusion: Our results demonstrated that the compound BBPT is non-toxic and BBPT modulated Caspase-3/BCL-2 levels to inhibits apoptosis and decreases the TNF-α and IL-6 levels leading to restore the neuronal damage in unilaterally lesioned 6-OHDA induced SD rats. Thus, the research amply supported BBPT's eminence as a potent anti-parkinsonian drug with a significant capacity to prevent neurodegeneration. This might have an impact on the pathophysiology of PD and potential treatment targets in the future.
Acknowledgements: Jyoti Mishra is thankful to the University Grant Commission (UGC), CSIR, New Delhi, India for the award of Junior Research Fellowship. Pratibha Mehta Luthra is thankful to the IoE, University of Delhi for sanctioning research funds to carry out this study. We acknowledge the Central Instrumentation facility (CIF), ACBR, University of Delhi, India for providing necessary support.

P52: Exploring gene regulation and electro-behavioral alterations in Pilocarpine-induced epilepsy in rats

Jyoti Tyagi, Shweta Saran, KC Upadhayay, and Deepak Sharma School of Life Sciences, Jawaharlal Nehru University, New Delhi-110067

Background: Epilepsy is a neurological disorder characterized by episodes of recurrent seizures. The prevalence and onset of epilepsy is multifactorial and contributed by mis regulation in the expression of multiple vital genes. 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 can change the idea for therapy. Hence, in our study, we evaluated the expression pattern of STX1B, KCNN2, FOXO, GABRA and GRIK1 genes, and electro-behavioural alterations in pilocarpine-induced epilepsy.
Methods: Male Wistar rats (~250gms) to induce epilepsy pilocarpine (127mg/kg) was injected in Wistar rats. which resulted in progressive evolution of seizures. To reduce the mortality rate in rats Diazepam (8mg/kg) was administered 120 min after Status epilepticus (SE) induction Epileptiform seizures were confirmed by Racine scale and electroencephalographic (EEG) from the cortex and hippocampus of the brain, post 25 days of injection. Electro-behavioral assessment was carried out by using Morris water maze (MWT) test to investigate spatial learning in epileptic rats. The mRNA expression of STX1B, KCNN2, FOXO, GABRA and GRIK1 genes was analyzed using real time-PCR.
Results: Our results demonstrated the occurrence of discrete epileptiform episodes in the cortex and hippocampus suggesting epilepsy in pilocarpine-induced rats. It was further confirmed by the electro-behavioural analysis. Decreased spatial learning was observed in epileptic rats. The expression of STX1B, KCNN2, FOXO, GABRA and GRIK1 genes was seen to be down-regulated in both cortex and hippocampus of pilocarpine-Induced Epileptic Rats.
Conclusion: The product of these genes STX1B, KCNN2, FOXO, GABRA and GRIK1 could be involved in the altered electro-behavioural expression affecting spatial learning and collectively inducing epilepsy in pilocarpine - injected rats. Hence, this model can be further explored to get an insight into the gene expression patterns, observed in human epileptic conditions.
Acknowledgment: Financial assistance for the present study was provided from ICMR, New Delhi, India

P53: Understanding anxiety-like behaviors manifested in rodent model of Alzheimer's disease (AD)

Jyotsna Pandey[1], Amrutha S[2], Sakshi Sharma[1], Suman Jain[3], Varsha Singh[4]
[1]School of Interdisciplinary Research, Indian Institute of Technology (IIT), Delhi; [2]Indian institute of Technology, Delhi [3]Department of Physiology, ALL INDIA INSTITUTE OF MEDICAL SCIENCES New Delhi [4]Humanities and Social Sciences, IIT Delhi

Background: AD is a neurodegenerative disorder that affects cognitive functions, leading to memory loss, impaired thinking, and difficulty in performing daily activities. However, AD is not limited to cognitive symptoms; it can also manifest with a range of neuropsychiatric symptoms, including psychological distress and mood alterations such as anxiety and depression. We aimed to examine the anxiety-like behaviors with AD to provide insights into the interplay between cognitive decline and emotional states.
Materials and Method: Open filed test paradigm was performed in adult males (n=20) albino Wistar rats weighing 220- 250g to examine the anxiety-like behavior. The variables taken for the assessment of OFT were total time spent in the periphery, corner, and center of the chamber, frequency of climbing and rearing which may provide insights into the animal's level exploration and anxiety,
Results: Analysis showed that AD rats spent less time in the center (inner zone) than the healthy control rats ($p=0.003$, $t=3.434$, $df=18$), and chose to spend more time in the corners of the chamber ($p=0.01$, $t=2.628$, $df=18$). Further, when the ethological parameters were assessed, we observed increased climbing ($p=0.03$, $t=2.324$, $df=18$) and rearing ($p=0.04$, $t=2.213$, $df=18$) in AD rats, suggesting increased emotional distress in AD rat model.
Discussion and Conclusion: Our analysis suggests that there is a connection between AD- related neuropathology and anxiety-like behavior. However, the results from studies examining anxiety-like behavior in AD have been inconsistent. The findings highlight the complexity of the relationship between AD, anxiety-like behavior, and the need for more comprehensive approaches to studying emotional dysfunction in AD models. This could lead to a better understanding of the underlying mechanisms and potential avenues for treatment strategies targeting both cognitive and emotional symptoms in AD.
Acknowledgements: VS and SJ supervised the study, JP collected the data and guided the interns to perform the analysis, AS performed the data analysis. This work was under DST SERB Vritika Research Training Grant of the author (VS) supporting the Trainee (AS).

P54: Navigating the neural labyrinth: A technical exploration of age-related changes in brain complexity

Kalpana Dhanik and Uttam Kumar
Center of Biomedical Research, SGPGIMS Campus, Lucknow

Background: Brain complexity, encompassing attributes like gyrification and fractal dimension, is an indicator of brain health and neurological disorders. Age-related declines in complexity are linked to cognitive impairment and neurodegenerative diseases. This study probes these changes to enhance understanding and potential early detection of related issues.

Material & Methods: Forty participants were analyzed using a 3T Siemens Magnetom Skyra scanner with a T1-weighted MPRAGE sequence. The study used computational anatomy toolbox (CAT12/SPM12) for processing and included surface-based morphometric analysis. Statistical analysis identified complexity differences between aging and early adult groups, with corrections made using the FDR method.

Results: The quantitative analysis demonstrated pronounced differences in brain complexity between normal aging and early adult groups. These disparities were particularly evident in the frontal, temporal, parietal, and occipital regions of the brain. These areas are integral to cognitive functions, including memory, attention, language, and spatial reasoning. The observed variations may underline substantial shifts in neural connectivity and processing, reflecting the age-related changes that affect essential cognitive abilities, thereby contributing to the broader understanding of aging's impact on the brain.

Discussion and Conclusion: This study reveals significant age-related changes in brain complexity, particularly in regions governing cognitive functions. The differences may indicate alterations in neuronal connectivity and function, leading to cognitive decline and increased risk of neurodegenerative disorders. The findings contribute to understanding the aging brain, offering potential pathways for early diagnosis or targeted therapies, thus emphasizing the importance of complexity measures in neuroscience and clinical practice.

Acknowledgement: We acknowledge CBMR for providing intramural funding**.**

P55: Stereological analysis of microglia in rat hippocampus following partial sciatic nerve ligation

S Kamalesh, Mamta Bishnoi, Tony George Jacob, Saroj Kaler Jhajhria
All India Institute of Medical Sciences, New Delhi

Background: Neuropathic pain, a complex and debilitating condition, poses challenges in understanding its underlying mechanisms and impact on brain regions such as the hippocampus. This project aimed to investigate the effects of partial sciatic nerve ligation (PSNL), a model of neuropathic pain, on microglia in the rat hippocampus through design-based stereology.

Materials and methods: Male Sprague Dawley rats were divided into Sham and PSNL groups, with a 28-day observation period. Optical fractionator was used to quantify the total number of microglia. Nucleator probe was used to measure the approximate volume of the microglial cell body. Cavaliery probe was used to measure the approximate volume of the contralateral hippocampus.

Results: Design-based stereology provided quantitative insights into microglial changes. The PSNL group demonstrated a significant increase in the total count of IbA1-positive microglia in the contralateral hippocampus. Furthermore, analysis using the nucleator probe revealed a noteworthy increase in the average volume of microglia in the PSNL group. The cavaliery probe indicated no significant differences in the volume of the contralateral hippocampus between the PSNL and Sham groups.

Discussion: This study highlights the impact of neuropathic pain on the hippocampus, shedding light on microglial activation and potential alterations in behaviour. The project also demonstrates the utility of design-based stereology in precisely quantifying microglial parameters and hippocampal volume, offering a comprehensive view of neuropathic pain induced alterations. This work contributes to the broader field of neuropathic pain research and encourages further investigation into the complex relationships between pain, microglia and brain function.

Acknowledgement: We would like to thank the Department of Anatomy, AIIMS, New Delhi for funding this project.

P56: Neurochemical alterations in Primary Visual cortex (V1)during Retinal Degeneration

Kashish Parnami, Anwesha Bhattacharyya
Amity Institute of Neuropsychology and Neurosciences, Sector 125, Block- J1, Amity University Noida, UP 201313

Background: Retinal degeneration (RD) involves gradual retina deterioration, including light- sensitive photoreceptor loss. Electrophysiological studies explored photoreceptor death's impact on V1 neuron responses. Our study examines GABAergic neuron subtypes to reveal neurochemical changes that shape excitatory neuron output. Thisinsight enhances understanding RD's effects on visual processing and neuronal communication.
Materials & Methods: Changes in parvalbumin and somatostain groups of interneurons were studied in a mouse model of RD, C3H/HeJ (rd1) mice and compared with C57BL/6 wild type mice. Animals were intracardially perfused, brains were dissected, postfixed followed by sectioning in cryostat. Sections were immunostained, visualized in confocal microscope and images were quantified.
Results: A trend of higher number of GABAergic neurons were observed in the upper layersof the V1 as compared to the lower layers. Next, we evaluated the changes in the GABA neurons in different age groups (early and late). No clear changes inparvalbumin (PV) and somatostatin (SST) were observed in either stage of wildtypeanimals. However, there was a decline in the population of PV neurons in the earlystages of RD**.**
Discussion: Here, we show that there is a decrease in the population of subtypes of GABAergicneuron during RD, indicating a possible connection between visual impairment andchanges in inhibitory interneuron populations. This reduction in specific GABAergic subtypes may contribute to disruptions in inhibitory-excitatory balance within V1, possibly affecting the processing of visual information and the overall functionality of the visual cortex.
Acknowledgment: AB was supported by the Ramanujan Fellowship of Science and EngineeringResearch Board (SERB), Department of Science and Technology (DST), Government of India (Grant: RJF/2019/000040), and the Core Research Grant (CRG) of SERB, DST (CRG/2021/003472

P57: Glycemic fluctuations and their effect Semaphorin 4D in Frontal Cortex ofDiabetic Rats

Kavya Shah, Amee Krishnakumar
Institute of Science, Nirma University, Ahmedabad

Intricate arborization of neuronal dendrites is crucial for signal processing. Sema4D binding with plexinB1 is involved in process that modulates dendritic branching via cytoskeletal dynamics including actin and microtubule organization in CNS neurons, including those in frontal cortex. Alterations in the Sema4D/plexinB1 signalling are associated with neurological disorders characterized by abnormal dendritic morphology, highlight its role in circuit maintenance. ATP powers actin polymerization and its hydrolysis within filaments, while microtubule motor proteins use ATP hydrolysis for movement during growth cone formation. Altered glycemic levels could disrupt ATP-dependent cytoskeletal dynamics. Unexplored effects of glycemic variations on Sema4D/plexinB1 signalling could potentially interrupt branching, revealing metabolic impacts on neurodevelopment. The primary functionof the frontal cortex involves integrating sensory stimuli, executing decisions, and generating motor responses through its dendritic architecture, which might get altered during disrupted glycemic regulation. Diabetes (D) was induced in adult male Wistar rats (250-300g), by a singleintravenous dose of streptozotocin (30 mg/kg body weight). Hypoglycemia was induced by administering daily two doses of insulin in control (C+IIH: 1.5 IU/kg body weight), and in diabetic (D+IIH: 10 IU/kg body weight) rats via subcutaneous dosing for 4 weeks. Gene expression analyses of Sema4D and PlexinB1 and Adhesion Removal behavioural assay wereconducted in experimental rats. Alterations in gene expression levels in experimental conditions can be a causing factor of changes in frontal cortex dendritic structure. Thus, our study highlights the underlying role of Sema4D in dendritic arborization under glycemic alterations offers a promising avenue for further investigation.
Acknowledgement: Dr. Amee Krishnakumar thanks Institute of Science, Nirma University for infrastructural facility. Ms. Kavya Shah acknowledges the fellowship grant (202101569) from ScHeme of Developing High quality search (SHODH), Education Department, Gujarat State and Instituteof Science, Nirma University for Research Budget for PhD Scholars (E1A07A).

P58: Association of Pax6, Parkin and α-Synuclein in Parkinson's disease

Khushboo Srivastava and Rajnikant Mishra
Biochemistry and Molecular Biology Laboratory, Department of Zoology,Institute of Science, Banaras Hindu University, Varanasi- 221005, India

Background: Pax6, evolutionary conserved transcription factor, is required for the functionalanatomy of the eyes, brain, pituitary, pineal and pancreas. However, mechanisms of Pax6 functions and it association with Parkin and α-synuclein in Parkinson are unavailable.
Material and methods: Adult male mice (*Mus musculus*) of AKR strain were used for developing the Parkinson's model by using MPTP (20mg/kg, SC, 21 days). Brains were removed, fixed and process for cryo-sectioning, Nissl staining and Immunohistochemical analysis. SH-SY5K, NIH-3T3 cell lines were also used to evaluate association of Pax6, Parkin, α-Synuclein.
Results: Cell types and numbers decrease in the striatum (SNc, DV) and layers of cerebral cortex; molecular layer (MoLr), external granular layer (ExGl), pyramidal layer or external plexiform layers (PyLr/ExPl), inner granular layer (InGl), ganglionic layer (GaLr), multiform layer (MuLr) in brain of MPTP-treated Parkinson's mouse model. The Pax6, Parkin and α- Synuclein co-localize but their expression and co-localization change in the MPTP treated mice and SH-SY5Y cell line.
Discussion and Conclusions: Reduction in Pax6 and Parkin-positive cells and increase in α- Synuclein immuno-positive cells in brain of MPTP induced mice, and co-localization of Pax6with Parkin and α-Synuclein in SH-SY5Y cell line indicate their association in Parkinson disease.
Acknowledgements: DBT, India, BT/PR28908/MED/122/174/2018 Dt 10/02/2020

P59: Unravelling the Therapeutic Potential of Atomoxetine in Animal Model of Burn-Injury induced Chronic Pain

Krushna Eknath Yadav, Nipun Pundeer, Vinod Tiwari
Neuroscience and Pain Research Laboratory, Department of Pharmaceutical Engineering and Technology, Banaras Hindu University, Varanasi,221005, U.P. India.

Background: Burn injuries is the most burdensome and common problem which is the main cause of mortality along with severe and long-lasting pain. The pathophysiology of burn pain is poorly understood due to various pathways associated with it & the lack of clinical and pre-clinical shreds of evidence. It is generally caused by physical contact with harmful elements such as flames, electricity, scalding etc. Through behavioural assessments, biochemical, mRNA and protein expression, the study aimed to uncover the mechanism by which atomoxetine modulates pain perception and to assess its potential as a novel therapeutic option. In this study we are investigating the antinociceptive effect of atomoxetine, suggesting its potential to alleviate burn-injury induced chronic pain by targeting different types of nociceptors.
Materials and methods: Animals: Male Sprague Dawley rats (200-220gm)
Drugs: Atomoxetine (1,3,10mg/kg i.p.), Morphine 5mg/kg i.p.)
Behavioural assessment: Mechanical Allodynia-Von Frey test, Thermal hyperalgesia-Hargraves test, Cold Allodynia- Acetone drop test, Cold Hyperalgesia-Ice Floor test.
Biochemical Analysis: GSH, MDA and Nitrite.
Discussion and conclusion: According to Behavioral studies, atomoxetine exhibits effective anti-nociceptive activity in burn-injured rats. The effect is also maintained for nearly 120minutes after drug administration in various pain behavior tests and for 240 minutes in the case of mechanical allodynia.
These results from Hargreaves test, von Frey hair test, acetone evaporation test and ice floor test support that atomoxetine can modulate thermal hyperalgesia, mechanical allodynia, cold allodynia and cold hyperalgesia in burn injury rats.
Atomoxetine has also shown a significant effect on the levels of Glutathione, Malondialdehyde, and nitrite stress indicating that it can attenuate the oxidative stress in the sciatic nerve of burn-injured rats. This promising finding may pave the way for further research that could lead to a novel treatment for burn pain.
Results: Results suggest that burn injury reduced the level of antioxidant enzyme glutathione which was further elevated by the atomoxetine treatment. The level of malonaldehyde was found to be increased by the

burn injury which was attenuated by the atomoxetine treatment and the nitrite level was found to be significantly reduced by the atomoxetine treatment.
Results indicate that Atomoxetine (Strattera®), a selective norepinephrine (NE) reuptake inhibitor and potential NMDA blocker, may be able to treat burn injury-induced chronic pain by significantly reducing thermal hyperalgesia, mechanical allodynia, and the effects of potentially noxious or innocuous cold stimuli. Hence, may show antinociceptive effects.
Acknowledgements: We acknowledge the Department of Pharmaceutical Engineering and Technology, Indian Institute of Technology, Banaras Hindu University, Varanasi, Uttar Pradesh, India, for providing the necessary facilities and infrastructure.

P60: Microglia extracellular traps: In health and disease

Lipika Sha and Sushmita Jha
Department of Bioscience and Bioengineering, Indian Institute of Technology Jodhpur, Jodhpur, Rajasthan - 342037

Background: Extracellular Traps (ETs) are extracellular web-like structures composed of nuclear or mitochondrial DNA. ETs are released from various immune cells in response to different stimuli. Circulating ETs can be markers of cancer. Our group discovered dopamine-induced microglia ETs. Our work confirmed the presence of ETs in glioblastoma tissue.
Materials and Methods: Microglia cells (BV2) were stimulated with dopamine, cellular, molecular and transcriptomic techniques to assess the structure and function, revealed key differences from Neutrophil Extracellular traps.
Results: Dopamine induces extracellular traps in microglia. Additionally, Dopamine induces microglia glioblastoma cell proliferation. Cellular, molecular and transcriptomic techniques reveal differences from neutrophil extracellular traps.
Conclusion: In the GBM microenvironment, tumour cells secrete and respond to dopamine in an autocrine mechanism. Different cells in the GBM microenvironment, such as astrocytes and tumour cells, respond differently to dopamine. The role of dopamine-induced microglia Extracellular Traps (miETs) in the GBM microenvironment plays a vital role in GBM pathophysiology, this may be investigated as a potential therapeutic intervention.
Acknowledgement: We are thankful to IIT Jodhpur for infrastructure, administrative and financial support. Lipika Sha is supported by MoE (Ministry of Education) fellowship from IIT Jodhpur.

P61: Understanding the role of biased and unbiased KOR agonist in modulation of affective behaviour

Manish K. Dash[1,3], Poonam Kumari[1, 4], Lalan Kumar[2, 4], Sanjay Batra[2], Prem N.Yadav[1]
[1]Neuroscience and Ageing Biology Division, [1]Medicinal and Process ChemistryDivision, CSIR-Central Drug Research Institute, Lucknow, India; [3]Academy of Scientific and Innovative Research (CSIR-HRDC) Ghaziabad, Uttar Pradesh (India); [4]Jawaharlal Nehru University, New Delhi, 110067

Biased Kappa Opioid Receptor (KOR) agonists have emerged as promising candidates for the treatment of chronic pain conditions. Neuropathic pain is a highly unmet medical need as the available analgesics are either very moderately effective or mired with serious adverse effect profiles. Furthermore, neuropathic pain is highly associated with severe debilitating mood impairments, such as depression, anxiety, and loss of motivation. Although KOR agonist has been shown to attenuate nociceptive pain, role of biased KOR agonist on affective components of neuropathicpain is not known. Therefore, we evaluated the effect of G-protein biased and unbiased KOR agonist on neuropathic pain using Chronic Constriction Injury (CCI) and Chemotherapy-induced peripheral neuropathic pain (CIPN) models in SD rats and C57BL/6J mice, respectively. We observed that following biased KOR agonist CDRI4/105 (10mg/kg; p.o., 7 days), significantly alleviated hyperalgesia and allodyniain CCI and CIPN model of neuropathic pain. Conversely, unbiased KOR agonist U50488 (5mg/kg; i.p.) didn't elevate paw withdrawal threshold significantly. These results highlight CDRI4/105's potential therapeutic use in chronic pain conditions. Furthermore, we observed

that CDRI4/105 alleviated the neuropathic pain induced increased in the anhedonia, anxiety like behaviors. Significantly, we also found that CDRI4/105 did not induce aversion/dysphoria in contrast to unbiased KOR agonist U50488. Further studies are in progress to delineate the molecular mechanisms of biased KOR signaling in the modulation of affective neurocircuitry.

P62: Noradrenaline stimulates Na-K ATPase expression by increasing its mRNA stability by modulating HuR: Implications with rapid eye movement sleep and its loss

Manjeet Kaur[1], Rachna Mehta[2], Rohini Muthuswami[1] and Birendra Nath Mallick[2]
[1]School of Life Sciences, Jawaharlal Nehru University, New Delhi -110067
[2]Amity Institute of Neuropsychology and Neurosciences, Amity University, NOID

Background: Rapid Eye Movement Sleep (REMS) is an evolutionary conserved instinct behavior expressed in higher vertebrates. Although one spends the least time in REMS, it is essential for the homeostatic maintenance of normal physiological processes. Consistence research including contributions from our lab has shown that REMS deprivation (REMSD) increases noradrenaline (NA) level in the brain and that stimulates Na-K ATPase. Based on our findings it has been proposed from this lab that "evolutionary significance of REMS is to maintain brain level of noradrenaline (NA)" (Singh et al., 2019) and one of the functions of REMS is to maintain brain excitability by NA-mediated regulation of Na-K ATPase activity (Mallick and Singh, 2011). Subsequently, while understanding the molecular mechanism of sustained expression of Na-K ATPase molecules, we observed that although REMSD-associated elevated NA increased Na-K ATPase protein expression, that was not supported by corresponding increase in its mRNA abundance (Amar and Mallick, 2015). To resolve this apparent puzzle, we hypothesized that increased mRNA stability and its recycling might be responsible for increased Na-K ATPase protein translation We investigated the NA-induced HuR mediated Na-K ATPase mRNA stability.
Material and Methods: Male Wistar rats (220-250g) were REMS deprived for four days using classical Flowerpot method. The mRNA stability was assayed using *in vitro* cytoplasmic degradation method. The HuR protein expression was evaluated by western blotting in cytoplasmic and nuclear fractions from the same brain sample.
Results: REMSD-induced elevated NA indeed increased Na-K ATPase mRNA stability. mRNA stability was measured from control and REMSD rat brain with or without *in vivo* (intraperitoneal) treatment with α_1-adrenoceptor (AR) antagonist, prazosin (PRZ). Upon REMSD, Na-K ATPase α1-, and α2-mRNA stability increased significantly, which was prevented by PRZ. We also observed that the increased mRNA stabilization was induced by increased cytoplasmic abundance of HuR through PLC- mediated activation of PKC pathway.
Summary and Conclusion: REMSD-associated elevated NA acting on ARs modulates HuR and increases Na-K ATPase mRNA stability leading to increased expression of Na-K ATPase. This explains REMSD-associated sustained effect on brain excitability and chronic disease-associated symptoms.
Acknowledgement: MK received fellowship from DBT. Research funding to BNM under JC Bose fellowship and Institutional umbrella support under DST-PURSE& FIST and UGC-DRS.

P63: Decoding the molecular mosaic of age-related shifts in CNS neuron regeneration through Bioinformatics

Manojkumar Kumaran[1], Yogesh Sahu[1], Anisha S Menon[1]and Ishwariya Venkatesh[1]
[1]Department of axon growth and regeneration, CSIR-CCMB, Hyderabad.

Background: While numerous neurons display a sustained regenerative capacity throughout their lifespan, central nervous system (CNS) neurons uniquely exhibit heightened regenerative potential predominantly during their youthful phase. The underlying mechanisms governing this age-related shift, particularly at the molecular level, remain incompletely elucidated. Understanding the intricate molecular alterations accompanying the decline in regenerative aptitude of CNS neurons is pivotal for therapeutic advancements. The interplay between transcriptional, epigenetic, and 3D genomic landscapes could offer crucial insights into this complex phenomenon.
Methods: Employing advanced bioinformatics algorithms and machine learning techniques, we modelled the trajectory of age-dependent changes in CNS neurons. Comprehensive analyses were conducted using

combined single nuclei RNA-seq, ATAC-seq, and Hi-C to scrutinize modifications in transcriptional networks, epigenetic arrangements, and 3D genomic conformation.
Results: Preliminary data pinpoint nuclear receptors and stripe factors as significant molecular entities influencing the decline in regenerative capability of CNS neurons. Current endeavours are concentrated on assessing alterations in pertinent enhancers to furnish a comprehensive molecular portrait.
Discussion: By meticulously tracing the molecular dynamics associated with the waning regenerative potential of CNS neurons, this study aims to unveil novel determinants governing this process. The insights gleaned will not only deepen our understanding but also pave the way for innovative therapeutic strategies targeting CNS neuron regeneration.
Funding acknowledgment: Council of Industry and Scientific Research (CSIR).

