that require binding at the behavioral level. While these findings provide some new answers, they also require additional observations and extensions to determine whether neural synchrony in motor structures truly represents motor binding.

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Declarative versus Episodic: Two Theories Put to the Test

The question of whether the hippocampus plays a selective role in episodic memory or a more general role in both episodic and semantic memory (together termed declarative memory) is an unresolved and much-debated topic in the current literature. In two back-to-back articles in this issue of *Neuron*, Squire and his colleagues describe findings from a group of six patients with damage thought to be limited to the hippocampus. The reported findings provide new evidence toward resolving this much-debated controversy.

It would be fair to say that most neuroscientists polled today would agree with the statement that the hippocampus plays an important role in memory. Asked specifically what form of memory the hippocampus participates in, and this initial consensus will quickly dissolve into a raucous clash of two strongly divergent views. One camp has proposed that the hippocampus plays a selective role in episodic memory with little or no contribution to semantic memory. This has been termed the episodic theory of hippocampal function. Perhaps the most dramatic evidence in support of this view comes from the description of a group of patients who sustained damage to the hippocampus early in life and who exhibit impaired episodic memory in the face of surprisingly good semantic memory (Vargha-Khadem et al., 1997). Related to this view, others have argued that the hippocampus is not only specifically involved in laying down new episodic memories, but that even very remote episodic memories remain dependent on the hippocampus (Fujii et al., 2000). The opposing camp argues that the hippocampus together with the surrounding entorhinal, perirhinal, and parahippocampal cortices contribute to both semantic and episodic memory. This has been termed the declarative theory of medial temporal lobe function. This view is supported by a large body of convergent findings from studies in human amnesic patients together with parallel findings in animal model systems (Manns and Squire, 2002; Squire and Zola, 1998). The declarative view also holds that the medial temporal lobe plays a time-limited role in the consolidation of declarative memory such that memory for both episodic and semantic information encountered well before the onset of amnesia is unaffected.

A handy feature of such diametrically opposed theories is that each of them makes very distinct and testable predictions. For example, the episodic theory predicts that selective damage to the hippocampus should result in little or no impairment in semantic memory. In contrast, the declarative theory predicts significant semantic memory impairment resulting from selective hippocampal damage. A second clear prediction of the episodic theory is that remote episodic memories should be impaired in patients with selective hippocampal lesions. In contrast, the declarative theory predicts that remote episodic memories would be intact. One might ask, how is it that these clear and obvious predictions have not yet been tested? The short answer is that it is very difficult to gather a large enough group of patients with the kind of selective bilateral hippocampal damage necessary to test these predictions in a robust way. Using a rare group of six such amnesic patients with damage thought to be restricted primarily to the hippocampal region, Squire and his colleagues have tested these key predictions of the episodic and declarative views in two studies published in this issue of *Neuron* (Bayley et al., 2003; Manns et al., 2003).

The first experiment in the study by Manns et al. examined the performance of this group of hippocampal-damaged patients and matched controls on semantic memory for news events. The news events were either encountered before (retrograde memory) or after (anterograde memory) the onset of amnesia. The patients with hippocampal damage exhibited significant impairments on either recalling or answering multiple choice questions about the news events occurring after the onset of amnesia (i.e., anterograde amnesia for semantic information). On the retrograde component of this task, Manns et al. found evidence for a temporally graded retrograde amnesia such that recall for new events occurring 0–10 years before the onset of amnesia was impaired relative to the performance of control subjects. In contrast, remote memory for events occurring 11–30 years before the onset of amnesia did not differ from control performance. One potential problem in interpreting these findings is that control subjects but not amnesic patients may have access to episodic details that may, in turn, help them recall the related semantic infor-

mation. Manns et al. addressed this possibility in a second experiment in which subjects were asked about the names of famous and nonfamous people who came into prominence before 1970 (test of retrograde memory). If subjects and controls were able to correctly identify the name as being famous, they were then asked if that person was living or dead. Since, in most cases, the judgement of whether the person was living or dead relied on information learned after the onset of amnesia, this was a test of anterograde memory for semantic information. To eliminate the possible facilitating effect of intact episodic memory, the control subjects were asked to recollect any specific events associated with the correctly identified famous names. Those names for which control subjects recollected any circumstance in which they had heard that the individual had died were eliminated from the analysis. Even after removing those items, the patients with hippocampal damage still exhibited significant anterograde impairment for the famous names relative to controls. Thus, consistent with the declarative view, patients with selective hippocampal damage exhibit an anterograde memory impairment and a temporally graded retrograde memory impairment for semantic information.

