

04 - 21.4 Major or Minor Neurocognitive Disorder D

21.4 Major or Minor Neurocognitive Disorder Due to Another Medical Condition (Amnestic Disorders)

Watson PD, Voss JL, Warren DE, Tranel D, Cohen NJ. Spatial reconstruction by patients with hippocampal damage is dominated by relational memory errors. *Hippocampus*. 2013;23:570.

21.4 Major or Minor Neurocognitive Disorder Due to Another Medical Condition (Amnestic Disorders) The amnestic disorders are coded in the DSM-5 as “major or minor neurocognitive disorders due to another medical condition.” All of these disorders cause impairment in memory as the major sign and symptom, although other signs of cognitive decline may coexist. The authors of Synopsis believe amnestic disorder to be a clinically useful descriptive category of illness, but they are coded in DSM-5 as a neurocognitive disorder due to another medical condition with the specific medical condition noted. The amnestic disorders are a broad category that results from a variety of diseases and conditions that have amnesia as the major complaint. The syndrome is defined primarily by impairment in the ability to create new memories. Three different etiologies exist: amnestic disorder caused by a general medical condition (e.g., head trauma), substance-induced persisting amnestic disorder (e.g., caused by carbon monoxide poisoning or chronic alcohol consumption), and amnestic disorder not otherwise specified for cases in which the etiology is unclear.

EPIDEMIOLOGY No adequate studies have reported on the incidence or prevalence of amnestic disorders. Amnesia is most commonly found in alcohol use disorders and in head injury. In general practice and hospital settings, the frequency of amnesia related to chronic alcohol abuse has decreased, and the frequency of amnesia related to head trauma has increased.

ETIOLOGY The major neuroanatomical structures involved in memory and in the development of an amnestic disorder are particular diencephalic structures such as the dorsomedial and midline nuclei of the thalamus and midtemporal lobe structures such as the hippocampus, the mamillary bodies, and

the amygdala. Although amnesia is usually the result of bilateral damage to these structures, some cases of unilateral damage result in an amnestic disorder, and evidence indicates that the left hemisphere may be more critical than the right hemisphere in the development of memory disorders. Many studies of memory and amnesia in animals have suggested that other brain areas may also be involved in the symptoms accompanying amnesia. Frontal lobe involvement can result in such symptoms as confabulation and apathy, which can be seen in patients with amnestic disorders. Amnestic disorders have many potential causes (Table 21.4-1). Thiamine deficiency, hypoglycemia, hypoxia (including carbon monoxide poisoning), and herpes simplex encephalitis all have a predilection to damage the temporal lobes, particularly the

hippocampi, and thus can be associated with the development of amnestic disorders. Similarly, when tumors, cerebrovascular diseases, surgical procedures, or multiple sclerosis plaques involve the diencephalic or temporal regions of the brain, the symptoms of an amnestic disorder may develop. General insults to the brain, such as seizures, ECT, and head trauma, can also result in memory impairment. Transient global amnesia is presumed to be a cerebrovascular disorder involving transient impairment in blood flow through the vertebrobasilar arteries. Table 21.4-1

Major Causes of Amnestic Disorders Many drugs have been associated with the development of amnesia, and clinicians should review all drugs taken, including nonprescription drugs, in the diagnostic workup of a patient with amnesia. The benzodiazepines are the most commonly used prescription drugs associated with amnesia. All benzodiazepines can be associated with amnesia, especially if combined with alcohol. When triazolam (Halcion) is used in doses of 0.25 mg or less, which are generally equivalent to standard doses of other benzodiazepines, amnesia is no more often associated with triazolam than with other benzodiazepines. With alcohol and higher doses, anterograde amnesia has been reported. **DIAGNOSIS** The recognition of amnestic disorder occurs when impairment in the ability to learn new information or the inability to recall previously learned information, as a result of which there is significant impairment in social or occupational functioning and which is caused by a general medical condition (including physical trauma). Amnestic disorder may be transient, lasting for hours or days or chronic lasting weeks or months. A diagnosis of substance-induced persisting amnestic disorder is made when evidence

