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Chapter 21

Binding memory fragments together to form declarative memories depends on cross-cortical storage

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Introduction

What happens in your brain to allow you to remember a recent acquaintance, your favourite film, your last summer vacation, or your first kiss? Investigations of such phenomena are founded on contemporary classification systems for memorial abilities. The category of **declarative memory** refers to the ability to remember prior autobiographical episodes and complex facts, as assessed by tests of recall or recognition (Squire 1987). Declarative memory provides each of us with a vast but imperfect storehouse of information, and a basis for our own life story.

What would constitute a comprehensive scientific understanding of declarative memory? Relevant evidence concerning declarative memory includes physiological recordings in animals, cognitive modelling with computers, neuroimaging in patients with memory disorders, reversible magnetic neurodisruption in willing human volunteers, and more. A long-standing and venerable approach to exploring both neural and psychological underpinnings of memory is to investigate memory deficits in neurological patients.

Neuropsychological investigations of amnesia have provided many insights into memory functions of the human brain (Schacter and Tulving 1994; Schacter 1996; Squire and Kandel 1999; Eichenbaum and Cohen 2001; Squire and Schacter 2002). Contemporary theoretical explanations of declarative memory based on this evidence generally describe how memory storage depends on representations distributed across networks in the cerebral cortex. Although it is beyond the scope of the present chapter to summarize each of these theories, I will attempt to present some views on declarative memory that fit well within the current zeitgeist.

A core goal of research into declarative memory is to answer the question: ‘How is declarative memory different from all other types of memory?’ By analogy with the 'Four Questions' traditionally recited by the youngest child at Passover celebrations, consider the following answers to this overarching question (Paller 2002), which will be elaborated on in subsequent sections.

1. Declarative memory is behaviourally distinct in that it is assessed using recall and recognition tests for facts and episodes.
2. Declarative memory has distinct subjective characteristics in that it is often accompanied by the experience of conscious recollection.
3. Declarative memory has a distinct cognitive structure that entails retrieving a conjunction of discrete informational fragments.
4. Declarative memory has a distinct neural basis that depends on storage across a set of neocortical modules, with enduring storage dependent upon a cross-cortical consolidation process mediated by cortico-hippocampal and cortico-thalamic networks.

Although each of these four points is important, I take the position that our understanding of declarative memory can be significantly improved by striving to elucidate the connections between them. Thus binding is at the core of this understanding. Cross-cortical storage is a way to bind together the distinct neocortical ensembles that comprise a declarative memory. At the same time, these ensembles represent a set of discrete informational fragments that must be bound together. This **neurocognitive binding** of declarative memories is essential for the recall and recognition of facts and episodes, and it may also be a critical ingredient for the experience of conscious recollection.

Neurocognitive foundations of declarative memory

Investigations of amnesia have focused on patients who experience memory difficulties, but whose intellectual functioning is otherwise preserved. An amnesic patient may carry on an intelligent and detailed conversation but, shortly afterwards, be unable to remember that the conversation ever occurred. On the other hand, such patients often produce completely normal performance when it comes to a set of other memory phenomena collectively referred to as **non-declarative memory** (Table 21.1). These selective memory deficits imply that certain neural computations are essential for recalling and recognizing episodes and facts, but not for perceiving and manipulating the same types of information in other ways. Indeed, it appears that cortical networks play a major role in perceiving and manipulating the information inherent in an episode, whereas alterations in connections among neurons in these same networks are responsible for declarative memory storage.

Table 21.1 Comparing declarative memory with other types of memory

Type of memory	Definition	Findings in circumscribed amnesia
Declarative memory	Recall and recognition of episodes and facts (i.e. episodic memory and semantic memory)	Impairment in storage, producing deficits in new learning (anterograde amnesia) and in remembering information acquired prior to illness or injury (retrograde amnesia)
Immediate memory	Information kept in mind by continuous rehearsal (e.g. verbal working memory)	Preserved
Non-declarative memory[a]		Generally preserved, but with some notable exceptions
Perceptual priming	Speeded or more accurate responses to a stimulus when repeated, based on altered perceptual representations	Preserved if performance is not contaminated by declarative memory (i.e. implicit memory testing with no explicit retrieval)
Conceptual priming	Speeded or more accurate responses to a stimulus when repeated, based on altered conceptual representations	Preserved in some cases, but further investigation is required, particularly across stimulus domains
Skills	Behaviours that improve gradually with practice, including cognitive skills (e.g. reading mirror-reversed text) and motor skills	Preserved when skill acquisition is accomplished without reliance on declarative memory (which is not the case for many skills learned outside the laboratory)
Classical conditioning	Learned associations between two stimuli, one of which elicits an automatic response	Preserved under conditions with temporal overlap between conditioned and unconditioned stimuli

[a] Also includes non-associative learning, habits, category learning, and artificial grammar learning.

