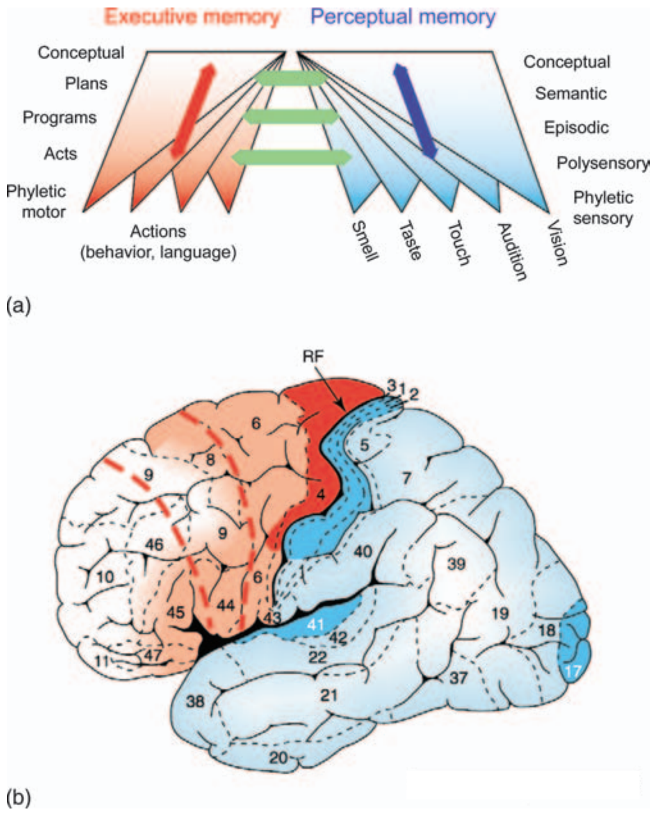
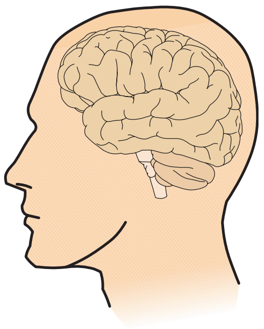
What sort of life (if any), what sort of world, what sort of self, can be preserved in a man who has lost the greater part of his memory and, with this, his past, and his moorings in time?

Oliver Sacks (1995)





How memory might be encoded in many parts of cortex. The neuroscientist Joaquin Fuster's conception of long-term memory traces encoded in cortex. Posterior cortex has more perceptual varieties of stored traces, while the frontal lobe has executive and action-related traces. The principle is believed to be that neocortex (the visible large cortex) encodes memory by strengthening synaptic connections among vast arrays of neurons that perform higher cognitive functions. *Source*: Fuster, 2004.

CHAPTER

9

Learning and memory

Morris Moscovitch, Jason M. Chein, Deborah Talmi, and Melanie Cohn

OUTLINE

1.0 INTRODUCTION

Memory can be defined as a lasting representation that is reflected in thought, experience or behavior. Learning is the acquisition of such representations, which involve a wide range of brain areas and activities. Human memory has some surprising limits and some very impressive capacities. For example, most students would like

Cognition, Brain, and Consciousness, edited by B. J. Baars and N. M. Gage
ISBN: 978-0-12-373677-2

to have a 'better memory' – by which we mean a capacity deliberately to store and recall information, at will, easily and accurately. However, the human brain has not evolved for academic study and testing, which is a very recent cultural invention. Rather, it has evolved for the tasks of survival. Our best memory performance is not for the exact symbol sequences that conventional computers handle so well. Rather, our brains are exceptionally good in dealing with complex, ill-defined, and novel challenges, the kinds that people have to deal with in the real world.

Humans are exceptionally *flexible* in adapting to new conditions. Learning and memory provide the royal road to that flexibility. Our great capacity for learning allows us to use a brain adapted to a neolithic environment, and apply it with great success in a world of computers, brain science, and academic learning. There must be something special about our great ability to learn.

Memory storage is believed to involve very widespread synaptic alterations in many parts of cortex. This process is often taken to involve large-scale Hebbian learning, following the rule that 'neurons that fire together, wire together' (see Chapter 3 and Appendix A). Thus, correlated activity between neurons leads to strengthened connections between them, both excitatory and inhibitory. Temporary cell assemblies are thought to maintain immediate memories, while long-term memories require more lasting strengthening of synaptic connections, both excitatory and inhibitory ones. While evidence has been found for these phenomena, we cannot yet observe changed long-term connectivity directly throughout the brain regions where it is thought to occur. Thus, the Hebbian memory trace itself remains an inferential concept.

In some views, all of the cortex may be able to learn by changing synaptic connectivities, from the posterior perceptual regions to the frontal executive and motor cortex (Fuster, 2004). Others focus more on the temporal lobe, which traditional neurology associates with memory functions. The most important brain structures we look at in this chapter are the *neocortex* – the visible outer brain – and the *medial temporal lobes* (MTL), which contain the two hippocampi and their surrounding tissues ((b) on p. 254, Figures 9.1 and 9.2). The MTL is spatially complex, and you should devote some time to the drawing exercises at the end of this chapter, to get an overall sense of its shape and location.

Until recently, the hippocampus was believed to be mainly responsible for transferring experiences into memory, but better methods now implicate the entire hippocampal neighborhood, the medial temporal lobes. The MTL overlap with the ancient mammalian smell cortex, which has fewer than the six layers. The

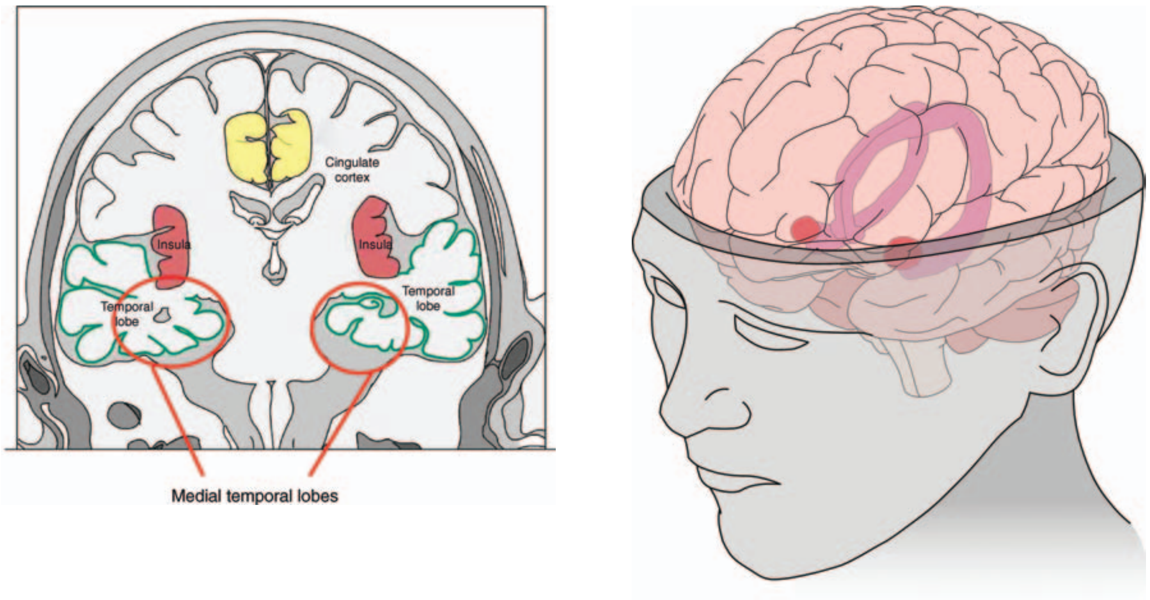


FIGURE 9.1 The medial temporal lobes and hippocampi. The memory regions are spatially complex and difficult to visualize. This collage shows two perspectives. The left panel shows a coronal cross-section of the brain, with the medial temporal lobes (MTL) circled in red. The right panel shows the hippocampi in both hemispheres, tipped by red structures, the amygdalae. Notice that the hippocampi are looped structures, nestled inside of each temporal lobe. The MTL includes the hippocampi and neighboring 'rhinal' structures (see Chapter 5). *Source*: Drawn by Shawn Fu.

neocortex, which is the 'new' cortex of modern mammals, consistently has six layers, one of its most distinctive features. The giant neocortex and the MTL are in constant dialogue with each other, as we store and retrieve the flow of our daily experiences.

Because of its ancient evolutionary lineage, the MTL has multiple functions. The hippocampus was first studied as a map for spatial localization in rats and other mammals. However, it also encodes olfaction, which is why parts of the MTL are called the 'rhinal', 'entorihinal', and 'perirhinal' cortex. ('Rhinos' means 'nose' in Greek, as in the word rhinoceros, 'nose horn' – Figure 9.3.)

MTL also interacts with visual area IT, the inferior temporal lobe (see Figure 9.2). You may remember that area IT has been shown to integrate high-level visual object information (see Chapter 8). Neurons firing in this region correlate with conscious visual perception (Sheinberg and Logothetis, 1997). Thus, the MTL is strategically located to take in high-level, presumably conscious visual information.

Just around the corner from the MTL is the auditory cortex, suggesting that auditory information can be fed to MTL as well (see Chapter 7), and the amygdalae reside near the tip of the hippocampi, a major hub of emotional information (Figure 9.3). Thus, MTL is a highly interactive crossroads, well-placed for integrating multiple brain inputs, and for coordinating learning and retrieval in many parts of the neocortex. It is a 'hub of hubs'.

Most of human cortex is neocortex, which ballooned out from earlier regions over more than a hundred million years of mammalian evolution. As mentioned above, the neocortex is believed to encode long-term memories by altering synaptic connections between billions of neurons. There are literally trillions of such synapses in the cortex and its satellite organs, especially the thalamus (see Chapter 3). The hippocampus is ideally situated to combine information about the cognitive (neocortex) and emotional (limbic) areas, and bind that information into a memory trace that codes for all aspects of a consciously-experienced event (Moscovitch, 1995).

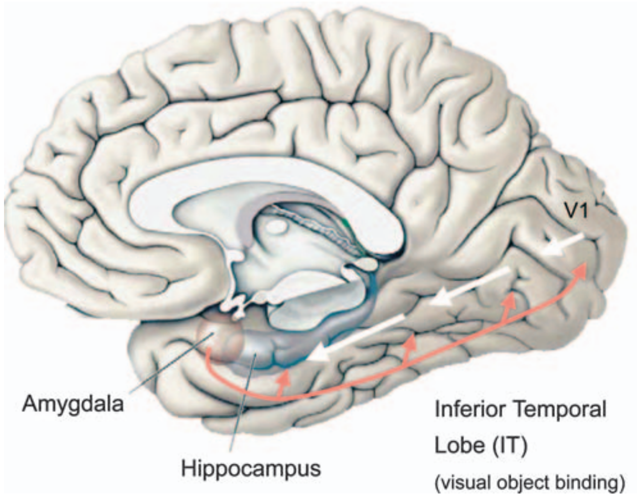


FIGURE 9.2 Memory areas receive visual object information. This midline view shows that the medial temporal lobe (MTL) is closely connected to area IT, the inferotemporal cortex. Area IT seems to support conscious visual object perception (see Chapter 8). MTL also includes the amygdala. Auditory cortex is located just around the corner, on the outside of the temporal lobe. *Source*: Vuilleumier, 2005.

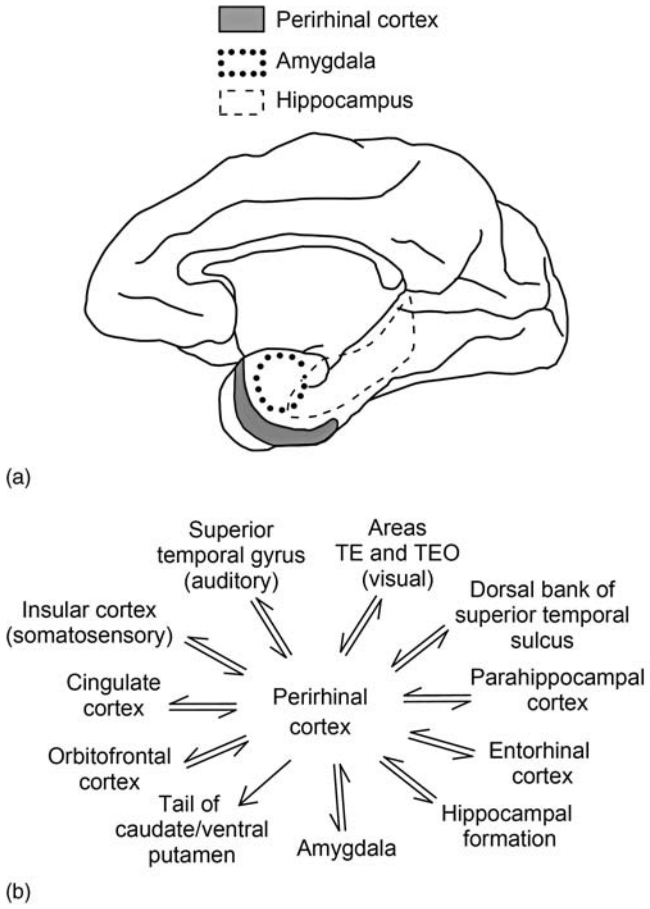


FIGURE 9.3 The medial temporal lobe is a hub with widespread connections. The MTL, including the perirhinal cortex, has very wide connectivity to visual, auditory, somatosensory, emotional, motor, memory and executive regions. This makes the MTL an ideal place to receive, bind and distribute information for long-term memory. Notice that almost all connections run in both directions (double arrows). *Source*: Murray and Richmond, 2001.

1.1 A functional overview

Figure 9.4 suggests that the visual cortex (for example) first takes in the sight of a coffee cup on a table. Cortical activity corresponding to the perceived coffee cup then spreads to the MTL, which activates and 'binds' widespread memory traces in both the visual cortex and other regions. Some scientists believe that, for a brief period of time, a few tenths of a second, the visual input regions and other parts of the 'bound' neocortex resonate with each other, as shown in coordinated gamma electrical activity (often called the '40 Hertz hypothesis') (Llinas and Pare, 1991; Engel and Singer, 2001; Freeman *et al*., 2003). Comprehending a visual stimulus like a coffee cup probably requires several hundred milliseconds. Thus, in less than a second, visual cortex has identified an object in front of our eyes, and triggered MTL to bind many regions of the neocortex to start making memory traces. However, as we will see, a permanent memory takes more time to consolidate.

Memory is for use in the real world, and retrieval is therefore as important as learning. When we encounter a reminder of a specific past experience of the coffee cup, the bound memory traces 'light up' the corresponding regions of cortex again. We thereby *reconstruct* some part of the original memory, again using the MTL to integrate memory traces into a coherent conscious experience. That experience – of imagining yesterday's coffee cup – makes use of visual cortex again. Because this is the central theme of this chapter, we begin with a cartoon version in Figure 9.4.

Learning is not limited to the neocortex. Other types of learning use other parts of the brain (see Section 8.0). However, in this chapter we will focus on learning and retrieving everyday memories.

1.2 Learning and memory in the functional framework

According to our functional framework, sensory input goes to 'working storage', which is part of *working memory* which, in turn, allows information to be actively maintained and manipulated (Figure 9.5; see Chapter 2). Working memory allows us temporarily to retain small

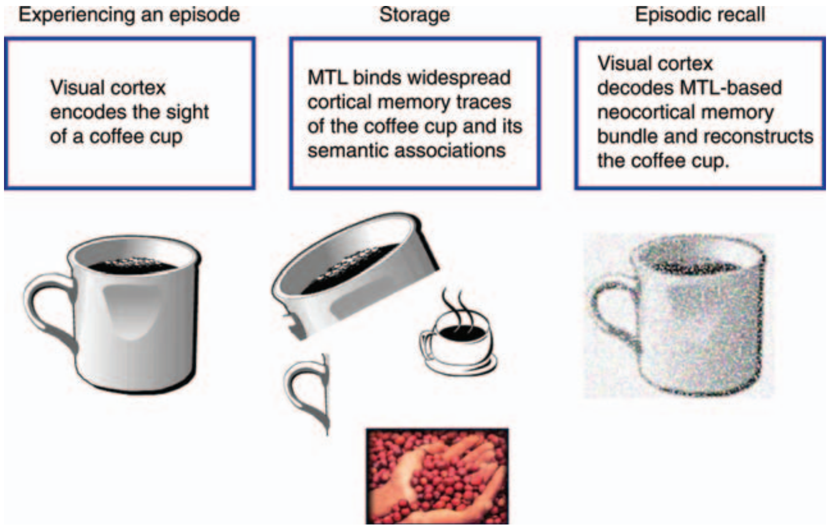


FIGURE 9.4 How MTL is believed to help store and retrieve episodic memories. In the left panel, the sight of a coffee cup standing on a table activates visual cortex up to the level of object perception (see Chapter 6). In the middle panel, storage is achieved when MTL coordinates widespread memory traces (involving synaptic modification) throughout many parts of cortex. These include semantic associates of the coffee cup, such as the coffee beans in the picture below. Visual features of the cup, like the handle, are also part of the associative complex that becomes activated. When the *episodic memory* – the sight of the coffee cup – is cued the following day, maybe by someone asking, 'Did you like the way I made the coffee yesterday?', MTL is once again involved in retrieving and organizing widespread cortical memory traces. Visual cortex is therefore needed to reconstruct the sight of the coffee cup, which is never identical to the original cup, but rather a plausible recreation of a pattern of visual activation that overlaps with the first one. Notice that visual cortex is involved in perception, learning, and episodic recall.

amounts of information in an accessible form. Many everyday tasks call upon this working memory capacity, such as keeping a phone number in mind for the several seconds it takes to dial the number. Working memory also gives us a sense of continuity over time, by embedding our immediate conscious experiences into a longer psychological present. There is debate about the exact relationships between conscious events, working memory and selective attention. Some scientists believe that working memory (WM) gives rise to our conscious experiences; others suggest that working memory is itself coordinated by conscious cognition (Baars and Franklin, 2003). But there is good agreement that all three interact very closely. That is the most important point.

Two key properties of WM are its relatively small capacity and its limited duration. In his famous paper on the *span* of immediate memory, George Miller (1956) concluded that only seven (plus or minus two) items can be held in immediate memory at any one time. More recent work suggests that the true WM span may be even smaller, closer to four items when rehearsal is prevented (Cowan, 2001; see Chapter 2). Likewise, the time an item is available is quite short, on the order of seconds.

Why have we evolved a memory system with these limits? The answer is not known. One possibility is that WM limits give special status to only the few pieces of information that are most relevant to our present goals, thus protecting them from interference from irrelevant information. It might also be adaptive for items in working memory to fade quickly. If material lingered beyond its period of relevance it might block out new information.

How we interpret and deal with material in working memory is determined by our current goals and concerns, as well as by our existing knowledge. Sensory and internal information may be brought to consciousness using attention. Once it becomes conscious, a number of theorists maintain that information is rapidly *encoded* into long-term memory (e.g. Moscovitch, 1990). There is also evidence for some unconscious learn-

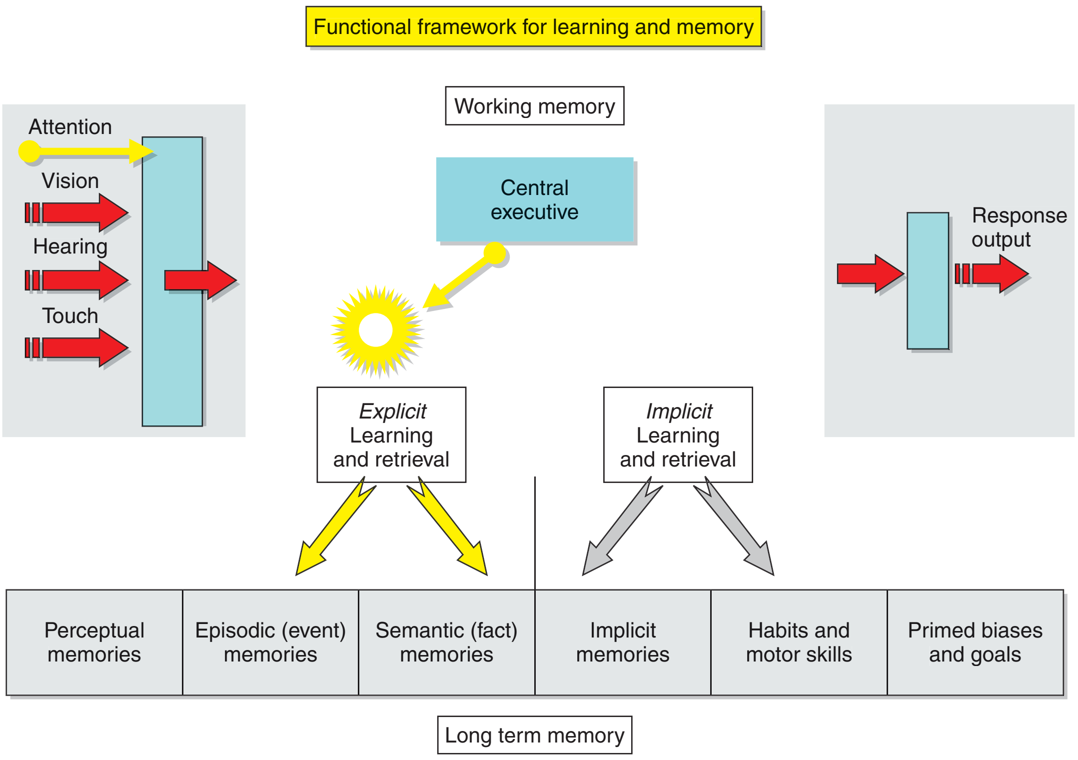


FIGURE 9.5 Explicit and implicit aspects of memory. A functional diagram for learning and memory. Working Memory (on top) can now be viewed as input to different types of long-term memory, divided into *Explicit and Implicit* ones. Explicit learning and retrieval involves conscious knowledge, both for facts and autobiographical experiences. Memory for facts is called *semantic* memory, while autobiographical memory is also called *episodic* because it reflects life episodes. Working Memory can manipulate explicit memories, like words, numbers, semantic facts and autobiographical episodes. Implicit learning and retrieval involves primed tasks, highly practiced habits and motor skills.

ing, but so far only unconscious fear conditioning has been shown to result in long-term memory (LeDoux, 1996). In general, conscious exposure correlates well with learning. While details of this broad picture continue to be debated, it is a useful outline to start with.

