Dissociative amnesia: Epidemiology, pathogenesis, clinical manifestations, course, and diagnosis

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INTRODUCTION — Dissociative amnesia is a potentially reversible memory impairment that primarily affects autobiographical memory [1-3]. In dissociative amnesia, the patient cannot recall important autobiographical information, usually of a traumatic or stressful nature, although more extensive memory loss may be reported.

Dissociative fugue, a subtype of dissociative amnesia in DSM-5 [3], is characterized by sudden unexpected travel or wandering in a dissociated state, with subsequent dissociative amnesia for the fugue episode, and often for some or all of the patient's life history.

Dissociative amnesia and dissociative fugue (a subtype) are discussed here. Other dissociative disorders, including dissociative identity disorder, depersonalization disorder, and dissociative aspects of posttraumatic stress disorder, are discussed separately. (See "Dissociative identity disorder: Epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis" and "Depersonalization/derealization disorder: Epidemiology, pathogenesis, clinical manifestations, course, and diagnosis" and "Psychotherapy of depersonalization/derealization disorder" and "Dissociative aspects of posttraumatic stress disorder: Epidemiology, clinical manifestations, assessment, and diagnosis".)

DEFINITIONS

- Autobiographical memory [1] Episodes recollected from a person's life, with a combination of
 episodic autobiographical memory and semantic autobiographical memory [4]. Autobiographical
 memory includes recall of cognitive, emotional, and motivational aspects of events.
- Semantic memory Memory of objects, facts, and concepts, including words and their meaning, such as learning the skill of reading
- Episodic memory Memory of specific events and their context such as "the first day of school when I tried to read a book"
- Procedural memory Memory of how to perform different actions and skills, such as riding a bike or tying shoes.

EPIDEMIOLOGY — The prevalence of dissociative amnesia found in population-based samples ranges from 1.8 percent in the previous 12 months to 7.3 percent lifetime.

12 month prevalence

- 1.8 percent (1 percent male, 2.6 percent female) in the United States (US)
- Lifetime prevalence
 - 6 percent, Winnipeg, Canada [5]
 - 7.3 percent, Turkey (all female sample) [6]

The prevalence of dissociative amnesia diagnosed using standardized diagnostic inventories in psychiatric outpatients and inpatients has been found to range from 7.3 to 11.4 percent [7,8].

PATHOGENESIS — The pathogenesis of dissociative amnesia is unknown, though environmental, genetic, and other neurobiological factors are believed to play a role in the development of the disorder.

Conceptual model — Development of dissociative disorders has been conceptualized based on an epigenetic model, which posits that the disorders result from genes and the environmental factors that influence their expression.

Dissociation is posited to be an expression of a genetic diathesis to dissociative disorders combined with the occurrence of overwhelming and/or traumatic experiences during childhood or later life [2].

Genetic — Initial twin studies did not show a genetic contribution to "pathological dissociation" [9]. Subsequent twin studies reported that about 50 percent of the variance in the development of dissociative symptoms could be accounted for by genetic factors, and the remainder to "non-shared" environmental factors, eg, traumatic experiences [10,11]. (See "Depersonalization/derealization disorder: Epidemiology, pathogenesis, clinical manifestations, course, and diagnosis", section on 'Neurobiology'.)

Several studies have found associations between genetic variants and dissociation/related symptoms:

- A cross sectional survey of 935 adults drawn from the general population found a relationship between dissociation, a history of childhood interpersonal trauma, and genetic polymorphism in the promoter region of the serotonin transporter (5-HTT) gene (SS 5-HTTLPR genotype) [12,13].
- A study reported an interaction among a functional catechol-O-methyltransferase (COMT)
 polymorphism, Val158Met, and trauma scores (primarily physical abuse not sexual abuse), and
 dissociation scores [14]. The Val/Val genotype was associated with increased dissociation in
 subjects reporting higher levels of childhood trauma. The Met/Met genotype subjects displayed
 decreased dissociation with increasing self-reported childhood trauma.
- The twin study, described previously, reported an independent association between dissociation scores and the SS 5-HTTLPR genotype variant, traumatic experiences, and depression [13].

