PAVOL JOZEF ŠAFARIK UNIVERSITY IN KOŠICE

FACULTY OF MEDICINE

Dissociative amnesia: a clinical and theoretical reconsideration

Paulo Alexandre Rocha Simão

DEGREE THESIS

Košice 2017

PAVOL JOZEF ŠAFARIK UNIVERSITY IN KOŠICE

FACULTY OF MEDICINE

FIRST DEPARTMENT OF PSYCHIATRY

Dissociative amnesia: a clinical and theoretical reconsideration

Paulo Alexandre Rocha Simão

DEGREE THESIS

Thesis supervisor: Mgr. MUDr. Jozef Dragašek, PhD., MHA

Košice 2017

Analytical sheet

Author	Paulo Alexandre Rocha Simão
Thesis title	Dissociative amnesia: a clinical and theoretical reconsideration
Language of the thesis	English
Type of thesis	Degree thesis
Number of pages	89
Academic degree	M.D.
University	Pavol Jozef Šafárik University in Košice
Faculty	Faculty of Medicine
Department/Institute	Department of Psychiatry
Study branch	General Medicine
Study programme	General Medicine
City	Košice
Thesis supervisor	Mgr. MUDr. Jozef Dragašek, PhD., MHA
Date of submission	06/2017
Date of defence	09/2017
Key words	Dissociative amnesia, dissociative fugue, dissociative identity disorder
Thesis title in the Slovak language	Disociatívna amnézia: klinické a teoretické prehodnotenie
Key words in the Slovak language	Disociatívna amnézia, disociatívna fuga, disociatívna porucha identity

Abstract in the English language

Dissociative amnesia is a one of the most intriguing, misdiagnosed conditions in the psychiatric world. Dissociative amnesia is related to other dissociative disorders, such as dissociative identity disorder and dissociative fugue. Its clinical features are known since Janet's studies on hysteria. However, conceptualization, pathophysiological bases and even diagnosis are source of intense discussion and disagreement. The disagreement involved in this matter is evident on nosological classification of the condition: International Statistical Classification of Diseases and Related Health Problems (ICD) – by World Health Organization (WHO) - and Diagnostic and Statistical Manual of Mental Disorders (DSM) – by American Psychiatric Association (APA) – have different classifications and diagnostic guidelines for the condition. The objective of this thesis is to make a review of the available information on this subject, trying to reach a common ground and providing a short personal insight on the diagnostic status and scientific validity of the diagnosis.

Abstract in the Slovak language

Disociatívna amnézia je jednou z najzaujímavejších, a nesprávne diagnostikovaných stavov v psychiatrickom svete. Disociatívna amnézia súvisí s inými disociatívnimy poruchami, ako je disociatívna porucha identity a disociatívna fúga. Jej klinické vlastnosti sú známe od Janetových štúdií o hystérii. Avšak konceptualizácia, patofyziologické základy a dokonca diagnóza sú zdrojom intenzívnej diskusie a nesúhlasu. Nesúhlas s touto záležitosťou je zrejmý z nosologickej klasifikácie tohto stavu: Medzinárodná štatistická klasifikácia chorôb a súvisiace zdravotné problémy (ICD) - a Svetová zdravotnícka organizácia (WHO) - diagnostický a štatistický manuál duševných porúch (DSM) - vytvorený Americkým Psychiatrickým združením (APA) - majú rozdielne klasifikácie a diagnostické usmernenia pre tento stav. Cieľom tejto práce je urobiť prehľad dostupných informácií o tejto téme, a taktiež snažiť sa dosiahnuť spoločný základ a poskytnúť krátky osobný náhľad na diagnostický stav a vedeckú platnosť diagnózy.