P64: NLRX1 a novel regular regulator of innate immunity in the Glioblastoma tumor microenvironment

Durgesh Meena[a], Sushmita Rajkhowa[a], Sushmita Jha[a]
[a]Department of Bioscience and Bioengineering, Indian Institute of Technology Jodhpur, Jodhpur, Rajasthan

Background: Glioblastoma (GBM) is the most aggressive glioma. Innate Immune cells such as microglia and macrophages account for >50% of the cellular population within the GBM microenvironment. Innate immune cells express pattern recognition receptors (PRR). One PRR, NLRX1, regulates mitochondrial signaling and cancer progression but the *role of NLRX1 in GBM is unexplored.*
Material and Methods: To understand the subcellular expression pattern of NLRX1, immunocytochemistry and immunohistochemistry were performed on glial and GBM cell lines, GBM primary cells and brain tissue sections. Western Blot was performed to quantify the NLRX1 differential expression, and NLRX1 gene knockdown was utilized for functional assessment across cell populations.
Results: Differential subcellular localization of NLRX1 in various cell lines shows the cell-specific role of NLRX1 in the GBM microenvironment.
Discussion and Conclusion: NLRX1 is an innate immune pattern recognition receptor (PRR), expressed in the cytosol and mitochondria. NLRX1 plays a critical role in inflammation, antiviral signaling, ROS production, apoptosis, and autophagy. Our data demonstrates that NLRX1 may act as a regulator of GBM progression. This research will help improve the understanding of GBM pathophysiology leading to novel diagnostic/prognostic markers and signaling/pathway discovery that, in turn, may help create better GBM therapy approaches and improve overall survival.
Acknowledgments: We acknowledge infrastructure and funding support from the Indian Institute of Technology, Jodhpur, and funding support from the Ministry of Electronics and Information Technology, Government of India ((No.4 (16)/2019-ITEA)). Durgesh Meena is supported by a fellowship from the Council of Scientific & Industrial Research (CSIR)-NET-JRF.

P65: Investigation of *Helicobacter pylori* secretome on the gut-brain axis

Meenakshi Kandpal[1], Budhadev Baral[1], Nidhi Varshney[1] and Hem Chandra Jha[1]
[1]Infection Bioengineering Group, Department of Biosciences and Biomedical Engineering, IndianInstitute of Technology Indore, Indore, Madhya Pradesh, India

Background*: Helicobacter pylori* is pathogenic bacterium causes gastritis and gastric carcinoma. *H. pylori's* influence extends beyond the stomach, potentially causing neurological disorders by disrupting the gut-brain axis. Thecurrent study investigated the plausible association between clinical *H. pylori* isolates: HB10, HJ9 and HB1 and neuroinflammation that might lead to neurological modalities like Alzheimer's disease (AD).
Material and Methods: Assessment of Anti-microbial resistance in *H. pylori* isolates done via broth dilution method. Inflammation was studied by qRT-PCR and Western Blot of inflammatory, STATs and AD markers in *H. pylori* derived conditioned media (HPCM) treated neuroblastoma and neuro-astrocyte co cultured cells. ROS was estimatedthrough, DCFDA staining. Immunofluorescence were performed for the glial fibrillary acid protein (GFAP) and pSTAT3.
Results: The HPCM-induced inflammation with differential expression of inflammatory markers compared to control.Elevated expression of STAT-1, STAT-3 and AD associated proteins- APP and APOE4 ($p<0.05$)

was determined in HPCM-treated neuronal cell and neuro-astrocyte co cultured cell. Excessive ROS generation has been found in these cells. The HPCM treatment to LN229 cause astrogliosis evidenced by increase in glial fibrillary acidic protein ($p<0.05$). Our results indicate the association of STAT3 as an important regulator in the *H. pylori*-mediated pathogenesis in neuronal cells. Notably, the inhibition of STAT3 by its specific inhibitor, BP-1-102 marked a reduction in the expression of pSTAT-3 and AD markers ($p<0.01$).

Discussion and Conclusion: Our study demonstrate that *H. pylori* infection exacerbates inflammation in AGS cells and modulates the activity of STAT3 regulatory molecule. *H. pylori* secretome could affect neurological compartments by promoting STAT3 activation and inducing the expression of AD associated signature markers particularly withHJ9 strain. The study suggest that pSTAT-3 inhibition may be a potential therapeutic strategy for mitigating
H. pylori-induced neurodegeneration.

Acknowledgement: We gratefully acknowledge IIT Indore for providing facilities and support. We acknowledge ICMR for the research grant (BMI/12(82)/2021) and (ECD/CSTPU/Adhoc/COVID-19/28/2021-22. We are also grateful to Prime Minister's Research Fellowship, MHRD for fellowship.

P66: Early and delayed neurobehavioral consequences of lateral fluid percussion-induced mild traumatic brain injury

Mohd. Aleem, Kailash Manda
Institute of Nuclear Medicine and Allied Sciences, INMAS, Delhi

Traumatic brain injury (TBI) contributes to significant death and disability more than any other trauma-related injury. The most common form of TBI among human patients is mild TBI (mTBI) leading up to 80% of all TBI clinical cases. TBI represents two complex damage spectra, primary/acute and secondary/delayed injury cascades, each of which may affect neurobehavioral functions differently. Therefore, the present study was carried out to compare the mTBI-induced early (at 7^{th} day) and delayed (at 30^{th} day) changes in neuronal architecture, neurogenesis, neuroinflammation, and associated behavioural functions. For this purpose, C57BL/6J male mice were exposed to lateral FPI and assessed for potential changes in the structural and functional outcomes of the brain. The functional observations on acute time point revealed that mice with mild TBI showed significant locomotor hyperactivity and risk-taking behavior. Similarly, neuromuscular strength was significantly impaired without affecting the motor coordination. On the contrary, functional observations at later stage revealed no significant effect on locomotor and exploratory functions, whereas higher anxiety, stress, and depression-like functions were found similar to acute functional changes. Moreover, cognitive functional impairment was reported after mTBI at a later time point. Furthermore, at both time points, structural observations revealed significant cortical tissue damage, neuronal cell death, and neuroinflammation in mTBI mice. The dendritic and axonal morphometric and quantitative analysis revealed significant damages when compared to the control. The study reports that the pattern of few functional changes was common for anxiety, stress, and depression, while locomotor and exploratory activities were affected differently at both time points. The subsequent neuronal cell death and dendritic damage at a later time point appeared to be an exacerbation of the secondary and delayed damages.

P67: Dental Pulp Stem cells (DPSC)-derived mitochondrial transfer as a neuroprotective biomolecule to rescue neurons against neurodegeneration in Alzheimer's disease like cell model

Mohil Mishra[1]; Shalini Raik[1], Vidya Rattan[2], Shalmoli Bhattacharyya[1]
[1]Department of Biophysics, Post Graduate Institute of Medical Education and Research,Chandigarh, India; [2]Oral Health Sciences Centre, Post Graduate Institute of Medical Education andResearch, Chandigarh, India

Background: Mitochondrial activity is essential to support neural functions and can contribute to synaptic plasticity. Mitochondrial dysfunction is considered one of the major factors for Alzheimer's disease progression. Thus, transferring DPSC-derived healthy mitochondria may serve as a means to rescue neurons against the detrimental effect of AD.

Material and method: In this study, pre-neuroblastoma cells were differentiated into mature neurons, subsequently, treated with streptozotocin and Aβ1-42 oligomer to develop AD-like *in* vitro models. Neuronal morphology and cell viability assays were performed to validate the model. Further, the therapeutic potential of DPSC-mitochondria was analyzed by ROS and an immunofluorescence assay.
Results: The results have shown a significant neurotoxic effect on mature neurons after treatment with streptozotocin and Aβ1-42 oligomer that act as *in vitro* AD models. Further, no decrease in cell survival efficacy of mature neurons after the transfer of functional DPSC- derived mitochondria that demonstrated a significant neuroprotective effect after transplantation in *vitro* AD model.
Discussion: Our study has primary evidence that isolated autonomous mitochondria fromDPSCs can prevent neurotoxic effects, maintained neurite extension, and attenuated ROS production against Aβ and STZ. Thus, these findings might provide a novel approach toward the use of mesenchymal cells-derived mitochondria which may be considered as potential neuroprotective biomolecules for the treatment of Alzheimer's disease.
Acknowledgment: Gratefully acknowledges the extramural funding provided by IndianCouncil of Medical Research (ICMR), Govt. of India to conduct the study.

P68: Exploring USP14 as a Potential Therapeutic Target for Neurodegeneration: Insights from Rat Brain Studies

Moumita Roy[1,2], Chayan Banerjee[1,2], Rupsha Mondal[1,2] and Joy Chakraborty[1,2]
[1]Department of Cell Biology and Physiology, CSIR-Indian Institute of Chemical Biology-TRUE, Kolkata, India, [2]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad- 201002, India

Background: Deubiquitinases (DUBs) have emerged as potential regulators of mitochondrial clearance. Among these, USP14 stands out for its dual impact on proteasome activity and autophagy. USP14 inhibition enhances mitochondrial clearance and protect against Parkinson's disease progression in Drosophila. However, its role in higher animal models of neurodegenerative disorders remains unexplored.
Materials and Methods: Male Sprague Dawley rats (1 month, 6-7 months, and 10-12 months old) were subjected to intraperitoneal injections of 3-nitropropionic acid (3-NP; 20 mg/kg) and Rotenone (1 mg/kg) for 2 consecutive days. Brain homogenates from treated rats were immunoblotted and probed for Actin and USP14.
Results: In the adult rat brain, USP14 levels showed an elevation in the substantia nigra (SN) and cerebellum. However, there are no notable changes observed in the cortex, striatum, ventral tegmental area and hippocampus. Post rotenone exposure, marked upsurge of USP14 was manifested solely in SN, while other regions remain unaltered.
Discussion and conclusion: The reduced mitophagy during aging adds to neurodegeneration related complexities. This study explores the potential of USP14 as a therapeutic target in the rat brain, focusing on age-related and disorder-specific fluctuations in USP14 protein levels. Given the predominant rise of USP14 within SN due to ETC complex I inhibition, there is a strong rationale to consider it a promising target for therapeutic development, particularly regarding the abnormal mitophagy seen in Parkinson's disease.
Acknowledgement: This research received partial support through the Early Career Research Grant provided by the Department of Science and Technology-Science and Engineering Research Board (DST SERB). Additionally, a segment of the study was financially backed by the International Society of Neurochemistry (ISN) – Committee for Aid and Education in Neurochemistry (CAEN), which facilitated research supplies for utilization within the researcher's home laboratory.MR and RM are currently pursuing their Ph.D. studies and hold the position of Senior Research Fellows under the Council of Scientific and Industrial Research (CSIR) in India. CB is a recipient of a Senior Research Fellowship granted by the University Grants Commission (UGC) of India.

P69: Effects of Curcumin on hyperglycaemia induced Caenorhabditis elegans

Mrunmayee Rade, Dr. Sree Nair, Sukaina Abbas
Department of Life Sciences, Sophia College (Autonomous), Bhulabhai Desai Road, Mumbai 400026.

Background: Hyperglycaemia can occur in the body due to paucity of insulin or non- responsiveness to

insulin. Ensuing diabetic neuropathy harms neuronal functions. Curcumin is known to have curing abilities. Therefore, more research into the impact of curcumin on hyperglycaemia is desirable. In the present study we attempt to learn the effect of curcumin using *Caenorhabditis elegans* at hyperglycaemic conditions.
Materials and methods: This study assess the effects of Curcumin using a Hyperglycaemiainduced Wild-type model of *Caenorhabditis elegans*. Toxicity assays, specifically those of Glucose and Curcumin were analysed. Lifespan assays were performed to examine the survivalrate. Two behavioural assays, including thrashing and pharyngeal pumping were used to evaluate motor and feeding activities respectively.
Results: According to preliminary data, at certain concentrations, curcumin shows rescue effect in *C. elegans* exposed to hyperglycaemic conditions. The results showed that curcuminmight considerably increase *C. elegans'* ability to survive without affecting its growth. Antioxidant properties of Curcumin were evaluated with the help of DPPH (2,2-Diphenyl-1-picrylhydrazyl) that also takes into account the utilisation of free radicals in determining a substance's capacity to act as a source of hydrogen or a free-radical scavenger (FRS).
Discussion and Conclusion: Behaviour of the worms vary as the glucose concentrations increases, showing motor and feeding defects. Survival rate hampers because of high concentrations of glucose however curcumin exhibits its own beneficial impacts in retrieving the normal lifespan of worms. Administration of the antioxidant properties of curcumin is hypothesized to consider the use of free radicals when assessing curcumin's ability to serve asa free radical scavenger (FRS) and needs to be further investigated.
Acknowledgements: I want to express my heartfelt thanks to Sophia College, the Department of Life Sciences, and the Suman Tulsiani Research Centre for giving me this chance. I also expect to gain a lot of knowledge from this opportunity. RUSA (Rashtriya Uchchatar Shikshan Abhiyan) 2.0 provided funds for this study in exchange for supportingmy initiative.

P70: Deciphering the anti-tumor activity of limonene and azelaic acid in neuroblastoma cells

Muqadas Wani, Dr. Geetanjali Ganguli
Department of Life Sciences, Sophia College (Autonomous), Bhulabhai Desai Road, Mumbai 400026

Background: Neuroblastoma, an extracranial tumor originating from neural crest progenitor cells offers low median rate of survival and recurrence in patients. Hence, new treatments are required. Phytochemicals are potent therapeutic alternatives due to their efficient anti-tumor activity and easy accessibility. Authors are studying the effect of Limonene and Azelaic acid on N2a cells.
Materials and Methods: MTT assay is to detect cytotoxic effects of drugs at concentrations; 2mM, 4mM, 6mM, 8mM and10mM. Giemsa staining is to observe the morphological changes in cells post treatment. Scratch assay is to examine cell migration factors at concentrations as mentioned at time intervals; 0hrs, 24hrs and 48hrs. ROS estimation is conducted using Dichlorodihydrofluorescein diacetate and dihydroethidium fluorescence staining in treated cells.
Results: Cell cytotoxicity increased with increase in concentration of LMN and AZA as less formazan crystals were observed post addition of MTT assay. Cell migration property was reduced with increasing concentration when scratch assay was performed. Interestingly, changes in cell morphology were observed with increase in phytochemicals concentration: the cells lost their neural projections. The ROS levels were visibly higher as more green fluorescence was observedwith increasing concentrations of drugs.
Discussion and Conclusion: According to literature, phytochemicals and their derivatives provide exciting possibilities for increasing the effectiveness of cancer patients' treatments and lowering negative side effects. Limonene and Azelaic acid have shown cytotoxicity, effect on the cell morphology and migration properties with increasing concentration in the assays conducted thereby indicating therapeutic applications. To validate the likelihood that both the phytochemicals are promising therapy against Neuroblastoma, more study must be done in this area.
Acknowledgements: I extend my gratitude to the Principal, Dr. Anagha Patil Tendulkar and the Head of Departmentof Life Science, Dr. Sree Nair and my supervisor, Dr. Geetanjali Ganguli for giving me invaluable guidance, in sights, moral support and direction. Heartfelt gratitude to the department of Life Sciences for allowing me to use the Cell Culture Lab, Suman Tulsiani Research Centre atSophia College (Autonomous), Mumbai. I would also like to thank Dr. Bhaskar Saha from Saint Xavier's College, Mumbai and National Centre for Cell Science (NCCS), Pune for providing Neuroblastoma cells.

P71: Uncovering sex-specific epigenetic regulatory mechanism underlying neural and recovery mechanism in the internal carotid artery occlusion mouse model

Mydhili Radhakrishnan[a, c], Aditya Undru[b, c], Arvind Kumar[b, c], Sumana Chakravarty[a, c]
[a]Applied Biology, CSIR- Indian Institute of Chemical Technology (IICT), Hyderabad500007, India; [b]Centre for Cellular and Molecular Biology (CCMB), Hyderabad,500007, India; [c]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, India

Background: Cerebral ischemic stroke is one of the foremost global causes of death and disability. Apart from inadequate therapies, another lacuna in the field is stroke-related studies failed to consider sex as a critical variable. In this study, we are elucidating the sex-specific epigenetic mechanisms in cerebral ischemia induced neural damage and recovery.
Materials and methods: ICAO (Internal carotid artery occlusion) were surgically performed for 90 minutes in both males and females at different timepoints. Behavioural tests were conducted to evaluate different motor coordination and neurodeficits induced by ICAO.RT-PCR, Immunoblotting and highthrouput RNA sequencing analysis was employed for molecular studies.
Results: Results showed early restoration of H3k9me2 marks on the promoters of inflammatory genes in female striatum compared to that in males post-ICAO; this resulted in attenuation of the expression levels of various inflammatory cytokines leading to the accelerated recovery. Further, mild occupancy of H3k27me2 mark on the promoters of different neurogenic genes at an early time point triggered neurogenesis in female striatum. Thus, our findings suggest that H3k9me2and H3k27me2 differentially regulates ICAO-induced neural damage and recovery across the sexes**.**
Discussion and conclusion: ICAO induced neurological deficits and subsequent recovery mechanism differentially in male and female CD1 mice. Our novel findings highlighted the role of the H3k9me2, H3K27me2, *kdm4b/jmjd2b* and *kdm6b* epigenetic modifications, which harness thesubstrate H3k9 and H3k27, in the inflammation and regeneration processes post-ICAO. Basedon the findings, we propose H3k9me2 and H3k27me2 as a novel target for the therapeutic development with sex or gender as a crucial factor to be taken into consideration.
Acknowledgements: This research was initiated by the Council of Scientific and Industrial Research (CSIR), India network projects [(BSC0103-UNDO)] and ICMR grant [5/4-5/3/17/Neuro/2022-NCD-1 to SC]. MR and AU acknowledges CSIR India, for their doctoral fellowships. In addition, the authors would like to specially acknowledge CSIR-IICT and CCMB for the support.

P72: long-term neurobehavioral and neurodegenerative effects of nerve agent (vx) exposure in an animal model

Naveen Singh[1], Ankush Rajput[1]and Ramarao Golime[1]
[1]Biomedical verification division, DRDE, Jhansi Road, Gwalior (M.P)

Introduction: Nerve agents belongs to organophosphorus compounds (OPs) that pose a real threat to civilian and defense populations due to their deadly toxic nature and ability to cause high mortality. Nerve agents are used both in military and civilian conflicts and terrorist attacks in the recent history. Nerve agents block the function of acetylcholinesterase irreversibly at neuronal synapses causing an excess of the neurotransmitter acetylcholine buildup. Excessive acetylcholine causes hyper activation of cholinergic receptors leading to many toxic symptoms including death. However, the mechanisms behind nerve agents induced long term neurological effects; cognitive impairments are not well known.
Material and Methods: VX was obtained from PTD division, DRDE, Gwalior. DTNB, Acetylthiocholine iodide, and all other chemicals supplied by Sigma Chemicals Co unless otherwise mentioned. Neuronal damage assessed by FJ-C stain and acetylcholinesterase activity measured by Ellman method. Wistar rats were used for this study.
Result & Discussion: Results showed that AChE activity significantly inhibited after nerve agent exposure. Neurobehavioral studies including elevated anxiety levels, decreased working memory, and impaired muscle strength were observed in animals after nerve agent exposure indicating the nerve agent induced neurobehavioral effects. Neuronal damage in discrete rat brain areas were observed in the 30day post exposure, indicating nerve agent induced long term neurotoxicity caused by single VX exposure and no

substantial damage was observed in the 3 months when compared to the control animal groups. Understanding the mechanisms underlying these long-term toxic effects of nerve agents will help us to develop better antidotes.

P73: Combined exposure to chlorpyrifos and cypermethrin induces neuroinflammation and Parkinsonian indices in a rat model of Parkinson's disease

Neeraj Rawat [1, 2], Mahendra Pratap Singh [1, 2,3]
[1]Systems Toxicology Group, FEST Division. CSIR-Indian Institute of Toxicology Research (CSIR-IITR), Vishvigyan Bhawan, 31, Mahatma Gandhi Marg, Lucknow 226 001, Uttar Pradesh, India; [2]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201 002, Uttar Pradesh, India; [3]Capacity Building and Knowledge Services, ASSIST Division, CSIR-Indian Institute of Toxicology Research (CSIR-IITR), Vishvigyan Bhawan, 31, Mahatma Gandhi Marg, Lucknow 226 001, Uttar Pradesh, India

Background: Parkinson's disease (PD) is a common neurodegenerative disease characterised by the nigrostriatal dopaminergic neurodegeneration, striatal dopamine depletion and motor deficits. While cypermethrin (CYP) acts as a Parkinsonian neurotoxicant, chlorpyrifos (CPF) is reported to produce neurotoxicity. Exposure to CYP induces behaviour abnormalities, dopamine depletion, dopaminergic neurodegeneration and neuroinflammation. However, the effect of chlorpyrifos on cypermethrin-induced Parkinsonism is not yet known.
Objective: The study aimed to assess the effect of CPF exposure on CYP-induced changes in Parkinsonian indices and expression of toll like receptor-4 (TLR-4) and inflammatory cytokines in the rat nigrostriatal tissue.
Methods: Rats were exposed to CPF for 4, 8, and 12 weeks in the presence/absence of CYP along with respective controls. Rotarod and grip strength tests were performed to check the behaviour abnormalities. Dopamine content, number of TH-positive neurons and level of TLR-4, cyclooxygenase-2 (COX-2), tumor necrosis factor alpha (TNF-α), interleukin-1β (IL-1β) were measured employing standard procedures.
Results: Both CYP and CPF individually altered the behaviour indexes, dopamine content and number of TH-positive neurons. Besides, an alteration in the expression of TLR-4, COX-2, TNF-α and IL-1β was also observed after 12 weeks of CYP or CPF exposure. The alterations produced by half of the combined exposure were more pronounced than that of individual one.
Discussion and Conclusion: The result indicate that CPF increases CYP-induced Parkinsonian indices. Besides, CYP and/or CPF could impart toxic effect on the nigrostriatal dopaminergic neurons probably by an alteration of TLR-4, COX-2, TNF-α, and IL-1β.
Acknowledgement: The Council of Scientific and Industrial Research, New Delhi, India is gratefully acknowledged for providing research fellowship to Neeraj Rawat.

P74: Zebrafish as an alternative model for investigating sporadic Alzheimer's Disease

Neha Dhiman and Rajat Sandhir
Department of Biochemistry, Basic Medical Sciences Block II, Panjab University, Chandigarh-160014

Background: Alzheimer's Disease is a progressive neurodegenerative disorder with a heavy global burden. Recently, zebrafish have become a popular choice of model organism for neuroscience research. Their high similarity to humans, conserved pathological genes, short duration of model induction and cost effectiveness have promoted chemically induced and transgenic models of zebrafish models for studying AD.
Materials and Methods: In this study, ICV-STZ injection was given to adult zebrafish in different doses (1 to 30 mg/kg body weight STZ). The selected doses (1, 5 and 10 mg/kg body weight STZ) where subsequently used to evaluate behaviour using novel tank diving test. Gene expression analysis was done using RT- PCR. Histological analysis was done by hematoxylin and eosin and congo red staining. The presence of amyloid beta plaques was further confirmed using immunohistochemistry.
Results: STZ injection at higher doses proved fatal to the zebrafish. STZ injected fish displayed symptoms of anxiety and stress with cognitive impairment from day 5 onwards. The fish exhibited increased expression of genes involved in AD pathology. Histological examination revealed marked signs of neurodegeneration with fragmented nuclei and vacuolation. Immunohistochemistry confirmed the presence of amyloid plaques.

ICV-STZ injection of 5 mg/kg body weight for 7 days proved to be the most effective dose for inducing sAD pathology.

Discussion and Conclusion: Zebrafish have become the model of choice for neurodegenerative diseases since they have a CNS which shares all major nuclei, receptors and neurotransmitters with humans. sAD has been successfully modelled in non-transgenic rodents as well as zebrafish. ICV-STZ induced sAD in zebrafish has been described as a novel, robust and reliable model. The model displayed all the hallmarks of AD pathology at behavioural, molecular and histological level while preserving the cost effectiveness and efficiency this model organism offers. The behavioural parameters analysed demonstrated clear signs of anxiety, stress and cognitive impairment in the fish.

Acknowledgements: The funding for this study from DST-INSPIRE is acknowledged.

P75: Identification of significant differentially expressed miRNA and their targets common inIdiopathic Parkinson's disease and Parkinson plus syndrome

Neha Srivastava[1], Gyaneshwer Chaubey[2], Bhupendra Kumar[3], Abhishek Pathak[4], Vijaya NathMishra[1]
[1*]Department of Neurology, Institute of Medical Sciences, Banaras Hindu University,Varanasi-221005, India; [2]Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi-221005,India; [3]Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi-221005,India; [4]Department of Neurology, Institute of Medical Sciences, Banaras Hindu University, Varanasi-221005, India

Background: Idiopathic Parkinson's disease is the most common type, causing oxidative stress, glutamate excitotoxicity, protein aggregation, and neurodegeneration. Parkinson's plus syndromepresents progressing symptoms and no effective dopaminergic therapy. This study aims to identify differentially expressed miRNAs targeting neurodegeneration genes using microRNA expression profiling and bioinformatics tools.

Methods: The present case study includes 10 patients from IPD and PD plus with their respective 2 respective control. We have performed Microarray profiling, GO, KEGG and miRNA-mRNA network analysis in order to find out the candidate DE miRNAs in IPD and PD Plus by using bioinformatics tools and algorithms.

Results: A total of 163 DE miRNAs identified, and 11 of them, including hsa-miR-34/150/374/128/304/135/390/4473/6803, and 6809, was found to be common in IPD and PD plus patients. Network analysis pragmatically demonstrated that DE miRNAs such as: hsa-miR- 34, hsa-miR-29, hsa-miR-128, hsa-miR-3175, and hsa-miR-6809 were most prominent interactormiRs and its selected target genes (SNCA, PAK1, and PRKN) show maximum interaction with selected miRNAs and also play a potent role in Parkinson's disease pathway and neurodegeneration.

