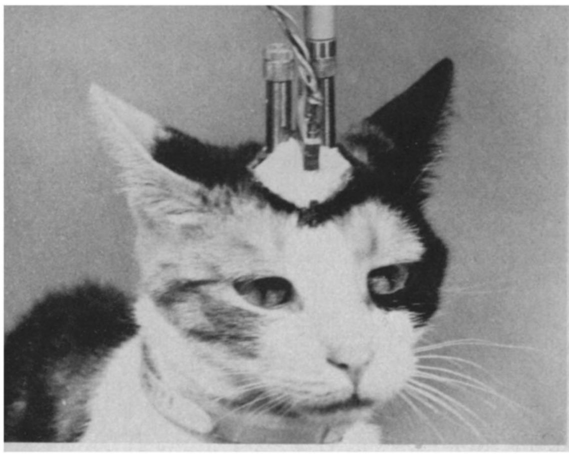
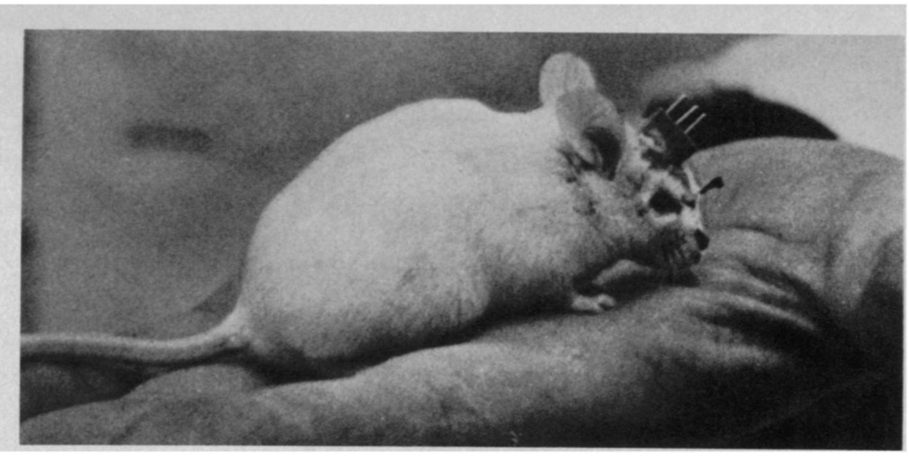


John



Ungar

Electrode implants, ponderous yet painless, provide researchers with valuable data about the processes of memory.

The Biology of Memory

Can conflicting evidence be reconciled? Not until researchers start cooperating.

by Joan Arehart-Treichel

Brain investigators have attempted in recent decades to define the biological bases of memory. If such bases could be delineated, researchers might learn how to manipulate them. And manipulation of the biological processes of memory could have a profound impact on society, both positive and negative. Memory manipulation might be exploited by teachers, by physicians correcting brain diseases involving memory, by Madison Avenue in subliminal advertising, by nations engaging in psychological warfare.

"Memory research has widespread ramifications," says Robert Grenell, psychiatrist and neurobiologist at the University of Maryland Hospital. "People think memory researchers are engaged in fun and games, but it's not so."

Memory research today is largely concentrated in two areas—the chemical bases of memory and the electrophysiological bases of memory.

A leader in the field of the chemistry of memory is Georges Ungar, a pharmacologist at the Baylor College of Medicine. During the past decade, Ungar has trained animals to perform various tasks. He has then extracted chemical material from their brains and purified and isolated it. When he injects the isolated chemical material back into the brains of untrained animals, the animals act like the trained animals from which the material was taken. So it looks as if the chemical material might contain memory that can be transferred from one animal brain to another. Hence Ungar's material has come to be called "memory molecules."

The memory molecules Ungar has extracted are proteins. One, called "scotophobin," from the Greek for "fear of the dark," was taken from the brains of rats trained to fear the dark. When scotophobin was injected into untrained rats, they also feared the dark. Another molecule was taken from the brains of rats trained to ignore the sound of a loud bell. When the molecule was injected into the brains of untrained rats, they too ignored the bell. Memory molecules were also taken from goldfish trained to avoid certain colors, and to swim against adverse conditions (SN: 4/28/73, p. 268). A few months hence, Ungar intends to inject one of his memory molecules into himself and some other human volunteers.

