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Report on the Brain-Storming Session on Neurobiology held at NIMHANS, Bangalore in November 1984.

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Preface

In its endeavour to promote research in identified thrust areas in life sciences, the Department of Science & Technology, at the initiative of the Programme Advisory Committee on Neurobiology, and in view of the recommendations of the Science & Engineering Research Council (SERC) supported the organization of a Brain Storming Session on 'Neurobiology' at the National Institute of Mental Health & Neuro Sciences, Bangalore - 560 029 from 21-23 November, 1984.

This Brain Storming Session on Neurobiology was organized by Prof. G N Narayana Reddy, Director, NIMHANS primarily with the aim of ascertaining the areas in which work is being done in Neurobiology in India, to explore the facilities and potentials available for future research and to identify new areas and centres for developing research and scientific activity in the area of Neurobiology.

A major achievement of this Brain Storming Session was the identification of specific areas and problems for investigations in Neurobiology. A report on the Brain Storming Session prepared by Dr. P M Bhargava former Chairman of this Advisory Committee is being published with the hope that it will help in creating awareness about the areas in which research can be initiated in Neurobiology. As a result of the discussions held during the Brain Storming Session, a major programme on Neural Transplantation has been initiated with DST support at All India Institute of Medical Sciences under Prof. P. N Tandon. Other institutes where work in the area of Neurobiology is being actively pursued with DST support are Madurai Kamaraj University, Indian Institute of Science, Bangalore; and Christian Medical College, Vellore . It should enable younger scientists to take the initiative of working in some of the areas identified at this Brain Storming Session and focus on the need to develop coordinated research programmes in Neurobiology.

I. Problems and attitudes that have come in the way of initiating and pursuing first-rate work in the area of neurobiological sciences

(a) We have, by and large, not yet learnt to think in terms of a question but continue to think, in the traditional mode, in terms of disciplines. Modern biology is largely question - or problem-oriented where one learns all that is needed to solve a problem; the solution often requires acquaintance with more than one discipline.

(b) It is not yet adequately realised in our country that the challenge in modern biology demands an

understanding of the basic fundamentals of physics, chemistry and mathematics, and of a variety of biological disciplines, such as immunology, genetics, virology and physiology. Multi-disciplinary approach does not mean merely getting together people who are specialists in their own area but unaware of the other areas. Such an approach, for it to be viable, requires getting together people who, while being specialists have a conceptual understanding of the whole problem, and can work together, with each one understanding, in principle, what the other is doing and why, and appreciating each other's difficulties, success and failures. There cannot be a discipline hierarchy in such an approach in which all the participants are equal partners in a venture, no one being more equal than the other. One of the main reasons why this has not happened in our country, is the nature of our educational system in which knowledge is compartmentalised.

(c) Our scientists have not realised that a question is a viable question only if for answering it, means are available or could be made available within the framework of existing knowledge; and that hypothesis is a hypothesis only if it is testable. We also do not often realise the difference o between a trivial question and an important question. We shy away from answering 'difficult' questions. Our attitude being that if it has not been done 'elsewhere', how could we do it here. This attitude is not conducive to producing leaders in science. We do not realise that it is only when we endeavour to handle difficult questions that we can hope to acquire world leadership. We need to be driven by the ambition and desire to acquire such world leadership in science, specially neurobiology where their is still so much to be done.

(d) We still do not seem to realise that creativity is not the prerogative of any particular age or sex; consequently we set up age or position hierarchies. Such hierarchies are totally non-conducive to first class creative effort.

e) As already implied above, our objectives of investment in the area of neurobiology (as indeed in many other areas) should be to:

(a) acquire world leadership in this area by solving some of the major unsolved problems;

(b) find practical solutions to some of our local problems.

n the process of doing the above, we would naturally generate new knowledge. To do the above, our scientists must obviously know what the state of art in the world as well as in India is; they must be specially aware of what is available within the country in terms of expertise, materials such as chemicals and instruments.

II The achievement of the Brain Storming Session

We believe that the recognition of the above lacunae was an important achievement of the Brain Storming Session, as such awareness is always a first step in finding solutions to a problem. The other major success of the Seminar was

(a) the identification of some of the basic requirements which can be met in the country for progress in several areas of neurobiological sciences, and

(b) identification of specific areas and problems for investigations, as detailed in the next two sections.

III Some basic requirements

(a) The expertise and facilities for basic techniques such as hybridoma technology, use of radioactive isotopes, techniques of micro-fractionation (e.g. two dimensional gel runs of proteins) and micro-estimation, and use of small computers, should be available in virtually every institution. These facilities and techniques must not be regarded as exotic. They are, indeed, within the

intellectual and financial means of every institution and every group that intends doing worthwhile pioneering research in neurobiology. They should be looked at only as techniques and as means to an end, not as the end itself. In other words, there should be no "section" on hybridoma technology or radioactivity isotope usage, in the institution.