Figure 9.5 brings out several features of learning and memory. Notice that conscious cognition leads to *explicit* learning and memory retrieval in this figure. An obvious example is deliberately trying to memorize a technical term in cognitive neuroscience. What may not be so obvious, however, is that *implicit* learning also happens along with learning of conscious or explicit stimuli (Section 2.4).

Thus, Figure 9.5 shows both explicit or conscious *and* implicit or unconscious learning. Episodic memory is the storage of conscious episodes (also called autobiographical memory). Semantic memory, usually viewed as memory for facts, is also conscious, in the strict sense that people can accurately report the facts they believe. This is the standard operational definition of conscious brain events (see Chapter 8). Finally, perceptual memory capacities, such as our ability to 'learn to hear' music and art, also involve conscious, explicit kinds of memories.

On the right-hand side of Figure 9.5 we also see the learning of implicit memories. Infants may hear sequences of speech sounds, but they are not explicitly learning the rules and regularities of grammar. Those are apparently learned unconsciously, as we will see later. In general, implicit learning is often evoked by explicit, conscious events, but it often goes far beyond the events given in conscious experience (Banaji and Greenwald, 1995). Over-practiced habits and motor skills are also largely implicit. As we will see, priming effects are often implicit. Contextual phenomena are often implicit, such as the assumptions we make about visual space, the direction of the incoming light in a visual scene, the conceptual assumptions of a conversation, and so on. These are often hard to articulate, implicit, and to some degree unconscious (Baars, 1988).

As we will see, the 'Central Executive' of working memory plays an important role in long-term learning and retrieval. For example, if you are trying to learn a word, you might deliberately rehearse it to yourself, using your executive capacities to control inner rehearsal and to shut out distractions. When you are studying for a test, it is a good idea to monitor your own performance 'metacognitively' – i.e. to think about your own thinking process, and to see if your understanding of the material is good enough to pass the exam. All these are examples of executive processes (see Chapters 10, 11, and 12).

1.3 Implicit and explicit memory

Implicit memory is not accompanied by conscious awareness that one has a memory; the memory's existence is inferred only from the effects it has on behavior. Implicit memories may be retrieved without an intention to remember. Priming effects are used extensively to test for implicit memory.

Priming refers to the effect of a stimulus in creating readiness for a similar one. For example, showing a picture of a face will increase the processing efficiency of a following face, as measured by faster reaction time and greater accuracy. Priming can be either perceptual or conceptual.

Suppose you are asked to read a set of words and then your memory for them is tested a week later. We could test your memory directly by asking you to recall as many of the studied words as you can remember, or to recognize the words by picking them out from a list of old and new words. If the interval is long enough, you are likely to recall or recognize only a small subset of the items, and mistakenly classify old words that you studied as new ones that did not appear on the list.

However, if your memory is tested indirectly by asking you to read the words as quickly as you can, you will be able to say old words faster than new words. The old words are *primed*. On such an indirect test no mention is made of memory, and the subject is typically not even aware that memory is being tested. Yet by looking at how quickly subjects read a word we can tell whether the previous experience left a residue in memory. The same result can be seen in amnesic patients who cannot recall studying the words at all.

In the case of conceptual or semantic priming, words such as 'food' may increase the processing efficiency of words like 'water', even though they share little perceptual content. Priming can be viewed as a way of tapping into the general tendency of the brain to engage in predictive processing at every moment.

Perceptual priming is based on alterations of perceptual representation in posterior neocortex associated with perceptual processing. Conceptual priming is associated with alterations of conceptual systems in prefrontal cortex.

1.3.1 Procedural memory

Procedural memory refers to sensorimotor habits or automatic skills, which are largely unconscious. The structures implicated in these habits are the basal ganglia.

> Imagine you are riding a bicycle, and you start falling to the right. How would you avoid the impending crash?

> Many cyclists say they would compensate by leaning towards the left, but that action would precipitate the fall. When responding to the same situation while actually riding a bicycle, these same cyclists would turn their handlebars in the direction of the fall. The example highlights the distinction between implicit and explicit knowledge. Implicit learning refers to the ability to learn complex information (e.g. skills such as bicycle riding) in the absence of explicit awareness. Anecdotes such as the bicycle example offer subjectively compelling demonstrations for the existence of implicit forms of knowledge that are distinct from (and possibly in conflict with) explicit knowledge . . . (Curran, 2001).

The basal ganglia-frontal networks are the mediators of different classes of sensorimotor learning (Yin and Knowlton, 2006).

2.0 AMNESIA

Chapter 2 touched on the case of Clive Wearing, who has lived with a dense amnesia since 1985, when a viral infection destroyed some brain areas for memory. Over a few days, Wearing was transformed from a rising young musician to a man for whom each waking moment feels like the first, with almost no recollection of the past, and no ability to learn for the future.

Little has changed for Wearing since 1985. While he cannot recall a single specific event, some aspects of his memory are spared. He can carry on a normal, intelligent conversation. Some short-term memory is spared, allowing him to stay with a topic over several seconds. His has retained general world knowledge, an extensive vocabulary, and a tacit understanding of social conventions. Wearing also remains a skilled musician, able to play complex piano pieces from sheet music. Though he cannot remember specific events, he does recall a limited number of general facts about his life. Among the few memories that have survived is the identity of his wife, Deborah. He greets her joyfully every time she comes into his room, as though they have not met for years.

However, just moments after she leaves, Wearing has forgotten that she was there at all. In a recent book, Deborah Wearing (2005) tells of coming home after visiting Clive at his care facility, and finding these messages on her answering machine:

> Hello, love, 'tis me, Clive. It's five minutes past four, and I don't know what's going on here. I'm awake for the first time and I haven't spoken to anyone . . .
>
> Darling? Hello, it's me, Clive. It's a quarter past four and I'm awake now for the first time. It all just happened a minute ago, and I want to see you. . . .
>
> Darling? It's me, Clive, and it's 18 minutes past four and I'm awake. My eyes have just come on about a minute ago. I haven't spoken to anyone yet, I just want to speak to you.

Wearing's history suggests that amnesia is selective – certain kinds of memory may survive while others are lost. Skills like the ability to speak or play the piano are distinct from our memories of specific events. Thus, *memory is not unitary, but consists of different types*. Wearing's history also hints that different parts of the brain may be involved in different kinds of memory.

Figure 9.6 shows how specific Clive Wearing's memory loss is. Organic amnesia – the kind that is involves damage to both MTLs – interferes with episodic learning and recall. In addition, semantic learning is impaired, but not semantic retrieval. Clive Wearing still understands the world in much the way he understood it in 1985; his previous semantic knowledge is remarkably intact. But he cannot learn new ideas. And he can neither learn nor remember specific events. We will see later why this pattern of impairment makes sense.

Although all amnesic patients have memory loss, it varies in degree. Clive Wearing's amnesia resembles that of other patients, but he is unusual in his recurrent sense that he has just awoken from some unconscious state. He also 'perseverates' more than most amnesics, repeating the same thoughts and actions over and over again, as in the repetitive telephone messages he leaves for his wife. These symptoms may result from additional damage to prefrontal structures that allow us to monitor our own actions.

2.1 HM: the best-studied amnesia patient

We know a great deal about Clive Wearing's life from the extensive publicity about his case. However, another patient, known only as HM, is by far the best-studied victim of amnesia. In the case of HM we know exactly where the lesion occurred (Figures 9.7 and 9.8). This makes him very rare. Most brain injuries are very 'messy', can spread wider than the visible lesions, and may change over time. Clive Wearing's viral infection apparently destroyed hippocampal regions on both sides of the brain, but also some frontal lobe areas. Wearing may also have suffered brain damage that we simply do not know about. In the case of HM, however, because his lesion was carefully performed by a

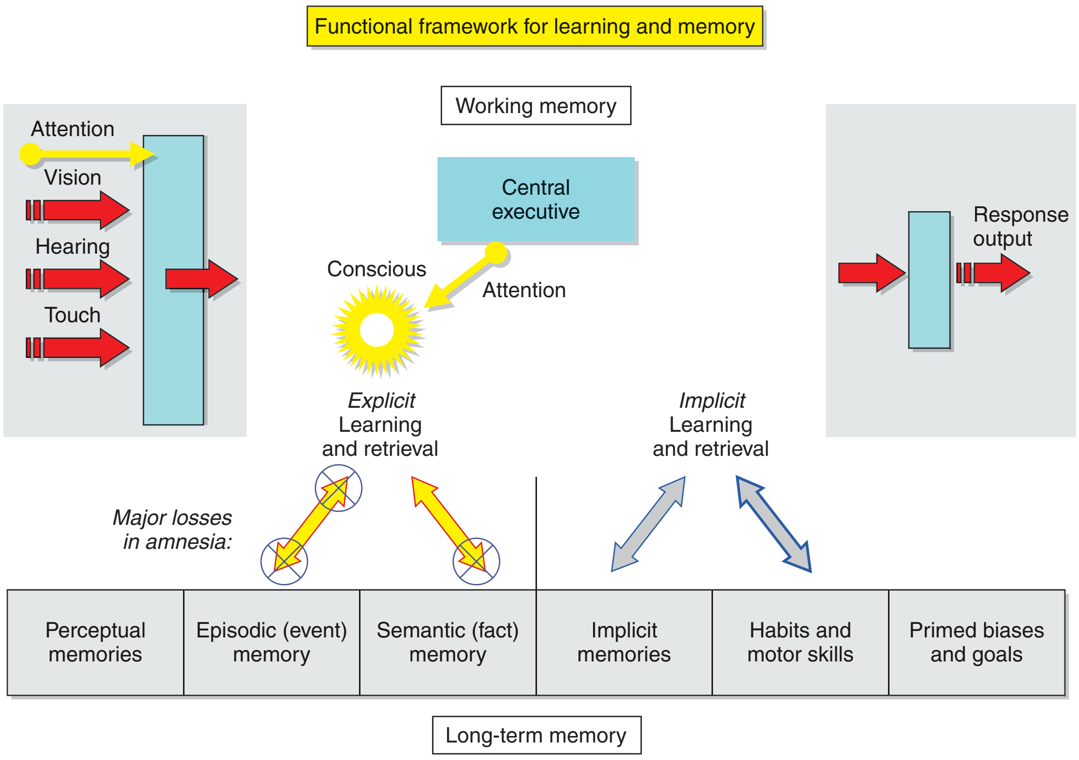


FIGURE 9.6 Functional framework: the typical loss in organic amnesia. Amnesia due to bilateral damage to MTL is highly specific. It impairs recollection of episodic (autobiographical) memories and blocks episodic learning. It also makes it impossible to learn new facts and concepts (semantic learning). However, amnesics like HM and Clive Wearing can carry on a normal-seeming conversation because they can still *retrieve* semantic information that was learned before the injury. *Implicit* learning and retrieval also continue. Since the MTL and neocortex work together to enable episodic learning, damage to MTL on both sides of the brain seems to explain these specific deficits. (Notice that the terms 'explicit' and 'conscious' are essentially equivalent; both are indexed by accurate report, as discussed in Chapter 8. Similarly, 'implicit' and 'unconscious' are equivalent for our purposes).

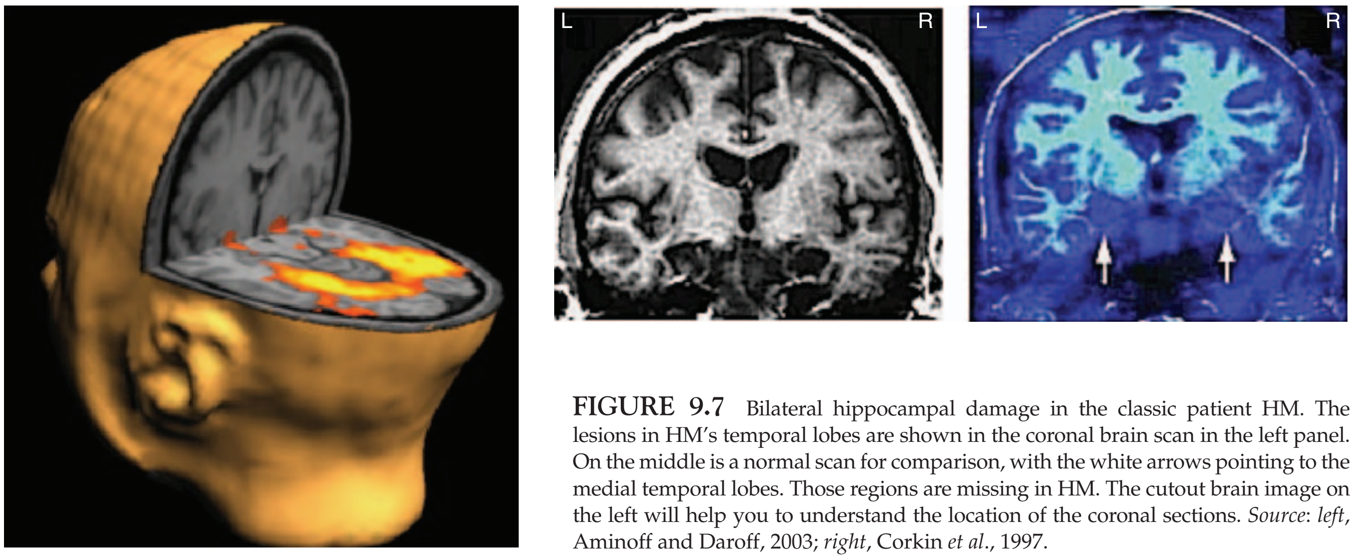


FIGURE 9.7 Bilateral hippocampal damage in the classic patient HM. The lesions in HM's temporal lobes are shown in the coronal brain scan in the left panel. On the middle is a normal scan for comparison, with the white arrows pointing to the medial temporal lobes. Those regions are missing in HM. The cutout brain image on the left will help you to understand the location of the coronal sections. *Source*: *left*, Aminoff and Daroff, 2003; *right*, Corkin *et al*., 1997.

surgeon, we know that both sides of the medial temporal lobe (MTL) were removed as accurately as was possible at the time. The extent of HM's brain damage and functional deficits have been verified with great care, in more than 100 published articles. This has made HM one of the most important patients in the history of brain science (Box 9.1).

Olfaction and taste – the chemical senses – are often thought to be the earliest sensory systems to emerge in evolution, simply because detecting nutrients and avoiding poisons is a fundamental requirement for life. Some scientists therefore believe that human senses like vision and speech audition built on an earlier foundation of the chemical senses. If that is true, it would explain

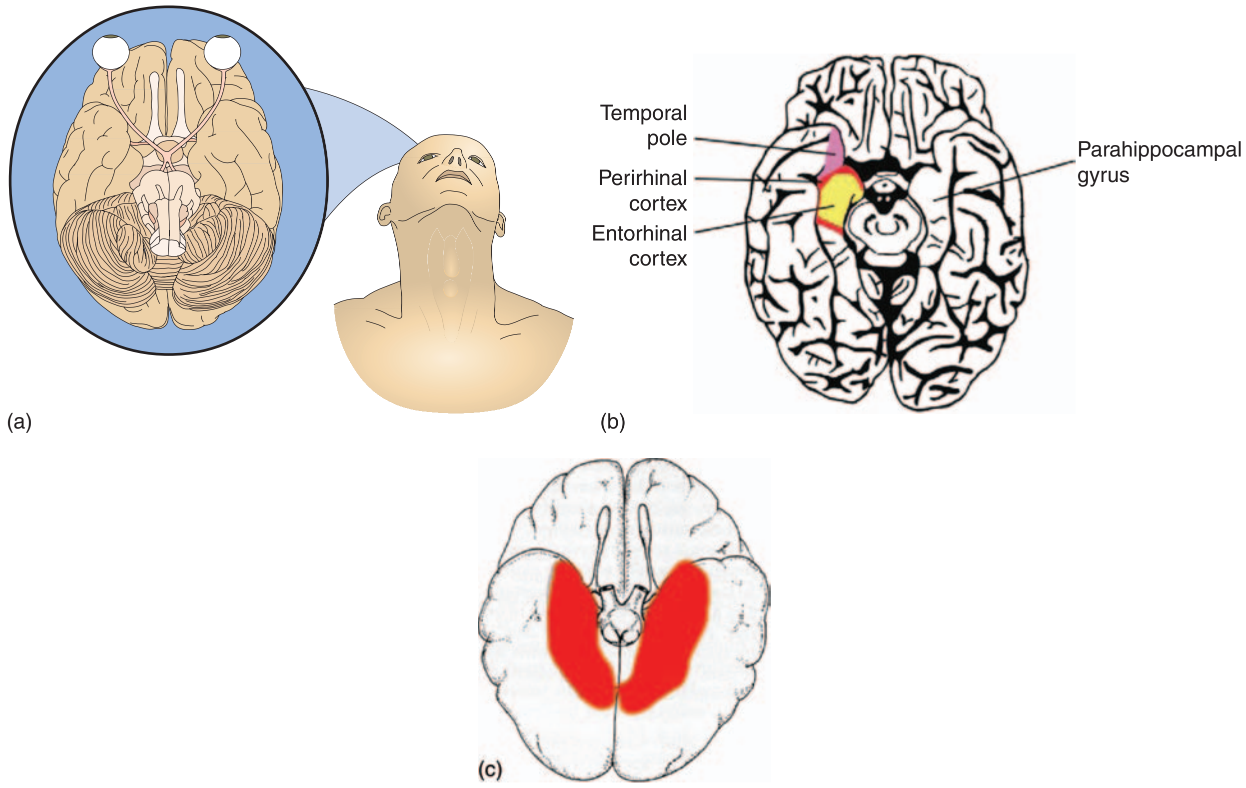


FIGURE 9.8 The medial temporal lobes and HM's lesions, seen from below. (a) The orientation of the head and brain; (b) the bottom of the MTL, with major subregions for memory labeled. Notice that the rhinal (smell) cortices indicate the ancient origin of this region. In all figures you can see the two olfactory bulbs pointing upward, an important landmark for orientation. (c) The surgical lesion in HM's brain. The surgeon at the time was unaware of the importance of this region for memory. *Source*: (b) Buckley and Gaffan, 2006; (c) Moscovitch, personal communication.

BOX 9.1 The case of HM

The cognitive neuroscience of memory arguably began with Herbert Scoville and Brenda Milner's (1957) report of a memory disorder in HM after bilateral removal of his medial temporal lobes to control severe epileptic seizures. As a result of a head injury from a bicycle collision when he was a young boy, HM was beset with epileptic fits that increased in frequency and severity into his late 20s. As a treatment of last resort, Scoville performed an operation in which he removed tissue in and around the hippocampus on both sides of HM's brain (see Figure 9.8). While the surgery reduced HM's seizures, it had a profound and unexpected impact on his memory. This result was unknown at the time, and Scoville would undoubtedly have changed the procedure had he known about this harmful result. The report of HM's case by Scoville and Brenda Milner (1957) was the first to demonstrate directly the importance of the hippocampus and surrounding structures for memory.