Environmental — A history of psychological trauma is strongly associated with dissociative amnesia, and is widely believed to contribute etiologically to the development of the disorder [2,15,16].

Dissociative amnesia has been reported subsequent to a variety of different types of traumatic events, including [17,18]:

- Childhood physical or sexual abuse [19-22]
- Adult sexual assault [23]
- Sexual trafficking [24]
- Military combat [25]

- Natural disaster such as an earthquake [26] or firestorm [27]
- Nazi and Cambodian holocausts [28-30]
- Torture [31]

The association between traumatic experiences and dissociative amnesia has been found in clinical and community samples of individuals drawn from many different populations, and in studies using a wide variety of designs and data collection methods. Documentation supporting the occurrence of the index trauma has included medical records, social service records, and other corollary sources [12,18,19,26,28,29,32-52].

Studies of varied designs, clinical and population-based samples, and varied types of trauma have found the following characteristics of traumatic experiences to be associated with an increased likelihood of subsequent dissociative amnesia [2,53-55]:

- Trauma caused by human assault rather than natural disaster
- Repeated traumatization as opposed to single events
- Longer duration of trauma
- Fear of death or significant harm during trauma
- Trauma caused by multiple perpetrators
- Close relationship between perpetrator and victim
- Betrayal by a caretaker as part of abuse
- Threats of death or significant harm by perpetrator if victim discloses
- Violence of trauma (eg, leading to physical injury)
- Earlier age at onset of trauma

Other neurobiological — There is preliminary evidence from neurobiological studies in dissociative amnesia of inhibition by frontal systems of temporal/hippocampal and occipital areas associated with autobiographical memory, although other circuitry has been described as involved as well [56-59]. These frontal inhibitory neural network patterns are similar to those found in experimental studies of post-hypnotic amnesia and memory suppression using non-clinical subjects [60,61].

CLINICAL MANIFESTATIONS — In a typical clinical presentation of dissociative amnesia, relatively large groups of memories, perceptions, and associated affects have become unavailable, not just single memories, feelings, or thoughts [62]. The unavailable memories usually relate to autobiographical information, for example [32]:

- Who a person is
- What he or she did
- Where he or she went
- With whom he or she spoke
- What was said
- What he or she thought and felt at the time

Dissociative amnesia can be characterized by localized, selective, or generalized amnesia [3]:

- Localized amnesia Lack of autobiographical memory for a specific period of time
- Selective amnesia Partial memory for a period of time, eg, remembering only parts of year when the person was in combat

 Generalized amnesia — Person cannot recall the entirety of the life history, usually accompanied by loss of memory for the person's identity

Dissociative amnesia is characterized by retrieval deficits in both episodic and semantic aspects of autobiographical memory. The ability to remember new factual information is generally intact, as are general cognitive functioning and language capacity. Procedural memory is not typically affected, but can be lost in extreme forms of the disorder [63]. (See 'Definitions' above.)

Dissociative amnesia generally has a quality of clear-cut onsets/offsets, whereas ordinary autobiographical memory usually has a gradient, with better recall of more recent information [64].

Other symptoms of memory loss in dissociative amnesia include:

- Fragmentary recall of life history
- Unrecalled behavior
- Unexplained possessions
- Inexplicable changes in relationships
- Fluctuations in skills/habits/knowledge
- Not remembering people who describe significant interactions with him/her
- Brief lapses of memory during clinical interview or other interactions

The duration of the period subject to amnesia has been observed to vary, ranging from:

- Failure to recall some or all of the details of the index trauma [65]
- Unavailability of everyday non-traumatic memories [42]
- Gaps in retrospective recall of long periods of life [42]

Most patients who present with dissociative amnesia have a history of one or more traumatic experiences [15]. Longer gaps in memory have been seen more commonly subsequent to chronic childhood physical and sexual abuse [42].

