CHAPTER

24

The Hippocampus, Memory, and Consciousness

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OUTLINE

ABSTRACT

This chapter reviews the cognitive and neurological profile of medial temporal-lobe (MTL) amnesia as relates to conscious phenomenology. Topics include the selectivity of the memory deficit vis-à-vis other cognitive functions; the selectivity of the deficit, within the myriad abilities that can be called mnemonic, to the conscious accessing of information acquired post trauma; the seeming normalcy of many aspects of the patient's conscious experience; and the severe constraints that damage to the MTL places on the candidate information and qualia that can make up the contents of consciousness. Particularly relevant to the latter are relatively recent, still controversial ideas that ascribe to the hippocampus important functions that extend beyond its traditionally accepted role in memory encoding – retrieval of autobiographical episodic memory, relational binding, and imagining new experiences.

PROLOGUE: ROAD TRIP

One of the privileges afforded graduate students at MIT's Behavioural Neuroscience Laboratory has been the opportunity to transport the renowned amnesic patient H.M. from and to his home, a handful of hours distant, for his roughly semiannual research visits[1]. His renown derived from the profound influence that the study of his global amnesia, first described by Scoville and Milner in 1957 [2], had had on the neuroscience and psychology of memory. For example, it had provided the impetus for lesion studies of the role of the hippocampus and adjacent structures in learning and memory in rodents, nonhuman primates,

[1] Anecdotes relating to H.M.'s life as a celebrated patient can be found in [1].

and humans [3], for electrophysiological studies of long-term potentiation (LTP) [4, 5], for the idea of the hippocampus as a cognitive map [6], and for many theoretical models of learning and memory [7].

The convention for H.M.'s transport was for the designated graduate student to travel with a companion, and there was never a shortage of volunteers (typically a fellow student or a postdoc) eager to take a 'road trip' with this famous patient. On one such trip the two scientists-in-training and their charge sought to pass the time by playing a game in which each player selects a colour – on this occasion, green, blue, and white – and accumulates points for each car painted in his or her colour that passes in the opposite direction on the highway. Each player counts aloud, and the gaps between passing cars are typically filled with cheering and good-natured banter. H.M. participated fully in the game, selecting his colour, accurately keeping track of his running total, and participating in the debate about whether a teal-coloured car should be scored as blue, green, or neither. Indeed, on this occasion H.M. won, accruing a score of 20 first. A round of congratulations was exchanged, followed by a lull as the car rolled through the undulating central Massachusetts countryside. A few minutes later, the guest traveller, eager to maximize his once-in-a-lifetime opportunity to gain first-hand insight from this famous patient, asked 'H___, what are you thinking about right now?' H.M. replied that his count of white cars had now increased to 36.

The driver and guest were both impressed that this patient, famously incapable of remembering virtually anything that had occurred in his life since his 1953 surgery, had accurately maintained and updated a running count of arbitrarily selected 'target stimuli' across a span of several minutes, with no evident source of external support or reinforcement. The three travellers commented on this before the guest traveller redirected the conversation to a line of questions that was typical of these trips: *Do you know what today's date is? Do you know who the current President is? Do you know who we are; where we're going today?* H.M. complied with good-natured responses, as always, clearly enjoying the interaction with and attention from these young, engaged travelling companions. Very quickly, however, H.M. initiated another typical element in the driving-with-H.M. script, by steering the conversation towards a reminiscence from his youth, the portion of his life still mentally accessible after his surgery. (The story, about riding the Silver Meteor passenger train on a multi-day trip to visit an Aunt in Florida, had already been told several times at that point in the trip, a product of the teller not remembering the previous tellings.)

At that point, sensing a 'teachable moment', the driver of the car interjected with a question of his own:

'H_____, do you remember what game we were playing a few minutes ago?'

No, he didn't.

'It involved counting cars of different colours; do you remember what your colour was?'

No.

'The three colours were green, blue, and white; do you remember which was yours?'

No, the cues didn't help.

'Do you remember who won the game?'

No recollection even of the triumph that had, only a few minutes before, produced in H.M. a modest chuckle and satisfied smile.

This vignette illustrates several points about the cognitive profile and conscious phenomenology of medial temporal-lobe (MTL) amnesia that will be taken up in this chapter: the selectivity of the memory deficit vis-à-vis other cognitive functions; the selectivity of the deficit, within the myriad abilities that can be called mnemonic, to the conscious accessing of information acquired post trauma; the seeming normalcy of many aspects of the patient's conscious experience; and the severe constraints that damage to the MTL places on the candidate information and qualia that can make up the contents of consciousness.

