COGNITIVE NEUROSCIENCE AND NEUROPSYCHOLOGY

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Introduction

The review covers the work done in the fields of Cognitive Neuroscience and Neuropsychology. While both fields study brain - behavior relationships, there is a difference in the predominant method used. Neuropsychology studies patients with brain damage using the lesion method. Cognitive Neuroscience studies normals as well patients using the methods of functional human brain mapping such as EEG, ERP, fMRI and lesion method. In our country, majority of the studies are in the field of Neuropsychology and have covered three fields i.e., Neuropsychological profiles in Neurological, Neurosurgical and Psychiatric conditions; Development of neuropsychological tests; Neuropsychological rehabilitation. Studies in Neuropsychological profiles in Neurological, Neurosurgical and Psychiatric conditions have combined neuropsychological assessment with EEG/ERP. Studies on normal subjects with functional brain mapping using EEG, ERP, fMRI are a few. Publications of the studies have been sparse. Hence the review has included published articles, research undertaken as part of the Ph.D., M.D., D.M., M.Ch., M.Phil degrees which have been examined and degree awarded. The review does not cover the field of language and the brain as it is a vast area and merits a separate review. It is restricted to work done in India. Studies on cognition alone and studies which have merely documented cognitive deficits in clinical condition have been excluded. Omissions are not deliberate but inadvertent and request to be excused.

Neuropsychological Profiles in Neurological, Neurosurgical and Psychiatric Conditions

Neurological Conditions

Neuropsychological studies have been undertaken in different neurological disorders with the aim of understanding the nature of brain dysfunction.

Epilepsy

Neuropsychology and psychophysiology were combined to understand the nature of divided attention in epilepsy. Ten epileptic patients with well-controlled seizures and matched normal controls formed the sample. Divided attention was studied with the dual task paradigm. The P300 component of the event related brain potential was recorded as an index of attentional resource. The P3 was recorded from CZ channel. An initial recording of P300 to the auditory odd-ball paradigm alone served as the baseline measure. In the divided attention paradigm I and II, the primary tasks were verbal tasks and figural tasks respectively, which required classification. The P300 was recorded using the auditory odd-ball paradigm

as a secondary task in both divided attention paradigms. The behavioural measures were foot tapping on hearing 'infrequent' tone in the odd-ball task and accuracy and reaction time of classifying the stimuli in the two primary tasks. In the baseline condition, epileptic patients and controls did not differ significantly in attentional resources as indexed by P300. Both groups could divide attention in the dual task paradigm. In both groups only some persons could divide attention probably due to a deficit in attention-allocation strategies. The two groups did not differ on the measures of the primary and secondary tasks in case of subjects who could divide their attention and those who could not. The primary tasks employing verbal stimuli were difficult for both patients and controls. Epileptic patients were able to divide their attention and there was no decrement on secondary task performance as compared to controls (Chandiramani & Rao, 1997).

Recognition of Facial Expression of emotion was studied in 80 patients with epilepsy, 20 of their relatives and 20 normal controls. The patients with left sided seizure focus were significantly poorer in labeling emotions. The accuracy of recognition did not differ between left and right sided seizure focus (Ismail, 1998). The performance of 21 temporal lobe epilepsy patients was compared with that of twenty one matched normal controls on measure of Prospective Memory. The two groups were comparable in their performance on the prospective memory tasks. As TLE is associated with hippocampal sclerosis, adequate prospective memory in TLE indicates that hippocampus does not mediate prospective memory (Subramaniam, 2001). Memory and executive functions were examined in temporal lobe epilepsy (TLE). The performance of 30 TLE patients was compared with that of 30 normal controls on verbal (RAVLT) and visual (BVRT) tests of memory as well as on executive functions of set shifting (Trail making and WCST), working memory (Letter-number sequencing, Spatial span) and response inhibition (Stroop test). In TLE memory and the executive functions of concept learning and set shifting were impaired (Bhattacharya, 2006).

Parkinson's disease

The underlying brain structures of cognitive control were examined by studying inhibitory control in patients with Parkinson's disease (PD). Most PD patients have poor control of voluntary movement and poor capacity to inhibit prepotent responses on a variety of tasks, indicative of impaired inhibitory control. Basal ganglia dysfunction could cause poor inhibitory control. While inhibitory control of automatic motor responses is poor, the capacity of PD patients to inhibit in a corrective manner planned or ongoing motor behavior. Using oculomotor control as a model, a study examined 15 PD patients and 13 normal controls on a visually guided saccade task. The subjects had to cancel a partially prepared saccade on a fraction of randomly chosen trials. PD patients took longer to make this correction indicating poor inhibitory control even when ongoing behaviour needed correction. As basal ganglia is dysfunctional in PD, inhibitory control required for corrective behavior also appears to be a basal ganglia function.

Huntington's disease

Huntington's disease is characterized by choreaic movements and dementia. Cogntive deficits may precede onset of clinical symptoms. In view of the complete penetrance of the HD gene, asymptomatic gene carriers have shown varied patterns of cognitive dysfunction. A cognitive profile was derived by a comprehensive neuropsychological assessment in asymptomatic HD gene carriers. Eight HD patients and their first degree relatives were assessed. Of these 8 subjects were asymptomatic gene carriers and 10 subjects were non gene carriers. The neuropsychological profile of the HD group was a combination of cortical and subcortical dementia. The AGC group had deficits of varying severity suggestive of three profiles wherein deficits were comparable to the HD group, or milder than the HD group or absent. The deficits profile indicated interrupted flow of information in the sensorimotor and dorsolateral fronto striatal circuits impacted by the HD gene. The degree of severity was hypothesized to be a function of the extent of the mediation of the fronto-striatal circuits by the HD gene. Neuropsychological deficits could serve as early diagnostic markers for the illness (Udupa, 2007).

Dementia

The nature of utilization behavior (UB) in Indian patients with Fronto temporal dementia (FTD) was examined. Twenty one FTD patients underwent detailed neuropsychological assessment. Eighty percent (80%) of our patients with FTD exhibited utilization behaviour. Among patients with UB, a wide range of "incidental" utilization behaviour was observed in all. Imitation behaviour preceding UB was not seen in any of our patients. Utilization behaviour appears to be very common in FTD patients in India as opposed to those from the West. The nature and pattern of UB is very different in Indian patients with FTD than in their Western counterparts (Ghosh & Dutt, 2008). Environmental dependency was present in 2 patients who had probable AD but presented with frontal features. Patient 1 manifested frank and spontaneous utilization behaviour with garments. He also tended to toy with objects and also had hoarding behaviour. Echolalia, echopraxia or other imitation behaviour were not seen in him. Patient 2 manifested echolalia as well as touching and handling behaviour. Both patients also had neuropsychological evidence of temporo-parietal involvement (Dutt & Ghosh, 2008).

Duchene Muscular Dystrophy is a disorder associated with progressive muscular wasting and eventual death. Twenty-seven right-handed boys diagnosed with Duchene Muscular Dystrophy (DMD) between 6-11 years of age constituted the sample. The Wechsler Intelligence Scale for Children-III, Rey's Auditory Verbal Learning Test and Memory for designs were administered. The Full scale IQ (88.5) and Verbal IQ (86.59) were significantly lower than the Performance IQ (92.64). Deficits were present in information processing, complex attention, immediate verbal memory span, verbal working memory, comprehension and

vocabulary were present, indicative of prefrontal cortex and temporal lobe involvement (Perumal, 2007).

HIV infection has assumed epidemic proportions in our country. Neuropsychological deficits are indicative of brain dysfunction in clinically asymptomatic HIV infection. Most of the studies in HIV infection are from USA and Europe where the infection is by the clade B virus. In our country clade C virus is prevalent and studies of cognition are few. The neuropsychological profile of HIV seropositive cases and matched HIV seronegative controls were examined using a cross culturally valid neuropsychological test battery. HIV seropositive cases had deficits on color trails 1 & 2, Trail making test part A and Auditory verbal learning test indicating deficits in verbal memory, selective attention, sustained attention and cognitive flexibility. Global impairment in the neuropsychological test performance was present in 41.6% of the cases as against none in the controls (Madhu, 2000). One hundred and twenty HIV infected individuals who were clinically asymptomatic were administered the NIMHANS Neuropsychology Battery-2004 and a few other cognitive tests. Neuropsychological deficits were present in 73% of the sample. The deficits were sporadic and did not characterize a syndrome (Dasgupta, et al., 2007). The course of progressive brain damage can be mapped by the progression of the cognitive deficits as disease progresses. Following up the above sample of HIV infected persons over 2.5 years found a progression of the disease but no worsening of cognition indicating resilience of cognition to progression of HIV infection (Gopukumar et al., 2008).

Neurosurgical Conditions

Lateralization: The cerebral laterality of distractability of attention was investigated using an auditory distraction test, visual search test and a manual exploration test. The tests were administered on 8 right hemisphere lesion cases, 9 left hemisphere lesion cases and 9 nonclinical controls. Greater distractibility was present in right than left lesion cases. Visual search in the contralateral hemi space was impaired to a greater extent in the right hemisphere lesions. Manual exploration of visual space was impaired in both hemi spaces in both right and left sided lesions (Dwivedi & Mukundan, 1989). The lateralization of visual attention was studied with six subtests of the visual exploration task. The sample consisted of ten right and ten left lesion patients, (5 anterior and 5 posterior) and ten nonclinical controls matched on age and sex. Hemi inattention did not differ between the right and left sided lesions, or between the anterior and posterior lesions. Reaction items were faster for stimuli presented in the left hemi field. Further, reaction times were faster in the hand ipsilateral to the hemi field in which stimuli were presented (George, 1991). Laterality in brain dysfunction was examined by administering the WAIS performance scale to 20 patients each with both left or right brain tumors and a group of matched normal controls. The patient groups performed worse than normals. Right hemisphere tumor patients performed worse than the left sided tumor group only in the Digit symbol test (Gupta, & Jain, 1990).

Event related potential (ERP) evidence for the presence of hemispheric asymmetry for visual attentional processes was studied with a sustained attention visual detection task, two visual search tasks assessing focused and divided attention respectively and a covert orienting of attention task using trial-by-trial cueing of target stimulus location. The study sample consisted of a control group of normals and two groups of patients with cortical lesions in either hemisphere. ERP's in response to the tasks were recorded from 21 scalp locations. Findings indicated right hemisphere dominance for early attentional processes, as suggested by the amplitude and latency profiles for early ERP components of P1 and N1. The extreme right and left leads were found to be the most sensitive in tapping asymmetry. In the orienting of attention task, in sharp contrast to the other two groups, the right hemispheric lesion subjects showed reduced early ERP latencies in conditions of invalid target location cueing indicating distractability in right-sided lesions (Dwivedi, 1994).

The contribution of laterality of the brain to creativity was studied on thirty right and thirty left sided cortical lesions patients and a control group of 30 nonclinical subjects. Verbal and visual tests of creativity were administered. Neuropsychological tests included Standard Progressive Matrices, Stroop test, Rubin Vase Test, Embedded Figure Test, Ideational Fluency Test, Verbal learning and Memory Test and Visual Learning and Memory Test. Creativity was not material specific, but required an integration of verbal and visuo-spatial inputs. Patients performed poorly on tests of creativity irrespective of the lesion laterality. Right sided lesions affected tests using visuo-spatial processing, while left sided lesions affected verbal processing. Creativity was an independent dimension evidenced by the lack of correlation with neuropsychological tests in the control group. Interaction of both the cortical hemispheres was crucial for creative performance (Jamuna, 2000).