While there are a number of subtypes of dissociative amnesia (<u>table 1</u>) [2], there are two basic clinical presentations [15,66] (see <u>'Definitions'</u> above):

- Overt generalized or dense-localized dissociative amnesia (Type 1)
- Covert dissociative amnesia (Type 2)

Overt dissociative amnesia — Patients with overt dissociative amnesia usually present with a dramatic, profound loss of memory for personal history, often accompanied by amnesia for personal identity. Generalized dissociative amnesia affects all of a patient's autobiography. Dense localized dissociative amnesia affects some substantial parts of a patient's autobiography but not others.

Because of the extent of their overt memory deficits, these patients are usually brought rapidly to clinical attention, most commonly in the emergency department or in acute outpatient medical or neurologic services. Inpatients with the disorder are more commonly seen by consulting psychiatrists on general medical inpatient units rather than on acute psychiatric inpatient units.

Patients with overt dissociative amnesia can appear confused, perplexed, and baffled by their deficits, although others appear relatively unconcerned despite the extent of their symptoms. They may recall factual information about the outside environment (eg, historical events or famous faces) but recall only limited information pertaining to their own autobiographical experiences [67].

Dissociative fugue — A subset of patients with generalized dissociative amnesia present with dissociative fugue, involving "apparently purposeful travel or bewildered wandering that is associated with amnesia for identity or for other important autobiographical information" [3]. There are limited systematic data on individuals with dissociative fugue, in part because they may be resistant to being interviewed and may flee again after coming to clinical attention. A panel of clinicians with expertise in dissociative disorders has suggested that many cases of dissociative fugue may be a manifestation of dissociative identity disorder [2].

Covert dissociative amnesia — Based on the experience of clinicians specializing in dissociative disorders, the "covert" form of dissociative amnesia is more common than the overt form [2]. Patients rarely complain of this form of dissociative amnesia. It is usually discovered by careful questioning in the diagnostic interview or in subsequent interviews during psychotherapy.

This type of dissociative amnesia generally presents as a retrospective gap or series of gaps in autobiographical experience, often a mixture of significant localized, systematized, and/or selective dissociative amnesia (<u>table 1</u>).

These individuals often fit the clinical construct of "complex posttraumatic stress disorder" [68,69], where repeated early life maltreatment leads to a variety of deficits in emotional regulation, sense of self, body image, relationships, and somatization, as well as problems with dissociation, self-destructiveness, and posttraumatically distorted beliefs about the self, others, and the world. Patients with this form of dissociative amnesia may have additional dissociative symptoms, such as depersonalization, derealization, or spontaneous trance experiences [2,8,66]. (See "Dissociative aspects of posttraumatic stress disorder: Epidemiology, clinical manifestations, assessment, and diagnosis".)

Comorbidity — There are few systematic studies of psychiatric disorders co-occurring with dissociative amnesia. Many patients with dissociative amnesia have experienced physical and/or sexual abuse during childhood. Large population studies have described adverse psychiatric outcomes associated with such early life trauma including depression, suicidality, auditory hallucinations, substance use disorders, posttraumatic stress disorder, anxiety disorders, eating disorders, somatic symptom disorders, and personality disorders [70-75].

COURSE — There are limited systematically collected data on the course of dissociative amnesia.

Most patients who present with dissociative amnesia have a history of one or more traumatic experiences [15]. Longer gaps in memory have been seen more commonly subsequent to chronic childhood physical and sexual abuse [42]. In a retrospective study of over 13,000 HMO enrollees, the duration of sexual abuse experienced during childhood was associated with greater severity, frequency, and violence of the abuse. A longer period of amnesia of aspects of early life history, up to inability to recall years of the person's early life, was associated with greater severity of abuse [76,77].

In our clinical experience, many patients with the acute, overt form of dissociative amnesia respond rapidly to intervention such as removal from a traumatic environment (eg, combat) and provision of emergency, clinical treatment [15]. A subgroup of these patients, particularly those with dissociative fugue, may have prolonged, refractory dissociative amnesia for life history and/or identity. Our clinical experience suggests that these individuals are usually very impaired interpersonally and occupationally.