Here I will articulate a theoretical explanation for such memory disorders that postulates a core defect in a process called **cross-cortical storage**. This process is assumed to be essential for connecting the fragments of an episode or the various features of a complex fact together into a coherent and sturdy representation in the brain (Paller 1997, 2002). For example, fragments linked together in the cerebral cortex to form an enduring memory of an episode might include representations of various sights, sounds, smells, spatial layout of objects, people, actions, emotional colouring, a set of precipitating events, consequences of the episode, and so on. Cortical regions are clearly specialized for processing these different types of information.

The cross-cortical storage process is believed to depend on a group of representations instantiated not in a single brain region but rather in many neocortical networks, each specialized for a different set of computations. The fundamental characteristic of declarative memory is taken to be its dependence on a linking together of discrete representations in multiple neocortical zones. I propose that this fundamental neural characteristic strongly influences the form of the other characteristics of declarative memory: its cognitive characteristics, its behavioural characteristics, and its association with conscious recollection.

Binding is a key aspect of declarative memory, but the term 'binding' can take on substantively different meanings in different contexts. For example, binding of a different sort, feature integration, occurs during visual object perception when distinct features present at the same spatial location are processed such that representations of feature conjunctions are formed (see Chapter 12). Binding also occurs in immediate memory as multimodal and multidimensional representations of sensory input are formed and manipulated. With respect to declarative memory, binding concerns representational elements in memory that can be brought back together in a unitized way when a specific episode or fact is retrieved. Declarative memory binding (cross-cortical storage) is accomplished through network interactions that are not well understood but that probably involve changes in neuronal connectivity among various neocortical regions and the medial temporal region, as well as between the neocortex and the medial diencephalon. This hypothesis is based on the fact that amnesia generally results from damage to either the medial temporal or the diencephalic regions of the brain.

Furthermore, cross-cortical storage is not finalized immediately after a learning episode; rather, it can evolve over an extended time course as the information becomes integrated with knowledge already accrued as well as with information acquired subsequently. This process of **cross-cortical consolidation** may continue for many years for a fact or event that is re-evaluated, re-interpreted, and repeatedly integrated with other information. Cross-cortical consolidation may proceed not only during waking, but also during sleep (Maquet *et al.* 2003; Paller and Voss 2004). It may also continue beyond a point in time when the memory has become cortically self-sufficient, i.e. when the memory would not be disrupted by hippocampal damage because critical cortical storage sites would be sufficient to support retrieval. This brain damage leads to difficulties in remembering declarative memories that are not cortically self-sufficient, including memories formed prior to the onset of amnesia (retrograde amnesia) and memories formed after the onset of amnesia (anterograde amnesia). Because memories are less likely to be cortically self-sufficient if acquired recently, retrograde amnesia is typically worse for recently acquired information. Many amnesic patients can remember episodes from their childhood and early adulthood as well as anyone.

Normal declarative memory is a by-product of three stages of information processing. **Encoding** refers to the initial stage, when information arrives in the brain following sensory analysis or via imagination. The term encoding has been used to refer to the input and comprehension of this information (which is not problematic for amnesic patients), as well as to the transformation of the experience into a memory (which is impaired in amnesia).

As described above, declarative memory formation is often not finalized at encoding but rather can continue over a prolonged storage period when memory is subject to change, consolidation, interference, distortion, and forgetting. **Storage** denotes this second stage of information processing, which may actually begin as soon as new information is acquired.

