

# **Consolidating Dispersed Neocortical Memories: The Missing Link in Amnesia**

Ken A. Paller

*Northwestern University, Illinois, USA*

Consolidation is often conceptualised as a general process by which memory traces can be strengthened in the brain. An alternative idea, developed here, is that a particular sort of consolidation is required for establishing memories belonging to a neurobiologically defined category—memories dispersed across multiple distinct neocortical zones. These memories are consolidated via the formation of a neocortical cell assembly that confers coherence to the set of scattered neocortical memory traces. A set of memory traces linked in this manner can subsequently serve as the basis for conscious recollection. A disruption of this neocortical consolidation process is held to be responsible for the patterns of preserved and impaired memory observed in amnesic patients. A suitable strategy for empirically testing this sort of theory requires an examination of evidence from neuropsychological studies of amnesia and from studies of the neural substrates of memory functions in normal subjects.

## **INTRODUCTION**

In an influential paper published in 1976, Paul Rozin systematically contrasted various theories of human amnesia and came to a conclusion that may still be appropriate today. Rozin proposed that the core defect in amnesia is a severe consolidation block with normal memory-activation processes, and furthermore, he ended his review (1976, p.42) by expressing the hope that by 1990, “the intervening advances in the psychological understanding of human memory will permit someone to organize materials on the amnesic syndromes so that they can be covered in a few pages.” The literature on amnesia, however, has steadily expanded, as Mayes & Downes (this issue) demonstrated in their survey of the evidence that theories of amnesia must address. The number of theoretical positions has also expanded, but a clear consensus on which theory can best explain the evidence has not yet emerged.

---

Requests for reprints should be sent to Ken Paller, Department of Psychology, Northwestern University, 2029 Sheridan Road, Evanston, IL 60208-2710, USA. Email: kap@nwu.edu

I acknowledge support from NINDS grant #NS34639 and thank the many memory theorists who have influenced the ideas expressed here. Special thanks to Larry Squire and Andrew Mayes, who provided useful feedback on previous versions of this paper.

In this article I describe a new version of a consolidation theory and examine how well it can handle the challenge of explaining the evidence from amnesia. In addition, I argue that a reasonable goal is to seek connections between theories of amnesia and theories of normal memory so as to foster their synergistic development. This can be accomplished by considering the neuropsychological evidence from amnesia together with evidence about the neural substrates of normal memory functions. To support this view, the penultimate section summarises recent research using neuroimaging and neuromonitoring techniques to study memory functions in normal subjects, building on the knowledge gained through the study of amnesia.

In amnesia, brain damage undermines the ability to recollect previously experienced episodes and facts. In some cases of amnesia, a memory deficit occurs in the absence of other intellectual dysfunctions.<sup>1</sup> The selectivity of the memory deficit affords two key conclusions: (1) the preserved intellectual abilities do not require the integrity of the damaged brain areas, and (2) these brain areas contribute a function that is critical for the type of memory that is impaired. But what is the nature of this critical function?

Although it is possible to investigate the *functional deficit* of amnesia without regard to the nature of the *neural dysfunction*, the most suitable strategy for understanding amnesia is to simultaneously seek to understand the disorder from both perspectives. Thus, an adequate theoretical account of amnesia would include:

1. a psychological description of the disrupted memory function;
2. a biological description of the neural disruption;
3. a mapping between the psychological dysfunction and the brain dysfunction with reference to the neural implementation of memory functions in normal subjects.

Whereas psychological and biological aspects of a theory can be listed separately, they are highly interdependent. Ultimately it will be important to bridge the gap between these two levels of description—a key goal of the field of cognitive neuroscience.

---

<sup>1</sup> Mayes & Downes (this issue) note the lack of agreement about whether amnesia should be considered a heterogeneous syndrome. Indeed, amnesia often occurs together with additional symptoms that are dissociable from the memory impairment (e.g. confabulation, anosognosia, disorientation, perseveration, and remote memory loss). Despite this controversy, a working hypothesis is adopted here that the disruption of a single memory function gives rise to a set of core memory impairments.

## CONSOLIDATION OF DISPERSED NEOCORTICAL MEMORIES

The idea that amnesia arises because of the disruption of a consolidation process is not new. The construct of consolidation—the process whereby memories change to become stronger over time—has a long history in the study of memory, both in human and nonhuman subjects (Squire, Cohen, & Nadel, 1984). Early theorising by Burnham (1903, p. 396) construed consolidation as “a physical process of organization and a psychological process of repetition and association.” The view that human amnesia reflects a consolidation deficit was advocated by Brenda Milner in explaining the pattern of deficits in patient HM, who received a bilateral surgical excision to the hippocampus and adjacent temporal lobe regions (Scoville & Milner, 1957). Milner (1965) referred to this area as “the hippocampal zone” and suggested that it made possible the storage of information beyond the immediate present via the consolidation process. Milner also concluded that the hippocampal zone was not necessary for forming temporary associations between stimuli or for the variety of intellectual abilities that patients retained, including many uses of past learning. These abilities were thought to depend primarily on cell assemblies within the cerebral cortex (Hebb, 1949). Temporary associations could be recalled if attention was continuously maintained on the information. After attention was diverted, recall was thought to depend on the simultaneous activity of cortical and hippocampal cells. Furthermore, Milner explained the intact remote memories of amnesic patients by supposing that cortical cell assemblies could eventually mediate recall autonomously, without the hippocampus.

