Dissociative amnesia

Angelica Staniloiu, Hans J Markowitsch

Lancet Psychiatry 2014; 1: 226–41

Published Online July 2, 2014 http://dx.doi.org/10.1016/S2215-0366(14)70279-2

Physiological Psychology, University of Bielefeld, Bielefeld, Germany (A Staniloiu MD, Prof H J Markowitsch PhD); **Cognitive Interaction Technology, Centre of Excellence, Bielefeld, Germany** (Prof H J Markowitsch); **and Hanse Institute for Advanced Study, Delmenhorst, Germany** (A Staniloiu)

Correspondence to: Dr Angelica Staniloiu, Physiological Psychology, University of Bielefeld, PO Box 100131, 33501 Bielefeld, Germany **astaniloiu@uni-bielefeld.de**

Dissociative amnesia is one of the most enigmatic and controversial psychiatric disorders. In the past two decades, interest in the understanding of its pathophysiology has surged. In this report, we review new data about the epidemiology, neurobiology, and neuroimaging of dissociative amnesia and show how advances in memory research and neurobiology of dissociation inform proposed pathogenetic models of the disorder. Dissociative amnesia is characterised by functional impairment. Additionally, preliminary data suggest that affected people have an increased and possibly underestimated suicide risk. The prevalence of dissociative amnesia differs substantially across countries and populations. Symptoms and disease course also vary, indicating a possibly heterogeneous disorder. The accompanying clinical features differ across cultural groups. Most dissociative amnesias are retrograde, with memory impairments mainly involving the episodic-autobiographical memory domain. Anterograde dissociative amnesia occurring without significant retrograde memory impairments is rare. Functional neuroimaging studies of dissociative amnesia with prevailing retrograde memory impairments show changes in the network that subserves autobiographical memory. At present, no evidence-based treatments are available for dissociative amnesia and no broad framework exists for its rehabilitation. Further research is needed into its neurobiology, course, treatment options, and strategies to improve differential diagnoses.

Introduction

Amnesic disorders comprise severe memory impairment, occurring in an alert individual, in the absence of other major cognitive impairments.[1] Historically, these disorders have been classified as caused by a general medical disorder, attributable to the persisting effects of substance misuse, due to psychological mechanisms, or mixed mechanisms. This classification is still used in the International Classification of Diseases volume 10 (ICD-10),[2] but several changes have been made in the new (fifth) edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). DSM-5[3] incorporates the DSM–IV text revision (DSM-IV-TR) category of "amnestic disorders" under "neurocognitive disorders" and recommends specific descriptions of the types of impaired memories, implicitly discouraging the use of the term "amnesia". However, dissociative amnesia remains a diagnostic entity in DSM-5.[3] The amended definition of dissociation in DSM-5[3] (panel 1) is closer to the original description by Janet in 1894[6] and narrows the gap between the ICD-10[2] and previous editions of the DSM; it matches neuropsychological and neuroimaging findings and aligns with integrative neural models of cognition and emotion.[7]

In this Review, we provide an overview of recent research findings about the diagnosis, epidemiology, pathophysiology, course, and treatment of dissociative amnesia and its variant, dissociative fugue. We discuss debates pertaining to pathogeny, and future directions to improve differential diagnoses and guide treatment.

The concept of dissociative amnesia

Historically, attempts have been made to encapsulate the group of amnesic disorders caused by prevailing psychological mechanisms into several constructs (panel 1). Although sometimes used interchangeably, these constructs have different theoretical bases and treatment implications. In this Review, we use the term "dissociative" to align with existing nosologies, but we also discuss its limitations. The term dissociative amnesia is a priori theoretically loaded because it assumes dissociation to be the primary or sole pathogenic mechanism of the cognitive impairment. The weight of theoretical load differs between ICD-10 and DSM-5. The ICD-10 directly suggests that trauma or psychological stress are key players in the causes of dissociative amnesia.[8] In ICD-10, dissociative (conversion) disorders are operationalised diagnoses that explicitly need the finding of "convincing associations in time between the symptoms of the disorder and stressful events, problems or needs". By contrast with ICD-10, the DSM-5 does not list the existence of these associations as an explicit diagnostic criterion, although in its descriptive section it mentions that "dissociative disorders are frequently found in the aftermath of trauma". The DSM-IV specification of criterion A for dissociative amnesia that "the inability (to recall information) may be the outcome of an underlying trauma or stress" was abandoned in DSM-IV-TR. The evolution of DSM diagnostic criteria for dissociative amnesia could be interpreted as representative of openness towards a possible diversity of causal models and antecedents for these disorders.[8]

The term dissociative amnesia is used to describe a diagnostic entity or a negative dissociative symptom of another disorder. Negative dissociative symptoms refer to a decrease in function (eg, amnesia), whereas positive symptoms denote an increase in function (eg, hypermnesia). Although dissociative fugue is a separate entity in ICD-10,[2] clinical, neuropsychological, and neuroimaging data support its reclassification in DSM-5.[3,9–11]

Clinical and psychological features

The term dissociative amnesia includes a heterogeneous group of disorders in terms of clinical and neuropsychological presentations, associated features, disease course, antecedents, memory-related pathogenetic

mechanisms, and possibly underlying ideologies (ie, different definitions or conceptualisations). Some cases involve losses (retrieval blockades) of all autobiographical information for years of the patient's life. Other cases can involve amnesia for individual aspects of a traumatic event and might reflect incomplete encoding. In some cases diagnosed as dissociative amnesia, patients are believed to have amnesia for an entire traumatic event

Panel 1: **Common terms for dissociative amnesic disorders, subtypes, and related disorders, and the underlying mechanisms**[1–4]

Hysterical amnesia: Outdated term, used since the end of the 19th century to describe a stress-related disorder leading to extraordinary emotional excitement and memory loss.

Dissociative amnesia: Inability to consciously recall autobiographical information in the absence of significant brain damage (as detectable by conventional structural neuroimaging). It is a priori theoretically loaded since it assumes dissociation to be the primary or only pathogenetic mechanism.

Dissociative fugue: A retrograde variant of "dissociative amnesia" in DSM-5, with loss of personal identity and dislodging from the usual place of living (apparently purposeful travelling or wandering).

Psychogenic amnesia: Broader term than dissociative amnesia, potentially linking amnesia to a wider range of psychological mechanisms (dissociation, suppression, cognitive avoidance, motivated forgetting, and exaggeration of symptoms solely to assume the role of being ill).

Functional amnesia: Advocated by de Renzi and colleagues[5] as a "more suitable term to classify patients whose memory disorders cannot be traced back to organic or psychological causes". Might be more acceptable to patients than the term dissociative amnesia.

Mnestic block syndrome: Retrograde memory block, caused by psychological effects such as severe stress or psychological trauma.

Medically unexplained amnesia: Term suggesting that a medical explanation might arise in the future. Can also refer to non-psychogenic amnesia.

Idiopathic amnesia: Term suggesting an amnesic disorder of unknown or uncertain cause. The term might be suitable for amnesias that cannot be linked to neurological, psychological, or substance-induced causes.

Retrograde amnesia: In general, an inability to consciously access information from the past after a certain incident—usually brain damage or stress; sometimes denotes amnesia for events that happened just before the occurrence of a brain injury.

Post-traumatic amnesia: Term used in traumatic brain injury literature with two meanings. It can describe the phase after the resolution of delirium that is characterised mainly by memory impairments. In some cases, the term overlaps with delirium, including a period from injury until full recovery of consciousness and memory.

Isolated, focal, or disproportionate persistent retrograde amnesia: Disorders that might suggest a psychogenic or mixed cause. The disorders can also be caused by physical insults only.

Systematised amnesia: Amnesia for some categories of information (eg, for a particular person or group of people).

Selective amnesia: Amnesia for some, but not all, of the events from a time period.

Continuous amnesia: Ongoing forgetting within minutes to hours of all new personal events in life (anterograde amnesia).

Localised amnesia: Failure to recall events from a circumscribed period of time.

Dissociative identity disorder: Existence of two or more personality states, repeatedly taking control over a person's behaviour. Gaps exist in recall of traumatic material, but also of everyday events. In DSM-5, dissociative identity disorder (formerly called multiple personality disorder) is a separate disorder from dissociative amnesia, but amnesia is one of the main symptoms.

Malingering: Intentional reporting of symptoms (eg, memory complaints) for personal gain (eg, money).

Simulating: Imitating a disorder or symptom (eg, memory problems).

Feigning: Pretending or simulating a deficit. In factitious disorder, feigning occurs in the absence of obvious external rewards or incentives.

(Pathological) Dissociation: "A disruption and/or discontinuity in the normal integration of consciousness, memory, identity, emotion, perception, body representation, motor control, and behavior" (American Psychiatric Association[3]).

Suppression: Intentional, conscious operation that reduces the access to consciousness of target information.

Repression: Unconscious operation (strict definition); or both conscious and unconscious operations (less strict definition), reducing accessibility to consciousness of target information.

Post-hypnotic amnesia: Inability to recall events that had been present during hypnosis.

Confabulation: Narrative story of an event that has not been experienced.

Intrusion: Creation of a new or imagined part of an experienced event.

False recognition: A new item is claimed to be an old or studied one.

Ribot's law: Principle that in retrograde amnesia memories from childhood and youth are best preserved, whereas those from recent periods are lost most easily.

such as childhood sexual abuse, while nevertheless maintaining normal autobiographical memory for other aspects of their lives. It is often claimed that such individuals can later recover the formerly inaccessible memory of the traumatic event. This latter postulated form of dissociative amnesia remains highly controversial, with some authorities suggesting that it is common[12–14] and others suggesting that it is devoid of empirical support.[15–17] The debate about the delayed recall of trauma memories has been partly fuelled by differences in patient samples (patients routinely encountered in clinical and research practices *vs* extreme and atypical cases).[18]

Dissociative amnesias nevertheless share some core features. Their understanding is helped by the comprehension of the existing classification of memory according to time and content dimensions (figures 1, 2).[1] The memory impairment in dissociative amnesia is most frequently of a retrograde nature and is often limited to the episodic-autobiographical domain. It could be circumscribed or generalised. It does not always follow Ribot's law, which states that, in retrograde amnesia, memories from the remote past are better preserved than are those from recent past (panel 1). Old general knowledge, for example knowledge obtained during school time, is usually intact. Variable impairments of old public semantic memory (time-specific knowledge of public events and famous faces and names, which is typically shared in a cultural community) have been described,[19,20] but how these deficits are related to an impairment in semantic knowledge is still under debate.[21] First, the extent of premorbid immersion in the sociocultural environment affects performance on tests for public knowledge. Second, dissociations exist in processing of public semantic information—for example, when the public event information is linked to personal experiences (ie, it has autobiographical significance), it is integrated within autobiographical memory (figure 3) and is therefore more likely to be affected by disruptions of autobiographical memory.[21]

Autobiographical-semantic memory (figure 3) is usually preserved in selective or more circumscribed cases of dissociative amnesia. Major loss of personal identity characterises dense (generalised) retrograde dissociative amnesia and fugue, in which deficits in episodic-autobiographical memory and autobiographical-semantic memory co-occur. Components of autobiographical-semantic memory can be impaired in developmental amnesia or neurodegenerative dementias.[22] An abrupt loss of both autobiographical memory and identity is strongly suggestive of dissociative amnesia (table 1).