In the second article, Bayley et al. examined the performance of the same group of patients with presumed damage limited to the hippocampus as well as two patients with larger medial temporal lobe lesions on tests of remote autobiographical memory. Compared to earlier studies, a new and innovative aspect of this study was the detailed and quantitative analysis performed on the content of the autobiographical narratives generated by the experimental and control subjects. Each narrative was first scored using a 0 to 3 scale. Those narratives given a rating of 3 (corresponding to the recollection with the most detail) were further scored for the specific number of episodic and semantic pieces of information they contained. The amount of repetition in the narratives, latency, duration, and the number of prompts required were also examined. The major finding was that amnesic patients (some with profound anterograde memory impairments) not only generated a similar number of well-formulated (i.e., 3 point) autobiographical memories as controls, but those memories contained the same amount of episodic and semantic detail as control subjects. The two patients with larger medial temporal lobe lesions repeated details in their narratives and required more prompts during the narrative compared to controls, but the amnesic patients as a whole did not differ from controls in either the latency or duration of the narratives. Thus, consistent with the declarative view of medial temporal lobe function, both the depth and detailed content of remote autobiographical memories are intact in patients with damage thought to be limited to the hippocampal region as well as in patients with larger medial temporal lobe lesions.

How do we relate the results of Manns et al. and Bayley et al. to the predictions of the episodic theory of hippocampal function? Specifically, how do we reconcile the findings of Manns et al. with the findings of Vargha-Khadem et al. (1997), who reported severely impaired episodic memory in the face of surprisingly good semantic memory following hippocampal damage early in life (termed developmental amnesia)? One obvious difference between the Vargha-Khadem study and these reports by Squire and colleagues is the etiology of the two patient populations. While all the patients in the Vargha-Khadem study sustained hippocampal damage very early in life, all the patients in Squire's studies became amnesic as adults. This difference suggests the possibility that a striking amount of functional reorganization may be possible if medial temporal lobe damage is sustained early in life. However, additional studies comparing the performance of the subjects with early hippocampal damage on the tasks used by Manns et al. will also be important to help fully resolve this issue. Thus, while semantic memory may be relatively spared in cases of developmental amnesia (Vargha-Khadem et al., 1997), in the adult brain both episodic (Reed and Squire, 1998) and semantic memory (Manns et al., 2003) are significantly impaired following even discrete damage thought to be limited to the hippocampus.

A second key comparison is between the findings of Bayley et al. on remote autobiographical memory and previous reports of two single case studies with impaired remote autobiographical memory following medial temporal lobe damage (Cipolotti et al., 2001; Hirano and Noguchi, 1998). As discussed by Bayley et al., a major consideration in evaluating studies of remote autobiographical memory is the precise locus and extent of the brain damage in the patients studied. This is particularly critical for studies of remote autobiographical memories, since any extra damage outside the medial temporal lobe could potentially involve the cortical storage sites for the remote autobiographical memories themselves. Bayley et al. argue that because the hippocampal or medial temporal lobe-damaged patients in their study were not impaired on tasks of remote autobiographical memory, the severe impairments reported in those two single case studies (Cipolotti et al., 2001; Hirano and Noguchi, 1998) are probably not due to damage to the medial temporal lobe. Instead, they propose that the remote autobiographical memory impairment may be caused by as yet undetected damage outside the medial temporal lobe. Direct histological verification of damage in these amnesic patients may be the only way to ultimately resolve this issue. However, it is clear that detailed anatomical characterization of the amnesic patients used in these studies becomes even more critical as the hypotheses being evaluated become more and more specific.

These two new reports by Squire and his colleagues provide important new evidence in support of the declarative theory of memory and contradict two key predictions of the episodic theory of hippocampal function. Thus, while these findings suggest that the episodic theory is not valid in cases of adult onset amnesia, they do not rule out the possibility that the hippocampus may play a selective role in some other aspect(s) of memory. Indeed, a fundamental question remains understanding the specific contributions of the hippocampus and adjacent entorhinal, perirhinal, and parahippocampal cortices in memory function. The findings of Manns et al. and Bayley et al. suggest that future attempts to define a more specific set of mnemonic features or functions dependant selectively on the hippocampus must include features of both episodic and semantic memory.

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