The present consolidation theory of amnesia extends these ideas in several directions. Some similarities to other theories in the literature are discussed in a subsequent section. The theory can be summarised by eight chief propositions, as follows:

1. Episodes are experienced when a set of neocortical neurons representing relevant events and states are activated. This requires the participation of neocortical regions specialised for representing different types of information (various visual areas, various auditory areas, and so on). The term *neocortical zone* will be used to refer to these functionally distinct regions. Aspects of spatiotemporal context are essential features of episodes that depend on a large set of neocortical zones. Thus, encoding and storage of episodic information characteristically involves multiple neocortical zones. Likewise, many sorts of facts also rely on representations distributed across multiple neocortical zones. A set of neurons within each neocortical zone can function to represent a single memory feature (or “memory attribute” as described by Underwood, 1969). This set of neurons will be termed a *neocortical ensemble*. The collection of neocortical ensembles that represents factual or episodic

information dispersed across multiple neocortical zones will be termed a *neocortical consortium*.

2. Re-experiencing an episode as a memory requires the participation of the same neocortical consortium that was activated during the original experience. Consolidation of a dispersed neocortical memory (henceforth referred to simply as consolidation) involves a process whereby the constituent parts of the memory are linked together in an enduring way. Remembering an episode or fact is facilitated by consolidation because successful retrieval depends on the extent to which the individual elements of the memory are strongly integrated as a unit.

3. The consolidation process is accomplished via an interplay between the hippocampal zone and the neocortex. The retrieval of facts and episodes is made possible because this interplay results in the modification of synaptic connections at memory storage sites distributed across multiple neocortical regions. The contribution of the hippocampal–neocortical interaction is twofold. First, hippocampal neurons are instrumental in the re-activation of a dispersed neocortical memory at the time of retrieval. Second, the same hippocampal neurons function over extended time periods to promote the formation of what will be referred to as a *coherence ensemble*. Each coherence ensemble has connections to the constituent parts of a neocortical consortium and facilitates the activation of that consortium as a unit. Eventually, the coherence ensemble takes over the role of facilitating the re-activation of the neocortical consortium such that the hippocampal connections are no longer required.

4. Memory storage can be facilitated by consolidation for memories that rely on representations dispersed across multiple neocortical zones, and this can apply for episodes, facts, and perhaps for some associative priming effects. Brain mechanisms responsible for these memories can collectively be termed the *declarative memory* system. Varieties of *nondeclarative memory* are accomplished without the necessary participation of the declarative memory system and are intact in amnesia either because (a) the memories are stored in places other than the neocortex or (b) plasticity within individual neocortical zones is sufficient for memory storage.

5. Consolidation proceeds in proportion to the extent to which the neocortical consortium is re-activated as a unit. Processes critical for consolidation—memory access, association, and integration—are active processes and are markedly promoted during dreaming. Consolidation is not a passive process inexorably set into motion at encoding, but rather it is determined by the continuing relevance of the memorial information and relationships to other information in an individual's ongoing cognitive activities.

6. Consolidation depends on the concurrent re-activation of neocortical consortia through two neuronal routes. One pathway involves hippocampal connections through transitional cortex in the temporal lobe. The second pathway involves diencephalic projections to neocortical regions, along with

prefrontal interconnections. After consolidation is complete, coherence ensembles in anterior temporal and orbitofrontal cortex participate in the re-activation of neocortical consortia through direct cortical-cortical connections.

7. Hippocampal plasticity is rapidly and indiscriminately available to provide coherence to dispersed neocortical memories. The formation of coherence ensembles takes longer to achieve, but provides coherence to neocortical memories less indiscriminately and fades more slowly.

8. Consolidation and recollection occur under the supervision of prefrontal areas that provide critical activation of posterior regions in the service of memory retrieval. This prefrontal activation is instrumental for memory search operations that can selectively access coherence ensembles as well as individual neocortical ensembles that comprise declarative memories.