The final stage, **retrieval**, takes place when memory is accessed and used. Amnesic patients are generally able to retrieve some memories, particularly those already consolidated to the point of cortical self-sufficiency. However, memory retrieval can be quite demanding and require effortful search strategies, such as when one searches for a relatively insignificant childhood memory. In such cases, contributions from the prefrontal cortex are especially important with respect to conducting a systematic search, evaluating products of retrieval, escaping from the present moment to bring a prior experience to mind, maintaining information in working memory, inhibiting the intrusion of irrelevant information, constructing a remembered experience based on retrieved information, evaluating the suitability of each bit of retrieved information, and so on. Accordingly, prefrontal damage alone can lead to memory retrieval difficulties, and when combined with medial temporal damage can lead to exacerbated memory deficits.

The evidence that amnesic patients can show intact performance when it comes to various types of non-declarative memory (Table 21.1) emphasizes the idea that declarative memory depends on special storage mechanisms. Non-declarative memory does not require the linking of distinct representations across multiple neocortical zones. Often, tests of non-declarative memory do not make explicit reference to prior learning episodes; such tests are called implicit memory tests. For instance, behavioural responses to a specific stimulus may be faster or more accurate as a result of prior experience, even when a person is unable to remember that prior experience. This behavioural effect constitutes **priming** (also known as item-specific implicit memory). With respect to the concept of binding, declarative memory retrieval can be conceptualized as requiring the reinstatement of cross-cortically bound information; in contrast, priming may depend on locally bound information within some discrete cortical networks. Evidence relevant to this idea can be obtained in functional neuroimaging experiments which can succeed in dissociating these two types of memory and, ideally (as described below), contrasting them within the same experiment while other stimulus and task factors are held constant. For example, EEG measures of neural synchrony (e.g. von Stein *et al.* 1999; Weiss and Rappelsberger 2000) may also prove relevant for contrasting binding across multiple cortical regions in declarative memory retrieval as opposed to the more localized processing in priming. Ultimately, explorations of the fundamental differences between declarative and non-declarative memory should shed light on the neurocognitive mechanisms unique to declarative memory.

Furthermore, understanding special cases when non-declarative memory is not preserved in amnesia can provide pivotal insights into the core defect. Future research may be able to test one particular prediction that follows from the foregoing discussion, namely that priming should be preserved in amnesia only when performance can be mediated through neural plasticity within one or more isolated neocortical zones. Special tests in which priming is mediated through neural plasticity connecting separate neocortical zones (see discussion of cross-domain conceptual priming below) should show that priming is impaired in amnesia.

Electrophysiology of declarative memory

To gain further insight into the distinct cognitive functions that combine to support declarative memory, it will be crucial to be able to measure these functions independently. Recordings of the electrical activity of the brain have shown that such measures can indeed be obtained so as to track relevant memory functions on a millisecond-by-millisecond basis. I will outline this evidence below, emphasizing findings from my laboratory.

The EEG is a summation of electrical fields produced by the activity of vast numbers of neurons and recorded using electrodes placed harmlessly on an individual's head. Time-locked average responses known as event-related potentials (ERPs) can be calculated based on EEG responses to different categories of stimuli presented to the individual in a suitable experimental setting (for reviews of ERP studies of memory see Friedman and Johnson 2000; Mecklinger 2000; Paller 2000; Rugg and Wilding 2000; for a general review of ERP methods see Munte *et al.* 2000). ERPs can be characterized in terms of their latency (when they occur relative to the onset of a stimulus), their polarity (positive or negative at the recording location relative to a distant reference location), their amplitude (size of a potential deflection), and their topography (distribution of potential amplitudes across the head).

The extant findings suggest that future prospects are strong for using electrophysiological measures of brain activity in healthy individuals to test and advance theoretical frameworks developed from neuropsychological studies of memory disorders. Despite the emphasis on ERP research, the general approach advocated here also holds for other methods of directly or indirectly measuring brain activity, including neuromagnetic, haemodynamic, and optical neuroimaging.

Transforming experience into memory

One way of investigating the formation of declarative memories is to contrast neural activity at encoding that predicts successful versus unsuccessful memory performance. Brain potentials that predict successful subsequent recall and recognition have been observed in many experiments. These potentials generally have a positive polarity over parietal or frontal brain regions relative to a distant reference location, reach maximal amplitudes 400–800 ms or so after stimulus onset, and have larger amplitudes for remembered stimuli (reviewed by Wagner *et al.* 1999; Paller and Wagner 2002). Similar ERPs have been observed in a few experiments in which electrodes were implanted in the medial temporal region of the brain in patients who were candidates for surgery to relieve medically intractable epilepsy (Fernandez *et al.* 1999, 2002). ERPs have also been identified which predict whether a person will remember seeing a common object, as well as whether a person will claim to have seen an object than was not actually seen but rather was imagined (Gonsalves and Paller 2000). Stimuli to be remembered in the majority of these ERP studies have been visual words, but other stimuli have been used including pictures of objects, faces, spoken names, and environmental sounds.

