PREFRONTAL CORTEX-FROM 'SILENCE TO SURGE'

The frontal lobes are phylogenetically the newest neurostructures making up about 40% of the surface and the mass of cerebral hemispheres. They are unique in cytoarchitecture, functions and electro physiological response. Their development is not complete until 9-11 years of age in the humans. Only in recent decades our knowledge of their role, in diverse and complex forms of behaviour and integrative functions have been furthered. Luria (1973), considered frontal lobes as the 'summit of the brain's hierarchy'. Fuster (1980) saw the frontal cortex as a kind of 'superordinate functional system responsible for the formation of temporal structure of behaviour with a unifying purpose or goal'.

The rostral part of the lobe constitutes 'prefrontal cortex' (PFC) a term coined by Ferrier (1887). There are three subcontinents of frontal lobe—dorsolateral, orbitofrontal and mesiofrontal (limbic). PFC is marked by the presence of granular layer (granular cortex) which is absent in motor areas (agranular cortex). PFC was non responsive to electrical stimulation unlike other cortical areas; hence the term 'silent areas'. The granular layer establishes multitude of circuits with other areas of brain necessary for PF cortical integrative 'office'.

Earlier data on frontal lobe functions were derived from noting features consequent to lesioned lobes—from trauma (accidents), tumours and prefrontal leukotomy. Three sets of 'frontal lobe syndrome' features were described by Benton (1968) comprising personality changes, intellectual 'deficit' and 'adynamia'. 'Pseudo depressive and Pseudo psychopathic' syndromes were also described resulting from lesions in the dorsolateral and basofrontal areas respectively. However, recently the term "dysexecutive syndrome" (Baddeley, 1986) has come into usage that includes a major part of the frontal features.

This results from the impaired 'executive function of the PFC. The later receives afferents from many areas of the brain and thereby 'executes' the ultimate behaviour; it serves as a 'final outflow'. The changed personality of 'frontal lobe syndrome' is best illustrated by the case of Phineas Gage, an 'efficient and capable' foreman who was injured on September 13, 1848, when a tamping iron accidentally blew through the basofrontal region of the lobe. The consequence was: 'his mind was radically changed so that his friends and acquaintances said that he was no longer Gage' (Harlow, 1868).

The understanding of the functioning of the prefrontal cortex continues to be a challenge. The newer techniques assessing PFC functions have contributed towards unravelling complexity (e.g., study of regional cerebral blood flow, oxygen consumption, glucose utilisation, Wisconsin card sorting and stroop test and neuro imaging procedures). From these and other studies it is suggested that PFC enables forming and shifting abstract concepts, to code the temporal order of information, to sustain attention, to modulate mood and keeping information 'active' over a period of time to serve as 'working' memory (Grafman & Tamminga, 1995). Also from these studies has emerged the concept of 'hypofrontality' in schizophrenia and depression. This finding however has failed to endure. Molecular genetics, molecular biology, neurochemistry, neuroanatomy and cognitive neuroscience have found application in understanding neural substrate of mind and its disorders. One can now visualize brain chemistry in vivo which informs us about the patterns of chemical disruption in diseases. However, a single abnormality can seldom be equated with a single diagnosis. Nor can it be
diagnostic. There is no gold standard as yet for psychiatric diagnosis.

Traditionally executive cognitive function (ECF) deficit is associated with frontal cortical lesions. Executive control includes goal selection, formulation of an action plan, sequencing of steps, initiation, monitoring outcome, and inhibition of distracting or competing influences over behaviour. Each of these components is essential for completion of complex task. Executive deficits result from lesions of prefrontal cortex or and subcortical connection. The former include the three regions of prefrontal cortex, that are linked through the striatum, globus pallidus with the thalamus. The fibre connection from thalamus to prefrontal cortex complete subcortical circuits. These circuits ('frontal system') control by inhibition or stimulation the frontal cortical regions and thereby the frontal lobe behaviour. There are regional differences in sequelae from different frontal cortical lesion (Fuster, 1989). Dorsolateral prefrontal lesion leads to impairment of planning, hypothesis generation and control of behaviour. The Wisconsin card sorting test and verbal fluency specifically tests this area. Orbitofrontal lesion results in impaired insight, impaired judgement, and impulsivity (Piribram & Melges, 1969). Mesiofrontal anterior cingulate lesion leads to indifference (adynamia) consisting of poor spontaneous speech generation or behaviour with correct response to prompting. The 'Stroop Test' tests the integrity of these areas.

Frontal lobe is shown to be involved in an array of psychiatric disorders (David, 1992) e.g., personality disorders, obsessions, delusions, mania, hyperkinetic disorder, catatonia and hysteria.

In depression (Robinson et al., 1984) the psychomotor slowing, the dysfluency of speech and the failure to respond to the environment reflect frontal features. Depression is associated with focal dorsolateral and orbitofrontal metabolic defect demonstrable by PET and SPECT imaging (Baxter et al., 1987). Frontal cortical stroke especially of left side causes depressive syndrome clinically indistinguishable from functional mood disorder (Lipsey et al., 1984) or in its response to tricyclic antidepressant. Frontal metabolic deficit are reported in Alzheimer's disease and other dementing illnesses (Fukuda et al., 1990).