As a result of the operation, HM could not remember any of the events of his life thereafter – the people he met, the things he did, events taking place in the world around him. Even today, he cannot keep track of his age, and can no longer recognize himself in the mirror because he is unfamiliar with his changed appearance. In addition to this *anterograde* (post-damage) memory deficit, HM also can't

(*Continued*)

remember events or experiences from the years immediately before the surgery, a *retrograde* amnesia. While his episodic (autobiographical) memory loss is acute, other cognitive functions seem to be intact. He can reason, solve problems, and carry on a normal conversation. His intelligence is normal, and he has retained his language abilities.

HM has intact short-term memory. He performs like healthy controls on tests of working memory, like the digit span task. HM had been under the care of doctors from a young age, and his intellectual abilities before surgery were well documented. The specific locus of damaged tissue is both limited and well characterized. In most amnesias, the damage is more widespread and difficult to identify. HM has been tested and imaged a number of times since his surgery, giving a very complete picture of his condition.

As you can tell from Figures 9.1 and 9.2, HM has an apparently intact neocortex – the outer structures in brain scan. Like Clive Wearing, HM can carry on a normal conversation. He can discuss the immediate present, using his general knowledge of the world. He is conscious, has normal voluntary control over his actions, and appears to be emotionally well adjusted. It is only when his episodic memory is tested that he reveals that he simply cannot remember the past, or learn new memories for the future.

It is useful for you to review some important regions of the cortex (Figures 9.3, 9.9; also see p. 254). You should recall the location of the prefrontal lobes particularly, in front of the motor and premotor cortex. All of the neocortex is important for memory (see p. 254), but the prefrontal lobes may be especially important.

why vision, for example, has some of its highest levels of analysis in the smell brain, particularly the entorhinal cortex (ento – inside; rhinal – nose or smell).

2.2 A summary of amnesia

HM represents the features of amnesia in a very 'pure' form. More generally, amnesia is any loss of memory for personal experiences and other information, despite otherwise normal cognitive functions. The cause can be organic, including infection, stroke, tumor, drugs, oxygen deprivation, epilepsy and degenerative diseases, such as Alzheimer's disease. Amnesia can also be *psychogenic*, resulting from trauma or suggestion (Nilsson and Markowitsch, 1999).

As we have seen, organic amnesia is caused by bilateral damage to the medial temporal lobes, which includes the hippocampal formation. It generally reveals:

1. *Impaired memory but preserved perception, cognition, intelligence and action*. Amnesic people perform normally on standard tests of intelligence, but are impaired on standard tests of memory. They can play chess, solve crossword and jigsaw puzzles, comprehend complex instructions, and reason logically.
2. *Impaired long-term but not working memory*. Amnesic people have a normal digit span. They are impaired, however, if they are distracted. The same holds for words, stories, visual patterns, faces, melodies, smells and touch.
3. *Impaired recent but not remote memories*. Memory loss is most noticeable for events learned *after* the onset of the disorder, as well as in the period immediately preceding it, but not for information acquired years before. That is, amnesia victims have an *anterograde amnesia* that extends into the future but a limited *retrograde amnesia*. The length and severity of retrograde amnesia varies.
4. *Impaired explicit but not implicit memory*. Anterograde (post-injury) memory loss applies only to information that can be remembered consciously or *explicitly*. Learning, retention and retrieval of memory without awareness or *implicitly* is normal.

2.3 Spared functions in amnesia: implicit and procedural memory

As mentioned above, implicit memory is commonly assessed by priming tasks. Perceptual priming is mediated by sensory cortex, and conceptual priming is believed to involve both the temporal and prefrontal regions. Amnesics do not lose their capacity to perform well on priming tasks, such as word-fragment completion. For example, subjects may study a list of words (such as *metal*) and are tested with fragments of the words they studied, to see if they can complete them (*met*__). The study phase increases the speed of completion. On such tasks, amnesic patients can perform as well as normals.

Functional neuroimaging studies confirm the perceptual locus of perceptual priming. Unlike tests of explicit memory, which are associated with *increased activation* during retrieval in regions that support memory performance, such as the MTL and prefrontal cortex, perceptual priming is associated with *decreased activation* on repeated presentations in regions believed to mediate perceptual representations. Thus, repeated presentation of faces and words leads to decreases in activation in inferior temporal and extra-striate cortex which mediate face and word perception (Wigg and Martin, 1998; Schacter *et al*., 2004).

2.3.1 Conceptual priming

In conceptual priming the relationship between study and test items is meaning-based. Conceptual tasks include word association ('Tell me the first word that comes to mind for Elephant'), category exemplar generation ('Provide examples of animals') and general knowledge ('What animal is used to carry heavy loads in India?') (Moscovitch *et al*., 1993; Roediger and McDermott, 1993). Conceptual priming occurs if studied words (e.g. elephant) are retrieved more frequently than unstudied ones. Because conceptual priming depends on meaning, a change in the physical form of stimuli has little influence on conceptual priming.

Conceptual priming is impaired in people with damage to regions of cortex mediating semantics. Thus, patients with semantic dementia whose degeneration affects lateral and anterior temporal lobes show an inability to recognize repeated objects which share a common meaning, for example, two different-looking telephones. But they have no difficulty recognizing the object if it is repeated in identical form (Graham *et al*., 2000).

Likewise, patients with Alzheimer's disease show preserved perceptual priming but impaired conceptual priming. Functional neuroimaging studies of conceptual priming implicate semantic processing regions, such as prefrontal and lateral temporal areas. As in tests of perceptual priming, tests of conceptual priming lead to decreases in activation in those regions (Buckner *et al*., 1998; Schacter *et al*., 2004). Asking people repeatedly to generate examples of 'animals' results in *reduced* activation in the same regions.

Numerous studies have shown that priming on a variety of tests is normal in amnesic patients. This applies to most tests of perceptual and conceptual priming, indicating that the MTL does not contribute to them.

2.3.2 Spared procedural memory in amnesia

One of the earliest demonstrations of preserved memory in amnesia was on tests of learning perceptual motor skills called *procedural memory*. Corkin (1965) and Milner (1965) showed that HM was able to learn and retain a pursuit-rotor task, keeping a pointer on a moving target. HM showed improvement on these tasks even months later, though he could not recall doing it even minutes afterwards, if he was distracted. These findings have been repeated in other cases.

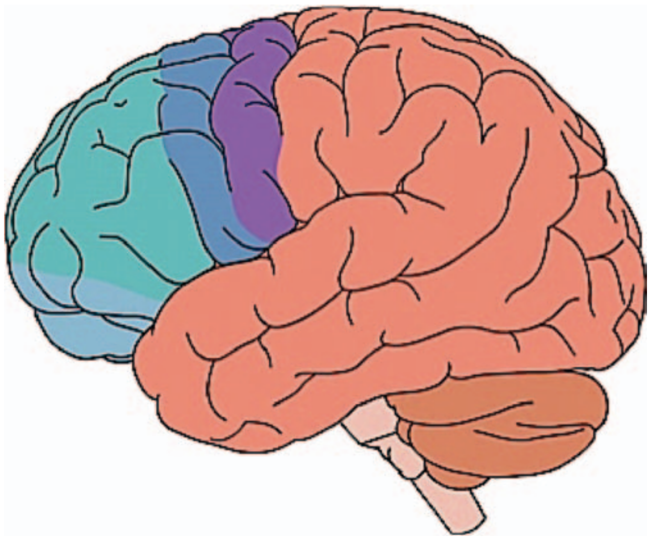


FIGURE 9.9 Neocortex: motor, premotor, and prefrontal regions. In this lateral view of the cortex, the motor strip is tinted purple, and just in front of it, the premotor area encodes the cognitive intention to move specific limbs. The true prefrontal cortex is in front of these motor regions (light green). The light blue area of the prefrontal lobe is sometimes called the orbitofrontal cortex, because it is located just above the orbital hollows of the two eyes. You are encouraged to review the other visible structures, including the major lobes, the Sylvian fissure and the central sulcus, which divides the posterior half of cortex from the frontal half. *Source*: Drawn by Shawn Fu.

Procedural memory depends on perceptual-motor regions, like the basal ganglia, which interact with the neocortex, both the posterior and frontal (see Chapter 5). Patients with impaired basal ganglia due to Parkinson's or Huntington's disease show little or no improvement after practicing sensorimotor tasks (Kaszniak, 1990; Gabrieli *et al*., 1994).

In the serial reaction time task (SRT), dots are presented on a computer screen in one of four locations, and participants are instructed to press a key corresponding to the location of the dots they see (Willingham *et al*., 1989). Some of the sequences are repeated while others change randomly. Reaction time to the repeated sequences becomes faster with repetition, but remain the same for the random sequences, even though participants cannot consciously distinguish one from the other (Willingham, 1998). Amnesic patients perform normally on the implicit SRT task but poorly on the explicit version (Nissen and Bullemer, 1987; Reber and Squire, 1998). Again, patients with basal ganglia disorders like Parkinson's disease perform poorly on both SRT tasks (Knopman and Nissen, 1987; Vakil *et al*., 2000).

Functional neuroimaging studies also show that learning on the implicit SRT task is associated with activity in the basal ganglia but not with MTL activity.

2.4 Spared implicit learning

Academic learning is often explicit: professors point out the things to be learned, and students try their best to memorize them. But most ordinary human learning is probably implicit. A hunter may teach young people how to track an animal, or how to kill and skin it. Most of the time such practical activities can be taught more easily by modeling than by explicit labeling. Many of the subtleties of hunting and gathering may not even have names. Experimentally, subjects who are given a set of stimuli generated by a simple set of rules, unconsciously infer the underlying regularities. Social habits are probably learned mostly implicitly. Children learning language surely don't label the words they hear as nouns or verbs. Rather, they pay attention to speech sounds and the underlying regularities are learned *implicitly*. We rarely become conscious of abstract patterns – the regularities of grammar, the harmonic progressions of a symphony, or the delicate brushwork of a work of art. Most knowledge is tacit knowledge; most learning is implicit.

Knowlton *et al*. (1994, 1996) used a probabilistic classification task to study implicit learning. Participants were shown sets of four cards that predicted the 'weather' with different probabilities (Figure 9.10). After each set of cards, participants were asked whether it predicted 'rain' or 'sunshine'. Some sets predicted 'rain' 20 per cent of the time, and others 80 per cent of the time. Learning this association takes about 50 trials in normal people, but it takes considerably longer for subjects to realize explicitly which card sequence predicted which kind of weather. That is, the weather prediction is learned *implicitly* before it can be stated *explicitly* (Knowlton *et al*., 1994, 1996).

Amnesia patients performed as well as controls in the early trials, the implicit association, but not in the later trials when performance was based on explicit, declarative memory. However, patients with Parkinson's disease, a basal ganglia dysfunction, performed poorly during the early trials, but caught up during the later ones. Brain imaging showed activity in the basal ganglia throughout the task, but a shift in MTL activity as the task progressed (Poldrack *et al*., 1998).

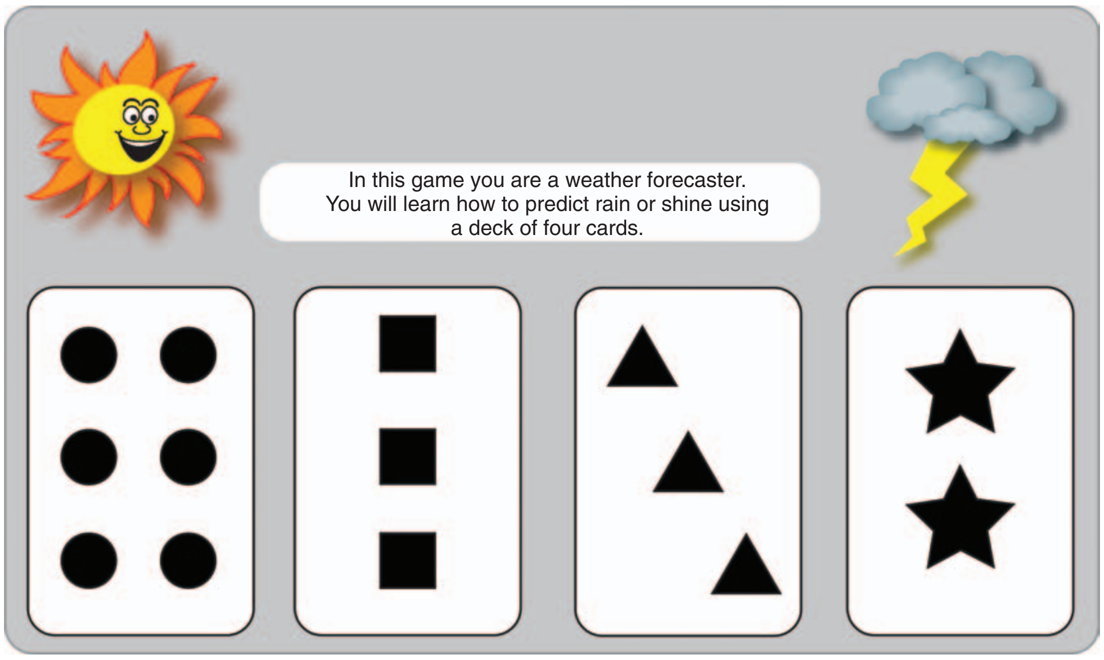


FIGURE 9.10 An implicit 'weather prediction' learning task. Knowlton *et al*. (1994) devised this 'weather prediction' task for four-card sequences. Participants learned to predict the probabilistic outcomes implicitly before they were able to state the pattern explicitly. Amnesic patients performed well during the implicit early part of the learning process, but did not learn to state the association between the cards and the 'weather' explicitly. *Source*: Knowlton *et al*., 2003.

In summary, amnesia due to bilateral damage to MTL seems to be primarily a disorder of *episodic memory*, resulting from impaired transfer of information from working memory into long-term memory. Because memories acquired long before the onset of amnesia are relatively spared, it is believed that the hippocampus and related structures in the medial temporal lobe are needed only temporarily to hold information in memory until they are consolidated elsewhere in the brain, presumably in neocortex.

3.0 MEMORIES ARE MADE OF THIS

Traditionally, a memory is considered to be a stable record of an event, which can be recalled accurately in the same form it was learned. In this commonsense view, memories can be retrieved, examined, and played back like a high fidelity music recording. Memories can also be forgotten without affecting other cognitive systems.

There are reasons to question this common sense idea. One is that real memories of past events are rarely accurate. The *process view* considers memory to be a product of a dynamic process, a reconstruction of the past influenced by past and current conditions, anticipations of future outcomes, and by other cognitive processes. In the process view, memory is based on stored information, but is not equivalent to it. It is dynamic and mutable, and interacts with other processes. Thus, two people experiencing the same event may have different memories of it. It is not simply that one person is right and the other wrong, but that in retrieving the memory each person's outlook, knowledge, motivation, and retentive abilities may alter what is retrieved.

Everyone's memory changes with time. We forget most of what has happened within minutes or hours, and what remains is commonly reorganized and distorted by other knowledge or biases. We would not want computer files or books to be that way. We do not want files to decay over time, or to leak into neighboring files. Computers and libraries are designed to keep everything as distinct and stable as possible. Yet normal memories do fade, and are often confused with others.

Try to reconstruct in as much detail as possible all the things you did two weekends ago, in the exact order in which you did them. To do that, most of us have to search for cues, to determine exactly what we did. Having found a cue, there is a process of reconstruction, especially in trying to figure out the sequence of events. Did I meet my friend before I spoke to my parents or afterwards? Did I go shopping, and what was the order of the stores I visited? In each store, in what order did I look at the merchandise and buy it? You can try this with a recent movie, and then see how accurate your memory is by checking it against a copy of the movie.

To answer these questions you must draw on a body of knowledge and inference that is unlike anything that is needed when you enter a file name to access a computer file, or use a call number to find a library book. You may confuse what you did two weekends ago with what happened another time. As we will see, some patients with brain damage have a disorder called *confabulation*, in which they make up false memories without any intention of lying, and without any awareness that their memories are incorrect.

Memories influence how other memories are formed and retrieved. They also shape our actions even when we are not conscious that they do so. Our memories and dispositions influence our thoughts and actions and, in turn, are influenced by them. In short, memory is needed to carry on the affairs of daily life and to plan for the future, and is, in turn influenced by the past, whether conscious or not, and by our thoughts about the future.

3.1 Electrically evoked autobiographical memories

For some fifty years, brain surgeons have reported that awake patients report vivid, specific conscious recollections during temporal lobe stimulation. Penfield and Roberts (1959) were among the first to use pinpoint electrical stimulation of cortex to map out functional regions. Their aim was to remove 'epileptic foci' in the cortex, regions of scarred tissue that can trigger the massive electrical storm of major seizures. In order to locate epileptic foci, and to avoid harming functionally important areas, the cortex of awake patients was mapped using low-voltage electrical stimulation in specific cortical locations.

This is only possible because the cortex itself has no pain receptors. As long as local anesthetic is used to block pain from the scalp incision, conscious patients can talk about their experiences without harm. Open-brain surgery provides a unique source of evidence for cognitive neuroscience.

Stimulation of the temporal lobe sometimes results in an unexpected flood of conscious memories. For example, a recent patient during brain stimulation

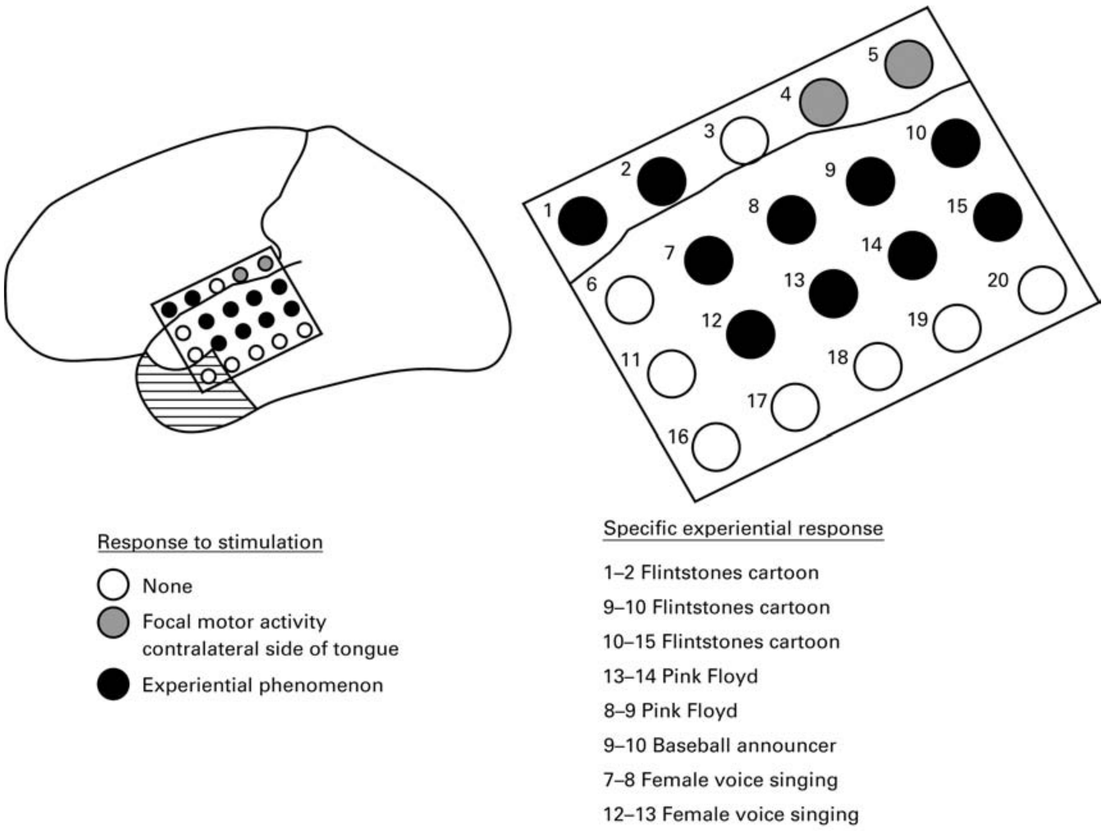


FIGURE 9.11 Autobiographical memories evoked by temporal lobe stimulation. Spontaneous reports of memory experiences by electrical brain stimulation in a patient with a surgical lesion in the left medial temporal lobe. Notice the electrode grid that was placed on the cortex as shown. Electrodes were places 1 cm apart. Different electrodes consistently evoked different memory episodes. Spontaneous reports of this kind are not unusual with temporal lobe stimulation, but are not routinely reported as a result of other locations of cortical stimulation. *Source*: Moriarty *et al*., 2001.

gave the following reports of his experiences (Moriarty *et al*., 2001):

1 At four electrode locations shown in Figure 9.11, re-experiencing Flinstones cartoons from childhood
2 At four different electrode locations, hearing the rock band Pink Floyd
3 At two other locations, a baseball announcer
4 At four more locations, an unknown female voice.

