Memories Are Made of This

"Without memory there can be no mind," Stanford University psychologist Richard Thompson said at a recent conference,* noting that the how and where of memory storage has been a "baffling" problem. Partly because the problem has been "solved" falsely on several occasions, some authorities on the issue have concluded that memories must be diffuse rather than localized. Recently, however, Thompson reached the opposite conclusion. He now says that memory trace circuits are "extremely localized"—surprisingly, partly within the cerebellum—and that lesions as small as 1 cubic millimeter in the appropriate region of a rabbit's brain "can completely destroy the trace for a particular learned response."

Thompson is not alone in trying to locate and describe memory traces. There is at least rough convergence with other studies, including those of Larry R. Squire at the Veterans Administration Medical Center in San Diego, California, and Mortimer Mishkin, who participated in a recent workshop on learning† (*Science*, 16 December, p. 1219), at the National Institute of Mental Health in Bethesda, Maryland, and their respective collaborators. Squire and Mishkin have identified two distinct memory systems in man and also in monkeys, providing something of a "rapprochement of the monkey and man results," according to Squire. Though there is yet no proof of any correspondence of these primate systems to the simpler memory system of the rabbit being studied by Thompson, Squire says, "Our notion of memory systems applies not just to man or monkeys but to all mammals, possibly to all vertebrates."

The two memory systems identified in primates are called "procedural," corresponding roughly to habit or behavioral functions, and "declarative," corresponding to cognitive and representational functions. "We think there are two [information] storage systems," Mishkin explains. "One is a habit system, and the other is based on stored representations of stimuli. Information can be present in both simultaneously, so behavior is an amalgam of both kinds of processes."

Importantly, these two systems are anatomically distinguishable. Also importantly, amnesia (including surgically induced global amnesia in monkeys) only affects the declarative form of memory, sparing the procedural form. Studies of certain patients, whose lesions have been well characterized, and of monkeys indicate that both the hippocampus and the amygdala (deep-lying brain structures in the medial temporal region) play important roles, Squire notes. Placing primate memory more precisely is difficult and made more so by its tendency to change, or consolidate, with time.

Thompson's success at pinpointing one kind of memory circuit in the rabbit brain is due, in part, to its being more akin to a procedural—rather than a declarative—type memory. The task his rabbits learn is to blink their eyes when they hear a tone. Training consists of hearing that tone shortly before a puff of air is blown in an animal's eye, a mild stimulus that elicits the blink reflex. Two kinds of lesions can stop a trained rabbit from blinking when it hears the tone, although neither procedure affects the animal's ability to blink when it feels an air puff.

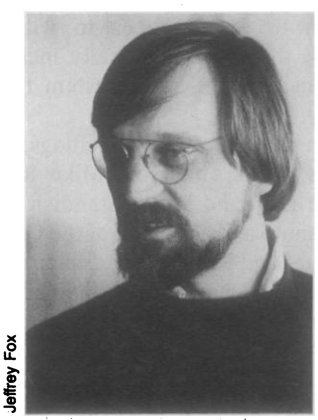
One lesion is permanent, the result of kainic acid (which selectively destroys nerve cell bodies) being placed in the correct region. Moreover, the procedure can be done on one side of the brain without affecting the other.

The other kind of lesion depends on introducing pharmacologically active agents, whose effects are reversible. For example, bicuculline temporarily and selectively abolishes the trained rabbit's blink in response to a tone, Thompson says. "It's a dose-dependent response clearly localized to the same region of deep nuclei and the cerebellar cortex." Picrotoxin exerts a similar effect, suggesting to him that the key circuits involved use gamma-aminobutyric acid (GABA) as a neurotransmitter, whose actions these agents are known to affect.

"I would not dream of suggesting that all of the learned response is in the cerebellum," Thompson says. "The red nucleus is part of the essential circuit." And, he adds, although the hippocampus is "not essential" for this simple learning task, it "may be needed for more complex learning." Some "plasticity" is established in the hippocampus during learning, but unlike the cerebellum there is no pronounced lateral effect in that the hippocampus does not "care" which side is doing the learning, Thompson finds. Also, he speculates that another brain structure, called the inferior olive, acts as the "reinforcing component of the stimulus" during the training of animals.

Though these clues about memory traces are temptingly concrete, they by no means solve the entire mystery. For example, Thompson points out, "We have not studied forgetting." Well-learned responses tend not to be forgotten by the animals, although they gradually cease blinking if they hear just the tone alone. The memory trace is there because retraining occurs so fast, he argues, concluding: "The fundamental question still is mechanism. But no one has known where to look to analyze mechanism."—JEFFREY L. FOX

Richard Thompson



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*Society for Neuroscience annual meeting, Boston, 6 to 11 November 1983.

†Dahlem Workshop, "The Biology of Learning," Berlin, 23 to 28 October 1983. Conference Proceedings will be available in mid-1984 from Springer-Verlag, Berlin/Heidelberg/New York.