Discussion and conclusion: Micro RNA expression profiling was used to identify DE miRNAs in IPD and PD plus patients. The analysis revealed that hsa-miR-34/29/128/3175/6809 was primarily involved in interactions with other miRNA targets, such as SNCA, PAK1, and PRKN. The candidate miRNAs were then chosen and assessed because they were interacting most strongly with other miRNA targets that were linked to neurodegenerative diseases. This research highlights potential therapeutic targets and a common pathway between IPD and PD plus.

Acknowledgements: The authors kindly acknowledge Information Centre for Bioinformatics, Institute of Science, Banaras Hindu University for providing software and the computational facilities for bioinformatics analysis. We are highly grateful to the Department of Neurology, Institute of Science, Banaras Hindu University, Varanasi for extending laboratory facilities.

Funding: This study was financially supported by IOE Scheme under R/Dev/D/IoE/Incentive 2021-2022-32135. Scheme No. 6031/2021) and ICMR-SRF, Research fellowship, Project (ICMR ID No: 2021-15613-F1). Sanction letter No 3/1/2(2)/Env/2021-NCD-II-; dt-27.07.20

P76: Fractal Dimensions and Lacunarity of Glioma Subcomponentsas a Marker of Genotypic Status

Neha Yadav, Ankit Mohanty, and Vivek Tiwari
Indian Institute of Science Education and Research, Berhampur

Introduction: Gliomas of similar histologic type and grades exhibit distinct geometries and variations in the

fractions of tumor subcomponents: enhancing, non-enhancing, necrotic, and edema fractions. Gliomas are irregular structures that do not conform to traditional Euclidean geometry. Instead, non-Euclidean geometric measurements, such as fractal dimension and lacunarity, better characterize tumor subcomponents. Gliomas with somatic mutations in isocitrate dehydrogenase (IDH) and epigenetic methylations in O6-methylguanine-DNA methyltransferase (MGMT) gene exhibit better prognosis and improved survival.
Methods: The study cohort consisted gliomas subjects with T1w, T2w, T2-FLAIR, and T1-Gd MRI images, alongside genomic data from TCGA-GBM and TCGA-LGG. Fractal dimension and lacunarity were estimated for enhancing, non-enhancing plus necrosis, and edema components using an in- house developed novel pipeline. Using the fractal dimensions of different subcomponents of tumor, a machine learning based Radiogenomic platform was developed which is predictive of IDH status.
Results: Fractal dimension and lacunarity of different tumor subcomponents varies between IDH mutant and wildtype tumors. wherein IDH wildtype tumors had significantly higher FD of the enhancingcomponent (EN) and lower lacunarity compared to IDH mutant tumors. Furthermore, we developed ML models to test whether Fractal dimensions of each tumor subcomponent is predictive of IDH status and MGMT status. SVM based ML model using fractal dimensions is predictive of IDH mutational status with an average accuracy of ~92%. We have also extended thesame process for predicting MGMT status**.**
Discussion: Fractal dimension and Lacunarity of different tumor subcomponents is distinctive of the IDH andMGMT status. Therefor FD and Lacunarity are representative of differential prognosis and IDH status, thus indicating that in vivo Fractal estimates have potential to serve a noninvasive variablein characterizing aggressive and non-aggressive *viz* IDH mutant and wildtype gliomas. Quantifying the geometry of different tumor components across diverse molecular backgrounds could establish non-invasive method of structural geometry as a molecular status indicator.

P77: Pax6 regulates pattern recognition receptor genes

Nidhi Ghosh and Rajnikant Mishra
Biochemistry and Molecular Biology Lab, Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi- 221005, India,

Background: The Pax6 is evolutionary conserved transcription factor required for the functional anatomy of central nervous system, eyes, nose, pituitary, pineal and pancreatic alpha-cells. Since it is also involved in immunological surveillance of brain, impacts of Pax6 has been evaluated in innate immune responses and neuroinflammation.
Methods: LPS (1mg/kg) was injected intraperitoneally for 5 days to develop neuroinflammatory AKR strain mice model. Equal volume of saline was injected as a vehicle control. Multi-omics study was performed using ChIP and ChIP-sequencing with anti-Pax6 and whole brain proteomics analysis of Control and LPS mice.
Results: Pax6 recognises promoter sequences, UTR, distal Intergenic and Intron regions of genes. Functional annotation of genes enriched in LPS-administered mice brain shows that Pax6 binds to genes participating in regulatory pathways ranging from Tlr4 activation, chemokines secretion, regulation of NF-κB pathway. Proteomics analysis sheds light into putative mechanism of Pax6 in Neuroinflammation via Tgfβ cascade and putative biomarkers of Neuroinflammation.
Conclusion: Pax6 acts as a grid for cascades in regulating innate to adaptive immunity switch and combating Neuroinflammation.Pax6 regulates initiation of neuroinflammation through Tlr4 (a part of innate immunity) and works as mediator to innate and adaptive immune response by regulating genes of Pattern recognition receptor, cytokines and Chemokines, inflammasome activation through non canonical regulation of Tgfβ and NF-κB pathways.
Acknowledgements: Financial support from IoE-BHU is gratefully acknowledged.

P78: Spatial pattern of cerebral small vessel disease with aging is distinctive of cognitive status

Niraj Kumar Gupta[1], Vivek Tiwari[1]
[1]Indian Institute of Science Education and Research (IISER) Berhampur, Odisha 760010

Background: Cerebral Small Vessel Disease is a prevalent aging brain pathology, characterized by small arterial infarcts, causing chronic ischemia and White Matter Hyperintensity (WMH) in white matter regions visible on T2-FLAIR MR images. Yet, the uncharted clinical significance of spatial-temporal cerebrovascular dynamics, their role in aging processes, and potential links to cognitive decline and Alzheimer's pathology warrant further investigation.
Methods: Post-MR image segmentation and WMH lesion extraction, WMH spatial distribution was estimated. Probability maps, representing voxel-wise WMH occurrence across age-groups within the normal cognition, cognitive impairment, and cognitive impairment with AD etiology cohorts, elucidate brain-wide probabilistic insights into the prevalence and localization of WMH, enabling insights into evolving cerebrovascular pathology with age and cognitive status.
Results: WMH burden increased exponentially with age across cognitive groups, notably accelerated in CI and CI-AD vs. CN. Probability mapping revealed peak WMH likelihood in the periventricular region, rising with age and cognitive impairment. Frontal and parietal lobes showed elevated WMH load. Periventricular WMH distinguished cognitive statuses at all ages. Decline in executive functioning/reaction time due to periventricular WMH load is mediated through atrophy of structures, which are paracentral, precentral gyrus thickness/volume, accumbens, cuneus, pericalcarine volume.
Discussion: White matter hyperintensity (WMH) load and distribution influence structural decline and cognition via chronic vascular insult. Certain brain regions exhibit higher susceptibility to CSVD-related damage. Disparate WMH accumulation may dictate cognitive deficits. Spatial WMH distribution differentiates normal cognition from impairment. CSVD emerges as a contributor to cognitive decline, notably in attention and executive function domains. Our study underscores CSVD's cognitive impact mediated through certain neuroanatomical atrophy and region-specific vulnerability.

P79: Pharmacological investigations on therapeutic potential of Gabexate Mesilate in animal model of rheumatoid arthritis

Nivedita Verma, Abhipshit Kalita, Vinod Tiwari
Neuroscience and Pain Research Laboratory, Department of Pharmaceutical Engineering and Technology, Indian Institute of Technology (Banaras Hindu University), Varanasi,221005, Uttar Pradesh, India.

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by persistent synovitis, pain, and progressive joint damage. The pathogenesis of RA mainly involves oxidative stress which is responsible for inflammation and pain. Gabexate mesylate, a serine protease inhibitor that has anti-inflammatory properties help in managing RA pain by suppressing NF-κβ and nitric oxide pathway.
Materials and Methods: Animals-Male S Drats (wt-200-220 gm)
Drugs-Gabexate Mesilate (Dose:10mg/kg,20mg/kg,40mg/kg), Indomethacin(5mg/kg)
Animal Model:
CFA-induced arthritis
Behavior essays
- Von-Frey test: Mechanical allodynia
- Pin-prick test: Mechanical Hyperalgesia
- Hargreaves test: Thermal Hyperalgesia
- Acetone Drop test: Cold allodynia
- Ice-floor test: Cold Hyperalgesia
- CNS toxicity: Rotarod test, open field test
- Biochemical tests-GSH, nitrite, LPO
- Molecular tests-rt-PCR, Western Blotting

Results-
1.Gabexate mesylate attenuates mechanical allodynia in CFA-induced arthritis rats.
2.Gabexate mesylate decreases heat hyperalgesia in CFA-induced arthritis rats.
3.Gabexate mesylate decreases cold allodynia in CFA-induced arthritis rats.
4.Gabexate mesylate restores paw thickness in CFA-induced arthritis rats.
5.Gabexate mesylate restores body weight in CFA-induced arthritis rats.
6.Gabexate mesylate did not affect locomotor or exploratory activity as well as did not observe a significant change in motor incoordination in the Rota-rod test.

Discussion and Conclusions: Gabexate mesylate prevents proteolytic destruction of Iκβ resulting in suppression of the NFκB signaling pathway and downregulates the activation of TRPV1 signaling in the spinal dorsal horn neuron. This leads to a decrease in the production of inflammatory cytokines and also prevents spontaneous ongoing pain. Findings from the current study revealed that gabexate mesylate could be a better and safer therapeutics for the treatment of rheumatoid arthritis pain and inflammation.
Acknowledgement: We would also like to acknowledge the Department of Pharmaceutical Engineering and Technology, Indian Institute of Technology (B.H.U), Varanasi for providing the necessary facilities and infrastructure.

P80: Region specific alteration and activation of protein tyrosine kinase 2 in temporal lobe epilepsy

Ozasvi R Shanker [a], Sonali Kumar[a], P Sarat Chandra[b], Manjari Tripathi[c], Jyotirmoy Banerjee[d], Aparna Banerjee Dixit [a]
[a]Dr. B.R. Ambedkar Centre for Biomedical Research (ACBR), University of Delhi, New Delhi, Indi; [b]Department of Neurosurgery, All India institute of medical sciences (AIIMS), New Delhi, India**;** [c]Department of Neurology, All India institute of medical sciences (AIIMS), New Delhi, India**;** [d]Department of Biophysics All India institute of medical sciences (AIIMS), New Delhi, India

Background: Research has demonstrated stress-related Pyk2 activation in the brain however its role in epilepsy remains unclear. Since, TLE is a network-level disorder it is crucial to investigate PYK2 activity in various temporal lobe areas. This study thus aimed to assess the region-specific alteration and activation of PYK2 in TLE.
Materials and methods: qRT-PCR and western blot were performed to detect changes in mRNA and protein levels respectively in MTLE patients versus control and in lithium pilocarpine model of epilepsy compared to control. Cell-specific expression was assessed using immunofluorescence, and flow cytometry was used to detect the calcium levels.
Results: The results revealed a significant increase in the levels of phospo-Pyk2 in the hippocampus and ATL of MTLE patients and lithium pilocarpine model of epilepsy as compared to control while no significant changed was observed in the levels of unphosphorylated form of Pyk2. Further, a positive correlation was observed between the levels of activated Pyk2 and increased calcium levels.
Discussion and conclusion: This was the first study to assess the activation of Pyk2 in a region-specific manner in TLE suggesting its possible contribution in the pathogenesis of epilepsy. The study also suggested a possible involvement of Pyk2 in the generation of independent epileptogenic networks in TLE and the role of calcium in activating Pyk2. Specific inhibitor for Pyk2 will be used in the future studies to understand its role as a potential therapeutic target in TLE.

P81: Histopathology of motor cortex in rats exposed to middle cerebral artery occlusion

Paalki Sethi[1], Laxmi T. Rao[2],
[1]School of Studies Neuroscience, Jiwaji University, Gwalior; **[2]**Department of Neurophysiology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Karnataka.

Background: Stroke is one of the major causes for disability of motor functions. Ischemic stroke is caused by permanent or transient decrease in cerebral blood flow that is restricted to area of a major brain artery. MCAO results in lesions associated with motor cortex affecting motor functions in the contralateral sides.
Materials and Methods: Animal: Sprague Dawley Rats; Adult male rats n=6. Rats were either exposed to sham surgery or MCAO surgery to induce stroke at PND 60, animals were tested for motor behavior and neurological examinations after 7th and 14th day of surgeries. Further Histomorphological analysis via cell quantification of motor cortex.
Results: Histomorphological analysis of motor cortex in rat brain showed comparable difference in terms of different parameters such as total cell count, area, volume, and density when both the groups were compared, clearly indicating the loss of neurons and synaptic connections between injured and uninjured hemisphere in

stroke affected rat brain. However, prominently indicating the contralateral inhibition in the uninjured hemisphere is an indirect consequence of stroke.
Discussion and Conclusion: In the current study, histomorphology of motor cortex is analysed when exposed to ischemic stroke induced by MCAO. There is a cascade of events that supports the progression of pathophysiological mechanisms and resulted into adverse conditions. From the core region to contralesional hemisphere, the effect of MCAO induced ischemic injury was clearly indicated. However, synaptic plasticity and other therapeutic mechanisms can help in overcome the gravity of the situation.

P82: Restorative potential of the mesenchymal stem cells secretome in neuralprogenitor cells receiving toxic insult of Monocrotophos

P Vatsa[1,2], R Negi[1,2], UA Ansari[1,2], VK Khanna[1,2], AB pant[1,2]
[1]Systems Toxicology & Health Risk assessment Group, Food Drug and Chemical, Environment and Systems Toxicology (FEST) Division, CSIR-Indian Institute of Toxicology Research (CSIR-IITR); [2]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad- 201002, India

Background: The mesenchymal stem cell (MSC) secretome comprising an array of neurotrophic factors, cytokines,nucleic acids, proteins, etc., imparts restorative potential by regulating the inflammatory responses, reducing apoptosis and cytotoxicity. The study intends to investigate the MSC secretome's proteomicprofile to understand its applicability in the therapeutic intervention in neurodegeneration**.**
Materials and methods: The proteome profiling of MSC secretome following cellular pre-conditioning was done by High- Resolution Mass Spectroscopy. The restorative potential of the MSC secretome was determined in theiPSC-derived neural progenitor cells (NPCs) exposed to Monocrotophos at 100 μM for 24 h.
Results: The MSC secretome reveals the predominant presence of proteins involved in glycolysis, oxygen transport, anti-inflammation, anti-fibrosis, neuroprotection, and cell proliferation pathways. A total of65 proteins were exclusive to the secretome of stimulated cells. In comparison to the baseline secretome, 146 proteins were common between pre-conditioned and normal MSCs while 65 were exclusive to former, of which 14 were upregulated and 10 downregulated. The secretome of MSC exhibits a significant restoration in cell viability, oxidative stress and mitochondrial membrane potential of NPCs receiving MCP exposure.
Discussion and Conclusions: Our findings show that MSCs can alter their secretion profile in response to their microenvironment, enabling them to play in different capacities according to the maladies. The study findings also demonstrate that MSC secretome can restore homeostasis in MCP-exposed NPCs. The components identified in the MSC secretome highlight the importance of cellular pre-conditioning, hence renderingthe MSC secretome a potential therapeutic intervention against neurotoxicity/ neurodegeneration.
Acknowledgement: The authors would like to acknowledge the Indian Council of Medical Research, New Delhi for financial assistance (IRIS Cell No. 2020-9465) and the Senior Research Fellowship to Ms. Pankhi Vatsa.

P83: Telomere Shortening in Leukocytes and Placenta: Links Gestational Diabetes Mellitus and Perinatal Depressive Symptoms

Thirumoorthy C[a], **Pavithra Rekha R[a]**, Shalu D[a], Nikhil PJ[a], Deepa M[b], Mohan V[b],
Gokulakrishnan K[a]; [a]Department of Neurochemistry, National Institute of Mental Health & Neuro Sciences (NIMHANS), Bangalore, India; [b]Madras Diabetes Research Foundation (MDRF), Chennai.

Aim: Studies reported a bidirectional relationship between depression and Gestational Diabetes Mellitus (GDM). While telomere length (TL) has been extensively studied in the contexts of GDM and depression individually, there has been a relatively limited exploration of TL in the specific intersection of GDM with comorbid depression. The present study aimedto examine the relationship of Leukocyte and Placental TL in antenatal women with GDM with and without perinatal depressive symptoms (PNS)].
Methods: Blood leukocyte TL was measured in 300 pregnant women between 24-28 weeks ofpregnancy [Normal Glucose Tolerance [NGT] without PNS (n = 80); NGT with PNS (n = 105);GDM without PNS (n = 75); GDM with PNS (n = 40)] and in a subset of 112 placental samplesfrom the ongoing STRiDE (Stratification of Risk of Diabetes in Early pregnancy) study. The depression score was derived using PHQ-9, and qRT-PCR was used to quantify TL.

Results: Blood Leukocyte TL at 24-28 weeks of pregnancy was lower in GDM (with and without PNS; $p<0.001$), and in individuals with NGT with PNS. This trend was similar in placental TL ($p<0.001$). Notably, GDM with PNS has the lowest expression of both leukocyteand placental TL and was negatively correlated with depression score ($p<0.05$) and 2-hour postprandial glucose levels ($p<0.05$).
Conclusion and Discussion: Our findings indicate that GDM and PNS are linked to lower TLlevels in blood leukocytes and placenta. This suggests a dynamic link between TL, GDM, andPNS throughout pregnancy.TL could serve as a potential biomarker for GDM and PNS. Furtherstudies are needed to validate the observed change over time and whether similar marks can bedetected in postpartum, and children born to these mothers, remains to be elucidated.
Funding: This study was supported by India Alliance/ DBT Wellcome Trust.

P84: In-silico evaluation of potential natural neuroprotective molecules for treatment of Parkinson's disease

Poonam Bhadauriya[a, b] , Ahsas Goyal[b] and Vibhav Varshney[b]
[a]Institute of Professional Studies-College of Pharmacy, Gwalior-474001, MP, India
[b]Institute of Pharmaceutical Research, GLA University, Mathura-281406, UP, India

Background: Mas Receptor is a G protein coupled receptor which plays a pivotal role in the treatment of PD via the activation of angiotensin II type receptor (AT-2R) and suppression of Angiotensin I type receptor (AT-1R). The activation of AT-2R activate Ang(1-7)\MasR axis which reduces an oxidative stress neuroinflammatory status that results is protection of dopaminergic neurons by the Ang(1-7)/MasR axis.
Methods: Fifty flavonoids were evaluated for the binding efficacy for Rat MasR by using molecular docking. On the basis of their binding efficacy best two flavonoids were selected from docking results then after molecular dynamic simulations for 100 ns for binding stability analysis with the MasR were done of two selected flavonoids. Then after *in silico* ADMET studies were performed to check the drug ability of the selected flavonoids.
Results: Pterosupin (–7.9 kcal/mol) and Amentoflavone (–7.6 kcal/mol) Pterosupin were the two selected flavonoids which has best binding efficacy with the MasR. The molecular dynamics simulation studies showed that both Pterosupin and amentoflavone were at stable state during duration of simulation period, root mean square deviation (RMSD) and root mean square fluctuation (RMSF), and protein flavonoids complex were stable until 100 ns.
Discussion and Conclusion: Pterosupin and Amentoflavone are potential lead molecules that could be used as effective agonists of MasR to treat Parkinson's disease. Thus ,further *in-vitro* and *in-vivo* analysis can be done for confirmation of effectiveness of these flavonoids.

P85: Association of air pollution with placental pathology in pregnant women of Odisha, India: A case study

Poonpun Das, Lucy Das, Manorama Patri
Ravenshaw University, Cuttack, Odisha

Background: The exposure of pregnant women to atmospheric pollutants is related to the period of early development of the foetus, low birth weight, preterm delivery and low placental weight which occurs due to oxidative stress and it may cause placental abnormalities.
Objective: The present cross-sectional study was conducted to know the effects of air pollution on placental pathology by taking 373 women volunteer participants with normal pregnancy from thickly populated, traffic-congested, industrial and remote rural areas of Odisha, India.
Methods: We collected the pollution level of air pollutants of the three study areas of Odisha State Pollution Control Board (OSPCB) Bhubaneswar. The placental tissue was collected immediately after delivery. The effect of air pollutants on the placental pathology was analyzed by Histopathological studies done by using Hematoxylene and Eosin staining methods and photographed by florescent microscope.
Results: The present study showed the level of pollution, percentage of exposure of pregnant mothers to ambient air pollution, preterm delivery, significant increase in preterm birth in heavy traffic congestion areas (Cuttack zone) and industrial areas (Jajpur zone) in comparison to rural non-industrial areas (Nilagiri zone).

The histopathological study of placenta showed presence of $PM_{2.5}$, Neutrophil granules, damaged tissues, desquamated epithelial tissues, thrombus and less number of villi in heavy traffic and industrial areas as compared to non-industrial areas.
Conclusion: Our findings advocate that the exposure of pregnant women to air pollutants may adversely affect the growth and development of placenta and fetus in highly polluted areas. More studies are required for confirmation.

P86: Generation of drug induced model to study Parkinson's Disease

Prajwal BG[1], Priyajit changdar[1,2], Shrilaxmi MS[1], Varshith M[1] and Somasish Ghosh Dastidar[1,3]
[1]Centre for Molecular Neurosciences, Department of Anatomy, Kasturba Medical College, Manipal Academy of Higher Education, Manipal; [2]Department of Physiology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal; [3]Centre for Emerging and Tropical Diseases, Kasturba Medical College, Manipal Academy of Higher Education, Manipal.

Background: Rotenone, a mitochondrial complex-1 inhibitor is a naturally occurring insecticide and pesticide. High lipophilic nature of rotenone enables it to cross biological membranes including the blood-brain barrier to target the dopaminergic neurons and cause neuronal death. It can be developed as the best drug-induced model for Parkinson's disease.
Material and method: Male Swiss albino mice of age 4 and 8 months were considered for the study. The mice were housed in individually ventilated cages, with 12hrs day-night cycle, *ad libitum*. The mice were treated with rotenone for 21 days via intraperitoneal injection and behavioural tests were conducted to examine the disease progression.
Result: The rotenone-injected mice were subjected to a battery of behavioural tests. The hind and fore limb grip strength test, hind limb clasping, the vertical pole test, Ledge test, gait analysis and kyphosis was performed to check the progression of the disease. The tests were performed to assess the motor coordination, in which the rotenone treated mice showed significant decrease.
Discussion: Rotenone, is one among the best chemicals to develop drug-induced model of PD. It replicates most of the pathologies that are observed in PD. Our studies reveal that injection of rotenone caused severe decrease in the motor coordination, bradykinesia, gait abnormalities in the mice compared to the normal mice.
Acknowledgement: We would like to thank Department of Biotechnology (under the Ministry of Science & Technology) and KMC, MAHE for providing financial and instrumental supports to pursue this research work.

P87: Chronic rewarding stimulation alleviates depression-induced motivation and memory deficit in rats

Pratik D. Dange[1], Biru B. Dudhabhate[1], Vinod K. More[1], Nishikant K. Subhedar[2],Dadasaheb M. Kokare[1]
[1]Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj NagpurUniversity, Nagpur 440 033, Maharashtra, India; [2]Indian Institute of Science Education and Research, Dr Homi Bhabha Road, Pune411 008, Maharashtra, India

Background: Major depressive disorder is associated with motivation and memory deficit that leads to severe disability in patients. Recently, the deep brain stimulation(DBS) of LH-MFB evolved as an effective therapeutic strategy to treat depression. However, DBS effect on motivations and memory deficit, and its mechanism of action is yet elusive.
Material and Methods: Rats were exposed to unpredictable stressors (42 days) to induce depression and implanted with electrodes in LH-MFB. DBS (14 day) treatment was provided and behavioral screening performed by sucrose preference,forced swim, operant and novel object recognition tests. Expression of neuropeptideCART and BDNF were tested in different brain subregions.
Results: Chronic stress exposure leads to behavioral despair, reduction in sucrose intake, lever pressings under fixed and progressive ratio schedules, and impairs recognition memory. CUMS rats showed decrease in BDNF expression in the lateralhypothalamus, cornu ammonis 3, arcuate nucleus and ventral tegmental

area, and neuropeptide CART expression in central amygdala, dentate gyrus, dorsal raphe nucleus, lateral hypothalamus and ventral tegmental area compared to control rats. LH-MFB DBS reversed the all altered parameters in stressed rats.
Discussion and conclusion: Previously, the unilateral stimulation of LH-MFB produces an antidepressant effect in TRD patients. The LH-MFB is a crucial locationfor DBS because it has connections with the several brain areas that are affected bydepression. Herein, the application of 14 days DBS treatments reversed the depressive behavior, affected reward motivations and memory deficit in the CUMS rats. Moreover, increased expressions of BDNF and CART, indicate its involvement in the antidepressant effect of DBS of LH-MFB.
Acknowledgment: We acknowledge Science and Engineering Research Board (SERB) (CRG/2020/004971) and Indian Council of Medical Research (ICMR) (SRF-2021-15699/F1) for providing funding support for this work.

P88: Machine learning driven transcriptome analysis reveals MTRNR2L1 as the potent biomarker in intellectual disability disorder

Prekshi Garg[1], Farrukh Jamal[2], Prachi Srivastava[1]
[1]Amity Institute of Biotechnology, Amity University Uttar Pradesh, Lucknow Campus, 226028; [2]Department of Biochemistry, Dr. Rammanohar Lohia Avadh University, Ayodhya-224001, U.P.