P. J. Šafárik University in Košice
Faculty of Medicine

1219559102

THESIS ASSIGNMENT

Name and Surname:	Paulo Alexandre Rocha Simão
Study programme:	General Medicine (Single degree study, doctor I.II. deg., full time form)
Field of Study:	7.1.1. General Medicine
Type of Thesis:	Diploma thesis
Language of Thesis:	English
Secondary language:	Slovak

Title: Dissociative amnesia: A clinical and theoretical reconsideration

Title SK: Disociatívna amnézia: Klinické a teoretické prehodnotenie

References:

Staniloiu, A., & Markowitsch, H. J. (2014). Dissociative amnesia. The Lancet. Psychiatry, 1(3), 226–241. https://doi.org/10.1016/S2215-0366(14)70279-2

Spiegel, D., Lewis-Fernandez, R., Lanius, R., Vermetten, E., Simeon, D., & Friedman, M. (2013). Dissociative disorders in DSM-5. Annual Review of Clinical Psychology, 9, 299–326. https://doi.org/10.1146/annurev-clinpsy-050212-185531

Kihlstrom, J. F. (2005). Dissociative disorders. Annual Review of Clinical Psychology, 1, 227–253. https://doi.org/10.1146/annurev.clinpsy.1.102803.143925

Aims: Since the 1980s, the concept of dissociative disorders has taken on a new significance. Dissociative disorders are a group of psychiatric syndromes characterized by disruptions of aspects of consciousness, identity, memory, motor behavior, or environmental awareness. DSM 5 now includes 3 dissociative disorders and one category for atypical dissociative disorders. These include dissociative amnesia, dissociative identity disorder, dissociative fugue, depersonalization/derealization disorder, and dissociative disorder not otherwise specified. The aim of the work is to prepare a systematic review of this topic with the emphasis on dissociative amnesia.

Keywords: dissociative amnesia, dissociative fuga, dissociative identity disorder

Supervisor: Mgr. MUDr. Jozef Dragašek, PhD., MHA
Clinic : 1. PK - 1st Department of Psychiatry

Approved: 10.04.2017 Mgr. MUDr. Jozef Dragašek, PhD., MHA
Head of Department

Declaration on honour

I hereby declare that I have written this thesis on my own and used the sources quoted.

In Košice, 2017

.....

Signature

Acknowledgement

To Mgr. MUDr. Jozef Dragašek, PhD, who provided invaluable knowledge, advice and consideration during the construction of this thesis, my deepest gratitude.

Foreword

Living my days of a normal medical student, some discussions arise among friends considering the most different topics in Medicine. My personal interest has always been related to the brain and mind, the mechanisms which makes us a living, conscious being. It is not surprising, then, that my two favourite areas of medicine are Psychiatry and Neurology.

My interest in these areas lead me to search for a subject which comprises, in some way, a little of both worlds, hence my degree thesis being about dissociative amnesia.

In the words of Angelica Staniloiu and Hans J Markowitsch (2014), two of the leading specialists in this matter, in Europe, “dissociative amnesia is one of the most enigmatic and controversial psychiatric disorders“in the world. It is a condition known (although in the form of another concept - hysteria) since Janet’s studies, during 19th century, considered the father of the concept of dissociation. However, the pathological processes involved in this condition are still not clear.

There has been a lot of debate considering the proper terminology for the disorder, which correlates with the disagreement regarding all the etiology and disease mechanisms.

With the realization of this thesis project, I hope I can shed some light considering the subject and, at the same time, provide my own personal opinion on the scientific validity of the diagnosis.

Table of contents:

List of Figures

List of Tables

List of Symbols and Abbreviations

ACT – Acceptance and commitment therapy

AD – Alzheimer's disease

ADHD – Attention-deficit/hyperactivity disorder

APA – American Psychiatric Association

CADSS – Composite International Diagnostic Interview

CBT – Cognitive behavioral therapy

CD – Conversion disorder

CIDI – Composite International Diagnostic Interview

CNS – Central nervous system

DA – Dissociative amnesia

DBS – Deep brain stimulation

DD – Dissociative disorder

DDNOS – Dissociative disorder not otherwise specified

DES – Dissociative Experiences Scale

DF – Dissociative Fugue

DHEA – Dehydroepiandrosterone

DID – Dissociative identity disorder

DLPFC - Dorsolateral prefrontal cortex

DPD – Depersonalization disorder

DSM-I - Diagnostic and Statistical Manual of Mental Disorders, First Edition

DSM-II - Diagnostic and Statistical Manual of Mental Disorders, Second Edition

DSM-III - Diagnostic and Statistical Manual of Mental Disorders, Third Edition

DSM-IV - Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

DSM-V - Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

EAM – Episodic-autobiographical memory

fMRI - Functional magnetic resonance imaging

HD – Huntington's disease

HF – Hippocampal formation

ICD-10 - International Statistical Classification of Diseases and Related Health Problems, 10th revision

