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Teacher-to-teacher

Brain and Behavior

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Cognitive neuroscience is a new interdisciplinary approach to an understanding of mind-brain relations that combines cognitive psychology and neurological sciences. These two fields of study seek answers to many of the same questions and have methodological and conceptual contributions to offer one another. Further envisioned is the possibility of going beyond the levels of mutual contributions towards developing a unified, interdisciplinary science of human nature.

The physiological basis for the storage of information in the nervous system—or the formation of memory—is an important problem that requires an interdisciplinary effort. One theoretical framework of cognitive psychology, the consolidation model for memory, states that information storage involves a sequential process, which begins with a short-term sensory store. The shortest of memory stores is the sensory register and is called the iconic store. Here sensory items are perceived and subsequent attention to material in this iconic store may lead to literal copy of the input and transfer to short-term store. Information can be maintained for only a second or two; and if it is not transferred to short-term stores, there is much information loss. Short-term memory, the next stage of processing, has a time duration measured in minutes and seems to have capacity limitations as well. Transfer of short-term information to long-term stores may be accomplished through rehearsal, and long-term memory may last a lifetime. The transitions from one store to the next probably require neurochemical processes.

Recent developments of this consolidation model suggest that short-term memory may be the active state of long-term memory (Posner 1977). In this more unitary view of memory processes, any stimulus can have multiple representations including visual, tactile, phonemic, or semantic systems. Minimizing the distinction between short-term and long-term stores, this hypothesis emphasizes the existence of "levels" of human memory where depth of processing may play an important role. In this theoretical framework, preliminary analysis includes physical features as edges, angles, brightness, hue, pitch, and loudness. Later stages consist of recognizing patterns and matching these against stored patterns. A word, for example, is immediately processed phonemically and morphemically, only to trigger further semantic associations based on the subjects' experiences. This enrichment and elaboration of the word allow the subject to extract meaning, and of course, this depth of processing approach is not restricted to verbal material.

A recent clinical experience with an elderly patient illustrates the disruption of the ability to choose and maintain an appropriate memory level. This man had great difficulties organizing the trivialities of his daily life. Formerly automatic events, such as putting on both shoes and tying them, or finding his way to his office, had become insurmountable chores. Forgetting the time and often his exact location, he frequently wandered to distant corners of the hospital. When confronted with the apparent aimlessness of his direction, he responded with a gruffness and indignation that befitted his former brilliance. Throughout his long life he had been the creator of a number of powerful scientific theories. His philosophical treatises had also gained him worldwide recognition; yet, at moments he could not remember the time of year and had only a vague glimmer of intuition regarding the reasons for his hospitalization.

To the ordinary medical examiner he appeared hopelessly demented, but further analysis revealed several tantalizing possibilities. By establishing contexts with linguistic cues he verbally reconstructed past episodes about his life. For example, the mere mention of a former colleague prompted an emotive and accurate

verbal report of events and related scientific experiments. If the memory for events of one's life are viewed as a by-product of a multilevel perceptual analysis, then the ability to use or recall this memory can be viewed as a function of the different characteristics associated with each level. Cueing this patient then with the arguments he once explored, resulted in focused and cogent conversation, presumably because of the intensity and the multiplicity with which these events were processed. His problem may now be viewed as a difficulty with attention response to a specific level of perceptual ability. He is no longer just an old man losing his memory.

Certain other factors relating time of processing, and stability of memory also are important. For example, immediately following learning, memory is highly susceptible to interference and loss. This shift in susceptibility leads to the hypothesis that the physiological basis of a given memory shifts from initial neurobiological processes with short lifetimes, as exemplified by the electrophysiologic experiments of John, *et al.* (1973), to processes with longer lifetimes (for example, the experiments of altered synaptic anatomy by Berlucchi and Buchtel 1975). Thus, short-term memory has become associated with electrical events that are easily disrupted by shocks. Long-term memory, on the other hand, may entail some permanent change involving protein synthesis and altered synaptic organization.

The question of where memory stores are located within the brain also remains unresolved. Lashley (1950) investigated this question by systematically lesioning different areas of rat's brain and quantifying maze learning ability. He concluded that memory was critically affected by the amount of cortex removed (principle of mass action) and did not depend on the area removed (principle of equipotentiality). However, experimental and clinical evidence has since suggested these principles do not hold. For example, a cerebrovascular accident that disrupted 5-10% of the left temporal parietal cortex would cause a more radical deviation from normal speech and thinking when compared to complete corpus callosum transection. This latter procedure would effectively remove 100% of the cortical contribution of one hemisphere to the other. In any case, the memory trace that Lashley called the "engram" probably does develop whenever learning occurs. Further, it is generally true today that this engram cannot be pinpointed to a specific brain area.