A leader in the field of the electrophysiological bases of memory is E. Roy John of the New York Medical College. During the past 20 years, John has acquired increasing evidence that memory consists of electrical patterns that sweep through populations of nerve cells in the brain. When animals are taught certain tasks, John can see certain patterns of brain waves flicker through their brains. These waves represent a brain response to a stimulus; they are called exogenous brain waves. Soon afterward, other electrical waves ripple through the animals' brains. These waves, which appear to represent brain reaction to the stimulus, are called endogenous waves.

As an animal learns a task better and better, its endogenous brain waves become stronger and stronger. And when the animal that has learned a task is later asked to remember the task, the identical endogenous wave patterns flicker through the animal's brain. So in John's view, the endogenous waves represent traces of memory, or "engrams."

Recently John found that while memory traces are widely distributed throughout the brain, they tend to cluster in strategic areas. Traces that concern memory of a visual event are seen mostly in the visual area of the brain. Traces that concern memory of an auditory event concentrate in the auditory area of the brain.

However fascinating the chemical evidence for memory and the electrophysiological evidence for memory, they present a dilemma. Is memory chemical, or is is electrical? Might evidence from the two camps of research be reconciled?

"It's not a question of reconciliation, but of definition," Grenell insists. Learning and memory constitute a number of intricate processes. There is input of information, recognition and comparison, evaluation, short-term memory, consolidation of short-term memory, long-term memory storage, memory retrieval. Ungar, says Grenell, concerns himself with long-term memory storage. Ungar agrees. John, says

Grenell, concerns himself with memory retrieval. John agrees.

So if Ungar's molecules represent long-term memory storage, and John's engrams represent memory retrieval, might memory molecules and engrams be reconciled? Ungar thinks so. "Both," he says, "are based on the assumption that new connections are established in the brain during learning."

John agrees that new connections may be established during learning, although there is no evidence for such connections. But he does not agree, on the basis of his own laboratory evidence, that memory depends on specific pathways. He does not believe that Ungar's molecules could be "produced by such pathways, or produce such pathways" in a naive brain. So John feels "there is a pretty substantial problem" in reconciling memory molecules with engrams.

On the other hand, John does not deny that Ungar's molecules do something to the brains of untrained animals. John suspects that the molecules stimulate nerve cells in the brain, as do pep pills, hormones or a number of other chemicals. As a result, an animal's behavior is altered.

J. Anthony Deutsch of the University of California at San Diego agrees. "It seems reasonable to assume," he says, "that the molecules Ungar is extracting are simply altering an animal's motivational status at the time of performance, and this is producing significant alterations in his behavior. It has nothing to do with memory as we understand it."

Yet Deutsch doesn't think electrophysiological experiments show anything about learning or memory either. On the basis of his own work, he believes that memory constitutes chemical changes as one nerve passes an electrical impulse to an adjoining nerve.

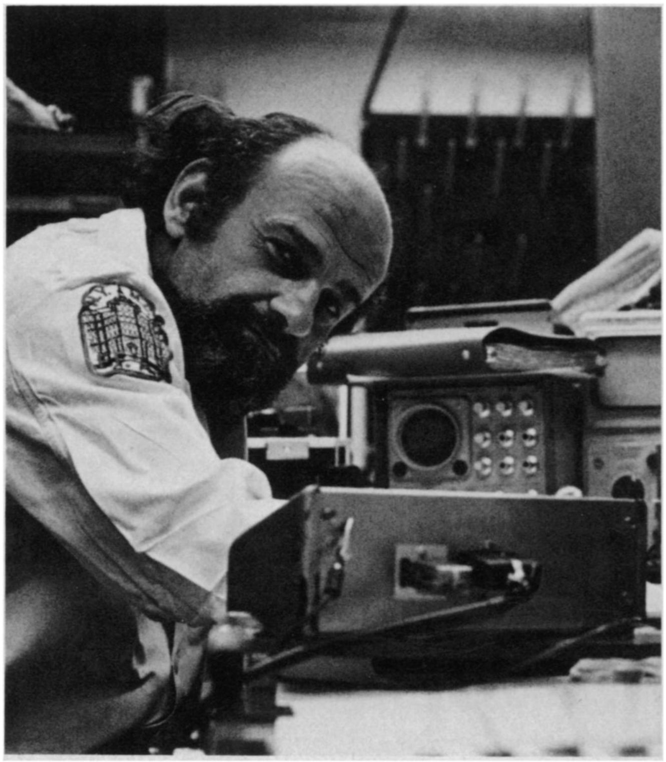
Grenell more or less agrees with Deutsch, at least as far as the recognition-comparison stages of learning, and of short-term memory, are concerned. After eight years of research, Grenell has found that the nerve chemical acetylcholine facilitates the ability of a nerve to pass an electrical message to an adjoining nerve, and this facilitation is necessary for the recognition-comparison stage of learning, and for short-term memory as well. He also has results that nerve transmitters known as the catecholamines are able to inhibit nerve facilitation. He has not yet looked at the specific effects of the catecholamines on recognition-comparison and memory.