ICD-11 - International Statistical Classification of Diseases and Related Health Problems, 11th revision

ISSTD – International Society for the Study of Trauma and Dissociation

MID – Multidimensional Inventory of Dissociation

MMPI-2 – Minnesota Multiphase Personality Inventory 2

MPD – Multiple personality disorder

MRI – Magnetic resonance imaging

MS – Multiple sclerosis

MTL – Medial temporal lobe

OMD – Organic mental disorder

PAI – Personality Assessment Inventory

PCP – Phencyclidine

PD – Parkinson's disease

PET – Positron emission tomography

PTSD – Post-traumatic stress disorder

SCID-D – Structured Clinical Interview for Dissociative Disorders

SCID-D-R – Revised Structured Clinical Interview for Dissociative Disorders

SIRS – Structured Interview of Reported Symptoms

TGA – Transient global amnesia

TOMM – Test of Memory Malingering

VIP – Validity Indicator Profile

WHO – World Health Organization

Introduction

Dissociative amnesia is a condition characterized by inability to recall autobiographical memories in the absence of structural, organic brain damage (or, at least, undetected by conventional neuroimaging methods). Recently, cognitive research and brain imaging methods have provided some information concerning the mechanisms underlying the condition. However, the disorder remains considered, by some, mostly as a form of malingering or feigning behavior rather than a disease.

The prevalence of this condition differs across countries and populations. A definitive major study, or compilation of studies, with the same diagnostic and scientific value, is needed to assess correctly the prevalence.

Currently, there is no evidence-based treatments available and even the rehabilitation framework is scarce.

Further research is needed in order to understand the pathophysiology, predict the course and provide some reliable treatment, in the future.

There has been some debate considering the correct terminology for this condition. It is, often, mistaken in literature with psychogenic amnesia or functional amnesia.

Some sources, such as DSM-V, classify psychogenic amnesia as the older terminology for dissociative amnesia. Functional amnesia, on the other hand, cannot be traced either to organic or psychological causes.

For the purpose of this thesis, the three terms will be incorporated to the same condition, with the same theoretical base, dissociative amnesia as defined in DSM-V.

1. Dissociative process

Dissociation, in simple terms, is a process by which someone disconnects from his own thoughts, memories, feelings, actions or self-awareness. It is a process that most people experience at some point, more commonly in mild forms, such as “daydreaming” or highway hypnosis, being these experiences more prevalent among youngsters. In the normal population, dissociative experiences that are not clinically significant are highly prevalent with 60% to 65% of the inquired indicating that they have had some dissociative experiences (Waller, Putnam, Carlson, 1996). In more severe cases, further along the continuum of the condition, occur the so-called dissociative disorders (some examples include: dissociative amnesia, dissociative fugue, depersonalization disorder, dissociative identity disorder), which are fortunately less common and, sometimes, may even stay undiagnosed for years. The lifetime prevalence of dissociative disorders varies from 10% in the general population to 46% in psychiatric inpatients (Ross et al., 2002).

The process of dissociation occurs, for example, during traumatic experiences (e.g. child abuse, accidents and crimes), believed to be a coping mechanism in extremely stressful, unbearable situations. It works as a way of escaping negative feelings like pain or horror, by dissociating from the memories or feelings of the event.

1.1 Definition

“Dissociation represents a process whereby certain mental functions which are ordinarily integrated with other functions presumably operate in a more compartmentalized or automatic way usually outside the sphere of conscious awareness or memory recall" (Ludwig; 1983). In others terms, dissociation is a process by which mental functions usually integrated in conscious awareness or memory recall are compartmentalized originating a detachment from reality. (Should not be mistaken with psychosis, in which it is characteristic a changed or lost reality).