In fact, more data from the neurological clinics (Gazzaniga 1976), supports experimental notions that we should search for the network that interconnects a variety of different processing systems all contributing to the reconstruction of past experience rather than searching for the engram. This formulation from the neurological clinics is reminiscent of the hypothetical models proposed above by cognitive psychology groups. The engram, then, is a hypothetical construct referring to as yet undefined neurochemical or electrophysical alterations in the nervous system. It is likely that the physiological basis of even the simplest type of memory involves the interaction of many systems incorporating biochemical changes in many specific areas of the nervous system. Memory has aspects of component parts that are interlocking nets of specific sensory processing modes widespread throughout the brain.

The search for this molecular substrate of memory has involved at various times one or more of a number of brain biochemicals. One example from a long litany of animal experiments is the work of Deutsch (1971). These experiments suggested that cholinergic mechanisms are intimately involved in memory and learning. Cholinergic mechanisms depend on the synthesis of acetylcholine in the body of the neuron. This biochemical joining of choline and acetyl-CoA is catalyzed by the enzyme choline acetyltransferase. The acetylcholine is packaged at the presynaptic neuron terminal for release into the synapse. Upon release acetylcholine attaches to specific receptors on the postsynpatic neuron which causes transmission of the electrical impulse to the next neuron. Acetylcholine is then inactivated by the enzyme acetylcholinesterase. Neural transmission can be accomplished by several other biochemicals as well. Norepinepherine, serotonin, and dopamine are examples of other discrete neurotransmitters.

The specific cholinergic animal experimental models, however, described disruption of the retrieval aspect of the memory system in rats after intracerebral or intraperitoneal injection of an anticholinergic drug like scopolamine. Escape task ability was decreased after treatment with this anticholinergic drug. Scopolamine, through competitive inhibition, decreases the amount of acetylcholine that binds to the postsynaptic receptor and so acts in an anticholinergic manner. Acetylcholinesterase is the enzyme that inactivates acetylcholine and in a sense is also anti-cholinergic. The inhibition of this enzyme permits acetylcholine to remain in the synapse longer. Physostigmine is a specific inhibitor of acetylcholinesterase and therefore enhances the activity of remaining acetylcholine. In these animal studies physostigmine treatment improved the ability of the animals to recall the trained escape task.

Pursuing the acetylcholine experiments and the involvement of this transmitter in memory processes, Rosenzweig (1970) showed increased brain acetylcholine in rats raised in "rich" environments compared to a control group raised in "poor" environment. The rats living in rich environments where they had much to do also had an increased number of dendritic spine synapses on cortical neurons.

Other experiments, such as Drachman's (1977) work with young

healthy human volunteers, suggest that memory can be disrupted specifically by blocking acetylcholine activity with anticholinergic drugs. Neuropsychological memory tests were administered to test and control groups of young people before and after anticholinergic drug administration. The anticholinergic-treated group revealed significant decrease in performance levels after drug treatments. Further testing included the administration of different antidotes to reverse the action of the anticholinergic drug (like physostigmine in Deutsch rat experiments). Strikingly, memory performances improved with the antidote that specifically increased acetylcholine levels. Memory performance did not improve with other less specific antidotes.

Extending this observation to aged volunteers, the pattern of performance on memory tests appeared to have certain similarities to the group of young people who were treated with anticholinergic drugs (presumably those with decreased acetylcholine activity). These results suggest that memory decline seen in normal human aging may be a function of acetylcholine activity.

In several laboratories, methods for quantifying the activity of acetylcholine in brain tissue obtained at autopsy have been developed (Volpe, *et al.* 1978). Using radioactive toxins that specifically bind to acetylcholine synaptic receptors, binding activity can be assayed and compared to other brain regions. Correlations are possible with the antemortem status of the patient. Specifically, it appears that in groups of patients who suffer with dementing illness, the level of acetylcholine activity may be decreased in excess of that decrease apparent with normal aging processes.

Experimental results like those reported are a direct result of the combination of brain and cognitive science investigations. The results may be far reaching and not only theoretical but practical as well. Cognitive disorders of aging may result from a relatively specific dysfunction of a neurotransmitter system rather than from a general mass dropout of neurons. This may suggest a group of patients for whom a treatment program is possible. Clinical trials are now in progress all over the country to evaluate the behavioral effects of increased acetylcholine activity at the postsynaptic receptor.

Results from neuroscience laboratories suggest discrete neuroanatomic and biochemical clues underlying the normal memory process. Simultaneously, results from behavioral science laboratories suggest new theoretical constructs underlying memory processes. The interaction of these research paradigms has been reviewed recently in a textbook entitled *Functional Neuroscience* (Gazzaniga, *et al.* 1979), which integrates the fundamental discoveries of neuroanatomy and neurophysiology with experiment and theory derived from behavioral research. The book also includes clinical case histories that describe in detail a series of neurologic problems that affect humans.

Understanding the mind and brain is a formidable challenge for scientists. The combined approach of these disciplines provides a platform for future research and a pedagogical paradigm of unparalleled excitement.

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