Background: Differentially expressed genes (DEGs) have been widely used to understand not only gene function but also the molecular mechanisms underlying different biological processes. In the present study, key biomarker in intellectual disability (ID) was identified using transcriptome data analysis and robust machine learning approaches.
Materials and Methods: Data for 29 control and 31 patients of ID were retrieved from GEO and BioProject database of NCBI (GSE77742, GSE74263, GSE108887, GSE90682, GSE98476, GSE145710, and PRJEB21964). The DESeq2 package was used for identifying DEGs. The feature selection algorithms (InfoGain, Correlation feature selection, and ReliefF) of Weka 3 software was used to identify important features among DEGs. The accuracy of these algorithms was tested through logistic regression, logistic model trees (LMT), and Random Forest. The key biomarker in intellectual disability was identified using NeuralNet.
Results: The DESeq2 analysis identified 15 upregulated genes in patient sample. Out of these 15 genes, feature selection algorithm discarded 2 genes as non-significant and identified 11 genes as the important attributes for the analysis of intellectual disability The machine learning algorithms showed improved accuracy after removal of non-significant attributes from the dataset. The artificial neural network formed using the important attributes only revealed the MTRNR2L1 expression as an important parameter when the level of all other genes was kept constant.
Discussion and conclusion: This indicate that gene MTRNR2L1 is expressed considerably in patients of intellectual disability even if the levels of all other DEGs remain constant. The increased expression of MTRNR2L1 gene can be easily identified in patients indicating their increased risk of development of intellectual disability. Thus, MTRNR2L1 can act as a potent biomarker for the early diagnosis of intellectual disability.

P89: BMAA induces myeloperoxidase-based HOCl production and aggravates lipid peroxidation in microglia

Abir Mondal[1], **Prince Upadhyay[1]**, Chaheti Goyal[1] Subrata Munan[2], Animesh Samanta[2], Shailja Singh[3] and Soumya Pati[1]
[1]Department of Life Sciences, School of Natural Sciences, Shiv Nadar Institution of Eminence, Delhi-NCR, India; [2]Department of Chemistry, School of Natural Sciences, Shiv Nadar Institution of Eminence, Delhi-NCR, India; [3]Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi, India.

Background: Humans have been chronically exposed to bacterial toxins through their biomagnification in the food chain. When consumed with food, these microbial toxins cause several neurological diseases like-Amyotrophic Lateral Sclerosis (ALS) and Parkinson's Dementia Complex (PDC). However, the molecular mechanism of toxins-induced neurodegeneration is yet to be elucidated.

Materials and Methods: Myeloperoxidase activity in human microglia was evaluated by microscopy using our in-house probe. Bacterial toxin BMAA was used for our experiment to observe the production of HOCl, loss of mitochondrial potential, and accelerated lipid-peroxidation in microglia by flow cytometer. Erastin was taken as a positive control.
Results: Treatment of bacterial-toxin BMAA increased in percentage (56%) of reactive oxygen species (ROS) positive microglia. Further, 50% of microglia showed reduced mitochondrial potential 24 hours after treatment with BMAA. We also found that BMAA induces myeloperoxidase activity and increases the production of mitochondrial HOCl similar to erastin-treated microglia. Additionally, BMAA increases lipid peroxidation in microglia which is comparable to erastin treatment. Potential small molecule flavonoid decreases the BMAA-induced HOCl production and lipid peroxidation in microglia.
Discussion and conclusion: BMAA is reported to enter the brain via crossing the blood-brain barrier (BBB) or gut-brain axis. BMAA increases ROS production and negatively regulates mitochondrial health. Additionally, BMAA activates myeloperoxidase activity and lipid peroxidation in microglia. Lipid peroxidation is the crucial step that promotes cell death called ferroptosis. Thus, the bacterial toxin BMAA can alter microglial functions, and increase the rate of ferroptosis which are also one of the causes of sporadic form of neurodegeneration.
Acknowledgments: We are grateful to the DST-CSRI, India (DST/CSRI/2018/247). We also highly acknowledge the Shiv Nadar Foundation for supporting our research work.

P90: Development and validation of high throughput screening platform using genetic cell line model for Parkinson's disease and Gaucher Disease

Priya Gagansingh Thakur, Sivaprakash Ramalingam
CSIR-IGIB, Mathura road, New Delhi, India; 2. ACSIR, Ghaziabad, India

Background: The glucocerebrosidase 1 (GBA1) gene is the most common genetic risk factor for Parkinson's disease (PD). The L444P mutation is the most frequent occurrence and is known to cause early onset and severe forms of PD. The accumulation of misfolded mutant GCase leads to ER stress, which in turn causes GCase to move to the cytoplasm and interact and stabilize soluble α-synuclein (αsyn) oligomers. This accelerates the formation of pathological α-syn in PD pathology.
Approach: HTS using patient-derived iPSCs can provide more accurate results, but it is a labor-intensive and costly process to screen large libraries. To address these challenges, we have devised an economical genetic model that employs low substrate concentration in SH-SY5Y cells carrying the L444P mutation. This is supported by a platform that integrates fluorescence-based assay and flow cytometry to assess GCase activity.
Results: An initial screening of small molecule compounds (1st: approximately 1280 compounds, 2nd: approximately 10,000 compounds) to boost GCase activity using the SH-SY5Y GBA1L444P/L444P and GBA1L444P/+ cell lines. Additionally, our aim is to select the top 5 hit compounds through secondary screening of the top 10.
Discussion: Assessment of the efficacy of these 5 compounds in alleviating the disease symptoms in human DA neurons differentiated from iPSCs of GBA1L444P/L444P-carrying. Evaluation of the potential of these compounds to mitigate the defects in dopaminergic differentiation of neuronal progenitor cells, improve mitochondria dysfunction, and prevent the accumulation of lipids, as well as to reduce susceptibility to α-syn PFF-induced PD.
Acknowledgments: DBT, Government of India, CSIR, and DBT-JRF.

P91: Graphene based nanomaterials to support neuronal growth and function post injury

Priyadharishini Veeraraghavan
Department of Biotechnology, PSG Institute of Advanced Studies, Coimbatore 641 004

Damage to neurons in the central nervous system (CNS) can have catastrophic consequences due to the loss of function and limited ability to recover. Injuries to the CNS occur in two stages: primary or acute injury, and secondary injury. The primary injury is the initial impact to the CNS, which leads to a prolonged

secondary injury that further expands the loss of function. Secondary injuries involve a range of cellular events and molecular factors, including excitotoxicity, inflammation, oxidative stress, and axon degeneration, which can last from hours to days after the initial injury. Additionally, many secondary injury factors are exacerbated by the loss of physical support for neurons and their sub-cellular structures after an injury. Therefore, it is essential to support and treat existing neurons to improve their functional recovery quickly. Graphene-based nanomaterials (GBNs) are emerging as promising tools for tissue engineering due to their excellent biocompatibility with various cells, including neurons. However, the potential functional effects of GBNs on injured neurons in the CNS are still unclear. My lab aims to study the membrane and functional properties of neurons during and after injury with GBNs. This research will provide us with more insights into the use of GBNs as a supportive material for treating CNS injuries and their potential for clinical translation.

P92: Neuroprotective effect of Virgin Coconut Oil against chronic drug induced Parkinson's disease

Priyajit Changdar [1,2], Prajwal BG[2], Shrilaxmi MS[2], Varshith MR[2], Saradindu Banerjee[2], Vasudev R Pai[4], Roberto Hirochi Herai[5], Manjula S.D[1], Somasish Ghosh Dastidar[2, 3]
[1]Department of Physiology, Kasturba Medical College, Manipal, Manipal academy of higher education (MAHE), Karnataka-576104; [2]Center for Molecular Neurosciences, Kasturba Medical College, Manipal, Manipal academy of higher education (MAHE), Karnataka-576104; [3]Center for Emerging Tropical Diseases, Kasturba Medical College, Manipal, Manipal academy of higher education (MAHE), Karnataka-576104; [4]Department of Pharmacognosy, Manipal College of Pharmaceutical sciences, Manipal academy of higher education (MAHE), Karnataka-576104; [5]School of Medicine and Life Sciences, Pontifícia Universidade Católica do Paraná (PUCPR), Curitiba - Paraná – Brazil

Background: Virgin coconut oil (VCO) is a nutraceutical, with anti-oxidative and anti-inflammatory properties. Parkinson's disease (PD) is a progressive neurodegenerative disorder caused by dopaminergic neuronal death due to oxidative stress and neuroinflammation. We propose VCO can be neuroprotective against PD.
Materials & Methods: Swiss albino male mice were divided into five different groups. To induce PD features three groups of mice were injected with Rotenone. Post PD induction two groups of mice received VCO treatment for 28 days while another one remained untreated. We assessed motor behavioural parameters weekly during our treatment period.
Results: We observed a drastic reduction of motor and coordination activities in mice after 21 days of rotenone injection in comparison to control mice. When PD mice were treated with two different doses of VCO, a symptomatic improvement was noticed. Weekly assessment of fore limb and hind limb grip strength, gait, kyphosis, hind limb clasping, and vertical pole activity showed a sign of amelioration of PD progression by VCO treatment in comparison to untreated PD mice.
Discussions: The possible reason for VCO's ameliorative effect in PD mice models could be due to its antioxidant and anti-inflammatory properties. We have done RNA sequencing analysis of the SNPc of the 5 groups of mice understudy. A thorough analysis of the transcriptome data might reveal common pathway(s) shared in genetic or environmental models of PD and mechanisms by which VCO offers protection against PD.
Acknowledgement: We would like to thank Department of Biotechnology (under the Ministry of Science & Technology) and KMC, MAHE for providing financial and instrumental supports to pursue this research work.

P93: Neuroprotective effect of Vitamin B12 Supplementation on neuronal morphology and spine density after traumatic brain injury

Priyanka Yadav and Thamil Mani Sivanandam
Biochemistry and Molecular Biology Laboratory, Department of Zoology, Institute ofScience, Banaras Hindu University, Varanasi-221005

Introduction: Traumatic brain injury leads to the transmission of external force to the head. Changes in neuronal morphology and spine density are directly associated with the pathophysiology of TBI. The present study aims to investigate the effect of Vitamin B12 supplementation on 3rd day, 7th day, and 14th day after TBI.
Methods: To check the effect of Vitamin B12 supplementation on neuronal morphology and spine density, Swiss albino males (12±2 week) were divided into three groups: Control, TBI, and TBI+Vitamin B12 supplementation (1.5mg/kg body weight, intraperitoneally). The mice were sacrificed on the 3rd, 7th, and 14th day and performed Golgi-cox staining.
Results: The results show that TBI+Vitamin B12 supplementation significantly increases the number of intersections, and length as compared to TBI on the 3rd, 7th, and 14th day. The total number of nodes was only found to be significantly increased in TBI+Vitamin B12 supplementation as compared to TBI on 3rd day. The total spin density, filopodia, and mushroom-shaped spines were found to be increased in TBI+Vitamin B12 supplementation as compared to TBI on the 14th day.
Discussion and conclusion: Neuronal morphology and spine density are closely associated with structural plasticity. The study revealed that TBI leads to changes in neuronal morphologysuch as the number of dendritic intersections, dendritic length, and nodes, and Vitamin B12 supplementation markedly restored the same parameters. Similarly, spine density was also increased by Vitamin B12 supplementation after TBI. Altogether these changes indicated that TBI-mediated disruption in the neuronal architecture and structural plasticity was improved byVitamin B12 supplementation.
Acknowledgments: ICMR, UGC-Start up grant for providing funds to STM lab.CSIR for senior research fellowship to PY, interdisciplinary School of Life Science, Banaras Hindu University for vibrotome and Light microscope Facilities

P94: Identification of natural product inhibitors of TRPA1 channel against neuropathic pain

Priyanka Yadav[1], Asif Ali [2] & Aravind Sing Kshatri
[1]Neuroscience and Ageing biology Division[1], Medicinal and Process chemistry Division; [2]CSIR- Central drug Research institute, Lucknow, India

Chronic pain control is frequently ineffective and associated with adverse side effects, and thus prompted a frantic search for new natural therapeutic molecules. TRPA1 channel has emerged as a critical target for pain relief since its antagonists target the beginning of the pain transduction pathway. To identify the TRPA1 antagonists we have developed and optimized a fluorescent based screening assay using GCaMP6s as a Ca2+ indicator. Molecular docking was performed to identify the binding sites of the hit molecules. The in vivo efficacy was evaluated using Chemotherapy induced peripheral neuropathy (CIPN) mice model. We identified that Phialomustin-B (PHL-B) derived from endophytic fungus exhibited potent TRPA1 inhibitory activity (IC50= 0.4 μM). Its effects were selective to TRPA1 but not to TRPV1 and TRPV4 channels. Molecular docking of PHL-B on TRPA1 channels revealed a binding pocket in a hot spot region for gain of function mutations which result in pain syndromes. Furthermore, our preliminary in vivo data also shows that PHL-B effectively reversed neuropathic pain behavior in a translational-CIPN rodent model. Although PHL-B appears to be a promising analgesic candidate displaying TRPA1 selectivity, its optimization with systematic SAR, structural & mechanism of action studies, and detailed in vivo efficacy remains to be established. Based on the obtained structural information, we envisage that PHL-B binding to this region may hinder the movement of S4-S5 linker and prevents the TRPA1 channel opening. Together, PHL-B appears to be a promising analgesic candidate targeting the nociceptive pain pathway.
Acknowledgment: This work is supported by CSIR- CDRI & UGC-JRF fellowship to Priyanka Yadav.

P95: Unveiling the Neuroprotective Mechanisms of Agmatine in Huntington's Disease: Implications for Therapeutic Interventions

Raj Katariya, Nandkishor Kotagale, Milind Umekar, Brijesh Taksande
Department of Pharmacology, Smt. Kishoritai Bhoyar College of Pharmacy, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur- 441002, Maharashtra, India

Background: Huntington's disease (HD) is a rare incurable progressive neurogenetic disorder caused by repeated expansion of CAG trinucleotide in the huntingtin gene (Htt) with gradual loss of GABAergic neurons in the striatal part of the basal ganglia. Agmatine is a novel neurotransmitter in the brain reported to exhibit a diverse range of biological properties.
Materials and methods: 3-nitropropionic acid (3-NP), a neurotoxin, was used to induce HD-like symptoms in rats like progressive behavioral, biochemical, neurochemical, and histopathological alterations. Rats were pre-treated with 3-NP (10 mg/kg, i.p.) on alternate days and then from the 10^{th} day continued on agmatine treatment (5-20 mg/kg, i.p.) up to the 32^{nd}day of the treatment protocol.
Results: The findings of the current investigation revealed that the manifestations of HD induced by 3-NP were restored by agmatine treatment. Agmatine intervention not only improved the 3-NP induced motor incoordination, beam walking, rota-rod performance, and learning and memory impairment but also normalized the GABA/glutamate levels as well as the oxidative stress markers in discrete brain areas. Moreover, agmatine (20 mg/kg) ameliorates the observed histopathological changes and modulates the expression of GFAP, a recognized immunohistochemical marker indicative of astrocytic activity.
Discussion and conclusion: The outcomes of the present study demonstrate that agmatine treatment effectively counteracted HD manifestations induced by 3-NP. It ameliorated motor deficits, cognitive impairments, and neurotransmitter dysregulations while restoring oxidative equilibrium. Notably, agmatine exerted positive influences on histopathological alterations and GFAP modulation. These multifaceted improvements underscore the
neuroprotective potential of agmatine for mitigating the diverse aspects of HD pathology. In conclusion, agmatine holds enormous promise as a comprehensive therapeutic intervention for HD management, warranting further exploration for clinical translation.
Acknowledgements: I would like to express my heartfelt gratitude to my supervisor for their invaluable support and guidance, which have been instrumental in shaping my progress. We also acknowledged the DST-SERB (EEQ/2021/000955), New Delhi for generously providing the funding that enabled us to conduct our research work.

P96: Early diagnosis of Alzheimer's disease by Electrocorticogram and ameliorative effects of low intensity magnetic field stimulation in Streptozotocin rat model

Reena Chittora, KP Kochhar[1], Suman Jain
Department of Physiology, All India Institute of Medical Sciences, New Delhi, India

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 intracerebroventricularly, 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.
Results: A significant improvement in cognitive functions was observed following MF exposure in AD rats. The improvement in behaviour was supported by viable neuronal count which was higher after MF treatment than in the AD rats. Electrocorticogram from frontal and occipital lobes showed reduced delta power of EEG waves in AD rats, whereas, MF exposure for short duration of 8 days only, increased the wave power in comparison to AD. Significant neurogenesis was also evident in MF exposed rats.
Discussion & Conclusion: These findings illustrate that the alteration in delta activity can be a potential early diagnostic measure of cognitive impairment in AD. It further confirms the correlation of neurodegeneration with impaired memory deficits. Present findings also suggest that non-invasive magnetic field stimulation has the potential to ameliorate the functional, morphological and cognitive deficits in STZ rat model of AD.
Acknowledgement: Authors wish to thank ICMR for financial assistance. The overall mentorship and supervision was provided by Prof. Suman Jain.

P97: Elucidating the mechanisms underlying the induction of neurotoxicity upon low-dose malathion and radiation exposure

Rekha Koravadi Narasimhamurthy[1], Gireesh G[2], Bola Sadashiva Satish Rao [1,3], Kamalesh Dattaram Mumbrekar[1]
[1]Department of Radiation Biology & Toxicology, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal, 576104, India; [2]Department of Cell and Molecular Biology, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal, 576104, India; [3]Directorate of Research, Manipal Academy of Higher Education, Manipal, 576104, India

Background: Neurodegenerative disorders are one of the most prevalent problems that the ageing population globally suffers from. Among the many etiological factors responsible for their onset, co-exposure to pesticides and radiation has also been stated to play a role. However, a holistic insight in to their regulative mechanism is scarcely explored.
Materials and methods: One-month old C57BL mice were singularly administered with malathion (50mg/kg) or subjected to irradiation (0.5Gy) or co-exposed. Behavioral tests for memory, recognition and exploratory behavior were conducted. Following euthanizing, neuronal morphology, neuroinflammation, neuronal survival and antioxidant enzyme levels were assessed. Further, hippocampal tissues were subjected to transcriptomic and metabolomic analysis.
Results: Altered neuronal morphology, neuroinflammation, neuronal death, increased oxidative stress and acetylcholinesterase enzyme inhibition were observed in the single and co-exposure groups. Transcriptomic analysis revealed activation of pathways involved in neurodegenerative diseases like MAPK, PI3k-Akt, Notch, Fox-O, Hippo signaling etc. Several processes regulating neuronal cell survival, synaptic transmission, plasticity, neurotransmitter synapses showed synergistic enrichment in co-exposure group. Metabolomic signatures showed alterations in metabolic pathways including tyrosine, glutathione, arginine, glutamine, tryptophan metabolism.
Discussion and **conclusions**: Malathion and radiation single and co-exposure induced changes in antioxidant status, inflammation and gene expression, leading to changes in metabolites and regulation of neuron morphology, synaptic plasticity and survival. Several neuronal processes along with genes and metabolites implicated in the onset of neurodegenerative diseases were altered, demonstrating their role in neurotoxicity. Co-exposure resulted in augmented effects compared to individual exposure and alteration of several unique pathways important in neuronal homeostasis, indicating importance of co-exposure toxicity studies.
Acknowledgements: The support and research facilities at the Manipal School of Life Sciences and Manipal Academy of Higher Education is gratefully acknowledged. The authors also thank the DBT-BUILDER for the support and financial assistance under the grant (ECR/2017/001239) from SERB, Govt of India. RKN would like to thank MAHE, Manipal, for the Dr. T.M.A Pai fellowship and KSTePS, Govt of Karnataka, for the DST-PhD scholarship.

P98: Identification of potential protein targets of Amyotrophic Lateral Sclerosis in TDP-43-mutated hiPSCs-derived 3D organoid model

R Negi, P Vatsa, UA Ansari, VK Khanna, AB Pant
Systems Toxicology Group, Food, Drug & Chemical, Environment and Systems Toxicology (FEST) Division, CSIR- Indian Institute of Toxicology Research (CSIR-IITR), Vishvigyan Bhavan, 31, Mahatma Gandhi Marg, P.O. Box No. 80, Lucknow-226 001, Uttar Pradesh, India, Academy of Scientific and Innovative Research (AcSIR), Ghaziabad- 201002, India

Background and objectives: Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder that causes motor neuron degeneration, progressive motor impairment, paralysis, and death. Human iPSC-derived 3D organoid models have emerged as better predictive tools for understanding the etiology of neurodegenerative disorders. We investigate the proteomic profile of the TDP-43-mutated hiPSCs-derived 3D organoid to understand its applicability in the therapeutic intervention of ALS.
Materials and methods: Human episomal iPSC cell lines were grown in Essential 8 media to generate a significant number of iPSCs, which were then characterized for pluripotency markers. The mutation in hiPSCs was accomplished using CRISPR/Cas-9 technology and predesigned gRNA. Normal and mutated organoids were produced and subjected to global proteomic profiling by high-resolution mass spectrometry.

Results: The proteomic analysis of normal and mutated organoids revealed the proteins associated with pathways of neurodegenerative disorders, proteasomes, autophagy, and hypoxia-inducible factor-1 signaling. Differential proteomic analysis revealed that the mutation in TDP-43 gene caused proteomic deregulation, which impaired protein quality mechanisms. Furthermore, this impairment may generate stress conditions that may ultimately lead to the development of ALS pathology.
Conclusion: The developed organoid model identifies potent proteins and their associated biological mechanism altered in ALS pathology. This study offers potential protein targets that may shed light upon the precise disease pathological mechanism and could be used for future diagnostic and therapeutic purposes for various neurodegenerative disorders.

P99: Insilco study for the identification of biomarker for Tuberculous meningitis

Ritika, Varun Kumar Singh
Department of Neurology, IMS, BHU, Varanasi-221005

Background: Tuberculous meningitis (TBM) is a common form of meningitis caused by infection of Mycobacterium tuberculosis and is the most severe form of tuberculosis (TB). Although the proportion of TBM may only be 1–5% of all TB cases. Its mortality is unacceptably high (range 10–36.5%), especially in developing countries. The estimated mortality due to TBM in India is 1.5 per 100,000 population. Despite being an endemic country for TB, data regarding clinical, radiological and laboratory (biochemical and microbiological) parameters and final outcome of adult TBM patients is sparse in India. Analysis of such variables in various countries has shown association of various factors with the prognosis of the disease like age, stage of disease, level of consciousness, presence of extraneural TB, isolation of Mycobacterium tuberculosis from CSF, biochemical studies and hydrocephalus. The availability of such data in a high burdened developing country like India. Thus, its required to develop diagnostic and prognostic biomarker for the identification of TBM.
Aim: The present work is planned to identify diagnostic and prognostic biomarkers for TBM.
Materials &Methods: In the present study we have used DisGeNET (gene and protein repository) and STITCH tool.
Result: We have found from DisGeNET, that TBM has disease gene id: C0041318 and have 68 genes reported from various databases. Further, we identify their interaction among themselves using STITCH tool and found that Cathelicidin antimicrobial peptide have higher interaction with rest of the proteins as matrix metallopeptidase-2, matrix metallopeptidase-6, Interleukin-6, Interleukin-4, Interleukin-1 beta, Estrogen receptor-1 and Vascular endothelial growth factor A.
Discussion & Conclusion: We found that these genes (Cathelicidin antimicrobial peptide have higher interaction with rest of the proteins as matrix metallopeptidase-2, matrix metallopeptidase-6, Interleukin-6, Interleukin-4, Interleukin-1 beta, Estrogen receptor-1 and Vascular endothelial growth factor A) might be used for the diagnosis and prognosis of TBM.
Acknowledgement: IMS-BHU, Varanasi-221005, India.

P100: Neuroprotective effects of Nootropic drug *Bacopa monnieri* in Alzheimer's disease

Roshani Singh, Deepesh Parashar and Manoj Sharma
School of Studies in Pharmaceutical Sciences, Jiwaji University, Gwalior (M.P), 474001

Background: Alzheimer's disease (AD) is a disorder that causes degeneration of the cells in the brain and it is the main cause of dementia, which is characterized by a decline in thinking and independence in personal daily activities. AD is considered a multifactorial disease: two main hypotheses were proposed as a cause for AD, cholinergic and amyloid hypotheses. In the present study we have taken Bacopa monnieri for Cognitive enhancement and neuroprotective effects. Based on its reputation for nerve tonic and its antioxidant activity, we hypothesized that this plant extract could mitigate the memory impairment and neurodegeneration in animal model of Alzheimer's disease.
Method: Bacopa monnieri (40mg/kg-ip) and Piracetam (200mg/kg-ip) were administered 30 min before Scopolamine (0.4mg/kg-ip) on the first day and followed up to 7^{th} days. On day 8^{th} animals were sacrificed, brain tissue homogenate was prepared and neuroprotective effects were measured followed by lipid

peroxidation (LPO) assay, and antioxidant markers such as GSH, SOD and CATalase. Body weight changes, estimation of hematological variables and behavioural changes were also accessed.
Results: Based on previous findings that this plant extract could directly inhibit the superoxide anion formation and could increase the hippocampal superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) activities, we suggested that the neuroprotective and cholinoprotective effects of the plant extract might be partly due to its antioxidant
Discussion and Conclusion: In conclusion, the present data supported the efficacy of Bacopa monnieri according to the traditional system and provided supported document about the neuroprotective effect against the cholinergic degeneration and cognitive enhancing effect of Bacopa monnieri in Alzheimer's disease model. Therefore, this plant is a valuable candidate for cognitive enhancer and neuroprotective agent in Alzheimer's disease.