Perceptual memory has not been formally assessed in patients with dissociative amnesia, but variability in familiarity judgments has been reported.[23,24] Complaints of loss of previously acquired procedural skills have mostly not been objectified by formal testing.[24] Learning of new procedural skills is usually possible, although emotional and motivational factors can interfere.[23,25] Priming is typically preserved; reports of impaired priming suggest non-specificity of task and testing methods.[24] The conscious acquisition of new information for long-term storage is often spared,[23,26] but concomitant impaired performance on standard anterograde memory tasks can sometimes occur.[19,20,27] In patients with dense retrograde amnesia, qualitative differences of newly acquired personal events were recorded compared with healthy participants.[28] Dissociative amnesia with anterograde memory impairments that occur in the absence of significant retrograde memory impairments (also named continuous amnesia or "amnésie actuelle"[29,30]) is diagnosed rarely (table 2). Its purported underlying mechanisms are deficits in conscious acquisition of new information for long-term storage with or without a retrieval blockade.

Impairments in executive functions and complex attention tasks and changes in perception (eg, impaired self-face or face-emotion processing), social cognition, and behaviour have been described,[27,34] but the results are not uniform. Intelligence is usually preserved, although pseudodementic presentations have been recorded.[37] Language is spared, but semantic memory and executive function deficits can interfere with performance on language production tests.[24,38,39] An absence of concern about the symptoms ("la belle indifférence")[30,40] does not always or exclusively accompany dissociative amnesia.[30] Many patients with dissociative amnesia report feeling distressed by their amnesic symptoms.[41]

No systematic studies have been done on the propensity for false memories (false recognition, intrusions, and confabulations; panel 1) in patients with dissociative amnesia. The hypothesis that dissociation renders individuals prone to fantasy, and subsequently leads to false memories of trauma after the recovery from amnesia, has no robust empirical support.[8,42]

Dissociative amnesia can occur suddenly; at times, a lag exists between the psychologically traumatic incident and the onset of amnesia. The antecedent factors range from massive psychological trauma to seemingly objective minor incidents. In the latter case, there is usually a history of recurrent psychological stresses or traumata.

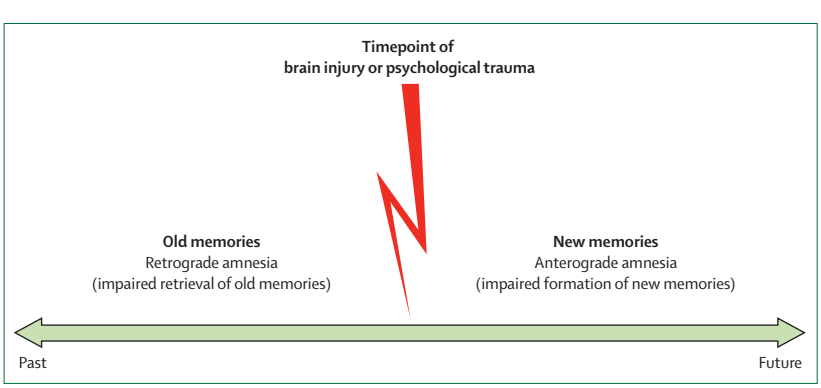

Figure 1: **Possible effects of a brain injury or psychotraumatic event on old and new memories**

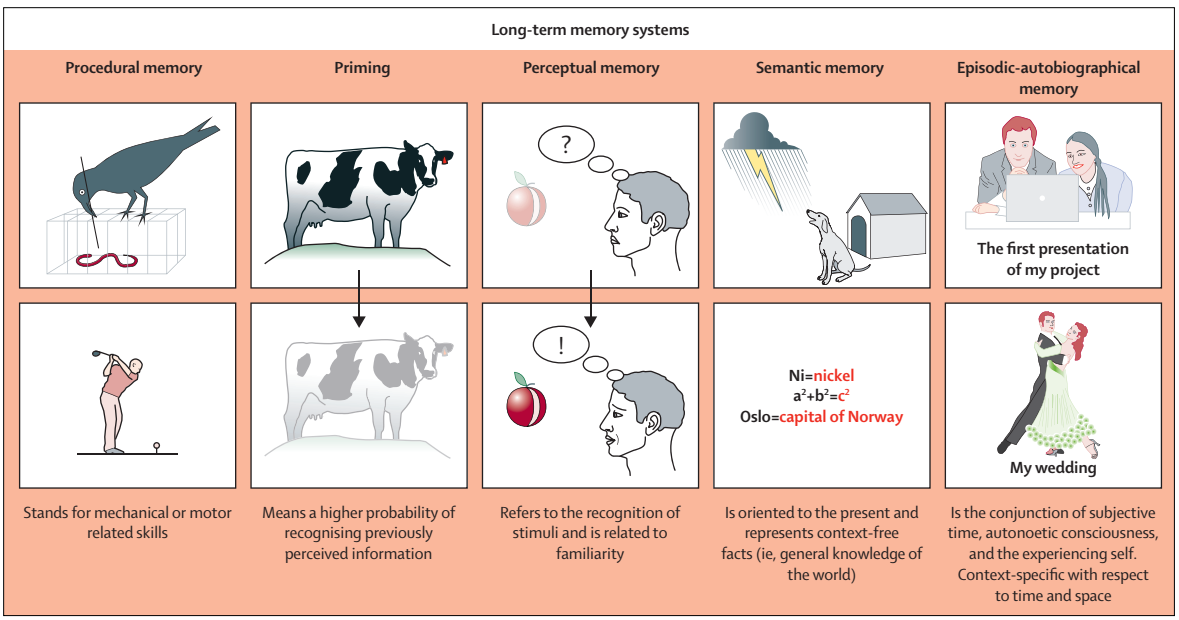

Figure 2: **The five long-term memory systems**
During ontogeny (and during phylogeny), memory development is thought to start with procedural and priming memory systems and end with episodic autobiographical memory; the latter system exists only in human beings, whereas all the other systems occur in other animal species.[1] The terms remember and know describe the distinction between the episodic-autobiographical memory and semantic memory systems, based on the nature of the subjective conscious experience during retrieval. The process of remembering refers to conscious (autonoetic) recall of experiences with a high degree of reliving or re-experiencing, whereas the process of knowing needs conscious (noetic) yes–no distinctions without further connotations.

Many dissociative amnesias are predated by a combination of psychological and physical stresses. The physical incidents are usually of mild intensity (mild traumatic brain injury or electrocution). Cases of dissociative amnesia can also arise after more severe brain insults,[43,44] which makes the diagnosis process more difficult.[43] In some cases diagnosed as probable dissociative amnesia, the amnesia occurs in the absence of any obvious stress, trauma, or other precipitating event. Amnesia itself and insufficient informant data might account for the absence of readily identifiable psychological factors. In a subset of patients, the amnesia might later turn out to be an early neurodegenerative disorder that at the time of the assessment escapes capture by existing neuropsychological and imaging investigation, but might become obvious later.

Epidemiological and demographic data

Epidemiological studies of dissociative amnesia have been done in more than 16 countries. Differences in terminologies, case definitions, assessment methods and settings, sample size, and selection criteria hinder accurate estimates of the prevalence of dissociative amnesia and fugue. Prevalence studies have shown rates of dissociative amnesia of between 0·2% and 7·3%.[9,45–47] Data for the prevalence of dissociative fugue alone are scarce. In a representative sample of 628 women in Turkey, only one participant (0·2%) satisfied criteria for dissociative fugue.[45] Xiao and colleagues[46] found that 1·3% of 304 Chinese outpatients of a mental health centre had

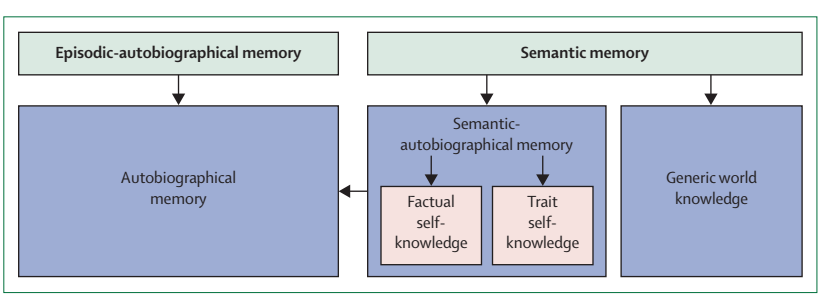

Figure 3: **The relations between autobiographical memory and the semantic and episodic-autobiographical memory systems**
The episodic-autobiographical memory can feed episodes or events directly into autobiographical memory. The semantic memory system contains generic world knowledge, but also semantic-autobiographical memory that is part of the autobiographical memory.

an episode of dissociative fugue throughout life and none had a fugue in the other comparison groups. The comparison groups were 423 inpatients of the mental health centre and a non-clinical sample of 618 factory workers. However, the prevalence of the symptom of dissociative amnesia in the general population is much higher than the estimates for the disorder of dissociative amnesia.[41] Dissociative amnesia and fugue are often diagnosed between 20 and 40 years of age, but cases have been reported in children and in older people.[43,48–50] An inverse association between age and dissociative amnesia is not supported by all studies.[51]

The prevalence of dissociative amnesia is similar between sexes.[41,51] Studies done in forensic settings draw attention to possible underestimations of the disorder in

	Dissociative amnesias	Organically based amnesias (neurocognitive disorders)
Age at diagnosis (years)	20–40	Variable
Course	Acute or chronic	Acute or chronic
Autobiographical-episodic anterograde amnesia	Less common	Most common
Autobiographical-episodic retrograde amnesia	Most common	Uncommon and rarely without anterograde amnesia
Loss of personal identity	Common	Uncommon
Preservation of learning of new facts	Usually, but not always	Rarely reported
Onset related to psychological trauma or psychological stress or conflicts	Common	Uncommon
Precipitants	Psychological stress with or without physical events	Neural tissue damage (but also emotional precipitants in transient global amnesia)
Reversal of memory loss with hypnosis	Sometimes	No
Improvement with sedative hypnotics (eg, pharmacologically facilitated interview)	Sometimes	No, or might worsen
Affected brain regions	Prefronto-temporal areas/ limbic system	Variable, usually limbic areas

Some criteria have been adapted from table 4 of Spiegel and colleagues.[9]

Table 1: **Distinct features of dissociative amnesias compared with direct organically based amnesias**

	Patient characteristics
Kessler et al (1997)[31]	29-year-old male student with no conspicuous events before the onset of his persistent anterograde amnesia
Markowitsch et al (1999)[32]	27-year-old female student with a history of two car accidents with whiplash injuries before the onset of her chronic amnesia, persisting for 20 years
Kumar et al (2007)[33]	34- or 38-year old man with psychological stress immediately before the onset of his anterograde amnesia. However, retrograde episodic-autobiographical memory was not formally tested and initially he showed some indications of retrograde amnesia; furthermore, he received treatment with benzodiazepines, electroconvulsive therapy, and antipsychotics
Smith et al (2010)[25]	51-year-old woman with history of a car accident (mild traumatic brain injury?) immediately before the onset of her anterograde amnesia
Markowitsch and Staniloiu (2013)[34]	51-year-old man with two mild physical insults (hitting his head against a cigarette automate door) before the onset of his chronic anterograde amnesia

One of the earliest cases of disproportionate anterograde amnesia of probable dissociative nature is Mrs D, described by Charcot,[29] Janet,[30,35] and Souques.[36]

Table 2: **Cases with severe anterograde amnesia in the absence of evidence for retrograde amnesia**

men.[52] The recurrence rates of dissociative amnesia cannot be ascertained accurately because there are very few longitudinal studies, and these have insufficient sample sizes and variable selection criteria.[43,48,50] High values were reported by Coons and Milstein,[48] who reported that 40% of their 25 studied patients had recurrent episodes of psychogenic (dissociative) amnesia. The authors attributed their results to the specifics of their assessment setting (a tertiary care unit). Incidentally, a substantial rate of recurrence was also reported in other dissociative (conversion) disorders, such as psychogenic non-epileptic seizures.[53]

The socioeconomic burden of dissociative amnesia has not been formally assessed, but case series indicate long-lasting disability in many patients.[19,20,27,48] Dissociative amnesia is associated with substantial functional impairment, irrespective of the presence of comorbidity.[41,51,54] Severe and broad impairments characterise chronic generalised dissociative amnesia.[11,24,48] Comorbidities of dissociative amnesia with affective and anxiety disorders, substance misuse, somatoform disorders (somatic symptom and related disorders), personality disorders (eg, borderline personality disorder), and other dissociative disorders (eg, depersonalisation disorder) have been reported,[9,20,41,48,51] but await replication in larger scale epidemiological studies.

