

# Amnesia

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Amnesia is a general term that refers to a serious memory deficit typically associated with medial temporal lobe or diencephalic lesions. Reference to amnesia implies a memory impairment in the absence of, or out of proportion to, deficits in other intellectual domains, such as problem solving or general cognitive function.

## Introduction

Amnesia can be defined as a memory loss in the absence of, or out of proportion to, other cognitive problems that the affected individual might suffer. Much of what we now know about memory and the loss of memory came not from intentional experiment but from the unexpected consequence of a surgical treatment for epilepsy conducted on a particular patient in 1953. It had been known for many years that the serious seizures associated with psychomotor epilepsy are most often associated with abnormal neural activity beginning in the temporal lobes of the brain. An operation that had been performed for some years to treat this disorder had involved surgical removal of parts of the temporal lobe of one hemisphere. In the case in question, the patient had especially frequent and severe seizures and it was decided to remove both sides of a structure called the hippocampus, a band of fibres that is embedded deep within the temporal lobes. (The term 'hippocampus' literally means 'seahorse'. The name was derived from its irregular curved appearance.)

After the operation the frequency and severity of the patient's seizures were greatly reduced. It was soon discovered, however, that the patient, whose initials were H.M., had as a result of the operation an intriguing and tragic kind of memory deficit. His memory for events years prior to the surgery was quite well maintained. There was, however, an almost complete absence of memory for any events that occurred after his surgery. This included events in his personal life as well as broader events in the world. He could hold new information very briefly in memory for a matter of minutes (and less if distracted), but he showed an almost complete inability to transfer these short-term memories into more permanent long-term memory.

From 'case H.M.' students of memory learned two important lessons. The first was that it is possible to dissociate behaviourally short-term from long-term memory. We can define the term short-term memory (also called immediate memory or primary memory) as referring to knowledge of the 'just past'. By this we mean events that occurred or facts that were learned a few seconds ago and that are recalled immediately. By contrast, long-term memory (also called secondary memory) refers to informa-

## Introductory article

### Article Contents

- Introduction
- Features of the Amnesic Syndrome
- Retrograde and Anterograde Amnesia
- Other Forms of Amnesia
- Summary

tion from the past minutes, hours, days or years. The second lesson from case H.M. was that the areas important for consolidation of a short-term memory trace into a more enduring long-term memory can be anatomically localized.

## Brain lesions that produce amnesia

We now know that the amnesia expressed by H.M. is characteristic in type, if not in severity, of damage to a number of related areas of the brain. These areas include the medial temporal lobe structures comprising the hippocampus, the amygdala, the entorhinal cortex and the perirhinal cortex. Besides surgical resection of these medial temporal structures that caused the amnesia in H.M., other causes of damage to these areas that result in amnesia include stroke, closed head injury and herpes simplex encephalitis. Patients with Alzheimer disease have memory loss associated with damage to these same medial temporal structures, although their neuropathology is not restricted to medial temporal areas and accordingly their cognitive deficits are not restricted to memory loss alone. These patients suffer from dementia, which is memory loss plus impaired functioning in at least one other psychological domain, such as language, visuospatial function, judgment, abstract thought or personality.

A second brain region associated with amnesia is the midline diencephalic region, which includes the mamillary bodies of the hypothalamus and the dorsomedial nucleus of the thalamus. Causes of damage to these diencephalic structures include stroke, brain tumours in this region and a disorder called Korsakoff syndrome.

## Korsakoff syndrome

The most commonly studied single group of amnesics are those with Korsakoff syndrome. These patients have damage to the above-mentioned brain tissue in and around the diencephalic brain structures as a consequence of long-term alcoholism which often results in poor diet and vitamin deficiency. In the case of Korsakoff syndrome the vitamin implicated is thiamin (vitamin B<sub>1</sub>).

Korsakoff syndrome is a permanent condition in which the individual has difficulty acquiring new information

(anterograde amnesia), combined with a memory loss for information acquired before the onset of the brain damage (retrograde amnesia). In the case of the retrograde amnesia, the memories acquired long before the onset of the damage are far better recalled than memories that had been acquired closer in time to the onset of the damage. These features of the amnesic syndrome will be described in more detail. The consequence of this damage, however, is that the Korsakoff patient is unable to learn new information even when it has been repeated many times. When interrogated, these patients often confabulate, giving what to them might be a reasonable answer in place of the actual information that is not available.

It is not uncommon for Korsakoff patients to show source amnesia, in which they may remember an item of information but not recognize that it had just been told to them by the examiner. Source amnesia can also occur in normal elderly individuals who may correctly recall or recognize material that was learned previously but may misidentify where and when the material was learned.

## Features of the Amnesic Syndrome

The general features of the amnesic syndrome have been characterized in some detail in the literature. One major feature of amnesic patients is that while some forms of memory are devastated by the brain damage, other forms of memory may be relatively spared.