BACKGROUND

The study of patients with anterograde amnesia resulting from damage to the hippocampus and adjacent structures of the MTL has contributed enormously to our understanding of the organization of memory, of its relation to other aspects of cognition and behaviour, and of its neural bases. Perhaps the most important principle to derive from the study of anterograde amnesia is that it is inaccurate to depict *memory* as a unitary domain of cognition, in the way that one might characterize *vision* or *language*. Indeed, a hallmark of a 'pure' case of anterograde amnesia is the inability to encode (or learn) new information, despite relatively intact abilities to retrieve premorbid memories[2], to remember a small amount of information, such as a phone number, for tens of seconds or

[2] As we shall see, although there is ongoing controversy about the quality of some types of premorbid memories in these patients, neurologists find it 'clinically useful to describe amnesia as a failure to learn new information, which is distinct from a retrieval deficit' [8] p. 41.

even longer, and to demonstrate the improvements that accompany repeated performance of routine behaviours or repeated exposure to stimuli. Also spared in anterograde amnesia is every other major domain of cognition – sensory perception, language comprehension and production, motor control, intelligence, and so on. Because this condition produces so circumscribed a deficit of cognition, it provides an interesting case with which to examine the relation of consciousness to memory vs. other domains of cognition. The analysis in this chapter will begin with a review of the neurological exam and its implications, followed by the anatomical and physiological profile of the amnesic brain, followed by considerations of cognitive effects of damage to the MTL. It will end with a consideration of phenomenology (Box 24.1).

THE NEUROLOGICAL EXAM AND ITS IMPLICATIONS FOR CONSCIOUSNESS

Anterograde amnesia is diagnosed when a neurological exam and neuropsychological testing reveal a specific deficit in the ability to learn new information, as assessed by poor performance on subsequent tests of memory for this new information. In a case described by Mega [8], for example, the patient had a normal general medical exam. She could, upon hearing a spoken list of digits, correctly recite lists of six in the forward order, and lists of five when instructed to recall them in reverse order. On the Mini Mental State Exam (MMSE), a dementia screen that evaluates knowledge of where one is and when it is (year, season, month, date, day of the week) at the time of testing, counting backward from 100 by sevens, and following simple instructions, she responded correctly to 28 out of 30 questions, missing only two that required recall of information provided earlier in the exam. Her vocabulary was intact, as assessed by the ability to name 59 of 60 black-and-white drawings of objects from the Boston Naming Test. When asked to name as many animals as possible within a minute, an index of retrieval from semantic memory and, particularly, the control of this retrieval, she named 19. Executive function was intact, as assessed by tests evaluating the ability to perform mental arithmetic, to change strategy after covert changes of the rule in the Wisconsin Card-Sorting Test, and to withhold responses on a speeded responding test. Finally, and perhaps most striking for one not familiar with such cases, her full-scale intelligence quotient (IQ) as assessed by the Wechsler Adult Intelligence Scale-Revised (WAIS-R) was within the normal range.

Against this backdrop of normal functioning, however, the patient exhibited marked impairment on several formal tests of recall and recognition. For example, she demonstrated marked impairments on tests requiring recall of a list of 16 words several minutes after she had heard them (California Verbal Learning Test, CVLT), requiring recall of the content

BOX 24.1

ANTEROGRADE VS. RETROGRADE MEMORY

Although the severity of anterograde amnesia can differ across patients as a function of the nature and size of the lesion, it remains stable within a patient for the remainder of his or her life. This is illustrated by case H.M., who has been tested numerous times, across a span of greater than 25 years, on his ability to identify from photographs people who were famous during specific decades (e.g., Oliver North from the 1980s, John L. Lewis from the 1940s, Warren G. Harding from the 1920s, and so on). On each occasion that he was tested on this Famous Faces test [9] – in 1974, 1977, 1980, 1988, 1989, 1990, 1994, 1997, and 2000 – his performance never varied between 0% and 20% correct for photos taken after the onset of his amnesia (i.e., portraying people from 1950s to 1980s). For stimuli assessing premorbid knowledge, in contrast, H.M.'s performance never varied between 50% and 75% correct for photos from the 1940s and 1930s, and it dropped off to between 15% and 50% for photos from the 1920s, the decade in which he was born. By contrast, the mean performance of 19 age- and education-matched control subjects starts high and declines steadily, and nearly monotonically, from approximately 75% correct for the 1980s to 30% for the 1920s [10]. (It is interesting to note that, for items from the 1940s and 1930s, H.M.'s performance exceeds the control group's mean performance of approximately 40% correct. This is perhaps because the remote memories of the neurologically healthy group have endured more interference over the years than have those of H.M.) A more detailed consideration of retrograde amnesia is provided in Box 24.4.

of two short stories 30 minutes after they had been read aloud (Wechsler Memory Scale (WMS) delayed paragraph recall), and requiring recall of a complex nonsense figure 30 minutes after she had first seen it and successfully copied it (Rey-Osterrieth complex figure recall).[3] One concise (if overly simplistic) way to summarize this patient's clinical profile, which is characteristic of anterograde amnesia, is that she displayed a normal full-scale IQ but an abnormally low *memory quotient* (as assessed by the WMS). Another important distinction revealed here is between long-term memory (LTM) and short-term memory (STM). Although these terms can have different meanings in different contexts, to the cognitive neuroscientist the former refers to memory for information that has not been in conscious awareness for at least several tens of seconds (but possibly for as long as several decades) prior to its retrieval, whereas the latter refers to the temporary retention of a limited amount of information beginning the moment that this information is no longer accessible to the senses. (Thus, for example, your memory for what time you woke up today is an example of LTM, not STM. Sceptics of this convention need only consider the penultimate vignette that concludes this chapter.)