Preliminary data suggest that dissociative disorders pose a high risk for suicide,[55] but estimates for dissociative amnesia and fugue are not available. Cases of dissociative amnesia with postpartum onset indicate a role for screening of dissociative symptoms in perinatal mental health programmes.[56,57]

Genetic and epigenetic factors

The genetic underpinnings of dissociative amnesia are unknown. Quantitative genetic studies reported heritability rates for dissociation of 50–60%.[58,59] Candidate gene studies suggest that various dissociative disorders result from interplays between genes and the environment (trauma events).[59,60]

Pathophysiology

The centrality of the trauma or stress-related explanatory model is shown by the placement of dissociative disorders in the proximity of trauma and stress-related disorders in DSM-5. Retrospective and prospective studies have accumulated substantial support for the trauma model of dissociative amnesia.[9,34,42,61]

Within the trauma model, two theoretical frameworks were espoused. Both models view retrograde dissociative amnesias as the result of a retrieval deficit. Kopelman postulated that psychological stress in combination with other predisposing psycho-socio-biological factors[43,62] afflicts the frontal executive system,[63,64] which subsequently leads to deficits in generative retrieval from episodic-autobiographical memory and in severe cases from the personal semantic belief system (autobiographical -semantic memory; figure 3).[22,65] The prefrontal cortex is involved in several functions related to episodic-autobiographical memory retrieval: searching, monitoring and verification, reconstructive and self-referential processes, and autonoetic consciousness. Neuroimaging studies of episodic-autobiographical memory retrieval show a differentiated contribution of prefrontal subregions.[22,65] Although the contribution of executive

functions to memory recall is accepted, which subcomponents of the executive system are involved in different components of the episodic-autobiographical memory system is still debated.[22,65] Furthermore, executive functions work in tandem with subcomponents of working memory (feature binding) to retrieve episodic-autobiographical memory.[22] The neural correlates of feature binding might extend beyond the frontal system to encompass portions of the medial temporal lobe.[65]

Executive functions have not been studied systematically in patients with dissociative amnesia; when examinations were done, standard executive skills were assessed, resulting in non-uniform results, probably because of different tests and testing procedures used and different comorbidities of the assessed patients.[23,27,38,66] Fujiwara and colleagues[19] reported more pronounced retrograde memory impairments in patients with dissociative amnesia who showed deficits on standard executive functions than in those without such deficits. Tramoni and colleagues[23] showed that a patient with retrograde dissociative amnesia performed within normal limits on standard executive function tests. However, on the "think–no think" task designed to study memory suppression,[67] the patient was able to suppress more items than were healthy participants. Since the test was carried out after the onset of amnesia, the contribution of overactive suppressive ability to his amnesia is difficult to gauge.

Fujiwara and Markowitsch[68] argued that the executive control system is engaged in holding distressing or undesired memories out of self-awareness or autonoetic consciousness. This process could overload the executive system and reduce the frontal cortex-associated cognitive reserve that is necessary for performance of other functions, especially those involved in successful retrieval of other non-stressful personal memories. Partial empirical support for this hypothesis comes from work by Anderson and colleagues[67,69] who showed that healthy participants can suppress unwanted memories.

Individual differences in the capability of suppression are accounted for by the strength of interactions within a right lateralised dorsolateral prefrontal-cingulate-parietal-hippocampal network, which might be supported by the cingulum bundle.[67] Anderson[69] also suggested that suppression acts through the right dorsolateral prefrontal cortex that inhibits the activity of the hippocampal formation. Extension of this work to samples of traumatised individuals might clarify the degree to which a heightened capacity for cognitive inhibition (as estimated by laboratory memory suppression tasks) contributes to the development or maintenance of dissociative amnesia.[42]

In the second main trauma model, Markowitsch and colleagues[34,70] argue that in retrograde dissociative amnesia, precipitating incidents lead to a release of stress-related hormones resulting in a mnestic block syndrome, characterised by a desynchronization of fronto-temporal regions during retrieval, especially in the right hemisphere. This neurochemical model is supported by studies showing a dysregulation of the hypothalamic-pituitary-adrenal axis in dissociative amnesia[71] and by experimental work in healthy people.[63,64,72] Increased levels of acute stress hormones were shown to exert a differentiated effect on encoding or consolidation and retrieval of episodic-autobiographical memory.[63,64,72] Improved experimental designs allow a separation between the stress effects on retrieval and consolidation. Retrieval impairments of episodic-autobiographical memory and semantic memory were recorded in healthy participants after the acute administration of glucocorticoids or psychosocial laboratory stressors.[63,64] However, inconsistent effects were noted in patients with various stress-related disorders.[72]

How chronic stress leads to dissociative amnesia has not yet been fully elucidated. Several studies link chronic glucocorticoid elevations to poor performance on memory tasks.[64] Consistent with epigenetic models, changes in stress hormones and brain function that arise from gene–environment interplays before the onset of amnesia can increase the likelihood of the development of dissociative amnesia after trauma or psychological stress exposure.[37,73,74]

Deficits in encoding and consolidating or binding and reassembling details of personal past events might have a role in some cases of dissociative amnesia.[16,37] Consolidating impairments were conjectured to account for anterograde dissociative amnesia.[34,37]

By contrast with trauma models, sociocognitive models do not postulate a significant role for trauma in the causation of dissociative amnesia or fugue. Some models emphasise cultural contamination and iatrogenesis as primary causes.[75] Others regard cognitive deficiencies intrinsic to dissociation as main explanatory mechanisms for the cognitive impairments of dissociative amnesia. In line with a strong sociocognitive position, mild executive dysfunctions and voluntary suppression could solely account for the retrieval impairment in dissociative amnesia; reports of traumatic experiences could be false memories that are caused by heightened fantasy proneness or a labile sleep–wake cycle leading to intrusions of dream-like content into the awake state.[76] Very little empirical evidence exists for the sociocognitive model of dissociative amnesia.[42,46] Either–or polemics[77] precluded the development of a successful reconciliatory framework.[8,18,76] A newly emerging model of dissociative amnesia that can advance understanding is grounded in cultural neuroscience and integrates cultural, societal, psychological, and neurobiological factors.[77] This framework might shed light on how precipitants, severity, and accompanying features of dissociative amnesia differ across cultural or minority groups.[41,46,51,78]

The two-hit hypothesis

Two-hit hypotheses that postulate an additive or synergistic interaction between psychological and physical incidents have been proposed for some cases of dissociative amnesia that are predated by mild traumatic brain injury (including blast-related mild traumatic brain

injury), electrocution, or general anesthesia.[20,34,43,79,80] Cases of dissociative amnesia after mild traumatic brain injury received the most attention. Diffusion tensor imaging studies showed microstructural changes in the white matter after mild traumatic brain injury, which were associated with the patients' performance on executive tasks.[81] Consistent with Kopelman and Fujiwara and Markowitsch's models, executive or prefrontal dysfunctions arising after mild traumatic brain injury could reduce the frontal cortex-associated cognitive reserve that is necessary for retrieval of episodic-autobiographical memory and subsequently act as a predisposing factor for the development of dissociative amnesia.

Clarification of the degree to which physical incidents provide psychological or biological grounds for the development and maintenance of dissociative amnesia is essential for treatment prioritisation and needs careful interpretation of anamnestic, neuropsychological, and neuroimaging data.[43] This goal is a challenge in cases with more severe brain damage, accompanied by massive and persistent retrograde amnesia.[34,44,82,83]

Neuroimaging

Refinements in structural and functional imaging methods began to sweep away the old distinction between mind and brain disorders and improve the understanding of the neural basis of dissociative amnesia.[84] With standard MRI, substantial brain changes are usually not found.[85,86] Recent studies suggest a role for voxel-based morphometry, diffusion tensor imaging, or magnetisation-transfer ratio measurements in elucidating the biological substrate of dissociative amnesia.[23,79] Several single case or small group studies that used functional imaging methods such as glucose PET, single photon computed emission tomography (SPECT), and functional MRI provided evidence for metabolic or blood flow changes in areas that are agreed to be involved in memory processing (figure 4).[11,23,85,87]

Comparisons of results between studies are hampered by the variability in paradigms, samples, and time of investigation. Most investigations have compared one or two patients with a control group (tables 3, 4). In one study in which glucose-PET data obtained at rest from 14 patients with dissociative amnesia with severe

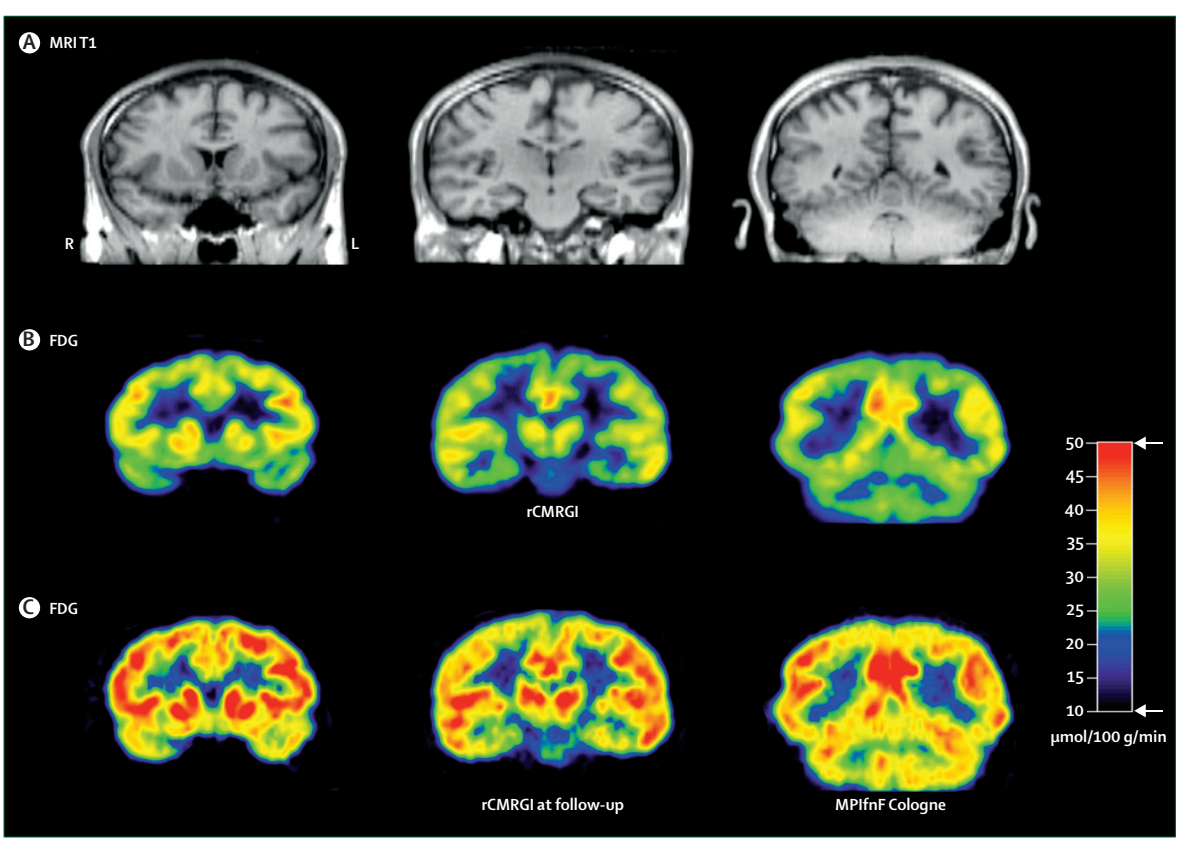

Figure 4: **Changes in brain metabolism in a patient with dissociative amnesia before and after treatment**
(A) MRI coronal sections through the brain of a patient with dissociative amnesia, with retrograde and anterograde memory impairments, showing no visible abnormalities. (B, C) Resting state FDG PET-based coronal sections from an anterior-to-posterior (left-to-right) orientation through the brain of the patient 2 months (B) and 12 months (C) after the onset of his mnestic block syndrome. A reduction in the metabolism of the cerebrum is visible in widespread cortical and subcortical areas 2 months, but not 12 months, after amnesia onset. The patient was treated with antidepressants and psychotherapy and largely recovered by the 12th month from his initial amnesia. FDG=fluorodeoxyglucose. rCMRGl=regional cerebral glucose metabolism. Reproduced from figure 1 in Markowitsch and colleagues.[85]