### Explicit memory

The typical amnesic patient is unable to recall recent information, whether it is what they had for breakfast that morning, a new address or a new telephone number. These memories can be referred to as 'explicit' memory, in the sense that they are memories for facts and events that are capable of being consciously recalled or recognized. These kinds of memories have sometimes been called 'declarative' memories because one can declare this knowledge, or the understanding that we have this knowledge, to others.

### Implicit memory

By contrast to the deficit in explicit memory, some forms of memory can be retained in amnesic patients, even in severely impaired individuals such as H.M. These are forms of memory called 'implicit' memory. Implicit memory refers to a patient's ability to demonstrate by his or her responses that material has been registered and retained in memory, but the patient neither has the ability to retrieve this information through conscious effort, nor even has the knowledge that he or she has this information. For example, we would not expect a severely amnesic patient to be able to remember a word-list such as 'camel,

table, train, basket, cloud', even after many presentations. This would illustrate a failure in explicit memory. At this point one could demonstrate that the patient had spared implicit memory using a technique referred to as stem-completion. In this case the person would be given word beginnings, such as 'cam...', 'ta...', 'tr...' and so forth, and be asked to produce the first words that come to mind that begin with those letters. For example, the patient might produce 'camel' for the stem 'cam...', 'table' for the stem 'ta...' and 'train' for the stem 'tr...', rather than other words of equal or greater frequency in the language such as 'camp', 'take', or 'tree'.

Studies of amnesic patients show that they will very often complete the stems with words from the studied list, thus showing that some trace of the word was in memory even though it could not be produced in attempted recall. Indeed, being told that the stems were completed with words that had been studied, the patient may deny any memory of having seen them before or having studied them. Stem completion and other forms of 'priming' are thought to rely on cortical areas that are not usually affected in amnesia.

Amnesics can also demonstrate normal or near-normal skill learning on a variety of tasks. Consider, for example, attempting to trace a geometric shape with a pencil with direct sight of your hand obscured such that you are able only to see your hand and the form you are trying to trace reflected in a mirror. This task, known as mirror tracing, is at first quite difficult to perform because of the reversed image of your hand and the form produced by the mirror. With sufficient practice, however, speed and accuracy of tracing the reflected image will improve. Amnesics show a similar ability to learn this task, even as they may have no memory of ever having seen the apparatus or of using it before. Mirror tracing is an example of 'procedural' learning that is preserved in amnesic patients. A real-world example of procedural learning is learning to ride a bicycle. This is a skill that is acquired with substantial amounts of practice, and one that may remain intact even in patients with severe deficits in explicit memory.

Besides motor tasks, procedural learning occurs in perceptual tasks, such as mirror reading. For example, if one holds a page of text to a mirror and attempts to read it, the task is difficult because of the reversals of the printed letters. Like its production counterpart, mirror tracing, performance at mirror reading improves with practice. Amnesic patients will also show a learning curve for this task (good implicit memory), even though they may not remember ever having practised it (poor explicit memory). Skill learning of these sorts is thought to depend upon brain structures that are not ordinarily affected in amnesia, such as the basal ganglia.

Other capabilities, such as classical conditioning, are also relatively preserved in amnesic patients. For example, an eyelid blink response may be conditioned to an auditory tone by giving repeated presentations of an airpuff to the

eye preceded on each occasion by the tone. The conditioning process is complete when presentation of the tone alone elicits the eyelid blink response. Classical conditioning is another example of implicit learning. Animal studies implicate the cerebellum in such conditioned response learning. Because this sort of classical conditioning can be demonstrated in amnesic patients with medial temporal lobe damage, it would suggest that the medial temporal structures are not necessary for this form of implicit learning.

## Retrograde and Anterograde Amnesia

### Anterograde amnesia

Besides providing evidence of dissociations between short-term and long-term memory, and explicit and implicit memory, case H.M. and patients with Korsakoff syndrome also illustrate the difference between anterograde and retrograde amnesia. H.M.'s main impairment was in the recall and recognition of new events and facts. That is, he could remember events and facts that had been acquired well before his surgery but he was unable to learn new information since his surgery. H.M. had a dense anterograde amnesia: an inability to learn new material. The same characteristic anterograde amnesia is seen in the Korsakoff patient, in which the patient shows great difficulty in learning new information.

### Retrograde amnesia

As indicated previously, retrograde amnesia refers to an inability to remember information that had been acquired before the injury or disease that produced the amnesia. Typically in amnesic patients the extent of the retrograde amnesia decreases for information more temporally remote from the time of brain damage, with very poor recall of events that occurred closer in time to the occurrence of the brain damage, or in the case of H.M., to the time of his surgery. This is referred to as the temporal gradient of retrograde amnesia. For example, when tested for recent history, such as knowledge of famous persons or events, amnesic patients are more likely to correctly supply information about persons and events who were in the news well before their injury. By contrast, memories for events or persons that were newsworthy just before their injury are not remembered.