Localisation of neuropsychological dysfunction by correlating it with structural abnormalities on MRI was done on 10 patients with structural lesions of the brain. MMSE, Luria Nebraska Neuropsychological battery and PGI Memory scale were administered. Use of the structural imaging alone does not give enough information. Neuropsychological assessment gives additional information on the nature of brain dysfunction (Mukhopadhyay, et. al., 2005). Immediate memory was assessed by administering the digit span test and the sentence recall test form the PGI battery of brain dysfunction on 27 patients with specific brain lesions. Immediate memory was impaired in 82% of cases. In 77% impairment was present in both tests. Immediate memory was subserved by multiple systems. In addition to the lesions of the left parieto-frontal network, lesions of the different subcortical areas also disrupted immediate memory indicting that widespread areas connected by a network system mediated immediate memory (Dutta, et. al., 2001).

Frontal Lobe Lesions: In the past twenty years the functions of the frontal lobes have been intensely studied in the domain of brain behavior relationships.

The frontal lobes being the center of executive functions, understanding of frontal lobe functioning is critical to understanding behavior. The neuropsychological profile in frontal lobe lesions was investigated on 110 patients with frontal lesions, 22 patients with non-frontal lesions and 30 normal subjects by administering a comprehensive battery of neuropsychological test.. The left frontal cortex was involved in spontaneous arousal of attention, flexibility of control, sequential motor behavior, kinetic melody, regulation of voluntary behavior by verbal processes, concept formation, field independency and complex learning and memory functions. The right frontal cortex was involved in directive component of attention and behavior, visual scanning, anticipation, planning, visuo spatial organization, inhibitory functions, ability to do withhold a response and personality changes. Deficits associated with bi-frontal pathology are associated with inhibitory functions, response control, anticipation, regulation, integration and personality changes. The nature of frontal deficits was not only determined by the laterality of the tumor but also by its intra-frontal localization (Shailaja, 1989).

The relative contribution of cerebellum and frontal lobes to executive functions was studied by comparing the performance of fifteen patients with cerebellar lesion with those of twenty patients with frontal lobe lesions and thirty matched normal controls on neuropsychological tests of attention, intelligence, motor speed, executive functions of planning, fluency and working memory tasks, verbal comprehension, visual learning and memory, and verbal learning and memory. Both frontal and cerebellar lesion groups were impaired on all the executive functions and most of neuropsychological functions. The pattern of deficits differed between the two groups. On discriminant function analysis six variables discriminated between the two groups. The underlying process that led to the deficits in frontal lesion group was hypothesized as an inhibitory control component, whereas in cerebellar lesion group it was hypothesized as an 'agility' component. An interactive model was proposed in which the inhibitory control and agility components interact in a complimentary way, in order to process the motor and cognitive functions through the reciprocal anatomical connections of frontal lobes and cerebellum (Ajayan, 2002).

The capacity of the Central Executive of the Working Memory (WM) to allocate attention and manipulate information for the comprehension of syntactic and semantic aspects of a sentence was studied on three patients with right frontal lesions and 2 patients with left frontal lesions. Working Memory was studied with Digit Backwards, N-Back Task, Self-Ordered Pointing Task and Trade Task. Syntactic and Semantic comprehension tasks were also administered. Both syntactic and semantic comprehension was correlated with working memory. Deficits of comprehension were greater in left frontal lesions (Nair, 2002).

The role of the central executive in identifying and utilizing the organizational strategy in encoding and working memory was examined on a sample of 10 left frontal and 14 right frontal lesion patients and 17 normal subjects. They were

tested on encoding and working memory tests of Verbal Working Memory Test, Matrix Test, Self-Ordering Pointing Test, Sentences Recall Test, Complex Figure Test, Information Missing Test, Categorization Test, Related Sentences Test and Related Words Test. The left frontal lesion patients showed significant deficits of the central executive functioning in identifying and organizational strategy in tests of Verbal Working Memory and Sentences Recall Test, as well as in encoding of relational representation. The right frontal lesion patients showed significant impairment in "passive" storage task of Visuo-Spatial Working Memory (matrix) Test and deficits in self-ordering the responses (Roopesh, 2000).

The role of frontal lobes in memory was examined through neuropsychological and electrophysiological paradigms. The sample comprised of three groups of patients (frontal, sub-cortical lesion patients and a group of alcohol dependent subjects) and control group of normals. The neuropsychological tests included Mini Mental State Examination for screening cognitive dysfunction, Trail making test I and II, Stroop Test, Digit Span, Digit Symbol Test, Delayed Response Learning to assess the executive component of working memory, Visual and Verbal Learning and Memory and Wordlist Learning Memory. A Mirror Drawing Test was also given to assess the implicit learning in memory. The Psycho-physiological test included a visual odd ball test to assess target detection, visuo-spatial search memory test and number sequencing test to assess sequential memory. Working memory deficits were present in the frontal and sub-cortical group of patients. The frontal lesion group in addition manifested deficits in delayed recall and sequential memory. The sub-cortical lesion group showed deficits in immediate memory and implicit learning and memory. The alcohol dependent group showed minimal deficits in working memory and in other learning and memory tests. (George, 1997).

The brain structures mediating the executive function of set shifting was investigated by administering WCST to 54 patients with focal cortical (n=30), subcortical (N=13), and cerebellar damage (n=10) patients. The classification and regression Tree (CART) analysis was used to determine the brain substrates of WCST performance. The CART showed that frontal lobes are essential mediators of the set shifting capacity. However for its optimal execution, the participation of other cortical (temporal and parietal), subcortical (thalamus) and cerebellar regions is required (Mukhopadhyay, et. al., 2008).

Head Injury

The nature of divided attention and its relation with post concussion syndrome was examined in 19 patients with mild head injury and a group of matched normals. Following a multiple resource model of attention, dual tasks which tapped either attention resources of the right and left hemispheres or dual tasks which tapped attentional resource from the same hemisphere were administered. The efficiency of sharing attention and neurobehavioral changes were noted. Both groups could divide attention, but resource sharing was deficient when sharing from the same

pool compared with sharing between two pools. Patients had a constricted resource volume and deficient strategic allocation of available resource on both paradigms as compared to controls. The clinical factors, i.e. severity of injury, severity of symptoms and post injury duration were not related with efficiency of sharing and volume of the attentional resource (Mishra, 1989). Intelligence as measured by the Bhatia's Battery of performance tests was lower in head injured patients (N=20) compared to matched normal controls (Gupta & Baveja, 1990). Head injured patients (N=24) had deficits of immediate memory (digit span forward and backward), associate learning and visual reproduction (subtest of WMS), and information processing (PASAT). Severity of the head injury did not significantly worsen the deficits (Gupta & Ghai, 1996). Head injury was associated with deficits in sensory gating of stimuli possibly leading to an overflow of stimulation and consequent overload of information. In turn this would lead to post concussion syndrome (Sanjakumar, et. al., 2005). Executive functions and decision making ability were correlated in head injured patients but not in normal controls. Poor visuospatial working memory was associated with good decision making in patients (Ray, 2008).

The cognitive deficits and post concussion syndrome in head injury do not appear to be correlated with the nature of structural brain damage as evident on MRI. Twenty patients with PCS, 11 of whom had structural abnormalities on MRI underwent neuropsychological assessment. All the patients had neuropsychological deficits. Specificity of MRI in diagnosing neuropsychological deficits was low. The pathophysiological basis of PCS was related to a functional cerebral dysfunction rather than any specific structural brain damage (Datta, 2006). Apolipoprotein E (APOE) plays a major role in repair of cell membrane and growth of neurites following injury to cells. Studies carried out on Western population have shown that the APOE e4 genotype is associated with poor survival (acute as well as chronic) following traumatic brain injury. Eighty one patients with mild to moderate head injury were followed up for six months. APOE polymorphism status determined by PCR technique was available for 59 patients. APOE e4 was present in 8 patients and absent in 51 patients. The two groups did not differ on Digit vigilance test (sustained attention), Digit symbol substitution test (mental speed), Complex figure test (visuoconstructive ability and memory) and Token test (verbal comprehension) indicating lack of an effect of the APOE e4 on the cognitive functions tested (Pruthi, 2006).

Attention was the focus of an ERP study on head injury. Fifty five closed head injury patients divided into mild, moderate and severe head injury, and 30 normal controls formed the sample. EEG was recorded from 6 active electrodes – Fz, Pz, T3, T4, P3 and P4 referenced to linked mastoids. ERP tasks were Auditory and Visual Evoked Potential tasks, the Auditory and Visual P300 tasks and the Divided Attention tasks I and II. Slow latency was present in tasks requiring complex stimulus analysis. Amplitudes were reduced on tasks requiring the maintenance of a passive attentional state, indicative of a lowered arousal level,

but were normal on tasks requiring focused attention, the patients were comparable to the control group. Amplitudes were reduced on tasks requiring complex cognitive analysis. Lateralized deficits were also observed with right-sided deficits being elicited on tasks requiring the maintenance of a passive attentional state. Left-sided deficits were seen on tasks requiring complex cognitive analysis. The interaction of arousal level, channel capacity and task complexity appeared to influence the deficits. Severity of injury had no association with the deficits (Easvaradoss, 1991). Neuropsychological tests, EEG and ERP were used to assess the nature of recovery at 3 months and 6 months after closed head injury. The battery of neuropsychological tests measured sustained attention, visual and verbal learning and memory and visuo perceptual processing. EEG recorded from 7 active electrodes- F3, T3, P3, F4, T4, P4 and PZ, measured absolute and relative power of resting EEG (eyes closed condition). Seven experimental tasks were employed for ERP analysis: auditory and visual evoked potential, auditory and visual P300 tasks, divided attention tasks and tasks of arithmetic ability and visuo-spatial processing, which were presented in divided visual field conditions. Neuropsychological assessment showed diffused involvement at first assessment. In the second assessment there was marked recovery in verbal tasks and simple visual memory tasks. But sustained attention, visual learning and memory and visual scanning tasks continued to be impaired. Patients had reduced power on alpha and higher power on delta frequency bands in the EEG at both assessments. The ERP findings indicated significantly delayed latencies on tasks requiring complex stimulus analysis and information processing. Significantly decreased amplitudes were obtained on some of the tasks. At second assessment, performance of the patients did not improve consistently. The right hemisphere functions recovered slowly after head injury (Thakur, 1993).

Neuropsychological assessment and high density EEG with 128 channels were used to understand the brain dysfunction in mild head injury. Thirty patients with mild head injury and thirty normal controls formed the sample. Neuropsychological assessment measured mental and motor speed, attention, executive functions, verbal comprehension and verbal and visual memory, and comprehension. EEG measured relative power in the eyes closed rest. ERP measured brain activity during auditory odd ball paradigm, dual task paradigm, working memory with the Sternberg paradigm. Neuropsychological tests found deficits in motor speed, word reading speed, verbal comprehension and visuo-constructive ability in patients. EEG relative power was similar in resting and working memory conditions. The power in various frequency bands differed across the task conditions and between the two groups. Longer latencies in N200 and P300 were observed in two-stimuli auditory oddball task. No differences were found on coherence values in theta, alpha-1, and alpha-2 frequency bands between MHI and normal group during eyes closed resting condition. MHI patients had poor intra-hemispheric long range and inter-hemispheric coherence in alpha-1, alpha-2, and theta frequency band in verbal and visuo-spatial working memory condition.