retrograde episodic-autobiographical memory impairments were analysed, the authors noted that the right temporo-frontal region was hypometabolic in patients compared with matched healthy participants, with a significant reduction in the right inferolateral prefrontal cortex (figure 5).[27] These results are congruent with findings from other non-clinical and clinical populations, which suggest an important role of this area in the retrieval of remote personal events.[34,85] Other single or small case studies using resting state PET or SPECT showed decreased metabolism or perfusion in the fronto-temporal areas (tables 3, 4).

Functional imaging studies undertaken during tasks—preponderantly contrasting performance in episodic-autobiographical or semantic memory conditions using stimuli from the time before and after amnesia onset—have used a wide range of testing paradigms (tables 3, 4). This variability has led to heterogeneous results, which are amenable to various interpretations. For example, depending on methods and neuropsychological results, findings of increased prefrontal activity could be interpreted as either supporting the executive or prefrontal dysfunction model or the stress hormone-mediated fronto-temporal desynchronisation model of dissociative amnesia.

Overall, the results of functional neuroimaging studies suggest a disruption of prefrontal–temporal connectivity or a cortico-limbic dysfunction, which has been identified in other dissociative (conversion) or stress-related disorders.[9,101] Changes in white matter integrity might underlie this disruption.[23,67]

Functional neuroimaging studies of patients with anterograde dissociative amnesia are scarce.[32] Glucose PET undertaken in a patient with retrograde dissociative amnesia with concurrent anterograde memory impairments suggested that hypometabolism of bottleneck structures important for transfer of semantic and episodic-autobiographical information into long-term memory (hippocampal formation and thalamus) could account for the anterograde memory deficits.[85,94]

Follow-up studies that incorporate both neuropsychological and neuroimaging methods in dissociative amnesia are rare.[10,26,85,91] In a single case study, glucose PET

	Technique	Results
Markowitsch et al (1997)[11]	$H_2{}^{15}O$-PET	Patient with psychogenic fugue; brain activation was mostly confined to the left prefrontal hemisphere when he was confronted with events from his personal past, whereas healthy people showed a corresponding right hemispheric activation.
Markowitsch et al (1997)[88]	$H_2{}^{15}O$-PET	Paradigm: identification of own paintings from an epoch that the patient did not retrieve consciously. Results: activation was largely confined to the right anterior temporal lobe and the occipital lobes.
Reinhold et al (2006)[87]	$H_2{}^{15}O$-PET	Patient had to imagine events in response to photographs from the time she did not remember consciously, and from the time period that followed the traumatic event that had led to her dissociative amnesia. Her brain showed right hemispheric activity in the infero-frontal and anterior temporal regions only for the recent and therefore remembered events (similar to healthy participants); for the non-remembered events, activations in regions linked to retrieval effort were obtained.
Yang et al (2006)[89]	fMRI	In a woman with dissociative amnesia, the investigators used a paradigm with photographs. For the recognised photographs, amygdalar, hippocampal, parahippocampal, and insular activations were recorded.
Botzung et al (2007)[90]	fMRI	Trigger words were used to remember events from the past before and after onset of dissociative amnesia. Medial temporal and prefrontal activations were recorded only for successfully retrieved memories.
Yasuno et al (2000)[91]	$H_2{}^{15}O$-PET	The patient had to identify faces of politicians. Initial PET resulted in right anterior medial temporal activation that, with recovery, after 12 months (second PET) diminished and led to increased right hippocampal activation.
Kikuchi et al (2009)[26]	fMRI	Two patients with dissociative amnesia perceived photographs from friends and colleagues; some of these were unrecognisable to them, whereas they recognised others. Unrecognised faces led to increased prefrontal and decreased hippocampal activity, suggesting a role of the prefrontal cortex in hippocampal memory suppression. In a second fMRI undertaken after treatment, this pattern disappeared in the successfully treated patient but not in the unsuccessfully treated patient. The large right prefrontal activation in particular faded away in the patient who recovered.
Hennig-Fast et al (2008)[10]	fMRI	The authors used a design with four conditions of stimulus sentences: sentences with (a) real autobiographical events, (b) fictitious autobiographical events, (c) real public facts, and (d) fictitious public facts. Furthermore, the patient was tested initially and 1 year later, after he probably had relearned portions of his biography, although he claimed to still be amnesic. Subtraction of conditions (b) minus (a) during initial testing showed activations in the left subcallosal and cingulate region. The mesial frontal region was activated when subtracting condition (d) from (c). 1 year later, the (b) minus (a) condition showed activations mainly in left parahippocampus and left temporo-frontal regions, probably indicating relearning of his past, but not vividly and emotionally remembering it. Compared with healthy control participants, the patient had bilateral activation of the insulae and the parahippocampal gyrus. After 1 year, the patient showed more frontal activation, whereas the healthy controls had activations in occipital regions (indicating imagining events). The results therefore show several differences in brain networks during normal conscious recall as opposed to unsuccessful recall attempts and—in line with several other studies on functional imaging—point to the importance of portions of the prefrontal cortex for retrieval success.
Arzy et al (2011)[92]	fMRI	A woman was apparently amnesic for one time period. Although the patient responded correctly to all events from her amnesic period, her brain activity differed from that of controls in showing hyperactivation in the left posterior parietal cortex for the amnesic period.
Brand et al (2009)[27]	Glucose PET	The authors used resting glucose PET in 14 patients with preponderantly retrograde dissociative amnesia, and recorded hypometabolism in right prefrontal-temporal areas, with a further reduction in the inferolateral prefrontal region.

fMRI=functional MRI. $H_2{}^{15}O$-PET=water (blood-flow) positron emission tomography.

Table 3: **Functional brain imaging with fMRI, glucose PET, and $H_2{}^{15}O$-PET, mostly during performance of memory tasks**

	Technique	Metabolic, perfusion, or subtle structural changes
Markowitsch et al (1997)[11]	^{15}O-PET	Left PFC activation towards autobiography, whereas healthy participants show right PFC activation
Markowitsch et al (1997)[93]	SPECT	Reduced right temporo-frontal perfusion
Markowitsch et al (1997)[93]	^{15}O-PET	Bilateral activations in precuneus, lateral parietal, and right prefrontal areas during (partly successful) attempts to retrieve autobiographical memories
Markowitsch et al (1997)[88]	^{15}O-PET	Right temporo-polar activation when attempting to remember semi-conscious events
Markowitsch et al (1998)[94]	GPET	Bilateral, but especially right-hemispheric reductions in glucose metabolism in temporo-frontal and surrounding cortical areas
Markowitsch et al (2000)[85]	GPET	Normal metabolism after therapy-induced recovery from dissociative amnesia
Reinhold et al (2006)[87]	GPET	Reductions in temporo-frontal areas
Brand et al (2009)[27]	GPET	Reductions in right temporo-frontal areas, especially in the inferolateral prefrontal cortex
Tramoni et al (2009)[23]	MTR	Decrease in MTR values in right prefrontal lobe white matter
Tramoni et al (2009)[23]	MR spectroscopy	Metabolic changes in right prefrontal lobe
Thomas-Antérion et al (2010)[95]	GPET	Left medial temporal lobe and insular/opercular hypometabolism
Sellal et al (2002)[96]	SPECT	Right temporal hypoperfusion
Hennig-Fast et al (2008)[10]	GPET	8–15% decrease in tracer uptake in right temporo-mesial cortex
Stracciari et al (2008)[50]	GPET/SPECT	Frontal hypometabolism or hypoperfusion
Piolino et al (2005)[66]	GPET	Right ventral prefrontal hypometabolism
Arzy et al (2011)[92]	GPET	Hypermetabolism in bilateral posterior parietal cortex and left inferior frontal cortex
Glisky et al (2004)[38]	GPET	Prefrontal hypometabolism
Sehm et al(2011)[97]*	VOX	Decreases in left temporopolar cortex and a region between right posterior parahippocampal and lingual cortex
Kunii et al (2012)[98]	SPECT	Mainly prefrontal hypoperfusion
Magnin et al (2014)[99]†	SPECT	Bilateral temporal, frontal, and right caudate head hypoperfusion
Back et al (1998)[100]	SPECT	Perfusion disturbances in temporo-basal areas not detected despite old temporal lesion (low resolution?)

^{15}O-PET=water (blood flow) positron emission tomography. PFC=prefrontal cortex. SPECT=single photon computed emission tomography. GPET=glucose positron emission tomography. MTR=magnetisation transfer ratio. VOX=voxel-based morphometry; MR=magnetic resonance. Data from functional MRI are excluded. *The authors themselves do not consider their case as having dissociative amnesia; they term him to be functionally retrogradely amnesic. †The authors consider this to be a mixed case (dissociative amnesia, Ganser syndrome, and somatoform disorders).

Table 4: **Studies reporting brain changes in patients with dissociative amnesia or possible dissociative amnesia**

was used to show that the reinstatement of the patient's ability to consciously process mnemonic information was paralleled by a normalisation of his brain metabolism.[85]

Diagnosis

The assessment of dissociative amnesia encompasses psychiatric, physical, and neurological examination; laboratory investigations (including toxicology screening, structural neuroimaging, and sometimes electro-encephalography); neuropsychological evaluation; and psychiatric questionnaires. To gather reports from different sources is especially important in children. In some cases, functional brain imaging[10,26] and psycho-physiological parameter measures that estimate emotional processing of relevant personal past information can help diagnosis.[23]

Principally, a patient without substantial brain damage (as assessed with conventional structural imaging) but persistent retrograde amnesia (usually longer than 1 day[102]) for salient personal episodes might alert the assessing physician to the possibility of dissociative amnesia. As stated previously, dissociative amnesia can also manifest after traumatic brain injury or other types of brain damage. When brain damage is present, the extent and nature of amnesia do not match the locus or severity of the brain lesion. Loss of personal identity and presence of antecedent trauma or severe psychological conflict or stress enhance the validity of the diagnosis. If the memory loss occurs on a background of litigation, a careful assessment for malingering should be done. Feigned memory impairments can also occur in the absence of obvious external rewards in factitious disorder, and exaggeration of symptoms is more common than is full malingering. Although assessment of retrograde episodic-autobiographical memory with structured interviews might be impossible, if the patient reports that they do not remember anything, combined assessment of several neuropsychological tests can be used to judge feigning or malingering tendencies. Some symptom validity tests assess feigning of cognitive deficits in general and are embedded in standard neuropsychological tests,[103,104] and thus offer some protection against coaching.