Given this theoretical framework, how can the central findings from amnesia be explained? Table 1 lists the chief characteristics of amnesia and

TABLE 1  
Accounting for the Chief Characteristics of Amnesia as the Outcome of a Defect in Consolidating Dispersed Neocortical Memories

Impaired recall and recognition of facts and episodes (anterograde)	In the absence of consolidation, re-activation of the scattered components comprising the memorial information occurs only inefficiently.
Preserved immediate memory	Once activated, dispersed neocortical representations can be maintained in an activated state via prefrontal connections.
Preserved retrieval of remote memories	Remote memories can be efficiently accessed via previously established coherence ensembles.
Temporal gradient of retrograde amnesia	The temporal gradient corresponds to the protracted timespan of consolidation, which varies greatly from one memory to another.
Preserved motor skills, conditioning, and nonassociative learning	These types of learning are not mediated cortically but instead depend on other brain regions such as the cerebellum and basal ganglia. Different sorts of consolidation may be required.
Preserved semantic memory	General knowledge of the world is available because it is already consolidated or because it is contained within a single neocortical zone.
Preserved item-specific priming	This type of priming depends on the storage of information within a single neocortical zone. Temporary effects of the activation of these representations do not require consolidation.
Impaired association-specific priming	New associations across multiple neocortical zones are facilitated by consolidation, and so are stored less efficiently in the absence of normal consolidation.

corresponding explanations based on the core deficit proposed in the present theory. A salient feature of this theory is that neurobiological criteria are used to define declarative memory, the type of memory impaired in amnesia. Declarative memories are those that rely on dispersed neocortical memory traces, and furthermore, the process of consolidation specified here is taken to apply only to this type of memory. One shortcoming of this approach is that these neurobiological criteria are not transparent from the behaviour of the subject, although in essence these distinctions pertain to the brain. Memory distinctions *are* biological distinctions. Furthermore, tying well-established psychological conceptualisations to the biology of cortical storage has the virtue of connecting them to a long tradition of neuroscience research concerned with understanding the physiology of nervous systems (Squire, Knowlton, & Musen, 1993).

The theory posits that consolidation confers coherence to elements of a declarative memory. The elemental unit of information is thought to be contained within a single neocortical zone. The plasticity takes the form of changes in synaptic connection strengths such that the memorial information is represented using a large number of neurons, as in a Hebbian cell assembly. The cell assembly, or neocortical ensemble, might involve neurons in more than one cortical column, but these columns would share common representational principles and would be considered part of the same neocortical zone. Although general methods for empirically delineating neocortical zones cannot be given, presumably there are distinct zones for each of the ways in which sensory input is analysed. For example, within the arena of representing facial information, a variety of visual analyses may be conducted, and there may be corresponding zones for representing the results of these different analyses. Judging from the number of distinct visual areas found in the neocortex, the sum total of neocortical zones may be quite large.

The nature of a neocortical zone is central here because consolidation is defined as a process that links neocortical information *across* zones. Declarative memories are fundamentally characterised by a dependence on connections among neocortical ensembles in multiple zones. Preserved priming effects in amnesia are characterised by a dependence on plasticity within single neocortical zones. Consider item-specific and association-specific priming. An example of the former is enhanced identification for studied words compared to nonstudied words; an example of the latter is enhanced identification for studied word pairs compared to studied words combined to form new pairings (Paller & Mayes, 1994). Item-specific priming is preserved because the relevant plasticity occurs within a neocortical zone concerned with representing one aspect of an item, such as visual word-form. Such representations involve a large number of neurons, but the crucial factor concerns the scale of the distributed representations—whether they are distributed within versus across neocortical zones. Association-specific priming is generally impaired because the relevant

plasticity occurs with respect to connections among multiple neocortical ensembles not restricted to a single zone, as in the semantic associations formed between words. Schacter (1987) used the term "free fragments" to denote the isolated memory components that an amnesic patient can retain. Representations maintained within a single neocortical zone may correspond to so-called unitised representations or free fragments (Hayes-Roth, 1977; Schacter & McGlynn, 1989).

Retrieval factors can have a strong influence on whether a priming effect relies on within-zone plasticity or across-zone plasticity. A given test of association-specific priming that yields impaired performance in amnesia could be construed as a test that relies on across-zone plasticity. Similarly, disproportionate deficits in recall versus recognition can arise if the circumstances are such that the recall test places relatively more demands on across-zone plasticity. Unfortunately, an independent metric for within- versus across-zone plasticity has not been identified. In addition, the situation is complicated by the possibility that behavioural priming effects may depend more on one or the other type of plasticity as a function of subtly different retrieval circumstances. In any event, further research is needed to more precisely specify the boundaries of preserved priming in amnesia. Note that the use of an implicit memory test does not guarantee a preserved priming effect in amnesia. Therefore, the contrast between implicit and explicit memory is not adequate for defining the categories of preserved and impaired memory functions in amnesia.

Burnham's (1903) description of consolidation cited both physical and psychological processes. One way to construe the physical or neural mechanism of consolidation is as an automatic firming up of neural connections necessary for long-term storage. Many have speculated on how long such a process would require. The completion of such a process might indeed require a constant time period due to some passive molecular process. In contrast, consolidation in the present formulation is considered an active process that depends on intervening rehearsal and association; it does not inexorably run its course. Consolidation can be thought of as the reorganisation of memory traces that occurs when information is rehearsed and also when any portion of the memory is accessed. By this view, consolidation takes place at many points in time after the initial experience. The time span of consolidation depends on the complexity and meaningfulness of the memorial information, the number of times the memory is accessed, and the nature of concomitant reorganisation.