Notice that the open circles in the figure show electrode locations that led to no experiential memories at all. Some of the electrode sites are close to the auditory cortex of the upper temporal lobe, but some are not. And these auditory regions are not known to provide such rich memories of experiences that patients report having heard at specific points in their lives. However, this particular patient had a surgical lesion in the medial temporal lobe, and we must be careful about generalization to other cases.

The patient in this case is not told which electrode is currently stimulating the temporal lobe, so that it is not possible to fake this pattern of results. Scientists have been skeptical about these reports, since stimulation in one place might activate other regions as well. Epileptics have atypical brains, since cortex commonly changes in response to disorders. However, it is extremely unlikely that so many different patients would report a flow of conscious memories over fifty years of stimulation of the temporal lobe. After numerous animal experiments, careful studies of amnesic patients and brain imaging of memory tasks, there is little doubt today that there is something about the temporal lobe that is specific to long-term episodic memory. One reasonable hypothesis is that temporal lobe stimulation somehow activates specific memories by way of the MTL.

Figure 9.12 shows a possible explanation of this phenomenon. What we are seeing in the neurosurgical patient is an established memory pattern, which is

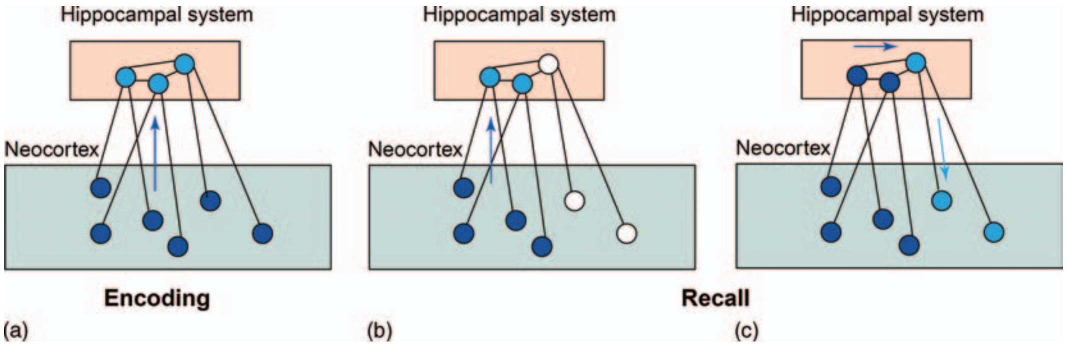


FIGURE 9.12 The hippocampal system (MTL) and neocortex in learning and recall. A neural net model of MTL (the hippocampal system) in interaction with neocortex. During the encoding or learning process, information from cortex is transferred to the hippocampal system. During recall, a neocortical event serves to evoke an overlapping pattern of neural activation in the MTL (the blue dots). The hippocampal system responds by activating neocortical regions that provide the experience of recall of some part of the original event. *Source*: Gluck *et al*., 2003.

re-evoked by direct electrical stimulation to the temporal lobe. Thus, the flow of information is from the neocortex (temporal) to the hippocampal system (MTL), which causes the hippocampal system to resonate with the original neocortical memory traces to produce the original episodic experience, or something very much like it. However, this still leaves many questions unanswered, such as, what is the relationship between the electrical stimulus and the normal process of episodic memory retrieval? Why are such extremely specific memories evoked under these circumstances, among the many millions of episodes the average person has experienced? Is there perhaps a relationship between the electrical stimulus and the oscillatory EEG phenomena that are observed in connection with retrieval, like the theta rhythms that seem to coordinate MTL-neocortical retrieval (see below)? Episodic memories reported by patients in neurosurgery after electrical stimulation are fascinating, and appear to be robust and reliable phenomena. But we do not have a good specific explanation as yet.

3.2 Long-term potentiation and long-term depression: excitatory and inhibitory memory traces

Most synapses in cortex are excitatory, using the neurotransmitter *glutamate* (see Chapter 3). A very large minority use inhibitory neurotransmitters like *GABA* (gamma amino butyric acid). To encode long-term memory traces in changed synaptic efficiency, these excitatory and inhibitory connections must somehow be made more permanent. These two processes are believed to occur in what is called long-term potentiation (LTP) for excitatory synapses and long-term depression (LTD) for inhibitory ones. These events, which have been observed in specific regions, are simply an increase and a decrease in the firing probability of a postsynaptic potential given a presynaptic spike.

LTP has been observed within the hippocampus itself, using single-cell recording in one of the neuronal layers of the hippocampus (Figure 9.13). Single cell recording has been extensively done in animals, but there are cases of such recordings in human epileptic patients as well (Kreiman *et al*., 2002).

While we can observe LTP and LTD in specific locations like the hippocampus, the standard hypothesis about long-term memory involves billions of synapses in cortex and its satellites, amounting to literally trillions of synapses. We have no way of taking a census of all of the synapses in this system, or even a substantial fraction of them, at this time. Rather, we have a number of studies showing increased LTP and LTD in experiments like the one described in Figure 9.14, supplemented by studies of brain damage and of population activity among billions of neurons as measured by EEG, ERP, fMRI and so on. In addition, we have evidence from stimulation studies, like temporal lobe stimulation of awake patients during neurosurgery, and transcranial magnetic stimulation (TMS) in normal subjects. What we know about memory is therefore an inferential picture, in which many hundreds of studies have been performed. But we cannot yet come close to observing large numbers of changed synaptic connectivities directly at the submicroscopic level.

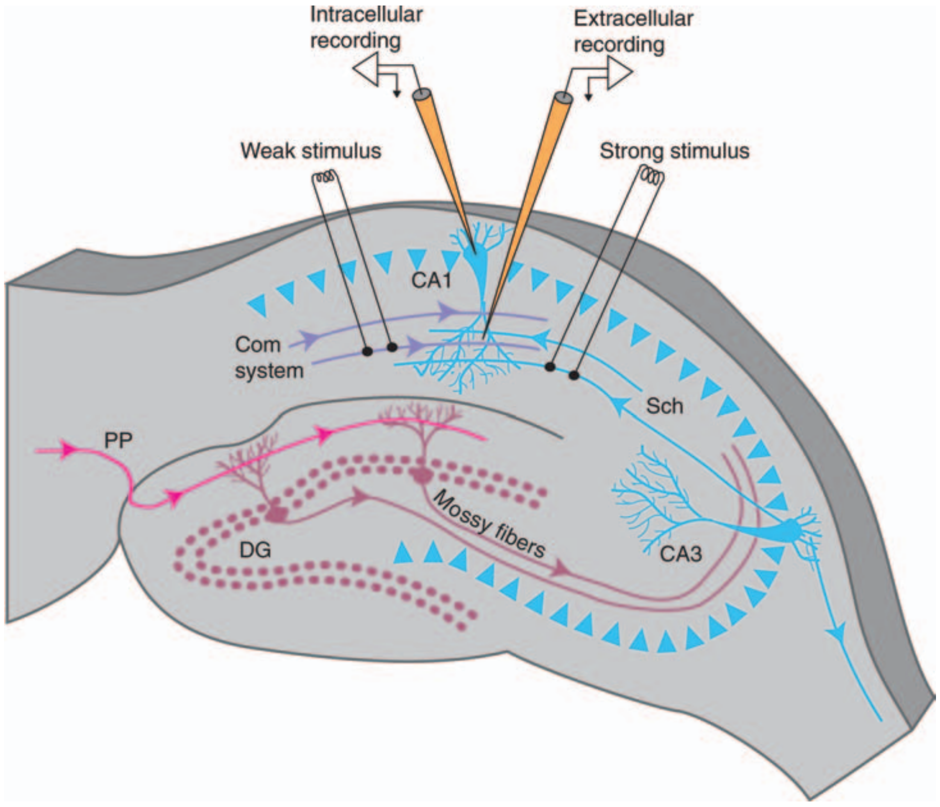


FIGURE 9.13 Single-cell recording in hippocampus. A schematic of single cell recording and stimulation either inside of hippocampal neurons, or outside. An electrode placed outside of a neuron can pick up electrical field potentials, which are similar to EEG but much more localized. Electrical field potentials often reflect the activity of small populations of neurons, as opposed to the axonal or dendritic potential of a single neuron. Notice that a very similar technique can be used to stimulate single cells, or small sets of cells, in the hippocampus. *Source*: Squire *et al*., 2003.

With that caution in mind, there is good agreement today that the evidence is consistent with these propositions:

1. Episodic input is initially represented via neocortex.
2. It is integrated for memory purposes in the MTL (medial temporal lobes), containing the hippocampi and related structures, and perhaps also the thalamus and surrounding regions.
3. Consolidation: MTL and related regions then bind and integrate a number of neocortical regions, a process that transforms temporary synaptic connectivities into longer-lasting memory traces in both MTL and neocortex. The main mechanism for such changes is believed to be LTP and LTD.

We focus on the last point next.

3.3 Consolidation: from temporary to permanent storage

We can now add the final steps. Chapter 2 suggested a widely accepted hypothesis about the relationship between immediate memory and long-term memory called the *consolidation hypothesis*. Consolidation is generally defined as a progressive stabilization of long-term memory traces so that they are relatively resistant to decay or disruption. It is this process which is absent or severely disrupted in amnesic patients and accounts for their poor ability to transfer information from short- to long-term memory.

Figure 9.15 shows one version of learning with consolidation, in which input into the neocortex and the hippocampal regions (MTL) evoke an active state, with neuronal processes making new synaptic connections. As mentioned above, immediate memory is encoded in

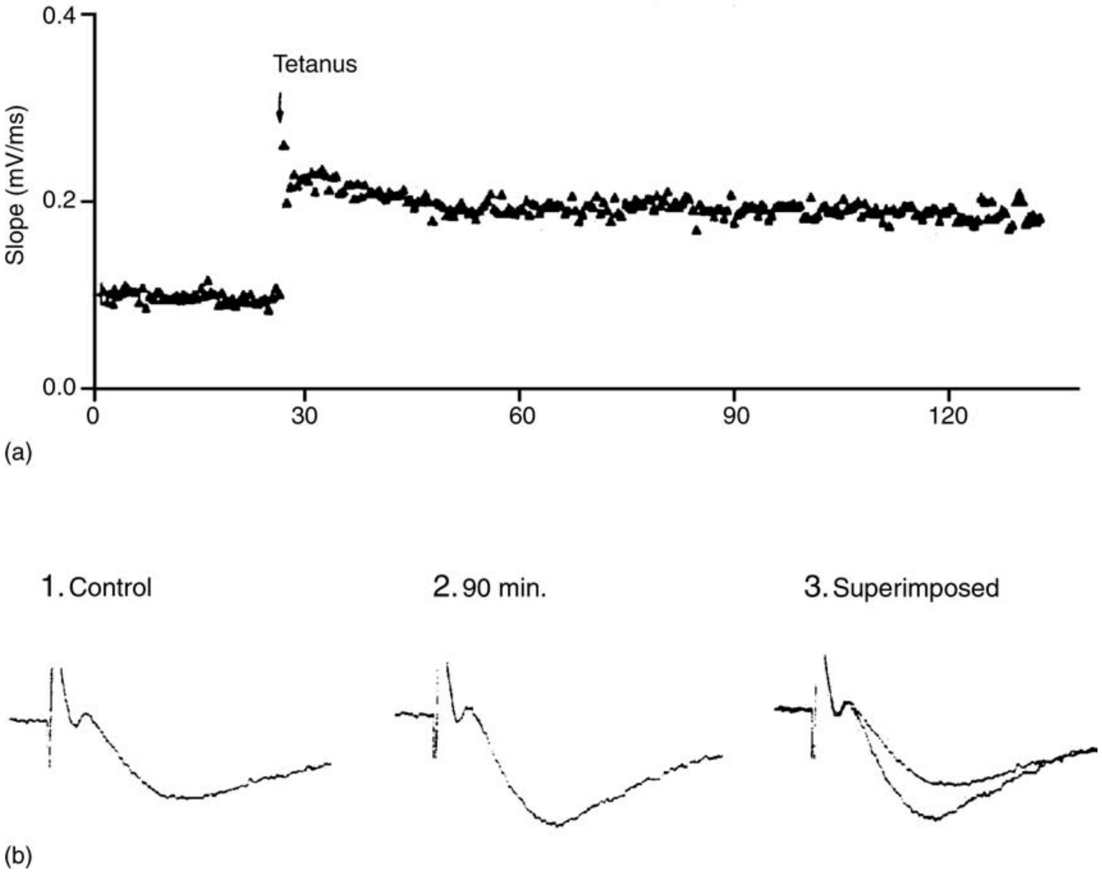


FIGURE 9.14 Long-term potentiation in the hippocampus. Memory traces are believed to be encoded in changed synaptic efficiency among billions of neurons in the neocortex and MTL. These are called long-term potentiation (LTP), corresponding to a permanent increase in excitatory transmission, and long-term depression (LTD), a permanent increase in inhibitory neurotransmission. Direct evidence for LTP has been obtained in hippocampal single cell recordings, as shown above. The lower half of the diagram shows three cases of changed EPSP (excitatory postsynaptic potentials) after strong electrical stimulation presynaptically (called tetanus). Notice that after 90 minutes, the EPSP dips more deeply (remember that a more negative potential means more electrical spiking activity). The graph above shows a long-lasting change in the conductivity of the synapse, as measured by the slope of the EPSPs for two hours after the strong electrical stimulus (tetanus). *Source*: Byrne in Squire *et al.*, 2003.

improved synaptic connectivity between billions of neurons in the neocortex. Normal sleep, especially the slow-wave stage, is important to turn these temporary connectivities into long-lasting memory traces.

However, more permanent memories are believed to require protein synthesis – such as the growth of dendritic spikes, tiny stalks that grow on top of axons and dendrites, bearing new synaptic connections with neighboring neurons.

The idea that new learning takes some time to 'fix' is quite old. In 1904, Burnham wrote that:

> The fixing of an impression depends on a physiological process. It takes time for an impression to become so fixed that it can be reproduced after a long interval; for it to become part of the permanent store of memory considerable time may be necessary. This we may suppose is not merely a process of making a permanent impression upon the nerve cells, but also a process of association, of organization of the new impressions with the old ones (quoted by Moscovitch).

Figure 9.16 shows these two kinds of consolidation conceptually. The LTP-LTD process discussed above involves cellular consolidation, a local change of connective efficiency in trillions of synapses. However, there is also believed to be *systems consolidation*, in which large-scale reorganization of memories may occur. There is considerable evidence that different sleep stages may have different effects upon this systems consolidation

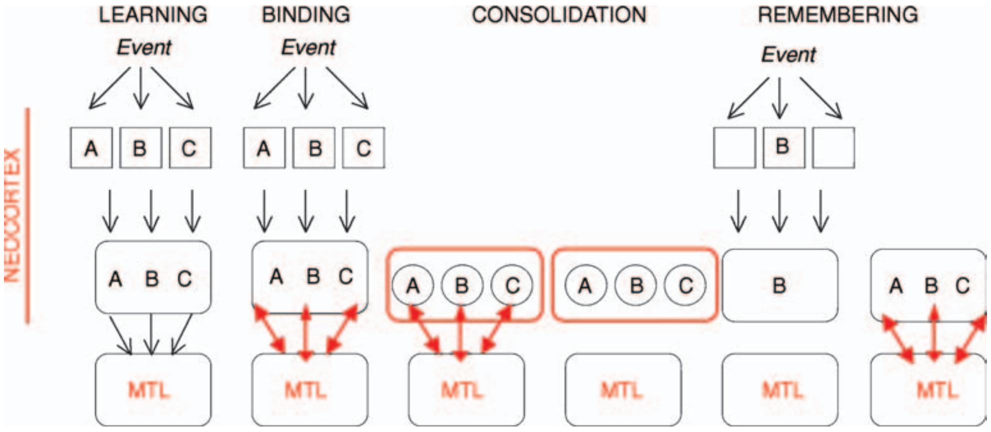
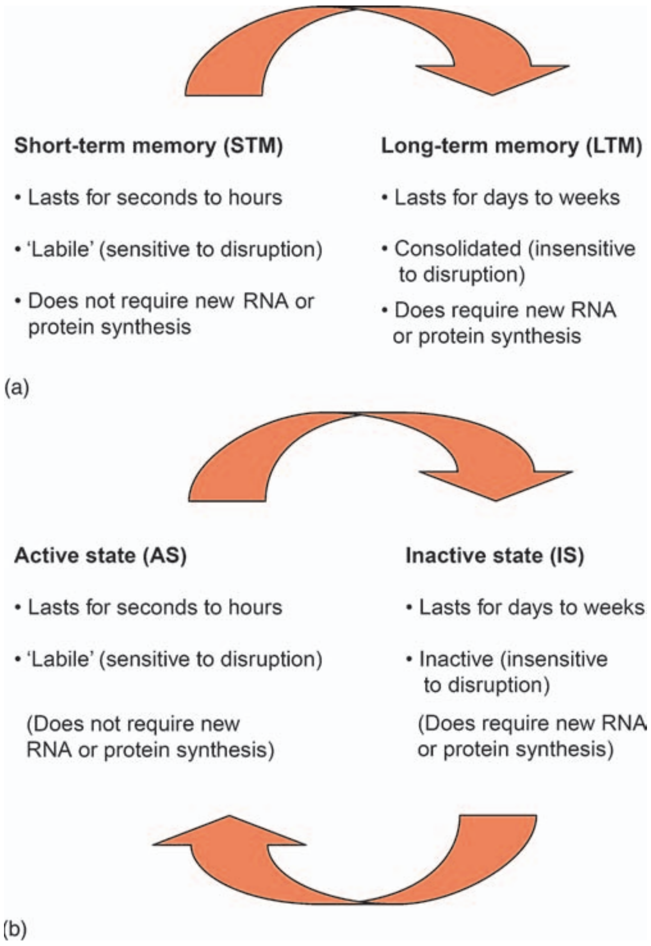


FIGURE 9.15 The steps of learning, binding, consolidation and remembering. In this summary, Step 1 is the learning of an event, consisting of three elements, A, B, and C. It is initially encoded by neocortex (such as the visual cortex) and sent to MTL. In Step 2, MTL and neocortex resonate with each other to begin establishing the memory trace. In Step 3, the stimulus event is no longer available, and the MTL-neocortical resonance is now independent of external support. Step 4 shows how consolidation leads to permanent, separate memory traces (synaptic changes) in both the MTL and neocortex, which now exist separately from each other, while other input is being processed. In Step 5, element B of the original event (A-B-C) is presented as a reminder or recall cue. In Step 6, the memory traces of A-B-C are activated by resonating activity between MTL and neocortex. At this point, the episodic memory has been retrieved in the absence of the original stimulus. *Source*: Moscovitch, modified with permission.



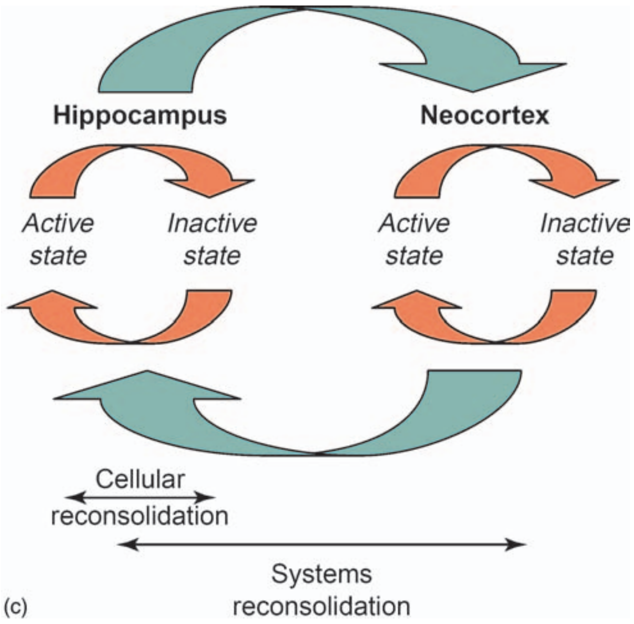


FIGURE 9.16 Reconsolidation turns active neuronal connections into lasting ones. Two kinds of consolidation are believed to exist, cellular and systems consolidation. Both are evoked by activation of MTL and neocortex. This diagram emphasizes the degree to which MTL (also called the hippocampal complex) and neocortex establish active cell assemblies corresponding to the learned input, in which neurons resonate with each other until more permanent connections are established. *Source*: Nader, 2003.

process. Notice that both types of consolidation are thought to involve an active dialogue between the MTL (hippocampus) and neocortex.