(b) We need to set up a brain-bank and a Central Neurosciences Information Bureau (CNIB). The ICMR could be persuaded to do the former and the DST the latter, through an institution such as the NIMHANS at Bangalore. The CNIB could bring out a newsletter made up solely of contributions sent by subscribers, and designed to serve as a medium of communication for the exchange of ideas, the raising of questions and a source of information regarding techniques, etc.

(c) Adequate state-of-art facilities for positron emission tomography (PET) and whole-body NMR studies, should be made available at two or three selected places in the country, which could be used by workers all over the country. At places and institutions where these techniques are made available, there should be accommodation for visitors to stay and laboratory space for them to process their material. All this may need an investment of about Rs. 10 crores which would be a trivial investment at the national level in the next plan compared to the likely return. The DST and the ICMR could share this expenditure.

(d) Suitable intensive short-term training courses in neurobiology (lecture courses and laboratory training where possible) should be arranged periodically (at least once a year) under the auspices of the DST. A committee consisting of two or three persons (say Dr. V Nanjundiah & Dr. P N Tandon) could prepare a plan and submit it to the DST for their approval.

IV Some areas / specific problems identified which deserve attention of workers in the field of neurobiological sciences in the country.

(This list is only illustrative and must not be taken as being exhaustive. The items listed here are not arranged in any specific order).

- Development of immunodiagnostics for diseases of the central nervous system (CNS) and peripheral nervous system (PNS), such as neurotuberculosis, neural leprosy and neurocysticercosis. (This would require identification of disease-specific markers.)
- Neural transplantation.
- Neural prosthesis.

Tissue culture of various kinds (e.g. organ culture, monolayer culture), using various types of cells derived from or related to the nervous system. Development of our own cell lines from both diseased and normal tissue, and studies such as the following using the above techniques

(a) Somatic cell hybridisation

(b) Receptor-ligand interactions

(c) Interaction between neural and glial cells

- Developmental neuroanatomy in humans using material obtained in MTPs.
- Developmental anatomy in cattle : use of abnormalities to study the relationships between structure, function, chemistry and biochemistry in the nervous system.
- Neuroanatomy of insects.
- Dendritic changes (structural, chemical, functional) after birth: control of such changes by nutrition and by varying sensory inputs in animals and humans.
- Methods for following movement of molecules in single cells (such methods may turn out to be specially useful in studying compartmentation in neurons, which compartmentation may be related to

their function).
- Control or modification of microvascularisation by various factors.
- Determination of dosages appropriate for the Indian population, of drugs used for treatment of CNS/PNS diseases.

Mechanism(s) of intra axonic (axoplasmic) transport.

Relative contribution of nutrients to axons, by intraaxonix transport and Schwann cells.

Chemical, biochemical, structural and functional differences between neurons of the CNS and the PNS.

Chemical and functional compartmentation (and the relationship between the two) in the neuron : chemical composition of different parts of a neutron / axon. (This would require further developments in the techniques for separation of the different parts, and could lead to identification of the part-specific surface proteins or antigens).

A study of the cytoskeletal components in the cells of the nervous system.

Development of an 'assay' for synapses (what would be the lowest common denominator of markers for a synapse?)

Synapse formation in tissue culture.(Will neuroblastoma cells form junctions with cells other than muscle cells?)

Differences in the myelination process between cells of CNS and PNS.

Difference in the surface characteristics of cells of CNS and PNS.

Effect of environmental factors (e.g., herbicides, pesticides, heavy metals, and other toxic agents) on the structure, bichemistry, chemistry and function of the brain and of its components, eg., on the dendritic processes, signal transmission, immunological markers, etc.

Modulation of brain chemistry, biochemistry, structure and function by factors such as alcohol and tobacco, and conditions such as malnutrition, and the age factor in such modulations.

Effect of ageing on the chemistry, biochemistry, structure and function of the brain, the CNS and the PNS.

Metabolic compartmentation in brain and in its cells.

Neurogenetics : genetic changes modulating or affecting a specific aspect of chemistry, biochemistry, structure and / or function. (Such an approach would help answering questions such as : How many genes are involved in control of, say, vision, hearing, taste, touch, or smell?)

Receptor-ligand interaction in, say, taste, smell and vision.

Mapping of pathways in the sensory responses, using genetics.

Use of genetic observations in man and other animals, e.g, cattle, nematodes, and Drosophila, to understand normal function in the nervous system (would, for example, disorders of the frontal lobe, affect "anticipation"?).