P101: Electrophysiological brain mapping in infantile hemiplegic cerebral palsy patients

Rudraksh Banga[1], Aliya Mufti[1], Kanwal Preet Kochhar[1], Sheffali Gulati[2], Suman Jain[1]
[1]Department of Physiology, All India Institute of Medical Sciences, New Delhi, India; [2]Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India

Introduction: Infantile cerebral palsy (CP) is a neurodevelopmental disorder that affects children's sensorimotor functions, which may be associated with functional reorganization of somatotopic maps. The present study aims to standardize the procedure for cortical brain mapping in children with cerebral palsy and study the effect of rTMS on it.
Materials and Methods: Three different groups of participants (active, sham and control) aged between 5-15 years with infantile hemiplegic CP were subjected to brain mapping procedure before and after administration of low frequency rTMS intervention over the contralateral motor cortex for 4 weeks in 10 sessions along with Modified Constraint-Induced Movement Therapy (mCIMT).
Result: A grid targeting predefined locations around the hotspot of abductor pollicis brevisin cardinal directions was manually designed. Single pulse TMS was used to record motor evoked-potential at 41 stimulation sites on the grid for construction of brain maps. Heat maps of the hand area generated in the MATLAB software showed modulation of cortical excitability and somatotopic maps after rTMS intervention in CP patients. QUEST scores confirmed the recovery of sensori-motor function in these children.
Conclusion: We were able to standardize the procedure for mapping motor cortex in CP children using single-pulse TMS. This technique was found to be effective in understanding the alterations in cortical excitability and plasticity. Further rTMS intervention induced reorganization of cortical motor maps that lead to enhanced sensory and motor functional recovery in hemiplegic CP children.
Acknowledgment: We acknowledge the financial support provided by ICMR, Delhi.

P102: Calcineurin inhibition rescues dopamine inducedcytotoxicity and protects against behavioural decline in MPTP induced Parkinson's disease model

Rupsha Mondal[1,2], Chayan Banerjee[1,2], Sumangal Nandy[1], Moumita Roy[1,2], Joy Chakraborty[1,2]
[1]Department of Cell Biology and Physiology, CSIR-Indian Institute of Chemical Biology- TRUE, Kolkata,India; [2]Academy of Scientific and Innovative Research (AcSIR), CSIR-Human Resource Development Centre, Ghaziabad, India

Background: Dopamine (DA) cytotoxicity plays a key role in the development of Parkinson's disease (PD) progression. Effect of L-DOPA therapy on PD progression is still a matter of debate. We determined the effect of Calcineurin (CaN) inhibition on DA cytotoxicity and PD progression in a mice model.
Materials and Methods: Cytotoxicity assays, confocal microscopy and immunoblotting were performed to determine the effect of DA (± Calcineurin inhibition). MPTP, L-DOPA and CaN inhibitor FK506 treated C57BL/6 mice (30, 10 and 1 mg/kg respectively, for 7 and 14 days) wereused to determine the behavior, neurochemistry, neuronal death and neuronal architecture.
Results: DA induces cytotoxicity and mitochondrial fragmentation in vitro by enhancing CaN activity. This

leads to mitochondrial translocation of DRP1, which is protected by the applicationof FK506. Further, evaluation of the impact of DA exposure on PD progression in a mice model reveal that LD mediated behavioral recovery diminishes with time, because of continued DAergic cell death and dendritic spine loss. CaN inhibition, alone or in combination with LD, offer long term behavioral protection.

Discussion and Conclusions: Application of FK506 alone or in combination with L-DOPA in MPTP induced PD mice resulted in increased neuronal spine density and behavioural recovery. However, inhibition of other CaN substrates including proteins involved in neuro-inflammation (e.g., NFAT) did not show improved neuronal spine density, thus behavioural decline was not
protected. Hence, our findings suggest that CaN inhibitors might extend therapeutic effectivenessof LD therapy to treat PD progression.

Acknowledgements: The study is supported by grant from Indian Council of Medical Research (ICMR) and Science and Engineering Research Board (SERB). MR and RM are supported by Council of Scientific and Industrial Research (CSIR)-Senior Research Fellowship. CB is supported by The University Grants Commission (UGC)-Senior Research Fellowship

P103: RNA binding protein hnRNPA1 regulates O^6- Methylguanine DNA-methyltransferase expression in T98G glioma cells

Sachin Bhardwaj, Ajay K. Yadav
Dr. B.R. Ambedkar Centre for Biomedical Research, New Delhi

Background: Glioblastoma multiforme (GBM) is most invasive brain tumor with poor patient survival, recent studies showed O^6- Methylguanine DNA-methyltransferase (*MGMT*) as a poor prognosis marker. Epigenetic silencing of *MGMT* by promoter methylation compromises DNA repair and has been associated with the longer survival of the patients with glioblastoma received alkylating drugs.

Material and Methods: We tested the relationship between *MGMT* expression and RNA binding protein in T98G glioma cells, along with expression of *MGMT* at mRNA level was analysed in T98G and U87MG using PCR. RNA binding protein hnRNPA1 was knocked down using specific siRNA and *MGMT* expression was studied using RT-PCR and immnunoblotting.

Results: *MGMT* was predominantly expressed at mRNA level in T98G glioma cells but not in U87MG cells. To study the further relation between hnRNPA1 and *MGMT* we chosen T98G glioma cells and knocked down hnRNPA1 variants showed downregulation of *MGMT* at mRNA as well as protein level.

Discussion and Conclusion: Around 50-60% glioblastoma patients have a methylated *MGMT* promoter; yet, those expressing *MGMT* due to an unmethylated promoter or alternate mechanism will likely respond poorly to standard alkylating therapy. It is very important to elucidate the molecular mechanism of *MGMT* regulation at mRNA and protein level besides of the *MGMT* promoter methylation. Combined evaluation of *MGMT* methylation and expression may provide better insight into better therapeutic approach.

Acknowledgements: We thanks CSIR- Senior Research Fellowship support (File no.-09/045(1769)/2019-EMR-I) to S.B for financial support and we also acknowledge the support given to A.K.Y from Institute Of Eminence Grant, 2021-22 by University of Delhi, and Internal Maintenance Grant, University of Delhi, Delhi, India.

P104: Unraveling the timeline: Neuronal and skin regeneration dynamics after injury in Zebrafish

Saida Sayyed, Bushraa Nirban and Tressa Jacob
Department of Life Sciences, Sophia College (Autonomous), Mumbai

Background: Skin injuries stimulate the growth of nerve fibers in the injured area, where the actin cytoskeleton is crucial for maintaining the structural integrity of cells and is involved in various cellular processes, including neuronal development and function. The role of actin polymerization during skin and neuronal regeneration in zebrafish is being studied.

Material and method: Adult zebrafish (1.5-2 years) were used to study neuronal regeneration by inducing a superficial wound. Different timepoints after wounding were fixed using PFA, and immunostaining with mouse anti-acetylated tubulin was used to detect regenerating neurons during various post-injury time intervals.

Result: Presence of neurons was examined in the descaled region 24 hours post descaling (24hpd) using

immunostaining with mouse anti-acetylated tubulin. Zebrafish at 0 hours post descaling (0hpd) displayed an absence of neuronal growth in the descaled region, while regions with intact scales in the same fish exhibited the presence of neurons.
Discussion and Conclusion: In this study, neuronal regeneration was successfully observed at the 24-hour post-descaling timepoint in zebrafish. To strengthen the validity of our findings, further investigations involving a larger sample size are essential. Exploring additional time points, both earlier and later, will provide a comprehensive understanding of the regenerative process. Moreover, ongoing effortsto unravel the role of actin polarization in neuronal regeneration are being carried out.

P105: Understanding the role of Dopamine Receptor D5 (DRD5) modulator in working memory and cognitive functions

Sakesh Kumar[1, 3], Kajal Sharma[1, 3], Prem P Yadav[2] and Prem N Yadav[1]
[1]Neuroscience and Ageing Biology Division; [2]Medicinal and Process Chemistry Division CSIR-Central Drug Research Institute, Lucknow, Uttar Pradesh, India; [3]Academy of Scientific and Innovative Research (CSIR-HRDC) Ghaziabad, Uttar Pradesh (India)

Neurological diseases are on rising in all age groups, and the hardest hit ones are elderly citizens all over the world. Cognitive impairment, motor disability, are serious age associated debilitating conditions the occurs in about 8% percent of Indian population. One of the major underlying mechanisms considered for age associated dementia or motor disabilities is perturbed dopaminergic neurotransmission. Dopamine, a major neurotransmitter action through five (D1-D5) receptors belonging to the GPCRs superfamily. Also, dopamine plays important role in several critical processes, such as reward, motivation, attention, and learning. In this study using HTS assay, we discovered the thydroalcoholic extract of *Tinospora cordifolia* plant **(135/C002)** exhibit selective DRD5 receptor agonist activity. Using GloSensor assay, a live cell assay to measure cAMP formation, we determined that 135/COO2 extract exhibitEC50<0.5µg/ml at DRD5, while <2.2µg/ml at the DRD1 receptor. We further evaluated the effect of 135/C002 on cognitive behaviors in scopolamine-induced amnesia model. We observed that 135/C002 Significantly alleviated scopolamine-induced impairments in spatiotemporal learning and memory (measured by Y-Maze Test), working memory (measured by T maze test). Furthermore, to elucidate the molecular mechanisms of 135/C002procognitive effect in vivo, we measured the expression of BDNF, phosphorylation of AMPA ion channel subunit-GluR1 and cFOS activation. We observed that 135/C002 significantly blocked the effect of scopolamine-induced decrease in BDNF and phsopho-GluR1. Furthermore, we found that 135/C002 treatment induced the expression of cFOS (a marker of increased neuronal activation and synaptic plasticity) in the prefrontal cortex. These neurobehavioral and neurobiological studies for the first time demonstrated that *Tinospora cordifolia* plant extract 135/C00 enhances spatiotemporal learning and working memory in C57BL/6J mice. These results suggest that selective modulation of the D5 receptor as a plausible therapeutic strategy for treating cognitive disorders and highlights the therapeutic importance of *Tinospora cordifolia* plants for CNS disorders.

P106: Agmatine-NPY interplay in paraventricular nuclei regulates pubertal endocrine physiology

Sakshi Nalkande, Manish Aglawe, Brijesh G. Taksande, Milind J. Umekar
Division of Neuroscience, Department of Pharmacology, Smt. Kishoritai Bhoyar College of Pharmacy, Kamptee

Background: Puberty onset is a complex, organized biological process with multilevel regulation, and its physio-pathological mechanisms are yet to be fully elucidated. NPY is known regulator, however, the role of agmatine in neuroendocrine physiology of puberty is unknown.
Objective: To study the effect of agmatine on puberty and evaluation of neuropeptide Y involvement in it and associated conditions.
Method- On PND 29 to 35 & PND 45-52 daily administration of agmatine (4, 8 µg i-pvn) & l-Arginine (5,10 µg i-pvn)) in pre- & post-puberty male/female rats was done Onset of puberty was examined through body weight, age of vaginal opening, oestrus cycle, testis development & plasma hormone levels. Estimation of LH, FSH, ACTH, TSH, oestrogen, progesterone, testosterone, T3 & T4 level in plasma by ELISA. The involvement of NPY wasdone by implying NPY (peptide) agonist and antagonist - BIBP3226 (1 µg i-pvn).

Result: Testes development, vaginal cytology and estrus microscopy verified normalpubertal onset in all the experimental groups. Intra-pvn administration of agmatine have significant influenced the hormonal levels in HPG axis in pre- & post-puberty male/female rats. NPY receptor antagonist BIBP2336 have shown significant reduction in the effect of agmatine and l-arginine on release and inhibition of hormones in HPG axis.
Conclusion: These data suggest the influence of agmatine within paraventricular nucleuson release and regulation of hormones from HPG axis. Furthermore, our study also highlightsthe implication of NPY within PVN in the regulatory effect of agmatine in pre- and post- pubertal animal. Thus, this interplay can be novel therapeutic target for management of pubertaldisorders.
Acknowledgement: I am very thankful to AICTE for providing a GPAT stipend. Also,thankful to all teaching and non-teaching staff for helping me throughout my research.

P107: Comparative ethological analysis of behavior in healthy male and female Wistar rats on elevated plus maze

Sakshi Sharma[b], Martina Narzary[c], Suman Jain[d], Varsha Singh[a]
[a]Humanities and Social Sciences, Indian Institute of Technology, Delhi; [b]School of Interdisciplinary Research, Indian Institute ofTechnology, Delhi; [c]Indian Institute of Technology, Delhi; [d]Department of Physiology, All India Institute of Medical Sciences, New Delhi

Background: The Elevated Plus Maze (EPM) is a standard task for the assessment of anxiety in rodents. The ethogram derived from the EPM provides precise measure of behaviour enabling objectiveinterpretation of anxiety. We report parameters assessing the behaviour on EPM critical for quantitativeand quantitative analysis of EPM with reference to sex-differences.
Materials and methods: Adult Male (n=10) and Female (n=10) albino Wistar rats weighing240-280g were used for this study. EPM paradigm was used for the investigation of basal levels of anxiety in healthy male and female Wistar rats (Walf and Frye, 2007). Video-tracking of behavior of the animal was done with CCD camera.
Results: Results confirmed that males spent more time in the open arms compared to the closed arms and showed more non-anxious behaviours, reflecting low anxiety and increased risk-taking in males. Females exhibited more anxious behaviour when parameters assessing the quantitative measuresof behaviour like time spent and number of entries to each arm were investigated. Blind analysis of theethological behaviours like head dips, stretched posture and rearing also gave the similar results. Whenthe behaviour was analyzed in the two separate halves of the task duration, these observations persistedin the females when compared with the males.
Discussion and conclusion: Our study reports the differences in the behaviour of the two sexes on EPM. We examined sex-specific quantitative and qualitative measures in the elevated plus maze performance. Our understanding of males and females' approach-avoidance and anxiety state explaining the behaviour on EPM might be improved by cumulatively analyzing the quantitative parameters along with the changes in ethology, producing alternate insights.
Acknowledgement: Authors, VS and SJ supervised the study. SS collected and analysed thedata. MN helped with the data analysis. This work was under DST SERB Vritika Research Training Grant of the author VS supporting the Trainee MN.

P108: Subacute metabolic markers of repetitive mild head injury rat model

Samiya Zehra[1], A K Baranwal[2], Kamlesh Bhaisora[3], Ahmad Raza Khan[1]
[1]Department of Advanced Spectroscopy and Imaging, Centre of Biomedical Research, SGPGIMS Campus, Lucknow; [2]Experimental Animal facility, SGPGIMS, Raebareli Road, Lucknow; [3]Department of Neurosurgery, SGPGIMS, Raebareli Road, Lucknow

Background: Repetitive mild traumatic brain injury (RmTBI) is a strong risk-factor for neurodegenerative diseases.[1] So far, no objective diagnostic test is available for RmTBI[2], therefore we hypothesize that NMR-based metabolomics can suggest potential biomarker for RmTBI. NMR spectral analysis shows significant alterations in serum and urine metabolites inmTBI and RmTBI.
Material and Method: Thirty male, Wistar rats were employed and blood, urine samples were collected on

day 21 from control, mTBI and, RmTBI group. NMR spectra wereacquired on 800 MHz NMR Spectrometer (Bruker, Germany). Each metabolite was integratedwith respect to the TSP and NMR data were analyzed as our previous work.

Results: Serum metabolites N-acetyl Glycoproteins (NAG) ($p<0.05$), and Lipids L3/L4($p<0.05$) were significantly altered. Among urine metabolites, creatinine ($p<0.01$), trans-aconitate ($p<0.01$), were significantly altered in both groups, while acetoacetate($p<0.01$), and taurine ($p<0.01$) only in RmTBI group with respect to control. AUC of serum metabolites are, NAG (0.843) and L3/L4(0.81). AUC values of creatinine,acetoacetate, trans-aconitate and taurine from urine are AUC=1.0,0.98, 0.98, 0.95 respectively.

Discussion and Conclusion: Present study showed serum metabolic markers such as N-acetylglycoprotein (NAG) significantly increased in both group in comparison to control. NAG is a marker of inflammation and has been observed in many diseases such as cardiovascular, cancerand metabolic diseases[4]. A significant increase in creatinine and significant decrease in Trans-aconitate, and acetoacetate observed in urine, that suggest impaired energy metabolism after injury. While a significant decrease in taurine suggests impaired osmoregulation.

Acknowledgement: The work is funded by the Department of Biotechnology, Govt of India under the Ramalinga swami Re-entry Fellowship grant 2019. We would also like to thank our host institute, the Centre of Biomedical Research (CBMR), under the Department of Healthand Family Welfare, UP Govt. We also thank our collaborators for their support for animalexperimentation at SGPGI.

P109: Metabolic rewiring during neuronal differentiation and its interplay with toxicant-induced epigenetic alterations

Sana Sarkar[1,2], Anuj Pandey[1], Mohammed Haris Siddiqui[2], Sanjay Yadav[3], AB Pant[1]

[1]Systems Toxicology Group, Food, Drug & Chemical, Environment and Systems Toxicology (FEST) Division, CSIR-Indian Institute of Toxicology Research (CSIR-IITR), Vishvigyan Bhawan, Lucknow, UP, India.; [2]Department of Bioengineering, Faculty of Engineering, Integral University, UP, India.; [3]All India Institute of Medical Sciences (AIIMS), Raebareli, UP, India.

Background: The metabolic program in neuronal cells undergoes critical alterations during neuronal differentiation and degeneration. Further, epigenetic modulators like miRNAs deregulated by toxicant exposure drive several processes triggering energy crises leading to neuronal death. Thus, the present study was designed to explorealterations in mitochondrial functions during differentiation, toxicant exposure, and miRNA-mediated regulation in neuronal cells.

Materials and Methods: Real-time bioenergetics was performed using a Seahorse XFp analyzer. OpenArray profiling was conductedto identify miRNAs deregulated by arsenic exposure (10μM for 24h) in human-derived RA+BDNF-induceddifferentiated SH-SY5Y cells. Target identification and pathway analysis were done using *in-silico* tools. Gene expression and transient transfection studies were carried out using mimics and inhibitors of miRNAs via RT-PCR assay**.**

Results: Bioenergetics studies revealed that differentiated SH-SY5Y cells exhibited an "anti-Warburg effect," a metabolic shift from glycolysis to oxidative phosphorylation indicated by higher OCR and lower ECAR thanproliferating cells. Further, differentiated cells possessed enhanced bioenergetics functions and mitochondrialdynamics relative to undifferentiated cells. However, arsenic significantly decreased both OCR and ECAR inmature SH-SY5Y cells. Transfection studies confirmed the involvement of miR-29b and miR-153 inregulating mitochondrial bioenergetics and dynamics in neuronal cells.

Discussion and Conclusion: Induction of metabolic reprogramming during neuronal differentiation marked the transition of cells from aerobic glycolysis to oxidative phosphorylation. However, drastic alterations in mitochondrial bioenergetics in response to arsenic or ectopic expression of miR-29b and miR-153 have been associated with impaired mitochondrial function and dynamic behavior. The miRNAs (i.e., miR-153 and miR-29b) and their associatedtargets identified in the present study have the potential to develop as predictive biomarkers and mediators ofmultifactorial neurodegenerative conditions.

Acknowledgments: Financial support for the study was provided by CSIR-IITR, Lucknow, India, and Science and Engineering Research Board (SERB), New Delhi, India. The Indian Council of Medical Research, New Delhi, India, gavefellowship for carrying out the research.

P110: Exploring the relationship of hyperhomocysteinemia with executive functioning in older adults

Sandhya G, Palash Kumar Malo, TLSA study team, Thomas Gregor Issac
Centre for Brain Research, Indian Institute of Science

Background: Hyperhomocysteinemia (HHcy) is a known risk factor for cardiovascular diseases. Since dementia more often involves cerebrovascular pathology, it becomes important to study homocysteine as a potential risk factor for cognitive impairment. The current study aims to examine whether plasma homocysteine levels affect cognitive performance especially executive functioning in older adults.
Materials and methods: This study used baseline data from CBR-Tata Longitudinal Study of Ageing (CBR-TLSA). Participants were assessed for cognitive performance and executive functioning using Addenbrooke's Cognitive Examination-III (ACE-III) and Trail Making Test-B (TMT-B) respectively. Homocysteine was quantified using chemiluminescence immunoassays. Mann-Whitney U test was used to compare means of scores between groups.
Results:1212 participants were stratified into three groups based on age (45-54, 55-64, ≥65 years). Homocysteine levels higher than median 17.22µmol/L were considered HHcy. People ≥65 years with HHcy had significantly lower ACE-III than people without HHcy of same age group ($p=0.005$). Further analysis showed that only women ≥65 years of age had significant difference among HHcy groups ($p=0.014$). The scores in TMT-B did not show differences with HHcy across all age groups and genders ($p>0.05$).
Discussion and conclusions: The present study showed that, in women ≥ 65 years of age, people with HHcy scored significantly lesser in ACE-III than those without HHcy. The observed result might be due to uneven prevalence of HHcy among the genders and the post-menopause effects in women. But such a difference among people with different HHcy status was not observed in TMT-B.
Acknowledgements: I would like to thank the CBR-TLSA study team who were involved in data collection. I would also thank the participants of the study for their active participation and cooperation. I also express my gratitude to Tata Trusts and Centre for Brain Research for funding the research.

P111: Development of novel therapeutics for mitigation of burn injury-induced chronic pain

Sangam Barnwal, Vinod Tiwari
Department of Pharmaceutical Engineering and Technology, Indian Institute of Technology., Banaras Hindu University, Varanasi-221005

Burn injuries are among the underappreciated injuries associated with substantial morbidity and mortality. Burn injuries, particularly severe burns are accompanied by an immune ad inflammatory response, metabolic changes, and distributive shock that can be challenging to manage and can lead to multiple organ failure. In India, over 100,000,0 people are moderately or severely burnt every year. Burns not only lead to physical trauma but also psychological trauma. Burn injury treatment follows a series of events such as wound healing, suppression of chronic pain, and stabilizing the proinflammatory cytokines. The major neuroinflammatory mediators are starting from NGF, TRPVI to NR2B, and some voltage-gated ion channels. This further activates PKA/PKC pathway, increases the influx of Na+ ions as well as Ca+2; sensitizes the AMPA channel, and simultaneously microglial activation. Current therapeutics are morphine and its analogs, some antipsychotic drugs, and antiepileptic drug but all of them have their own limitations like CNS toxicity. Amiloride is a reversible blocker of the Acid Sensitive Ion Channel (ASIC) and has been reported as a potent analgesic in CCI-induced pain, Bone cancer pain, Neuropathic pain, and Ulcerative colitis pain. Moreover, ASIC is colocalized with TRPV1 in DRG so we hypothesize to use ASIC as a target. So far we have performed Evoked pain behavior studies and Biochemical; further, we are going to quantify mRNA expression ASIC and its protein concentration in DRG.

P112: Parkinson's disease -related neuroinflammation controlled by the phosphorylation of cytosolic phospholipase A2 through cyclin-dependent kinase 5

Sangita Paul[1,2], Saman Fatihi[1,2], Srishti Sharma[1,2], Rintu Kutum[1], Raymond Fields[3], Harish C Pant[4], Lipi Thukral[1,2] and Binukumar BK[1,2]
[1]CSIR Institute of Genomics and Integrative Biology, New Delhi, India; [2]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad- 201002, India; [3]Viral Production Core Facility, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA; [4]Neuronal Cytoskeletal Protein Regulation Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA

Abstract not available

P113: Small Organism, Big Hope: Secondary metabolites from *Dictyostelium discoideum* as innovative interventions for Alzheimer's disease

Nil Patil[1,2], Rupal Dhariwal[1,2], Mukul Jain[1,2]
[1]Cell and Developmental biology lab, Research and Development Cell, Parul University, Vadodara 391760, Gujarat,India; [2] Department of Life Sciences, Parul Institute of Applied Sciences, Parul University, Vadodara 391760, Gujarat, India.

Background: *Dictyostelium discoideum,* a eukaryotic microorganism, produces diverse secondary metabolites (polyketides, terpenes, flavonoids) across various developmental stages with antibacterial, anti-aggregative, and anti-amyloidic properties. This study focuses on isolation and characterization of screened secondary metabolites against AD.
Materials and methods: Screening of metabolites (SWISS - ADME) and receptors specific to AD were scrutinized through network pharmacology (CytoHubba, GO, and KEGG resources) and subsequent screening through AutoDock and GROMACS. Among these, the selected compound was isolated from *D. discoideum*, and subjected to characterization using analytical techniques - GC-MS and NMR
Results: Following initial screening, six compounds were selected and underwent hybrid approach involving database and compound-centric target identification led to the selection of three receptors (CYP19A1, COX2, mTOR), prioritized over GO enrichment and KEGG analysis. The resulting metabolite-receptor complexes underwent validation via molecular docking and molecular dynamics (MD) simulation. The ultimate compound was isolated and subjected to characterization using GC-MS, which identified Discoidol (a Terpene) as a prominent constituent with a retention time of 19.23 minutes and 100% abundance in the extract.
Discussion/Conclusion: This study explores the utilization of secondary metabolites from a eukaryotic model organism in a therapeutic approach to develop a cost-effective, less harmful, and relatively efficient drug for AD treatment. The extract was highly comprised with Discoidol and had affinity for COX2. The COX2 enhances amyloid-beta production and thus,its targeted inhibition using Discoidol was focused on. Moreover, the Discoidol's PROTOX validation indicates its least toxic behavior towards human cells and organs in comparison with the referred drug Indomethacin that have a hepatotoxic property causing upraised level of drug degrading enzymes. Thus, Discoidol could be considered for pre-clinical and drug discovery purpose against AD in near future.
Acknowledgments: The Parul University, Vadodara for providing funding support to this project.