Other symptom validity tests are specifically designed to detect poor effort and malingered anterograde amnesia (standalone measures; table 5).[105] Although cutoff scores for intelligence are often given in these tests, the results need to be related to the general intellectual level, and in particular to the level of memory performance of the individual as estimated with a number of corresponding methods, and contrasted with the embedded validity indicators.[106] Assessment of malingering in dissociative

retrograde amnesia creates several challenges.[19] Standard tests of memory malingering assess anterograde and not retrograde memory; patients with dissociative amnesia might quickly relearn their past (through the semantic memory system[107]), which makes it difficult to distinguish between relearned (known) and remembered personal information; and differentiation of conscious from unconscious motivations with symptom validity tests is very difficult. However, the additional use of self-report personality assessment inventories could give hints about the presence of repressive coping styles.[19] Two recent studies[10,26] of retrograde dissociative amnesia that used functional imaging investigated deceptive or fictitious elements; their results open a pathway for the use of combined neuropsychological and functional neuroimaging methods to differentiate between dissociative and simulated amnesia in the future. Furthermore, Bayesian methods can complement existing tests for assessment of malingering, since they can be more resistant to coaching effects. Ortega and colleagues[108] used a Bayesian latent group analysis approach to detect poor effort and performed experiments to compare the accuracy indices (sensitivity and specificity) of their method with those of a symptom validity test. They also assessed how coaching affects the classification accuracy indices in the two conditions. The study showed higher sensitivity for the Bayesian method compared with the symptom validity test. The results also suggested that a Bayesian latent group analysis approach is more resistant to possible effects of coaching than is a traditional symptom validity test.

The diagnosis of dissociative amnesia can be strengthened if patients obtain scores indicative for the disorder in dimensional and classificatory scales (table 5, panel 2). Based on a factorial analysis of 2569 datasets from healthy participants and patients, Dell[4] suggested that three amnesia factors might be more useful to frontline clinicians than the DSM categorisation of dissociative amnesia: First, "discovering dissociated action" that is "preceded by the amnesic individual being unaware of having done something"; second, "lapses of recent memory and skills"; and third, "gaps in remote memory." Panel 3 provides an overview of clinical features indicative of dissociative amnesia.

To assess the nature and severity of the memory impairment, a detailed neuropsychological assessment should be done (table 5 and panel 2).[123]

In retrograde dissociative amnesia, the memories of personal events are believed to still exist, but their retrieval from the episodic-autobiographical memory system is blocked. According to Tulving's "serial, parallel, independent" (SPI) model,[107] indices of these memories could still be accessed through other memory systems. The SPI model posits that information is encoded serially, stored in parallel in different memory systems, and can be retrieved independently of the system in which encoding occurred. Patients with retrograde dissociative amnesia might therefore still be able to make familiarity judgments about their past familiar surroundings. Since their priming memory system is intact, they can also react to indices of old information in an implicit way.[123] However, changes in heart rate or galvanic skin conductance during the presentation of old, consciously inaccessible information should be interpreted with caution.[38] Evidence exists for impaired somatic responses to emotional stimuli in dissociative amnesia, which could account for features of emotional flattening ("la belle indifférence").[23,28] Several studies show that heart rate variability is lower in patients with dissociative (conversion) disorders than in healthy participants. This outcome differs from hypnosis, in which an increase in heart rate variability occurs without changes in heart rate.[23,124]

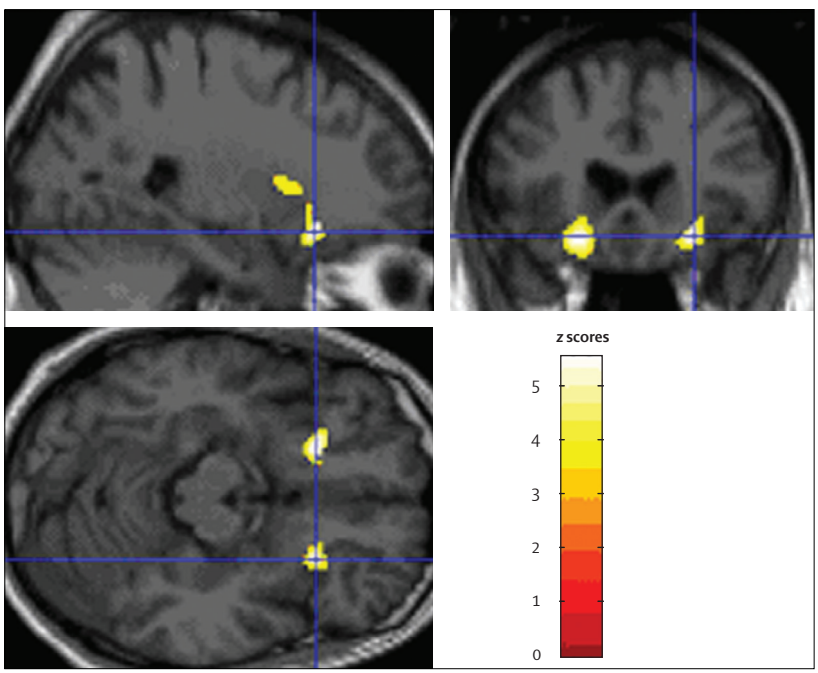

Figure 5: **Relative decreases in regional cerebral glucose metabolism in 14 patients with dissociative amnesia with pronounced retrograde memory impairments compared with 19 healthy participants**
The images show sagittal, frontal, and horizontal views superimposed on MRI sections (MRI template). The blue cross indicates the locus of the only significantly deactivated spot in the right inferolateral prefrontal cortex. The homologous hypometabolic region within the left cortex did not reach significance.
Adapted from figure 1 in Brand and colleagues,[27] by permission of Elsevier.

Differential diagnosis

The differential diagnosis of dissociative amnesia encompasses amnesic disorders caused by general medical conditions or substance misuse-related disorders, other dissociative or trauma-related or stress-related disorders in which dissociative amnesia is a symptom, borderline personality disorder, and mood or anxiety disorders. Pseudodementic presentations should be distinguished from neurodegenerative dementias, especially in elderly people. In this age group, physicians might have a tendency to preponderantly attribute

	Function, symptoms, or disorders assessed
Laterality	
Laterality assessment scale	Handedness, footness, earness, and eyeness
Intelligence	
Wechsler Intelligence Scale—4th edition	General intelligence
Language	
Aachen Aphasia Test	Various aspects of language
Token test	Understanding verbal commands
Reading, writing, and naming	Ability to read, write, and name
Tests for attention and concentration	
Wechsler Memory Scale—IV	Attention and concentration
Trail Making Test A and B	Attention and concentration
Semantic anterograde memory	
Wechsler Memory Scale—IV	Anterograde verbal and non-verbal short-term and long-term memory
California Verbal Learning Test	Anterograde verbal memory
Doors and People Test	Anterograde nonverbal memory
Rey-Osterrieth Figure	Anterograde nonverbal memory
Procedural memory	
Mirror reading or writing	Subconscious learning and memory
Pursuit rotor task	Subconscious learning and memory
Retrograde autobiographical and semantic memories (see panel 2)	
Symptom validity tests	
Test of Memory Malingering	Malingering
Word memory test	Malingering
Amsterdam Short Memory Test	Malingering
Effort measures (eg, recall vs recognition of items)	Effort (indirectly malingering)
Questionnaires (self-report)	
Dissociative Experiences Scale	Pathological and non-pathological dissociation
Steinberg Dissociative Amnesia Questionnaire	Dissociative symptoms
Beck Depression Inventory	Depressive symptoms
Childhood Trauma Questionnaire	Occurrence of traumatic events in childhood
Harvard Trauma Questionnaire	Traumatic events and emotional responses
Trauma History Questionnaire	Experiences with potentially traumatic events
Early Trauma Inventory	Occurrence of childhood trauma and impact
Impact of Event Scale	Subjective response to a specific trauma event
Toronto Alexithymia Scale	Alexithymia
Personality Assessment Inventories	Might give indices of repressive coping tendencies
(Semi)-structured interviews for dissociative disorders (clinician-administered)	
Structured Clinical Interview for Dissociative Disorders	Gold-standard diagnostic instrument
Dissociative Disorders Interview Schedule	Dissociative disorders and other disorders
Clinician-administered measures for dissociation	
Clinican-Administered Dissociative States Scale (CADSS)	Dissociative symptoms
Emotional processing/theory of mind	
Reading the Mind in the Eyes test	Theory of mind
Florida Affect Battery	Visual and auditory affect processing
Executive functions	
Wisconsin Card Sorting Test	Cognitive flexibility, and perseverative and inhibitory tendencies
Game of dice task	Risk-taking behaviour
Go–no go tests	Cognitive inhibitory abilities
Word fluency tasks	Cognitive flexibility
Stroop Interference Procedure`	Interference sensitivity
Tower of Hanoi/Toronto/London	Problem solving, cognitive flexibility
Trail Making Test B	Cognitive flexibility

Table 5: **Examples of tests used to assess patients with dissociative amnesia**

memory impairments to neurological or more common psychiatric disorders.[125]

Dissociative fugues alone are rare and might later be rediagnosed as dissociative identity disorder.[9,45] In children, they could be falsely attributed to disruptive disorders.[126] The differential diagnosis of dissociative amnesia and fugue also includes transient epileptic amnesia,[126] which is characterised by recurrent, transient episodes of isolated memory loss that usually last for less than 1 h and occur in middle-aged and elderly people.[1,43,82] Neuropsychological testing, electroencephalography, and pattern of response to anticonvulsant medication help to clarify diagnosis.

In the past, cases of transient global amnesia have often been misdiagnosed as psychogenic amnesia. They are triggered by psychological factors, physical factors, or both. In comparison to dissociative amnesia, transient global amnesia affects older people (usually older than 60 years of age), is mainly of an anterograde nature, and lasts for less than 24 h.[102] Variable retrograde memory impairments might occur, but identity is always preserved.