Further, discriminant function analysis indicated that based on verbal and visuo-spatial working memory coherence and comprehension ability, 80% of MHI and 86.2% of normal individuals can be classified correctly. However, poor correlation was found between neurobehavioral symptoms and neuropsychological and electrophysiological deficits. The study indicated that MHI patients have comparable overall cognitive ability, but utilization of cognitive ability is slowed. Further, functional disconnections between brain regions are evident in MHI upon taxing the cognitive resources (Sanjay kumar, 2006).

Affective Neuroscience

The social and emotional responses in right and left hemisphere lesions were examined in 10 stroke patients with left hemisphere lesions and 11 stroke patients with right hemisphere lesions with a mean age of 52 years. Both males and females were included. None of the cases had any other psychiatric or neurological diagnosis. The Mini Mental Status Examination was administered as a screening instrument to rule out dementia and global comprehension deficit. The patients were rated on - Hamilton's Depression Scale, Hamilton's Anxiety Scale, Bech et al's Mania Scale and the Anhedonia Symptom Checklist. There was no significant difference between the two groups on scales of depression, mania and anxiety. Anxiety, dpression and mania were prevalent in 76%, 60%, and 21% of the sample respectively. The symptoms of anhedonia significantly differentiated the two groups, with patients in right hemisphere group obtaining higher scores (Rajendran, 1990). Emotional changes' following brain tumors was preoperatively investigated in 51 brain tumor patients above 18 years of age. The Neurophysiology Behavior and Affect Profile's (NBAP) others report version was administered on the significant other, after obtaining patients CT/MRI and Neuropsychological assessment report. Emotional changes following brain lesion are widespread. The most common change is depression followed by indifference. Emotional changes are present, both with presence and absence of cognitive dysfunction. The more the time elapsed since the lesion, the more a person is likely to develop depression. There is a significant relationship between presence of psychosocial stressor and emotional change. This relation holds good for both depression and indifference (Tewari, 2002).

The effect of brain lesions on perception of facial emotion was examined. Patients with unilateral brain damage and normal controls judged emotions in terms of similarities within the photographs of six facial emotions. They judged the intensity of expression within the hemi facial composite photographs. Right brain-damaged patients could differentiate between the emotion of happiness and all other emotions. Left brain-damaged patients differentiated between aroused-non aroused emotions. Normal controls differentiated between positive-negative as well as aroused-non aroused emotions. All the groups judged the Left-left facial composites to have expressed more intensely than right-right facial composites or normal/mirror reversed facial orientations of emotions excepting fear (Mandal, et.

al., 1993). Patients with right or left hemisphere-damage and normal control groups were asked to judge facial emotions from photographs presented in two orientations - upright, inverted. Responses were elicited with a matching and a verbal labeling task. Normal controls were significantly superior in the judgment of facial emotions than left hemisphere-damaged patients, who in turn were significantly superior to right hemisphere-damaged patients. Negative-aroused (fear, anger) and negative-non aroused (sadness, disgust) facial expressions were recognized with significantly greater accuracy by left hemisphere-damaged patients compared to right hemisphere-damaged patients; the group difference in performance was nonsignificant for positive (happiness, surprise) emotions (Mandal, et. al., 1991). The effects of valence, motoric direction (approach/withdrawal), and arousal on the perception of facial emotion in patients with unilateral cortical lesions was examined in 30 right-hemisphere-damaged (RHD) and 30 left-hemisphere damaged (LHD) male patients with focal lesions restricted primarily to the frontal, temporal, or parietal lobe. The influence of lesion side, site, and size on emotional perception was also examined. Patient groups were comparable on demographic and clinical neurological variables. The ability of the subjects to match photographs of four facial emotional expressions: happiness, sadness, fear, and anger was tested. Overall, RHD patients were significantly more impaired than LHD patients in perceiving facial emotion. Lesion side, but not site, was associated with motoric direction and valence dimensions. RHD patients had specific deficits relative to LHD patients in processing negative and withdrawal emotions; there were no group differences for positive/approach emotions. Lesion size was not significantly correlated with accuracy of emotional perception (Mandal, et. al., 1999). In order to examine whether the impairment of RHD patients in judging facial expression of emotions was due to deficit of visuo-spatial processing and emotion processing or only due to emotion processing, emotions were depicted in unusual faces. Patients with focal brain damage, right and left hemisphere damage, and normal controls were asked to match photographs of emotion expressions that were depicted in unusual (line drawings, strange, and schematic) and normal (usual) representations of faces with the target emotion expressions of normal face. Normal controls were significantly superior to right hemisphere damaged patients in matching photographs of emotion expressions that were depicted in line drawings of normal face and schematic face. LHD patients were found superior to RHD patients in matching emotional expressions represented by line drawings of usual (high-pass) faces and schematic faces. Right hemisphere damage groups are doubly disadvantaged as the right hemisphere processes both visuo spatial information and emotions (Mandal, et. al, 1998). Patients with right or left hemisphere-damage (RHD/LHD) focal brain damage, and anterior or posterior region-damage (ARD/PRD), and normal controls (NC) were asked to match the photographs of (left right) hemi facial expressions of emotions. The emotions depicted could be positive (happy-surprise), negative-aroused (fear-anger), negative-non aroused (sad-disgust). The patients were poorer than normals in their performance. The lesion laterality did not make a difference as RHD and LHD patients did not differ. But the PRD patients performed

better than the ARD patients, indicating that irrespective of the lesion laterality the anterior lesions were most impaired (Mandal, et. al., 1992).

The central (ERPs) and peripheral (EMG and ECG) co-activation patterns with subjective experience of affect during emotional processing in normal subjects and patients with functional mental disorders were examined. 15 patients each (Generalized Anxiety Disorder, Panic and Phobic Disorders and Depressive Disorders) and one group of 15 matched normals formed the sample. Emotional and neutral stimuli were presented. The ERPs, ECG and EMG recordings were carried out during pre and post stimulus presentation. In linear analysis averaging for extracting the ERP waveform from EEG signals was used. For ECG, RR intervals were calculated and subsequently converted into beats per minute. Average voltage was calculated for the EMG signals. Four invariants of non-linear analysis viz- Fractal dimension, Correlation dimension, Principal Lyapunov Exponent and Kolmogorov-Sinai Entropy were calculated for the averaged ERP data. All the groups reliably discriminated pleasant, unpleasant and neutral stimuli on valence and arousal. On the EMG measure, the corrugator and the zygomatic muscle groups failed to discriminate between pleasant, unpleasant and neutral stimuli statistically. The ECG measures showed initial heart rate deceleration prompted by unpleasant stimuli, where as pleasant pictures occasioned acceleration of heart rate. With respect to the ERP measures late positive potential was observed for the emotional pictures in comparison to neutral pictures. Moreover, evidence of slow positive potentials was noted. Non-linear analysis indicated more frontal activity, during task engagement. The implications of the study show observable changes in depression group, suggesting possible difficulties of resource amount and resource allocation of attention. In panic and phobic disorder group, their waveform abnormality reflected possible dysfunctional inhibitory modulation of affective information processing (Pandey, 2005).

Psychiatric Conditions

Schizophrenia

The nature of information processing deficits were studied in 30 patients with schizophrenia of whom 15 had positive symptoms and 15 had negative symptoms. Their performance was compared with 15 normal controls. Two versions of the continuous performance test were administered in which one version required abstraction and primacy or recency error could be produced. The patients had poorer short term memory and when the tasks involved categorization and/or an increased processing load. They also made more primacy errors relative to controls. However the two clinical groups did not significantly differ from each other. Schizophrenic patients appear to have a reduced processing capacity (Shenoy, 1989). The correlation of neuropsychological performance with psychopathology was examined in 30 recent-onsets, neuroleptic-naïve schizophrenic/ schizophreniform disorder patients. Reality distortion dimension was not

significantly associated with impairment of performance on the frontal lobe neuropsychological test scores. Disorganization dimension was positively correlated with increase in the time taken for Trail Making B test thus indicating an impairment in inhibition of an inappropriate response. Psychomotor poverty dimension was found to be inversely correlated with delayed response learning and verbal fluency indicating impairment in word generation and working memory. These findings point towards a differential pattern of frontal lobe involvement across the three psychopathological dimensions (John, et. al., 2001). The postulate of a left hemisphere deficit in nonparanoid schizophrenics was investigated by presenting structured and unstructured dot arrays in a dot enumeration task presented to the right and left hemispheres. The structured task would elicit automatic or global processing with a right hemisphere advantage, while the unstructured task would elicit controlled processing with a left hemisphere advantage. Non paranoid patients processed both tasks using an automatic strategy indicating a left hemisphere deficit (Gupta, 1993). However the hemisphere differences did not show up in a letter naming task. Paranoids (N=10), Non paranoids (N=10) and normal controls (N=10) performed equally with a left hemisphere advantage (Gupta, & Sachdeva, 1991). The nature of encoding deficits and the difference in encoding between the acute and chronic phase of the schizophrenic illness was studied. A battery of tests consisting of Verbal Working Memory test (VWM), Self-ordered Pointing Test (SOPT), Visuo-Spatial (Matrix) Working Memory test (VSWM), Complex Figure Test (CFT), Sentences Recall Test (SRT), Information-Missing Test (IMT), Related Sentence Test (RST), Related Words Test (RWT) and Categorizing Test were administered on 10 acute schizophrenic and 20 chronic schizophrenic patients and a group of matched normal controls. The patients performed poorly on the tests indicating poor encoding. Organizational ability was impaired in both patient groups. While the control and acute groups benefited from organizational cues, the chronic group did not (Udupa, 2002). The relationship of cognitive functions, clinical symptoms and social functioning in patients with schizophrenia was studied on 140 consecutive schizophrenic patients. A comprehensive battery of neuropsychological tests was administered. The caregiver rated the social occupational functioning of the patients. Patients had deficits in all the cognitive domains in comparison to controls. Severity of negative symptoms and general psychopathology were significantly correlated with poor performance on verbal fluency and social cognition test. Positive symptoms and age at onset (AAO) did not correlate with any of the cognitive factors and social cognition, while longer duration of untreated illness (DUI) was correlated with poor processing speed. Negative symptoms, education, course of illness and social cognition emerged as significant predictors of social functioning. Patients with good social functioning were characterized by higher education, more likely to be employed, having single episode of illness, lesser negative and general psychopathology symptoms and better cognitive functions in the areas of processing speed, planning and social cognition. Multiple factors determined functional outcome (Saraswat, 2006). The intelligence and memory of paranoid (N=20) and non paranoid (N=20) schizophrenic

patients were compared with 20 normal controls. Both patient groups had lower intelligence and memory in comparison with normals. Compared with paranoid patients non paranoid patients had lower verbal IQ but the memory deficits were similar. Frontal lobe dysfunction was measured with neuropsychological tests on paranoid (N=20), non paranoid (N=20) and normal controls (N=20). The non paranoid patients performed significantly poorer on tests of frontal lobe functions such as attention under distraction, vigilance, abstraction, motor tasks, expressive speech and constructional ability, (Srivastava, 1990). However on a grosser test of frontal lobe functions using an intelligence test, there were no differences between chronic and acute schizophrenic patients who were subdivided into paranoid and non paranoid groups. Only the information subtest differed between the groups (Chakraborty, 1997). A range of attention tasks such as Vigilance task, Letter Cancellation task, Digit span Test, Digit span test with distraction were administered on 40 schizophrenic patients consisting of acute (N=14), chronic (N=26), paranoid (N=16), non paranoid (N=26). The performance of the patient groups were compared with that of 20 normal controls. Schizophrenic patients had impairments on all the tests of attention. While the acute and chronic groups did not differ in their performance, the non paranoid were impaired to a greater extent than the paranoid group. Positive symptoms were associated with errors of commission while negative symptoms were associated with both errors of omission and commission (Pandey, 1990). The association with the nature of symptoms and working memory was examined. Thirty schizophrenic patients were compared with fifteen normal controls on verbal and visual working memory tasks. Patients with either positive or negative symptoms were worse than normal controls. Patients with negative symptoms were the most impaired (Saxena, 2002). Activity based and event based prospective memory was assessed in 42 schizophrenic patients and 42 normal controls. Set shifting and verbal working memory tasks were also administered. The patients were impaired on all the parameters. Activity based prospective memory correlated with working memory and set shifting. Neither activity nor event based prospective memory correlated with severity of the illness or with positive or negative symptoms (Kumar, et.al., 2007a, b).

