Problems and prospects in neurochemistry

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The importance of neurochemistry in understanding the functional basis of the nervous system was emphasized. Attention was drawn to the role of lipids, particularly the sphingolipids, whose metabolic abnormalities lead to 'sphingolipidosis' in the brain and to gangliosides, which show growth-promoting and neuritogenic properties. Several questions that remain to be answered in this area were enumerated. It was pointed out that neurons make a large number of proteins, an order of magnitude higher than other cells, and several of these are yet to be characterized and their functional significance established. Myelination and synaptogenesis are two fundamental processes in brain development. Although much is known about myelin lipids and proteins, it is not known what signals the glial cell receives to initiate myelin synthesis around the axon. In fact, the process of myelination provides an excellent system for studying membrane biogenesis and cell–cell interaction. Great strides were made in the understanding of neurotransmitter receptors and their function in synaptic transmission, but how neurons make synapses with other specific neurons in a preprogrammed manner is not known and requires immediate study. In this context, it was stressed that developmental neurobiology of the human brain could be most profitably done in India. The importance and complexity of signal transduction mechanisms in the brain was explained and many fundamental questions that remain to be answered were discussed. In conclusion, several other areas of contemporary research interest in the nervous system were mentioned and it was suggested that a 'National Committee for Brain Research' be constituted to identify and intensify research programmes in this vital field.

ABOUT four years ago, I was asked to review the past and present of neurochemical research activities in India. There I wrote: 'All phenomena which characterize life processes should ultimately be amenable to explanation in chemical and physical terms. The functioning of the nervous system, the most challenging one among the biological phenomena, is no exception. Even higher functions of the brain such as thought and memory will have to be explained eventually in terms of the chemistry of the constituent molecules and their physical properties. Therefore, neurochemistry – the chemical approach to the study of the nervous system – would be vital to our understanding of the nervous system[1]. Even 'consciousness' is likely to have a molecular basis.

The chemical exploration of the brain began at the turn of the century. The basic biochemical components of the nervous system are now identified and we can account for almost 100% of the mass of the neuron. It is unlikely that any new class of organic molecules peculiar to the nervous system will be discovered in future. This means that the special functions of the nervous system will have to be explained in terms of the molecules that are already known. Much has been discovered regarding the biochemistry of the brain. Its continuous dependence on the blood supply of glucose is now well known and the metabolic pathways of carbohydrates are also well established. Brain contains a very large amount of lipid and a bewildering variety of lipid components exist in it[2]. While no particular lipid component is characteristic of the nervous tissue, some lipids occur in large amounts in the brain. Their functional significance is unknown at present. The sphingolipids occur in high concentrations in the brain and their abnormal metabolism, usually due to the lack of a particular catabolic enzyme, leads to their accumulation specifically in the nervous tissue, causing a number of diseases, commonly known as 'sphingolipidosis', which result in severe mental retardation. Why should the accumulation of a single sphingolipid component lead to mental retardation? What role does it play in neural communication and eventually in thought and higher functions of the brain?

Ethanolamine and choline plasmalogens are major phospholipid components in the nervous tissue and in muscle. Do they have any role in excitability of the membranes? Similar questions can be asked of many other lipids. Interestingly, gangliosides – another major group of lipids in the brain, have been implicated in cellular recognition as adjuncts at receptor sites and show growth-promoting and neuritogenic properties. Much remains to be discovered about the function of these complex lipids in the brain. By far, proteins are the most important molecules with an array of biological functions. It appears that gene expression is maximal in neurons among the various cells, i.e. species of mRNA that are found in neurons are about an order of magnitude higher than in other cells. This means that a very large number of proteins are made and most of these are yet to be identified. While several of them are