Isolated (episodic-autobiographical) chronic retrograde amnesia after neurological insults has been reported.[1,127] Initially, anterograde memory impairments are present in this disorder, but they then remit or become subtle. Debate is ongoing about the extent of the contribution of psychological factors to the onset or maintenance of this disorder.[1,24,34,43] In post-traumatic stress disorder, the memory impairment is usually more circumscribed than in dissociative amnesia, and is limited to aspects of the traumatic event.[9]

The main challenge posed by the differential diagnosis of dissociative amnesia is to distinguish between true and feigned or malingered amnesia.[34,43,82] This challenge is even greater when various mechanisms co-occur. In some cases of dissociative amnesia, a mixture of true amnesia and feigning or malingering might be present.[9] Furthermore, both dissociative amnesia and feigned amnesia can occur in a patient with severe brain damage.[43]

Management and treatment

Medical investigations should be balanced to avoid reinforcement of maladaptive illness beliefs. Repetitive medical examinations, solely motivated by the intent to calm the patient or health-care provider, should be avoided because they can promote feelings of diagnostic uncertainty, strengthen conviction in a primary neurological causation, and increase the tendency not to make a connection between the memory impairment and stress or emotional problems.[128] Education is crucial because it might help patients to accept their illness and subsequently improve outcomes.[53] Studies in patients with other dissociative (conversion) disorders, such as psychogenic non-epileptic seizures, showed that acceptance of and belief in the diagnosis had a bearing on recovery outcomes.[129]

No evidence-based treatments exist for dissociative amnesia.[1] Treatment studies often have methodological limitations, such as regression towards the mean, inadequate sample sizes, and non-randomised designs.[130,131]

Antidepressants can effectively treat comorbid depression.[25,85] Barbiturate derivatives or benzodiazepines have been used in drug-assisted interviews to help memory recovery, with some mixed results.[26,38,132] So far,

***Panel 2:* Examples of tests used to assess retrograde autobiographical and semantic memories**

- Autobiographical Memory Interview[109]
- Survey of Autobiographical Memory[110]
- Test Episodique de Mémoire du Passé[111]
- Autobiographical Interview[112]
- Verbal Autobiographical Fluency Task[65]
- Episodic Autobiographical Memory Interview[113]
- Crovitz Trigger Words[114]
- Autobiographical Memory Test[115]
- Autobiographisches Altgedächtnis-Altgedächtnisinventar[116]
- Semantisches Altgedächtnisinventar[116]
- Famous Faces Test[117]
- News Events Test[118]
- Dead/Alive Test[119]
- Cities Test[25]

***Panel 3:* Overview of criteria suggestive of a diagnosis of dissociative amnesia[120–122]**

Absence or exclusion of:

- Major and long-standing deficits in memory systems other than the episodic-autobiographical system
- Cognitive impairments involving lateralised abilities
- Concomitant neurological symptoms
- Preceding illnesses, such as malnutrition, intoxication, traumatic brain injury, or hypoglycaemia
- Transient global amnesia or transient epileptic amnesia

Presence of:

- Severe impairment of autobiographical event retrieval
- Loss of personal identity
- Potential for reversibility of episodic-autobiographical memory blockade
- Possible changes in brain metabolism or subtle changes in fibre structures
- Cognitive impairment greater than expected from injury or that does not match the locus of injury, or both
- Psychiatric history of depressive episodes, previous episodes of dissociative amnesia or fugue
- History of a stressful childhood or youth or a major psychotraumatic event in the past plus a proximal distressing event
- "La belle indifférence" (however, although this is a textbook symptom, it is not always present)
- Other associated conversion symptoms (eg, paralysis, psychogenic blindness)

Search strategy and selection criteria

This Review is based on material identified through searches of PubMed and Medline for original research or review articles, from 2007 to May, 2014, and written in English, German, Dutch, and French, with combination of the search terms "dissociative", "psychogenic", "functional", "fugue", "isolated", "disproportionate", "focal", "amnesia", "memory disturbances", "dissociation", and "dissociative disorders". We selected articles on the basis of their quality, originality, and relevance to the subject. We also cited a few relevant book chapters and older seminal or commonly referenced articles on the topic.

no randomised placebo-controlled trials have been done of pharmacologically assisted interview in dissociative amnesia.[132] Furthermore, sodium amytal creates a risk for respiratory depression.[132,133] Single case reports have described opposite responses to electroconvulsive treatment.[33,134] Remediation of any concomitant sleep deficits or irregularities has also been suggested as a potential adjunctive approach.[25,76]

Non-somatic approaches include hypnosis or hypnotherapy,[135] and various forms of psychotherapy (eg, psychodynamic or imagery-guided therapy). The use of hypnosis to help the retrieval of blocked memories has yielded variable results.[132] This approach is guided by the idea that similar neurobiological mechanisms underlie both hypnosis and dissociative amnesia.[136–138] Some evidence suggests that hypnosis leads to changes in confidence judgments (increased conviction in the correctness of a retrieved item after having gone through hypnosis), which might have legal ramifications.[138] Confidence judgment and correctness of memory are two different variables. Although they are related, situations exist in which subjective confidence in the correctness of a retrieved item and correctness of the retrieved memory diverge. Yet, eyewitness testimony studies suggest that eyewitnesses who are highly confident about their identifications are very persuasive to jurors.[139]

Psychotherapeutic treatment in dissociative amnesia usually follows a phasic approach. Initial goals are stabilisation, securing of patient safety, and symptom reduction. Dealing with possible traumatic events or psychological conflicts follows thereafter; physicians should avoid asking suggestive questions.[140] Additional important treatment goals of therapy are to increase the patient's motivation to participate in psychotherapy and to establish a psychosomatic model of illness.[44,140]

Data about neuropsychological rehabilitation for dissociative amnesia are sparse.[34,44] Neuropsychological findings in dissociative amnesia suggest a role for the development of a broad theoretical framework for rehabilitation of dissociative amnesia,[141] to improve psychological, social, and vocational wellbeing. In trauma-related or stress-related disorders (eg, post-traumatic stress disorder), a reduction in the symptoms of dissociative amnesia can lead to reductions in overall symptom severity and distress symptoms.[131]

Prognosis and course

Follow-up studies are scarce and are limited by the small number of patients and high variability in follow-up rates and intervals, definitions of recovery or favourable outcome, and the level of sophistication of neuropsychological assessment.[20,50] Clinical experience indicates that dissociative amnesias differ greatly in terms of outcome. Some amnesias remit spontaneously or after treatment, others decrease in symptoms and severity, and still others show a chronic or even deteriorating course.[125] Some patients with dissociative amnesia are re-diagnosed with post-traumatic stress disorder.[9] Several case series pointed to chronic disease courses in many patients, but referral bias might have partly affected these results.[20,27] Patients with brief, less severe amnesia or a better outcome might be missed by follow-up studies.[53] Variables that independently predict prognosis in dissociative amnesia have not been systematically studied. A short duration of symptoms and the presence of comorbid depression have been suggested to be good prognostic factors, but longer disease duration does not preclude successful treatment.[25,53,132]

Conclusions and future directions

Dissociative amnesias vary in their clinical manifestations, precipitants, and course. Further research is needed to understand the neurobiological, psychological, and cultural underpinnings of this variation. Larger functional neuroimaging studies with improved rigour are needed to disentangle the neurobiology of these disorders. These studies should not only investigate patients with dissociative amnesia, but also those with other dissociative disorders or trauma-related or stress-related disorders in which dissociative amnesia is one of the main symptoms. Some cases of dissociative amnesias with onset after a combination of psychological and physical factors suggest a pathogenetic model of mixed causation, through additive or synergistic effects. Empirical testing of this model might generate results that could affect existing nosologies and lead to a rethink of treatment approaches. In 1935, an annotation in *The Lancet*, entitled "Psychogenic amnesia", warned about the "incompleteness of purely psychological explanations of amnesia, and the occasional practical risks of accepting them as final".[142] Treatment and rehabilitation studies in dissociative amnesia are greatly needed.[143] Future research that combines the use of existing effort methods, Bayesian approaches, and functional neuroimaging will hopefully improve the way in which effort and malingering are assessed and subsequently increase the chances of a successful differential diagnosis of dissociative amnesia.

Contributors

Both authors contributed equally to this Review.

Declaration of interests
We declare no competing interests.

Acknowledgments
We thank an anonymous reviewer for suggesting the term idiopathic amnesia (used in panel 1).