Our clinical experience suggests that the course of dissociative amnesia during treatment may be positively associated with better social and occupational functioning, the presence of social supports,

and lack of major, chronic comorbidities such as refractory substance abuse, eating disorders, and severe health problems. (See 'Comorbidity' above.)

Among patients with dissociative amnesia and a history of childhood sexual or physical abuse, studies have found that recall of previously dissociated memory frequently occurs outside of therapeutic settings. Memories of the abuse were triggered by a variety of stimuli [43,53,65], including a patient's own child reaching an age at which the patient was abused, a patient's child being abused, media accounts of trauma or abuse, death of an abusive parent, experiences of contemporary trauma (even minor ones), a variety of sensory cues, and feeling safe in one's life situation.

ASSESSMENT — Clinical assessment of a patient with dissociative amnesia would typically identify a pattern of deficits in autobiographical memory with normal cognitive functioning, intact memory for everyday information, facts, and skills, normal orientation to current circumstances, and normal interpersonal grasp of the interview. A comprehensive psychiatric assessment, including a mental status exam, and a medical history and physical exam, should be done to rule out medical conditions, substance use disorders, and cognitive disorders such as dementias and delirium prior to diagnosing dissociative amnesia. Brain imaging and/or an electroencephalogram may be needed in patients with focal findings on the neurologic exam.

In more complex or ambiguous cases, a detailed review of the patient's medical and psychiatric records may be needed as well as consultation with corollary sources of the patient's history to rule out factors such as substance abuse, factitious or malingered amnesia, and co-morbid brain injury [78].

Questions useful for testing memory in cases of suspected dissociative amnesia include:

- Do you have gaps in your memory of your life?
- Are you missing parts of your memory for your life history?
- Are you missing memories of some important events in your life, for example, weddings, birthdays, graduations, pregnancies, birth of children?
- Do you remember some parts of your life better than others? As an example, when you were growing up, do you recall home better or school better?
- Do you "lose" periods of time or have gaps in your experience of time? What is the longest period of time you have lost, eg, minutes, hours, days, weeks, months, years?
- Do you ever have blackouts or blank spells?

A careful sequential history may be needed to identity periods of amnesia, to distinguish between dissociation and substance use, and sort out other more clinically complex clinical presentations. A more systematic inquiry may include asking for the patient's first memory, then asking for subsequent memories in turn. This may reveal significant gaps in the person's autobiographical memory. In patients who appear to have problems with memory for childhood, the clinician can ask the names of the patient's teachers and schools. Patients with dissociative amnesia may not recall many of their teachers in early school years, or even what occurred at school.

It is helpful to ask patients for specific, detailed examples when the patient gives a positive answer one of these queries. The patient should be asked if he or she was intoxicated on alcohol or drugs during some or all of the time that they report memory problems. Drug, alcohol, and dissociative memory problems may co-exist in the same person, and some dissociative amnesia patients may also have

cognitive disorders related to traumatic brain injury. Some patients with dissociative amnesia rationalize their amnesia by ascribing it to substance abuse.

Patients should be assessed for other dissociative symptoms including (see "Dissociative aspects of posttraumatic stress disorder: Epidemiology, clinical manifestations, assessment, and diagnosis", section on 'Concepts and definitions'):

- Depersonalization Detachment or estrangement from one's self
- Derealization The sense that the external world is strange or unreal
- Spontaneous trance experiences

Dissociative amnesia may be associated with memory that is derealized, ie, the person does not experience memory as first hand, but as something that they "know" about, as if they read it in a book. Some may only know about their childhood history from what relatives tell them, or from looking at family photo albums. It may be helpful to ask if the person "knows" information about the past as if 'You were there", or do you more "know about it", "were told about it" by your family or friends, or it feels like "you read about it in the paper, or saw it on television".