In one experiment, words were presented visually in an encoding phase followed by either an implicit or an explicit memory test (Paller 1990). In the implicit memory test, participants were instructed to complete three-letter stems with the first word to come to mind. The extent to which their completions matched words from encoding, compared with a baseline completion rate, provided a measure of priming. In the explicit memory test, participants attempted to recall words from the encoding phase to complete the stems. ERPs from the encoding phase were more positive for words recalled later than for words not recalled later. This systematic difference in brain potentials can be referred to as Dm-recall (an ERP **D**ifference based on later **m**emory performance on a **recall** test). On the other hand, ERPs did not reliably predict later priming. These findings, together with others, are consistent with the idea that Dm-recall indexed encoding activity specific to declarative memory formation, most likely

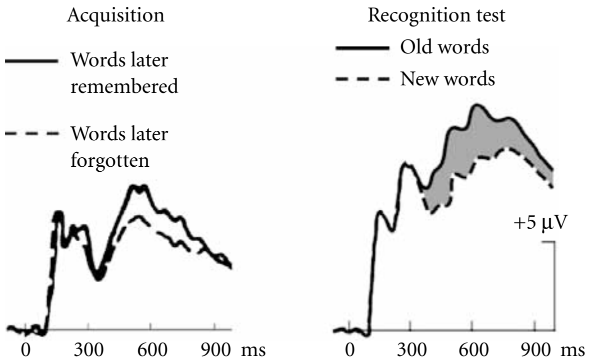

Figure 21.1 Examples of ERPs investigated in memory paradigms demonstrating (a) a subsequent memory effect and (b) an old–new effect. ERPs were elicited by words presented visually in the study and test phases of the same experiment (Paller *et al*. 1987). The recordings shown were obtained from electrodes located at the midline parietal scalp location in a group of 16 young adults. During the study phase (acquisition), participants responded to each word according to task requirements in four different tasks. During the test phase (recognition test), participants made yes–no recognition judgements followed by a three-choice confidence rating. The subsequent memory effect was observed by averaging ERPs recorded during acquisition as a function of later recognition performance. The ERP difference between responses to subsequently remember and subsequently forgotten words (Dm) was apparent from about 400–800 ms after word onset. The old–new effect was recorded during the recognition test and is shaded in (b). ERPs elicited by old words were more positive than ERPs elicited by new words. Results also showed that this old–new effect was greater for words recognized with high confidence. However, old–new effects of this sort cannot be unequivocally linked to declarative memory, given that priming also occurs (see Fig. 21.2). (Adapted from Paller ***et al***. 1987.)

pertaining to the meaning of each word rather than merely to its visual appearance. Similar Dm phenomena have also been observed using recognition tests, as shown in Figure 21.1(a).

In an experiment with faces, ERPs at initial encoding predicted not only whether later recognition was successful, but also the experiential quality of the recognition experience (Yovel and Paller 2003). Positive ERPs from parietal regions over both hemispheres predicted recognition accompanied by retrieval of episodic detail, whereas only right-parietal ERPs predicted successful recognition without episodic detail, a phenomenon referred to as **pure familiarity**, i.e. when a face seems familiar but is not remembered.

Other studies of ERPs, frequency-domain EEG measures, functional magnetic resonance images of brain activity, and spiking from single neurons have suggested that many cortical regions can be involved in memory encoding, and that hippocampal activity may be particularly relevant for the storage of declarative memories (Cameron *et al*. 2001; Fell *et al*. 2002; Paller and McCarthy 2002; Reber *et al*. 2002; Sederberg *et al*. 2003).