A prime opportunity for this memory access is in the context of the retrieval of the memory in question. Significantly, retrieval does not only occur in the waking state. In all likelihood, consolidation regularly occurs in the context of retrieval that takes place during sleep. In dreams, a multitude of memories are accessed, particularly recent memories. Consolidation may occur whether or not there is any lasting memory for the dream. Indeed, a peculiar characteristic of

dreams—that they are quickly forgotten upon awakening unless rehearsed during the waking state—suggests that memory functions have switched to another mode. Winson (1985) and others have shown that changes in the functional connectivity of hippocampal subregions correlate with sleep stage (e.g. hippocampal gating patterns change such that output from CA3 neurons is enhanced during slow-wave sleep). Furthermore, firing patterns of ensembles of rat hippocampal neurons demonstrate a degree of synchrony during waking that is specifically maintained during subsequent slow-wave sleep (Wilson & McNaughton, 1994). Thus, dream sleep may be a vital time for the “off-line” processing of memories (e.g. Marr, 1971; Winson, 1985). In this way, memories can be retrieved and integrated with the individuals’ long-term plans and goals, although this is not necessarily apparent in dream content. Associations thus forged among recent memories and old, well-established memories provide a critical part of the consolidation process. Importantly, the reorganisation of memories does not happen randomly but is regulated according to higher-level goals such that certain memories are more likely to be accessed and thus more readily consolidated.

Another fundamental issue that theories of amnesia must address is whether the impairment applies to only certain types of information or to all types of information. Cohen and Squire (1980) suggested that consolidation is preferentially required for the particular type of information termed *declarative knowledge*, which includes autobiographical episodes as well as facts and is directly accessible to conscious recollection. Others have emphasised configurational processing, in the sense that some memories require relational connections among multiple informational elements (Eichenbaum, Otto, & Cohen, 1992; Sutherland & Rudy, 1989). I also place central importance on configurational connections, but not fundamentally with respect to informational elements. Rather, representations that exist within discrete neocortical zones constitute the elements that must be associated via consolidation. Thus, consolidation operates by strengthening connections among a set of neocortical ensembles, each localised within a single neocortical zone. In the absence of consolidation, not all types of information are lost. The boundary between impaired and preserved memory depends on the biology—memory is impaired when it depends on connections among neocortical ensembles. A lingering problem is to be able to determine whether or not connections among neocortical ensembles are required for any given instance of memory performance.

In addition to specifying the functional characteristics of consolidation, it is also necessary to specify the outcome of consolidation. What is it that changes over the course of consolidation? So far I have speculated that a new declarative memory requires a special sort of neocortical plasticity that is capable of linking memory traces from disparate neocortical regions. The key change is the formation of a new neocortical ensemble in the anterior temporal region and/or



associated orbitofrontal regions. This newly formed coherence ensemble differs from the proverbial “grandmother cell” in that it does not operate independently. It maintains the integrity of the consortium of neocortical ensembles but it does not redundantly re-represent all the same information. Global aspects of a fact or event may be represented by the coherence ensemble, whereas the consortium of neocortical ensembles represents the various components of the memory. Neocortical ensembles can also be used concurrently in other memories (just as neurons participating in each neocortical ensemble can also be used concurrently in other neocortical ensembles). Recollection thus involves the conjoint activation of the coherence ensemble and the consortium of neocortical ensembles. In short, consolidation can be conceptualised as the transfer of the coherence contribution from a set of neurons in the hippocampus to a set of interconnected neocortical neurons constituting a coherence ensemble. This neocortical coherence function takes some time to develop, whereas the hippocampal coherence function develops more quickly, perhaps even in a single trial, but also fades more rapidly with disuse (see McClelland, McNaughton, & O’Reilly, 1995; Milner, 1989).

The present proposal accounts for the common coexistence of anterograde and retrograde amnesia, while it also allows for dissociations between anterograde and retrograde amnesia, as follows. First, hippocampal damage causes anterograde amnesia because new coherence ensembles can only be created slowly and inefficiently. Hippocampal damage also produces some retrograde amnesia because of incomplete consolidation of recent memories—the formation of coherence ensembles occurs over a time period that depends on the extent to which the memories are retrieved, integrated, and associated. Second, damage to anterior portions of temporal and/or orbitofrontal cortex can lead to retrograde amnesia (see reviews by Kapur, 1993; Markowitsch, 1995) because some of the storage sites of coherence ensembles have been destroyed such that retrieval of the formerly associated neocortical consortia is inefficient. Third, a more severe amnesia is produced after damage to both the hippocampus and anterior temporal areas because neocortical consolidation is more severely hampered without either the hippocampus to promote the formation of coherence ensembles or anterior temporal regions to act as the substrate for these new ensembles.

## THE NEURAL DYSFUNCTION OF AMNESIA

Each of the multifarious neurological conditions associated with amnesia disrupts function in one or more of a set of brain structures generally regarded as components of the limbic system. Prominent among these structures are the hippocampus, neighbouring cortical areas in the temporal lobe, structures in the diencephalon (the mammillary bodies and certain midline thalamic loci, although precisely which is controversial), and the basal forebrain. An

exhaustive list of the critical brain lesions might thus include a large number of areas that may or may not comprise a single functional system. For present purposes, a key question is how these areas function in the service of consolidation.