suggests that the symptoms are causatively related to the use of a substance. The DSM-5 refers clinicians to specific diagnoses within substance-related disorders: alcohol-induced disorder; sedative, hypnotic, or anxiolytic-induced disorder; and other (or unknown) substance-induced disorder. **CLINICAL FEATURES AND SUBTYPES** The central symptom of amnestic disorders is the development of a memory disorder characterized by an impairment in the ability to learn new information (anterograde amnesia) and an inability to recall previously remembered knowledge (retrograde amnesia). The symptom must result in significant problems for patients in their social or occupational functioning. The time in which a patient is amnestic can begin directly at the point of trauma or include a period before the trauma. Memory for the time during the physical insult (e.g., during a cerebrovascular event) may also be lost. Short-term and recent memory are usually impaired. Patients cannot remember what they had for breakfast or lunch, the name of the hospital, or their doctors. In some patients, the amnesia is so profound that the patient cannot orient himself or herself to city and time, although orientation to person is seldom lost in amnestic disorders. Memory for overlearned information or events from the remote past, such as childhood experiences, is good, but memory for events from the less remote past (over the past decade) is impaired. Immediate memory (tested, for example, by asking a patient to repeat six numbers)

remains intact. With improvement, patients may experience a gradual shrinking of the time for which memory has been lost, although some patients experience a gradual improvement in memory for the entire period. The onset of symptoms can be sudden, as in trauma, cerebrovascular events, and neurotoxic chemical assaults, or gradual, as in nutritional deficiency and cerebral tumors. The amnesia can be of short duration. A variety of other symptoms can be associated with amnesic disorders. For patients with other cognitive impairments, a diagnosis of dementia or delirium is more appropriate than a diagnosis of an amnesic disorder. Both subtle and gross changes in personality can accompany the symptoms of memory impairment in amnesic disorders. Patients may be apathetic, lack initiative, have unprovoked episodes of agitation, or appear to be overly friendly or agreeable. Patients with amnesic disorders can also appear bewildered and confused and may attempt to cover their confusion with confabulatory answers to questions. Characteristically, patients with amnesic disorders do not have good insight into their neuropsychiatric conditions. A 73-year-old survivor of the Holocaust was admitted to the psychiatric unit from a local nursing home. She was born in Germany to a middle-class family. Her education was truncated because of internment in a concentration camp. She immigrated to Israel after liberation from the concentration camp and later to the United States, where she married and raised a family. Premorbidly, she was described as a quiet,

intelligent, and loving woman who spoke several languages. At 55 years of age, she had a significant carbon monoxide exposure when a gas line leaked while she and her husband slept. Her husband died of carbon monoxide poisoning, but the patient survived after a period of coma. After being stabilized, she displayed significant cognitive and behavioral problems. She had difficulty with learning new information and making appropriate plans. She retained the ability to perform activities of daily living but could not be relied on to pay bills, buy food, cook, or clean, despite appearing to have retained the intellectual ability to do these tasks. She was admitted to a nursing home after several difficult years at home and in the homes of relatives. In the nursing home, she was able to learn her way about the facility. She displayed little interest in scheduled group activities, hobbies, reading, or television. She had frequent behavioral problems. She repeatedly pressed staff to get her sweets and snacks and cursed them vociferously with racial epithets and disparaging comments on their weight and dress. On one occasion, she scratched the cars of several staff with a key. Neuropsychological testing demonstrated severe deficits in delayed recall; intact performance on language and general knowledge measures; and moderate deficits on domains of executive function, such as concept formation and cognitive flexibility. She was noted to respond immediately to firmly set limits and rewards, but deficits in memory prevented long-term incorporation of these boundaries. Management involved development of a behavioral plan that could be implemented at the nursing home and empirical trials of medications aimed at amelioration of irritability.