Insight which influences treatment compliance in schizophrenia was studied in relation to its association with frontal executive functions. Insight was measured with the Scale to Assess Unawareness of Mental Disorder. Executive functions were measured with the Wisconsin Card Sorting Test (WCST), Trail Making Test, Stroop Test, Letter Number Sequencing and Spatial Span Test. Insight was absent in 70-80% of patients. WCST scores explained 40% of the variance in insight. While insight, executive functions improved and symptoms reduced with treatment, neither symptoms nor changes in symptomatology was associated with insight or executive functions (Chaudhary, 2005). The value of executive functions as endophenotypes of schizophrenia was examined in a group schizophrenic patients (N=30), their first degree relatives (N=30) and 30 normal controls. Their executive functioning was measured with the Stroop Test, Trail Making Test and Number-

Back Test. Schizophrenic patients had significant impairment in executive functioning which increased with increasing severity of negative symptoms. Similar sets of deficits were replicated in their first- degree relatives too, indicative of genetic predisposition to schizophrenia. The impairments in the domain of executive functions are not an epiphenomenona but a stable trait marker, thus an endophenotypic marker (Vegar, 2004).

P300, an event related potential is a measure of stimulus updating by the brain. The latency of P3 is a measure of processing speed. Amplitude is a measure of resource allocation. Deficits of P3 were measured in 58 patients divided into schizophrenics with positive symptoms, those with negative symptoms, depressives and normal controls. The P3 was recorded with the auditory odd – ball tone task, a task requiring a simple semantic discrimination between two words, and a task that required a complex semantic categorization of words. No deficit in attention related N100 and P200 amplitudes were observed. Both schizophrenia groups manifested markedly decreased P300 amplitude on each of the experimental tasks. The depression group did not have P300 deficits in amplitude. P300 latency deficit was specific to negative schizophrenia and was seen in the semantic categorization task. The results indicate brain dysfunction in schizophrenia (Gonzalves, 1990). The nature of brain dysfunction in schizophrenia was examined through documenting neurological signs and changes in P300 and N200 components of ERP in twenty one drug naïve schizophrenic patients. Thirteen of their first degree relatives and twenty normals formed the control sample. Significant excess in neurological sign scores in the patients (67%) compared to the first degree relatives (15.4%) and the normal controls were found. At the PZ site, the P300 amplitude was significantly lower and the P300 latency was prolonged in patients. Changes in P3 and the increased frequency of neurological signs are indicative of brain dysfunction in schizophrenia (Pavan kumar, 2000). A high-resolution EEG study investigated spontaneous gamma coherence and power spectrum and their relationship with psychopathology in unmedicated schizophrenic patients. Resting EEG was recorded in 30 unmedicated male schizophrenic patients and 30 matched normal controls. Power spectrum and coherence of gamma band activity was analysed using Matlab 6.5. Raw EEG signals, obtained through a 64-channel digital EEG system, were filtered with finite impulse response (FIR) digital filter and for spectral analysis Welch averaged periodogram was used. Schizophrenic patients had significantly less interhemispheric and increased bilateral intrahemispheric (front temporal) spontaneous gamma coherence and increased gamma power compared to normal controls. Gamma coherence had no significant relation with PANSS subscale scores except that there was a negative correlation between general psychopathology scores and right intrahemisphric gamma coherence. The results indicate that there is cortical hyper activation and a differential (hypo and hyper) spontaneous gamma coherence abnormality in schizophrenia (Agarwal, 2003).

The effect of rTMS n cognitive processing was examined on 20 schizophrenic patients. The ERP components of P300 and CNV measured cognitive processing. A group of 10 normal subjects were the control group for ERP. The patients had lower amplitude of P3 at the left fronto-central region (FC3) and of CNV in the right temporal region (T4). Low frequency rTMS was administered over the left temporo parietal cortex as adjunct to antipsychotic medication for 10 sessions spread over two weeks. Post rTMS symptoms reduced, P3 latency reduced over the right central (C6) region (Jain, 2008).

Bipolar affective Disorder

Disability and cognitive functioning was studied in patients with remitted bipolar affective disorder. Compared to normal controls, the patients had greater disability and greater neuropsychological deficits. The neuropsychological deficits were diffuse and involved attention, executive functions, memory and visuospatial organization. Further overall disability, the roles of family, citizen, social and occupational functioning was correlated with neuropsychological deficits (Vijay, 2002). The role of executive function deficits during the asymptomatic stage in symptom recurrence was studied in single episode and multiple episode bipolar mania. The executive functions of set shifting (WCST), response inhibition (Stroop Test), complex attention (Trail Making Test) and planning (Porteus Maze Test) were administered on asymptomatic thirty single episode and thirty multiple episode manic patients as well thirty matched normal controls. The bipolar manic patients performed worse than matched controls on all four tests of executive functioning. Multiple episode manic patients performed worse than single episode manic patients on all but one test, i.e., Porteus Maze Test (PMT). Deficits in executive functioning remain even during asymptomatic phases of bipolar (manic) illness, and are progressive with the illness (Chatterjee, R., 2005). The association of creativity with bipolar disorder was investigated by studying creativity in adolescents with mania. Twenty five adolescents between 13-19 years of age and twenty five matched normal controls were administered Passi test of creativity and Raven's Progressive Matrices test to measure intelligence. The patients were poorer in intelligence and creativity. The well known finding of cognitive deficits in mania could have contributed to the deficits of creativity and intelligence (Rautela, 2006). Neurocognitive deficits in Bipolar disorder were studied in 30 patients with Bipolar disorder I and 30 patients with bipolar disorder II. Wechsler Adult Intelligence Verbal subtest, PGI Memory scale, and executive function tests of Verbal working memory N back, Stroop test and Wisconsin Card sorting test were administered. Bipolar I patients showed deficits in recent memory, mental balance, delayed recall visual retention and total scores with visual recognition deficits. These deficits were greater in Bipolar II in comparison with Bipolar I. No significant differences were found between groups in deficits of attention, concentration and immediate recall. A number of clinical variables affected the cognitive deficits (Goyal, 2006). The literature on euthymic patients with bipolar disorder is fraught with confounds such as multiple episodes, chronic illness and residual mood symptoms. To

overcome these confounds, 30 euthymic young persons who had no more than 2 episodes of bipolar I disorder were assessed on sustained attention and executive functions of set sifting, planning and response inhibition. Their performance was compared with 30 matched controls. The patient group was impaired in sustained attention and executive functions indicating a trait status to the deficits as they are present even in the absence of clinical confounds of the illness (Kolur, et.al., 2006).

Comparison of brain dysfunction between mental disorders

Abstract thinking was examined in patients with different psychiatric diagnosis using the Kahn test of symbol arrangement. Fifteen patients each of bipolar disorder, paranoid schizophrenia and non paranoid schizophrenia and fifteen matched normal controls formed the sample. The categorization of the patient groups was different from that of normals. Manic patients were quick to symbolize objects. Depressives did not estimate their performance adequately. Paranoid patients placed more objects in love and less in hate (Manoj Kumar, 1996). Formal thought disorder a core feature of psychosis was studied by administering the object sorting test on 30 Schizophrenic and 30 with manic patients, 30 same sex first degree relatives of the each of the Schizophrenic and manic patient groups were also tested. The schizophrenics had impoverished responses; the manics had peculiar responses corresponding respectively to the presence of negative and positive symptoms. Interestingly both groups of relatives also tended to have deviant OST scores but they had more adequate responses than the patient groups. Thus a distinct pattern of thought deviance was present in each of the four groups (Dotivala, 2005). The performance on trail making test I and II were compared in 50 each of Acute schizophrenics, chronic schizophrenics, depressives, manics, normals and 35 epileptics. Each of the clinical groups performed worse than normals. There were significant differences between the clinical groups. The chronic schizophrenic group was most impaired. Trail making B was more sensitive than Trail making A test (Kumari, 1996). Cognitive models assume that attentional bias is not simply a by-product of emotional disorder but plays a vital role in its causation and maintenance. But this hypothesis has not been well tested in Obsessive Compulsive Disorder (OCD) and depression. Forty patients in each of the two clinical groups and a group of forty normal were tested on Emotional Stroop test, Trail making test and Digit symbol substitution test. On all the tests the two clinical groups performed worse than normals with the depressive patients performing the worst. Both clinical groups had an attentional bias for anxiety related information as seen by the poor performance on the emotions stroop and also on attention as seen on the trail making test and DSST (Sharma, 2005). The nature of subcortical functioning in 20 OCD patients and 20 normals was examined through EEG coherence. EEG coherence values were calculated across delta (0.5-3.5 Hz), theta (4-7.5 Hz), alpha (8-12 Hz), beta1 (12.5-20 Hz) and beta2 (20.5-30 Hz) bands. As coherence between distant brain regions reflects physiological activities at sub-cortical neural networks, EEG channels at four distant brain regions

- anterior interhemispheric, posterior interhemispheric, fronto-temporal and fronto-occipital were chosen. Patients had a significant increase of theta band EEG coherence in the fronto-occipital region, which did not correlate significantly with either medication status or disease severity. The results suggest hyperactivity in the subcortical circuitry in OCD providing external validity for sub-cortical dysfunction hypothesis of OCD (Desarkar, et. al, 2007).