One difficulty in identifying the lesions that are critical for the emergence of amnesia is that many of the conditions that produce it cause additional damage to other regions. These additional lesions can cause memory and cognitive disturbances that are dissociable from the deficits caused by the critical lesions. Patients with amnesia due to Korsakoff's syndrome, for example, usually have brain damage that superimposes additional symptoms on the amnesia. Even taking such superimposed deficits into account, the available neuropsychological evidence is insufficient to support firm conclusions about whether the core deficits of amnesia differ as a function of qualitatively different configurations of brain damage.

Although the anatomy of amnesia has been studied intensively for many years, *in vivo* neuroimaging technology now provides a significant source of information that was not previously available. Moreover, functional neuroimaging can provide a vital new perspective on the neural dysfunction. The majority of the extant evidence on the neuroanatomy of amnesia specifies only structural damage, whereas functional alterations can also be highly relevant for understanding amnesia. This point can be made more concretely with reference to a study of alcoholic Korsakoff's syndrome (Paller et al., in press). Functional neuroimaging of glucose utilisation with positron emission tomography was used to investigate the neural dysfunction responsible for the amnesic impairment. Results suggested that the known diencephalic lesions in these patients had remote effects on other brain areas. In particular, metabolic abnormalities were found in the frontal lobe, the parietal lobe, and both anterior and posterior cingulate regions. In contrast, abnormalities were not found in temporal lobe areas, including the hippocampus. Therefore, the idea that amnesia reflects an across-the-board disruption of processing within the medial temporal region and parts of the diencephalon must be supplanted by a theory that confers a degree of independence to these two brain areas.

A likely alternative is that hippocampal-neocortical interaction is not the sole factor mediating consolidation. Specifically it can be hypothesised that midline thalamic nuclei function to activate widespread cortical regions such that two types of interactions with neocortical storage sites can occur simultaneously. One is mediated by projections from the hippocampus to posterior neocortical regions via entorhinal cortex. The other is mediated by projections from several midline thalamic nuclei to prefrontal cortex and to other parts of the cerebral cortex. Prefrontal projections to posterior cortical regions also figure in related mechanisms for immediate or working memory (e.g. Fuster, 1995). In short, two types of interactions must be active in order for neocortical ensembles to store declarative memories normally. Synaptic alterations may occur through Hebbian

principles such that concurrent input from both sources is required. This speculation is consistent with the notion that many different configurations of brain damage produce basically the same sort of memory defect.

## COMPARISONS WITH OTHER CONSOLIDATION VIEWS

Neural interactions between the hippocampus and distributed neocortical locations in the service of consolidation have been emphasised in many more theories than can be cited in the space available here. For example, the need for linking information from multiple cortical regions was recognised in a proposal developed by Damasio (1989), although that formulation did not include specifics about consolidation. Squire et al. (1984) described a consolidation process in which neocortical activity was modified by input from the hippocampal region, leading to neocortical reorganisation. Importantly, reorganisation was portrayed as occurring in concert with forgetting, in that some connectivity is improved while some is lost. Several computational models of hippocampal consolidation have been developed (McClelland et al., 1995; Squire & Alvarez, 1995; Treves & Rolls, 1994). Halgren (1984) postulated that the hippocampus contributes to the retrieval of recent memories and to the experience of familiarity though reciprocal connections between hippocampus and neocortex forming positive feedback loops. Highly specific connections would thus be required such that particular hippocampal and neocortical cells mutually excite each other. A different sort of hippocampal–neocortical interaction was proposed in the memory-indexing theory of Teyler and DiScenna (1986). The information stored in the hippocampus was thought to provide a map or index of the sets of neocortical ensembles representing particular experiences. Thus, reactivation of a hippocampal index would lead to the reactivation of an array of neocortical loci and thereby a memorial experience. Consolidation was conceived of as a process of continual reactivation of a hippocampal index, leading to incremental effects on the associated cortical circuitry and the establishment of a cortically based memory trace. Squire, Shimamura, and Amaral (1989) argued for an alternative view based on anatomical evidence suggesting that specific reciprocal feedback between the hippocampus and neocortex is not anatomically possible. Instead, hippocampal output was hypothesised to act nonspecifically. Whether hippocampal output can topologically access specific neocortical ensembles remains a point of contention. The present theoretical stance does not solve this controversy, but it does emphasise the idea that temporal lobe pathways and diencephalic/frontal pathways function together in mediating neocortical consolidation. Wickelgren (1979) described a learning process in which the hippocampus regulates how new representations are assigned to neuronal ensembles. The present concept of the formation of coherence ensembles has

much in common with Wickelgren's use of the concept of "chunking" and is also related to the idea of unitised representations discussed by Schacter and McGlynn (1989) and others.