From this profile we see that many domains of mental function remain intact after the onset of anterograde amnesia. One can infer from these results that this patient can, when prompted, call into conscious awareness much of the impressively vast amount of knowledge that she (like most typically developing humans) has acquired during her life (such as the names of a plethora of different kinds of animals and common objects, facts about political history, knowledge about numbers and their mathematical manipulation, etc.); consciously recite to herself lists of digits and think about how to reverse their order; consciously reason about what the rules of a novel card-sorting game might be, come to the realization that the rules have changed, and think about what the new rule might be; and so on. As an interim conclusion, then, we might infer that many aspects of consciousness are largely unaffected by anterograde amnesia. This conclusion is also consistent with the impression that one might draw from the vignette that opened this chapter. Next we will consider how the evidence about the damage sustained by the amnesic brain, as well as the effects of this damage on the brain's functioning, informs our understanding of the conscious phenomenology of the anterograde amnesic patient.

THE IMPLICATIONS OF MTL DAMAGE FOR NEUROANATOMICAL AND NEUROPHYSIOLOGICAL CORRELATES OF CONSCIOUSNESS

Patients demonstrating the classic neuropsychological profile of a pure anterograde amnesia, such as the patient profiled in the preceding section, invariably have sustained damage that is largely confined to one or more elements of the *medial temporal lobe-diencephalic memory system*, which comprises the hippocampal complex (dentate gyrus, cornu Ammonus (a.k.a., the hippocampus proper), and subiculum), and adjacent structures of the MTL – the parahippocampal, perirhinal, and entorhinal cortices – and two closely anatomically linked structures – the mammillary bodies of the hypothalamus and the anterior thalamic nuclei. Also important to the MTL memory system is the fornix, a bundle of fibers leaving the hippocampal complex that synapse on the mammillary bodies and on neurons of the basal forebrain. A postmortem examination of the brain of Mega's patient revealed bilateral hippocampal sclerosis – cell loss in the CA1 fields of the hippocampus accompanied by gliotic change – and an absence of pathological changes in cortex. Importantly, there was no evidence of the widespread cortical damage that is associated with such neurodegenerative disorders as dementia of the Alzheimer's type[4] [8]. The possible aetiology of this damage was not considered. (In contrast, a retrieval deficit, as considered in Box 24.2, would be associated with damage to the dorsolateral prefrontal cortex (PFC) [8]).

The bilateral damage to H.M.'s MTL, produced by surgical aspiration intended to treat his intractable epilepsy [2], was considerably more extensive. Detailed structural imaging with magnetic resonance imaging (MRI) indicates that H.M.'s lesion is bilaterally symmetrical, and includes the medial temporal polar cortex, most of the amygdaloid complex, most of the entorhinal cortex, and the rostral half of the hippocampus proper. The caudal half of the hippocampus (approximately 2 cm in length), although intact, is atrophic. The mammillary nuclei are shrunken. In addition, the cerebellum

[3] Details about the testing procedures for each of the tests listed here, as well as the brain systems and mental abilities that they are intended to measure, can be found in [11].

[4] *Dementia* is distinguished from *amnesia* by the clinical presentation, along with a memory impairment, of marked impairment of one or more nonmnemonic domains of behaviour, including perception, receptive or productive language, executive control, and motor control.

BOX 24.2

LOST FOREVER OR TEMPORARILY MISPLACED?[5]

The presence of anterograde amnesia, alone, does not permit one to distinguish between a 'consolidation block' (i.e., impaired encoding) account vs. disordered storage or disordered retrieval accounts of hippocampal function. In the years following the report of case H.M. [2], which launched the modern study of the MTL and of amnesia, the emphasis was on 'the central role of the learning impairment' [12] (p. 233). By the late 1960s, however, accumulating evidence that many kinds of learning could be spared in amnesic patients ([12, 13]) led to the alternative proposal that the amnesic syndrome was best characterized not as a disorder of encoding, but rather as one of storage or retrieval [14]. For example, when Warrington and Weiskrantz [15] tested amnesic subjects and neurologically healthy control subjects 10 minutes after reading 16 words, the patients performed as well as control subjects on what the authors termed a 'cued recall' task, but were markedly impaired on a test of Yes/No recognition. (The cued recall task from [15] used a procedure that came to be known as word-stem completion, in which the first three letters of a studied word were presented and the subject was 'required to identify the stimulus word' (p. 420). It will be revisited in Box 24.3.) These results, together with evidence of disproportionate sensitivity to interference from items presented prior to or after the critical information, were taken as evidence for 'altered control of information in storage' (p. 419) in amnesia, and against the consolidation block account.

These early studies illustrated that the study of amnesia could provide powerful insight into the organization of human memory, and the 1970s witnessed an explosion of LTM research, in both memory-impaired and normal populations. One result of this development was increased understanding of the differences between anterograde and retrograde memory (Box 24.1), which led to a convincing refutation of strong versions of storage- and retrieval-based accounts of anterograde amnesia [9, 16].