References

1 Markowitsch HJ, Staniloiu A. Amnesic disorders. *Lancet* 2012; **380:** 1229–45.
2 ICD-10. Classification of mental and behavioral disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization, 1992.
3 American Psychiatric Association. Diagnostic and statistical manual of mental disorders—fifth edition (DSM-5). Washington, DC: American Psychiatric Publishing, 2013.
4 Dell PF. Three dimensions of dissociative amnesia. *J Trauma Dissoc* 2013; **14:** 25–39.
5 de Renzi E, Lucchelli F, Muggia S, Spinnler H. Is memory loss without anatomical damage tantamount to a psychogenic deficit? The case of pure retrograde amnesia. *Neuropsychologia* 1997; **35:** 781–94.
6 Janet P. État mental des hystériques. Paris: Rueff, 1894 (in French).
7 Lindquist KA, Wager TD, Kober H, et al. The brain basis of emotion: a meta-analytic review. *Behav Brain Sci* 2012; **35:** 121–43.
8 Lynn SJ, Lilienfeld SO, Merckelbach H, et al. The trauma model of dissociation: inconvenient truths and stubborn fictions. Comment on Dalenberg et al. (2012). *Psychol Bull* 2014; **140:** 896–910.
9 Spiegel D, Loewenstein RJ, Lewis-Fernandet R, et al. Dissociative disorders in DSM-5. *Depress Anxiety* 2011; **28:** 824–52.
10 Hennig-Fast K, Meister F, Frodl T, et al. A case of persistent retrograde amnesia following a dissociative fugue: neuropsychological and neurofunctional underpinnings of loss of autobiographical memory and self-awareness. *Neuropsychologia* 2008; **46:** 2993–3004.
11 Markowitsch HJ, Fink GR, Thöne AIM, Kessler J, Heiss W-D. Persistent psychogenic amnesia with a PET-proven organic basis. *Cogn Neuropsychiatry* 1997; **2:** 135–58.
12 Elliott DM. Traumatic events: prevalence and delayed recall in the general population. *J Consult Clin Psychol* 1997; **65:** 811–20.
13 Brown D, Sheflin AW, Hammond D. Memory, trauma treatment, and the law. New York: WW Norton & Co, 1998.
14 Dalenberg C. Recovered memory and the Daubert criteria: recovered memory as professionally tested, peer reviewed, and accepted in the relevant scientific community. *Trauma Violence Abuse* 2006; **7:** 274–310.
15 Brandon S, Boakes J, Glaser D, Green R. Recovered memories of childhood sexual abuse: implications for clinical practice. *Br J Psychiatry* 1998; **172:** 296–307.
16 McNally R. Remembering trauma. Cambridge, MA: Harvard University Press, 2003.
17 Pope HG, Hudson JI. Repressed memories: scientific status. In: Faigman DL, Cheng EK, Mnookin JL, Murphy EE, Sanders J, eds. Modern scientific evidence: the law and science of expert testimony (2011–2012 edition). Eagen: West Group, 2012: 828–913.
18 Dalenberg SJ, Brand BL, Loewenstein RJ, et al. Reality versus fantasy: reply to Lynn et al (2014). *Psychol Bull* 2014; **140:** 911–20.
19 Fujiwara E, Brand M, Kracht L, et al. Functional retrograde amnesia: a multiple case study. *Cortex* 2008; **44:** 29–45.
20 Kritchevsky M, Chang J, Squire LR. Functional amnesia: clinical description and neuropsychological profile of 10 cases. *Learn Memory* 2004; **11:** 213–26.
21 Manning L, Denkova E, Unterberger L. Autobiographical significance in past and future public semantic memory: a case-study. *Cortex* 2013; **49:** 2007–20.
22 Picard L, Mayor-Dubois C, Maeder P, et al. Functional independence within the self-memory system: new insights from two cases of developmental amnesia. *Cortex* 2013; **49:** 1463–81.
23 Tramoni E, Aubert-Khalfa S, Guye M, Ranjeva JP, Felician O, Ceccaldi M. Hypo-retrieval and hyper-suppression mechanisms in functional amnesia. *Neuropsychologia* 2009; **47:** 611–24.
24 Staniloiu A, Markowitsch HJ. The remains of the day in dissociative amnesia. *Brain Sci* 2012; **2:** 101–29.
25 Smith CN, Frascino JC, Kripke DL, McHugh PR, Treisman GJ, Squire LR. Losing memories overnight: a unique form of human amnesia. *Neuropsychologia* 2010; **39:** 2823–40.
26 Kikuchi H, Fujii T, Abe N, et al. Memory repression: brain mechanisms underlying dissociative amnesia. *J Cogn Neurosci* 2009; **22:** 602–13.
27 Brand M, Eggers C, Reinhold N, et al. Functional brain imaging in fourteen patients with dissociative amnesia reveals right inferolateral prefrontal hypometabolism. *Psychiatry Res* 2009; **174:** 32–39.
28 Reinhold N, Markowitsch HJ. Retrograde episodic memory and emotion: a perspective from patients with dissociative amnesia. *Neuropsychologia* 2009; **47:** 2197–206.
29 Charcot JM. Sur un cas d'amnésie rétro-antérograde. *Rev Med* 1892; **12:** 81–96 (in French).
30 Janet P. L'amnésie continue. *Rev Gen Sci* 1893; **4:** 167–79 (in French).
31 Kessler J, Markowitsch HJ, Huber R, et al. Massive and persistent anterograde amnesia in the absence of detectable brain damage—anterograde psychogenic amnesia or gross reduction in sustained effort? *J Clin Exp Neuropsychol* 1997; **19:** 604–14.
32 Markowitsch HJ, Kessler J, Kalbe E, Herholz K. Functional amnesia and memory consolidation. A case of persistent anterograde amnesia with rapid forgetting following whiplash injury. *Neurocase* 1999; **5:** 189–200.
33 Kumar S, Rao SL, Sunny B, Gangadhar B. Widespread cognitive impairment in psychogenic amnesia. *Psychiatr Clin Neurosci* 2007; **61:** 583–86.
34 Markowitsch HJ, Staniloiu A. The impairment of recollection in functional amnesic states. *Cortex* 2013; **49:** 1494–510.
35 Janet P. L'amnésie hystérique. *Arch Neurol* 1892; **24:** 29–55 (in French).
36 Souques A. Essai sur l'amnésie rétro-antérograde dans l'hystérie, les traumatismes cerebraux et l'alcoolisme chronique. *Rev Med* 1892; **13:** 367–401 (in French).
37 Staniloiu A, Markowitsch HJ. Towards solving the riddle of forgetting in functional amnesia: recent advances and current opinions. *Front Psychol* 2012; **3:** 403.
38 Glisky EL, Ryan L, Reminger S, Hardt O, Hayes SM, Hupbach A. A case of psychogenic fugue: I understand, aber ich verstehe nichts. *Neuropsychologia* 2004; **42:** 1132–47.
39 Iglesias A. Diagnosis and hypnotic treatment of an unusual case of hysterical amnesia. *Am J Clin Hypnos* 2009; **52:** 123–31.
40 Breuer J, Freud S. Studien über Hysterie. Wien: Deuticke, 1895 (in German).
41 Sar V, Alioglu F, Akyuz G, Karabulut S. Dissociative amnesia in dissociative disorders and borderline personality disorder: self-rating assessment in a college population. *J Trauma Dissoc* 2014; published online March 28. DOI:10.1080/15299732.2014.902415.
42 Dalenberg CJ, Brand BL, Gleaves DH, et al. Evaluation of the evidence for the trauma and fantasy models of dissociation. *Psychol Bull* 2012; **138:** 150–88.
43 Kopelman MD. Focal retrograde amnesia and the attribution of causality: an exceptionally critical review. *Cognit Neuropsychol* 2000; **17:** 585–621.
44 Pommerenke K, Staniloiu A, Markowitsch HJ, et al. Ein Fall von retrograder Amnesie nach einer Resektion eines Medulloblastoms – psychogen, organisch, funktionell? *Neurol Rehab* 2012; **18:** 106–16 (in German).
45 Sar V, Akyüz G, Dogan O. Prevalence of dissociative disorders among women in the general population. *Psychiatry Res* 2007; **149:** 169–76.
46 Xiao Z, Yan H, Wang Z, et al. Trauma and dissociation in China. *Am J Psychiatry* 2006; **163:** 1388–91.
47 Mohammadi MR, Ghanizadeh A, Rahgozart M, et al. Suicidal attempt and psychiatric disorders in Iran. *Suicide Life Threat Behav* 2005; **35:** 309–16.
48 Coons PM, Milstein V. Psychogenic amnesia: a clinical investigation of 25 cases. *Dissociation* 1992; **5:** 73–79.
49 Reinhold N, Markowitsch HJ. Emotion and consciousness in adolescent psychogenic amnesia. *J Neuropsychol* 2007; **1:** 53–64.
50 Stracciari A, Fonti C, Guarino M. When the past is lost: focal retrograde amnesia. Focus on the "functional" form. *Behav Neurol* 2008; **20:** 113–25.
51 Johnson JG, Cohen P, Kasen S, Brook JS. Dissociative disorders among adults in the community, impaired functioning, and axis I and II comorbidity. *J Psychiatr Res* 2006; **40:** 131–40.

52 Spitzer C, Freyberger HJ. Geschlechtsunterschiede bei dissoziativen Störungen. *Bundesgesundheitsbl Gesundheitsforsch Gesundheitsschutz* 2008; **51:** 46–52 (in German).

53 Gelauff J, Stone J, Edwards M, Carson A. The prognosis of functional (psychogenic) motor symptoms: a systematic review. *J Neurol Neurosurg Psychiatry* 2014; **85:** 220–26.

54 Mueller-Pfeiffer C, Rufibach K, Perron N, et al. Global functioning and disability in dissociative disorders. *Psychiatry Res* 2012; **200:** 475–81.

55 Foote B, Smolin Y, Neft DI, Lipschitz D. Dissociative disorders and suicidality in psychiatric outpatients. *J Nerv Ment Dis* 2008; **196:** 29–36.

56 Tharoor H, Dinesh N, Chauhan A, et al. Dissociative amnesia related to pregnancy. *German J Psychiatry* 2007; **10:** 119–21.

57 Spinelli MG. A systematic investigation of 16 cases of neonaticide. *Am J Psychiatry* 2001; **158:** 811–13.

58 Becker-Blease KA, Deater-Deckard K, Eley T, et al. A genetic analysis of individual differences in dissociative behaviors in childhood and adolescence. *J Child Psychol Psychiatry* 2004; **45:** 522–32.

59 Pieper S, Out D, Bakermans-Kranenburg MJ, Van IJzendoorn MH. Behavioral and molecular genetics of dissociation: the role of the serotonin transporter gene promoter polymorphism (5-HTTLPR). *J Traumatic Stress* 2011; **24:** 373–80.

60 Savitz JB, Van der Merwe L, Newman TK, et al. The relationship between childhood abuse and dissociation. Is it influenced by catechol-O-methyltransferase (COMT) activity? *Int J Neuropsychopharmacol* 2008; **11:** 149–61.

61 Bremner JD. Cognitive processes in dissociation: comment on Giesbrecht et al. (2008). *Psychol Bull* 2010; **136:** 1–6.

62 Amrhein C, Hengmeth S, Maraqkos M, Hennig-Fast K. Neuropsychological characteristics of highly dissociative healthy individuals. *J Trauma Dissociation* 2008; **9:** 525–42.

63 Wolf OT. Stress and memory in humans: twelve years of progress? *Brain Res* 2009; **1293:** 142–54.

64 Lupien SJ, McEwen BS, Gunnar MR, Heim C. Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nat Rev Neurosci* 2009; **10:** 434–45.

65 Piolino P, Coste C, Martinelli P, et al. Reduced specificity of autobiographical memory and aging: do the executive and feature binding functions of working memory have a role? *Neuropsychologia* 2010; **48:** 429–40.

66 Piolino P, Hannequin D, Desgranges B, et al. Right ventral frontal hypometabolism and abnormal sense of self in a case of disproportionate retrograde amnesia. *Cogn Neuropsychol* 2005; **22:** 1005–34.

67 Paz-Alonso PM, Bunge SA, Anderson MC, Ghetti S. Strength of coupling within a mnemonic control network differentiates those who can and cannot suppress memory retrieval. *J Neurosci* 2013; **33:** 5017–26.

68 Fujiwara E, Markowitsch HJ. Durch Angst- und Stresszustände ausgelöste Gedächtnisblockaden und deren mögliche hirnorganische Korrelate. In: Börner I, ed. Trauma und psychische Erkrankungen—Borderline Persönlichkeitsstörungen. Senden: Verlag für Medizin & Wissenschaft, 2003: 19–48 (in German).

69 Benoit RG, Anderson MC. Opposing mechanisms support the voluntary forgetting of unwanted memories. *Neuron* 2012; **76:** 450–60.

70 Markowitsch HJ. Functional retrograde amnesia—mnestic block syndrome. *Cortex* 2002; **38:** 651–54.

71 de Kloet ER, Rinne T. Neuroendocrine markers of early trauma. In: Vermetten E, Dorahy MJ, Spiegel D, eds. Traumatic dissociation. Neurobiology and treatment. Arlington, VA: American Psychiatric Publishing, 2007: 139–56.

72 Wingenfeld K, Driessen M, Terfehr K, et al. Cortisol has enhancing, rather than impairing effects on memory retrieval in PTSD. *Psychoneuroendocrinology* 2012; **37:** 1048–56.

73 Labonté B, Suderman M, Maussion G, et al. Genome-wide epigenetic regulation by early-life trauma. *Arch Gen Psychiatry* 2012; **69:** 722–31.

74 Heim CM, Mayberg HS, Mletzko T, Nemeroff CB, Pruessner JC. Decreased cortical representation of genital somatosensory field after childhood sexual abuse. *Am J Psychiatry* 2013; **170:** 616–23.

75 Pope HG, Poliakoff MB, Parker MP, Boynes M, Hudson JI. Is dissociative amnesia a culture-bound syndrome? Findings from a survey of historical literature. *Psychol Med* 2007; **37:** 225–33.

76 Lynn SJ, Lilienfeld SO, Merckelbach H, et al. Dissociation and dissociative disorders: challenging conventional wisdom. *Curr Direct Psychol Sci* 2012; **21:** 48–53.

77 Seligman R, Kirmayer LJ. Dissociative experience and cultural neuroscience: narrative, metaphor and mechanism. *Culture Med Psychiatry* 2008; **32:** 31–64.

78 Igwe MN. Dissociative fugue symptoms in a 28-year-old male Nigerian medical student: a case report. *J Med Case Rep* 2013; **7:** 143.

79 Mishra NK, Russmann H, Granziera C, Maeder P, Annoni J-M. Mutism and amnesia following high-voltage electrical injury: psychogenic symptomatology triggered by organic dysfunction? *Eur Neurol* 2011; **66:** 229–34.

80 Roberts I, Gluck N, Smith MS, Morrison MF. Postanesthesia persistent amnesia in a patient with a prior history of dissociative fugue state: the case for the two-hit hypothesis. *Am J Psychiatry* 2013; **170:** 1398–400.

81 Lipton ML, Gulko E, Zimmerman ME, et al. Diffusion-tensor imaging implicates prefrontal axonal injury in executive function impairment following very mild traumatic brain injury. *Neurology* 2009; **252:** 816–24.

82 Stuss DT, Guzman DA. Severe remote memory loss with minimal anterograde amnesia: a clinical note. *Brain Cognit* 1988; **8:** 21–30.

83 Cantagallo A, Grassi L, Della Sala S. Dissociative disorder after traumatic brain injury. *Brain Injury* 1999; **13:** 219–28.

84 Markowitsch HJ. Organic and psychogenic retrograde amnesia: two sides of the same coin? *Neurocase* 1996; **2:** 357–71.