## RECOLLECTION, NEUROIMAGING, AND NEUROMONITORING

Consolidation theories of amnesia generally postulate that retrieval processes are not directly disrupted. However, the memory loss that amnesic patients experience is a failure of recollection, so some comments on the subjective experience of remembering are in order. The feeling of familiarity is not a function solely of memory retrieval. Jacoby and colleagues have argued that familiarity arises as an unconscious inference based on current situational factors as well as on retrieved memories (e.g. Jacoby, Kelley, & Dywan, 1989; for a related view see Mandler, 1989). Unconscious inferences can also give rise to priming effects in paradigms wherein prior experience with studied material is not attributed to familiarity with the material but is instead attributed to another factor (e.g. the fame of a face or name, the loudness of a sound, or the duration of a visual presentation). Amnesic patients are not deficient in making inferences in these priming paradigms, yet they are deficient when it comes to inferences regarding recognition (Paller et al., 1991; Squire & McKee, 1992). The functional deficit of amnesia is clearly not in the ability to make these inferences. Nonetheless, it can be useful to consider recollection as an outcome of an inference process, rather than as an inherent characteristic of memory. It remains to conceptualise the neural processes whereby memory retrieval events can provoke the type of inference that is critical for recollective experience.

Research on amnesia has taught us that the recollection of facts and events is associated with a type of memory distinctly different from priming phenomena, although both types of memory rely on neocortical storage mechanisms. These two types of memory are biologically dissociable in their dependence on nonidentical brain regions. Configurations of brain damage that give rise to circumscribed amnesia spare priming, whereas particular types of priming can be disrupted in the absence of declarative memory deficits (e.g. Gabrieli et al., 1995). The distinct neural correlates of these two types of memory can also be studied in normal subjects.

Neuroimaging studies using positron emission tomography (PET) have begun to examine cerebral blood-flow changes correlated with recollective processing. These blood-flow changes are used as a proxy for neuronal activity. For example, studies using a stem-completion paradigm showed that frontal lobe areas were activated more strongly during recall than during baseline conditions (Buckner et al., 1995). Results from other PET studies are also consistent with the conclusion that the frontal lobe plays an important role in recollection (e.g. Grasby et al., 1993; Schacter et al., 1996; Shallice et al., 1994; Tulving et al.,

1994). In contrast, a bilateral blood-flow reduction in occipito-temporal neocortex was shown in the priming relative to the control condition (Buckner et al., 1995). This effect was interpreted as supporting the idea that sensory-specific areas necessary for representing visual word-form are important for priming, in that they are activated less by words when those words have been recently encountered compared to when they have not. These results readily accord with prior ideas on the neural substrates of recollection and priming.

Neuromonitoring studies using electrophysiological measures called event-related potential (ERPs) offer a different perspective on memory functions of the brain. Whereas neuroimaging techniques can be used to show which brain areas are active during particular types of cognitive processing, neuromonitoring techniques—in which the electrical activity of the brain is monitored with high temporal resolution—can be used to find out more precisely when and in what circumstances these memory functions come into play. In this manner, it may be possible to use ERPs to monitor the neural events underlying recollection as they unfold (for review, see Rugg, 1995). For example, Paller and Kutas (1992) isolated an ERP correlate of recollection that occurred during a word-identification priming test. This ERP measure was recorded 500–900ms after words were flashed and was evident at all scalp locations examined. The intracranial sources of this ERP effect have not been established, but scalp topographic evidence suggests that frontal lobe activity was likely to have made a contribution. Moreover, the ERP effect was evident over the frontal lobe 100ms prior to being evident at other locations. In contrast, qualitatively different results were found in experiments wherein ERP correlates of visual word-form priming were isolated (Paller & Gross, submitted; Paller et al., submitted), indicating that ERPs are selectively sensitive to the different retrieval processing underlying recollection and priming.

The process of consolidating dispersed neocortical memories cuts across encoding–retrieval distinctions because it begins when encoding occurs and it continues with subsequent retrieval events so that the neocortical memory becomes self-sufficient. Most memory studies with neuroimaging or neuromonitoring have focused on encoding or retrieval. Intracranial ERP recordings have suggested that the hippocampus is active both during initial stimulus presentation and at retrieval when retention intervals are fairly short (Paller, Roessler, & McCarthy, 1990). In future, it may be possible to investigate consolidation by probing the intervening events of rehearsal. This is when retrieval happens—and also when consolidation happens.

With future technical advances, evidence from neuromonitoring and neuroimaging will probably become increasingly more relevant for understanding the neural substrates of recollection and other memory functions. Hypotheses that once appeared untestable in human subjects may thus turn out to be subject to empirical test. The use of these techniques in memory research may be most advantageous when neuropsychology provides a foundation upon

which neuroimaging and neuromonitoring can build more elaborate and comprehensive theoretical structures.

