1962
94

Chapter 15

PROBLEMS OF MOLECULAR CODING

Roger W. Sperry

With regard to possibilities for the molecular coding of memory it becomes critical to ask: What distinguishes the mnemonic traces for different memories? Are the memory trace systems distinguished from one another (a) by differences in molecular configuration that may be laid down in numbers within a single brain cell or (b) by the patterns of distribution within the brain of essentially the same type of molecular change? Discovery of the molecular nature of the engram will be much more exciting if the former is the case. On the other hand, if the latter proves to be true, the coding of mnemonic information becomes largely a metamolecular problem. The tendency in the past has been to think more in terms of (b) than of (a), but the evidence is not yet sufficient to rule out one or the other.

In either case, it is probably true that a large part of the "information content" involved in any given "memory" as observed at the behavioral level is handled in the contextual dynamics rather than in the static molecular changes, i.e., in the background excitation pattern that is differential and critical for reactivation of any given engram. Memories that undergo active and sometimes creative change even to the incorporation of some calculation and reasoning (as illustrated in certain posthypnotic memory phenomena) present additional problems for molecular coding.

When one turns to the neural basis of behavior patterns that are inherited rather than acquired, problems of chemical coding can be more clearly outlined. At present, however, they seem to relate less to functional information content directly than to the tagging, sorting, orderly assembling, distribution, and interconnection of the neuronal elements in the ontogenetic organization of the neural machinery.

For example, in the genesis of visual perception, problems of chemical coding are involved in the differentiation of retinal specificity, the chemotactic guidance of the optic axons to their central terminals, their selective synapsis with central neurons, and the selective synapsis of these in turn with deeper elements in the system. The chemical tagging of the neurons for perception of directionality, for color discrimination, for brightness, and for the on-

off and other physiological properties requires several dimensions of chemical specificity within a single neuron. These chemical tags extend throughout the length of the frequently long axon into all its numerous arboreal ramifications, without loss of specificity. These tags are critical in determining the functional linkages with other neurons.

The characteristics of embryonic and regenerative phenomena including developmental gradients and fields seem to require chemical units or complexes for the neuronal specificities that can be graded in their properties through hundreds of continuous steps, any one of which can be rigorously replicated and spread throughout the long fiber extensions of a given nerve cell. These chemical specificities may arise by self differentiation or may be transmitted or induced by fiber tip (but not fiber length) contacts with end organs and associated neuronal elements. Once they are established in a neuron, they tend to be permanent, irreversible, and immutable, except for some plasticity in the lower vertebrates, especially in embryonic and larval stages. These chemical properties and the specialized intercell affinities which they involve seem to be responsible in large part for the inherited patterning of central nervous pathways and for the development and maintenance of synaptic connections. It is quite possible that the chemical changes associated with learning and memory in the mammalian cerebrum represent an evolvement, more or less direct, of these basic properties underlying selective chemical affinity.

Acknowledgments

This work was supported by U. S. Public Health Service Grant M-3372 from the National Institute of Mental Health, National Institutes of Health, and by the F. P. Hixon Fund of California Institute of Technology.

References

Brazier, M. A. B., ed., The Central Nervous System and Behavior, Transactions of the First Conference, Josiah Macy, Jr., Foundation, New York, 1958.

Galambos, R., and Morgan, C. T., The neural basis of learning. In Handbook of Physiology, Sect. I, 3, 1960, pp. 1471-1499.

Gomulicki, B. R., The Development and Present Status of the Trace Theory of Memory, British Journal of Psychology, Monograph Suppl., No. 29, University Press, Cambridge, 1953, pp. 1-94.

Lashley, K. S., In search of the engram. In Physiological Mechanisms in Animal Behavior (Soc. Exp. Biol. Symp., No. 4), Academic Press, New York, 1950, pp. 454-482.

Sperry, R. W., Physiological plasticity and brain circuit theory. In Biological and Biochemical Bases of Behavior, H. F. Harlow and C. N. Woolsey, eds., University of Wisconsin Press, Madison, 1955, pp. 401-424.

Sperry, R. W., Regulative factors in the orderly growth of neural circuits. In Growth Symp., Vol. 10, 1951, pp. 63-87.

Sperry, R. W., Cerebral organization and behavior, Science, 133, 1749-1757, 1961.

Teuber, H.-L., Perception. In Handbook of Physiology, Sect. I, 3, 1960, pp. 1595-1668.