The ambiguity of whether the patient's deficit is one of encoding vs. one of retrieval also has implications for the clinic, in that, for example, evidence of impaired recall of recently presented information, alone, cannot distinguish an isolated deficit in *learning* new information from a deficit in *retrieving* it. To differentially diagnose anterograde amnesia from a retrieval deficit, it is important to follow up a finding of poor 10-minute recall with retrieval cues. If the availability of cues produces a marked improvement in performance, the diagnosis of a retrieval deficit is indicated [8].

demonstrates marked atrophy (a finding assumed to have resulted not from the surgery, but rather from the patient's decades-long history of taking anticonvulsant medication [17]). Importantly, the lateral temporal, frontal, parietal, and occipital lobe cortices appeared normal for a 66-year-old individual [18].

When we contrast the lesions of these two patients, one quite circumscribed and the other considerably more extensive, we see that they do not invade the brain regions whose function is implicated in waking consciousness. The brain regions whose level of activation differentiates conscious from unconscious mental states include lateral and medial frontal and parietal cortex, and thalamus (for more detail, see Chapter 15, and [19–21]). Similarly, the lesions of these MTL amnesic patients largely spare the territories of the so-called 'default network' of cortical regions that display elevated levels of activity when subjects are at rest: medial posterior cingulate and dorso- and ventromedial frontal cortex; lateral inferior parietal cortex; and medial and lateral aspects of temporal polar cortex. (Portions of this latter area were resected during H.M.'s surgery.) Ideas about functional significance of activity in this network include 'unconstrained, spontaneous cognition – [e.g.,] daydreams', maintaining balance within neural networks and systems, and 'instantiat[ing] the maintenance of information for interpreting, responding to, and even predicting environmental demands' [22] (pp. 1249–1250).

Turning to the functioning of the brain of MTL amnesics, there is a surprising paucity of published information on this topic (this despite an abundance of data for patients with, for example, mild cognitive impairment and with Alzheimer's disease). H.M. has undergone a brain scan with single photon emission computed tomography (SPECT), a method that can measure blood flow in tissue. In comparison to the scan of a healthy, age- and education-matched control

[5]A more thorough treatment of this question can be found in [16], from which the title of this box was appropriated.

subject, H.M.'s thalamus and cortical mantle appear to show normal levels of blood flow, with the exception of the MTL, from which no signal is detected [23]. Other evidence for normal cortical functioning in H.M. comes from a functional MRI (fMRI) scan acquired while he performed a novel picture encoding task. This scan revealed task-related activity in a portion of caudal MTL that was spared by the surgeon, an effect that was comparable to what was seen in control subjects [17]. This rather thin set of observations from the human is supplemented, however, by controlled studies in experimental animals. In baboons with surgically produced neurotoxic lesions of entorhinal and perirhinal cortex, positron emission tomography (PET) scans revealed pre-to-postoperative hypometabolic changes in several brain regions, including inferior parietal, posterior cingulate, sensorimotor, posterior temporal, and rostral occipital regions, as well as in thalamus. No differences were observed in lateral prefrontal, anterior cingulate, anterior temporal, or insular cortex [24]. (These rhinal cortex lesions produced significant impairment of recognition memory [25].) A study in rats that used a similar procedure found significant hypometabolism (as measured by PET) in bilateral frontal, parietal, and temporal regions four days after unilateral chemical lesion of entorhinal cortex, an effect that persisted 4 weeks later only in temporal cortex [26].

This summary of the structural damage associated with relatively pure cases of anterograde amnesia, and its physiological sequelae, leaves equivocal the question of whether the lesions that are sufficient to produce anterograde amnesia would be expected to affect directly the phenomenological consciousness of these patients. Considering data from amnesic patients themselves, it is clear that their lesions do not directly invade brain regions known to be necessary for conscious awareness. Additionally, the scant amount of information available from case H.M. does not show any obvious alterations in the physiology of consciousness-related regions. In the baboon, however, bilateral damage to entorhinal cortex produced lasting alterations in many cortical and subcortical regions, some of which may correspond to regions that, in the human, contribute importantly to conscious awareness. An analogous effect may be more transient in rats, although the lesion in this case was unilateral. Finally, it is worth noting that the lesions in the animal studies, although targeting portions of the MTL memory system, spared the hippocampus proper. Thus, at this point in our exploration we have found, at best, only indirect hints that conscious awareness may be altered in patients with MTL amnesia. We shall see in the next section, however, that targeted evaluation of specific cognitive functions in these patients uncovers deficits that are not readily evident from standard clinical and neuroradiological exams.