## TOWARDS A PSYCHOBIOLOGICAL UNDERSTANDING OF HUMAN MEMORY

Combining the multiple perspectives of neuropsychology, neuroimaging, and neuromonitoring provides a way to approach both the psychological and biological aspects of human memory in an integrated manner. The theoretical stance taken here to address the evidence from human amnesia, along with evidence concerning the neural substrates of memory functions in normal subjects, is at once psychological and biological. The consolidation theory that I have articulated includes many aspects borrowed from prior theories, and yet it is still incomplete and in need of additional empirical support. Obviously there is much more to learn about the neural substrates of human memory functions. Optimistically, attention to theory should guide future research, and new evidence guide theory development, such that the consolidation view may continue to change and improve—like a ship that is rebuilt plank by plank on the open sea, all the while staying afloat (paraphrasing Neurath, 1932).

### REFERENCES

- Buckner, R.L., Petersen, S.E., Ojemann, J.G., Miezin, F.M., Squire, L.R., & Raichle, M.E. (1995). Functional anatomical studies of explicit and implicit memory retrieval tasks. *Journal of Neuroscience*, *15*, 12–29.
- Burnham, W.H. (1903). Retroactive amnesia: Illustrative cases and a tentative explanation. *American Journal of Psychology*, *14*, 382–396.
- Cohen, N.J., & Squire, L.R. (1980). Preserved learning and retention of pattern analyzing skill in amnesia: Dissociation of knowing how and know that. *Science*, *210*, 207–209.
- Damasio, A.R. (1989). Time-locked multiregional retroactivation: A systems-level proposal for the neural substrates of recall and recognition. *Cognition*, *33*, 25–62.
- Eichenbaum, H., Otto, T., & Cohen, N.J. (1992). The hippocampus—What does it do? *Behavioral and Neural Biology*, *57*, 2–36.
- Fuster, J.M. (1995). *Memory in the cerebral cortex: An empirical approach to neural networks in the human and nonhuman primate*. Cambridge, MA: MIT Press.
- Gabrieli, J.D.E., Fleischman, D.A., Keane, M.M., Reminger, S.L., & Morrell, F. (1995). Double dissociation between memory systems underlying explicit and implicit memory in the human brain. *Psychological Science*, *6*, 76–82.
- Grasby, P.M., Frith, C.D., Friston, K.J., Bench, C., Frackowiak, R.S.J., & Dolan, R.J. (1993). Functional mapping of brain areas implicated in auditory-verbal memory function. *Brain*, *116*, 1–20.
- Halgren, E. (1984). Human hippocampal and amygdala recording and stimulation: Evidence for a neural model of recent memory. In L.R. Squire & N. Butters (Eds.), *Neuropsychology of memory* (pp.165–182). New York: Guilford Press.
- Hayes-Roth, B. (1977). Evolution of cognitive structures and processes. *Psychological Review*, *84*, 260–278.
- Hebb, D.O. (1949). *Organization of behavior*. New York: Wiley & Sons.

- Jacoby, L.L., Kelley, C.M., & Dywan, J. (1989). Memory attributions. In H.L. Roediger, III & F.I.M. Craik (Eds.), *Varieties of memory and consciousness: Essays in honour of Endel Tulving* (pp.391–422). Hillsdale, NJ: Lawrence Erlbaum Associates Inc.
- Kapur, N. (1993). Focal retrograde amnesia in neurological disease: A critical review. *Cortex*, 29, 217–234.
- Mandler, G. (1989). Memory: Conscious and unconscious. In P.R. Solomon, G.R. Goethals, C.M. Kelley, & B.R. Stephens (Eds.), *Memory: Interdisciplinary approaches* (pp.84–106). New York: Springer-Verlag.
- Markowitsch, H.J. (1995). Which brain regions are critically involved in the retrieval of old episodic memory? *Brain Research Reviews*, 21, 117–127.
- Marr, D. (1971). Simple memory: A theory for archicortex. *The Philosophical Transactions of the Royal Society of London*, 262 (Series B), 23–81.
- Mayes, A.R., & Downes, J.J. (this issue). What do theories of the functional deficit(s) underlying amnesia have to explain? *Memory*, 5(1/2).
- McClelland, J.L., McNaughton, B.L., & O'Reilly, R.C. (1995). Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review*, 102, 419–457.
- Milner, B. (1965). Memory disturbance after bilateral hippocampal lesions. In P.M. Milner & S.E. Glickman (Eds.), *Cognitive processes and the brain* (pp.97–111). Princeton, NJ: Van Nostrand.
- Milner, P.M. (1989). A cell ensemble theory of hippocampal amnesia. *Neuropsychologia*, 27, 23–30.
- Neurath, O. (1932). Protokollsatz. *Erkenntnis*, 3, 204–212. [Translated by G. Schlick and reprinted as "Protocol sentences" in A.J. Ayer (Ed.) (1959). *Logical positivism*. New York: Macmillan.]
- Paller, K.A., Acharya, A., Richardson, B.C., Plaisant, O., Shimamura, A.P., Reed, B.R., & Jagust, W.J. (in press). Functional neuroimaging of cortical dysfunction in alcoholic Korsakoff's syndrome. *Journal of Cognitive Neuroscience*.
- Paller, K.A., & Gross, M. (submitted). *Brain potentials associated with perceptual priming versus explicit remembering during the repetition of visual word-form*.
- Paller, K.A., & Kutas, M. (1992). Brain potentials during memory retrieval provide neurophysiological support for the distinction between conscious recollection and priming. *Journal of Cognitive Neuroscience*, 4, 375–391.
- Paller, K.A., Kutas, M., & McIsaac, H.K. (submitted). *An electrophysiological measure of priming of visual word-form*.
- Paller, K.A., & Mayes, A.R. (1994). New-association priming of word identification in normal and amnesic subjects. *Cortex*, 30, 53–73.
- Paller, K.A., Mayes, A.R., McDermott, M., Pickering, A.D., & Meudell, P.R. (1991). Indirect measures of memory in a duration-judgement task are normal in amnesic patients. *Neuropsychologia*, 29, 1007–1018.
- Paller, K.A., Roessler, E., & McCarthy, G. (1990). Potentials recorded from the scalp and from the hippocampus in humans performing a visual recognition memory test. *Journal of Clinical and Experimental Neuropsychology*, 12, 401.
- Rozin, P. (1976). The psychobiological approach to human memory. In M.R. Rosenzweig & E.L. Bennett (Eds.), *Neural mechanisms of learning and memory* (pp.3–48). Cambridge, MA: MIT Press.
- Rugg, M.D. (1995). Event-related potential studies of human memory. In M.S. Gazzaniga (Ed.), *The cognitive neurosciences* (pp.789–801). Cambridge, MA: MIT Press.
- Schacter, D.L. (1987). Implicit expressions of memory in organic amnesia: Learning of new facts and associations. *Human Neurobiology*, 6, 107–118.
- Schacter, D.L., Alpert, N.M., Savage, C.R., Rauch, S.L., & Albert, M.S. (1996). Conscious recollection and the human hippocampal formation: Evidence from positron emission tomography. *Proceedings of the National Academy of Sciences, USA*, 93, 321–325.