Still, Grenell does not discount that Ungar's molecules and John's engrams represent some facet of memory. "It is unlikely," he says, "that memory is purely chemical, purely electrophysiological or purely any damn thing."

Robert Thatcher, a co-worker in John's lab, also sees hope for reconciliation between chemical evidence for memory and electrophysiological evidence for memory. He speculates that Ungar's molecules, rather than storing memory, activate nerve-firing patterns in recipient brains. And the activation of these electrical patterns is the same as if the patterns had been acquired (learned). He would like to get some of Ungar's molecules, inject them into brains and see what effects the molecules have on nerve firing patterns.

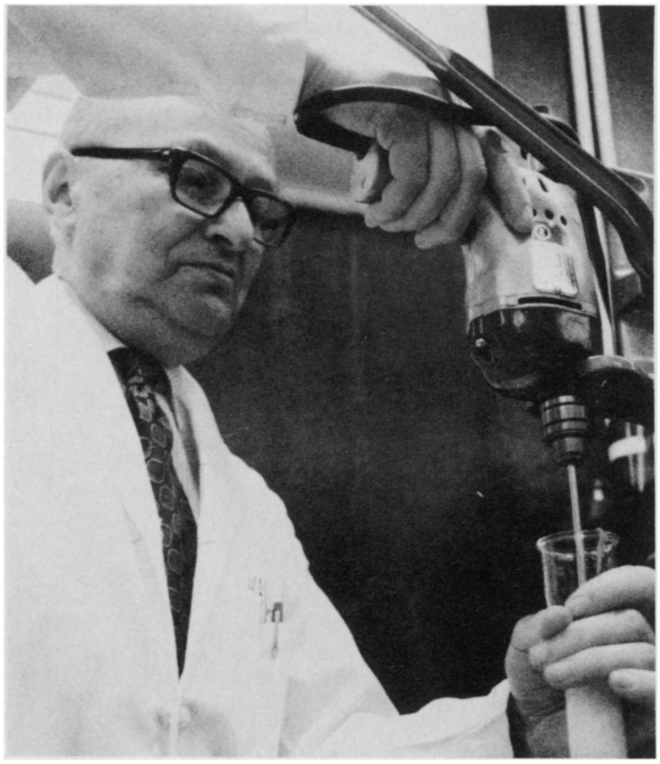
It is doubtful he will be able to conduct such experiments any time soon. Too much hostility exists between chemical researchers and electrophysiological researchers. A case in point—a declaration by James Old, an investigator of the electrophysiology of memory at the California Institute of Technology: "It is an interesting state of affairs right now. It is possible to think of theories being integrated, but some [Ungar's] are not compelling. The reason they are not compelling is that it is mainly people on the crackpot fringe who have done these experiments. They really believe what they say. . . . The advantages of believing are so great to them, and the cost so little, they can hardly help believing. The other side, the mainstream of science, has it almost as a matter of scientific superego to quell this heresy."

"The bias is pretty rough," Grenell admits. "Biochemists have not learned physiology. Physiologists have not learned biochemistry. And neither has learned biophysics. So it gets difficult trying to put things together." The ultimate unraveling of the biology of memory, he predicts, "will come from mathematicians and physicists." □



Baylor College of Medicine

Ungar: "Absolutely no discrepancy between the two."



New York Medical College

John: "There is indeed great disagreement between us."