Many different types of processing at encoding can promote successful memory storage. Accordingly, many avenues of investigation will be required to understand the formation and preservation of declarative memories. Measures of neural activity predictive of subsequent memory, such as Dm-recall, provide a way in to this problem, and will ultimately be most useful to the extent that connections can be built between these measures and specific neurocognitive processes. This goal will require analysing neural activity as a function of successful versus unsuccessful encoding in conjunction with experimental manipulations that systematically affect memory encoding and storage.

Memory retrieval

The effectiveness of encoding and storage becomes evident only when stored information is subsequently accessed. In studies of retrieval, differences between ERP responses to new and old items in recognition tests have been researched in considerable detail. These so-called old–new ERP effects are generally positive shifts in ERPs to old items relative to ERPs to new items, as shown in Figure 21.1(b). Early experiments on old–new ERP effects prompted a range of conclusions without leading to consensus. In retrospect, firm interpretations were difficult because remembering in these circumstances generally involves a variety of different cognitive processes such that multiple brain potentials are produced in overlapping time intervals. As a result, functionally distinct brain signals within old–new ERP effects were difficult to isolate from one another.

For example, consider two memory phenomena that can co-occur when a person views a face: retrieval of prior episodes involving the same face, and faster or more accurate processing due to prior perceptual analysis of that same face, as indexed by the behavioural phenomenon of perceptual priming. Thus special tactics are needed to isolate ERPs associated with these different sorts of memory (Fig. 21.2). Indeed, it is notoriously difficult to prevent people from systematically recalling prior episodes when stimuli are repeated, and this incidental retrieval can contaminate neural analyses of priming.

One approach to this problem made use of a condition in which faces were encoded only to a minimal extent (Paller *et al.* 2003a). Each face was presented at a central location for 100 ms while participants were required to make a difficult visual discrimination at another location. When the face disappeared, a noise stimulus appeared centrally to limit face encoding further. On a subsequent recognition test, participants' performance was no better than would be expected if they were purely guessing. However, priming was still observed for these faces in an implicit memory test. Thus ERPs elicited by these faces were associated with priming uncontaminated by conscious remembering. Within the same

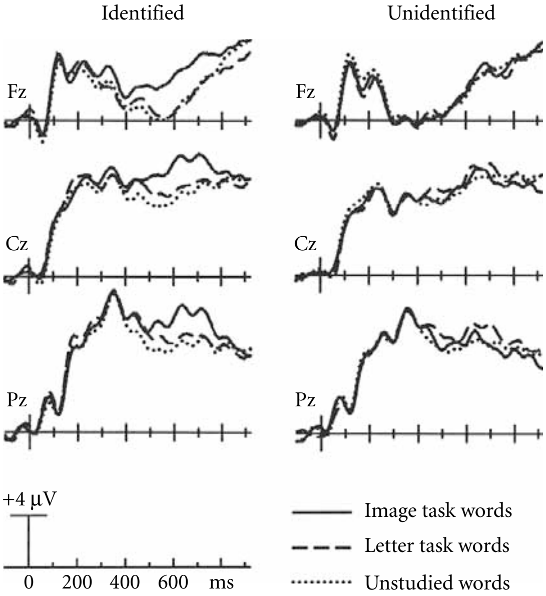

Figure 21.2 Specific electrophysiological correlates of recollection were first isolated by examining ERP old–new effects based on a study phase manipulation that dissociated priming and recollection (Paller and Kutas 1992). In general, ERP differences between old and new items cannot unequivocally be associated with declarative memory, but in the experiment conducted by Paller and Kutas (1992) two types of old items were compared to achieve this goal. Memory results were critical in showing that recall and recognition were superior for words studied in the image task compared with words studied in the letter task, whereas equivalent levels of word-identification priming were observed in these two conditions. ERP elicited during the test phase, when this priming test was given, differed very little for words that could not be identified correctly (right). However, words that participants identified (left) elicited ERPs that differed systematically between conditions. The usual old–new effect was observed, in that ERPs were more positive for old words than for new words. Importantly, the ERP difference between image task words and letter task words (two conditions with matched priming results) showed for the first time that this portion of the old–new effect beginning at a latency of 500 ms was associated specifically with declarative memory retrieval. Moreover, given that the manipulation influenced free recall performance, recollection was implicated. This ERP correlate of recollection was shown to be functionally distinct from an earlier portion of the old–new effect that was present for both types of old words and visible from 400–500 ms. Recordings shown were from midline frontal (Fz), central (Cz), and parietal (Pz) locations. (Adapted from Paller and Kutas 1992.)

