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Dedicated to Memory?

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ing evidence argues that a subset of BH3-only proteins function as direct activators of Bax and Bak, and indeed, may be indispensable for this. The work of Ren *et al*. provides strong support for the idea that Bim, Bid, and Puma are the central Bax-Bak activators, with the remaining BH3-only proteins functioning primarily as sensitizers. The major distinction between these two categories of cell death sensors may be their relative affinities for Bax-Bak compared to those of the prosurvival Bcl-2 proteins. The emerging view is that a combination model of activator-sensitizer appears to most accurately reflect BH3-only protein function.

The precise composition and structure of the Bax-Bak channel have yet to be elucidated, and how BH3-only proteins sense the multitude of signals that trigger apoptosis is not yet fully understood. However, there is progress toward developing targeted therapies aimed at selectively engaging the Bax-Bak channel in cell populations that resist death due to disturbances among the ranks of BH3-only proteins and their prosurvival Bcl-2 family antagonists (*9*). In the case of tumors that adopt the strategy of survival by avoiding cell death, direct activator BH3-only mimetic drugs may prove highly effective antidotes.

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NEUROSCIENCE

Dedicated to Memory?

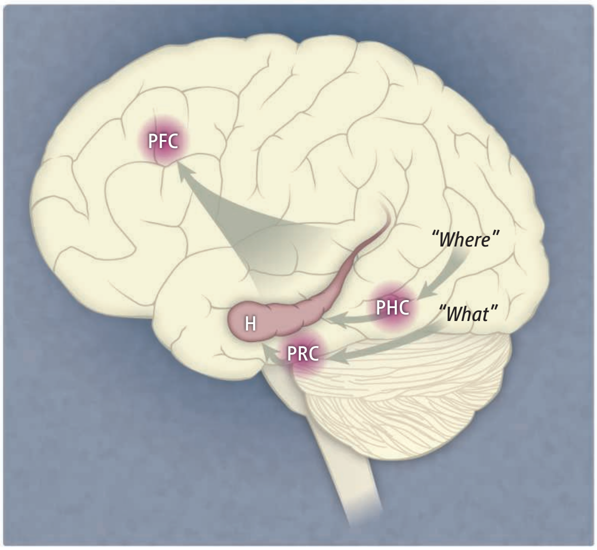
Howard Eichenbaum

Rats with a damaged perirhinal cortex exhibit false memory, raising questions about brain organization.

Early observations of individuals with circumscribed damage to the cerebral cortex led to a consensus that memory is not localized to any particular brain area. Rather, neuroscientists believed that memories were incorporated within the information processing functions of many specialized brain areas. In 1957, this view changed dramatically after Scoville and Milner (*1*) described a patient, known as H.M., in whom damage to the medial temporal lobe (MTL; including the hippocampus and surrounding cortex) resulted in global memory impairment but spared perceptual and cognitive functions. A principal interpretation of these findings was that the MTL is a dedicated memory system, and this perspective dominated subsequent research on memory (*2*). Recent studies have called this idea into question, however, and McTighe *et al*. (*3*) add another twist on page 1408 of this issue. They claim that one part of the MTL, the perirhinal cortex, has a specific information processing function not directly related to memory. Does this finding turn the clock back to the dedicated area view, or move it forward in understanding how the MTL memory system is organized?

McTighe *et al*. employed a clever variation of a popular memory-research paradigm. In the usual procedure, researchers initially present a rat with a novel object for a few minutes and then, after a significant delay period, simultaneously present the rat with two test objects: the now "familiar" one and a new "novel" object. Typically, rats that do not have brain damage spend less time exploring the familiar object (demonstrating memory). Rats with perirhinal cortex damage spend about the same amount of time exploring both objects, suggesting that they have forgotten the familiar object. In McTighe *et al*.'s variation, they presented the familiar and novel test objects separately, instead of simultaneously. They showed that animals with perirhinal damage did not forget the familiar object but rather treated the novel object as familiar, a kind of false memory. On the basis of this and previous findings, the authors argue that the perirhinal cortex's normal role in recognition is to configure, or bind, elemental features of stimuli already processed earlier in the perceptual pathway. If the perirhinal cortex is damaged, however, object memories exist only as fragmented representations of these featural elements formed at the earlier stages. These fragmented memories are susceptible to interference from a constant natural stream of subsequent perceptual input, leading to the false memory for test items that share features with the interfering inputs. Consistent with this idea, McTighe *et al*. were able to eliminate false memories in brain-damaged rats by placing the animals into a dark chamber during the delay, thus reducing new perceptual interference.