3.4 Rapid consolidation: synaptic mechanisms, gene transcription, and protein synthesis

Rapid or synaptic consolidation is accomplished within the first minutes to hours after learning occurs. Weiler and colleagues (Weiler *et al.*, 1995) showed that it correlates with morphological changes in the synapse itself. Stimulus presentation initiates a cascade of neurochemical events at the synaptic membrane and within the cell which increase the synaptic strength or efficiency with which neurons that form the memory trace can communicate with one another. The first of these processes involves local, transient molecular modifications that lead to an increase in neurotransmitter release at the affected synapse. If the stimulus is intense enough and/or repeated, additional processes are activated. These involve gene transcription and protein formation that lead to long-lasting cellular changes, including the creation of new synapses, that support the formation and maintenance of long-term memory. These processes may last from hours to days (Lees *et al.*, 2000; McGaugh, 2000; Dudai, 2004).

Though we are well on our way to understanding the basic cellular and molecular mechanisms of synaptic consolidation, we are far from understanding prolonged or system consolidation, which is being debated heatedly in the literature.

3.5 System consolidation: interaction between the medial temporal lobes and neocortex

System consolidation can take much longer to complete and may range from days to years or decades. Patients with MTL lesions show a retrograde memory loss that is temporally-graded, so that recent memory loss (before the amnesia) is greater than earlier memory loss. This temporal gradient is restricted to explicit memory, leaving implicit memory intact and stable over time (Scoville and Milner, 1957).

These observations suggest that the MTL forms a temporary memory trace needed for explicit memories until they are consolidated elsewhere in the brain, presumably in the neocortex (Squire, 1992; Squire and Alvarez, 1995). This standard model of consolidation makes no distinction between various types of explicit memory. For instance, it predicts a similar pattern for episodic and semantic memory.

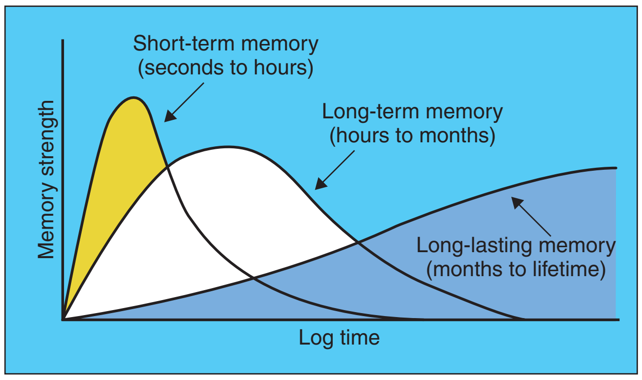


FIGURE 9.17 The time course of consolidation. McGaugh (2000) suggests that there are three overlapping time courses for consolidation. The fastest is referred to as 'short-term memory', from seconds to hours. Long-term memory consolidation takes place over hours to months. Finally, long-lasting memory is needed to account for certain facts, such as the retained long-term memory of early life events in amnesics, who do not have spared memory for some years before brain damage occurred, and none for the time afterwards. *Source*: McGaugh, 2000.

Nadel and Moscovitch concluded, contrary to the standard consolidation model, that MTL is needed to represent even old episodic memories for as long as the memory exists (Nadel and Moscovitch, 1997, 1998; Moscovitch and Nadel, 1998; Nadel *et al.*, 2000). Neocortex, on the other hand, is sufficient to represent *repeated* experiences with words, objects, people, and environments. MTL may aid in the initial formation of these neocortical traces, but once formed they can exist on their own. Thus, unique autobiographical memories are different from repeated memories, in that they continue to require MTL. Repeated experiences are proposed to create multiple traces, adding more traces each time the event is brought to mind.

Neuroimaging studies provide evidence for this interpretation (Box 9.2). These studies found that the hippocampus is activated equally during retrieval of recent and remote autobiographical memories (Conway *et al.*, 1999; Ryan *et al.*, 2000; Gilboa *et al.*, 2004; for review see Maguire, 2000; Moscovitch *et al.*, 2005, 2006). These questions continue to be debated at this time.

4.0 VARIETIES OF MEMORY

Memory is not unitary. Clive Wearing's memory for specific past events in his life is almost entirely destroyed, but he can maintain active knowledge of the immediate past for about 7 seconds (if he is not

BOX 9.2 Multiple trace theory versus traditional consolidation

Nadel and Moscovitch (1997) proposed a *multiple trace theory*, suggesting that the hippocampal complex rapidly encodes all information that becomes conscious. MTL binds the neocortical neurons that represent the conscious experience into a memory trace. MTL neurons act as a pointer, or *index*, to the neocortical ensemble of neurons that represent the experience (Teyler and DiScenna, 1986). A memory trace of an episode, therefore, consists of a bound ensemble of neocortical *and* MTL neurons. Formation of these traces is relatively rapid, lasting on the order of seconds or at most days (Moscovitch, 1995).

In this model, there is no prolonged consolidation process that slowly strengthens the neocortical memory trace. Instead, each time an old memory is retrieved, a new hippocampally-mediated trace is created, so that old memories are represented by more traces than new ones, and therefore are less susceptible to disruption. Because the memory trace is distributed in the MTL, the extent and severity of retrograde amnesia is related to the amount and location of damage to the MTL.

While each autobiographical memory trace is unique, the existence of many related traces facilitates retrieval. Episodic memories are integrated to form semantic memories. Thus, facts about people and events that are learned in specific episode become separated from their sources. This process may give the appearance of classical consolidation, but the brain mechanism is different from the classical view.

distracted). Clearly, some forms of memory have been targeted by his disorder and others not. This pattern is routine in amnesic patients, and suggests that different types of memory have different neural underpinnings. A standard view of the major long-term memory systems is shown in Figure 9.18. However, the exact relationship between memory types is still a matter of debate. For example, perceptual memory is classified under non-declarative memory, but this is rather arbitrary. Perceptual memory manifests in an improvement in sensory discrimination at the cortical level, often by reorganization of cortical receptive fields. The result is a change in conscious perception, as in learning to identify clearly the sound of a guitar in music. This has much in common with episodic memory, which can also be largely perceptual and which is generally believed to be conscious. Nevertheless, the memory classification shown in Figure 9.18 is widely used, and is part of the vocabulary students of the field are expected to know.

4.1 Episodic and semantic memory: 'Remembering' versus 'knowing'

As Figure 9.18 shows, declarative memory can be divided into two types, *episodic* and *semantic* (Tulving, 1972). *Episodic memory* refers to memories that have a specific source in time, space and life circumstances. Episodic memories are often autobiographical in nature, in that we can travel mentally back in time to relive the experience. By contrast, *semantic memories* involve facts about the world, about ourselves, and about other knowledge that we share with a community. Semantic memories are independent of the spatial and temporal context in which they were acquired.

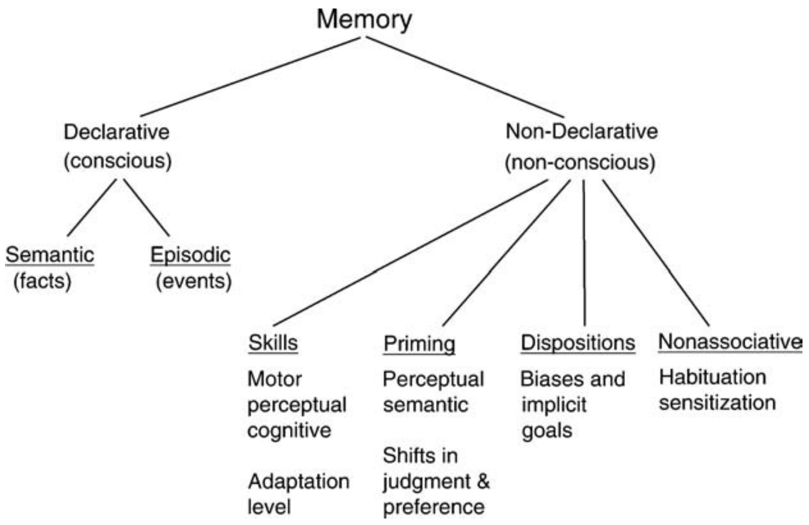


FIGURE 9.18 A classification of memory types. Schacter and Tulving proposed this classification of memory types. Declarative memories have been studied in great detail, and are believed to be explicit (conscious). Non-declarative memory types are said to be unconscious or implicit, but this claim is still debated. While the non-declarative memory types in this diagram undoubtedly have unconscious aspects, it is not yet clear that they can be learned without conscious input. *Source*: Adapted from Schacter and Tulving, 1994.

A semantic memory may refer to our knowledge of Paris as the capital of France, or Ottawa as the capital of Canada, or the knowledge that we attended a particular high school. By comparison, episodic memory may refer to an event that we experienced in Paris, Ottawa or in high school (Figure 9.19). We often have an autobiographical *source memory* about a specific time, place, and set of circumstances when our episodic memory was acquired. The terms 'episodic' and 'autobiographical' memory are near synonyms.

Episodic memories typically:

1 have reference to oneself
2 are organized around a specific time period
3 are *remembered* consciously, in such as way that we seem to be able to re-experience them
4 are susceptible to forgetting
5 are context-dependent, with respect to time, space, relationships with others, and other circumstances.

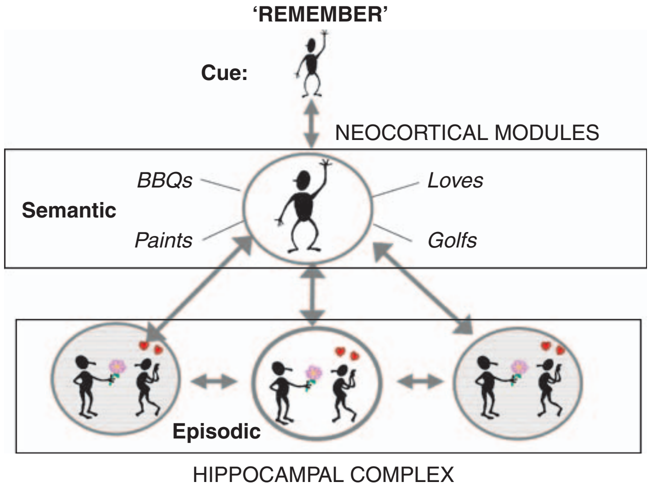


FIGURE 9.19 Remembering: autobiographical episodes. Remembering involves an active reconstruction of the original (conscious) episode. These conscious recollections seem to require hippocampal activity. *Source*: Moscovitch.

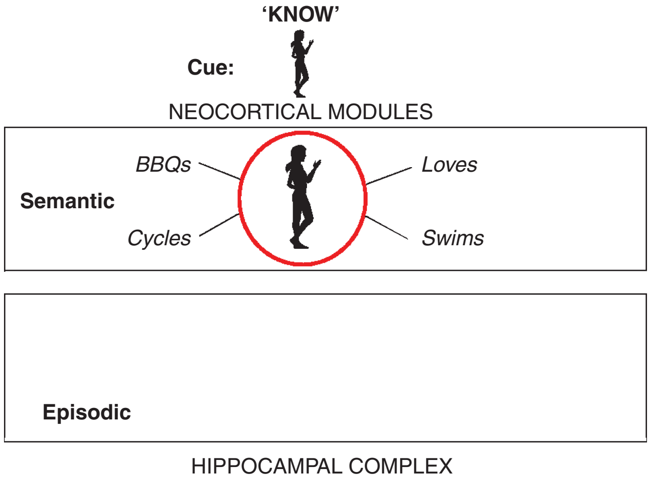


FIGURE 9.20 Knowing: semantic information. Semantic memories are assessed by feelings of knowing, which can be very accurate. However, they do not require active reconstruction of the original episode, and can apparently be accomplished by neocortex without the aid of the hippocampal complex. *Source*: Moscovitch.

BOX 9.3 False feelings of familiarity: AKP, a person with déjà vecu

People can falsely believe they have known something before when they have not. AKP was an 80-year-old Polish immigrant to Britain, a retired engineer who had a masters degree in his field. He presented to his family doctor with memory problems, and complaining of frequent sensations of what his wife described as déjà vu (actually, déjà vecu, the feeling of having lived through the same experience before). The sensation of déjà vecu was so strong that it influenced AKP's daily activities. He refused to read the newspaper or watch television because he said he had seen it before. The sensation of déjà vecu was extremely prominent when he went for a walk – AKP complained that it was the same bird in the same tree singing the same song, for instance. He also read car number plates and stated that the drivers must have very regular habits always passing by at the exact same time every day. When shopping, AKP would say that it was unnecessary to purchase certain items, because he had bought the item the day before. There was also further evidence of confabulation, including the belief that he had been married three times to the same woman, with three different ceremonies around Europe.

On formal testing, AKP had an above average IQ, scoring above the 90th percentile on some of the subtests. He scored poorly on some, but not all, tests of frontal function. His scores on standardized memory tests, however, were impaired, as were his scores on laboratory tests. Consistent with his condition, he would mistake the lures for targets. As in real life, he not only found new events familiar, but actually believed that he experienced them before.

Structural neuroimaging revealed atrophy of the medial temporal lobes but frontal lobes that appeared normal. Metabolic measures also showed only medial temporal abnormality. This medial temporal abnormality may cause 'memory' signals to be emitted continuously which tag on-going perceptions as memories.

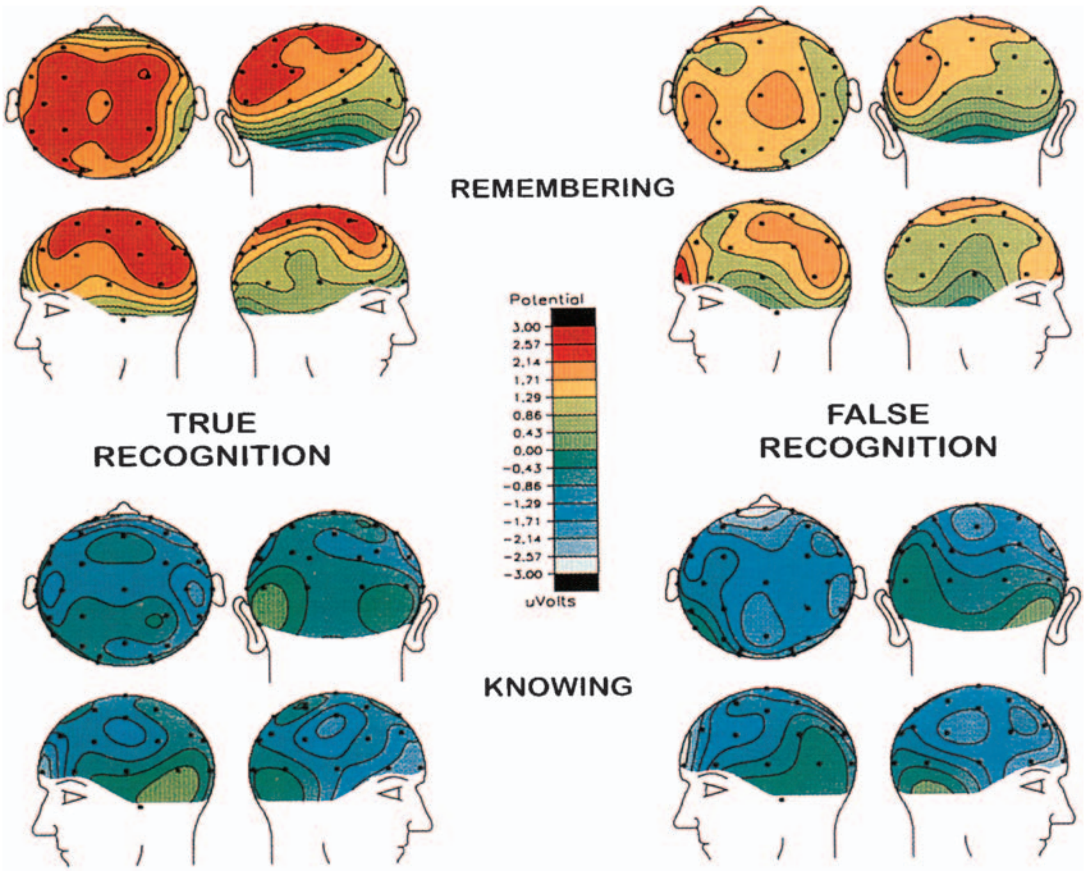


FIGURE 9.21 Even-related potentials for remembering versus knowing. The act of remembering (recollecting the original experience) results in much higher brain activation than the 'feeling of knowing', even for the same material. These brain images involve event-related potentials, scalp EEG traces averaged over trials. This is consistent with evidence discussed in Chapter 8 indicating that conscious stimuli evoked widespread forward activity, outside of sensory cortices, while unconscious stimuli evoke purely local activity. Recollecting original experiences may involve more consciously retrieved material, and it may also require more mental effort, which evokes high activity in prefrontal cortex (see Chapters 10, 11 and 12). *Source*: Duzel *et al*., 1997.

In contrast, semantic memories generally:

1 have reference to shared knowledge with others
2 are not organized around a specific time period
3 give a '*feeling of knowing*' rather than a fully conscious recollection of the original event
4 are less susceptible to forgetting than specific episodes
5 are relatively independent of context.

To investigate the types of consciousness in memory tasks, Tulving (1985) introduced the remember/know procedure. This involves asking participants to introspect about their conscious experience when they recognize studied items. If they believe an item was studied before, they must decide whether they *remember* the item (i.e. they can re-experience episodic details about the event) or whether they *know* the item (it feels familiar). Local hippocampus seems to affect only 'remember' judgments. Memory based on feelings of knowing is spared (Moscovitch and McAndrews, 2002; Yonelinas, 2002). Similarly, in functional neuroimaging studies, hippocampal activation is associated more with remembering than familiarity (Eldridge *et al.*, 2002; Yonelinas *et al.*, 2005).

Thus, the hippocampally-mediated memory trace is suffused with the consciousness that accompanied the original experience, or what Tulving called *autonoetic consciousness*. This is contrasted with simply having a sense of familiarity about an event, which Tulving refers this as *noetic consciousness*. Noetic consciousness is associated with semantic memory.

4.2 Episodic memories may turn into semantic memories over time

In 1958, Penfield and Milner wrote that:

> The record of the stream of consciousness . . . depends upon the integrity of the bilateral hippocampal structures. . . Later on, a person deals with what may be called generalizations, and he can summon them to his purposes. All events, even 'memorable' ones, slip away from the reach of voluntary recall unless he has talked about them or preserved them by reflective reconsideration. For example, one remembers a song or a poem that one has heard repeatedly, forgets each hearing or reading, but remembers the generalization. (p. 494)

Almost five decades later many memory scientists would agree. There is good evidence that semantic memories may be formed from repeated, similar episodes. Attending a high school is a long series of episodes. We may be able to recall dozens of those episodes, but much of the time they seem 'smeared' together in memory in the semantic belief that 'I attended such-and-such high school'.

Figure 9.22 shows how episodic and semantic memories may be related in the brain. Specific episodic memories are shown in the cartoon below: a man cooking on a barbecue grill, presenting flowers to a young lady, painting a picture, and playing golf. These are separate autobiographical memories, remembered as conscious events. Above, a small semantic network combines all these very specific and richly detailed episodes into a single figure: a semantic network of a man who BBQs, loves, paints and plays golf. The semantic network is more abstract and general than the episodes about particular events in the life of the person. Moscovitch (2004) claims that the bottom row of episodes depends upon the MTL, and the top figure depends upon neocortical modules.

We can summarize this concept in three steps:

1 Initially, memories are episodic and context-dependent
2 Over time, episodic memories are transformed into semantic memories
3 MTL is important for recovering episodic memories, which are linked to the specific autobiographical context in which they were acquired.

In this view, the hippocampal complex or MTL supports:

1 Storage and retrieval of detailed, remote autobiographical and spatial memories.
2 Formation and assimilation of semantic memory in neocortex.

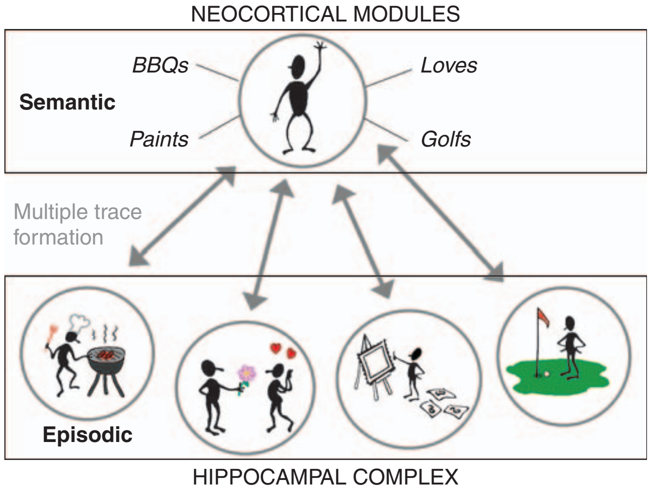


FIGURE 9.22 How semantic and episodic memories may be related: semantic memories may be the neocortical residue of many episodic memories. Thus one may have many experiences with the stick figure above, such as watching him or her cooking a barbecue, presenting flowers to a young lady, painting and playing golf. Over time, these episodes may be forgotten, and only the semantic knowledge remains, that this is the kind of person who does all those things. These are multiple traces, created each time there is another episodic experience with this person. Semantic memory may require only neocortex (particularly temporal and frontal lobes). Episodic information may require both neocortex and the hippocampal complex. *Source*: Moscovitch, 2004, modified with permission.