Cerebrovascular Diseases

Cerebrovascular diseases affecting the hippocampus involve the posterior cerebral and basilar arteries and their branches. Infarctions are rarely limited to the hippocampus; they often involve the occipital or parietal lobes. Thus, common accompanying symptoms of cerebrovascular diseases in this region are focal neurological signs involving vision or sensory modalities. Cerebrovascular diseases affecting the bilateral medial thalamus, particularly the anterior portions, are often associated with symptoms of amnesic disorders. A few case studies report amnesic disorders from rupture of an aneurysm of the anterior communicating artery, resulting in infarction of the basal forebrain region.

Multiple Sclerosis

The pathophysiological process of multiple sclerosis involves the seemingly random formation of plaques within the brain parenchyma. When the plaques occur in the temporal lobe

and the diencephalic regions, symptoms of memory impairment can occur. In fact, the most common cognitive complaints in patients with multiple sclerosis involve impaired memory, which occurs in 40 to 60 percent of patients. Characteristically, digit span memory is normal, but immediate recall and delayed recall

of information are impaired. The memory impairment can affect both verbal and nonverbal material.

Korsakoff's Syndrome Korsakoff's syndrome is an amnestic syndrome caused by thiamine deficiency, most commonly associated with the poor nutritional habits of people with chronic alcohol abuse. Other causes of poor nutrition (e.g., starvation), gastric carcinoma, hemodialysis, hyperemesis gravidarum, prolonged IV hyperalimentation, and gastric plication can also result in thiamine deficiency. Korsakoff's syndrome is often associated with Wernicke's encephalopathy, which is the associated syndrome of confusion, ataxia, and ophthalmoplegia. In patients with these thiamine deficiency-related symptoms, the neuropathological findings include hyperplasia of the small blood vessels with occasional hemorrhages, hypertrophy of astrocytes, and subtle changes in neuronal axons. Although the delirium clears up within a month or so, the amnestic syndrome either accompanies or follows untreated Wernicke's encephalopathy in approximately 85 percent of all cases. Patients with Korsakoff's syndrome typically demonstrate a change in personality as well, such that they display a lack of initiative, diminished spontaneity, and a lack of interest or concern. These changes appear frontal lobe-like, similar to the personality change ascribed to patients with frontal lobe lesions or degeneration. Indeed, such patients often demonstrate executive function deficits on neuropsychological tasks involving attention, planning, set shifting, and inferential reasoning consistent with frontal pattern injuries. For this reason, Korsakoff's syndrome is not a pure memory disorder, although it certainly is a good paradigm of the more common clinical presentations for the amnestic syndrome. The onset of Korsakoff's syndrome can be gradual. Recent memory tends to be affected more than is remote memory, but this feature is variable. Confabulation, apathy, and passivity are often prominent symptoms in the syndrome. With treatment, patients may remain amnestic for up to 3 months and then gradually improve over the ensuing year. Administration of thiamine may prevent the development of additional amnestic symptoms, but the treatment seldom reverses severe amnestic symptoms when they are present. Approximately one-third to one-fourth of all patients recover completely, and approximately one-fourth of all patients have no improvement of their symptoms.

Alcoholic Blackouts Some persons with severe alcohol abuse may exhibit the syndrome commonly referred to as an alcoholic blackout. Characteristically, these persons awake in the morning with a conscious awareness of being unable to remember a period the night before during which they were intoxicated. Sometimes specific behaviors (hiding money in a secret place and provoking fights) are associated with the blackouts.

Electroconvulsive Therapy Electroconvulsive therapy treatments are usually associated with retrograde amnesia for a period of several minutes before the treatment and anterograde amnesia after the treatment. The anterograde amnesia usually resolves within 5 hours. Mild memory deficits may remain for 1 to 2 months after a course of ECT treatments, but the symptoms are completely resolved 6 to 9 months after treatment.