In schizophrenia (Goldberg, 1985; Weinberger et al., 1986; McGrath, 1991) the avolition, poor judgement, lack of self-care, inappropriate behaviour, poverty of thought, poor insight, and lack of reason strongly correlate with frontal dysfunction (David, 1992). Schizophrenia is shown to be associated with frontal lobe structural changes, metabolic defects and failure on 'executive testing' (Taylor & Abrams, 1984; Weinberger et al., 1986). This has led schizophrenia being called a 'dysexecutive syndrome,' a model proposed by Zec et al. (1988).

A note on PFC and neurotransmitter radioligand techniques have now given place to 'cloning' to study the receptors. The important consequence of PFC research has been the emergence of novel theories regarding the pathophysiology of schizophrenia which are not limited to a single system as hitherto enunciated in the dopamine hypothesis. The new theory involved complex cellular interaction within PFC and its connection to other cortical and subcortical areas. The diversity of the symptoms of schizophrenia inevitably should shift the focus to a concept of multi-system pathology. Earlier, hyperactivity of subcortical dopamine system accounted for the positive symptom, leaving the negative symptoms unexplained. In the light of newer findings, 'dysfunctional prefrontal cortex' may play a role in the causation of negative symptoms and cognitive deficit. Dopamine theory, in its earlier form almost on the verge of abandonment has regained importance with the understanding of PFC systems. The atypical antipsychotics exert therapeutic efficacy by enhancing dopaminergic activity in the PFC (Matsubara et al., 1991) while the conventional ones target subcortical hyperdopaminergic activity. A typical antipsychotic is also a potent antagonist at multiple serotonin receptor subtypes.

A study of suicide victims revealed frontal cortex 5 HT1A receptor density to be higher in nonviolent suicide victims than in controls. Postmortem studies of brain of the depressive
suicidal patients have also revealed increased cortical 5HT$_{2A}$ receptor levels (Stanley & Mann, 1993). Decreases in 5HT$_{2A}$ receptor levels have been correlated with successful antidepressant treatment (Yates et al., 1990).

Knowledge about the neural mechanisms of the complex behaviour has moved on from the area of 'silence' to that of 'visibility' due to advances in technology. This is but a step towards complete understanding.

A. Venkoba Rao

REFERENCES

Baddeley, A. (1986) Working memory, London: Oxford University Press.

Baxter, L.R., Phelps, M.E. & Mazziotta, J.C. (1987) Local cerebral glucose metabolic rates in obsessive compulsive disorder: a comparison with rates in unipolar depression and in normal controls. Archives of General Psychiatry, 44, 211-218.

Benton, A.L. (1968) Differential behavioural effects of frontal lobe disease, Neuropsychologia, 6, 53-60.

David, A.S. (1992) Frontal lobology-psychiatry's new pseudoscience. British Journal of Psychiatry, 161, 244-248.

Ferrier, D. (1868) Functions of the brain, 2nd Edn, London: Smith, Elder.

Fukuda, H., Kobayashi, S. & Okada (1990) Frontal white matter lesions and dementias in lacunar infarction. Stroke, 21, 1143-1149.

Fuster, J.M. (1980) The prefrontal cortex, New York: Raven Press.

Fuster, J.M (1989) The prefrontal cortex, 2nd Edn., New York: Raven Press.

Goldberg, E. (1985) Akinesia, tardive dyskinesia and frontal lobe disorder in schizophrenia. Schizophrenia Bulletin, 11, 255.

Grafman, J. & Tamminga (1995) Images in neuroscience. American Journal of Psychiatry, 152, 163.

Harlow, J.M. (1868) Recovery from the passage of an iron bar through the head. Publication of the Massachusetts Medical Society. 2, 327-347.

Lipsey, J.R., Robinson, R.G. & Pearson, G.D. (1984) Nortryptamine treatment for post stroke depression. Lancet, 1, 297-300.

Luria, A.R. (1973) The working brain, alien labo. London: The Penguin Press.

Matsubara, S., Arora, R.C. & Meltzer, H.Y. (1991) Serotonergic measures in suicide brain: 5HT 1A binding sites in frontal cortex of suicide victims. Journal of Neural Transmission, 85, 181-194.

McGrath, J. (1991) Ordering thoughts on thought disorder. British Journal of Psychiatry, 158, 307-316.

Piribram, K.H. & Melges, F.T. (1969) The psychophysiological basis of emotion. In: Handbook of Clinical Neurology. Vol.2, (Eds.) Vinken, P.T. & Bruyn, C.W., Amsterdam.

Robinson, R.G., Kubos, K.L. & Starr, L.B. (1984) Mood disorders in stroke patients: The importance of location of lesions. Brain, 107, 81-93.

Stanley, M. & Mann, J.J. (1983) Increased serotonin 2 binding sites in frontal cortex of suicide victims, Lancet 1, 214-216.

Taylor, M.A. & Abrams, R. (1984) Cognitive dysfunction in Mania. Comprehensive Psychiatry, 27, 186-191.

Weinberger, D.R., Berman, K.F. & Zec, R.F. (1986) Physiological dysfunction of dorsolateral prefrontal cortex in schizophrenia. I. Regional cerebral blood flow evidence. Archives of General Psychiatry, 43, 114-124.

Yates, M., Leake, A. & Candy, J.M. (1990) 5-HT 2 receptor changes in major depression. Biological Psychiatry, 27, 489-496.

Zec, R.E., Ganobach, J. & Meyers, D. (1988) Improved adaptive functioning in schizophrenic patients using the executive board system. Journal of Clinical Experimental Neuropsychology, 10-20.