4.3 Episodic and semantic memory are often combined

When you are asked if the face of a particular person is familiar to you, say the movie star Brad Pitt, on what basis are you making your judgment? Are you relying on your semantic memory, episodic memory, or both? Westmacott *et al*. (2004) have shown that *both* systems may contribute, because performance on semantic tests is better if the participant also has some episodic memory associated with the famous name.

Semantic dementia is diagnosed in a subset of Alzheimer's disease patients who show widespread deficits in understanding meaning, often with spared perceptual abilities. These patients, whose degeneration of anterior and lateral temporal lobes leads to semantic loss, can identify common objects only if they can make a personal association to them. For example, they can identify a vase if it belongs to them, but not any other vase (Snowden *et al*., 1996; Graham *et al*., 1999).

Remarkably, however, if MTL is injured very early in development, during infancy, semantic memory develops relatively normally in most cases (Vargha-Khadem and Mishkin, 1997). However, episodic memory still remains impaired without an MTL. What these findings suggest is that early in life, the semantic system has the capacity to acquire knowledge on its own, without the help of the episodic system (MTL).

5.0 MTL IN EXPLICIT LEARNING AND MEMORY

MTL is necessary for conscious recollection of long-term, episodic memories. We do not have a way voluntarily to 'switch on' our MTL. Rather, all we need to do is to pay attention to some material we want to memorize. As pointed out in Chapter 8, that means in most cases that we become conscious of the material, and an episodic memory is apparently established without doing anything more.

That is, conscious experiences, such as the sight of the coffee cup in Figure 9.4, appears to be necessary and sufficient to record a conscious experience, using MTL; assuming of course that we are dealing with an intact brain. The episodic memory trace consists of an ensemble of MTL and neocortical neurons, while the MTL acts as a pointer to the neural elements in neocortex for the event. Retrieval occurs when a conscious cue triggers the MTL, which in turn activates the entire neocortical ensemble associated with it. When we recover episodic memories, we recover conscience experiences (Moscovitch, 1995). The recovery of these consciously-experienced events, in rich detail, always depends on the hippocampus no matter how long ago the memory was acquired. As Moscovitch (1992) has argued, the hippocampal complex acts as a module whose domain is consciously apprehended information. Much of the evidence seemed consistent with that view.

Some recent studies, however, have questioned this hypothesis. Using fMRI, Henke and her collaborators (Henke *et al.*, 2003; Degonda *et al.*, 2005) showed that the hippocampus can be activated by subliminal presentation of faces and their associated professions. Moreover, these activations are correlated with performance on subsequent explicit tests of memory for faces-profession pairs. Likewise, Daselaar *et al.* (2006) found that the posterior medial temporal lobe was activated more by old, studied items at retrieval, even when the person was not aware that the item was old. Finally, Schedon *et al.* (2003) showed that the hippocampus was activated on the SRT task if the repeated sequences were of a higher-order of association.

There also have been similar reports from studies with amnesic patients. Ostergaard (1987) was the first to suggest that performance on some priming tests was related to the extent of medial temporal damage. More recently, Chun and Phelps (1999) showed that non-conscious context effects in visual search were not found in amnesic patients, suggesting that the MTL was needed for retaining contextual information of which the person was not aware. Likewise, Ryan and Cohen (Ryan *et al.*, 2000) showed that amnesic people did not show the normal pattern of eye movements around the location where a change occurred in a studied picture, even though neither they nor the normal people were consciously aware of the change.

These are a handful of studies in an armful of older studies which claimed that the hippocampus is associated only with explicit memory. If the recent studies are replicated and not found wanting, then it would change our ideas about the relation of the hippocampus to consciousness and memory.

5.1 Divided attention interferes with learning

Learning works best when you pay attention. Trying to study in an environment where lots of other interesting things are happening is not likely to work. Psychologists have used this 'divided attention' or 'dual task' technique to understand the contribution of attention (or consciousness) to memory. In a typical study, participants are asked to process target material, such as words or pictures, while at the same time their attention is diverted with another task, such as tracking a dot on the screen, or deciding whether a running count of digits contains three successive odd numbers. Under such conditions, even if the participant is given a task that requires in-depth, meaningful analysis of the material, memory under divided attention is much worse than memory under full attention. Successful encoding requires a level of attention and presumably consciousness.

Exactly why that is the case is not well understood. One possibility is that deeper processing requires time to complete, and divided attention limits the time allotted to encoding. Another possibility is that consciousness or awareness is a necessary contributor to memory. If one is not fully conscious of the processed material, no matter how deeply it was processed, memory will suffer accordingly. A third possibility is that attention limits elaboration or organization, both of which contribute to good memory.

TABLE 9.1 Some types of learning and memory – explicit and implicit

Type	Learning	Retention	Retrieval
Episodic memory	Conscious or explicit	Unconscious	Conscious or explicit of the learning experience
Semantic memory	Conscious or explicit	Unconscious	Unconscious or implicit for the learning experience
Implicit learning	Conscious stimuli, but unconsciously learned regularities	Unconscious	Unconscious retrieval
Subliminal learning (rarely robust and long term)	Unconscious of target stimuli	Unconscious	Unconscious retrieval

Fletcher *et al*. (1995) found, in a PET study, that activation of the left inferior prefrontal region is reduced under divided attention. This finding was replicated by Anderson *et al*. (2000) in younger and older adults, with the additional observation that divided attention also reduced activity in the left medial temporal lobes, regions known to be important for verbal memory.

Memory and learning have both conscious and unconscious aspects. If we think about three phases – learning, retention and retrieval – we can lay out the possibilities in a 3 × 2 matrix (Table 9.1). Of the three, retention is generally viewed as unconscious, although it is shaped by conscious experiences. Learning is often thought to require consciousness and, intuitively, we certainly try to learn things by paying attention and becoming conscious of what we need to learn. That is perhaps the basic learning strategy we have as human beings.

However, there is some evidence for learning without consciousness, especially in the case of emotional stimuli. There is much stronger evidence for implicit learning, in which some inferential process takes conscious input and encodes unconscious results of conscious input. However, implicit learning tasks always ask subjects to pay attention and become conscious of a set of stimuli (Section 2.4). It is the rules and regularities that generate those stimuli that are learned without consciousness, just as we normally learn the rules of linguistic grammars without knowing those rules explicitly. But we must hear spoken words and word sequences consciously in order for implicit learning to occur.

The terms implicit and explicit memory are used in the context of remembering, i.e. retrieval of stored information. *Explicit memory* refers to memory with conscious awareness, namely, memory of which the individual is aware, can declare its existence, and comment on its content, either verbally or non-verbally (Schacter, 1987). For this reason, such memories also are known as *declarative memories* (Ryle, 1949; Cohen and Squire, 1980). They are the kind of memory to which we typically refer in everyday conversation when we ask 'Did you remember to call your aunt to thank her for the birthday present?' or, 'Do you remember who won the Academy Award for Best Actor or Actress?'

6.0 PREFRONTAL CORTEX, CONSCIOUSNESS AND WORKING MEMORY

The prefrontal cortex (PFC) plays a critical role in working memory. The prefrontal cortex is situated in front of the motor cortex in both humans and other primates (Figure 9.23). The macaque monkey has been the primary experimental animal in many studies of working memory. Obviously, humans have other abilities, like language, that are not directly paralleled in other species. But, in the case of working memory studies, the macaque has been a constantly important source of evidence.

Knowledge of a link between the PFC and short-term memory dates back to the 1930s, when it was first discovered that large bilateral lesions of the PFC in animals impaired performance on a delayed response task. In this task, a sample stimulus is presented (e.g. a color or location), and its identity must be maintained over a short delay period so that it can guide a later response (Figure 9.24). Using variants of this basic task with more recent neuroscientific techniques, modern research has firmly established the role of the PFC in active maintenance of WM information.

Much of the animal research has focused on a specific frontal region called the dorsolateral prefrontal cortex (DL-PFC, see Figure 9.23). (In the human cortex dorsal is 'upper' and lateral means 'to the side'.) One of the key early findings came from the laboratory of Joaquin Fuster (Fuster and Alexander, 1971). Fuster and his colleagues trained monkeys to perform a delayed-response task in which they had to remember a color over a brief delay, and then point to the correct color when later presented with two alternatives. Since no information about the

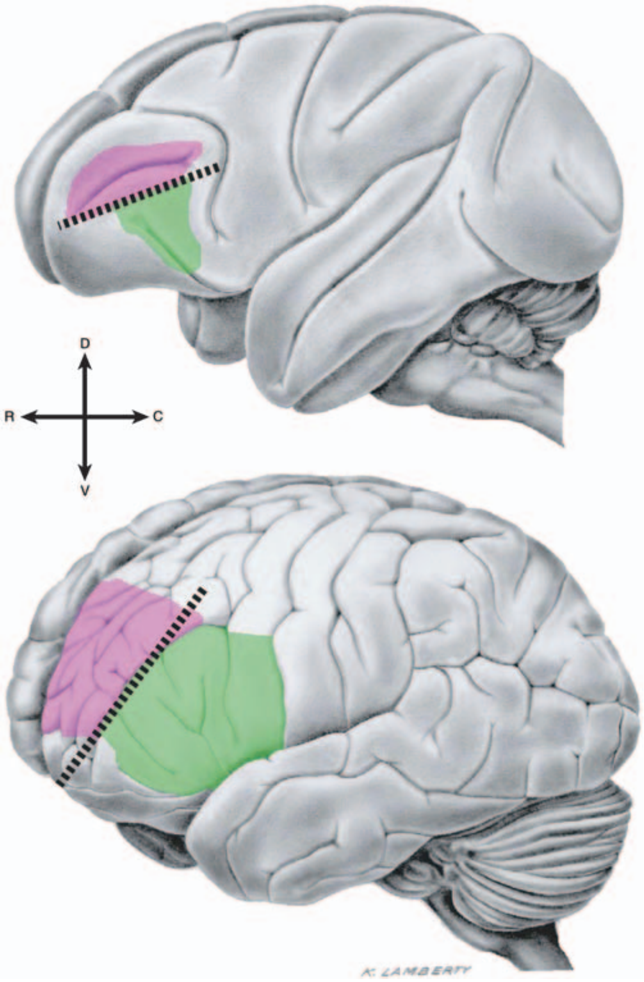


FIGURE 9.23 The prefrontal cortex in monkeys (top) and humans (bottom). The most common division is between upper and lower halves of the prefrontal cortex (PFC), called the dorsolateral prefrontal cortex (DL-PFC) for the light purple region, and the ventrolateral pfc (VL-PFC) for the light green area. Also notice the orientation cross, pointing to dorsal (upper), ventral (lower), rostral (toward the nose in humans), and caudal (toward the back of the head in humans). *Source*: Ranganath, 2006.

correct color was offered after the initial presentation, its identity had to be retained in working memory. Using implanted electrodes to record neural activity during performance of the task (see Chapter 4), it was found that individual neurons in the monkey DL-PFC exhibited sustained and persistent activity across the delay period. That is, after the color had been removed from the visual display, neurons in the DL-PFC continued to fire at an increased rate, and this activity then subsided once the match/non-match response was made (Figure 9.24).

This pattern of sustained delay-period activity in the DL-PFC has been replicated many times since, and in a wide variety of tasks. For example, to confirm that PFC contributions are truly memory-related, and not simply a reflection of subtle preparatory motor gestures, Patricia Goldman-Rakic and her colleagues developed a version of the task in which monkeys see a target presented briefly at one of several possible locations on a display, and then after a delay, must shift their gaze to that location in order to receive a reward. Importantly, the monkey is required to look straight ahead until the end of the delay period, so neural activity during the delay cannot be simply a byproduct of moving the eye, but must instead reflect memory processes. Again, this paradigm produces sustained neuronal activity in the DL-PFC and, what's more, the *amount* of delay-period activity predicts whether or not items will be remembered; when DL-PFC delay-period activity is weak there is a greater likelihood of forgetting (Funahashi *et al.*, 1993).

There is debate whether PFC is subdivided according to the content of the information that is stored, or according to the function that each region carries out. According to the content approach, the DL-PFC seems to be particularly involved in holding onto information about spatial locations, whereas different parts of the ventral and lateral PFC have been implicated in storing non-spatial types of information (e.g. objects, faces, words, etc.). Alternatively, each of these regions may have different functions, with DL-PFC implicated in manipulation of information and VL-PFC in maintenance (ventro-lateral, downward and to the side). The term ventral refers to the down direction in cortex; literally, 'ventrum' means 'belly' in Latin.

Monkey brain lesion studies have further implicated the PFC, and the DL-PFC in particular, in working memory function. With very precise techniques for localizing experimentally induced lesions, it has been shown that damage isolated specifically to the DL-PFC is sufficient to impair performance on working memory tasks (Fuster, 1997). Such findings show a causal role for the PFC in working memory. Not only are cells in this region active during a delay, but their lesioning impairs working memory. This impairment gets worse as the length of the delay increases, suggesting that there is more rapid forgetting when the PFC is prevented from sustaining them.

Studies in humans using neuroimaging have corroborated many of the findings from the animal literature. Hundreds of imaging studies have shown PFC activity when participants are trying to maintain task-relevant information. Consistent with the animal work, fMRI studies in humans show that PFC activity persists during the delay period of a working memory task (see Chapters 4, 10 and 12; Appendix B).

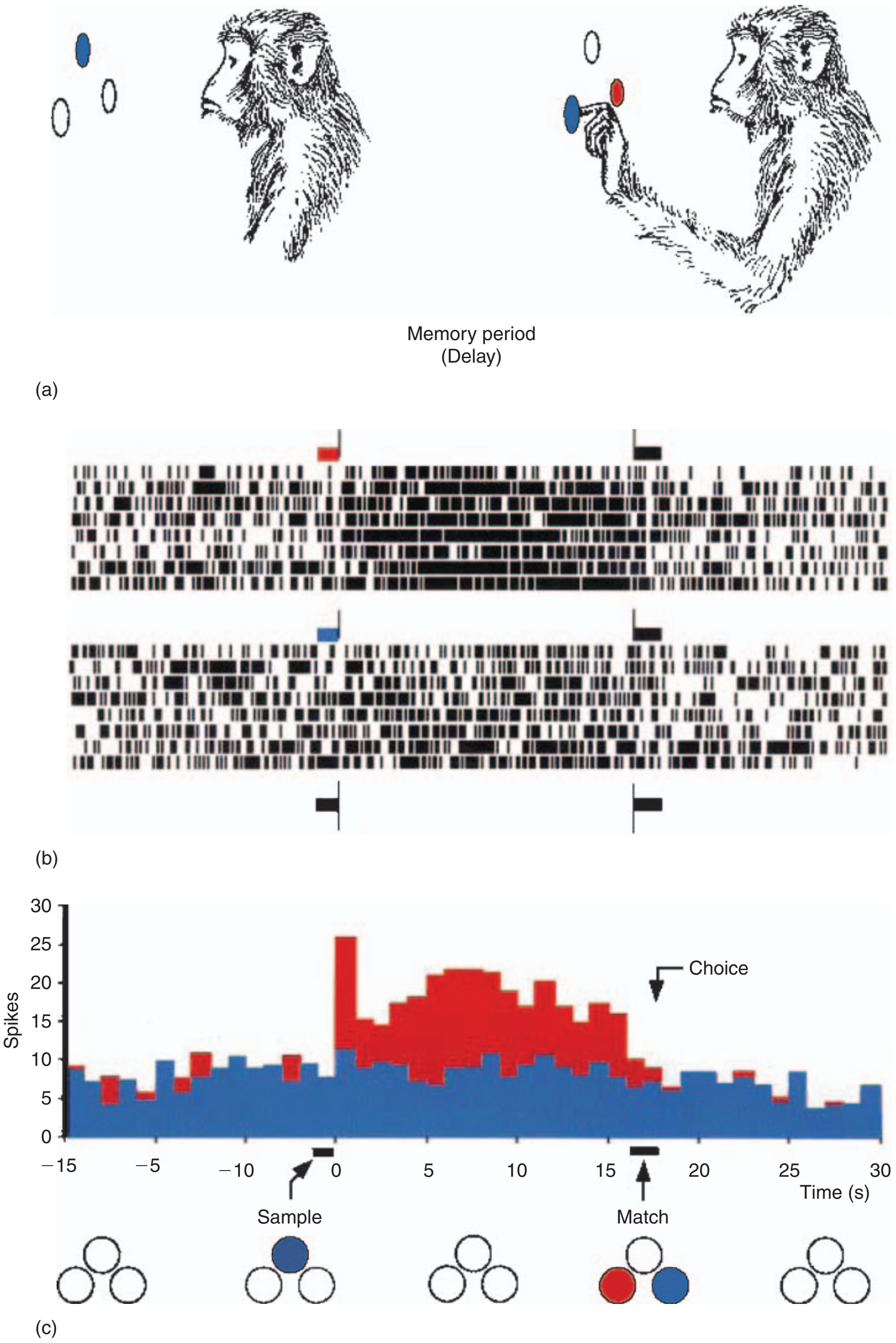
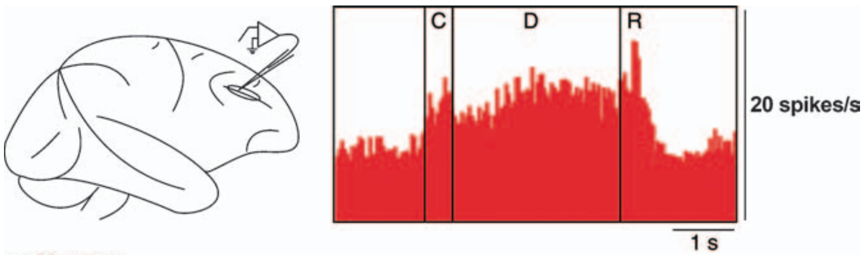
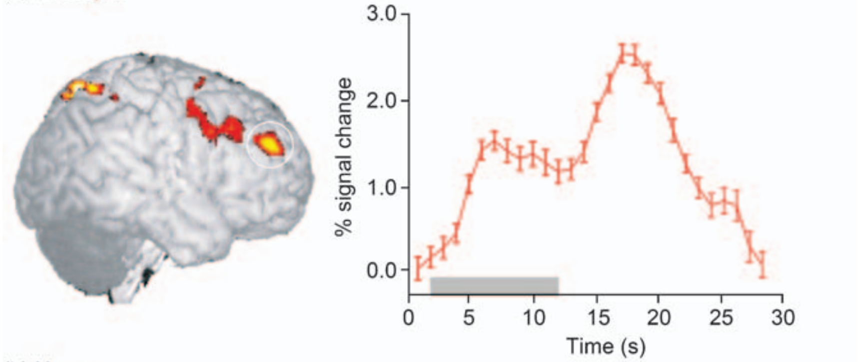


FIGURE 9.24 ‘Delayed match to sample’ in the macaque. In a classic experiment, a macaque monkey is trained to delay responding to a stimulus, in this case the location of a red, white or blue light. The monkey shows recognition of the stimulus after delay by matching it in the display, in a task called ‘delayed match to sample’. In effect, the monkey is communicating ‘this is what I saw’. DMTS methods are widely used in animals, non-verbal babies, and other subjects. *Source*: Fuster, 1997.



(a) **Macaque**



(b) **Human**

FIGURE 9.25 A delayed-response task to study working memory in monkeys and humans. It has been proposed that the PFC serves a specific role in the active *storage* of information in working memory (e.g. Goldman-Rakic, 1998). That is, sustained activity in prefrontal neurons reflects this region's role in maintaining specific representations of the items that must be kept in mind over the delay. This interpretation is supported by the finding that individual neurons in the PFC are selective for particular target stimuli. For example, a given cell may fire strongly over the delay period when the target is in the upper left portion of the display, but weakly when the target is elsewhere in the display. This pattern suggests direct involvement in the internal representation of target features. In this figure, neurons in prefrontal cortex respond during the delay period in a delayed-match-to-sample task. Results in macaques and humans are similar. *Source*: Curtis and D'Esposito, 2003.

Human neuroimaging studies have also varied *working memory load* – the number of items that must be held in immediate memory (Cohen *et al*., 1997; Rypma *et al*., 2002). In one study, memory load was varied between one and eight items, and subjects had to hold these items for a short delay. PFC activation was found to be positively correlated with the number of items in memory. Such 'load dependence' in the PFC supports the notion that this part of the brain is involved in working memory storage.

