The Amnestic Syndrome

Hillel Grossman, MD

Abstract This chapter focuses on the amnestic syndrome or an impairment in the ability to form new memories. The chapter first describes the history of amnestic disorder and provides a background on memory and memory function. Descriptions of the four amnestic syndromes (Wernicke–Korsakoff syndrome, transient global amnesia, mild cognitive impairment, and hysterical amnesia) are then provided. Finally, the etiology, evaluation, and treatment of amnestic syndrome are described.

Keywords Amnesia · Memory · Mild cognitive impairment · Transient global amnesia · Wernicke–Korsakoff syndrome

1. Introduction

1.1. History

This chapter focuses on a medical rarity that is far more common in artistic renderings of amnesia than it is in real life. The importance of the amnestic syndrome in research is substantial because it is a single symptom impairment that provides rare views into the function of memory processes. The amnestic syndrome is defined simply by impairment in the ability to form new memories. There are usually other associated features, some of which may be very striking, e.g., the patient’s indifference to their deficit, although these features are secondary in prominence to the overwhelming deficits in memory. There is some disagreement regarding how much impairment in other domains distinguishes an amnestic disorder from a dementia syndrome. The memory defect is in “new learning” or “short-term” memory, although some loss of remote memories is usual. Older memories tend to be protected and resistant to damage. Ribot’s first law articulated by the French psychologist, Theodule Ribot, in 1882, notes that amnesia affects memories in reverse order of their development—“The dissolution of memory is inversely related to the recency of the event” (1). Memories of recent events are most vulnerable; memories of events long ago are more resilient. The terms anterograde and retrograde memory are important here. Anterograde memory refers to the ability to lay down new memories and is sometimes called “recent memory” or new learning. Retrograde memory refers to the ability to recall previously learned material or previous experiences. Amnestic disorders are primarily disorders of anterograde memory, although some component of retrograde memory loss is invariably present. Some (2) have argued that the retrograde impairment is very prominent, although detection of this deficit requires a more specialized approach to cognitive testing.

Memory disorders can be classified based on phenomenology, on etiology, and on nosology. Nosology, e.g., the Diagnostic and Statistical Manual (DSM) or International Classification of Diseases (ICD) codes in their various iterations, is the least informative. The most recent DSM, the 4th edition, text revision (DSM-IV-TR), provides only four possible categories based on whether an etiology is known or not:

1. Amnestic disorder caused by a cerebral or systemic medical condition
2. Substance-induced amnestic disorder
3. Amnestic disorder caused by an unknown etiology
4. Amnestic disorder not otherwise specified

Phenomenology is a more useful approach to describing memory disorders.

1.2. Phenomenology of Memory

Memories can be described by their temporal occurrence or by their content.
1.2.1. Types of Memory

1.2.1.1. Temporal

The terms used to describe memory can be very confusing and lacking in uniformity of use. For example, how short is the term in “short-term” memory? Short-term memory can be used to refer to immediate recall or repetition of a list (registration), to keeping that list in mind while focusing on another task (working memory), to memories of events from minutes, hours, or days earlier. Memory is most often defined temporally, as in immediate, short term, or long term, or by its content.

Immediate memory, also known as working memory, attention span, or registration, refers to the first grasp of information in its original apperception, e.g., the visualization of a license plate or hearing a telephone number. This information is retained only as long as one is actively attending to it. Once attention is diverted, e.g., when one stops looking at the license plate or hearing the telephone operator, the numbers are lost from recollection. To retain such information, it must be passed to short-term memory, where it is transformed to a symbol or semantic construct, such as a word or number. Immediate memory involves parts of the prefrontal and parietal cortices, but does not involve the limbic lobes.

Short-term memory is very much a limbic phenomenon. Here, sensory information is encoded and initial consolidation of the sensory material into a symbolic representation begins. Further consolidation comes with rehearsing the new knowledge until the symbolic representation is formed.

Long-term memory refers to the enduring memory traces formed after consolidation is completed. Consolidation likely reflects a potentiation of neural circuits.

1.2.1.2. Content

Content definitions of memory distinguish between declarative memories, which require a conscious effort (e.g., what is the capital of Idaho?), and nondeclarative memories, which rely on unconscious retrieval of information (the association of fire to a burning smell).

Explicit and Implicit Memory. Explicit memory refers to the ability to consciously recollect facts and events. Explicit memory is sometimes known as declarative memory and can be subdivided into semantic memory, the recollection of facts and rules, and episodic memory, the recollection of past events and circumstances. Implicit memory refers to information that is learned or recollected without conscious effort.

Edouard Claparede (1873–1940), the French neurologist, provided an early description of a patient who illustrates the distinction between implicit and explicit memory. Claparede’s patient suffered from a classic Korsakovian amnesia with little ability to learn new semantic information. She was unable to learn the name of the hospital in which she had been residing for many years, could not report the city she was in, and could not recall her birth date. She was able, however, to learn her way around the facility and to find her room from the dining room and other public areas. This demonstrates intact visuospatial learning. Claparede’s famous experiment (which would not be approved by a contemporary institutional review board [IRB]!) involved introducing himself to the patient with a handshake that disguised a sharp pin in his hand. After a short lapse in time, Claparede reintroduced himself to the patient, who demonstrated no recognition of his face and no explicit recollection of having met him before. However, when he extended his hand with a handshake, the patient declined to take it, noting famously, “some people hide pins in their hands.” Here, we have learning without explicit knowledge of that learning and without semantic details, i.e., only the pain associated with the handshake is learned, not the name or face of the pain-inducing hand shaker.

Procedural memory is the nonconscious recollection of motor activities and skills. The motor skills of driving a car or hitting a golf ball rely on procedural memory. These are almost “automatic” activities that do not require conscious effort. As noted above, a different neuroanatomical circuit than that of new learning subscribes these memory functions and these memories are more resilient. Not infrequently, caregivers will report that an amnestic patient’s driving skills are very good although the patient cannot functionally drive because they cannot remember where they are going or how to navigate there (a failure of episodic memory) or they cannot recall the rules and etiquette of safe driving (a failure of semantic memory). Similarly, the amnestic golfer might hit true and strong strokes and putt evenly but will have great difficulty remembering whose turn it is, where his ball was resting, or with whom he golfed or even that he has golfed. Here, the implicit mechanisms of procedural memory are carrying the amnestic patient’s golf game.

2. Anatomy of Memory

2.1. Diencephalic Versus Hippocampal Amnesia: Korsakoff, Wernicke, and Milner

Korsakoff and Wernicke worked and wrote in the same decades of the late 19th century, but neither they nor any of their contemporaries saw a connection between their descriptions of amnestic conditions. Decades later, there emerged reports of patients who presented with acute Wernicke’s encephalopathy and then developed a chronic Korsakovian amnesia, demonstrating that the two syndromes represented different time points of the same condition. Not before the 1930s, however, when cases of Wernicke’s encephalopathy were described in nonalcoholic patients with gastric malabsorption, was it appreciated that the etiology was related to nutritional deficiency, namely insufficient thiamine or vitamin B1. Damage to the diencephalon, meaning mamillary bodies...