Memory (information storage, collation and recall): its properties and mechanisms (for example, do specific synapses relate to input of specific information, and is there any "reiterative determinism" in storage of information?).

Can we make specific monoclonals that would distinguish between a trained and an untrained animal?

Neurophysiology : mechanism of decision making, voluntary or involuntary, and its relation to consequential motor response.

The olfactory response (how does a dog distinguish between two individuals, but cannot distinguish between identical twins?): the chemistry (are there individual-specific odour-signals in men and if so, how is the variability in them generated?), physiology and response.

The taste and the touch response.

Development of techniques that will allow one to estimate, say, just a few hundred molecules of a substance (such techniques would be essential for the study of the olfactory response which is often to a single molecule).

Use of mathematical tools in reconstruction of 3D-vision.

What makes the visual space Riemanian and not Euclidean?

Use of diseases conditions such as epilepsy, leprosy, motor-neurone disease, schizophrenia, manic depression, and viral diseases that affect the nervous system, to understand normal brain function. To look for changes in chemistry, biochemistry and structure in such conditions, using the modern tools. (What happens, for example, to macromolecular synthesis in these conditions? What is the chemical, biochemical and functional basis of the left-hemisphere deficit in schizophrenia and the right-hemisphere-activation in manic depression? Is spontaneous neuroblastoma regression in children due to a depletion of growth factors necessary for the neuroblastoma?)

Pigeons and migratory birds: how do they compute directions?

Artificial intelligence : What are the hurdles? For example, how much information input is necessary before a machine can generate its own programme?

Neuroendocrinology : identification of new 'brain hormones'. Mechanism of endocrine control of function in the nervous system.

Language acquisition: structural, physiological, chemical and biochemical bases.

How much new information if any - and of what kind - can a single cell outside the nervous system, store. Any lessons from it ?

Studies on behaviour by narrowing the window of sensory input (e.g. bats respond differently to light of different wave length.)

Comparative study of behaviour and sensory responses in different species.

Mechanism of hallucination.

Why sleep? What happens (chemically, biochemically, structurally) during sleep?

Why dreams? What happens (chemically, biochemically, structurally) during the dreaming process?

Are there any culture-specific correlates of psychotherapy in India?

Epidemiological studies of
(a) muscle diseases,
(b) strokes,
(c) Subarachnoid Haemorrhage, and
(d) incidence of congenital neurological defects, in different parts of the country. (The true incidence and prevalence of these diseases are not known in our country, nor the distribution pattern.)

The role of consanguinity in neurological disorders and congenital neurological abnormality. (Such a study can easily be done in our country as there is little consanguinity in the North whereas there is much in the South.)

Use of a brain bank for the following:

(a) Study of the anatomy of the major cerebral blood vessels in Indians with a view to evolving better microsurgical techniques.
(b) A study of the cerebral vascularative in different age groups.
(c) A mapping of the internal structures of the brain to provide neuroanatomic correlates for CT-aided stereotaxic surgery.

Anatomical and biochemical mapping of the brain of Indian, e. g. through CT-scan study of the variations observed in the pineal gland and the chorid plexus .(Why the pineal gland cannot always be visualised readily in Indians?).

A study of incidence and prognosis in intracerebral hematomas. A controlled comparison of results after surgical and non-surgical treatments.

Why is there a recurrence of infestation by cysticercosis? Is it a re infection or reactivation ?

Can Ascaris lumbricoidus (round worm) cause convulsions?

Why are some tuberculomas of the brain not responsive to medical treatment? (Pathological and pharmacological studies of such lesions will lead to useful information.)

Development of immunotherapy of brain Tumours.

The role of vitamins in the therapy of brain Tumours(e.g. of Vitamin E).

Epilepsy: the use of anticonvulsants in pregnant women and possible terratogenesis.

Factors that cause spinal arachnoiditis.

Experimental spinal cord regeneration.

A study of the reasons for the absence of withdrawal symptoms after singulamotomy for morphine addiction : the use of animal (even tissue culture?) models

Operant conditioning and neurological disorders.

Nonvolitional biofeedback techniques e.g. visual and auditory.

The influence of electromagnetism on CNS functions, normal and abnormal.

Correlation of psychological changes with discrete lesions in the cerebral cortex as determined by CT scan.

Neurophysiology of awareness.

Is the "I" (the ego sense) situated in the temporal lobe?

A critical examination of correlates (such as the type of personality and the body structure) of neurological disorders (e.g. stroke, epilepsy, and headache) described in the Ayurvedic literature.

Are there any specific neuropeptide correlates of mediation and concentration?

Role of anion seekers and binders in treatment of cerebral edema.

Multiport (multipolar) EEG studies.

Are there psychological correlates to malignancy in the body, similar to enecephaloneuropathy in occult malignancies?