

## Editorial

### NEUROSCIENCE IN THE PAST - LIKELY TRENDS IN FUTURE

The scientific study in neurosciences has undergone rapid development in the last millennium. The subject has emerged as a great challenge, engaging the capabilities of creative offering the promises of better future towards the understanding of neurological disorders. There has also been an attempt in the understanding of human nature in cognitive behavioural sciences. However, still much remains to be accomplished in the structural componentry of the brain. Some of the important technical developments in the last millennium and likely trends in the forthcoming years are being projected here. We also look into the most intriguing questions of our mind, how does the brain understand itself? The subject has been discussed under following headings :

- (a) Tissue Slice, techniques.
- ✓(b) Neuro-imaging
- (c) Neuropharmacology.
- (d) Neuropsychopharmacology.
- (e) Genetics in neuroscience.
- (f) Neural transplants.
- ✓(g) Neurophysiology

#### TISSUE SLICE TECHNIQUE IN NEUROSCIENCE

Towards the middle of last century, Virchow reasoned that the brain, like all other organs must contain connective tissue. Examining tissue by gross dissection and under microscope, he recognised the 'neuroglia'. It took many decades of patient work and better staining methods used by the leading histologists of the latter half of 19<sup>th</sup> century which lead to the use 'neural cultures'.

#### NEURAL CULTURES

Techniques yielding tissue are used to examine isolated neural systems, which have been deprived of blood supply from their normal vasculature. That neural tissues can perform in isolation was first shown in slices of neo-cortex of rat, guinea pig and in cat.



The first experimental use of neural tissue cultures in neuroscience research was reported by Ross, Harrison while studying the growth of nerve fibres. Their elegant demonstration of the individuality of nerve cells by direct observation was the first development of this century.

Organised neuronal cultures have been used for basic studies in many areas of developmental neurobiology including synaptogenesis. Microiontophoretic horse-radish labelling, has been used for mapping of characteristic sensory evoked responses generated in various CNS target tissues. Arrays of neurons growing in a culture chamber on a thin glass slide, provide a remarkable window to facilitate direct microscopic observation of some of the intricate cellular networks. Techniques are available for preparation of neuronal cultures of varying complexity.

Neural tissue cultures provide a valuable model system for studies of various cellular mechanisms, such as EEG and neuronal plasticity in learning and memory. Finally, CNS cultures permit *in vitro* analysis of problems in regeneration after nerve injury and selective degeneration of specific types of CNS neurons as occurs in lateral sclerosis (ALS), Alzheimer's disease and other neuro-generative disorders.

#### NEURO-IMAGING

Then came the techniques of neuro-imaging. A new method of forming images from X-rays was developed and introduced into clinical use by the British physicist Godfray Housefield, in 1972. Neuro-imaging,

is a term used to describe the *in-vivo* depiction of normal and pathological CNS structures. A true representation of the brain became feasible in 1972, when Housefield introduced X-ray Commuted Tomography (CT) also know as Computer Assisted Tomography (CAT).

*Technical Aspects:* In computed tomography, the X-ray output is collimated to a very narrow beam. While passing through the patient it is partially absorbed, and the remaining photons of X-ray beam fall on radiation detectors instead of X-ray film. The information is fed into a computer which produces different readings and different images.

In addition, to non-invasive demonstration of CSF cavities, CT also gave the capability to differentiate the various brain structures. It is remarkable not only for specific capability to portray fine anatomical details, but also a technique for imaging of slices by the mathematical reconstruction of data, obtained from multiple projections. On the same lines further newer techniques have developed ECT, PET, SPECT, NMR, MRI, UCT.

The first NMR experiments were described by Bloch and Purcell independently in 1946, thus, paving the way for the development of NMR spectroscopy. A radiofrequency field applied at the same frequency as the processing nuclei excites small protons from a lower energy level to higher energy level. This release of energy can be recorded and indicates that resonance has occurred.



Due to their high resolving power one can detect extremely small amounts of  $\text{Ca}^{++}$  in various syndromes, tumours, inflammatory processes, and cerebral infarcts, brain tumours, extrapyramidal disorders. The sensitivity of the MRI, in the detection of CNS lesions is superior to that of CT. This breakthrough, which was made possible by the use of computers, soon led to the development of Emission Computed Tomography (ECT), Positron Emission Tomography (PET) and Single photon Emission Computed Tomography (SPECT) and Nuclear Magnetic Resonance (NMR). The resolution of the proton NMR images of the brain allows to visualise most of the newly developed finer structures of the brain, with great accuracy.

#### NEUROPHARMACOLOGY

Sine the beginning of neuroscientific research at the molecular level and behavioural level, various neuropharmacological agents have been discovered. The receptor concept of drug action has revolutionised the production of new-neuroactive drugs. With the availability of ligands of high specific radio-activity for receptors it is now possible to rapidly screen new compounds. In addition, with the development of recumbent DNA technology and its ability to isolate, identify genetic material, there has been a substantial further advancement.

#### NEURO PSYCHOPHARMACOLOGY

During the last few decades various methods have been used to localise and characterise neurons on the basis of transmitter substances. The first

attempts were made by Koelle and Friedenworld using Ach staining. These immunofluorescent studies were used to visualise peripheral, noradrenergic and DA neurons, and map some of the major neurotransmitter pathways.

The number of putative transmitter candidates, now exceeds forty. Besides there has been the discovery of more peptides, which act as chemical messengers in the central nervous system. Recent discovery of the action of L-glutamic acid and its high uptake has made them liable as putative neurotransmitter. The opioid peptides have attracted great attention. A bewildering number of encephalins have been identified. The peptide producing cells of the brain have been regarded as a separate division like the autonomic and somatic nervous system. The NMDA receptor complex has lately been excessively characterised physiologically and its distribution in the CNS has been traced.