experimental runs of this experiment, other faces were presented for a longer duration with no competing stimulus discrimination requirement to limit encoding; these faces were remembered well by the participants. The two conditions provide for a direct comparison between ERPs associated with conscious memory for faces and ERPs associated with priming. As illustrated in Figure 21.3, recognizing a repeated face was associated with positive ERPs at the rear of the head 400 to 800 ms after face onset (Fig. 21.3(a)), whereas priming was

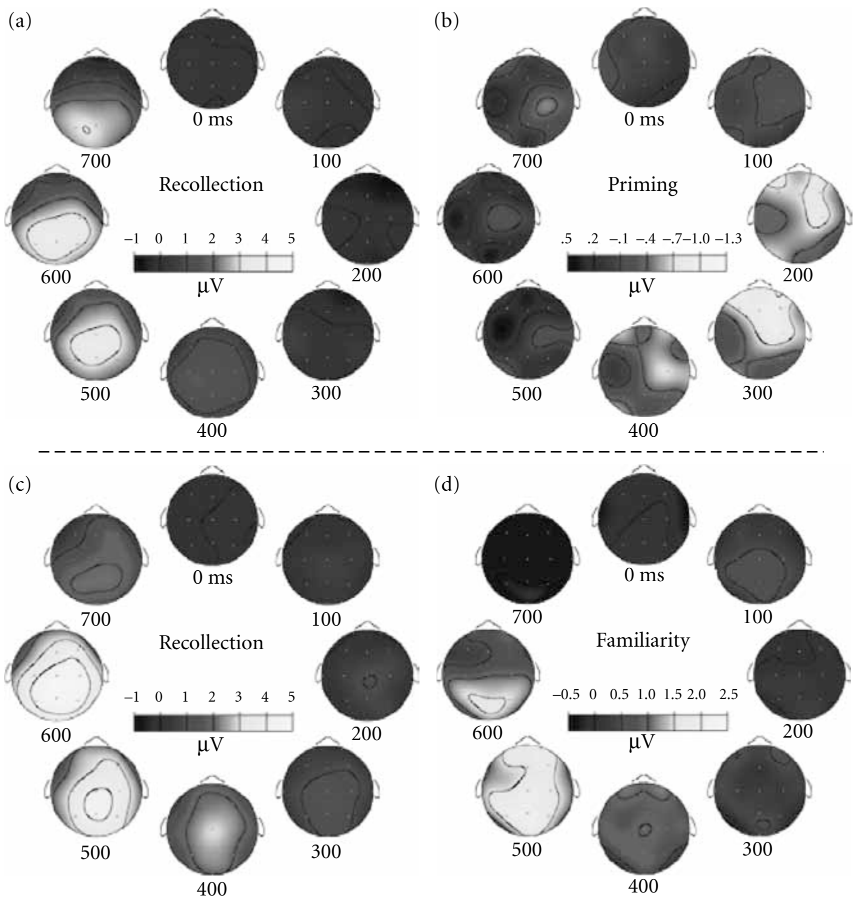

Figure 21.3 Topographic maps of brain potentials associated with different memory phenomena: (a) recollection and (b) perceptual priming in one experiment (Paller *et al*. 2003a); (c) recollection and (d) pure familiarity in another experiment (Yovel and Paller *et al*. 2004). Differences in potentials between pairs of conditions are shown on schematic heads as if viewed from above (nose at the top), interpolated from 21 scalp locations. Measurements were made over eight 100-ms intervals beginning at the time shown below each map, where time 0 is the time of stimulus onset. Thus each panel shows potential differences for eight time intervals, arranged like a stopwatch that runs for 800 ms. Potentials are displayed according to a different microvolt scale in each panel, together with isopotential lines. In all panels, the largest differences are signified by the lightest colours (yellow and white). Polarity is negative only in (b), and values beyond the negative range of the scale in the 700–800 ms map in (d) are shown as black. In one experiment (Paller *et al*. 2003a), subtractions were computed to isolate potentials associated with (a) recollection prompted by faces and (b) perceptual priming with faces. The two contrasts were between remembered faces and new faces, and between primed but forgotten faces and new faces, respectively. Quite different electrical signals were observed; priming was associated with negativity at 200–400 ms towards the front of the head, whereas recollection was associated with positivity at 400–800 ms towards the rear of the head. In the other experiment (Yovel and Paller 2004), subtractions were computed to isolate potentials associated with (c) recollection and (d) pure familiarity for faces. These two contrasts were between faces remembered with associative information and new faces, and between faces recognized without episodic retrieval and new faces, respectively. Electrical signals of pure familiarity did not resemble electrical signals of face priming, but rather seemed like reduced-amplitude versions of signals of face recollection. (Adapted from Paller *et al*. 2003a; Paller 2004; Yovel and Paller 2004.)