P114: Cell-free therapy against neurodegeneration as a double-edged sword of extracellular vesicles and organelles

Shalini Raik[1], Mohil Mishra[1], Vidya Rattan[2], Shalmoli Bhattacharyya[1]
[1]Department of Biophysics, Post Graduate Institute of Medical Education and Research, Chandigarh, India; [2]Oral Health Sciences Centre, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Background: MSCs have been involved in promoting neural repair, regeneration, axonal connection,

decreasing amyloid deposition, and tau-based neuronal death by transferring various factors to the site of injury. This study evaluates the neuroprotective efficacy of a stem cell-based cell-free approach via transferring dental pulp stem cell-derived exosomes and healthy mitochondrial.
Material and method: In this study, SHSY-5Y cells were differentiated into mature neurons, and later treated with streptozotocin to develop Alzheimer's disease-like *in* vitro model. An immunofluorescence assay was performed to validate the model. Subsequently, the therapeutic potential difference between DPSC-mitochondria and DPSC-EVs was analyzed by ROS andan immunofluorescence assay.
Results: Streptozotocin treatment to neuroblastoma cell line showed neurite distortion and accumulation of Tau protein which was confirmed by brightfield images and immunofluorescence assay; indicating successful establishment of Streptozotocin mediated AD-like *in* vitro model. Further, this neurotoxic effect was reversed by the uptake of DPSC- derived mitochondria and exosomes in a streptozotocin-treated neuroblastoma cell line which confirmed their neuroprotective role.
Discussion: This study has evaluated the comparative effect of exosomes and mitochondria derived from DPSC on mature neurons against Streptozotocin *in vitro* AD model. The isolated mitochondria and exosomes may have a role in preventing neurotoxicity and maintainingneurite extension. Thus, we observed that these findings may be considered potential dual- edged neuroprotective targets for the treatment of Alzheimer's disease.
Acknowledgment: Special thanks to Indian Council of Medical Research (ICMR) forproviding funding for this study

P115: Exploring the role of Imagery Rescripting and Imaginal Extinction in Reducing Generalized Threat Expectancies

Sharmili Mitra[1] and Manish Kumar Asthana[1,2]
[1]Department of Humanities & Social Sciences, Indian Institute of Technology Roorkee, India
[2]Department of Design, Indian Institute of Technology Roorkee, India

Background: Imagery rescripting (ImRS) is a UCS devaluation intervention where participants mentally reevaluate an aversive situation in a desirable direction. While Imaginal extinction (IE) is an exposure-based intervention where participants vividly imagine the conditioned stimuli. The current study attempted to compare the effectiveness of ImRS and IE in reducing generalized fear.
Materials and Methods: Forty-two healthy individuals (M=18.83, SD=0.44) were randomly assigned into three groups, ImRS, IE, and standard-extinction (SE as control group). On day 1, fear acquisition and generalization were performed. On day 2, the intervention and generalization tests were conducted. The outcome measures were skin conductance responses, UCS expectancy, and valence ratings.
Results: There was no significant difference in the UCS Expectancy ratings across the three intervention groups in the Acquisition, Generalization, Extinction, and Generalization Testing phases. Hence, the results indicate that the three interventions had a comparable effect on the expectancy ratings on extinction and generalization testing. A significant phase x group interaction effect [$F(6,117) = 2.519$, $p=0.025$, $\eta_p^2=0.823$] of CS+ valence was observed.
Discussion: The current study is the first to explore the effect of ImRs and IE on generalized fear. After the intervention, the expectancy ratings declined, although we did not find significant group differences. However, the CS+ valence of the ImRS group in the generalization testing phase was higher than the other groups indicating a possible effect of UCS devaluation. Therefore, ImRS may be more effective as it targets both expectancy-learning and UCS devaluation.
Keywords: fear generalization; imagery rescripting, imaginal extinction, expectancy; valence

P116: Scintillating effects of Vitamin D3 in combating the neuropsychiatric symptoms of schizophrenia

Sharon Mariam Abraham, Omalur Eshwari, Manjari SKV, Kishore Golla, and Pragya Komal
Department of Biological Sciences, Birla Institute of Technology and Sciences (BITS), Pilani, Hyderabad, Telangana - 500078.

Background: Schizophrenia is a multifactorial, neuropsychiatric, neurodegenerative, neurodevelopmental disorder in which the prefrontal cortex (known to be important for working memory and cognition) is severely impaired. Though glutamate receptor hypofunction has been previously investigated, there is a critical lack of insights into whether a common nutraceutical, Vitamin D3 (VD), combats neuropsychiatric symptoms observed in SCZ.
Materials & Methods: In the present study, we explored the effects of VD on SCZ phenotypes induced using MK-801 (dizocilpine) in a rodent model. MK-801 is capable of recapitulating the adult positive, negative, and cognitive symptoms of SCZ. C57BL/6 male mice were divided into four groups: (1) control (**Group I**), (2) SCZ (MK- 801, 0.5mg/kg; **Group II**), (3) only Vitamin D3 (VD; 500IU/kg, **Group III**), and (4) SCZ+ VD (**Group IV**). Mice were subjected to various behavioural assays like the open field test (OFT), novel object recognition test (NORT), and passive avoidance test (PAT) to assess locomotion, attention, cognitive and memory function.
Results: Our preliminary data shows that VD pre-administration remarkably restored movement deficit, anxiety, and cognitive dysfunction observed in SCZ mice. VD administration also rescued some major alterations in the gene expression of NR2B, NR2A, and NR1 subunits of the N-Methyl-D-Aspartate (NMDA) receptors in the prefrontal cortex brain tissue samples of SCZ mice.
Conclusion: Overall, we show that VD supplementation reflected a beneficial role in restoring the neuropsychiatric symptoms of SCZ via the rescue of the glutamatergic ionotropic receptor gene expression in the PFC.
Acknowledgements: Birla Institute of Technology & Science (BITS) Pilani- Hyderabad Campus
DBT-Boost to University Interdisciplinary Life Science Departments for Education and Research programme (DBT-BUILDER) International Brain Research Organization (IBRO)

P117: *Withania Somnifera* mediated microtubule stabilization: A novel approach for Parkinson's disease treatment

Shekhar Singh, Surya Pratap Singh
Department of Biochemistry, Institute of Science, Banaras Hindu University, Varanasi-221005 (U.P.), India

Background: Microtubule instability, a key feature of Parkinson's disease, disrupts vital neuronalprocesses. Impaired microtubule dynamics hinder intracellular transport, causing accumulation oftoxic alpha-synuclein aggregates. It also weakens neuronal structure, alters axonal transport, and declines mitochondrial function. These factors contribute to the degeneration of dopaminergic neuron, manifesting as motor symptoms. Understanding and addressing microtubule instability may offer novel therapeutic strategies to combat PD progression.
Objective: In the present study, we investigated the microtubule rescue effect of *Withania Somnifera* and explored its neuroprotective mechanism in the rotenone-intoxicated PD model.
Material and Methods: Mice were divided into four experimental groups: Vehicle control, rotenone (2 mg/kg body wt., subcutaneous), *Withania Somnifera* extract (WSE, 100 mg/kg body wt., oral) + rotenone, and WSE only]. Mice were pre-treated with WSE for a week and then simultaneously injected with ROT for 35 days.
Results & Discussion: *Withania Somnifera* mitigated the damage to dopaminergic neurons and prevented the disruption of microtubules caused by rotenone. Additionally, this was followed by increase in the post-transcriptional modifications on tubulins, helping to restore the balance of polymerized tubulins. In addition, *Withania somnifera* reduces α-synuclein accumulation and increases the expression of tyrosine hydroxylase that confirms the presence of viable dopaminergicneurons. These results demonstrated that WSE prevents the dynamic instability of MT by hyperacetylation of alpha tubulin rescuing the dopaminergic neurons from degeneration.
Conclusion: Taken together, our findings indicate that Withania somnifera has beneficial neuroprotective effects in PD and it might be a potential microtubule stabilizing agent for the treatment of PD and other diseases. In light of its favorable neuroprotective properties, Withania somnifera should be evaluated in the treatment of PD as well as related neurological disorders.
Keywords: Parkinson’s disease; *Withania Somnifera*; rotenone; α-synuclein; microtubules; tubulins.

P118: Analysis of Tmem119 for its possible involvement in microglia functions

Shweta, Himanshi Yadav, Shashank Kumar Maurya
Biochemistry and Molecular Biology Laboratory, Department of Zoology, Faculty ofScience, University of Delhi, Delhi-110007

Background: Microglia plays an important role in the regulation of neuroinflammation-drivenneurological disorders. Recently, Tmem119 has been identified as a marker of adult microgliawhose expression has been shown to alter during neuroinflammation. However, analysis of the Tmem119 protein and its possible involvement in neuroinflammation need to be deciphered.
Material and Methods: RT-PCR and western blotting were performed in an LPS-induced mice model of neuroinflammation to study the expression pattern of Tmem119. Physio- chemical properties, secondary and tertiary structures were predicted using ExPASy ProtParam, PSIPRED and Swiss-Prot, respectively. Protein-protein interaction and signalling pathways were predicted using STRING.
Results: The expression of Tmem119 at both transcript and protein levels was observed to increase in LPS-induced mice as compared to the control. Regarding physiochemical properties, the number of negatively charged residues was double the number of positively charges residues. The instability index and aliphatic index were very high. The GRAVY indexis negative. The secondary structure showed a large portion of α-helices. Tmem119 is predicted to interact with proteins of microglia involved in various physiological functions.
Discussion: The results of the present study demonstrated an increase in Tmem119 expressionin LPS-treated mice. Tmem119 is a single-pass transmembrane protein of 280 amino acids found in microglia. It is unstable in ex-vivo conditions and shows high thermostability due to the presence of a high number of aliphatic amino acids. Extracellular and intracellular domainsare hydrophilic and transmembrane is hydrophobic. Tmem119 interaction with microglial proteins using STRING predicts its role in microglial cellular processes.
Acknowledgements: Financial support of the Institution of Eminence, University of Delhi (IoE, DU) is gratefully acknowledged.

P119: Development of small molecules as potential mutant SOD-1 aggregation inhibitors for the amelioration of Amyotrophic lateral sclerosis

Siddharth Gusain, Manisha Tiwari
Dr. B. R. Ambedkar Center for Biomedical Research

Background: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by the loss of upper and lower motor neurons. Cu/Zn superoxide dismutase is one of the genes associated with the familial form of the disease (fALS). It is hypothesized that a toxic gain of function in the protein leads to ALS.
Material and Methods: Novel synthesized molecules were tested for their ability to prevent the aggregation of hSOD1 protein-associated toxicity in Neuro-2a cells overexpressing G85R hSOD1 mutation. Cells pre-treated with the small molecules were further treated by MG-132 and effects were analyzed by evaluating cell death, ROS generation, Apoptosis and Mitochondrial membrane potential.
Results: Small molecules SG-9 and SG-10 displayed very low toxicity to the transfected cells. Both the small molecules considerably prevented cell death as compared to the MG-132 treated cells. These small molecules were able to significantly reduce oxidative stress associated with the aggregation of mutant SOD1 protein. The molecules were also able to prevent apoptosis in the cells which was analyzed by Annexin V-PI staining and western blotting. These molecules were also able to restore mitochondrial membrane potential upon treatment.
Discussion: Currently, there are only two FDA-approved drugs; Riluzole and Edaravone, which are non-curative and marginally slow disease progression by a few months. Our study provides small molecules that can be further used for lead optimization and can provide targeted benefits and better therapeutic potential for SOD1-associated ALS. Our compounds were able to ameliorate the effects associated with SOD1 aggregation in a transfected N2a cell line model.
Acknowledgement: S.G. would like to thank DU-Non-NET and ICMR-SRF for providing the fellowship. M.T. would like to acknowledge the Institute of Eminence Grant,2021-22 and Maintenance Grant, ACBR, DU for providing the financial support to conduct the study.

P120: Identification and association of genetic factors: a cohort study of Post-Stroke Depression among eastern Indian population

Smriti Mishra[1], Dipanwita Sadhukhan[1], Biman Kanti Roy[2], Subhra Prakash Hui[3], Arindam Biswas[1]
[1]Molecular Biology & Clinical Neuroscience Division, National Neurosciences Centre, Calcutta, Kolkata, India; [2]Bangur Institute of Neurosciences, IPGME&R, Kolkata, India;
S.N. Pradhan Centre for Neurosciences, University of Calcutta.

Background: Post-stroke depression (PSD) is associated with increased morbidity and mortality. In Kolkata, the prevalence of PSD was 36.98% and ~17% developed depression annually. PSD is linked to worsen cognitive and physical outcomes**.** In this study, we aim to determine the association of polymorphic variants with PSD among eastern Indian population**.**
Materials & Methods: The patient cohort consisted of 91 Ischemic stroke and 68 ICH cases from eastern India. PCR-RFLP techniques was used to genotype the polymorphisms, based on associated literature. We used Geriatric Depression Scale (GDS) for assessment of depression. Statistical calculation was performed using Mann-Whitney U test calculator, on line web tool.
Results: Among the studied polymorphic variants, rs6559833 of *TRKβ* and rs6159 of *CRH* are found tobe statistically significant **(P=0.0455)** and **(P=0.01994)** respectively; with PSD in ischemic stroke patients. The mean GDS score for the "TT" survivors of rs6559833 was 14.45±6.36 andthe score for the "AA" survivors of rs6159 was 6.10 ± 2.02. Along with it, a trend has been observed in the variant, rs6265 of *BDNF* (P=0.08124) among post-stroke depressed individualsof ischemic stroke.
Discussion and Conclusions: A significant association of rs6559833 of *TRKβ* and rs6159 of *CRH* is observed with PSD among ethnic Bengali population of eastern India and a like-wise trend is observed for rs6265of *BDNF*. To best of our knowledge, this is first report from India, identifying the association of genetic variants with PSD. In future, a large number of samples from other ethnic populationneeds to be validated to understand the genetic pathobiology of depression after stroke.
Acknowledgements: The authors thank the patient and the family members who participated in the study. Supported by grants from the Department of Science & Technology, Govt. of India, underCognitive Science Research Initiative Programme toauthor Dipanwita Sadhukhan(DST/CSRI-PDF/2021/12) and the corresponding author Arindam Biswas (DST/CSRI-P/2017/22).

P121: Mouse brain development: Decoding developmental neurobiology through integrated multi-omics analyses

Sneha Manjunath, Vatsal Mehra, Manojkumar, Murray Blackmore and Ishwariya Venkatesh
CSIR- Centre for Cellular and Molecular Biology, Hyderabad

Background: Understanding the regulatory landscape of the developing mouse brain is crucial for unravelling the intricate processes driving brain development and function. However, analysing all regulatory layers simultaneously poses challenges for bioinformaticians, including the management and analysis of large and complex datasets generated by high-throughput sequencing techniques. This study introduces Mouse brain dev, an innovative user-interactive website designed to retrieve regulatory information in the field of neurobiology.
Methods: The Mouse brain dev database integrates diverse datasets, including gene expression, chromatin accessibility, transcription factor binding, and transcription factor footprints, obtained from the ENCODE consortia across multiple developmental time points. This comprehensive resource enables neurobiologists to explore intricate regulatory networks and uncover the molecular basis of complex brain functions**.**
Result: Mouse brain dev's unique feature is its intuitive graphical user interface (GUI), which overcomes the constraint of effectively visualising data and analysis. The GUI provides interactive and dynamic visualisations, facilitating the interpretation of complex regulatory patterns and relationships. This empowers researchers to identify trends, patterns, and potential regulatory interactions that may not beapparent in traditional formats. By addressing the challenges, Mouse brain dev offers a holistic approachto studying the dynamic regulatory landscape of the mouse brain during development**.**

Conclusion and Discussion: In conclusion, Mouse brain dev serves as a pioneering bioinformatics resource tailored for neurobiologists studying the mouse brain. Its integrated approach and user-friendly interface enable comprehensive analyses of complex biological systems, advancing our understanding of the regulatory mechanisms governing brain development and function. The application of Mouse brain dev has the potential to unlock the mysteries of the dynamic regulatory landscape of the mouse brain, contributingto the broader field of neurobiology**.**

Funding Acknowledgements: Council of Industry and Scientific Research (CSIR)

P122: Dopamine controls neuronal iron release by regulating ferroportin

Sanju Kumari, **Somya Asthana**, Abhishek Mukherjee, Chinmay K. Mukhopadhyay
Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi-110067

Background: Emerging evidences show degeneration of dopaminergic neurons and iron depositionin the substantia nigra of Parkinson's disease (PD) patients and animal models. Synthesis of dopamine (DA) in neurons is also dependent on iron. Despite the intimate relation between them,any role of DA on neuronal iron homeostasis remains unexplored.
Methods: SH-SY5Y neuroblastoma and HT-22 hippocampal neuronal cells were treated with DA.Western blot and RT-qPCR were performed for iron homeostasis components. Regulation of ironexporter ferroportin (Fpn) was determined by promoter assay, ChIP assay and protein stability assay. Intracellular iron level was determined using calcein fluorescence.
Results: Ferroportin (Fpn) is the unique cellular iron exporter in mammalian kingdom. It protectscells from iron-induced oxidative damage by releasing iron. Here we show that DA promotes ferroportin level to deplete of neuronal iron pool. DA regulates Fpn mRNA level by a transcriptional mechanism and as well as by a protein stability mechanism. Iron uptake componenttransferrin receptor 1 (TfR1) remains unaltered by DA treatment.
Discussions and conclusions: Our results reveal a novel role of DA in releasing iron by inducing Fpn in neuronal cells, whereas it does not influence iron uptake component TfR1. These results establish hitherto unknown role of DA on neuronal iron homeostasis. Our findings may be implicated in neuronal iron deposition in PD when DA synthesis is affected.
Acknowledgement: CKM acknowledges financial support received from DBT. SK was supported by fellowship from DBT and AM by DSK post-doctoral fellowship from UGC.

P123: Deregulated expression of HDAC4 and an insight into its interaction with a non-histone substrate in temporal lobe epilepsy

Sonali Kumar[a] Ozasvi R Shanker[a], P Sarat Chandra[b], Manjari Tripathi[c], Jyotirmoy Banerjee[d], Aparna Banerjee Dixit[a]
[a]Dr. B.R. Ambedkar Centre for Biomedical Research (ACBR), University of Delhi, New Delhi, India; [b]Department of Neurosurgery, All India institute of medical sciences (AIIMS), New Delhi, India; [c]Department of Neurology, All India institute of medical sciences (AIIMS), New Delhi, India [d]Department of Biophysics All India institute of medical sciences (AIIMS), New Delhi, India

Background: Several neurological disorders have been linked to the dysregulation of HDAC4, but the mechanisms underlying its role in establishment of distinct epileptogenic networks and specific molecular substrates in TLE remain unknown. The study thus, aimed to examine region-specific differences in HDAC4 expression and its interaction with Serum Response Factor (SRF).
Material and methods: HDAC4 and SRF mRNA and protein levels and their interaction were investigated via qRT-PCR, western blot and co-immunoprecipitation, respectively in MTLE patients versus autopsy control and in lithium pilocarpine model of epilepsy as compared to control. An immunofluorescence assay was used to examine cell-specific HDAC4 expression.
Results: The results revealed a significant increase in the levels of HDAC4 as well as its non-histone substrate-SRF in the hippocampus of lithium pilocarpine model and MTLE patients as compared to control. HDAC4 was found to be elevated in the cytoplasm of epileptic hippocampus as compared to control. Further, the interaction of HDAC4 and SRF was found to be altered in TLE with a significant decrease in the hippocampus.
Discussion and Conclusion: The results for the first time reveal a region-specific alteration in the levels of

HDAC4 in TLE and support the hypothesis that HDAC4 plays an important role in the pathogenesis of epilepsy. The results also highlight a potential dysregulation in HDAC4/SRF axis in TLE. Future studies will be focused on deciphering the contribution of dysregulated HDAC4/SRF axis in TLE and employing inhibitor study.

P124: Comparative evaluation of LXR modulators in STZ induced sAD rat model

Sonam Deshwal, Rajat Sandhir
Department of Biochemistry, Basic Medical Sciences Block-II, Panjab University, Chandigarh 160014, India.

Background: Alzheimer's disease (AD) is the most common cause of dementia. Majority of AD cases are of sporadic AD (sAD). Evidence indicates that progression of AD is linked to aberrant cholesterol metabolism and inflammation and can be modulated by liver X receptors (LXRs). Therefore, present study was designed to evaluate the potential of vitamin D (VD3) and podocarpic acid (PA) as LXR modulators in sAD model.
Material and methods: Male Sprague Dawley rats weighing 300-350g were used. Motor deficits and memory-related behaviour was done using rotarod and MWM test. Body weight, serum insulin and glucose levels were also done. Gene expression of LXRs and its target genes along with amyloid pathway were done using qPCR. Histological analysis was done using H&E and Congo red. IHC was done for inflammation.
Results: Neuro-behavior tests showed significant improvement in memory and cognition following both the treatments. Body weight of STZ-treated animals was significantly($P<0.001$) decreased initially and was recovered more significantly in STZ+VD3group ($P< 0.05$) and ($P<0.01$) as compared to STZ+PA and STZ treated animals respectively. There was no significant difference in peripheral fasting blood glucose levels among all groups. Fasting serum insulin was significantly increased by 3.8-fold (< 0.001) in the STZ treated animals. However, on VD3 and PA treatment in STZ animals, insulin level significantly decreased by 1.5-fold ($P< 0.001$) and 1.1-fold ($P<0.01$) respectively. Gene expression of LXRs and its target genes (ABCA1, ABCG1) and amyloid pathway genes (APP, BACE) were significantly altered in STZ-treated animals and found differentially restored on VD3 and PA treatment. VD3 treatment restored the cell loss and decreased amyloid deposition in the brain regions. Moreover, GFAP immunostaining suggested protective role of both the treatments.
Discussion and Conclusions: VD3 treatment elicited improved memory. VD3 evidenced efficacy in attenuating STZ-induced neuronal damage and decreased amyloid load displaying neurotherapeutic effects. However, PA failed to inhibit amyloid progression and behavioral dysfunctions. Moreover, VD3 and PA attenuated the neuroinflammation observed in STZ-treated animals as assessed by GFAP immunostaining which can be correlated with reversal of neuronal injury. On treatment with VD3 and PA, LXRs transcriptional activation seems to play a role in the above-mentioned beneficial effects. In conclusion, our results revealed thatVD3 and PA treatment attenuated ICV-STZ induced neurobehavioral, biochemical, and histological abnormalities. The neuroprotective effect of these treatments could be attributed to the activation of LXRs in modulating inflammatory brain damage, decreasing memory deficits and amyloid-load. Therefore, strategies like modulating the activity of LXRs in brain of AD individuals might offer prophylactic strategies to combat the disease.
Significance: Natural products have been an excellent and abundant source of therapeutics for many decades. Using VD3 and PA like compounds for sAD seems to be beneficial in terms of their non-toxicity and reproducibility. Natural products have been the single most productive source of leads for the development of drugs.
Acknowledgement: The financial assistance provided by the University Grants Commission (UGC), New Delhi, UGC-Ref. No.:584/ (CSIR-UGC NET DEC. 2018) is acknowledged.

P125: STAT3 is a critical mediator of diabetes-linked exacerbation of neurovascular dysfunction and cognitive impairment in Alzheimer's disease

Soni Tiwari[1,3], Ekta Yadav[1], Shweta Kaushik[1], Zaidan Mohammed[2], Anju Katyal[1], Simantini Ghosh[2], Amla Chopra[3], Itender Singh[1]
[1]Ambedkar Centre for Biomedical Research, Delhi University, Delhi; [2]Department of Psychology, Ashoka University, Rai; [3]Department of Zoology, Dayal Bagh EducationalInstitute, Agra

Background: Type 2 diabetes is known to aggravate neurodegeneration in Alzheimer's disease (AD). We hypothesizedthat Aβ generated in AD and advanced glycation end product (AGE) produced in type 2 diabetes or a dietwith high fat, sugar and salt together amplify STAT3 activation, leading to the exacerbation of AD pathology**.**
Materials and Methods: We conducted studies utilizing postmortem human brains, human brain vascular endothelial cells, pericytes and smooth muscles. To recapitulate human comorbidity condition of AD with diet-induced diabetes, we developed a rat model by injecting amyloid beta into the brain and feeding a diet with highlevels of fat, sugar and salt.
Results: The studies with blood micro vessels isolated from postmortem brains showed the enhanced activationof STAT3 in patients with AD and diabetes comorbidity. The *in vitro* blood-brain barrier studies utilizingthe primary endothelial cells and pericytes showed that the inhibition of STAT3 attenuated the trans-endothelial barrier impairment following exposure to amyloid beta and AGEs. Inhibition of STAT3 in therat model of AD with diabetes ameliorated the neurovascular pathology and improved cognitive function**.**
Discussion and Conclusions: Our *in vitro* and *in vivo* studies provide strong evidence that STAT3 is one of the primary mediators associated with neurovascular and cognitive dysfunction in AD and diabetes comorbidity. High fat-highsugar diet is known to increase AGE, which is one of the inducers of diabetic pathology. Our studies demonstrated that the presence of AGE along with amyloid beta amplify STAT3 activation and other downstream mediators leading to exacerbation of AD pathology.
Acknowledgement: This study was supported by Brain Aneurysm Foundation and Ramalinga swamy Fellowship to I.S., anintramural research grant from Ashoka University to S.G., and a graduate student fellowship from Ashoka University to Z.M.

P126: Effects of Methyl Cinnamate on GMR-Aβ42 *D. melanogaster* larvae

Sonia Joshi, Mayur Gaikwad
Department of Life Sciences, Sophia College (Autonomous), Bhulabhai Desai Road, Mumbai 400026

Background: *GMR-Aβ42 D. melanogaster,* a transgenic line of flies to study Alzheimer's Disease. Methyl Cinnamate having antioxidant properties stands to be a potential therapeutic option. Previouswork in our lab has shown it slightly restores phototactic behavior in adult flies. We show the
effect of Methyl Cinnamate on *Drosophila* larval behavior and levels of oxidative stress in larvalstages.
Materials and methods: Larval phototactic assay: was performed in the dark using third instar larvae on the Petri plate covered with light and dark zones. Each set of larvae (Wild type and *GMR-Aβ42*) were run under a white light bulb. Preference towards dark or light was noted.
Oxidative Stress assay: Lipid peroxidation assay
Results: Wild type (CsBz files) showed an average negative phototactic index, whereas *GMR-Aβ42* fliesshow a relatively positive phototactic index. Results indicated that owing to possibly impaired light avoidance in *GMR-Aβ42* larvae they show positive phototactic behaviour.
Discussion and Conclusion: Therapeutic effects of Methyl Cinnamate would be observed to see if the property of light avoidance is rescued. Other parameters to be considered in this experiment are oxidative stressand cell death in eye-antennal imaginal discs of larvae. Effects of Methyl Cinnamate would bechecked on the same.
Acknowledgement: I extend my gratitude to the Principal, Dr. Anagha Patil Tendulkar and the Head of Departmentof Life Science, Dr. Sree Nair and my supervisor, Mr. Mayur Gaikwad for giving me invaluable guidance, in sights, moral support and the direction to the project. Heartfelt thanks to my faculty of Department of Life Sciences as well as my lab partner Deepanjali Ghadge for unnerving support.