Head Injury Head injuries (both closed and penetrating) can result in a wide range of neuropsychiatric symptoms, including dementia, depression, personality changes, and amnestic disorders. Amnestic disorders caused by head injuries are commonly associated with a period of retrograde amnesia leading up to the traumatic incident and amnesia for the traumatic incident itself. The severity of the brain injury correlates somewhat with

the duration and severity of the amnestic syndrome, but the best correlate of eventual improvement is the degree of clinical improvement in the amnesia during the first week after the patient regains consciousness. Transient Global Amnesia Transient global amnesia is characterized by the abrupt loss of the ability to recall recent events or to remember new information. The syndrome is often characterized by mild confusion and a lack of insight into the problem; a clear sensorium; and, occasionally, the inability to perform some well-learned complex tasks. Episodes last from 6 to 24 hours. Studies suggest that transient global amnesia occurs in 5 to 10 cases per 100,000 persons per year, although, for patients older than age 50 years, the rate may be as high as 30 cases per 100,000 persons per year. The pathophysiology is unknown, but it likely involves ischemia of the temporal lobe and the diencephalic brain regions. Several studies of patients with SPECT have shown decreased blood flow in the temporal and parietotemporal regions, particularly in the left hemisphere. Patients with transient global amnesia almost universally experience complete improvement, although one study found that approximately 20 percent of patients may have recurrence of the episode, and another study found that approximately 7 percent of patients may have epilepsy. Patients with transient global amnesia have been differentiated from patients with transient ischemic attacks in that fewer patients have diabetes, hypercholesterolemia, and hypertriglyceridemia, but more have hypertension and migrainous episodes. PATHOLOGY AND LABORATORY EXAMINATION Laboratory findings diagnostic of amnestic disorder may be obtained using quantitative neuropsychological testing. Standardized tests also are available to assess recall of wellknown historical events or public figures to characterize an individual's inability to

remember previously learned information. Performance on such tests varies among individuals with amnestic disorder. Subtle deficits in other cognitive functions may be noted in individuals with amnestic disorder. Memory deficits, however, constitute the predominant feature of the mental status examination and account largely for any functional deficits. No specific or diagnostic features are detectable on imaging studies such as MRI or CT. Damage of midtemporal lobe structures is common, however, and may be reflected in enlargement of third ventricle or temporal horns or in structural atrophy detected by MRI. DIFFERENTIAL DIAGNOSIS Table 21.4-1 lists the major causes of amnestic disorders. To make the diagnosis, clinicians must obtain a patient's history, conduct a complete physical examination, and order all appropriate laboratory tests. Other diagnoses, however, can be confused with the amnestic disorders. Dementia and Delirium Amnestic disorders can be distinguished from delirium because they occur in the absence of a disturbance of consciousness and are striking for the relative preservation of other cognitive domains. Table 21.4-2 outlines the key distinctions between Alzheimer's dementia and the amnestic disorders. Both disorders can have an insidious onset with slow progression, as in a Korsakoff's psychosis in a chronic drinker. Amnestic disorders, however, can also develop precipitously, as in Wernicke's encephalopathy, transient global amnesia, or anoxic insults. Although Alzheimer's dementia progresses relentlessly, amnestic disorders tend to remain static or even improve after the offending cause has been removed. In terms of the actual memory deficits, the amnestic disorder and Alzheimer's disease still differ. Alzheimer's disease has an impact on retrieval in addition to encoding and consolidation. The deficits in Alzheimer's disease extend beyond memory to general knowledge (semantic memory), language, praxis, and general function. These are spared in amnestic disorders. The dementias associated with Parkinson's disease, AIDS, and other subcortical disorders demonstrate disproportionate impairment of retrieval, but relatively intact encoding and consolidation and thus can be distinguished from amnestic disorders. The subcortical pattern dementias are also likely to display motor symptoms, such as bradykinesia,

chorea, or tremor, that are not components of the amnestic disorders. Table 21.4-2 Comparison of Syndrome Characteristics in Alzheimer's Disease and Amnestic Disorder