While PFC contributions to working memory have been clearly demonstrated, its specific contribution to working memory storage has been recently questioned. Several other cortical and subcortical areas exhibit similarly persistent stimulus-specific activity over short delays. It appears that PFC may be part of a more distributed brain network supporting working memory. Other data suggest that the PFC may not be involved in storage *per se*, but in providing top-down, or *executive*, support to other regions where information is actually stored.

6.1 Working with memory: the frontal lobe works purposefully *with* memory

According to this model, both encoding and retrieval of consciously-apprehended information via the hippocampus and related structures is obligatory and automatic, yet we know from experience and from experimental investigation that we have a measure of control over what we encode and what we retrieve from memory. Moreover, if encoding is automatic and obligatory, the information cannot be organized, yet memory appears to have some temporal and thematic organization. How can we reconcile this model of memory with other facts we know about how memory works? One solution is that other structures, particularly those in the frontal lobes, control the information delivered to the medial temporal system at encoding, initiate and guide retrieval, and monitor, and help interpret and organize the information that is retrieved. By operating on the medial temporal and diencephalic system, the frontal lobes act as *working-with-memory* structures that control the more automatic medial temporal system and confer a measure of intelligence and direction to it. Such a complementary system is needed if memory is to serve functions other than mere retention and retrieval of past experiences (Moscovitch, 1992).

6.2 Prefrontal cortex in explicit (conscious) and implicit (unconscious) learning and memory

Figure 9.5 pointed out that working memory may help us to learn both explicit (conscious) and implicit (unconscious) information. One of the functions often attributed to consciousness is the integration of information across domains. In a very illuminating study, McIntosh *et al*. (1998) had subjects perform in a trace conditioning task which requires the person to make an association between a color and a tone separated by a blank delay of about a second. Previous work had shown that such conditioning is dependent on the hippocampus. Moreover, Clark and Squire (1999) showed conscious awareness of the association was a prerequisite for this kind of learning.

Using PET, McIntosh showed that learning, and the conscious awareness that accompanied it, was associated both with frontal activation and with coherence of activation across many areas of cortex. McIntosh *et al*. speculated that consciousness is associated with activation in prefrontal cortex which, in turn, leads to a correlated pattern of activity across disparate regions of cortex. It remains to be seen, however, whether frontal activation preceded or followed conscious awareness of the association. To do so, it is necessary to have a clear understanding of the sequence of activation across regions of cortex, using techniques that have a higher temporal resolution than fMRI, such as ERP or MEG. As yet few, if any, studies have used ERP and MEG to address issues regarding the time course of consciousness as it relates to memory.

If the prefrontal cortex plays a pivotal role in consciousness, as many people have speculated, deficits on all memory tests dependent on consciousness should be observed in patients with frontal lesions. However, so far, the evidence indicates that the effects of frontal lesions are much more selective and not nearly as debilitating as lesions to MTL and related nuclei of the thalamus.

The prefrontal cortex contributes to performance on implicit learning and memory if it requires search, sequencing, organization and deliberate monitoring. Implicit learning of language is a good example (Box 9.4).

BOX 9.4 Implicit learning of language. While we are given the words and sequences of language, the rules and regularities of grammar and perhaps meaning are often inferred unconsciously, i.e. using implicit learning (Cleeremans *et al*., 1998)

Implicit learning and language acquisition

The past few years have witnessed the emergence of increasing connections between implicit learning and psycholinguistics. This is perhaps not so surprising, in that language acquisition, like implicit learning, involves incidental learning conditions. Further, cogent use of language likewise does not require explicit knowledge of grammar. Recently, several authors have begun to explore this connection empirically. For instance, Saffran *et al.*[a] showed how incidental exposure to artificial language-like auditory material (e.g. *bupadapatubitutibu* . . .) was sufficient to enable both children and adult subjects to segment the continuous sequence of sounds they had heard into the artificial words (e.g. *bupada, patubi*, etc.) that it contained, as evidenced by their above-chance performance in a subsequent recognition test. Based on these data, Saffran *et al*. suggested that the word segmentation abilities demonstrated by these subjects were due to the transitional probabilities of successive syllables are higher *within* words than *between* words. Saffran and colleagues interpreted their findings as representing a form of implicit learning. The connection is obvious when one recognizes that language acquisition, like implicit learning[b,c] is likely to involve, at least in part, incidental learning of complex information organized at differing levels. Part of the convergence between language acquisition and implicit learning suggested by Saffran and colleagues can be attributed to the impact of computational modeling on the field of memory research. For instance, connectionist models such as the Simple Recurrent Network have been extensively used with significant success in both the language acquisition and implicit learning domains[d,e]. In effect, the problems faced in both domains are quite similar: how to best extract structure from a complex stimulus environment characterized by 'deep' systematic regularities when learning is incidental rather than intentional. The answer, in both domains, appears to be embodied by distributional approaches.

References

a Saffran, J.R. *et al.* (1997) Incidental language learning, listening (and learning) out of corner of your ear *Psychol. Sci.* 8, 101–105

b Berry, D.C. and Dienes, Z. (1993) *Implicit Learning: Theoretical and Empirical Issues*, Erlbaum

c Cleeremans, A. (1993) *Mechanisms of Implicit Learning: Connectionist Models of Sequence Learning*, MIT Press

d Christiansen, M.H., Allen, J. and Seidenberg, M.S. (1998) Learning to segment speech using multiple cues: a connectionist model *Lang. Cognit. Process.* 3, 221–268

e Redington, M. and Chater, N. (1997) Probabilistic and distributional approaches to language acquisition *Trends Cognit. Sci.* 1, 273–281

Even though we rarely try to make the rules of grammar conscious and explicit, we nevertheless need to direct our attention to the order of words in a sentence, for example, to learn a language implicitly. It is likely that unconscious inferences help us to discover rules or regularities, provided that we pay 'conscious attention' to a series of words, for example, from which we can discover the implicit regularities.

6.3 Different types of working memory

In proposing the concept of working memory, Baddeley and colleagues (2004) reasoned that subjects should have difficulty keeping items in memory if asked to perform other tasks simultaneously that disrupt specific components of the working memory system. Consistent with this view, Baddeley and others have shown that asking subjects to repeat aloud a simple utterance (like the word 'the') during retention can dramatically reduce short-term memory for verbal information, presumably because the repetitive speech task disrupts the rehearsal mechanism of the phonological loop. Importantly, the same repetitive speech task hasa much smaller effect on working memory for visuospatial information because holding such information does not make as much use of the phonological loop. Meanwhile, other tasks (e.g. visually tracking a moving object) have been found to disrupt visuospatial, but not verbal, maintenance.

We have already encountered examples of patients, like Clive Wearing and HM, who seem to have spared short-term memory but impaired long-term memory. Elizabeth Warrington and Tim Shallice (Shallice and Warrington, 1970) reported one of the earliest recognized cases of a patient, KF, with the opposite pattern of impairment – a severely impaired short-term memory but apparently intact long-term memory. For example, when asked to recall short lists of spoken digits, the *digit-span task*, KF could recall only one or two items reliably (as compared to a typical digit-span of around seven items). Still, KF had comparatively normal speech-production abilities, and could learn and transfer new information into long-term memory. The finding that a patient with severely impaired short-term memory could still transfer information into long-term memory presented a challenge to the standard hypothesis posited that a unitary short-term memory serves as the gateway into long-term memory. Baddeley's working memory model suggested that if verbal rehearsal is impaired, the visuospatial sketchpad might be used to compensate (see Figure 9.5).

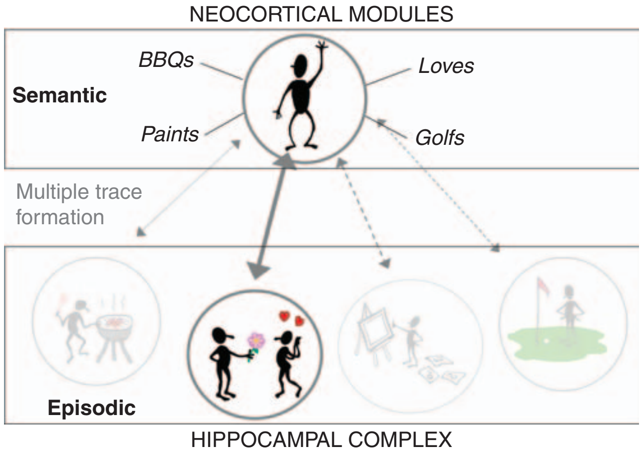


FIGURE 9.26 Damage in patients with this *auditory-verbal* working memory impairment is fairly consistently localized to a region near the left temporo-parietal junction, typically including the supramarginal gyrus of the parietal lobe. This region has accordingly been proposed as the site of the *phonological store*, the storage component of the verbal maintenance subsystem. In other patients this region is intact, but damage to more anterior areas in the VL-PFC and nearby cortex leads to working memory impairments consistent with disruption of the subvocal rehearsal process that supports verbal maintenance. (These areas are known to be involved in speech production, see Chapter 11). Still other patients have been identified with selective impairment of visuospatial memory, as evidenced for example by an inability to remember even a very small number of spatial locations presented sequentially. The selectivity of these deficits with damage to different parts of the cortex has been taken as strong support for the basic framework of the working memory model (Baddeley *et al.*, 2004). *Source*: Moscovitch, personal communication.

Indeed, the short-term memory impairment in patient KF, and a number of similar patients reported since, seems to be tied to particular types of information. For example, while these patients struggle to remember verbal items when presented auditorily, their performance is considerably improved when the items are presented visually. What might account for this pattern of findings? Baddeley's answer is that visually presented items can be coded directly into the visuospatial sketchpad, thus avoiding the damaged verbal rehearsal loop.

Neuroimaging has helped to clarify different kinds of memory. These include the distinction between verbal and visuospatial maintenance subsystems (e.g. Smith *et al.*, 1996), the dissociability of storage and rehearsal in verbal maintenance (Paulesu *et al.*, 1993; Awh *et al.*, 1996) and the assumption of a central executive processor that mediates the behavior of the subsidiary maintenance subsystems (e.g. Curtis and D'Esposito, 2003). In general, neuroimaging studies have tended to support the basic model (Smith and Jonides, 1998; Hartley and Speer, 2000; Henson, 2001).

Figure 9.27 illustrates the brain network implicated in neuroimaging studies of WM (Curtis and D'Esposito, 2003). The central executive corresponds to DL-PFC,

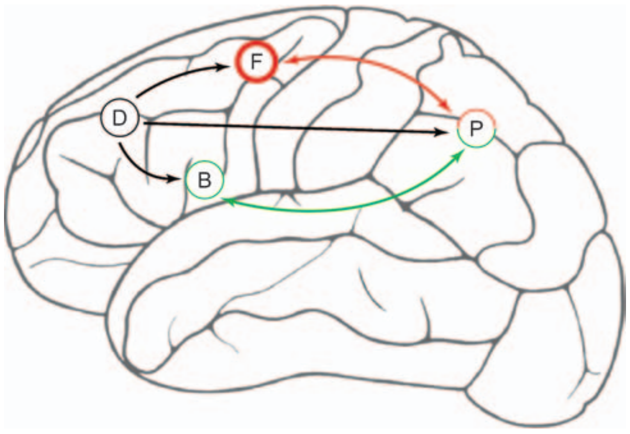


FIGURE 9.27 Brain areas believed to be involved in verbal and visual working memory. A simplified brain model of working memory (Figures 9.4 and 9.5). Abbreviations are D = dorsolateral prefrontal, B = Broca's area, also called the left inferior frontal gyrus (L-IFG), P = phonological loop for verbal rehearsal, also called the supramarginal gyrus; and F = frontal eye fields, believed to be involved in the visuospatial sketchpad of Baddeley's working memory model. *Source*: Curtis and D'Esposito, 2003.

the verbal maintenance subsystem in left lateralized regions of the temporo-parietal junction and VL-PFC, and the visuospatial maintenance subsystem in the superior parietal cortex, posterior PFC and frontal eye fields (FEF). However, we should be cautious in our acceptance of these findings as direct support for the framework, since few researchers have considered the applicability of these findings to alternative theories of working memory (Chein *et al*., 2003; Ravizza *et al*., 2005). In addition, the neuroimaging literature has at times challenged aspects of the standard working memory model. For example, neuroimaging evidence suggests that different types of visuospatial information may depend on different storage subsystems. For instance, there seem to be different neural substrates for the maintenance of *object* information as compared to the maintenance of *spatial* locations, a distinction that is not addressed by the traditional working memory model. (Recall that this 'what' versus 'where' dichotomy is important also in the visual processing pathways, see Chapter 6).

6.4 Prefrontal cortex – storage or process control?

In the beginning of this section on working memory, we reviewed several sources of evidence suggesting that the PFC is an important site for working memory function. According to one interpretation, this brain region participates directly in the storage of information. However, consideration of findings in the context of Baddeley's multiple-component model suggests an alternative account. Namely, that the PFC is more closely associated with control, or executive, aspects of working memory.

Specific evidence against a 'storage' interpretation of PFC function also comes from studies of humans. We discussed earlier a group of patients with left temporo-parietal damage who appear to have a storage deficit in working memory, and can't perform even simple maintenance tasks with auditory-verbal information. The findings from these patients can be contrasted with those from patients with damage to the PFC. In a review of published reports from patients with damage to large regions of the lateral PFC (D'Esposito and Postle, 1999), it was found that PFC patients showed little or no impairment on tasks that called for the passive maintenance of information over a delay (e.g. verbal and non-verbal memory span tasks). However, these patients were found to be substantially impaired at tasks that required information in working memory to be mentally *manipulated* or *acted upon*. This pattern of findings suggests that the PFC serves to support the mental 'work' performed on stored information, rather than as a site for storage itself. Few of the patients in this review had bilateral lesions, leaving open the possibility that storage and rehearsal are achieved via bilateral PFC representations and may thus allow functional compensation from the undamaged hemisphere (D'Esposito and Chen, 2006).

One possibility is that different parts of the PFC do different things. This proposal has generally focused on differences between dorsal (DL-PFC) and ventral (VL-PFC) areas. Advocates of this view have argued that the PFC is not organized by domain (e.g. spatial versus non-spatial), but by process, with ventral areas of the PFC supporting the passive storage and maintenance of items, while more dorsal areas are called upon when the task demands selection, monitoring, manipulation, or other 'mental work' to be performed on these items. This is the so-called 'maintenance' versus 'manipulation' processing distinction. While this view seems capable of explaining a wide range of findings, several studies have cast doubt on even the assumption that the VL-PFC contributes to storage in WM (e.g. Rushworth *et al*., 1997).

More recently, it has been argued that *all* of the PFC has an executive function in working memory, but that different subdivisions of the PFC perform this function at different levels of analysis (Ranganath, 2006). This emerging view asserts that the primary function of the

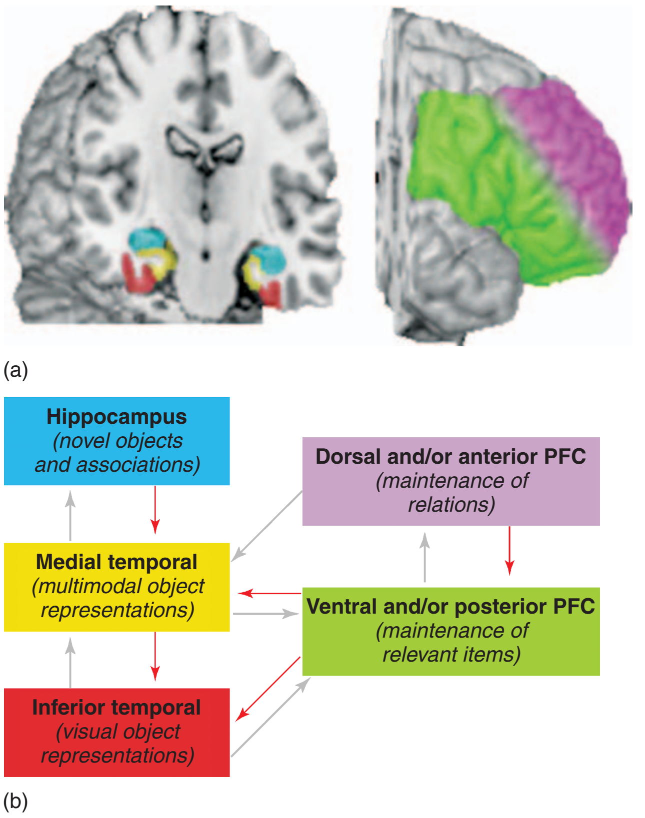


FIGURE 9.28 Combined brain regions work together for visual working memory. One view of visual working memory suggests that the hippocampus may encode WM items that are novel, the wider MTL may combine them with other modalities, and IT is involved in high-level visual object representation. The DL-PFCs and anterior PFC (purple) is involved with the short-term maintenance of relations, while the VL-PFC and posterior PFC is involved with maintenance of relevant items. As pointed out in the text, this is only one current hypothesis about the functions of these regions. However, it is widely believed that some network of functions like this may be needed to give a complete account of working memory. *Source*: Ranganath and D'Esposito, 2005.

PFC is to modulate the activity of other cortical areas where the items in memory are stored. Specifically, PFC representations enhance relevant information (or inhibit irrelevant information) represented in other parts of the cortex. When the information is specific to individual items in memory, more ventral PFC regions are engaged. When the information regards the integration of (or relations between) multiple items in memory, more dorsal PFC regions are engaged. Anterior regions of PFC, at the frontal pole, are implicated in coordinating and monitoring activity among different PFC regions to implement higher-order functions, such as planning. Accordingly, the primary role of the PFC is not in working memory, but in *working with memory* (Moscovitch, 1992; Moscovitch and Winocur, 1992).

6.5 Combining prefrontal and MTL regions for working memory

Working memory is usually believed to operate over a few dozen seconds or minutes. However, even within a few minutes' time, we can find differences between different kinds of memory. In particular, you may have seen the word 'combining' only a minute or two ago, and yet you may not be able consciously to recall it. We can therefore make a prediction, based on our previous understanding of the role of MTL in explicit memory: if you can recall seeing the word 'combining' a brief time ago, your MTL should show activity in an fMRI experiment in which you are asked to recall the first word of this section. On the other hand, if you do not have an explicit memory of it – even over a short time period – your MTL should show less activity. But perhaps you will still retain a semantic memory of the title of this section, based on your neocortical encoding of that word.

We can therefore even describe working memory in terms of MTL, prefrontal cortex, sensory cortex and the like. Figure 9.28 shows a model of how these brain areas may interact, based on a large number of studies of this kind (Ranganath and D'Esposito, 2005). Many of the specifics of this model are still debated, and we can expect new studies to cast some light on them. There seems to be an emerging consensus, however, that a complete explanation of working memory functions will require a multi-regional model of this kind.

7.0 RETRIEVAL AND METACOGNITION

Clive Wearing knows that something is terribly wrong, but he has no idea what it is. 'I've just woken up for the first time. I'm conscious for the first time' is his only way to express it. For more than twenty years he has expressed the most intense frustration with his condition. Wearing must therefore have some *metacognitive* conception of his own cognitive functioning, unlike patient HM, for example, who is spared the emotional pain of sensing what he is missing. Metacognition is defined as the ability to know our own cognitive functions, and to be able to use that knowledge. Many neurological patients who are severely impaired have no metacognitive insight that anything is wrong (Milner and Rugg, 1992).

For retrieval to be effective, information at retrieval must overlap with the information that was learned or encoded. In addition, the person must have the goal of

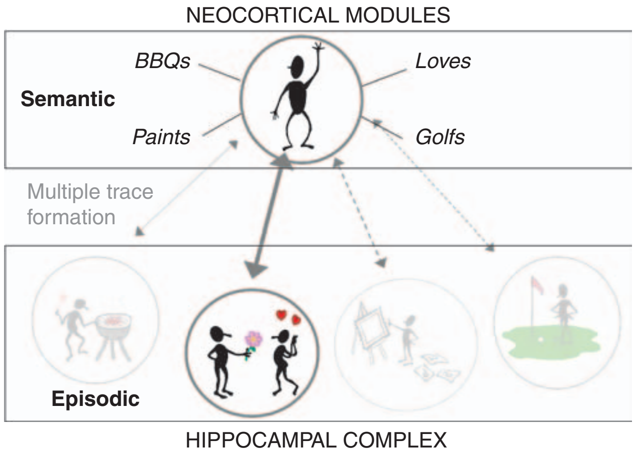


FIGURE 9.29 Retrieving semantic memories by using episodic cues and vice versa. We can often retrieve a semantic memory, like a fact about the world, by being cued with an episodic memory; the association can also go the other way. Thus episodic and semantic memory continue to be potentially connected, even if they exist relatively independently of each other in the hippocampal complex (MTL) and neocortex. Notice that most episodic memories for this semantic cluster of associations (on top) have faded. *Source*: Moscovitch, personal communication.

retrieving memories and paying attention to cues, as well as mentally searching for the desired memory. In all these processes, monitoring and verification are necessary, as is coordination of the various activities. Different regions of prefrontal cortex are implicated in many of these processes. The MTL is implicated most strongly with retrieval success for episodic memories. Automatic retrieval of a memory often occurs once the cue is found (Figure 9.29). Strategic or purposeful retrieval, however, is attention demanding and is impaired by any effortful competing task.