P127: Role of extra-telomeric TRF2 in Neural stemness

Soujanya Vinayagamurthy[1,2], Amit Kumar Bhatt[1], Sulochana Bagri[1,2], Shantanu Chowdhury[1,2,3$]
[1]Integrative and Functional Biology Unit, CSIR Institute of Genomics and Integrative Biology, New Delhi 110025, India; [2]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India. [3]GNR Knowledge Centre for Genome and Informatics, CSIR Institute of Genomics and Integrative Biology, New Delhi 110025, India.

Background: TRF2 is part of shelterin, protecting telomeres. G-quadruplex (G4) structures are common in telomeres and gene promoters. Bioinformatic analysis showed high G4 motifs in neuronal gene promoters. TRF2 binds to non-telomeric promoter G4s, and regulates transcription. It interacts with REST/NRSF for repression. Together hypothesizing, "TRF2 facilitates the repression of neuronal differentiation genes via REST recruitment".
Materials and methods: Model system: SH-SY5Y neuroblastoma cells and mNSCs from *Terf2*$^{F/F}$/*Nes:Cre* mice. TRF2 loss of function via silencing, and overexpressing dominant negative TRF2. Tamoxifen treated mNSCs to deplete TRF2. Amino acid mutants to investigate the function of post-translational modification.
Assays: Chromatin Immunoprecipitation (ChIP), Immunoprecipitation, Gene expression by RT-PCR, Immunofluorescence, and Flow cytometry.
Results: TRF2 loss and acetylation mutant K176R overexpression activated differentiation genes and exhibited differentiation phenotype. In mNSCs, neurosphere formation was compromised. RNA Pol II (Ser 5- transcription initiation) binding to differentiation genes promoters increased upon loss of TRF2. REST interaction with TRF2 was confirmed with IP. REST, H3K27me3, and EZH2 (the catalytically active component of PRC2) lost binding at the promoters upon TRF2 loss and K176R overexpression. ChIP indicated that the K176R mutant binds to promoters. Immunoprecipitation revealed lost REST interaction.
Discussion and conclusions: Results indicate that TRF2 binds to the promoters of neuronal differentiation genes, and recruits REST and PRC2 complex. This leads to the deposition of H3K27me3 for gene repression. Loss of TRF2 removes the repressor and increases RNA Pol ll on the promoter for transcription initiation and gene activation. Also, acetylation of TRF2 at K176 is crucial for its interaction with REST. Thus, TRF2 maintains neural stemness by repressing the different genes.

P128: Neurodevelopmental defects in the hippocampus caused by prenatal exposure to valproic acid

Sreyashi Chandra[1,2], Dr Prem Tripathi[1,2]
[1]Cell Biology and Physiology, CSIR- Indian Institute of Chemical Biology (IICB), Kolkata-700032, India; [2]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad- 201002, India

Valproic acid (VPA) is an antiepileptic drug whose prenatal exposure is linked with a high risk of neurodevelopmental defects including autism spectrum disorder (ASD). Here we investigated the effect of prenatal VPA on hippocampal neurogenesis, NSC proliferation, neuroblast migration, neuronal differentiation and the possible alterations in specific neuronal circuits. Pregnant FVB/N mice were gavaged with VPA once daily from E12.5 to E14.5. BrdU birthdating and immunofluorescence were used to pinpoint changes in the specific neuronal populations at various time points during development. A series of behavioural tests were performed in adolescence and adulthood to assess developmental and social deficits. We found the proliferative populations in hippocampal neuroepithelium (HNe) unaltered while their distribution was diminished at E14.5. At E16.5, these populations and the NSCs were increased in HNe, contrasted by their decrease in the dentate migratory stream (DMS). At P0, we observed reduced NSC and proliferative populations at DG. Behavioural data indicated delayed weight gain, delayed eye opening, and reduced swimming performance in neonatal mice, along with lower sociability and higher repetitive behaviours in adults. At the embryonic stages, the transient decrease in proliferative zones of the HNe, followed by the increase in proliferative zones and a diminished DMS during the tertiary dentate proliferative matrix formation window is explanatory towards the lower presence of proliferative population at the postnatal DG. The anomalies in hippocampal neurogenesis correlated with the behavioural changes might eventually help us understand the key basis of certain symptoms associated with ASD. We are thankful to Council of Scientific and Industrial Research and CSIR-Indian Institute of Chemical Biology for funding our project.

P129: Effect of 12 weeks of combined approach on frequency domain parameters of heart rate variability among major depressive disorder population (age 20-40 years)

Sharma S[1], Kacker S[2], Saboo[3]
[1]Department of Physiology, RUHS College of medical Sciences, Jaipur; [2]Department of Physiology, RUHS College of medical Sciences, Jaipur; [3]Department of Physiology, RUHS College of medical Sciences, Jaipur.

Background: Depression has frequently been linked to ANS-mediated heart rate control, as measured by heart rate variability (HRV). This aim of this study was to observe the effect of 12 weeks of yoga and diet intervention on frequency parameters of HRV in major depressive disorder population.
Materials & method: Study conducted on 40 subjects having major depressive disorder. Study group participants were given the combined approach which includes intervention of yoga and diet for 12 weeks. Frequency domain Parameters of HRV were recorded at baseline and after 12 weeks for both groups. Data was analysed and $p<0.05$ considered as significant.
Results: Yoga and diet group had significant increase in mean HF (48.2±10.55 to 60.92±15.99) and LF (45.39±10.80 to 68.08±3.44) and LF/HF ratio after 12 weeks of intervention whereas no changes was found in control group.
Discussion & conclusion: Analyses revealed HRV parameter differences between study and control group at baseline and after 12 weeks intervention may stimulate pressure receptors that lead to increased parasympathetic activity which is similar to the study conducted by K Gulati (2021). Change in HRV parameter values correlated with changes in symptom severity of depression. Combined approach towards healthy lifestyle was effective in increasing parasympathetic tone and reducing the depressive symptoms in population suffering from major depressive disorder.
Acknowledgments: we would like to thank all the participants who have given consent to participate in this study. We also want to acknowledge the faculty of department of physiology, all hospital staff. There was no source of funding.

P130: Does Presenilin 1 have a role in neural Stem cell quiescence?

Surya Suresh[1,2], Vankudoth Swathy[1], Jyothi P Nair[1,2], Meera V[1,2], Riya Ann Paul[1,2], Parvathy Surendran[1,2], Budhaditya Basu[1,3] and Jackson James[1]
[1]Neuro Stem Cell Biology Laboratory, Regenerative Biology Division, Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram, Kerala-695014, India; [2]University of Kerala, Thiruvanathapuram, Kerala-695014, India; [3]Regional Centre for Biotechnology, (DBT-RCB), Faridabad, Haryana - 121001, India

Background: During developmental neurogenesis, some of the proliferating neural stem cells (NSC) transit to a quiescent state and is retained till adulthood, a process involving molecules like VCAM1 which in turn is downregulated in Presenilin 1 (PS1) Knockout embryos. Hence, we hypothesize that Presenilin 1 has a role in NSC quiescence.
Materials and methods: Primary neural stem cells were derived from embryonic mouse brain. Quiescence was induced in vitro by addition of BMP4 and it was validated. Gene expression analysis as well as protein expression analysis were done on BMP4 treated quiescent neural stem cells and respective controls.
Results: We found that Presenilin 1 (Psen 1) is upregulated in quiescent NSCs, unlike other γ- secretase components. Also, γ-secretase activity (Cleaved Notch1 expression) is found to be absent in quiescent NSCs. However, PS1 is found to be more stable and localized to nucleus in quiescent NSCs. A significantly high proportion of phosphorylated PS1 is found in active NSCs compared to quiescent NSCs and in both cellular states, phsopho PS1 is localized to the nucleus.
Discussion and conclusion: When active neural stem cells transit to quiescent state, several attributes of Presenilin 1 seems to change, from expression level to stability. PS1 overexpression is reported to induce cell cycle arrest in glioblastoma. From our observations, we could arrive at the conclusion that Presenilin 1 might be executing its function in quiescence, independent of its γ-secretase activity. Identifying the interaction partners of PS1 in quiescence will unravel the mechanisms involved.
Acknowledgement: Supported by DST SERB (CRS/2021/005847) and Intramural grant from RGCB. Fellowship to SS (Reg No. 316695) and JPN (Reg No.366288) from UGC.

P131: Investigations on the functional status of regulated exocytosis in obesity-associated metabolic stress

Sushma Dagar, Souren Sadhukhan, Shivam Malviya, Krittika Biswas, Nikhitha Nair, Chandramouli Mukherjee, Bhavani Shankar Sahu
National Brain Research Centre, Manesar, Gurgaon, India.

Metabolic homeostasis regulates many biological functions, and its deregulation is responsible for severe pathophysiological conditions such as obesity and diabetes. Regulated exocytosis is an important cell physiological process during which dense-core vesicles (DCV) release cargo in response to an external stimulus. However, the effect of obesity-induced metabolic stress on regulated secretion isstill being determined. We modelled obesity-associated metabolic stress by feeding the mice with a high-fat diet and glucose tolerance test (GTT) was used to validate the obesity model.
We then used Neuropeptide-Y (NPY)-pHluorin imaging in primary chromaffin cells to discover impaired stimulus-coupled regulated secretion in obese animals. To further study which modes of exocytosis are affected by metabolic stress, we used Tetramethylrhodamine (TMR)-dextran staining and interestingly, we found a significant reduction in 40kDa dextran (full fusion) staining in obese chromaffin cells. We next used electron microscopy (EM) and found a significant increase in the dense core diameter of DCVs in obese chromaffin cells compared to control cells indicating a possible maturation defect caused by metabolic stress. Similar findings were documented in primary pancreatic islets. To understand the molecular determinants, we have conducted the transcriptomic analysis in chromaffin and pancreatic islets to discover specific pathways and genes associated with trafficking getting differentially expressed. We are in the process of validating some of those candidates using our cell culture systems.
In summary, we show that HFD-induced metabolic stress leads to a defect in DCVs maturation and an impediment in stimulus-coupled regulated exocytosis in chromaffin cells and primary islets.

P132: Molecular docking and simulation studies for identifying binding affinity of flavonoids for α7nAChR for the treatment of Alzheimer's disease

Sushma Singh[a, b], Ahsas Goyal[b] and Neetu Agrawa[b]
[a]Pharmacy college, Azamgarh-276128, UP, India; [b]Institute of Pharmaceutical Research, GLA University, Mathura-281406, UP, India

Background: Alpha-7-nicotinic acetylcholine receptor (α7nAChR) is one of the ligand-gated ion channels and one of the essential parts of the cholinergic pathway in the brain and thus it plays important role in Alzheimer's disease (AD). It has been reported that α7nAChR regulation by the phytoconstituent plays vital role in the treatment of AD.
Method: Fifty flavonoids were evaluated for the binding efficacy for human α7nAChR by using molecular docking. On the basis of their binding efficacy best two flavonoids were selected from docking results then after molecular dynamic simulations for 100 ns for binding stability analysis with the α7nAChRwere done of two selected flavonoids. Then after *in silico* ADMET studies were performed to check the drug ability of the selected flavonoids.
Result: Amentoflavone (–9.1 kcal/mol) and gallocatechin (–8.8 kcal/mol) were the two selected flavonoids which has best binding efficacy with the α7nAChR. The molecular dynamics simulation studies showed that both amentoflavone and gallocatechin were at stable state during duration of simulation period, root mean square deviation (RMSD) and root mean square fluctuation (RMSF), and protein flavonoids complex were stable until 100 ns.
Conclusion: Amentoflavone and gallocatechin are potential lead molecules that could be used as effective agonists of α7nAChR to treat Alzheimer's disease. Thus, to confirm their effectiveness in future invitro and in-vivo analysis can be done.

P133: NLRP3 and NLRP12 play distinct cell-specific roles in innate immune Cross-talk in Glioblastoma Pathophysiology

Sushmita Rajkhowa, Durgesh Meena, and Sushmita Jha
Department of Bioscience and Bioengineering, Indian Institute of Technology Jodhpur, Jodhpur, Rajasthan-342037.

Background: Glioblastoma (GBM), are malignant gliomas with poor survival. Nucleotide-binding domain LRR-containing receptor (NLR) family proteins NLRP3 and NLRP12 regulate inflammation and immunity and are known to play reciprocal roles with cell-specific tumour-promoting or anti-tumor functions. We aim to understand NLRP3 and NLRP12 differential expression and function in GBM pathophysiology.

Methods: RNA and Protein isolation from cell lines, and primary cells from patient-derived glioma tissue samples followed by endpoint and real-time PCR, Western blotting, and Immunocytochemistry. si-knockdown of *nlrp3* and *nlrp12* in cell lines and studying their effect on cell proliferation through colony formation assay and growth of 3D organoids.
Results: Differential expression of NLRP3 and NLRP12 in patient-derived cells as compared to GBM, astrocyte, and microglia cell lines.
Conclusion: Increased expression of NLRP12 correlates with poor survival of patients. Differential expression of NLRP3 and NLRP12 is linked to patient tumor heterogeneity and molecular pathophysiology. Hence, correlating the molecular and cellular cross-talk of the cells in the tumor microenvironment will improve our understanding of disease pathophysiology and aid possible future therapeutic strategies.
Acknowledgment: We are thankful to IIT Jodhpur and the Ministry of Electronics and Information Technology (MeitY), for infrastructure, administrative and financial support for this research (No.4(16)/2019-ITEA). Sushmita Rajkhowa is supported by MoE fellowship from IIT Jodhpur.

P134: Regulation of Drug resistance and epithelial-mesenchymal transition: Role of Extracellular Vesicles and implications for glioblastoma tumour progression

Swagatama Mukherjee, Prakash Pillai
Division of Neurobiology, Department of Zoology, The M. S. University of Baroda, Vadodara

Extracellular Vesicles (EV) play a crucial role in normophysiology as conduits of intercellular communication. Recently, EVs are being viewed as a cellular Cryptex unlocking new understandings of existing pathologies. Our study aims to elucidate the role of EVs and their specific cargo in mediating Temozolomide (TMZ) induced chemoresistance and epithelial- mesenchymal transition (EMT) via *in vitro* and *in silico* approaches. We also aim to identify the axis of operation of EV enriched lncRNA HOTAIR, a documented molecular scaffold and gene regulatory element, in epigenetically modifying the pathways of Chemoresistance and EMT. In regards to TMZ-induced resistance and involvement of EVs, U87 MG cells were treated with a TMZpulse (200µM for 7 days continuous) in the presence and absence of EV inhibitor GW4869 (10µM). We found a decrease (30% decrease compared to control) in percent survival in the group treated with TMZ only, however, U87 cells undergoing continuous TMZ pulse and GW4869 treatment have a significantly lower percent survival (80% decrease compared to control) whichinfers that the absence of EV release by the cells prevents TMZ from either being effluxed out or the absence of resistant cell-derived EVs prevents the sensitive cells from gaining the resistant phenotype. Additionally, with the help of TCGA database (with a cohort size of 595 GBM patients)and ExoCarta, we studied the correlation and enrichment analysis of lncRNA HOTAIR with various DNMTs and EMT regulatory elements ZEB isoforms (differentiation and subtype specifiers), SLUG and SNAIL (transcriptional repressors) TWIST (transcriptional activators), E-cadherin and N- cadherin (cell polarity mediators) suggesting its role as a master regulator of pathways affectingboth EMT and chemoresistance. The correlation of enrichment of specific EV cargo, lncRNA HOTAIR further indicates that EVs are vital carriers of various epigenetic modifiers that may contribute to the GBM aggressiveness and progression.
Acknowledgements: The authors are thankful to UGC Savitribai Jyotirao Phule Single Girl Child Fellowship (202223- UGCES-22-GE-GUJ-F-SJSGC-3102) and Junior Research Fellowship, DBT Builder CAT-III awardedto Ms. Swagatama Mukherjee. The authors also acknowledge the financial assistance received from various funding sources (ICMR, New Delhi and GSBTM, Gandhinagar) awarded to PP at Division of Neurobiology, Dept. of Zoology, The M.S. University of Baroda, in partially supporting the current research work**.**

P135: Role of Dopaminergic neurotransmission in the expression of key foraging regulatory molecules and structural plasticity in *Apis mellifera*

Swasti Sukanya[1], Adarsh Kumar[1], Mohammed S. Mustak[2] and Prakash P. Pillai[1]
[1]Division of Neurobiology, Department of Zoology, Faculty of Science, The M. S. University of Baroda, Vadodara, Gujarat 390002, India; [2]Department of Applied Zoology, Mangalore University, Karnataka, India

Dopamine is crucial during foraging behavior in honeybees. Understanding the dopamine mediated regulatory mechanisms in honey bee foraging at both cellular and molecular level are essential. Involvement of Immediate early genes and its related downstream genes in learning and memory pathways are highly expressed during foraging. Bees were collected at specified time point for pre, during- and post-foraging; and we employed pharmacological inhibitor (α-mT) in the study. Behavioral test was performed inside an enclosure. Dopamine levels in all experimental groups and expression levels of key genes were analysed through bionalyzer, LC-MS and qPCR respectively. Confocal imaging of honeybee brain sections performed for tracing dopaminergic neurons using α-TH antibody. Expression of target genes (CREB, EGR1, CaMKII, Ddc, Dopamine receptors, Kakusei) were found to be upregulated in in the foraging Group. Pharmacological manipulation of dopaminergic neurons led to significant down regulation of IEGs, and other downstream genes involved in learning and memory pathways during foraging activity. Tyrosine Hydroxylase immunostaining indicated dopaminergic neurons features that may be involved in structural plasticity. Dopamine levels were found to be significantly high in foraging group suggesting it's spatio-temporal expression pattern. Moreover, expression profile of various regulatory molecules during pre- and post-foraging were significantly lower compared to foraging group. Pharmacological manipulation of dopamine synthesis significantly altered the immediate early and target genes, suggesting expression of foraging genes depends on the neuromodulatory effects of dopamine in foraging activity. *Overall, the study confirms the necessity of involvement of aminergic control of modulation of regulatory molecules during foraging activity in Apis mellifera.*

Acknowledgements: The authors acknowledge DBT Junior Research Fellowship programme, Regional Centre for Biotechnology (RCB), Faridabad, awarded to Ms. Swasti Sukanya (Ref No: DBTHRDPMU/JRF/BET-20/I/2020/AL/391). The financial assistance in the form of Minor grant awarded by Research and Consultancy Cell, MSU Baroda to Dr. Pillai is highly acknowledged. The authors also are highly thankful for partial financial assistance received from Animal house facility, Dept. of Zoology, Faculty of Science, MSU Baroda. The authors would also like to thank all the assistance received from the Team of Botanical Garden, Faculty of Science, MSU Baroda.

P136: Investigating the impact of *Medhya Rasayana* on modifying behavioral and metabolomic alterations in mouse model

Swathi Maruthiyodan[1], Gagan M[1], Manjunath B. Joshi[1], Kamalesh D. Mumbrekar[2], Guruprasad K. P.[1]
[1]Department of Ageing Research, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal, 576104, India; [2]Department of Radiation Biology and Toxicology, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal, 576104, India

Background: Human memory involves retaining and recalling information from experiences and learning. Cognitive deficits may arise from ageing, neuropsychiatric conditions, or developmental issues, prompting interest in nootropics to improve cognitive abilities. Ayurveda focuses on healthy aging and *Medhya rasayana*, a class of Ayurvedic remedies, aims to enhance brain functions like memory, cognitive healing, and mental function. Hence, in this study, we aimed to explore the functional and mechanistic role of the *Medhya rasayana* plant *Bacopa monnieri* (Brahmi) in addressing cognitive impairment and metabolic disruptions in the cognition deficit mice.

Methodology: In the present investigation, we have developed and validated a mouse model with cognitive deficits. The efficacy of *Brahmi rasayana* on cognitive improvement was assessed by a battery of behavioral experiments on *rasayana* pretreated mice. In addition, the effects of *rasayana* pre-treatment on metabolome profile was evaluated by LC/MS analysis.

Results: Analysis of behavioral data revealed that *rasayana* pre-treatment improved cognitive ability. In addition, the effects of *rasayana* pre-treatment elicited metabolomic modulation in the mice serum. There was significant alteration in the carbohydrate, lipid, and amino acid metabolism. Further, analysis reveals the upregulation of metabolites that have neuronal functions.

Discussion and Conclusion: To summarise, our data suggest that Brahmi *rasayana* can reduce the risk of memory deficits may be by altering the metabolites related to neuronal health. As *rasayana*s are known as brain tonic and help in neuronal regeneration, early consumption of *Medhya rasayana* may improve brain health. The findings of the research could lead to the development of new principles based on the notion of Ayurvedic medicine for the translation of these medicines to enhance cognition.

Acknowledgment: The authors thank TIFAC-CORE, Government of India, BUILDER DBT and Manipal School of Life Sciences, Manipal Academy of Higher Education (MAHE), Manipal, India for the

infrastructure support and Centre for Ayurvedic Biology for valuable inputs. The authors are thankful to Dr. M S Valiathan, National Research Professor for the mentorship and also to Prathiksha Trust, Bengaluru for the financial support.

P137: Glutamatergic neuronal innervation from superior colliculus to hippocampal area regulates reward related memory in rats

Vaibhav A. Sabale[1], Akash M. Waghade[1], Sanjay N. Awathale[1], Nishikant K. Subhedar[2], Dadasaheb M. Kokare[1]
[1]Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur-440033, Maharashtra, India; [2]Indian Institute of Science Education and Research, Dr Homi Bhabha Road, Pune- 411 008, Maharashtra, India

Background: Glutamatergic neurons of superior colliculus (SC) receive visual inputs from external environment and terminate in hippocampal area via cingulate cortex. However, the activation of glutamatergic neurons of SC to hippocampal area for reward related memory has not been documented yet. Therefore, we test the hypothesis that the formation of reward related memory may be dependent on activation of glutamate system of the SC to hippocampus.
Materials and Methods: Adult male Wistar rats were trained with and without light cue conditioning in the operant chamber for food self-administration, and the number of lever pressings were counted. The MK-801 treatment (2 μg/rat; intra-DG) was given in rats. The cFOS immunohistochemistry and neurogenesis study was performed. Microdialysis and HPLC-ECD system was used for the estimation of dopamine (DA) and 3,4 dihydroxyphenyl acetic acid (DOPAC) samples collected from nucleus accumbens (NAc) of rats.
Results: The rats presented with light cue showed significant increased lever pressings as compared to without light cue and control rats. The cFOS immunoreactivity in SC was augmented in light cue conditioned group. The BrdU and NeuN immunoreactivity was elevated in light cue conditioned group as compared to without light cue and control. In MK- 801 treated rats, there was reduced lever press activity and DA and DOPAC level in NAc. The overall results suggest that the light cue helps to activate SC neurons to assist animals to form reward related memory in the hippocampus.
Discussion and conclusion: The visual light cue has improved rewarding behaviour in rats. The animal conditioned with light cue has activated more cFOS cells in SC region, it suggests that light cue assist to select and obtain food reward. The BrdU and NeuN immunoreactivity has revealed neurogenesis in the hippocampus, which shows the formation of reward memory in rats. We observed that the MK-801 treated rats reduced lever pressing, and DA and DOPAC level in the NAc, and reward memory. The present study reveals that the glutamatergic system of SC communicates with hippocampal area to regulate reward related memory in rats.
Acknowledgement: This work was supported by the grants from (DST-SERB) (CRG/2020/004971), Govt. of India, New Delhi, India.

P138: Effect of colored lights on performance in digit span tasks in healthy individuals

Vakode Vani, Pooja Ojha, Mahesh Arjundan Gadhvi, Abhinav Dixit
Department of Physiology, All India Institute of Medical Sciences Jodhpur-342005 Rajasthan

Background: Colored lights have been found to affect human physiology and cognition. Working Memory is a crucial component of human cognitive processes and plays a role in daily activities. The effects of different colored lights on performance in Forward and Backward Digit Span tasks (DST) have been assessed in this study.
Materials and Methods: Thirty-five males, with an age mean of 29.31 years, performed Forward and Backward DST under red, green, blue, and white lighting conditions. The order of four lights was randomized. The illumination was adjusted for all the lights using a lux meter and was maintained constant for all of the lights. Percent (%) accuracy was assessed for both tasks in all four lights.
Results: A statistically significant difference in % accuracy was found with repeated measures ANOVA during red light exposure in Forward DST as compared to white ($p=0.005$), green ($p<0.001$), and blue ($p=0.029$) lights. In addition, a statistically significant difference was found in Backward DST during red light exposure as compared to white ($p=0.009$), green ($p<0.001$), and blue ($p<0.001$) lights.

Conclusion: Exposure to colored lights affects performance in working memory tasks. Among the above four lighting conditions, the performance in forward and backward DST decreases, in that order, with red, white, blue, and green lights. Lighting color should be considered while assessing performance in working memory tasks and use of red light may be encouraged.
Acknowledgments:
No funding was received for this work. We are thankful to all the participants who took part in the study.