associated with negative ERPs at the front of the head, particularly on the right side 200 to 400 ms after face onset (Fig. 21.3(b)).

In another experiment we used a different strategy to isolate signals associated with face recollection (Paller *et al.* 1999). At encoding, participants attempted to memorize 20 faces accompanied by a spoken vignette (to simulate actually meeting the individual pictured) and were told to forget 20 other faces. One vignette, for example, was: 'I'm Alison; I won the Boston Marathon twice.' Later recognition was superior for the former compared with the latter faces, but the magnitude of priming observed during implicit memory testing was the same for the two groups of faces. In the implicit memory test face identification was made difficult by obscuring portions of each face with superimposed black pixels. In order to perform the famous–non-famous face discriminations required in this test, face identification was required, and prior exposure to a face presumably facilitated the processing of these partially obscured faces. Priming effects were observed as both faster response times and high response accuracy for faces repeated from the encoding phase compared with new faces. Therefore comparing ERPs for the two kinds of repeated faces revealed a neural signal of face recollection uncontaminated by face priming. This neural signal of recollection bore a strong resemblance to the spatiotemporal electrical patterns associated with face recollection in other studies (e.g. Fig. 21.3(a)). Analogous results have been obtained using verbal stimuli to obtain ERP correlates of recollection cued by words, as shown in Figure 21.2.

In one follow-up study using ERP and functional MRI methods in different groups of subjects, a contrast between remembered faces learned with a spoken vignette and new faces revealed left hippocampal, cortical (left insula and left temporal), and cerebellar activity (Paller *et al.* 2003b). Another experiment juxtaposed electrical signals of remembering a face *per se* and remembering a face together with corresponding biographical facts learned at encoding (Paller *et al.* 2000), such as the name Alison and the winning of the Boston Marathon. Brain activity was observed over posterior brain regions in both situations, whereas additional activity that was slightly more anterior was observed only when biographical retrieval occurred. Recalling person-specific information, as in the latter case, is dependent on a very high degree of binding, as diverse types of information must be linked together, and thus is perhaps a prototypical example of the sort of declarative memory retrieval that would naturally give rise to conscious recollection.

Awareness of remembering

Despite the strong connection between declarative memory and the experience of remembering, these phenomena need not always occur together. Declarative memory provides some of the necessary precursors at memory retrieval, but it is not sufficient to produce the awareness of remembering. Rather, conscious memory depends on a further inference—the explicit idea that the current contents of consciousness are derived from memory retrieval.

Thus dysfunctional cross-cortical storage in amnesia has an indirect impact on awareness of remembering. A strong and rather selective disruption of declarative memory will also disrupt awareness of remembering because memory for the spatiotemporal context of an episode is a critical factor that can help one to infer that a memory for a prior event has been retrieved (Johnson and Chalfonte 1994). This function falls within the aforementioned category of prefrontal functions that contribute to memory retrieval, together with strategic search, evaluation, and working memory (or 'working-with-memory' (Moscovitch 1992)). Indeed, frontal brain potentials associated with retrieval functions have been identified in many studies (Ranganath and Paller 1999; Rugg and Wilding 2000).

Thus neural signals of memory must be evaluated with respect to the possibility that declarative memory retrieval need not necessarily give rise to awareness of remembering. Sometimes a stimulus can seem familiar even in the absence of conscious remembering. This experience is called pure familiarity. The epitome of a pure familiarity experience is the so-called butcher-on-the-bus phenomenon (Mandler 1980), which is when one believes that a person is familiar (often upon seeing their face in an atypical context) while failing to recall any information whatsoever about that person. Indeed, when the butcher is encountered in the context of a bus, very few clues are available concerning the identity of the butcher compared with those typically present when the butcher is encountered in the butcher's shop.