Rating scales — The Dissociative Experiences Scale-Revised (DES-R) can be used to assess the initial severity of dissociative amnesia and monitor the response to treatment over time. The DES-R is a 28-item patient self-administered scale (<u>table 2</u>) that can be used for assessing and monitoring the severity of amnesia, absorption, identity alteration, and depersonalization/derealization [79,80].

DIAGNOSIS — DSM-5 diagnostic criteria for dissociative amnesia are as follows [3]:

• A. An inability to recall important autobiographical information, usually of a traumatic or stressful nature, that is inconsistent with ordinary forgetting.

Note: Dissociative amnesia most often consists of localized or selective amnesia for a specific event or events, or generalized amnesia for identity and life history.

- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The disturbance is not attributable to the physiological effects of a substance (eg, alcohol or other drug of abuse, a medication) or a neurological or other medical condition (eg, partial complex seizures, transient global amnesia, sequelae of a closed head injury/traumatic brain injury, other neurological condition).
- D. The disturbance is not better explained by dissociative identity disorder, posttraumatic stress disorder, acute stress disorder, somatic symptom disorder, or major or mild neurocognitive disorder.

Specifier — Specify if: with dissociative fugue, ie, apparently purposeful travel or bewildered wandering that is associated with amnesia for identity or for other important autobiographical information.

Differential diagnosis — The differential diagnosis of dissociative amnesia includes normal limitations in autobiographic memory, a cognitive disorder, acute and posttraumatic stress disorder, other dissociative disorders, substance use/disorders, traumatic brain injury, and factious disorder/malingering (table 3).

Normal autobiographical memory — Normal limitations in autobiographical memory typically include:

- Amnesia in adults for pre-verbal memories
- Fewer memories of life before age five or six
- A gradient for recall with more recent events more likely to be remembered and memories of earlier events diminishing with time.
- · Amnesia for sleep and dreaming

The gradient for recall seen in normal memory contrasts with a common presentation of dissociative amnesia as having a distinct boundary, onset, and offset, eg, a lack of memory for a specific age, such as fourth grade, or a lack of recall relating to a particular person, activity, or time of year [81].

Cognitive disorders — In cognitive disorders such as delirium and the dementias, autobiographical memory problems are embedded in a broad set of other cognitive and memory problems, as well as deterioration of the personality [2,53,82]. Dissociative amnesia affects autobiographical memory preferentially and does not affect the ability to learn new cognitive information or perform tasks. (See "Evaluation of cognitive impairment and dementia", section on 'Diagnostic approach' and "Diagnosis of delirium and confusional states".)

Memory problems in cognitive disorders are generally irreversible. In dissociative amnesia, the memories may begin to remit once the individual is removed from acutely traumatizing circumstances (eg, combat) [2,83] or may potentially be reversed through treatment [84,85].

Acute and posttraumatic stress disorder — Dissociative amnesia can share certain features with acute stress disorder (ASD) and posttraumatic stress disorder (PTSD) — eg, a history of trauma, amnesia for the traumatic event, and symptoms of numbing and dissociation. However, symptoms of hyperarousal and avoidance are not characteristic of dissociative amnesia, and memory loss in that disorder is typically far more extensive and pervasive than in ASD/PTSD. (See "Acute stress disorder in adults: Epidemiology, pathogenesis, clinical manifestations, course, and diagnosis" and "Posttraumatic stress disorder in adults: Epidemiology, pathophysiology, clinical manifestations, course, assessment, and diagnosis".)

Other dissociative disorders — Patients with other dissociative disorders may have amnestic features similar to those of dissociative amnesia, but have other clinical features distinguishing them from dissociative amnesia.

To be diagnosed with dissociative identity disorder (DID), a person would additionally have to experience two or more distinct identity states with differences in memory, affect, or clinical presentation among the identities. In contrast to dissociative amnesia, a patient with DID would experience intrusion of material from dissociated aspects of identity [86]. (See "Dissociative identity disorder: Epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis".)