Dissociation can be represented in a continuum, in which mild cases are non-pathological. Pathological dissociation involves all the spectrum of dissociative disorders (DD). The category of DD includes a variety of syndromes with a common central core – alteration of consciousness affecting memory and memory. These conditions should not be mistaken with organic mental

disorders. DD do not result from any brain injury or disease, but at the same time represent an abnormal impairment of brain processes related to consciousness. Because of its intimate relation with trauma, DD is also associated to post-traumatic stress disorder (PTSD), in which "voluntary recall of trauma is incomplete and fragmented, especially for individuals with higher levels of PTSD symptoms" (Berntsen D., Rubin D., 2014).

Dissociative disorders are widely believed to have roots in traumatic childhood experiences but symptomology often goes unrecognized or is misdiagnosed in children and adolescents (Steiner H., Carrion V., Plattner B., Koopman C., 2002).

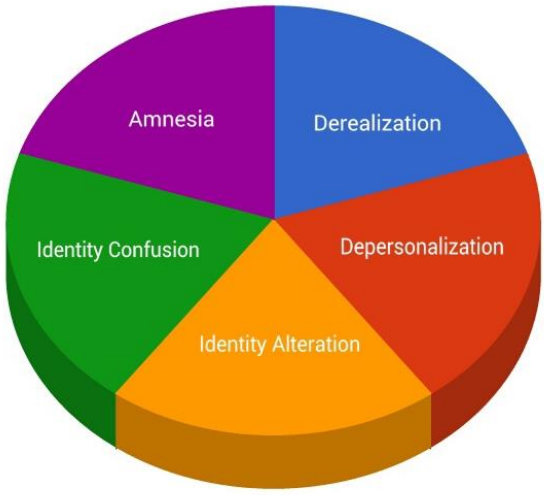

Figure 1 – The five core components of dissociative disorders (Steinberg, 1995)

1.2 Classification of dissociative disorders

According American Psychiatric Association's DSM-V, DD are divided in: dissociative amnesia (includes dissociative fugue), dissociative identity disorder, depersonalization disorder and dissociative disorders not otherwise specified - other specified dissociative disorder and unspecified dissociative disorder. ICD-10 classifies conversion disorder as a dissociative disorder, whilst DSM-V considers it to be a somatoform disorder.

1.2.1 Dissociative amnesia

Dissociative amnesia (DA), also known as functional amnesia or psychogenic amnesia, is the most common dissociative disorder. This condition is characterized by severely impaired memory functioning, usually precipitated by intense traumatic or stressful situations in the absence of organic causes - structural brain damage.

There are several subtypes of DA: localized amnesia, selective amnesia, generalized amnesia, continuous amnesia, systemized amnesia and dissociative fugue (DF). DF is characterized by symptoms of dissociative amnesia, as well as, loss of personal identity. It used to be a different diagnosis, but it is, nowadays, integrated as part of DA.

Dissociative amnesia and all its subtypes will be further discussed, in detail, in the third chapter of this thesis.

1.2.2 Dissociative identity disorder

Dissociative identity disorder (DID), previously known as multiple personality disorder (MPD), is probably the most famous of the dissociative disorders. It is well known from fictional productions which present it as a controversial condition: the possibility of malingering may provide, for example, an “insanity defence” in a court of law. The real condition, according DSM-V, is characterized by the presence of two or more distinct personalities (or alter-egos), plus the inability to recall important memories, not explained by ordinary forgetfulness. In most cases, one of the egos is the dominant one. Each ego may have its own personality, gender, age or language. It may occur that the experiences lived by one of the alter-egos are just integrated in the memory of that personality, being thus totally unrecalled by the other egos (Sadock B. J., Sadock V. A., 2007).

This disorder cannot be explained by any other medical conditions (e.g. complex partial seizures) or substance abuse (e.g. alcohol intoxication). It is, also, often combined with other comorbidities, such as PTSD, schizophrenia or borderline personality disorder (BPD), which make the diagnosis more difficult. The International Society for the Study of Trauma and Dissociation (ISSTD) considers that the prevalence of DID in the general population is comprised between 1 and 3 %.