Particularly informative results were obtained by comparing circumstances when a face provoked a full-blown recollective experience driven by remembering contextual features associated with that face with circumstances when a face provoked the unsubstantiated impression of memory known as pure familiarity (Yovel and Paller 2004). In comparison with the electrical signals associated with face-induced recollection (Fig. 21.3(c)), electrical signals associated with pure familiarity with faces (Fig. 21.3(d)) were similar but exhibited reduced amplitudes. Notably, electrophysiological correlates of pure familiarity with faces and of priming with faces (Fig. 21.3(d) and Fig. 21.3(b), respectively) were highly divergent, consistent with the notion that familiarity is not a straightforward outcome of priming, despite superficial similarities between familiarity and priming. Pure familiarity can instead be conceived of as a result of limited stimulus recognition without contextual retrieval adequate for triggering episodic recollection.

Border areas of declarative memory

Current theories of memory address a variety of memory phenomena and their neural implementation, but many questions remain open. Some subtle but critical questions concern memory phenomena at the border between declarative and non-declarative memory, such as some subtypes of priming. If amnesia fundamentally entails a disruption of memory functions dependent upon cross-cortical storage, as proposed, priming should remain preserved only if mediated within single neocortical zones.

Conceptual priming is one subtype of priming that deserves further study; it is believed to arise from altered representations of the meaning of a stimulus rather than merely the physical features of a stimulus. Conceptual priming can cross stimulus domains, such as when hearing a word primes its meaning so as to facilitate processing of that meaning when subsequently reading that word, or when reading the name of a famous person primes knowledge of their identity so as to facilitate processing of person identity when subsequently viewing that person's face. Indeed, a putative electrical signal of conceptual priming with words has been identified and shown to be preserved in patients with deficient declarative memory (Olichney *et al*. 2000; see also Yovel and Paller 2004). This signal may reflect a component of exactly the type of memory that allows amnesic patients to engage fully in complex conversations, all the while maintaining their comprehension abilities and focus on the topic at hand.

The neural processing responsible for conceptual priming is not well understood. Moreover, it may be useful to assume that there are multiple types of conceptual priming. For example, conceptual priming may in some circumstances reflect activation of the representation of the meaning of a word, in which case it is plausible that such a representation may be instantiated entirely within the neurons of a discrete neocortical zone. Likewise, in some cases new associations may be learned to the point where relevant information takes the form of a unitized representation dependent on a single neocortical zone. On the other hand, there may be many cases when conceptual priming depends on links among multiple neocortical zones, such as when very different types of perceptual objects are associated with one another. According to the present account, priming in such circumstances would be expected to depend on hippocampal processing and to be impaired in amnesic patients. Testing these predictions empirically will not be easy, but doing so will have important theoretical implications and thus may help to advance our understanding of the neural substrates of memory.

Conclusions

We now have the ability to record neural signals associated with several of the many processes that contribute to declarative and non-declarative memory. These neural signals provide a vital window on the physiology of memory that will become increasingly important for further explorations of the neurocognitive substrates of remembering.

Therefore future efforts should be aimed at elucidating exactly how declarative memory differs from priming and other types of non-declarative memory. What is unique about declarative encoding, storage, and retrieval? What memory processes support priming when is it preserved in amnesia, and how do they differ from those that support declarative memory? Does remembering in the absence of contextual retrieval, as exemplified by pure familiarity experiences, rely on any memory processing in common with priming, or is it more closely allied with declarative memory? What processing underlies priming phenomena that are impaired in amnesia, and what might this processing have in common with declarative memory?

A promising strategy to promote progress on these and related issues is to isolate and characterize neurophysiological events specifically responsible for memory functions. A variety of techniques for measuring brain activity can be used together to study human memory and memory disorders, and to provide data needed to advance and refine neurobiological hypotheses concerning memory, such as those outlined above. This approach may also lead to an eventual understanding of how neurocognitive processing gives rise to the conscious experience of remembering. We might thereby obtain a modicum of insight into the neurocognitive substrates of human awareness in general—a supreme challenge that has historically remained out of the reach of humankind but which now appears to be gradually yielding to determined scientific pursuit.

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