In depersonalization disorder (DPD), the patient generally has intact memory for life history, but experiences repeated or chronic states of depersonalization and derealization. Studies of DPD patients have found reports of childhood verbal and emotional abuse, but not the high rates of childhood physical and sexual abuse as reported for the dissociative amnesia and DID patients [87]. (See "Depersonalization/derealization disorder: Epidemiology, pathogenesis, clinical manifestations, course, and diagnosis".)

Substance use disorders — Amnesia can result from intoxication or chronic use of numerous substances, including alcohol, benzodiazepines, and marijuana. In most cases, a careful chronologic history of memory impairment and of periods of intoxication can help distinguish between substance-induced amnesia and dissociative amnesia. A period of abstinence for weeks or (in cases of more severe or longer-lasting substance use) months may be needed prior to assessment of the patient for dissociative amnesia.

Co-occurring substance abuse can complicate diagnosis in some patients with dissociative amnesia. It is common for patients with both disorders to ascribe their memory problems to substance-related "black outs". However, a careful history may reveal that at least some of the autobiographical memory problems relate to periods of sobriety (eg, in childhood or adolescence before substance use began).

Amnesia from chronic substance abuse/dependence can usually be identified by presence of additional signs and symptoms. As an example, the amnesia of Wernicke's encephalopathy is typically accompanied by disorientation, confabulation, inability to learn new information, and often by oculomotor dysfunction and/or gait disturbance. (See "Wernicke encephalopathy", section on 'Diagnosis'.)

Factitious disorder or malingering — Dissociative amnesia should be distinguished from a factitious disorder or malingering [82], presentations in which the symptoms of amnesia are feigned. No test or procedure reliably distinguishes dissociative amnesia from these disorders [88].

Factitious or malingered amnesia is more common in individuals presenting with the following [15,89,90]:

- Acute, florid forms of amnesia
- A context of financial, sexual, or legal problems
- A wish to escape from combat or similar extremely stressful circumstances

These factors may also be present in patients with non-feigned dissociative amnesia [91]. Detailed review of medical history and obtaining history from additional informants can aid diagnosis.

SUMMARY AND RECOMMENDATIONS

- Dissociative amnesia is a potentially reversible memory impairment that primarily affects autobiographical memory. Patients with the disorder cannot recall important personal information, usually of a traumatic or stressful nature. (See <u>'Introduction'</u> above.)
- The 12 month prevalence of dissociative disorders in the US general population has been estimated to be 1 percent in males and 2.6 percent in females. (See <u>'Epidemiology'</u> above.)
- While the pathogenesis of dissociative amnesia is unknown, genetic and environmental factors —
 particularly trauma are believed to play a role in the development of the disorder. Dissociative
 amnesia has been strongly associated with a history of traumatic experiences including childhood
 physical or sexual abuse, military combat, or natural disasters. (See <u>'Pathogenesis'</u> above.)
- Dissociative amnesia typically manifests with relatively large groups of autobiographical memories, perceptions, and associated affects that have become unavailable. Deficits are seen in episodic and semantic, but usually not in procedural memory. The ability to remember new factual information is generally intact, as are general cognitive functioning and language capacity.
 (See 'Clinical manifestations' above and 'Definitions' above.)

- Patients with overt dissociative amnesia usually present with a dramatic, profound loss of memory
 for personal history, often accompanied by amnesia for personal identity. In patients with the covert
 form of the disorder, the memory deficit is typically a gap or series of gaps in autobiographical
 experience that become apparent with careful questioning in the diagnostic interview. (See <u>'Overt dissociative amnesia'</u> above.)
- Assessment for dissociative amnesia should rule out medical conditions, substance use disorders (SUD), traumatic brain injury, and cognitive disorders such as the dementias and delirium as the cause of memory problems. Patients with dissociative amnesia may have a co-occurring substance use or mood disorder. (See <u>'Assessment'</u> above and <u>'Diagnosis'</u> above.)

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