The planning capacity of schizophrenics (N=30), Bipolar affective disorder (N=30), were compared to that of normal controls (N=30) using the Porteus Maze test. The two clinical groups had impaired planning. Schizophrenics performed worse than the bipolar affective disorder group (Sujeetha, 2005). The role of impaired face processing in the etiopathogenesis of Delusional Misidentification (DM) was examined with 64 channels QEEG on nineteen psychiatric patients with DM and nineteen others without it. Absolute power in each electrode was calculated and averaged to obtain regional scores of power in 13 areas. Interhemispheric coherence was calculated across 28 corresponding channel pairs and intrahemispheric coherence was calculated between 16 selected channel pairs on either hemispheres. Computations involved five frequency bands of delta (0.5-3.5 Hz), theta (4-7.5 Hz), alpha (8-13 Hz), total beta (13.5-32 Hz) and gamma (40-70 Hz). Neurological signs were recorded. Patients with DM had a) increased spectral power in temporal region, more prominent on the right side, b) increased interhemispheric coherence in the frontal and anterior parietal channel pairs, and c) increased intrahemispheric coherence maximally in fronto-parietal channels bilaterally. The findings are consistent with regional (temporal and fronto-parietal) as well as lateralizing (right hemisphere) abnormal neuronal activity in DM (Dayalnarayan, 2003). The cognitive style of schizophrenia (N=60) was compared to that of mania (N=60) using the Verbalizer-Visualizer questionnaire. Schizophrenia patients used the “visualizer” cognitive style, while bipolar-mania patients used the “verbalizer” cognitive style indicating difference in the modes of information processing between the two groups (Harikrishnan, 2003).

Obsessive Compulsive Disorder (OCD)

Working memory deficits in OCD patients with and without checking symptoms were examined on 8 OCD patients with symptoms of checking, 10 OCD patients without checking symptoms and 10 normal subjects. Five working memory test were administered. The verbal working memory tasks consisted of Delayed Recall, Competing Language Processing Test and Digit Span Test. The visuo-spatial tasks consisted of Cube Test and Card Position Test. OCD patients had verbal working memory deficits on competing Language Processing Test. OCD patients with checking symptoms showed spatial working memory deficits. Patients with checking symptoms performed poorer on the Digit span forward test as compared to patients without checking symptoms. There was no correlation between performances on the tests and severity of symptoms and also between the levels of co-morbid depression and anxiety in OCD patients (Singh, 1998).

The nature of explicit and implicit memory for contamination related verbal and nonverbal stimuli in OCD was examined by comparing 10 OCD patients for the experimental group with 11 anxiety disorder patients in the control group. The OCD patients remembered both verbal and non verbal contamination related material better than the anxiety patients. OCD patients remembered contamination material better than neutral material. The patients with anxiety disorder remembered neutral material better. Results indicate better memory for contamination related material (Ashok, 2006).

Whether executive function deficits in OCD are state or trait related was examined by administering WCST to a group of OCD patients. The deficits on WCST were not associated with OCD symptoms but were associated with each of anxiety and depression symptoms. The underlying orbitofrontal cortex dysfunction which would be reflected in WCST appears to be trait-related than state-related (Ghosh, 2008). The trait status of neuropsychological deficits was examined in a comprehensive manner in 30 recovered OCD patients and 30 healthy controls. Patients had deficits of set-shifting ability, alternation, response inhibition and nonverbal memory. Concept formation and delayed visual memory was particularly impaired. As these deficits were present in the recovered patients they are state independent and are potential endophenotypes (Rao, 2008).

The dysfunction of the fronto-striatal thalamic pathways in OCD can affect executive functions which are also mediated by the same. Executive functions being the basic mechanism of cognition, dysfunction of it can affect mode of cognitive processing and neuropsychological disposition. Hence the relation of neuropsychological disposition tested by the Adult Neuropsychological questionnaire with executive functions tested by WCST and cognitive style tested by the embedded figures test was examined in 20 patients with OCD. The subcortical – cerebellar – spinal domain of ANQ was associated with cognitive style and executive functions. The impairment of executive functions and poor activation of specific neurological circuitry in OCD patients confirmed the neurobiological basis of the disorder (Tarafder, et. al., 2006a). The nature of executive functioning in different levels of severity of symptoms was examined by administering WCST to 10 patients each in the moderate and extreme OCD categories. Their performance was compared with 10 normal controls. The patients performed significantly worse than normals. Severity of the illness did not have an effect on the WCST performance. Regression analysis showed that the executive functioning of patients were affected by distress associated with obsessive thoughts or time spent in obsessive thoughts (Mukhopadhyay, et. al., 2006).

Another study investigated neuropsychological and psychophysiological correlates of OCD during baseline. The response of the above variables to treatment was also examined. A sample of 41 patients was compared with 30 normal controls at the baseline level. 20 patients were compared before and after 12-14 weeks of pharmacotherapy. Further patients were divided into prospective responders and

prospective non-responders (retrospectively at pre-treatment level, sample size=10) and responders and non-responders to treatment (at post-treatment level, sample size=10). Neuropsychological, EEG and ERP assessment were carried out before and after 12-14 weeks of pharmacotherapy. Both linear and nonlinear dynamical measures were used for EEG and ERP analysis. The results showed that OCD patients had executive dysfunction, hypo activation and decreased functional autonomy in the brain, misallocation of attentional resources, more chaotic brain dynamics during resting conditions and inadequate brain dynamics during cognitive tasks condition. Treatment reduced executive dysfunction, misallocation of attentional resources and chaotic brain functioning in OCD patients. However, the improvement was not observed in all the areas and was not completely normalized. Inhibitory process was the one variable that clearly showed impairment in non-responders (at pre and post-treatment) (Roopesh, 2005).

Anxiety disorders

Response inhibition was assessed using the Stroop test and the Continous Perfomance test in a group of mildly to moderately ill panic disorder patients. Irrespective of severity response inhibition was impaired which may have a psycho-physiological role in perpetuating panic symptomatology (Thomas, 2002). Social phobia is a commonly occurring, chronic and seriously impairing disorder. Early studies in social phobia found reduced verbal learning and memory. The nature of executive functions was examined with a battery of six neuropsychological tests measuring planning, mental flexibility, sequencing, ability to form abstract concepts, shift and maintain sets, selective attention and immediate recall to a group of patients with social phobia and a control group with other anxiety disorders. Social phobia patients had poor immediate recall (digit forward), concept formation, conceptual learning (WCST) in comparison with the controls, and indicating brain dysfunction in social phobia (Wagle, 2006).

Alcohol related brain dysfunction

The cognitive functions of memory, intelligence and perceptual abilities were studied in 30 male alcoholics by administering the PGIBBD. Compared with the performance of thirty normal controls, the patients had deficits of concentration, memory, intelligence, and perceptual ability. Long duration of alcohol intake was associated with increased cognitive deficits (Singh, 1993). Set shifting ability was measured by the Trail making test and Stroop test in thirty alcohol dependent persons. The ADS patients had poor set shifting. Age, education and amount of alcohol consumed did not influence set shifting ability. Longer duration of alcohol consumption impaired performance on the Stroop test to a greater extent (Saraswat, 2002). A comprehensive examination of cognition in ADS was done by administering the Luria Nebraska Neuropsychological Battery to 10 detoxified ADS patients and 10 normal controls. The patients' performance was impaired as seen on the larger number of elevated scales on LNNB. Patients had impairment of C2-Rhythm Scale,

C3-Tactile Function Scale, C4-Visual function Scale, C5-Receptive Scale, C7-Writing Scale, C8-Reading Scale, C9-Arithmetic Scale, C10-Memory Scale, C11-Intellectual process Scale, and S1-Pathognomonic Scale in patients (Lal, 2002).

The vulnerability to alcoholism was examined by comparing children of alcoholic fathers with children of non alcoholic fathers. Children of alcoholic fathers had impairments of visual learning and memory, visuo-spatial functioning, verbal fluency, concept formation and delayed verbal recall. The mediators postulated for the deficits were heritability of brain structural abnormalities in the frontal and parietal regions, neurochemical or metabolic alterations in early development thereby altering brain structures, psychosocial influences of early family disruptions due to alcoholism in the father (Sunil Kumar, 2001). The nature of recovery of neuropsychological deficits with abstinence was examined. Three groups of alcoholics (1-2 weeks, 1-2 months, -> 6 months) were examined on neuropsychological measures of motor speed, attention, sequencing, visual search, planning and abstraction. Alcoholism was associated with significant neuropsychological deficits. Cognitive functioning improved with abstinence; longer the abstinence greater was the recovery. The extent of cognitive deficits and extent of cognitive recovery depended on age, education, lifetime consumption of ethanol and total lifetime years of consumption of alcohol (Bapat, 2005). Neuropsychological assessment in the OPD setting requires a short test, which is sensitive to cognitive deficits in alcoholism. Attention, motor speed, planning, fluency, working memory, verbal and visual memory was tested in 90 detoxified alcoholics. The functions, which were most vulnerable, were motor speed, verbal working memory, and verbal learning and memory. Finger Tapping test, Verbal N back test, Rey's Auditory Verbal Learning Test were chosen for the short battery (Gupta, 2006).

Cognitive deficit as a trait marker for alcoholism was examined by administering neuropsychological and electrophysiological measures to thirty alcoholics, 30 of their first-degree relatives and 30 normal controls. The tests administered were WAIS-III, WCST, Trail Making Test, part A and part B, Stroop Test, Controlled Oral Word Association Test, Letter Cancellation Test, Visual Continuous Performance Task, Visual Working Memory Test, Verbal Working Memory Test, Prospective Memory Test (event based, activity based and time based tasks), WMS-III and Finger Tapping Test. Electrophysiological evaluation of the three groups was done by; long-latency Event Related Potential (ERP) components N100, P200, N200 and P300, Movement Related Cortical Potential (MRCP)/ Bereitschaftspotential and Contingent Negative Variation (CNV).The three groups did not differ in intelligence. Executive functions were significantly impaired in patients. The first degree relatives also had deficits on some executive function tests. On the electrophysiological measures, the deficits were greatest in patients on the different parameters. But even the first degree relatives had deficits. Again deficits were greater in patients with positive history of alcoholism. The Trail Making Test-B (total number of error), Controlled Oral Word Association Test (word fluency),

N100 at midline frontal (Fz) site best predicted the AUDIT score in patients which together with the presence of cognitive deficits in first degree relatives and the presence of greater deficits in patients with positive symptoms indicate that cognitive deficits are a trait marker for ADS (Mukherjee, 2007). The role of P300 amplitude and latency as a endophenotype of alcoholism was examined. Thirty-three detoxified male ADS patients; their first-degree relatives and thirty-three normal controls formed the sample. Event related potentials using the auditory oddball paradigm were recorded to measure the N100/ N200/ P200& P300 waves from eight electrode positions of the 10/20 systems. Contingent Negative Variation (CNV) and Movement Related Cortical Potentials (MRCP) were also measured. Patients had longer latencies on N200, longer latency and reduced amplitude on P300, reduced amplitude on late CNV and the Beritshchafts potential. The first-degree relatives had reduced amplitude on late CNV and the Beritshchafts potential indicating a frontal dysfunction as a possible biological marker for alcoholism (Basu, S., 2002). QEEG of ADS patients (N=24), their first-degree relatives (N=23) and matched normal controls (N=22) were examined to discern patterns indicative of endophenotypes of alcoholism. EEG was recorded from 29 channels. Absolute and relative power was calculated from 21 monopolar channels for delta, theta, alpha, beta, beta 1 and beta 2 bands. Total absolute power was also calculated. Seven regional scores were constructed for statistical analysis. Coherence was calculated from 16 bipolar channels for 30 channel pairs (24 intrahemispheric and 6 interhemispheric). Seven sets were used for statistical analysis of coherence. Compared with the first degree relatives and normals, alcoholics had decreased power in delta and theta bands and increased power in beta, beta 1 and beta 2 bands, as well as increased coherence scores in delta, beta and beta 2 bands in fronto-temporal set. The first-degree relatives and normal controls did not differ in power spectral and coherence parameters indicating that EEG abnormalities were not a biological marker. EEG indicated frontal abnormalities in alcoholics (Lakra, 2002).