85 Markowitsch HJ, Kessler J, Weber-Luxenburger G, Van der Ven C, Heiss W-D. Neuroimaging and behavioral correlates of recovery from 'mnestic block syndrome' and other cognitive deteriorations. *Neuropsychiatry Neuropsychol Behav Neurol* 2000; **13:** 60–66.

86 Weniger G, Lange C, Sachsse U, Irle E. Amygdala and hippocampal volumes and cognition in adult survivors of childhood abuse with dissociative disorders. *Acta Psychiatr Scand* 2008; **118:** 281–90.

87 Reinhold N, Kühnel S, Brand M, Markowitsch HJ. Functional neuroimaging in memory and memory disturbances. *Curr Med Imag Rev* 2006; **2:** 35–57.

88 Markowitsch HJ, Thiel A, Kessler J, von Stockhausen H-M, Heiss W-D. Ecphorizing semi-conscious episodic information via the right temporopolar cortex—a PET study. *Neurocase* 1997; **3:** 445–49.

89 Yang J-C, Jeong G-W, Lee M-S, et al. Functional MR imaging of psychogenic amnesia: a case report. *Korean J Radiol* 2006; **6:** 196–99.

90 Botzung A, Denkova E, Manning L. Psychogenic memory deficits associated with functional cerebral changes: an FMRI study. *Neurocase* 2007; **13:** 378–84.

91 Yasuno F, Nishikawa T, Nakagawa Y, et al. Functional anatomical study of psychogenic amnesia. *Psychiatry Res* 2000; **99:** 43–57.

92 Arzy S, Collette S, Wissmeyer M, et al. Psychogenic amnesia and self-identity: multimodal functional investigation. *Eur J Neurol* 2011; **18:** 1422–25.

93 Markowitsch HJ, Calabrese P, Fink GR, et al. Impaired episodic memory retrieval in a case of probable psychogenic amnesia. *Psychiatry Res* 1997; **74:** 119–26.

94 Markowitsch HJ, Kessler J, Van der Ven C, Weber-Luxenburger G, Heiss W-D. Psychic trauma causing grossly reduced brain metabolism and cognitive deterioration. *Neuropsychologia* 1998; **36:** 77–82.

95 Thomas-Antérion C, Guedj E, Decousus M, Laurent B. Can we see personal identity loss? A functional imaging study of typical 'hysterical amnesia'. *J Neurol Neurosurg Psychiatry* 2010; **81:** 468–69.

96 Sellal F, Manning L, Seegmuller C, Scheiber C, Schoenfelder F. Pure retrograde amnesia following mild head trauma: a neuropsychological and metabolic study. *Cortex* 2002; **38:** 499–509.

97 Sehm B, Frisch S, Thöne-Otto A, et al. Focal retrograde amnesia: voxel-based morphometry findings in a case without MRI lesions. *PLoS One* 2011; **6:** e26538.

98 Kunii Y, Okano T, Mashiko H, Yabe H, Niwa S-I. Serial changes in cerebral blood flow single photon emission computed tomography findings during memory retrieval in a case of psychogenic amnesia. *Psychiatr Clin Neurosci* 2012; **66:** 622–24.

99 Magnin E, Thomas-Anterion C, Sylvestre G, et al. Conversion, dissociative amnesia, and Ganser syndrome in a case of "chameleon" syndrome: anatomo–functional findings. *Neurocase* 2014; **20:** 27–36.

100 Back T, Haag C, Buchberger A, Mayer T. Diffusionsgewichtetes MR–Imaging bei einem Fall von dissoziativer Amnesie. *Nervenarzt* 1998; **69:** 909–12 (in German).

101 Aybek S, Nicholson TR, Zelaya F, Neural correlates of recall of life events in conversion disorder. *JAMA Psychiatry* 2014; **71:** 52–60.

102 Bartsch T, Deuschl G. Transient global amnesia: functional anatomy and clinical implications. *Lancet Neurol* 2010; **9:** 205–14.

103 Kim N, Boone KB, Victor T, et al. Sensitivity and specificity of a digit symbol recognition trial in the identification of response bias. *Arch Clin Neuropsychol* 2010; **25:** 420–28.

104 Schwarz LR, Gfeller JD, Olivieri MV. Detecting feigned impairment with the digit span and vocabulary subtests of the Wechsler Adult Intelligence Scale—third edition. *Clin Neuropsychol* 2006; **20:** 741–53.

105 Reid WH. Malingering. http://www.reidpsychiatry.com/columns/Reid07-00.pdf (accessed Feb 11, 2014).

106 DGPPN. Zur Anwendung von Beschwerdevalidierungstests in der Psychiatrie, 2011 (in German). http://www.dgppn.de/publikationen/stellungnahmen/detailansicht/browse/1/select/stellungnahmen-2011/article/141/zur-anwendun.html (accessed Dec 12, 2013).

107 Tulving E, Markowitsch HJ. Episodic and declarative memory: role of the hippocampus. *Hippocampus* 1998; **8:** 198–204.

108 Ortega A, Wagenmakers E-J, Lee MD, Markowitsch HJ, Piefke M. A Bayesian latent group analysis for detecting poor effort in the assessment of malingering. *Arch Clin Neuropsychol* 2012; **27:** 453–65.

109 Kopelman MD, Wilson BA, Baddeley A. The Autobiographical Memory Interview. Bury St Edmunds: Thames Valley Test Company, 1990.

110 Palombo DJ, Williams LJ, Abdi H, Levine B. The survey of autobiographical memory (SAM): a novel measure of trait mnemonics in everyday life. *Cortex* 2013; **49:** 1526–40.

111 Piolino P, Desgranges B, Eustache F. Episodic autobiographical memories over the course of time: cognitive, neuropsychological and neuroimaging findings. *Neuropsychologia* 2009; **47:** 2314–29.

112 Levine B, Svoboda E, Hay JF, et al. Aging and autobiographical memory: dissociating episodic from semantic retrieval. *Psychol Aging* 2002; **17:** 677–89.

113 Irish M, Lawlor BA, O'Mara SM, Coen RF. Impaired capacity for autonoetic reliving during autobiographical event recall in mild Alzheimer's disease. *Cortex* 2011; **47:** 236–49.

114 Crovitz HF, Schiffmann H. Frequency of episodic memories as a function of their age. *Bull Psychonom Soc* 1974; **4:** 517–18.

115 Williams JM, Broadbent K. Autobiographical memory in suicide attempters. *J Abnorm Psychol* 1986; **95:** 144–49.

116 Schmidtke K, Vollmer-Schmolck H. Autobiographisches und semantisches Altgedächtnisinventar. *Z Neuropsychol* 1999; **10:** 13–23 (in German).

117 Jänicke C. Die Entwicklung des Bielefelder Famous Faces Test. Diploma thesis, University of Bielefeld, 2001. http://ebookbrowse.com/die-entwicklung-des-bielefelder-famous-faces-test-pdf-d92434850 (accessed March 14, 2014).

118 Smith CN, Frascino JC, Hopkins RO, Squire LR. The nature of anterograde and retrograde memory impairment after damage to the medial temporal lobe. *Neuropsychologia* 2013; **51:** 2709–14.

119 Kapur N, Ellison D, Smith M, et al. Focal retrograde amnesia following bilateral temporal lobe pathology: a neuropsychological and magnetic resonance study. *Brain* 1992; **115:** 73–85.

120 MacDonald K, MacDonald T. Peas, please: a case report and neuroscientific review of dissociative amnesia and fugue. *J Trauma Dissociat* 2009; **10:** 420–35.

121 Markowitsch HJ. Psychogenic amnesia. *NeuroImage* 2003; **20:** S132–38.

122 Staniloiu A, Markowitsch HJ. Searching for the anatomy of dissociative amnesia. *J Psychol* 2010; **218:** 96–108.

123 Markowitsch HJ. Memory: disturbances and therapy. In: Brandt T, Caplan L, Dichgans J, Diener HC, Kennard C, eds. Neurological disorders; course and treatment, 2nd edn. San Diego: Academic Press, 2003: 287–302.

124 van der Kruijs SJ, Bodde NM, Carrette E, et al. Neurophysiological correlates of dissociative symptoms. *J Neurol Neurosurg Psychiatry* 2014; **85:** 174–79.

125 Staniloiu A, Markowitsch HJ. Understanding psychogenic amnesia and psychiatric disorders as causes of dementia. *J Gen Med* 2010; **22:** 41–49.

126 Markowitsch HJ. Intellectual functions and the brain. An historical perspective. Toronto: Hogrefe, 1992.

127 Levine B, Svoboda E, Turner GR, Mandic M, Mackey A. Behavioral and functional neuroanatomical correlates of anterograde autobiographical memory in isolated retrograde amnesic patient M.L. *Neuropsychologia* 2009; **47:** 2188–96.

128 Henningsen P, Zipfel S, Herzog W. Management of functional somatic syndromes. *Lancet* 2007; **369:** 946–55.

129 Durrant J, Rickards H, Cavanna AE. Prognosis and outcome predictors in psychogenic nonepileptic seizures. *Epilepsy Res Treat* 2011; **274736.**

130 Brand B, Classen CC, McNary SW, Zaveri P. A review of dissociative disorders treatment studies. *J Nerv Ment Dis* 2009; **197:** 646–54.

131 Brand BL, Stadnik R. What contributes to predicting change in the treatment of dissociation: initial levels of dissociation, PTSD, or overall distress? *J Trauma Dissoc* 2013; **14:** 328–41.

132 McKay GCM, Kopelman MD. Psychogenic amnesia: when memory complaints are medically unexplained. *Adv Psychiatr Treat* 2009; **15:** 152–58.

133 Lee S-S, Park S, Park S-S. Use of lorazepam in drug-assisted interviews: two cases of dissociative amnesia. *Psychiatry Investig* 2011; **6:** 377–80.

134 Kosidou K, Lindholm S. A rare case of dissociative fugue with unusually prolonged amnesia successfully resolved by ECT. *Eur Psychiatry* 2007; **22:** 264.

135 Fine CG. Cognitive behavioral hypnotherapy for dissociative disorders. *Am J Clin Hypnosis* 2012; **54:** 331–52.

136 Oakley DA, Halligan PW. Hypnotic suggestion: opportunities for cognitive neuroscience. *Nat Rev Neurosci* 2013; **14:** 565–76.

137 Mendelsohn A, Chalamish Y, Solomonovich A, Dudai Y. Mesmerizing memories: brain substrates of episodic memory suppression in posthypnotic amnesia. *Neuron* 2008; **57:** 159–70.

138 Maldonado JR, Spiegel D. Dissociative disorders. In: Hales RE, Yudofsky SC, Gabbard GO, eds. The American Psychiatric Publishing Textbook of Psychiatry, 5th edn. Arlington, VA: American Psychiatric Publishing, 2008: 665–710.

139 Risius U-M, Staniloiu A, Piefke M, et al. Retrieval, monitoring and control processes: a 7 tesla fMRI approach to memory accuracy. *Front Behav Neurosci* 2013; **7:** 24.

140 Priebe K, Schmahl C. Dissoziative Störungen. *Fortschr Neurol Psychiatrie* 2009; **77:** 595–606 (in German).

141 Wilson BA. Neuropsychological rehabilitation. *Annu Rev Clin Psychol* 2008; **4:** 141–62.

142 Anonymous. Psychogenic amnesia. *Lancet* 1935; **26:** 953.

143 Tripathi R, Bharath S, Desai G, Mehrotra S. Therapist concerns and process issues in grappling with functional autobiographical amnesia. *Indian J Psychol Med* 2013; **35:** 305–08.