THE EFFECTS OF MTL DAMAGE ON VARIOUS MENTAL FUNCTIONS AND THEIR IMPLICATIONS FOR CONSCIOUSNESS

LTM

By far, the most influential framework for thinking of the relations between consciousness and memory has been Tulving's distinction between *autonoetic*, *noetic*, and *anoetic* states of awareness with respect to memory retrieval [27]. Derived from a Greek word appropriated by philosophers to refer to 'mind' or 'intellect,' the term 'noetic' in this context roughly corresponds to 'knowing'. Thus autonoetic (or 'self-knowing') awareness refers to an instance of memory retrieval that 'is not only an objective account of what has happened or what has been seen or heard … [but also] necessarily involves the feeling that the present recollection is a reexperience of something that has happened before' [28] (p. 597). 'At the core of autonoetic memory', writes Moscovitch [29], 'is a sense of personal self and the subjective experiences associated with that self or ascribed to it' (p. 611). In relation to the structure of memory, autonoetic awareness is the defining feature of episodic memory, the subcategory of declarative memory corresponding to events that one has personally experienced. Noetic ('knowing') awareness, in contrast, 'occurs when one thinks about something that one knows, such as a mathematical, geographical, or even personal fact, without reexperiencing or reliving the past in which that knowledge was acquired' [29] (p. 611). Noetic awareness characterizes the phenomenology associated with retrieving information from semantic memory, the other subcategory of declarative memory. Finally the concept of anoetic ('not knowing') awareness captures the fact that nondeclarative memory can be expressed without the individual's awareness that his or her performance is being influenced by a prior experience (see Box 24.3). For example, when H.M.'s performance on the completion of three-letter word stems or on the identification of briefly flashed words displays a robust level of influence of a prior study session [30], it does so despite an apparent lack of awareness on the part of the patient that there even was a study session 5 minutes prior to the test, let alone that his performance reflects the influence of that session. (Thus, perhaps 'anoetic performance' would be a better term.) There exists a large and complex literature, extending back even

BOX 24.3

'MEMORY WITHOUT AWARENESS'

A second major focus of memory research beginning in the 1970s was what came to be known as *implicit* or *nondeclarative* memory (for reviews, see [31, 32]). The consequent development of theoretical and methodological sophistication in this domain led to a more nuanced interpretation of some of the earlier reports of intact performance by amnesic subjects. With word-stem completion, for example, it was shown that the performance of amnesic subjects relative to age- and education-matched control subjects depended on the precise phrasing of instructions about how to process the three-letter stem: When subjects were instructed to complete the three-letter stem to 'the first word that comes to mind,' and no reference was made to the prior study episode, amnesic patients often generated target words at a level that was comparable to that of control subjects (i.e., they exhibited intact *repetition priming*); when, in contrast, they were instructed to use the three-letter stem as a cue with which to retrieve an item from the studied list, amnesic patients were typically impaired ([33]). (The former procedure, which most closely resembles that from ref. [15], came to be known as word-stem completion *priming*, the latter as word-stem *cued recall*.) Thus, the intact performance of amnesic patients in [15] came to be reinterpreted as an early demonstration of intact performance by amnesic subjects on a priming task, a phenomenon that fell under the rubric of *nondeclarative memory*.

In parallel to this research in nondeclarative memory, by the late 1980s, the dominant neuropsychologically inspired view was that memory was organized into distinct systems, with the principal distinction being between MTL-dependent declarative memory and MTL-independent nondeclarative memory[6]. From this perspective, the function of the *MTL memory system* was one of encoding information that is active in the subjective present (e.g., the products of the visual and auditory perception of an event, together with the emotions that they engendered) and effecting its 'transition from perception to memory' [34] (p. 1384) by binding together its anatomically discrete representations (in our example, visual, auditory, and affective). Only by undergoing this process of MTL-mediated *consolidation* could a memory later be called back into conscious awareness via volitional retrieval processes.

before Tulving's seminal paper [27], that grapples with the question of how to determine precisely the level of awareness that accompanies performance on different memory tasks. This literature is reviewed comprehensively elsewhere [29, 35], and the remainder of this section will draw on it only to the extent that it addresses directly the goals of this chapter.

The standard neuropsychological model of the MTL memory system, the development of which is sketched in Boxes 24.2, 24.3, and 24.4, includes two important tenets that we will examine in detail. One is the time-limited role for MTL-mediated consolidation, a feature necessitated by the temporal gradient that typifies retrograde amnesia following damage to the MTL (Box 24.4, [36]). The second is the hierarchical arrangement of the elements in the MTL memory system, with memory formation depending on the funnelling of activity from nonmnemonic cortical regions first into perirhinal or parahippocampal cortex, then into entorhinal cortex, and finally 'up' to hippocampus ('up' in the sense of the apex of the hierarchy) [37]. Recently, questions have been raised about both of these tenets of the standard neuropsychological model that have important implications for the neurobiology of consciousness.

A challenge to the idea of a time-limited role for the hippocampus in memory consolidation has come in the form of the *multiple trace theory* (MTT) of hippocampal function [38]. MTT posits that each instance of memory retrieval also prompts the encoding by the hippocampus of a new memory trace, such that over time a single memory comes to be stored as multiple traces. To the extent that elements of these traces overlap, this process leads to the development of semantic knowledge that is independent of the episodes in which the information was learned. So, for example, if learning about

[6] In parallel with the development of memory-systems models were transfer appropriate-processing models, which appealed to the overlap of mental processes engaged at study vs. test as the critical factor in determining memory performance. However, because this development emerged largely via the study of neurological healthy individuals, its application to the amnesic syndrome has been only indirect. A comprehensive overview of recent theoretical developments in human memory research can be found in [7].

BOX 24.4

RETROGRADE MEMORY AND CONSOLIDATION

Retrograde memory refers to memory for information encountered prior to the insult to the MTL. Were one to start from a strict assumption that the hippocampus is an engine of encoding, one might expect that memory for an event that occurred the day before the MTL insult would be as strong as (if not stronger than) memory for an event that occurred years earlier. However, no such cases of anterograde amnesia accompanied by the absence of any retrograde memory impairment have ever been reported. Instead, irreversible damage to the MTL invariably also produces some retrograde memory loss. However, there are marked differences in the effects of MTL damage on anterograde vs. retrograde memory. Whereas the former is stable across time, the latter is more variable, perhaps, as we shall see below, in systematic ways.