Lastly one of the most recent discoveries has been that the dendritic membrane of the large neurons in the central nervous system generate  $\text{Ca}^{++}$  dependant action potentials. The evidence is strongly in the case of Purkinje cells of the cerebellum and the pyramidal cells of hippocampal cortex.

#### GENERICIS IN NEUROSCIENCE

Heredity has been thought to play a role in the etiology of Alzheimer's disease (AD).

Most of the properties of the nervous system are built into it during embryonic and neonatal development. Important modifications of the nervous system, occur



as the result of experience. Hundreds of various types of neurons are present and are receiving multiple synaptic connections, which endow them with precise and complex receptive field properties. This great work, the reconstruction of the functioning cortex is coded somehow in DNA.

Through such genetic and molecular studies it may be possible for us to know about the specificity of the genes functions. Mutations may be used as biological tools.

#### NEURAL TRANSPLANTS

The first known reports of attempt to graft nervous tissue go back to Thompson, Forrsman and Saltykow, around the turn of the century. They grafted or reimplanted cortical tissue from adult donors into the cortex, but met with very poor survival. Later Ranson and Tolkow (1900) reported successful survival of peripheral nervous tissue, from neonatal donors in to adult brain.

In 1976, R.D. Lund and colleagues demonstrated that intracerebral grafts of developing CNS tissue can establish extensive afferent and efferent connections, with the mature host brain. The regions most extensively studied include the neocortex, the visual system, the hippocampus and cerebellum. This research has contributed significantly to the conceptual change that has taken place over the last few years.

Current intracerebral transplant research includes:

1. Studies in developing animals, associated with problem of neuroembryology.
2. Studies on the ability of neural grafts to promote regeneration in the CNS.
3. Graft induced restoration of brain or spinal cord circuitaries.
4. Intraocular grafting.
5. Studies on the grafts in neural tissue.

#### NEUROPHYSIOLOGY

- (a) *Synaptic Transmission*: In 1966, blockage of the action potential by tetrodotoxin, was shown indicating that there was a release of the transmitter from presynaptic terminal. Using micro-electrode voltage clamp technique, the properties of the presynaptic, calcium, sodium, and potassium conductance were shown. The fact that each of the ionic species  $\text{Na}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{H}^+$  and  $\text{Cl}^-$  has an inside concentration different from that of the extracellular medium and that this potential became well known and is given by the Nernst's equation.

$$E = (RT / 2F) \log \frac{(ci)}{(co)}$$

- (b) *Stimulus and Event Related evoked potentials*: Certain types of electrical potentials can be recorded from the human scalp, which can be elicited by sounds or visual stimuli presented at regular intervals. These stimulus related



EPs indicate functional integrity of sensory pathways. Another particular important human ERP, with a latency of 300 indicate cognitive functions of the brain.

(c) *Multi- sensory Neurons*: Neurons that can be excited or modulated by input from more than one sensory system are present in the nervous system.

(d) *Neural Coding*: Coding of information in the nervous system, by means of neural signals, either chemical or electrical which by acting on the various receptors lead to information processing.

(e) *Neuronal Networks*: Oscillating systems, representing a function of networks, and phenomenon of reciprocal innervation, lateral inhibition and amplitude signals has been shown.

(f) *Other developments*: Chief developments that came up were the regulation of feeding behaviour, drinking behaviour, memory consolidation, long term potentiation, sleep mechanisms and correlation with EEG learning and conditioned behavioural responses.

(g) *Stereotaxic Surgery*: Involving the location of specific structures within the brain, using the three dimensional approach, became excessively a popular, technique, during the last century.

#### FUTURE TRENDS IN NEUROSCIENCE

No comprehensive survey of the modern research is possible here, but a few brief

examples, may serve to indicate some of the forthcoming manoevers.

1. More information is expected on the receptor and gating mechanisms.

2. Very little information is available on the way hormones and peptides regulate the memory systems, more is likely to come.

3. Nerves and synapses in the human brain differ from this that make up the central nervous system of animals. We are consciously aware of a tiny fraction of intricate self-regulated processes that go to make up the human mind. We cannot describe another person's subjective experiences. We are more likely to be aware of some of the activities of others than ours. The existence of gravitational bonds, chemical bonds, and magnetic fields are deduced from such effects.

4. The role of conscious thinking in behaviour is likely to be exemplified. Psychobiology will be the most motivating force in the study of human mind. Neuroscience and psychobiology will probably be combined. The problem of computability in the human brain is likely to unfold itself. Sensory and motor coding will gain better perspectives. Neurochemical and behavioural relationships will be better understood.

5. Modern of philosophy is likely to be most important contributor to neurophysiology. Religious, social and economic values will be better



understood, and the science perhaps finally dealing with humanity will be the chief outcome of the forthcoming millennium..

6. Intelligence is still the most distinctive behavioural attributes of homo sapiens, and still the most controversial. Mental capabilities involved in these range of differences will be sought for. What are the biological foundations of intelligence? Precise linkages in neural systems are most distinctive features of human capabilities will be of primary importance.

7. New technical possibilities are likely to open up in studies of neuron, morphology, chemistry and function. Knowledge representation in the human brain will be studied by use of computers.

8. Molecular biology will open up new avenues on information systems of the human brain. Newer techniques to study the expression of neuron-specific polypeptides and proteins in defined cells will be made available.

Finally, the mystery behind human existence and mind will lay unfolded.

### Suggested Reading

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