Normal Aging Some minor impairment in memory may accompany normal aging, but the requirement that the memory impairment cause significant impairment in social or occupational functioning should exclude normal aging from the diagnosis. **Dissociative Disorders** The dissociative disorders can sometimes be difficult to differentiate from the amnestic disorders. Patients with dissociative disorders, however, are more likely to have lost their orientation to self and may have more selective memory deficits than do patients with amnestic disorders. For example, patients with dissociative disorders may not know their names or home addresses, but they are still able to learn new information and remember selected past memories. Dissociative disorders are also often associated with emotionally stressful life events involving money, the legal system, or troubled relationships. **Factitious Disorders** Patients with factitious disorders who are mimicking an amnestic disorder often have inconsistent results on memory tests and have no evidence of an identifiable cause. These findings, coupled with evidence of primary or secondary gain for a patient, should suggest a factitious disorder. **COURSE AND PROGNOSIS** The course of an amnestic disorder depends on its etiology and treatment, particularly acute treatment. Generally, the amnestic disorder has a static course. Little improvement is seen over time, but also no progression of the disorder occurs. The exceptions are the acute amnesias, such as transient global amnesia, which resolves entirely over hours to days, and the amnestic disorder associated with head trauma, which improves steadily in the months subsequent to the trauma. Amnesia secondary to processes that destroy brain tissue, such as stroke, tumor, and infection, are irreversible, although, again, static, after the acute infection or ischemia has been staunched.

TREATMENT

The primary approach to treating amnestic disorders is to treat the underlying cause. Although a patient is amnestic, supportive prompts about the date, the time, and the patient's location can be helpful and can reduce the patient's anxiety. After resolution of the amnestic episode, psychotherapy of some type (cognitive, psychodynamic, or supportive) may help patients incorporate the amnestic experience into their lives. **Psychotherapy** Psychodynamic interventions may be of considerable value for patients who have amnestic disorders that result from insults to the brain. Understanding the course of recovery in such patients helps clinicians to be sensitive to the narcissistic injury inherent in damage to the CNS. The first phase of recovery, in which patients are incapable of processing what happened because the ego defenses are overwhelmed, requires clinicians to serve as a supportive auxiliary ego who explains to a patient what is happening and provides missing ego functions. In the second phase of recovery, as the realization of the injury sets in, patients may become angry and feel victimized by the malevolent hand of fate. They may view others, including the clinician, as bad or destructive, and clinicians must contain these projections without becoming punitive or retaliatory. Clinicians can build a therapeutic alliance with patients by explaining slowly and clearly what happened and by offering an explanation for a patient's internal experience. The third phase of recovery is integrative. As a patient accepts what has happened, a clinician can help the patient form a new identity by connecting current experiences of the self with past experiences. Grieving over the lost faculties may be an important feature of the third phase. Most patients who are amnestic because of brain injury engage in denial. Clinicians must respect and empathize with the patient's need to deny the reality of what has happened. Insensitive and blunt confrontations destroy any developing therapeutic alliance and can cause patients to feel attacked. In a sensitive approach, clinicians help patients accept

their cognitive limitations by exposing them to these deficits bit by bit over time. When patients fully accept what has happened, they may need assistance in forgiving themselves and any others involved, so that they can get on with their lives. Clinicians must also be wary of being seduced into thinking that all of the patient's symptoms are directly related to the brain insult. An evaluation of preexisting personality disorders, such as borderline, antisocial, and narcissistic personality disorders, must be part of the overall assessment; many patients with personality disorders place themselves in situations that predispose them to injuries. These personality features may become a crucial part of the psychodynamic psychotherapy. Recently, centers for cognitive rehabilitation have been established whose rehabilitation-oriented therapeutic milieu is intended to promote recovery from brain injury, especially that from traumatic causes. Despite the high cost of extended care at these sites, which provide both long-term institutional and daytime services, no data have been developed to define therapeutic effectiveness for the heterogeneous groups of

Revision #1

Created 2026-01-04 19:51:19 UTC by Omar Ayman

Updated 2026-01-04 19:51:19 UTC by Omar Ayman