### Lessons from patient P.Z.

Temporal gradients are usually measured using tests such as pictures of famous persons (e.g. political figures and film stars) from different eras. Rarely do we have the opportunity to test with any exactness an individual's

recollection of actual events that had occurred at various times prior to the precipitating brain damage. A Korsakoff patient, P.Z., described by Butters and Cermak, presented an interesting research opportunity. P.Z. was an eminent university professor and scientist who had written his autobiography shortly before the onset of the clinical appearance of his disease. Using his own biography, the investigators were able to test his memory for events in his life beginning in his early years, through his undergraduate and graduate training, and into his career and family life beyond. P.Z. presented with a classic temporally graded retrograde amnesia in which the events over five decades leading up to the clinical appearance of the disorder showed a systematic decline in recall.

P.Z.'s temporally graded amnesia would not have been a consequence of an increasing deficiency in original learning, as he was unable to recall events that had registered sufficiently for him to have included them in his autobiography. P.Z. counters a simple view of long-term memory as a single stage of storage. With this patient for whom we have detailed autobiographical information, it can be seen that more recently acquired information, even spanning a decade or more, may be more vulnerable to interruption than more remote memories.

## Other Forms of Amnesia

### Amnesia after concussion

Concussion refers to nonpenetrating (closed) head injury that results in a temporary disturbance of consciousness. This is a not uncommon event in many active sports such as American football, rugby or boxing, or as a consequence of motor vehicle or bicycle accidents. In addition to a temporary loss or disturbance of consciousness there will typically be a retrograde amnesia for events just prior to the head trauma with the extent of the amnesia correlated with the length of time that consciousness was disturbed. This may be minutes or hours. Concussion offers an illustration of the fact that memories take time to consolidate and that they will become lost if there is a disruption of neural activity during this critical period.

### Electroconvulsive therapy and retrograde amnesia

Electroconvulsive therapy (ECT) is sometimes used for the treatment of severe chronic depression. ECT is the delivery of a brief but intense shock to the brain through scalp electrodes that induces a seizure. Our interest here is not in the efficacy of the treatment but in the side effect of ECT in producing a short-term retrograde amnesia. Like the effects of concussion, the retrograde amnesia observed following ECT is presumed to reflect a disruption in neural

activity that prevents the structural changes associated with long-term memory consolidation. It is for this reason that ECT is often administered only unilaterally, which helps treat the depression without causing such extensive retrograde amnesia as associated with bilateral administration.

## Transient global amnesia

Transient global amnesia is a general term for the sudden inability to acquire new memories combined with the inability to recover past memories formed prior to the appearance of the amnesia. These temporary amnesias can be associated with concussion, as indicated above, with hypoglycaemia, or with epileptic seizures. Perhaps the most common occurrence of transient global amnesia occurs in older adults in association with a transient ischaemic attack in which there is a temporary reduction in blood flow to the brain, presumably affecting those structures important to learning and memory. Transient global amnesia is so-named because the accompanying retrograde and anterograde amnesia is limited in time. In the typical case the anterograde amnesia lasts for minutes to days whereas the retrograde amnesia is limited to the period just prior to the onset of the attack.

## Psychogenic amnesias

The psychiatric literature holds reports of psychogenic amnesia involving loss of knowledge for items relating to personal identity. Ironically, although this might be the best-known form of amnesia, it is very rare, and highly influenced by film and TV depictions. In one variant of psychogenic amnesia, individuals may maintain personal identity but lose their memory for a particular episode or time period associated with exceptional stress. The loss is referred to as 'repressed memory', which may or may not be recovered later in life. In another variant, a dissociative identity disorder, a patient may share implicit knowledge among multiple personalities. By contrast, explicit knowledge of the life of a single personality is available only to that personality and not the others. This pattern of behaviour is consistent with the view that different types of memory may be functionally dissociable from each other.

The physiological substrates of psychogenic amnesia are unknown but such amnesias may share some behavioural

characteristics with amnesias already discussed, such as a temporally extensive retrograde amnesia. Unlike other amnesias, however, the psychogenic amnesias generally do not show a temporal gradient but instead are said to erase, temporarily or permanently, recollection of the patient's pre-traumatic identity or other selective knowledge. In addition, cases of psychogenic amnesia typically do not show anterograde amnesia.

## Summary

Although most dramatically described in case H.M., whose amnesia appeared following surgery for epilepsy, amnesia can be caused by stroke, or by brain damage associated with Korsakoff syndrome or other conditions. Amnesic patients illustrate a distinction between long- and short-term memory, and explicit versus implicit memory. In amnesic patients explicit long-term memories cannot be formed – or are difficult to form – even though implicit memory is spared.

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