The effect of social drinking on the brain was examined by comparing the neuropsychological and psychophysiological functioning of Social Drinkers (SDs) and teetotalers (TTs). Forty-four young male SDs and 22 matched TT controls were administered the Raven's Progressive Matrices, Auditory Verbal Learning and Memory Test, Visual learning and Memory Test, Trail Making Test, Digit Symbol Substitution Test, Koh's Block Design Test, and Tactual Performance Test. Psychophysiological measures were the power and coherence of EEG, amplitude and latency of the components of two auditory ERP paradigms, Contingent Negative Variation and Bereitschafts potential. SDs performed significantly poorer than TTs on neuropsychological tests. On EEG the power in right hemisphere leads and in the posterior frontal and anterior temporal leads were lower. The amplitudes and latencies of ERP components were similar for both groups except on a few leads. No significant correlations were obtained between age, indices of neuropsychological and psychophysiological functioning and drinking parameters.

The learning and memory tests best predicted drinking status. Cognitive decrements and altered psychophysiological functioning were seen even in young, educated light Social drinkers (Mariadas, 1989).

Child Neuropsychology

Conduct disorder(CD) is the precursor of antisocial personality. As ASPD is associated with neurocognitive deficits, it is necessary to know the nature of cognitive deficits in conduct disorder. Neuropsychological tests sensitive to prefrontal cortex dysfunction were administered to 10 adolescent boys with CD and 10 matched normal controls. The CD group was impaired on set shifting, planning, ideational fluency, inhibitory control, and response inhibition. However their aggression rating did not correlate with neuropsychological deficits. The results suggested the involvement of dorsolateral and ventromedial prefrontal cortex in CD (Mathew, 2005). The status of executive dysfunction as an endophenotype in autism was examined by comparing the WCST performance of 10 high functioning siblings of autistic children with 10 siblings of normally developing children. There was no statistical difference between the two groups. Profile analysis of the matched pairs revealed a greater percentage of errors, perseverative responses, perseverative errors, non-perseverative errors and poorer conceptual level responses among siblings of autistic children, lending support to the hypothesis of executive dysfunction as a cognitive phenotype in autism (Tarafder, et. al., 2006b). Another study examined the nature of executive function deficits in ADHD. Response inhibition was a core deficit. Working memory and Cognitive flexibility were also impaired but fluency and planning were not. ADHD was associated with prefrontal dysfunction (Sinha, 2006).

The nature of brain dysfunction in specific learning disability (SLD) was examined with QEEG absolute power spectrum and coherence in fifteen learning disabled and fifteen matched normal school children. QEEG was recorded in resting condition, from a 32 channel recording system. Absolute QEEG power was calculated from 31 referential channels over five frequency bands (delta, theta, alpha, low beta ,high beta). Coherence was calculated from 12 bipolar channels, for 14 electrode pairs (8 intra hemispheric and 6 interhemispheric) over the same frequency bands. SLD was associated with: a) significant increase in absolute power in low and total beta spectrum in right frontal and left fronto-temporal regions; b) significantly less coherence was significantly in left temporo -occipital, left fronto-parietal and left centro occipital regions, for the high theta, alpha and low beta frequencies. No difference was found in absolute power spectrum or coherence between reading and mathematics disabled subjects. There appears to be a left hemispheric localization of the cognitive deficits in learning disabilities (Basu, 2003). An inefficient synchrony of the underlying mechanisms of cognitive functions such as attention, motor control, working memory, word recognition and visual integration could cause dyslexia. The underlying deficient cognitive processes associated with reading disability were explored. Eighteen children between 3rd to 7th std. with dyslexia whose phonological decoding and reading comprehension were impaired,

were administered the Cognitive Assessment System (CAS) based on the PASS theory which measures simultaneous and successive processing. Deficits were present in the full scale and the attention and planning scales. Simultaneous processing was more deficient than successive processing, indicating difficulty in establishing a logical relationship between perceptual and conceptual components of language (Kar & Tripathi, 2008). The nature of executive functions was examined in 20 children with LD and 20 normal controls. The LD children were impaired on planning, verbal learning and memory, verbal working memory and response inhibition. Intelligence, which was lower in the LD GROUP, influenced the performance on all the executive functions tests except that of working memory (Padmakar, 2008). The multidimensional nature of learning disability was examined by assessing the academic skill deficits, intelligence, comprehensive neuropsychological assessment, psychiatric symptomatology in a sample of 130 school going SLD children. The profile was one of high frequency of mixed disabilities, diffuse neuropsychological deficits, predominantly externalizing symptoms with highest frequency of ADHD. Greater number of academic domains impaired was associated with greater neuropsychological deficits. There were three clusters of the association between the domains indicating different patterns of underlying brain dysfunction (Krishna, 2007).

Malnutrition is associated with both structural and functional pathology of the brain. Effect of chronic protein energy malnutrition (PEM) causing stunting and wasting in children could also affect the ongoing development of higher cognitive processes during childhood (>5 years of age). The effect of stunted growth on the rate of development of cognitive processes was examined using neuropsychological measures. Twenty malnourished and twenty adequately nourished children in the age groups of 5-7 years and 8-10 years were examined. NIMHANS neuropsychological battery for children sensitive to the effects of brain dysfunction and age related improvement was employed. The battery consisted of tests of motor speed, attention, visuospatial ability, executive functions, comprehension and learning and memory. Development of cognitive processes was governed by both age and nutritional status. Malnourished children had deficits of attention, working memory, learning and memory and visuospatial ability. Motor speed and coordination were adequate. Age related improvement was absent in design fluency, working memory, visual construction, learning and memory. However, age related improvement was present in attention, visual perception, and verbal comprehension, even though their performance was deficient as compared to the performance level of adequately nourished children. Chronic protein energy malnutrition (stunting) is associated with impairment of cognition, retards the ongoing development of higher cognitive processes during childhood years and slows down age related improvement in certain but not all higher order cognitive processes (Kar et. al., 2008).

Brain dysfunction in General medical conditions

A new path of understanding brain behavior relationship is the study of the nature of brain dysfunction in general medical conditions. The aim of these studies is to record the level of brain damage in clinical conditions, which do not primarily damage the brain.

Myocardial Infarction

Neuropsychological deficits in patients with myocardial infarction (MI) and in MI patients after cardiac bypass surgery was studied in 15 patients with MI and 15 patients with MI after CABG (cardio-pulmonary bypass). Neuropsychological tests administered were the Digit Symbol Substitution Test, Digit Vigilance Test, Phonemic Fluency, Category Fluency, Verbal N-back Test, Visual N-back test, Tower of London, Wisconsin's Card Sorting Test, Stroop Test, Auditory Verbal Learning Test and Complex Figure Test. On comparison with MI patients CABG patients showed significant deficits in Digit Vigilance (sustained attention), Tower of London (planning), Visuo-Spatial Working Memory, Auditory Verbal Learning Test (verbal learning & memory) Complex Figure Test (visual learning & memory). CABG is associated with greater deficits than MI in bilateral dorsolateral prefrontal, bitemporal dysfunction (Anthony, 2006).

Cancer

The effect of radiation to the head on cognition was examined on 20 patients with head and neck cancer before and after radiation therapy. There was significant decline in attention, ideational fluency, abstraction, visuo spatial functions, learning and memory indicating a global decline in cognitive functions after radiation to the head region. The reversibility of the cognitive decline needs to be examined with a long term follow up (Shanmukhi, 2000). Psychiatric morbidity occurred in a third of a sample of cancer patients receiving chemotherapy. Adjustment disorders and depressive disorders were common. Mild cognitive deficits were present. An overall increase in perceived physical and psychological distress was also present (Kumar, 2000).

Diabetes Mellitus

Cognitive functioning was examined in 48 patients with Non insulin dependent diabetes mellitus and an equal number of matched controls. In comparison with the controls the diabetic patients had impairments of focused and sustained attention, semantic fluency, planning, verbal learning and memory, visual memory. Only clinically evaluated attention, reading and visuoconstructive ability were spared. All the diabetes patients fulfilled the criteria for multiple domains Mild Cognitive Impairment (Dahiya, 2006).

Effects of Hypnosis on the Brain

The nature of alterations in the power of the different frequency bands of EEG under hypnotic trance was studied. After 6-8 sessions of hypnosis induction, EEG was recorded bilaterally at T3 and T4 channels during baseline eyes closed condition and during hypnosis in 3 low, 3 medium and 3 highly hypnotized normal subjects. A frequency band analysis (2-4 Hz, 4-8Hz, 8-10Hz., 10-13.5 Hz, 13.5-20 Hz, 20-30 Hz and 30-50 Hz) revealed that there was no statistically significant difference among any of these conditions. Increase in right hemisphere activity was associated with introduction of imagery under hypnosis and in hypnotic susceptibility. There was an increase in mean percentage of theta, delta and fast alpha powers during hypnosis. The state of hypnosis was found to be different from normal wakeful condition; it resembled more of light sleep and/or paradoxical sleep than deep sleep (Purohit, 1993). The next study examined the effects of hypnosis on information processing. Seven normal adults were hypnotized for 5-10 sessions after which EEG and ERP were recorded from 19 scalp electrodes. Power spectral values were calculated using Fast-Fourier Transformation. An oddball paradigm was used for auditory P300. On EEG there was reduction in the power of fast frequencies and increase in the power of slow frequencies. On the ERP, the function of sensory registration and attention as measured by P-N1-p2 complex was normal, while stimulus evaluation as indicated by the P300 component was either absent or significantly reduced in amplitude (Sharma, et. al., 2006).

The effect of hypnotic suggestion on event related potential (ERP) components of attention and information processing were studied in 7 high and 7 low hypnotizable subjects as assessed on Stanford Hypnotic Susceptibility Scale. Nineteen channels ERP recording was done during pre hypnotic and during hypnotic state. P300 was elicited with the auditory odd ball paradigm. The P300 amplitude could be reduced by hypnotic suggestion. Perception of stimulus intensity could be altered by hypnotic suggestion. High hypnotizability was closely associated with high P300 amplitude (Singh, 1997).

The next study investigated the EEG and ERP correlates of hypnosis in nonclinical and clinical groups as well as in different subgroups of hypnotisability. Sixty patients of four different diagnostic categories, i.e. Generalized Anxiety Disorder, Phobic Anxiety Disorder, Obsessive Compulsive Disorder and Dissociative Disorder and 30 matched normal controls formed the sample. The EEG and ERP recordings were carried out during baseline and hypnotic conditions. Absolute power in different frequency bands of the EEG and P300 amplitude and latency of P300 were calculated. Information processing capacity was altered or suppressed during hypnosis as evidenced by decreased P300 amplitude, implying their hypersensitivity to stimulus presentation during hypnotic state. Hypnosis was marked by predominant theta activity, implying a state that might be hypo aroused but vigilant to the internal cues and imageries. High hypnotizable subjects had

greater abilities to absorb themselves into the suggestive processes and enter the deeper trance (Kamarajan, 2000).

Forensic Neuropsychology

Neuropsychological deficits in impulsive (N=15) and premeditated (N=12) aggressive prisoners were measured on the functions of response inhibition, response conflict and verbal learning and fluency. Excepting one variable on the Go/No Go test, there was no difference between the two groups on any of the neuropsychological measures. The findings refuted the hypothesis of impulsive aggression as mediated by lack of cortical inhibitory control of overt aggression (Selvi, 2008).