Metacognition is an important aspect of normal memory retrieval. A memory trace may be retrieved spontaneously, or more often by cues or reminders. A cue could be as simple as 'Recall the words you just studied' or as complex as 'Describe in detail what you did today'. The kind of self-monitoring we tend to do when we try to remember a missing word is a kind of metacognition that involves prefrontal cortex.

Schacter and colleagues (Schacter *et al*., 1984) showed that memory for source in amnesic patients was related to the extent of their accompanying frontal deficits, rather than the severity of their amnesia. Extending these findings to older adults, Glisky (Glisky *et al*., 1995) showed that those with poor frontal function were impaired on tests of source memory but performed normally on tests of item memory, whereas the reverse was true of those with poor medial temporal function. Similarly, damage to prefrontal cortex leads to deficits in memory for frequency of occurrence (Smith and Milner, 1984) and temporal order (Milner, 1971; Shimamura, 1984) even when memory for the item itself is preserved.

The functional neuroimaging literature is consistent with the lesion literature. In comparison to tests of item memory, tests of source memory activate the DL-PFC and the frontal pole more strongly (Fletcher and Henson, 2001; Fletcher *et al*., 2005), as do tests of temporal order (Nyberg *et al*., 1996; Cabeza *et al*., 1997).

The role of metacognition, using prefrontal cortex, is especially dramatic when it fails. This is the case when people cannot recognize their own mistakes, as we see next.

7.1 False retrieval

There are deficits of retrieval that are quite remarkable. The case of confabulation is particularly important, the inability of some brain damage patients to tell that the 'memories' they are retrieving are entirely imaginary. One such case is illustrated in Box 9.5.

7.2 Hemispheric lateralization in retrieval

In light of the left hemisphere preference for language production (Chapter 11), it is perhaps unsurprising that memory functions may also be lateralized according to the nature of the material being processed. In working memory, for example, maintenance of verbal materials activates left regions in the parietal cortex and VL-PFC, whereas maintenance of non-verbal materials tends to be right-sided. Regions in the VL-PFC are also implicated in encoding information into long-term memory, and seem to interact with areas of the MTL in serving this function. Accordingly, both the VL-PFC and MTL have been found to exhibit hemispheric asymmetries in long-term memory encoding (Kelley *et al*., 1998).

Lateralization may depend upon the materials used (verbal, for example), and also upon the task and cognitive process. Endel Tulving and colleagues (Habib *et al*., 2003) proposed that, in general, learning is associated with greater involvement of the left PFC, while retrieval shows greater involvement of the right PFC (Figure 9.30). This model has received substantiation from a large number of neuroimaging studies.

Some researchers have questioned, however, whether this encoding/retrieval asymmetry may arise simply due to a greater dependence on verbal processes during learning than retrieval. The hemispheric bias seems to hold for episodic memories, while for semantic

BOX 9.5 HW, a confabulating patient

HW is a 61-year-old man who was married to the same woman, Martha, for over thirty years and had four grown children, ranging in age from 32 to 22. He worked in a management position at a factory. He had an aneurysm of the anterior communicating artery, which feeds the medial frontal lobes and basal forebrain. Surgical clipping of the aneurysm was followed by widespread bilateral ischemia (loss of oxygen) and infarction. CAT scans confirmed widespread frontal damage, with sparing of the temporal lobes medially and laterally.

His brain damage led to memory problems exacerbated by confabulations and an unawareness of his memory deficits. His intelligence was normal, as measured by standard tests. HW's confabulations were spontaneous and, because he believed they were true memories, he attempted to act on them, making it difficult to let him live on his own. For example, there were times in the hospital that he believed he was at work, even though the hospital had beds, nurses, etc., and he wore hospital clothes. Many days at 5 pm he would prepare to go home and became frustrated and belligerent when he was told he had to stay.

Here is a part of an interview with HW:

Q: How long have you been married?
A: About 4 months.
Q: What's your wife's name?
A: Martha.
Q: How many children do you have?
A: Four. (He laughs). Not bad for four months.
Q: How old are your children?
A: The oldest is 32 . . . the youngest is 22. (He laughs again).
Q: How did you get these children in four months?
A: They're adopted.
Q: Who adopted them?
A: Martha and I. . . .
Q: Does it all sound a little strange to you?
A: (He laughs) I think it is a little strange.
Q: Your record says that you've been married for over 30 years. Does that sound more reasonable to you?
A: No.
Q: Do you really believe that you have been married for four months?
A: Yes.

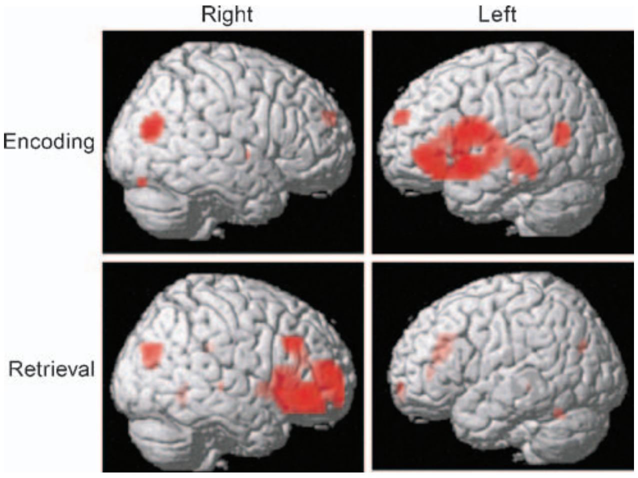


FIGURE 9.30 Left hemisphere for learning, right hemisphere for retrieval? Tulving and colleagues (Habib *et al.*, 2003) found that the left hemisphere shows greater activity in episodic learning (encoding), while the right side showed more activity in episodic retrieval. *Source*: Habib *et al.*, 2003.

memory, both learning and retrieval seem more dependent on left hemisphere mechanisms.

A recent study by Rossi and colleagues (Rossi *et al.*, 2006) using transcortical magnetic stimulation (TMS, see Chapter 4), a technique that allows temporary disruption to cortex in healthy subjects, supports the Tulving proposal. Their study showed that temporary disruption in the left PFC reduced learning efficiency, as measured by recognition accuracy. In contrast, TMS over the right PFC reduced retrieval efficiency. Thus, there seems to be a relationship between hemispheric lateralization and the learning-retrieval distinction.

7.3 Theta rhythms may coordinate memory retrieval

A new literature shows that theta rhythms (5–8 Hz) appear in the frontal lobes during memory retrieval. Depth electrodes placed in the hippocampi show that the MTL and prefrontal regions may be coordinated during retrieval (Siapas *et al.*, 2005). Figure 9.31 summarizes these findings, which begin to show how the neural networks of prefrontal and hippocampal structures may cooperate to draw out and coordinate memory traces during retrieval.

8.0 OTHER KINDS OF LEARNING

We have only discussed some kinds of memory. We can only briefly mention some others, which make use of other brain structures. For example, the amygdala mediates fear conditioning (see Chapter 14). The cerebellum and basal ganglia are needed for habits and skills, as well as some kinds of conditioning. The thalamus is one of the great information hubs of the brain, constantly trading signals with cortex. It is therefore believed to be involved with cortical learning mechanisms.

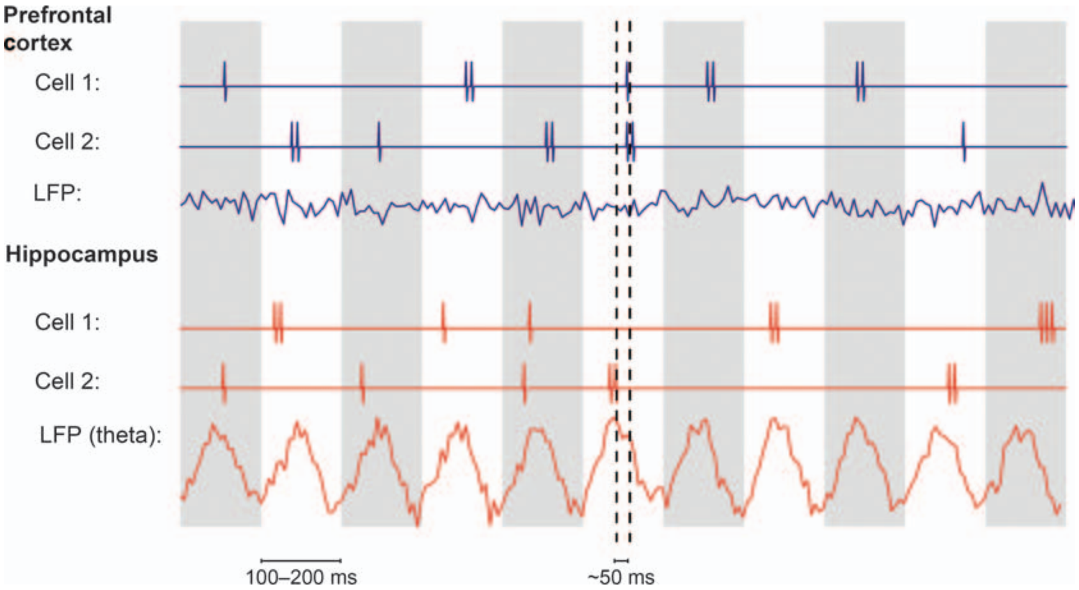


FIGURE 9.31 Theta oscillations may coordinate MTL and the prefrontal lobe during retrieval. Regular brain rhythms may serve to coordinate separate brain regions. Hippocampal theta is believed to reflect memory retrieval processes, and to coordinate prefrontal cortex with the MTL. *Source*: Jensen, 2005.

Perceptual and motor learning involve the dynamic organization and reorganization of cortical maps (Chapters 2 and 5). This is called *neural plasticity*. For example, losing a finger will change the motor map representing the finger in the macaque cortex. In humans, brain surgery can alter sensory body maps very quickly, even during the operation. Life development itself can be viewed as a process of learning, adaptation and memory formation (see Chapter 15). Finally, we now know that new neurons can be born throughout the lifetime, starting from stem cells (neural progenitor cells). The ongoing replacement of some neurons also involves a dynamic learning and adaptation process. There are many ways for the brain to learn. Though we have focused on more standard concepts of learning and memory, it is important to keep that in mind.

9.0 SUMMARY

The medial temporal lobes (MTL) are crucial to episodic memory in which we retain information about the conscious source of the memory. Amnesia patients with bilateral damage to the MTL are correspondingly unable to remember specific past episodes, or to learn new ones. However, implicit learning and memory may be spared in these patients. Patients suffering from semantic deficits typically have damage in the temporal lobe (especially the anterior and lateral parts) and prefrontal cortex. Such patients with semantic dementia, for example, may retain their episodic memory but are impaired on semantic tasks.

While explicit memory is assessed by accurate source memory reports, implicit methods like priming and sensorimotor performance may be needed to assess implicit memory types. Much of our learning is implicit, such as the learning of language. However, it is important to keep in mind that implicit learning requires conscious and attentive orienting to the stimuli to be learned. What is unconscious about implicit learning is not the original stimuli, but the inferential regularities that allow us to organize those stimuli. Sensorimotor skills are guided by the frontal cortex in collaboration with the basal ganglia and cerebellum. After overpracticing predictable tasks, such learned skills become less conscious and seem to rely only on subcortical structures like the basal ganglia.

Working memory can be decomposed into visual (the visuospatial sketchpad) and verbal (verbal rehearsal or the phonological loop). Further divisions are often possible, such as a separation between spatial and visual working memories.

A complete conception of human memory requires multiple brain regions: the MTL for explicit episodic memories, the prefrontal cortex for metacognition, maintenance, and use of memory, and sensory regions for perceptual and sensory memories. The cerebellum and basal ganglia are required for sensorimotor skill learning, in interaction with the frontal lobes. Further, sensory

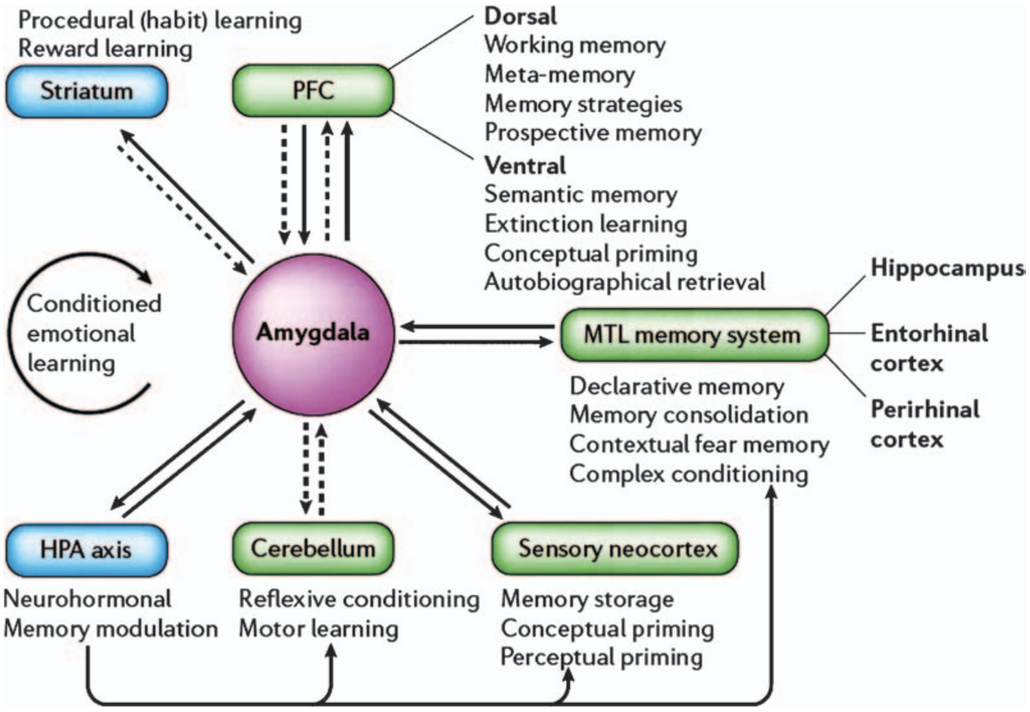


FIGURE 9.32 Different kinds of memory use different brain regions. An overview of multiple learning systems in the brain. The MTL system discussed in this chapter is involved in learning and recalling declarative, explicit memories; in memory consolidation; and the like. The PFC appears to be active in working memory tasks, metacognitive memory judgments, semantic memory, and conceptual priming. Perceptual priming involves sensory cortex, while motor learning and some kinds of classical conditioning seem to require the cerebellum. *Source*: Moscovitch.

and motor halves of the cortex are in constant dialogue with each other, as when we hear ourselves speak. Finally, the amygdala is deeply involved in emotional learning, along with associated regions in the limbic system.

A wide range of memory deficits can be used to separate different memory components from each other. You should know some examples of such dissociations.

10.0 DRAWINGS AND STUDY QUESTIONS

1 Fill in the missing labels in the functional diagram given in Figure 9.33. Define each of the terms.

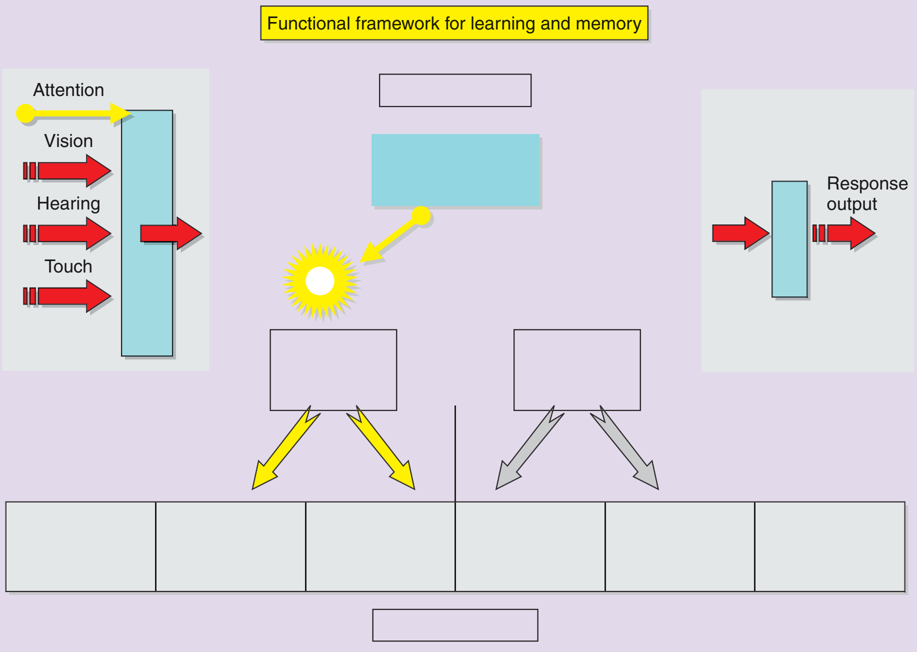


FIGURE 9.33 A functional diagram for learning and memory.

2 Label the regions and associated types of memory.

FIGURE 9.34 Relevant parts of the cortex.

3 Label the brain regions that are relevant to learning and memory in Figure 9.35.

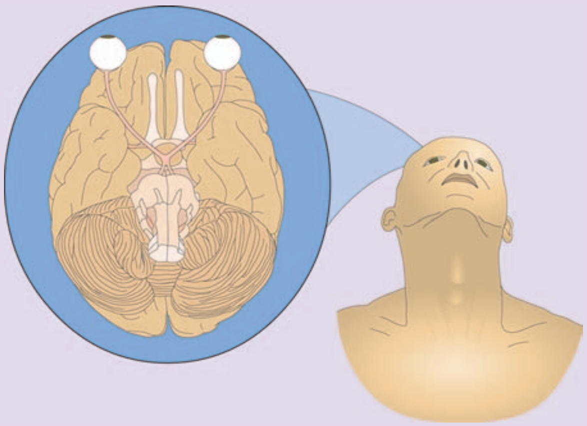


FIGURE 9.35 Location of some memory regions.

4 Label and describe:

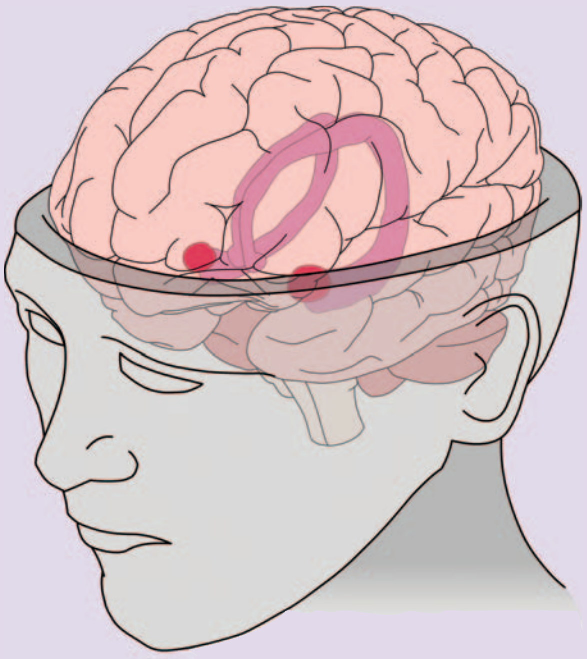


FIGURE 9.36 Location of some memory regions.

5 Label the abbreviations in Figure 9.37. What system does this describe?

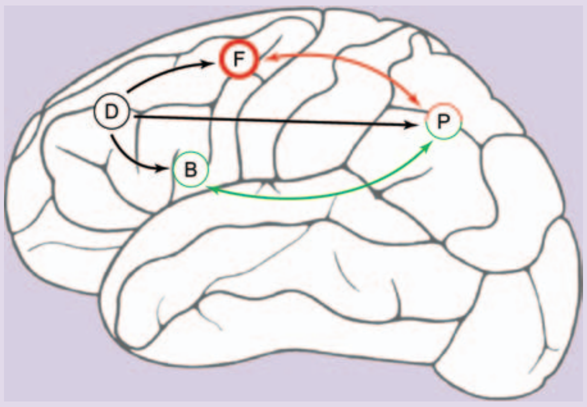


FIGURE 9.37