The strength and duration of retrograde amnesia can be sensitive to the amount of tissue damaged (particularly cortical tissue outside the MTL), the patient's age at the time of MTL trauma, and other factors [39]. For case H.M., his retrograde memory has been estimated to extend back to 11 years prior to his surgery [40]. Unlike anterograde amnesia, however, many studies suggest that retrograde amnesia can be characterized by a temporal gradient, such that memory for events that occurred shortly prior to the MTL trauma is worse than is memory for events that occurred several years earlier. Quantitative studies of this phenomenon, carried out in amnesic patients [41], in psychiatric patients undergoing electroconvulsive therapy [42], in a variety of animal preparations [36], and in formal computational modelling [43], indicate that this gradient takes the form of a monotonic function. Such a replicable, systematic pattern of results requires an explanation at the level of memory processing, and the explanation that has made its way into the textbooks is *consolidation*. More a description than a detailed account of a process, the concept of consolidation captures the logic that the MTL must continue to play a role in memory processing after the initial encoding of information, but that this role is time limited. Thus, memory for information that was encoded shortly before MTL damage was incurred is vulnerable to disruption, because consolidation of that memory is still underway. Memory for information that was encoded long before the trauma, in contrast, is more likely to be preserved, because the 'process' of consolidation had been completed. (A thorough summary of recent developments in the study of retrograde memory, including an intriguing phenomenon known as 'reconsolidation,' can be found in a special section of the journal *Learning Memory* (2006, 13(5)) that is devoted to this topic.)

US Presidents in primary school and taking a family trip to Washington DC both create traces representing the proposition that 'Thomas Jefferson was the third President of the United States,' repeated iterations of this process create a representation that can be retrieved independently of any reference to any one of the contexts in which this information was encountered. In this way, the memory that *Thomas Jefferson was the third President of the United States* becomes a *semantic* memory. Should damage to the hippocampus be sustained several years after the learning took place, the patient would nonetheless be able to retrieve this knowledge. On this prediction, the MTT and the standard neuropsychological model are in accord. The specific memory of the visit to the Jefferson Memorial during the family trip to Washington DC, however, remains an *autobiographical episodic* memory that is dependent on the hippocampus for the remainder of the subject's life. Thus, MTT would predict that access to this autobiographical episodic memory would be severely impoverished, if not completely impossible, after extensive damage to the MTL (particularly to the hippocampus). The standard neuropsychological model, in contrast, would hold that autonoetic awareness for remote autobiographical episodic memories can be comparable to that experienced by neurologically intact individuals when recalling a memory of the same vintage. At the time of this writing, this debate is far from being resolved [44, 39].

A second debate currently underway in the memory community relates to the retrieval of episodic memory, and can be thought of, for our present purposes, as a debate as to whether there are distinct processes corresponding to the autonoetic vs. noetic awareness that can accompany memory retrieval. No one disputes that recognition can either be accompanied by an autonoetic sense that '*yes, I've seen this person before and I recall distinctly when and where it was that I first encountered her*' or by a noetic 'feeling of

familiarity' such that '*I know that I've seen this person before, but I don't recall who she is, or where or when it was that I have previously encountered her.*' What is contentious, however, is whether there exist two processes – *recollection* and *familiarity* – that underlie these two phenomenological experiences. The alternative is simply that memories of different strengths can give rise to different phenomenological experiences, in this case autonoetic vs. noetic awareness, but that the actual underlying process of memory retrieval is the same in both cases. The details of this debate in the cognitive psychology community ([45, 46]) are beyond the scope of this chapter. What is relevant to our current interest, however, are reports that these two putative processes may be neurobiologically dissociable.

Results from fMRI in humans [47] and lesion studies in humans [48–51] and rats [52], have been interpreted as evidence that recollection is differentially supported by the hippocampus, whereas familiarity is supported by nonhippocampal elements of the MTL memory system, of which the perirhinal cortex is particularly emphasized [53]. An implication of this 'dual processes' account is that autonoetic awareness at the time of retrieval may depend on the hippocampus proper, whereas noetic awareness may be supported by nonhippocampal elements of the MTL. In contrast, the standard neuropsychological model would hold that any differences in retrieval-related phenomenology associated with damage to different elements of MTL memory system would be quantitative, rather than qualitative, because it denies the possibility that different elements of this system differentially support discrete memory-related processes. (Indeed, one recent account of this view aligns itself with 'single process' theories from cognitive psychology that deny a fundamental difference between recollection and familiarity [54]). As is the case with the differing views of the time-limited consolidation model vs. the MTT, satisfactory resolution of the question of one vs. two retrieval-related processes is probably several years off.