Neuropsychological Rehabilitation

Head Injury

Head injury is associated with morbidity in the form of post concussion syndrome, a constellation of impairments of cognition (poor memory and attention), disturbed emotions (anxiety, irritability and depression) and physical symptoms such as headache, fatigue and body pain contribute to impairments of social and occupational functioning. Slowed information processing, impairments of attention and memory are etiological to post concussion syndrome. Cognitive retraining is a treatment of choice for post concussion syndrome. The treatment improves basic cognitive functions such as information processing, attention, memory and executive functions. The pioneering studies on the efficacy of cognitive retraining in head injury in our country were conducted in the early 1980s (Rao, et.al., 1985). There have been a series of studies in the area since then. The approaches improved basic cognitive functions, using a hospital based or home based approach.

In the initial studies, computer based approach was used to improve speed and accuracy of information processing (Rao, et. al. 1985, 98). The lack of availability of the computer becomes a limitation in the administration of the treatment. Paper and pencil tasks and other non computer based tasks would ensure easy availability of the program. Paper and pencil tasks were devised to improve focused, sustained and divided attention using a multiple resource model of attention. A changing criterion design was used and four patients who had suffered closed head injury with post concussion syndrome underwent the program for one month. Daily sessions lasting for 45 minutes were held. Post retraining there was significant reduction of symptoms and improvement in neuropsychological functions and day to day functioning (Nag & Rao, 1999). As head injury is common in young adult males, due to the high prevalence of road traffic accidents in this age group, often the patient is the bread winner of the family. Hence it is difficult for the patient to come to the hospital daily for treatment. A home based approach was designed to improve the availability of the cognitive retraining program. Tasks which could be carried out either in the home or hospital settings, targeting to improve focused,

sustained and divided attention, information processing and contextual encoding of information were devised. Twelve patients with closed head injury were allotted to three groups with four patients in each..The treatment group underwent the retraining in the home setting supervised by a significant other with weekly supervision by the researcher. Control group I received the same tasks in the hospital while control group II did not receive cognitive retraining. Tasks were performed everyday in 45 minute sessions. Significant reduction of symptoms, improvement of neuropsychological, occupational and social functions occurred similarly in both the groups who underwent cognitive retraining compared with control group II. Cognitive retraining is similarly effective in both the hospital and home settings (Mishra, 1994).

The efficacy of the non computer based cognitive retraining program was tested in a large sample. Forty young adult patients with closed head injury were assigned to a treatment group (N=20) or control group (N=20). Both groups had equal numbers of severe (N=8-9), moderate (N=1) and mild (N=11) patients. The treatment group received cognitive retraining aimed at improving neuropsychological deficits of attention, information processing, memory, and executive functions. Retraining was administered in the hospital setting by the researcher on a daily basis and continued till patients were symptom free. The duration of retraining ranged from 4 to 12 weeks. Compared with the control group the patients in the treatment group had significant reduction of symptoms, improvement in well being, increased return to premorbid status. All the patients of the treatment group returned to gainful employment. Cognitive retraining was effective in severe and mild head injuries (Keshavkumar, 1999).

Child Neuropsychology

Treatment of *head injured children* requires special care as it is a developing brain which is being treated. Ten head injured children between 8-14 years with post concussion syndrome formed the sample. The treatment group of five children underwent 30 sessions of cognitive retraining targeting improvement of information processing, attention regulation, working memory and memory. Five of the children formed the wait listed control group. Post retraining, the treatment group improved in neuropsychological functions. Symptoms also reduced. Cognitive retraining was also effective in the damaged but developing brain (Ajayan, 1998).

Attention Deficit Hyperactivity Disorder (ADHD) is associated with deficits of attention. Seven children between 5-8 years with ADHD formed the sample. Four children underwent cognitive retraining which targeted deficits of attention (resource allocation, perceptual sensitivity and vigilance) and prefrontal deficits (perseveration and susceptibility to interference). Parental counseling and behavioral techniques were employed for both groups. After one month of retraining the treatment group improved in neuropsychological functions and overall functioning,

while the control groups improved only in overall functioning. One month of cognitive retraining did improve cognition even in ADHD children (Agarwal & Rao, 1997).

Remedial education is the conventional treatment for *specific learning disability* (SLD). The efficacy of computer-assisted cognitive retraining as an adjunct to remedial education was examined by comparing the performance of a group of SLD children who received computer assisted cognitive retraining as an adjunct to remedial education with another group of *learning disability* (LD) children who received only remedial education. Post remediation, there were no significant differences between the two groups on measures of reading, reading comprehension, spelling and arithmetic, indicating that the computer based cognitive retraining did not enhance scholastic skills in SLD children (Vidyasagar, 2007).

Cognitive retraining was also tried out in *adolescents with reading disorder*. Eight reading disabled children studying in the classes 7-9 with four children each in the treatment and control groups formed the sample. The treatment group underwent 30 sessions to improve Ideational Fluency, Rhyming, Temporal Ordering, Digit Span, Inter-hemispheric Transfer, Continous Performance Task, Coding, Naming and Phonetic Recognition. Individuals with severe disability required longer time and more intense inputs. Post training the control group did not improve, the treatment group improved in reading speed without committing too many errors. The students also reported improvements in emotions and motivation. (Sadasivan,1997). Dyscalculia in young children was treated with cognitive retraining in another study. Seventeen children with dyscalculia studying between 3rd to 6th standards formed the sample. The treatment group consisting of ten children underwent cognitive retraining wherein neuropsychological functions of working memory, attention and long term memory were improved. Content based arithmetic skills of number production, number comprehension, and procedural components were also sequentially improved. The control group consisting of seven children received remedial sessions for improvement of handwriting skills. The retraining program lasted for 6 to 8 weeks. Arithmetic skills significantly improved in the treatment group in comparison with the control group, indicating that this combination of cognitive retraining and content based training improved arithmetic skills (Bhasi, 2003).

Schizophrenia

Schizophrenia is a severe mental illness, associated with significant cognitive deficits even after clinical symptoms have abated. Medication reduces the positive symptoms but the negative symptoms of apathy and cognitive deficits cause disability. Cognitive retraining is a useful adjunct to medication in schizophrenia. A frequent cause of relapse in schizophrenia is the family dysfunction. A pioneering program integrated cognitive retraining with family intervention and administered it in the hospital setting. Three chronic schizophrenic patients with their family members formed the sample and were subjected to cognitive retraining, targeted

attention, information processing, working memory, response inhibition, comprehension, production of emotion, set shifting, and planning. The family intervention focused on the family assessment, psychoeducation, activity scheduling, handling family expectations, lowering expressed emotion, normalizing family routine, communication skills, problem solving skills, roles of the family members and enhancing social support systems. After the treatment, global and neuropsychological functioning of the patients improved. The general health and psychological well being of the caregivers also improved. Two month follow up on two patients showed deterioration in global functioning even though the neuropsychological functioning was sustained (Hegde, Rao, Raguram, 2007).

Epilepsy

Cognitive deficits are present even in well controlled epilepsy. Deficits of memory and attention are reported by these patients. The twin goals of epilepsy treatment are control of seizures without impairing cognition. Cognitive retraining, targeted, attention, categorization, information processing, planning, organization and encoding of contextual cues. Twenty eight patients each were in the treatment and control groups. The retraining program lasted for 45 days. The treatment group improved in cognitive and psychosocial functioning, while the control group remained status quo (Bharathy, 1998). A single case study of a patient with epilepsy was undertaken in a pre-post multiple baseline design. Cognitive retraining improved attention, memory and emotional status with paper and pencil tasks and real-life activities. Once a week session was held for 6 weeks. Supportive therapy and deep breathing relaxation were also given. Patients reported improvement in his cognitive difficulties (Gupta & Naorem, 2003).

Anxiety Disorder

Efficacy of Neurofeedback training to reduce self reported and observer rated anxiety in generalized anxiety disorder was examined. Three conditions were tried, a) Alpha frequencies were augmented while simultaneously beta frequencies were decreased b) alpha frequencies alone were augmented, c) beta frequencies alone were reduced. The expected changes in the bands of target frequencies were not present in any of the neurofeedback conditions. Self reported or observer rated anxiety did not show differences between the three conditions. However increased sense of wellbeing was associated with augmenting alpha frequencies while simultaneously suppressing beta frequency. Neurofeedback did not change the orientation of locus of control towards internality (Nangia, 1998). The relative efficacy of alpha neurofeedback (increasing alpha and decreasing beta) with theta feedback (increasing theta and decreasing beta) were compared in patients with generalized anxiety disorder. Neurofeedback given over fifteen sessions, was associated with a significant decrease in self reported and observer rated anxiety measures and a significant increase in quality of life measure. The two types of

neurofeedback were comparable in efficacy. However pre and post EEG spectral analysis did not change (Vanathy, 1997).

Development of Neuropsychological Tests

Neuropsychology requires a range of tests to measure deficits in different facets of cognition. Neuropsychological batteries consist of tests which measure a range of cognitive functions mediated by different brain structures or networks. The aim is to elicit deficits in functioning which would then lateralize and localize the brain lesion. The validity and reliability of the battery as a whole is established. In contrast neuropsychological tests measure individual cognitive functions which is mediated by a specific brain structure or network. The validity and reliability of the test is established. Each test in the battery and the individual test requires normative data.

Neuropsychological Battery

Four batteries were established. The NIMHANS Neuropsychology Battery-2004 consists of 21 neuropsychological tests. Internationally accepted neuropsychological tests were chosen and modified to suit our culture if required. Motor speed was measured by the Finger Tapping test, Mental speed was measured by the Digit Symbol Substitution test, Focused attention was measured by the Color Trails test, Sustained attention was measured by the Digit cancellation test. Among executive functions, verbal working memory was measured by the verbal n back and visual n back tests, and the self ordered pointing test, category fluency and phonemic fluency, planning by the Tower of London test, concept formation and set shifting by the Wisconsin Card Sorting Test, response inhibition by the Stroop test. Verbal comprehension by the Token test, verbal learning and memory by the Auditory verbal learning test, visual learning and memory by the Rey's Complex Figure test. The battery was administered on 540 normal adults belonging to both genders, aged between 16-65 years, with illiterates, and literates whose educational levels ranged from 1st standard to Ph.D. The education levels were divided into illiterates, school and college educated subjects. Age was divided into 16-30 years, 31-50 years and 51 -65 years. There were 30 subjects at each intersection of gender x age x education. Education significantly influenced performance followed by age. Gender had the least effect. Percentiles were calculated as normative scores for the 81 variables accrued from all the tests. Test retest reliability was calculated which showed adequate reliability for most scores. Validity was established by the differences in score profiles among head injured (N=182), brain tumors (N=30), epilepsy (N=102) Parkinsonism (N=20) patients (Rao, Subbakrishna et. Al., 2004, George, 2007).

NIMHANS Neuropsychology Battery for Head Injury was constructed by choosing the tests from the previous battery which were sensitive to head injury as well as to make the assessment comprehensive. Eleven tests were so chosen based on the performance of 182 head injured patients. The tests to measure

motor speed, mental speed, sustained attention, verbal working memory (N back), category fluency, planning, set shifting, response inhibition, verbal comprehension, verbal learning and memory, visual learning and memory were so chosen to form the battery (Rao, et. al., 2004).