P139: Pelvic irradiation-induced brain damage through gut dysbiosis in a rat model

Babu Santhi Venkidesh[1], Rekha K Narasimhamurthy[1], Krishna Sharan[2], Thokur S Murali[3], Kamalesh Dattaram Mumbrekar[1]

[1]Department of Radiation Biology and Toxicology, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal 576104, India; [2]Department of Radiotherapy and Oncology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal 576104, India; [3]Department of Public Health Genomics, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal 576104, India

Background: Pelvic radiotherapy is the primary choice for treating pelvic cancers. Recent studies indicate a link between gut microbes and brain function through the gut-brain axis. However, the consequences of pelvic radiotherapy on the gut-brain axis and its neurological outcomes remain unclear. Hence, this study aims to explore how pelvic irradiation affects the brain through gut dysbiosis.
Materials and Methods: A single dose of 6 Gy of pelvic radiation was given to 3–4-month-old Sprague Dawley rats. After treatment, faecal samples were collected at different time points (0, 7, 12 days), to determine the microbial diversity, using 16S rRNA sequencing. Further, behavioral, histological, and hippocampal gene expression analyses were performed to determine pelvic irradiation-induced changes in the brain.
Results: Distinct alterations in gut microbiota assemblages were noted at various time intervals following radiation exposure to the pelvic region. These changes were accompanied by changes in the structure and integrity of the intestine. Furthermore, a notable decline was seen in the number of viable and developing neurons, while there was an increase in reactive astrocytes. This shift led to a clear decrease in exploratory behaviour among the irradiated group. Additionally, the gene expression study indicated reduced neuronal plasticity.
Discussion and Conclusion: This study highlights the effects of pelvic irradiation on the gut microbiota and its impact on brain damage. Altered intestinal integrity points to negative gastrointestinal effects. Further, reduction in surviving neurons and increase in reactive astrocytes in the irradiated group associated with less exploratory behaviour, suggested pelvic irradiation-induced neural damage. Reduced expression of *Nmda2,* plasticity-related gene suggested that the brain's adaptive responses were hindered. These results highlight the need to understand and design formulated bacterial supplementation to mitigate pelvic irradiation-induced brain damage.
Acknowledgment: This study was supported by an MAHE intramural grant (2019). VBS would like to thank MAHE for the Dr. TMA Pai Ph.D. Fellowship.

P140: Loss of *NF1* results in cortical malformations, hydrocephalus, and motor deficits in mouse model

Vishal RL, Achira Roy
Neuroscience Unit, Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), India

Background: Neurofibromin 1 (NF1) is a critical regulator of RAS-ERK-MAPK pathway, which is instrumental for brain development. Patients with *NF1* mutations often exhibit cortical malformations, hydrocephalus, and epilepsy, intractable to current medication. Hence, understanding the origins and underlying mechanisms behind these disorders is important for developing better therapeutic strategies.
Materials and methods: We approached this question by generating a clinically relevant brain-specific deletion of *NF1* in mouse using cre-lox system. We used *GFAP-cre* to conditionally delete *NF1* in the mouse

brain. Subsequently, morphological, molecular, and behavioural alterations were examined at different developmental time points to elucidate the underlying mechanism.
Results: To understand the brain malformations due to *NF1* mutations, we performed *GFAP-cre* mediated deletion of *NF1* in subset of neural progenitors in mice. Biallelic loss of *NF1* caused an increase in brain size. Histological findings further revealed that *NF1* mutants have thicker corpus callosum, and a proportion of them developed severe hydrocephalus. Interestingly, these mutants also show smaller cerebellum and exhibit severe motor defects. These results suggest the importance of *NF1* in normal brain development.
Discussion: NF1 is a critical regulator of RAS-ERK-MAPK and its loss results in cortical malformation, hydrocephalus, and epilepsy in a proportion of patients. To understand the underlying mechanism, we performed clinically relevant deletion of *NF1* in mouse brains. Phenotypes resulted post *NF1* loss include thicker corpus callosum, motor deficits, and hydrocephalus which recapitulate all the key human pathological features. Our finding suggests a critical role of *NF1* in the normal brain development.
Acknowledgements: We thank Kathleen J Millen, Jackson Laboratories, USA and BLiSC Animal Care and Resource Center (ACRC), India, for gifting the mouse lines used in this project. We thank the animal facility of JNCASR for the maintenance of mouse lines. This work was funded by the Ramalingaswami Re-entry Fellowship from the Department of Biotechnology (DBT), India (AR), a research donation from M-CM Foundation, USA (AR), and the intramural funding from the Jawaharlal Nehru Centre for Advanced Scientific Research, India.

P141: LC-MS/MS based approach to study the altered brain proteome in aging rat due to Minimal Hepatic Encephalopathy

Vishal Vikram Singh[1], Shambhu Kumar Prasad[1], Arup Acharjee[2], Papia Acharjee[1]
[1]Department of Zoology, Banaras Hindu University, Varanasi; [2]Department of Zoology, Allahabad University.

Introduction: The work represents the impact of Minimal Hepatic Encephalopathy (MHE) on cognitive impairment in aging rat population by analysing hippocampal proteome dynamics. Mass spectrometry based proteomic analyses was used to unravel common and specific features in the neural systems associated with them and leveraging deep learning techniques to identify critical proteins that may be targeted for therapeutic intervention in aging population with MHE.
Material and method: Old male rats were divided into two groups: Old control (saline) and old MHE rats (Thioacetamide,50 mg/kg B.W, i.p for 14 days). The hippocampus was dissected out followed by sample preparation for LC-MS/MS. Statistical analysis and pathway enrichment analysis were performed using MetaboAnalyst and Metascape respectively. Validation of certain proteins using qPCR, Western blot, and Immunofluorescence was conducted.
Result: 1535 proteins were obtained and after filtering and 50% missing value imputation, a total of 1082 proteins were proceeded for further analysis. Statistical analysis of the protein sets identified a total of 40 dysregulated proteins among which 17 were upregulated proteins and 23 were downregulated proteins. We validated some upregulated protein namely p23, Interesectin 1 and fetuin-A.
Discussion and conclusion: Our findings highlight critical proteins as essential players impacting the age-associated hippocampal proteome dynamics due to MHE. Through network analysis tools, upregulated proteins are involved in the generation of precursor metabolites and energy, neurotransmitter release cycle, positive regulation of dendritic spine development, chaperone-mediated protein folding and protein stabilization. The validated protein p23 is upregulated in the presence of proinflammatory stimuli, fetuin-A is protective against lethal systemic inflammation and Intersectin 1 is a multidomain scaffolding and adaptor protein as a central regulator of synaptic vesicle cycling.
Acknowledgement: 1: UGC-JRF for financial assistance to Vishal Singh, DST-SERB project, IOE BHU grant to PA lab. Facilities: Prof SK Trigun Lab (Department of Zoology, BHU), ISLS BHU, CDC BHU and IIT Bombay MASSFIITB Facility.

P142: Transcriptional control of mammalian axon regeneration - Role of nuclear receptors (NR) family of transcription factors

Yogesh Sahu, Manojkumar Kumaran, Anisha Menon, Sneha Manjunath, Meghana Madhu, Arupam Biswas and Ishwariya Venkatesh
CSIR-Centre for Cellular and Molecular Biology, Hyderabad

Background: Neurons in the nervous system are connected through axons, cylindrical projections enclosed within the spinal cord that facilitate critical signal communication between the brain and other body parts. When injured, embryonic neurons exhibit a robust regenerative response, activating transcriptional networks that enable complete recovery. Yet, this regenerative potential faces an abrupt decline a week post-birth.
Material and methods: We employ CRISPR-based knockdown strategies to neutralize the anti-growth activity of repressors, coupled with *in vivo* overexpression of activators, to assess their impact on CNS axon regeneration. We employ combinatorial approaches like *in vitro* growth assays, *in vivo* mouse spinal injuries, and single-cell gene expression assays and chromatin accessibility.
Results: Our prior investigations highlight the synergistic action of Klf6, with Nr5a2 and Rarb, which can salvage a portion of the lost regenerative ability in adult neurons post-injury. Although regeneration is observed, it didn't translate into functional recovery, highlighting the knowledge gap. Recently we found a group of factors called Nuclear Receptor Transcription Factors (NRTFs) that modulate neuronal development but their role in regeneration is still vastly unknown.
Discussion and conclusion: Remarkably, around 18 out of 40 NRTFs display heightened expression within the mammalian cortex, exclusive to phases of axon growth across diverse cell types. Expression and binding analyses indicate that NRTFs have a dual role in regulating axon growth- as both activators and repressors depending on the developmental stage. Ultimately, the outcome of our research holds promising implications for identifying innovative therapeutic targets, potentially enhancing regenerative outcomes post-neural injuries.
Funding Acknowledgement: Council for Industry and Scientific research (CSIR)

P143: GluN2B NMDA subtype impairs long-term depression in an in vitro epilepsy model

Zubin Singh Rana and Pradeep Punnakkal
Department of Biophysics, Postgraduate Institute of Medical Education and Research Chandigarh, India

Background: Temporal lobe epilepsy (TLE) is one of the most common types of epilepsy in humans. It is commonly observed that patients with epilepsy suffer from memory-related problems. Long term potentiation (LTP) and long-term depression (LTD) are the two well characterized cellular models of memory. Here, we studied the effect of epileptiform activity on LTD. We induced LTD in rat hippocampal slices and studied how epileptiform activity affects LTD.
Material and Methods: Hippocampal slices were made from Wistar rat brain (p14-p28). Epileptiform activity was induced in the slices by perfusing HK-ACSF (high potassium- artificial cerebrospinal fluid). LTD was induced in CA1 region by stimulating the Schaffer collateral pathway and the application of low frequency protocol (1Hz, 900 pulses).
Results: Stable epileptiform activity was induced in the slices after perfusion of HK-ACSF. Low frequency protocol induced 20% LTD in control hippocampal slices. But in epileptiform induced slices 20% LTP was observed instead of LTD. Next, we studied the role of NMDA receptors in LTD and found that GluN2B subtype of NMDA receptor was responsible for the sign change of LTD to LTP.
Discussion: The epileptiform induced metaplasticity impaired LTD in hippocampal CA1 synapses. Moreover, this impairment was due to GluN2B subtype. Impairment in synaptic plasticity has been observed in various neurological disorder, the same was true in the present study. This provides new insight into the molecular mechanism of memory formation during epilepsy. This study identified GluN2B as a new target for memory impairment in epilepsy. Present investigation will trigger more studies in the direction of metaplasticity to understand the mechanism behind the memory impairment in patients with epilepsy.
Acknowledgement: The author ZSR was supported by CSIR (Fellowship No. (09/0141(12456)/2021-EMR-I), New Delhi, India.

P144: Neurocandidasis: Possible role of brain macrophages in eliminating *Candida albicans* infections

Siddhi S. Bangale, Gunderao H. Kathwate
[1]Department of Biotechnology, Savitribai Phule Pune University, Pune, Maharashtra, India

Background
Candida species are the major cause of fungal infections in humans. Systemic candidiasis may also result in conditions like neurocandidasis, where the pathogen enters the CNS. This pathogen is responsible to invade the entire neurons in the brain and lead the intracerebral haemorrhagic condition and stroke. Therefore, it is important to investigate the role of brain macrophages in the alleviation of neurological diseases.
Materials and methods
SC5314 strain of *Candida albicans* and *THP1* monocytes were used for the study. RNA extraction and imaging were done for co-culture of *Candida albicans* and *THP1* for 2 and 6 hrs for qPCR and microscopy respectively.
Results
Microscopy done to monitor phagocytosis at 2 and 6 hrs showed morphogenetic changes, when the monocyte gets activated and transforms into a macrophage, start occurring by two hours. Live cell imaging showed that these activated monocytes try to engulf the pathogen, and how the pathogen escapes. Both, the *THP1* and *C. albicans* cells were alive at this point and by 6 hrs most cells lost their viability.
Discussion
There is an interplay between host and pathogen cells, which decides their fate. *Candida* species are capable of inducing apoptosis or pyroptosis in macrophages, whereas macrophages are phagocytic cells. With the study undertaken, it was observed that phagocytosis by *THP1* cells starts occurring by 2 hr time point. By the end of 6 hrs, most of the cells lost their viability, they died either by phagocytosis or by apoptosis induced by *Candida*.
Acknowledgements
I would like to thank DBT, Government of India and Savitribai Phule Pune University, Prof. Smita Zinjarde, the Head of Department of the Department of Biotechnology, my guide and mentor Dr. GH Kathwate for providing me with guidance, insights and extending their valuable support to undertake this study.

P145: A high-throughput assay to study social interactions in *Drosophila*

Faizah Ansari, Navinchandra Venkatarama Puppala, Monalisa Ghosh, Paulami Dey, Rachagolla Sai Prathap Yadav, Pavan Agrawal
Centre for Molecular Neurosciences, Kasturba Medical College, Manipal Academy of Higher Education, Udupi-576104, Karnataka, India.

Background: Prior social experience or the lack of it can affect the interactions among social animals. *Drosophila melanogaster* is a social insect that communicates with conspecifics using complex social behaviors in a group setting. Stressors and drugs can disrupt these social behaviors making it an attractive model to identify underlying mechanisms.
Material and Methods: Here we devised a simple assay to identify changes by studying 79 behavioral parameters when flies interact in a group. We used high-resolution machine vision cameras to record group dynamics in flies which were group or single housed before introducing in the social arena. Using our high-throughput machine vision and machine learning pipeline, it is possible to analyze the effects of social isolation on group dynamics.
Results: The analysis of these recorded behaviors shows that prior experience in the form of stress caused by isolation affects the group dynamics and social parameters like walk, stop, chase, touch, body turns, etc. We also show effects of neurogenetic manipulation on group behaviors using this assay.
Discussion and Conclusion: Our recording and analysis setup can be implemented to study effects of stressors such as social isolation on group dynamics. It can also be extended to study effects of various drugs and identify mechanisms underlying complex social interactions.
Acknowledgement: DBT, extra mural research grant (PI- Pavan Agrawal); DBT, Ramalingaswami Fellowship (PI- Pavan Agrawal, Project Associate: Faizah Ansari); CSIR- JRF (Navinchandra Venkatarama Puppala); Manipal Academy of Higher Education- intramural funding.

P146: Regulation of social isolation-mediated sleep by dopaminergic neurons and epigenetic modulators in *Drosophila melanogaster*

Monalisa Ghosh, Manohar Vasam, Pavan Agrawal
Centre for Molecular Neurosciences, Kasturba Medical College, Manipal; Manipal Academy of Higher Education, Udupi-576104, Karnataka, India.

Background: Social isolation disrupts sleep across animal kingdom including in *Drosophila*. Our earlier work has identified the role of dopaminergic neurons (DANs) in regulating social isolation- mediated sleep disruptions. Specifically, Activity Regulated Genes (ARGs) and epigenetic modulators in DANs were shown to affect sleep disruptions in DANs.
Materials and methods: Here using a genetic toolkit, we screened DAN subsets and epigenetic modifiers that are responsible for these sleep disruptions. Targeted silencing and activation of specific DAN subsets by optogenetics or thermogenetics was used to monitor changes in sleep behaviors. RNAi-mediated knockdown of specific epigenetic modifiers and transcriptional modulators in DAN subsets was carried out to measure effects on sleep modulated by social isolation.
Results: We found specific DAN subsets in which rescue of disrupted daytime sleep was seen upon silencing. Conversely, neuronal activation led to dramatic increase in the baseline activity regardless of social experience. Down-regulation of ARGs and epigenetic modifiers in specific DAN subsets significantly reduced the disruption of daytime sleep.
Discussion and conclusions: Our results suggest that specific clusters of dopaminergic neurons play a role in the disruption of sleep under social isolation-mediated stress, probably modulating the activity in the mushroom body and central complex respectively, both of which are known sleep-regulating centers. Reversal in isolation mediated sleep disruption upon knockdown of specific epigenetic modifiers suggest role of epigenetic mechanisms in specific DAN subsets in regulating isolation mediated behaviors.
Acknowledgment: DBT extramural research grant (PI: Pavan Agrawal); DBT, Ramalingaswami Fellowship (PI: Pavan Agrawal); NFST Ph.D. fellowship to Manohar Vasam Intramural support by the Manipal Academy of Higher Education.

P147: Nerve Agent Induced Brain Damage: Comparative Efficacy Analysis of Midazolam and Diazepam Treatment in Mice

Poorna Shri, Rohit Chand Kabidayal, K.P Singh, Neeti Jain, D.P Nagar, A.S.B Bhaskar
Division of Pharmacology and Toxicology, Defence Research and Development Establishment, Jhansi Road, Gwalior-474002, India

Background: Nerve agents are highly toxic compounds that interfere with neurotransmission, leading to a range of symptoms including seizures, biochemical changes and cognitive impairment. Standard treatment with Atropine and 2-PAM do not control Status Epilepticus (SE). This study aims to compare the efficacy of two commonly used benzodiazepine drugs for SE, Midazolam (MDZ) and Diazepam (DZP) along with standard atropine and oxime treatment regimen for nerve agent poisoning.
Materials and Methods: The study design involved animal model exposed to a standardized dose of a representative nerve agent Vx. The animals are divided into four groups: Control, Atropine+2-PAM-treated (Std), MDZ+Std-treated, and DZP+Std-treated. The effects of the treatments are measured through a cholinesterase and neurotransmitter like monoamine oxidase activity analysis and histopathological evidences.
Results: Brain tissue samples are collected to analyze the impact of midazolam and diazepam as anticonvulsant on neurotransmitter levels and status epilepticus. Midazolam shows the better efficacy over diazepam treatment in all aspects in our results. Level of %AChE activity is high in MDZ treated groups. Increased MAO activity shows the level of neurotransmitter degradation in std group, equal to control in MDZ group. Preliminary observations indicate comborative histopathological changes in brain tissue. MDZ+Std group show better efficacy in protecting brain.
Discussion and Conclusion: This study contributes to a deeper understanding of the pharmacological management of nerve agent (Vx) induced brain poisoning. The results have implications for the development of novel therapeutic interventions to counteract the deleterious effect of nerve agent induced brain damage.

AChE, MAO and histopathological analysis of brain tissue shows that midazolam as a better anticonvulsant over diazepam along with standard treatments.
Acknowledgements: We are thankful to the Director, Defence Research and Development Establishment, Gwalior for providing all facilities required for this study. The study is funded by DRDO, Ministry of Defence.

P148: Benzodiazepine drugs: A comparative neurobehavioral study for better neuroprotective drug against nerve agent toxicity

Rohit Chand Kabidayal, Poorna Shri, KP Singh, DP Nagar, ASB Bhaskar, Neeti Jain
Pharmacology and Toxicology Division, Defence Research and Development Establishment, Gwalior 474002.

Background: Nerve agents are organophosphorus chemical warfare agents that disrupt the nervous system by inhibiting the function of enzyme Acetylcholinesterase (AchE) by forming a covalent bond with its active site, where acetylcholine would normally be broken down. Signs of acute intoxication with nerve agents or OP are miosis, profuse secretions, bradycardia, bronchoconstriction, hypotension, and diarrhea. Overstimulation of nicotinic receptors triggers muscle fasciculation and short-term/long-term CNS-related effects include anxiety, restlessness, confusion, tremors, seizures and central cardiorespiratory paralysis. This study is designed to select the most suitable drug amongst the various benzodiazepines recommended in case of nerve agent induced tremors.
Materials and Method: To conduct this study; Nerve agent (VX), Pralidoxime chloride(2-PAM), Atropine (ATP), Midazolam (MDZ) and Diazepam (DZP) were used. Open field box test, Forced swim test and Object Recognition tests were performed on Swiss albino mice to access behavioural pattern. Four groups (Negative control, VX only, and VX with available treatments) were used. Behavioural studies, and whole brain protein profiling were conducted at 1st day,10th day & 30th day after primary exposure. Statistical analysis was done using GraphPad Prism 5.
Results: Out of four groups VX exposed followed by MDZ treated group showed most protective efficiency and neuroprotective symptoms compared to traditional countermeasure treated group (i.e DZP with 2-PAM+ATP and 2-PAM+ATP alone). SDS PAGE profile of whole brain homogenate indicate the intense band of 120Kda & 70KDa protein in MDZ treated mice and control mice, this could be one possible reason for protective action of this anticonvulsant.
Conclusion: The behavioural data of MDZ treated groups certainly showed better therapeutic efficacy towards neurotoxicity of VX compared to DZP. This directs that administering 2-PAM with ATP is far less promising therapy for acute as well as delayed organophosphorus / nerve agent exposed mice. Further studies are in progress to validate the findings through biochemical, molecular pathways and gene expression.
Acknowledgements: The study was funded by DRDO, Ministry of Defence, Govt. Of India. The authors are thankful to the Director, DRDE-DRDO, Gwalior, for providing facilities to carry out the research.

P149. Effect of HDACi Sodium Valproate on the light-sensing ability of *Hydra viridissima*

Riddhesh Ahire, Mayur Gaikwad, Nawalkar Rhea
Department of Life Sciences, Sophia College (Autonomous), Bhulabhai Desai Road, Mumbai 400-026

Introduction: Hydra is a freshwater cnidarian and widely used model system for Regeneration studies. Sodium valproate (VPA), an aliphatic acid is a known HDACi. Apart from its role in regeneration not much has been reported of its role in Behavior. We show the effect of VPA on its behavioural parameter (phototactic behaviour) and Anatomical parameter (Quantification of Battery cell complex).
Material and methods: LC50 assay was performed to determine the least toxic concentration of VPA for *Hydra viridissima.* A range of various concentrations of VPA were used to perform the following assays. A phototactic performance assay was performed to assess the light-sensing ability of hydra. Staining of BCC with methylene blue and its quantification was performed to analyse the effect of VPA on BCC and sensory neurons using ImageJ.

Results: 100% mortality of hydra was observed after 48 hours of treatment with 2.5mM VPA. Hydra exhibited positive phototactic behaviour. The average phototactic performance value increases after 24 hours of interval. Staining and quantification of BCC was done using 0.1% methylene blue.
Conclusion: Concentration up to 2.5 mM was lethal to hydra. Therefore, a lower concentration would be considered for further analysis. At lower magnification, clusters of BCCs were observed as bands, and single BCCs were observed at higher magnification.
Acknowledgement: I extend my gratitude to Dr. Sree Nair and Sophia College for this exceptional opportunity. Special thanks to Mr. Mayur Gaikwad, and Ms. Rhea Nawalkar, for their mentorship. I also wish to acknowledge the dedicated faculty and staff members whose contributions have been pivotal to my journey.

P150. Orexin-expressing cells in cerebellum are involved in goal-directed behaviour to seek reward

Sharavi Kulkarni, Namrata Pawar and Amul Sakharkar
Department of Biotechnology, Savitribai Phule Pune University, Pune, India

The recent discovery that reward signals can be traced to the deep cerebellar nuclei (DCN) has gained new traction. Orexin, a neuropeptide, serves in wakefulness, motivation, arousal, and feeding behaviour. We for the first time report the orexin-expressing neuronal populations in the dentate nucleus (DN) and dentate-interpositus (IN) region of the cerebellum. Further, we decipher the role of this orexinergic system in goal-directed behaviour for seeking natural food reward. Adult male Wistar rats were subjected to Y-maze conditioning and nose-poke operant conditioning paradigms for seeking sweet pellets. Orexin siRNA in DN and tracer in Ventral Tegmental Area (VTA) were administered by stereotaxic cannulation. Conditioning for reward stimuli triggered over-expression of orexin in different subnuclei of DCN in both paradigms. On the contrary, the conditioning of rats to unbaited arm to avoid aversive stimuli in Y-maze did not alter orexin levels in DN. Moreover, orexin expression was not affected in rats exposed to sucrose water in home-cage. Interestingly, orexin siRNA administration in DN dramatically reduced the number of nose-pokes as well as time spent and entries in baited arm of Y-maze. These results highlight the significance of orexin neurons in DN in goal directed behaviour for reward seeking. Notably, these orexin neurons send projections to the VTA as shown by retrograde tracing study. The current results provide strong evidence for an essential role of orexin-expressing cells in DN in the processing of goal directed behaviour for rewarding stimuli.
Acknowledgements: SERB-DST and UGC, Government of India.

P151. Dissecting the role of miRNA in Cell cycle Related Neuronal Apoptosis (CRNA)

Komal, Monika Chauhan, Soumya Kusumakshi, Chen Chongtham, Aneeshkumar A.G. and Pushkar Sharma
National Institute of Immunology, New Delhi-110067, India

Background: Aberrant activation of the cell cycle of terminally-differentiated neurons results in their apoptosis and is known to contribute to neuronal loss in various neurodegenerative disorders like Alzheimer's Disease. However, the mechanisms that regulate Cell Cycle Related Neuronal Apoptosis (CRNA) are poorly understood. It is important to know how cell cycle related genes are up regulated in this situation. While microRNA are implicated in the process of cell cycle regulation but their correlation with the neuronal cell cycle regulation and neuronal loss has remained unknown.
Materials and Methods: We have used APP/PS1 transgenic mouse model for AD (TgAD) and cultured cortical neurons to study CRNA, which was assessed by assessing levels of cell cycle and apoptotic markers. Water Maze and Y-Maze test were performed to study learning and memory in AD mouse model.
Results: RNAseq was performed to identify miRNA deregulated in AD model, which was validated by qRT-PCR. Deregulation of miRNA that target cell cycle related genes was observed in neurons of TgAD neurons. Investigations on two of these miRNAs revealed that they suppress the cell cycle during neuronal differentiation. In response to neurotoxic amyloid peptide $A\beta_{42}$, their expression was impaired, which contributed to Cell cycle Related Neuronal Apoptosis (CRNA). Molecular mechanisms via which these miRNAs are deregulated, which in turn may contribute to CRNA, were also deciphered. Morris water maze

and Y- maze revealed that overexpression of one of these miRNAs can improve memory and learning in TgAD mice.

Conclusion: We have identified two miRNA that keep the neuronal cell cycle suppressed. Their repression in response to Aβ42 results in CRNA, which can be prevented by their over expression and can revert defects in learning and memory exhibited by TgAD mouse model.

Acknowledgements: Funding support for this work was provided by NII core grant and a grant from DBT, India