greater positive potential for recalled than for nonrecalled words).

These results are broadly consistent with the earlier fMRI studies (*6*) in that both the fMRI and ERP data directly implicate MTL structures in memory encoding associated with both subsequent remembering and forgetting. The two avenues of research appear to differ, however, in that the fMRI studies demonstrate that activity in the posterior MTL (posterior parahippocampal gyrus) is associated with subsequent retention of memory, whereas the ERP results indicate that activity in the anterior MTL (anterior parahippocampal gyrus and hippocampus) is associated with memory retention. Fernandez *et al.* did not record from the posterior MTL and it may be that if ERPs had been recorded from this region then an association between activity during encoding and memory formation would have been found. The fMRI and ERP data suggest that there may be at least three distinct regions of the MTL involved in memory encoding.

Why did the earlier fMRI studies fail to find an association between activity during encoding and subsequent memory in anterior MTL regions? Meta-analyses of neuroimaging data indicate that, whereas PET studies reveal activation during encoding in both anterior and posterior MTL, fMRI experiments demonstrate activation almost exclusively in the posterior MTL (*9*). These contrasting results could reflect differences in experimental protocols between the studies, or could be attributable to loss of fMRI signal (susceptibility artifact) in the anterior MTL. Further experiments comparing PET, fMRI, and electrophysiological techniques will be required to settle these apparently conflicting findings.

The Fernandez study brings into bold relief a critical and as yet unanswered question: exactly what computations do each of the MTL regions perform, and how is the later encoding activity in the hippocampus influenced by, or dependent on, earlier activity in the MTL? Consistent with the observation of temporally staggered encoding events within these structures, the MTL is the principal cortical input pathway to the hippocampal region. However, additional evidence is necessary to determine whether these structures support encoding of the same or similar types of information, or whether they support the encoding of fundamentally different kinds of information. This distinction bears on a current debate about the architecture of memory and the specific roles of MTL structures in memory formation (*10*). One theory proposes that parahippocampal and hippocampal regions support the encoding of the same type of declarative information, which supports later recall and recognition of facts and events. An alternative theory postulates that the parahippocampal gyrus contributes mainly to the encoding of information about the occurrence of an item (required for subsequent recognition) whereas the hippocampus supports encoding of relations between an item and its context (primarily useful for subsequent recall) (*10*). Although the Fernandez findings do not settle this debate, they will provoke future studies melding electrophysiological and fMRI techniques with behavioral observations. Such studies should help to elucidate how the parahippocampal and hippocampal MTL structures encode and form memories of items and their connections to other objects and, more broadly, how memories are organized (*11*).

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NOTA BENE: NEUROSCIENCE

For Time Is the Longest Distance Between Two Places

TENNESSEE WILLIAMS, *THE GLASS MENAGERIE*

Imagine that you can vividly describe the neighborhood in which you grew up 60 years ago but are unable to remember anything about the area in which you now live. This is the plight of a 76-year-old amnesic man who suffered damage to the hippocampus and other structures in the medial temporal lobe (MTL) of the brain (see the figure, previous page) after encephalitis. His misfortune has proved providential for neuroscientists studying how the brain forms memories, a process known to involve the hippocampus.

Teng and Squire, the University of California researchers who studied the amnesic patient, report in a recent issue of *Nature* (*1*) that he could recall as readily as several of his old schoolmates how to navigate from his boyhood home to school and gave comparable responses to a series of questions about the neighborhood in which he grew up. But, he could give no directions at all from his current residence to particular locations in his new neighborhood (to which he moved after becoming amnesic). The investigators conclude that the hippocampus is essential for forming new memories of places but that these memories are stored for long-term retrieval in other parts of the brain.

A neuroimaging study in mice, reported in a companion paper (*2*), supports that conclusion and identifies regions of the neocortex where place memories are eventually stored. Bontempi *et al.* (University of Bordeaux) taught their mice to discriminate between eight arms of a radial maze (three arms contained food, the other five did not). Five or 25 days after learning the task, the mice (injected with a radioactive tracer) were again presented with the maze, and changes in metabolic activity in different brain regions were visualized by neuroimaging. Mice negotiating the maze after a 25-day hiatus showed decreased metabolic activity in the hippocampus but increased activity in several neocortical structures compared with mice that had traversed the maze just 5 days previously. But presenting mice with a new maze (in which food appeared in different arms), 25 days after they had memorized the original version, reactivated hippocampal activity as new memories were formed. Although the hippocampus is active in the early formation of spatial memories, it appears that they are gradually consolidated and stored outside of the MTL in the neocortex. With the finding that other regions of the MTL (within the parahippocampal gyrus) are important for the initial step in memory encoding (see page 1503), the intricate skeins of memory's web are slowly becoming untangled.

—ORLA SMITH

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