NIMHANS Neuropsychological Battery for Mesial Temporal Sclerosis was constructed for use in presurgical evaluation of temporal lobe epilepsy patients, which requires neuropsychological assessment in addition to EEG, MRI and clinical findings. Epilepsy surgery being an elective surgery an elaborate presurgical evaluation is mandatory to assess the suitability of the patient for the surgery. Hence a neuropsychological battery sensitive to the lateralization of the epileptic focus is necessary. Twenty-five patients with right MTLE, 26 patients with left MTLE and 25 patients with non-MTLE, between the age ranges of 16-50 years were assessed on a range of neuropsychological functions for obtaining a comprehensive neuropsychological profile. The tests measured the functions of Motor speed, mental speed, sustained attention, verbal & visual working memory, planning, set shifting, response inhibition, verbal comprehension, verbal learning and memory, paired associate learning, logical memory, visual learning and memory with a complex figure test and the design learning test, facial recognition memory, memory for designs constructed using sticks (DCSR test) and a test of egocentric and allocentric space (nine box test). The researcher was blind to the clinical, MRI and EEG findings. MTLE patients were found to be more impaired on learning and memory functions than non-MTLE patients. The left MTLE patients were more impaired on verbal learning and memory than right MTLE patients. On discriminant function analysis, motor speed was found to discriminate the MTLE from non-MTLE and the right MTLE group from the left MTLE group. The final battery included the tests that discriminated MTLE from non-MTLE and tests that discriminated right MTLE from left MTLE; tests on which more than 50% of patients had deficits, as well as tests that fulfilled the criteria of comprehensiveness of the battery (Kavitha, 2006).

NIMHANS Neuropsychological battery for children was constructed to identify brain dysfunction in children between 5-15 years. The growing brain poses a challenge for neuropsychological assessment as brain functions rapidly alter due to maturation. Consequently age appropriate tests require to be chosen and norms are constructed for each year. The tests used in the test battery assessed frontal lobe functions such as motor functions, expressive speech, executive functions of verbal and design fluency, verbal and visuospatial working memory, planning and shift of set; parietal lobe functions such as visuoperceptual ability, visuo conceptual and visuo constructive ability, reading, writing and calculation skills, focal parietal signs; and temporal lobe functions such as verbal comprehension, verbal and visual learning and memory. The tests were administered to 400 school going children half of whom were girls. A clinical sample of 16 children with supratentorial tumors, 18 with intractable epilepsy and 15 with diffuse brain damage were assessed to establish the validity of the test battery in terms of localization and lateralization

of brain dysfunction. The 5th percentile was the criterion for a deficit. The test-retest reliability of all the tests included in the test battery was good. The battery was able to localize and lateralize brain dysfunction. The relation of age with neuropsychological functions was non linear. Age related rate of growth was different across the neuropsychological functions. The functional connectivity was found to develop gradually with bivariate relationships such as fronto-temporal and parieto-temporal relationships, and it was significantly present only in older children. The neuropsychological functions appeared to be more discrete in younger children and more interdependent in older children. (Kar et al., 2004).

Adaptation and Standardization of WMS-III: Wecshler Memory Scale is widely used internationally to assess memory dysfunction. The following subtests of WMS-III were modified to suit our culture, Information and Orientation, Logical Memory, Faces, Verbal Paired Associates, Family Pictures and Word Lists. This modified WMS-III was administered on 240 normal volunteers classified into equal number of males and females. In each gender there were thirty school educated and thirty college educated persons. A deficit was defined as a score falling below the 15th percentile of the normal distribution. Eighty normal subjects were retested after six weeks and the test retest reliability ranged from 0.4-0.9. The test was administered to a clinical sample of intractable epilepsy patients (N=18; 10 Right & 8 Left MTS), head injury cases (N=20) and patients with Alcohol Dependence Syndrome (N=20). The profiles of the clinical groups differed from the normals and between each other. But the sensitivity was moderate in the intractable epilepsy group but low in the head injury and ADS groups. Specificity was high and ranged from 60-100%. Factorial validity yielded four independent factors of logical memory, general memory, associative learning and face recognition (Pushpalatha, 2004).

Kolkata Cognitive Screening Battery was developed to assess the cognitive function of the elderly normal persons between 50-95 years. The battery was administered on 745 healthy urban subjects. Women scored lower on all parameters. Education was correlated with better performance. Age related cognitive decline was observed unevenly across the cognitive parameters (Das, et. al., 2006).

Neuropsychological Tests

Individual neuropsychological tests which measured specific functions were standardized.

***Tests of Attention*:** Figural visual scanning test and the Auditory Target Detection test were standardized on a normal sample of 60 subjects (30 males and 30 females) in the age range of 16-30 years and education ranging from 1 to 10 years. Norms were established with the criterion of deficit being a score below 15th percentile of the normal mean. Twenty subjects were retested after one month which indicated adequate reliability. The tests could differentiate between normals, patients with unilateral brain lesions (Thomas, 2005).

***Tests of Inhibition*:** Inhibition is the capacity to stop an ongoing motor response, thought or emotion. Inhibition or inhibitory control is mediated by the dorsolateral, orbitofrontal and anterior cingulate regions of the brain. Norms were developed on 80 males and 80 females between the ages of 16-30 years with 1-10 years of education, for the Go/no go test and stop signal test which measured the ability to stop an ongoing response. Test retest reliability ranged from 0.56-0.89. Discriminant validity was established by comparing the performance of ten patients with frontal tumors and 20 patients with unilateral lesions with that of normal controls. A score below 1 SD or the 15th percentile of the distribution of the normal subjects was a deficit. Sensitivity of Go/no go test was 70% while that of stop signal test was 80%. Specificity was 93% (Devender kumar, 2000, Thomas, 2005).

Facial recognition memory test: measured memory for faces. Face recognition is mediated by the right temporal lobe, hence this test is useful to detect damage in the right temporal lobe. The faces were photographs of twelve males and twelve females who posed a neutral expression. After the first exposure the faces were mixed with another twenty four photos and recognition of the previously seen photos was required. Norms were established for males aged 15-50 years. Split half reliability was 0.46. Criterion of deficit was a score which was below 15th percentile of the normal mean. The test could differentiate between normal and twenty patients with head injury indicating adequate discriminant validity (Sanjay kumar, 2002). Norms were also established for females aged 15-50 years with the same criterion of deficit. Split half reliability was 0.82. The test could differentiate between normals and patients with temporal lobe epilepsy (Kavitha, 2006). DCS-R test is a measure of constructional capacity using sticks. The patient constructs designs which are later recalled. The test is useful for identifying constructional apraxia and visual memory to detect dysfunction of the parietal and right temporal lobes respectively. Norms were developed for both men and women aged from 18-45 years in the form of percentiles. Criterion of deficit was a score below 15th percentile of the normal mean. Test retest reliability for the different variables ranged from 0.46 to 0.81. The test could differentiate between normals and patients with temporal lobe epilepsy (Kavitha, 2006).

Tests of Parietal Lobe functions: Parietal lobe mediates visuo spatial perception and visuo constructive abilities. Deficits in these functions distort the construction of the sensory template of the world. Bender-Gestalt Test (BGT), the Stick Construction Test and the Three dimensional Block Construction Test were standardized on one hundred and twenty, school-educated normal subjects with thirty males and thirty females in each age group of 16-30 years and 31-50 years. The clinical sample consisted of 15 patients with frontal lesions and 15 patients with non-frontal lesions. Criterion of deficit was score below 15th percentile of the normal distribution. Thirty two normal subjects were retested after 6-8 weeks and the test retest reliability was adequate. Discriminant validity was adequate as known by comparing the performance of the patients with that of the normals (Kashyap, 2006).

Test of Arithmetic Ability: Dyscalculia affects 6% of children. Test of arithmetic ability of Shalev a well known measure of arithmetic ability was administered on a sample of 284 children studying in standard III to VI. The test consists of three parts measuring the different facets of arithmetic with a range of difficulty. Test retest reliability after a span of 8 months was 0.76 for the total score. A score falling below the 5th percentile or below 2 S.D. was defined as a deficit. Standard wise cut off scores were obtained to identify Specific Learning Disorder for Arithmetic (Bhasi, 2003).

Studies on normals

Functional Neuroanatomy of Perceptual load

The functional neuroanatomy of perceptual load was studied with 3 tesla fMRI. The task consisted of presentation of neutral words varying in set size from 2 words to 4 to 6 words. The Visuo motor and verb generation tasks were used to validate the activations obtained in the neutral word task. Predominantly motor activity was seen in set size 2. Increased left lateralized activity was observed as perceptual load increased. Different nodes in the fronto-parietal attention network were activated for set sizes 4 & 6. Posterior parietal activations were greater in set size 4 indicating a recruitment of spatial attention. Dorsolateral prefrontal activations were greater in set size 6 indicating the recruitment of executive attention (Das, 2007).

Meditation

Non linear dynamics of the meditative state was understood using the measures of fractal dimension 'D1', correlation dimension of the attractor D2, and complexity dimension 'C', Lyapunov exponent lambda 1. Vipassana meditation was associated with decrease in 'C' as compared to other measures. This is indicative of high coherence across channels and maximum spread of activity originating from the focal region of the minimum locus (Pradhan, et. al, 2000). Experienced practitioners of Bramhakumari Raja Yoga meditation with practice of over 3 years participated in a 1.5 tesla fMRI study. Meditation was associated with increase of heart rate, bilateral activation of prefrontal lobes extending laterally in 4 subjects and right frontal lobe activation in 3 subjects. The left occipital lobe was activated in two subjects with over 15 years of meditation practice. Directed attention and visual imagery explained the activation. Meditation is an alteration of consciousness. Brain changes are associated with meditative practices. Sudarshan Kriya Yoga is a yogic practice comprising of mudra pranayama, sudarshan kriya (cyclic breathing) and focused meditation (Sahaj Samadhi). The change in preattentive processing was examined at the end of each of these three stages using mismatch negativity as the measure of pre attentive processing. The effect of meditation on standards and deviants were also examined. EEG was recorded from 64 channels on 10 long-term practitioners of Sudarshan Kriya Yoga and 10 normal controls. MMN was elicited by infrequent (20% of trials) 540Hz

tones presented together with frequent (80% of trails) 500Hz tones. MMN was recorded pre and post each o the 3 stages of sudarshan kriya yoga. The controls were asked to relax and read a book, while MMN was recorded at comparable intervals. The amplitude of MMN was higher in meditators overall. In meditators MMN was higher after meditation as compared with breathing. Meditators had higher peak amplitudes for the infrequent tones. The meditative state of consciousness lead to restructuring of the perception i.e. enhanced perceptual and preattentive processing. Meditation induces definitive state changes and possibly trait changes in frontal lobe function (Srinivasan & Baijal, 2007).

Conclusions

During the period under review the following developments have taken place in our country:

1. Neuropsychology with the lesion method has been the dominant force in understanding brain behavior relationships in our country during the period under review.

2. Cognitive Neuroscience with the functional brain mapping methods of EEG and ERP has developed well and have been used to understand psychiatric, neurosurgical conditions.

3. The newer technique of fMRI has been introduced.

4. Development of neuropsychological tests with Indian norms has flourished.

5. Neuropsychological rehabilitation has matured and is routinely used for patients.

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