STM

STM can be thought of as the retention in conscious awareness of information that is no longer accessible to the senses. As we shall see here, it represents yet another case in which received wisdom about the mnemonic functions of the hippocampus has come under reappraisal. In this instance, however, a function previously believed to be independent of the integrity of the hippocampus is now being shown, under some conditions, to depend on it. As we saw in the earlier section on the neurological exam, anterograde amnesia is characterized by a preserved ability to prehend a spoken list of items (in this case, digits) and to recite it back to the speaker. Formal demonstrations of this [55–58] contributed to the development of cognitive models specifying a fundamental distinction between STM and LTM [59], as well as to the idea that STM is independent of the MTL memory system. (To be thoroughly precise, therefore, this name would need to be expanded to 'MTL declarative LTM system'.)

The recent reconsideration of the dependence of STM on the MTL has its roots in a detailed theory of what might be the specific operations performed by the hippocampus that give it its privileged function with respect to the formation of LTM. In brief, this theory holds that the hippocampus effects the operation of representing and learning the relationships between items in the environment. This might include the arbitrary rule for written English of '*i* before *e*, except after *c*,' or the concrete spatial content of 'Zidane struck the free kick from the left side of the field, lofting the ball over the heads of the Brazilian defenders and into the right side of the goal box, where Henry, running in unmarked, volleyed it into the back of the net'. (Incidentally, Eichenbaum [60] has argued that the demonstration of a necessary role for the hippocampus for nondeclarative memory for the relationships between stimuli (e.g., learning cue–context relationships embedded in a visual search task [61]) rules out the view that the hippocampus 'could be a "gateway" for awareness to enter into memory' (p. 775).) Motivated by this 'relational binding' model, recent studies have demonstrated that patients with hippocampal damage are impaired on tests of STM, with lags as short as 1 second, for spatial relationships between items in a display [62, 63]. This suggests that one qualitative effect of hippocampal damage on phenomenological consciousness is to disrupt the ability to represent the relationships between discrete objects.[7] Whether this is also true for the real-time perception and experience of complex scenes, or only for instances when a mental image of the relationship between no-longer-perceivable items must be retained, will require additional research. A suggestion of what the answer might be, however, has already appeared in the form of the study to which we now turn.

[7] Another recent study has described a deficit in MTL patients in 4-second delayed recognition of visually presented stimuli that impose no explicit relational binding requirements (location of squares, face identity, color identity [64]). However, in view of the small number of amnesic subjects tested (three) and the heterogeneity of their lesions, it would be premature to draw strong conclusions about the implications of this one study for our understanding of the role of the MTL in STM.

Imagining New Experiences

The debates summarized at the beginning of this section relate to whether the hippocampus is necessary for autonoetic awareness during memory retrieval. But what about thinking about experiences that have never actually occurred, such as might happen when one daydreams, or when one thinks about what might happen at an upcoming event? One group has reasoned that because these phenomenological experiences would seem to draw on many of the same psychological processes required for autonoetic awareness of an episodic memory (e.g., mental imagery, a sense of 'being there', maintenance of a narrative structure), the ability to imagine new experiences might also be dependent on the hippocampus. (This line of reasoning depends on many precepts of the MTT.) In their experiment they asked patients with bilateral hippocampal damage to construct new imagined experiences, such as 'Imagine you are lying on a white sandy beach in a beautiful tropical bay' and 'Imagine that you are sitting in the main hall of a museum containing many exhibits'. Their results indicated that the imagined experiences of the patients contained markedly less experiential richness than did those of healthy control subjects. A more detailed analysis also revealed lower 'spatial coherence' (a measure of the contiguousness and spatial integrity of an imagined scene) in the performance of the patients, and the authors speculated that this might be at the root of the overall poor performance of the patients [65]. Although these results and their interpretation are also likely to be met with scepticism from some circles, they raise the possibility that the constraints on conscious phenomenology imposed by damage to the hippocampus are not limited to memory retrieval, but may also extend to prospective thought.

To summarize this section, many recent developments in memory research, although some of them are still controversial, point to the possibility that the contributions of the hippocampus to phenomenological consciousness may extend beyond the processing of the present so that the events of the present can later be revisited. They suggest that the hippocampus may also be necessary for rich autonoetic awareness, as well as for spatially coherent thinking about the very recent past, the present, and even the future.

WHAT IT IS LIKE TO BE AMNESIC?

Despite the currently unsettled state of the domains of contemporary memory research that were summarized in the preceding section, the first two analytic sections of this chapter established that many quantitatively measurable correlates of the conscious experience of the MTL amnesic patient are not appreciably changed from what they must have been prior to the neurological insult. This might justify what is arguably the most direct approach to investigating the phenomenal consciousness that is characteristic of MTL amnesia – interrogating patients. Before embarking on this exercise, however, a brief review of a few concepts from the philosophy of consciousness will prove to be useful. Within the tradition of phenomenology, the *stream of consciousness* is held to provide coherence and continuity to conscious experience. As summarized by Thompson and Zahavi [66], 'Phenomenological analyses point to the 'width' or 'depth' of the 'living present' of consciousness: our experience of temporal[ly] enduring objects and events, as well as our experience of change and succession, would be impossible were we conscious only of that which is given in a punctual now and were our stream of consciousness composed of a series of isolated now points, like a string of pearls. According to Husserl [67], the basic unit of temporality is not a "knife-edge" present, but a "duration block" …' (p. 77). The relevance of this concept to anterograde amnesia is clear, and is further bolstered by empirical evidence that relates to H.M.'s perception of the passage of time. In his experiment, Richards [68] asked 'Without the normal recall for events, how fast does time pass for H.M.? Does one hour, one day or one year seem just as long to this unique individual as to us?' (p. 279). The results indicated that whereas time reproduction (and thus, by inference, the experienced passage of time) was normal for intervals less than 20 second, it was grossly distorted for longer intervals. In answer to his passage-of-time question, Richards concluded by extrapolating from the data that 'one hour to us is like 3 minutes to H.M.; one day is like 15 minutes; and one year is equivalent to 3 hours for H.M.' (p. 281). Thus, for H.M., the width of his 'living present' may, in fact, be best characterized as a knife-edge.