- Schacter, D.L., & McGlynn, S.M. (1989). Implicit memory: Effects of elaboration depend on unitization. *American Journal of Psychology*, *102*, 151–181.
- Scoville, W.G., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery and Psychiatry*, *20*, 11–21.
- Shallice, T., Fletcher, F., Frith, C.D., Grasby, P., Frackowiak, R.S.J., & Dolan, R.J. (1994). Brain regions associated with acquisition and retrieval of verbal episodic memory. *Nature*, *368*, 633–635.
- Squire, L.R., & Alvarez, P. (1995). Retrograde amnesia and memory consolidation: A neurobiological perspective. *Current Opinion in Neurobiology*, *5*, 169–177.
- Squire, L.R., Cohen, N.J., & Zola-Morgan, L. (1984). The medial temporal region and memory consolidation: A new hypothesis. In H. Weingartner & E. Pader (Eds.), *Memory consolidation* (pp.185–210). Hillsdale, NJ: Lawrence Erlbaum Associates Inc.
- Squire, L.R., Knowlton, B., & Musen, G. (1993). The structure and organization of memory. *Annual Review of Psychology*, *44*, 453–495.
- Squire, L.R., & McKee, R. (1992). Influence of prior events on cognitive judgments in amnesia. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *18*, 106–115.
- Squire, L.R., Shimamura, A.P., & Amaral, D.G. (1989). Memory and the hippocampus. In J. Byrne & W. Berry (Eds.), *Neural models of plasticity* (pp.208–239). New York: Academic Press.
- Sutherland, R.J., & Rudy, J.W. (1989). Configural association theory: The role of the hippocampal formation in learning, memory, and amnesia. *Psychobiology*, *17*, 129–144.
- Teyler, T.J., & DiScenna, P. (1986). The hippocampal memory indexing theory. *Behavioral Neuroscience*, *100*, 147–154.
- Treves, A., & Rolls, E.T. (1994). Computational analysis of the role of the hippocampus in memory. *Hippocampus*, *4*, 374–391.
- Tulving, E., Kapur, S., Markowitsch, H.J., Craik, F.I.M., Habib, R., & Houle, S. (1994). Neuro-anatomical correlates of retrieval in episodic memory: Auditory sentence recognition. *Proceedings of the National Academy of Science, USA*, *91*, 2012–2015.
- Underwood, B.J. (1969). Attributes of memory. *Psychological Review*, *76*, 559–573.
- Wickelgren, W.A. (1979). Chunking and consolidation: A theoretical synthesis of semantic networks, configuring in conditioning, S–R versus cognitive learning, normal forgetting, the amnesic syndrome, and the hippocampal arousal system. *Psychological Review*, *86*, 44–60.
- Wilson, M.A., & McNaughton, B.L. (1994). Reactivation of hippocampal ensemble memories during sleep. *Science*, *265*, 676–679.
- Winson, J. (1985). *Brain and psyche: The biology of the unconscious*. New York: Vintage Books.