How do these findings affect the dedicated memory system view? McTighe *et al*. support a return to the idea that brain areas contribute to memory only as a by-product of their specialized information processing functions, in this case the perirhinal cortex's perceptual binding function. However,



Functional organization of a memory system. Information about specific objects and events arrives through the "what" cortical stream into perirhinal cortex (PRC), while information about the spatial-temporal context in which events occurred arrives through the "where" cortical stream into parahippocampal cortex (PHC). These two streams of information combine within the hippocampus (H), which represents relationships between objects and events and their context. When cued for a memory, feedback pathways from the hippocampus to the cortical areas generate representations of object and context memories that are tested for a match in prefrontal cortex (PFC).

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other recent studies that distinguish between forgetting and false memories due to damage in other parts of the MTL system offer a broader perspective. In these experiments, rats initially study items chosen from a large list each day, and then investigators measure their memory performance in terms of "hits" (correct identifications of stimuli that were on that study list) and "false alarms" (errors where subjects incorrectly judge new stimuli as appearing on the study list). Damage to the hippocampus results in a decrease in hits with no effect on the false alarm rate (*4*), indicating that the deficit is due to forgetting rather than false memories—the opposite of the pattern observed by McTighe *et al*. In contrast, damage to the prefrontal cortex results in an increase in false alarms and no effect on the hit rate (*5*), similar to the pattern observed by McTighe *et al*. These studies suggest that distinguishing forgetting from false memory provides researchers with a powerful tool for identifying the contributions of different brain areas to memory.

Furthermore, these diverse findings can be integrated into a model of the anatomical pathways of MTL system and its interactions with cortical areas (see the figure) (*6*). The perirhinal cortex is the end point of the so-called "what" stream, a cortical hierarchy of perceptual processing areas that represents information about objects (*7*). There is also a parallel "where" stream in the cortex, ending in the MTL within the parahippocampal area, which represents the spatiotemporal contexts in which objects have been experienced. These streams merge within the hippocampus, which represents relationships between objects and between objects and their context. In this model, the role of the perirhinal cortex is to bind perceptual features into representations of whole objects, and make these representations resistant to perceptual interference—just as McTighe *et al*. describe. The hippocampus normally encodes and retrieves representations of the objects and context when cued, and damage to the hippocampus prevents this retrieval, resulting in forgetting. The prefrontal cortex normally receives that information from feedback pathways through the MTL, and monitors the match between object and context memories ("Is this object from today's list?"). Lacking that monitor, the animals cannot tell whether an object is from today's list or a previous list—leading to the increase in false memories following prefrontal damage.

A decade ago (*2*), available evidence led to the conclusion that different forms of memory should be viewed as the outcome of plasticity within systems organized to perform particular information processing functions. The MTL's information processing functions, however, were unclear. In their study, McTighe *et al*. offer a partial answer: The MTL's perirhinal cortex binds featural elements into cohesive configural memories, and this function is supported by known plasticity mechanisms (*8*). The hippocampus and prefrontal cortex, as well as other key brain areas of this system, also contribute directly to memory through plasticity in their particular information processing tasks. These findings, then, support the view that there is a dedicated MTL memory system. They also further our understanding of that system as a set of specialized areas that interact to coordinate the information processing functions required for successful memory.

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MATERIALS SCIENCE

High-Temperature Rubber Made from Carbon Nanotubes

A mixture of carbon nanotubes creates a material that can recover its shape after deformation over a wide temperature range.

Yury Gogotsi

Carbon nanotubes have been among the most studied materials for the past two decades (*1*); they display several remarkable properties, such as extremely high tensile strength and electrical conductivity. On page 1364 of this issue, Xu *et al*. (*2*) report another case of extreme mechanical performance of a carbon material—viscoelastic behavior of nanotubes in a wide temperature range—that no other solid has shown so far.

Viscoelasticity is the ability of a material to dissipate energy through viscous behavior (think honey) and reversibly deform through elasticity (think rubber band). Polymer foam earplugs are a typical viscoelastic material; they conform to any shape of ear channel but fully recover to the original form after being pulled out. Viscoelasticity is exhibited by a large number of materials (*3*), including amorphous and semicrystalline polymers, biomaterials, crystalline materials experiencing reversible phase transformations, and some metallic alloys.

Viscoelastic behavior is determined by measuring stress-strain curves: The material is pushed on or pulled at a given force (stressed), and deformation (strain) is measured. A viscoelastic material exhibits "memory" (hysteresis) effects in its stress-strain behavior. For example, the amount of stress needed to maintain the same level of strain will drop over time, and for a given stress, the material will continue to deform.

The material reported by Xu *et al*. is a special case of a viscoelastic material; it behaves like rubber under moderate deformations. Rather than store energy in permanent deformation, like a bent metal part, a rubber releases the energy when the applied force is removed. Viscoelastic behavior of nanotubes has been observed for vertically aligned brushes and foams of tubes (highly intertwined random networks) tested at room temperature (*4*–*7*). The groups of Gogotsi and Greer independently observed buckling and irreversible compressibility

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