A second concept from philosophy that is germane to our pursuit is that of *fringe consciousness* [65], summarized by Seager [69] as 'the background of awareness which sets the context for experience … [a]n example is our sense of orientation or rightness in a familiar environment' (p. 10). Fringe consciousness situates a person, preventing the feeling that one has simply popped into the world at that moment.

Moving on, then, to the interrogation, self-report from H.M. suggests that one phenomenological quality of anterograde amnesia is a pervasive anxiety about what may have happened just beyond the edge of the truncated duration block of the living present:

'Right now, I'm wondering, have I done or said anything amiss? You see, at this moment everything

looks clear to me, but what happened just before? … It's like waking from a dream; I just don't remember … Every day is alone, in itself. Whatever enjoyment I've had, whatever sorrow I've had.' [1] (p. 138).

On another occasion, during an exchange between H.M. and researcher William Marslen-Wilson (relayed by Hilts [1]) the patient confessed to worrying about giving the wrong answer, whether during formal testing or just in conversation.

'It is a constant effort, H____ said. You must always "wonder how is it going to affect others? Is that the way to do it? Is it the right way?" … Asked if he worried about these things a lot, struggled with his thought to get right answers, he said yes, all the time. "But why?" "I don't know," said H____.' (p. 140)

The experience of disordered fringe consciousness is evident in amnesic patient Clive Wearing, a distinguished British musicologist, conductor, and keyboardist whose amnesia resulted from herpes encephalitis, a condition that can produce severe damage to the hippocampus while leaving the rest of the brain relatively unscathed. Wearing has been featured in several television documentaries, one of which, at the time of this writing, can be viewed on the World Wide Web[8]. The video clip opens with the camera panning in on Wearing and his wife sitting in a city park.

Wife: 'Do you know how we got here?

'Wearing: 'No.'

Wife: 'You don't remember sitting down?'

Wearing: 'No.'

Wife: 'I reckon we've been here about 10 minutes at least.'

Wearing: 'Well, I've no knowledge of it. My eyes only started working now …'

Wife: 'And do you feel absolutely normal?'

Wearing: 'Not absolutely normal, no. I'm completely confused.

Wife: 'Confused?'

Wearing (agitatedly): 'Yes. If you've never eaten anything, never tasted anything, never touched anything, never smelled something, what right have you to assume you're alive?'

Wife: 'Hmm. But you are.'

Wearing: 'Apparently, yes. But I'd like to know what the hell's been going on!'

(In making these pronouncements about his senses, it is clear that Wearing is speaking figuratively, not literally.) Thus, for Wearing, too, each waking moment feels as though he is just waking up from sleep. The journal that he keeps is filled with multiple entries that all contain variants of the same message. For example, directly under the entry '10:49 am I Am Totally Awake – First time', which appears on the first line of a page, is a second entry '11:05 am I Am Perfectly Awake – First time', and so on. When left alone in his room, the patient fills entire pages in this way with entries made at intervals ranging from 5 to 45 minutes.

These anecdotes capture an essential quality of the conscious phenomenology of the MTL amnesic patient, the near-continual experience of just having awakened from unconscious sleep. The plight of the MTL amnesic patient, then, is to be fully cognizant of, if not preoccupied by, the fact that one is not cognizant of the daily events of one's life.

CONCLUSIONS

The MTL's contributions to conscious awareness are at once minimal and profound. They are minimal in that they would seem to contribute little to the ongoing operations that comprise the contents of our moment-to-moment conscious awareness – perception, retrieval and contemplation of semantic knowledge, language processing (receptive and productive), social interactions, and so on. They are undeniably profound, however, in that they underlie the width of the stream of consciousness and the integrity of fringe consciousness. This chapter has highlighted several important questions that remain to be resolved. Physiologically, what are the contributions of the MTL to the quality and quantity of activity in the main complex of brain structures whose activity underlies awareness [20, 70]? Psychologically, what explains the phenomenological difference between autonoetic and noetic awareness? Empirically, are the recent findings that suggest a necessary role for the MTL in some kinds of STM and in the ability to imagine new experiences replicable and generalizeable?

EPILOGUE: A FINAL WORD

'"What happened to you? …' asked researcher Marslen-Wilson. 'Well,' said H____, 'I think of an operation. I have an argument with myself right there – did the knife slip a little? Or was it a thing that's naturally caused when you have this kind of operation?' 'That caused what?' Marslen-Wilson asked. 'The loss of memory, but not of reality', H_____ said." [1] (pp. 139–140)

[8] http://www.youtube.com/watch?v = OmkiMlvLKto&mode = related&search =

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