Some of the symptoms associated with DID may be: impaired memory, self-aware or perception; hallucinations; depressive symptoms; anxiety; somatizations; substance abuse; borderline personality features.

The cause of DID is unknown, even though in many cases patients report early childhood abuses, physical and/or sexual. Despite of the average age for ego appearance being three years old (Piper A., Merskey H, 2004), the disease is rarely diagnosed in children. It has been also reported that some symptoms may even be precipitated by therapy memory retrieval techniques, especially on suggestive individuals.

There is no consensus on diagnostics or treatment. Diagnosis is based on presence of two or more alter-egos with memory impairment, not explained by other conditions or substances. Various psychotherapy techniques have been used in the effort of treating the condition. Regardless, there is no unified solution. Medication can be used, especially to control the comorbidities or isolated symptoms.

1.2.3 Depersonalization disorder

Depersonalization disorder (DPD) is a mental disorder characterized by persistent and/or recurrent feelings of depersonalization and/or derealization. In depersonalization, the individual may feel completelly detached from his normal self, either his entire being or parts of it (feelings, thoughts, body parts or sensations). A particularly important characteristic is the possibility of rejection of own reflection as being part of the individual. In episodes of derealization, the subject may feel detached from the world outside, in form of individuals, objects or surroundings. Still, patients with this condition remain somehow in touch with the reality.

Prevalence of the disease is estimated to be between 0.8% and 1.9%. In one-third of the patients, the condition is episodic.

The depersonalization causes clinically significant distress or impairment in social, occupational, or other important areas of functioning (Bressert S., 2016). Some symptoms outside the spectrum of depersonalization/derealization may also occur, such as: depressive symptoms,

panic attacks, anxiety, blurry vision, widened/narrowed visual field, macropsia/micropsia, nausea and pain.

The exact cause of DPD is unknown, but some studies point out childhood trauma as a significant predictor of the disease (Simeon D., Guralnik O., Schmeidler J., Sirof B., Knutelska M., 2001). DPD is thought to be associated with dysregulation of the hypothalamic-pituitary-adrenal axis, where the "fight-or-flight" response occurs. Also, these patients demonstrate abnormal cortisol levels and basal activity (Simeon D., Guralnik O., Knutelska M., Hollander E., Schmeidler J., 2001).

Diagnosis of the condition is based on clinical assessment from patient's reports. Exclusion features are depersonalization occurying exclusively with other mental disorder (e.g. schizophrenia, panic disorder) or being caused by a substance or a general medical condition. The use of cannabis is well know to cause depersonalization symptoms.

As treatment methods, numerous psychotherapy techniques have been used, but without much agreement. Cognitive behavioral therapy (CBT) is the most agreed-upon technique. Medication such as antidepressants or antipsychotics, have been found useless.

1.2.4 Dissociative disorder not otherwise specified

Dissociative disorder not otherwise specified (DDNOS) is a condition in which a dissociative symptom does not meet the criteria to be included in any of the above mentioned dissociative disorders. Some examples are: dissociation occurying after long periods of coercive persuasion (e.g. brainwashing); loss of consciousness which is not related to a general medical condition; Ganser Syndrome/Nonsense Syndrome[1].

[1] Ganser Syndrome – is a syndrome characterized by nonsense wrong answers to questions, or doing things incorrectly (Miller P., Bramble D., Buxton N.,1997). It is famous for being called prison psychosis: inmates fake the condition to get some advantage of their situation.

1.2.5 Conversion Disorder*

*Conversion Disorder (CD) is classified as a dissociative disorder according to ICD-10, thus it should be mentioned.

This condition is characterized by neurological symptoms (e.g. paralysis, numbness, blindness or aphasia), which are not consistent with an organic cause.

CD affects from 0.1 to 0.5% of the general population, affecting mostly teenagers and young adults (Tollison C. D., Satterthwaite J. R., Tollison J. W., 2002)

The term “conversion“, which comes from Freud’s studies on hysteria, results from the conversion of anxiety into physical symptoms. CD is known to cause great social and occupational distress in the lives of the patients. Part of the differential diagnosis consists in preventing cases of malingering or searching for possible hidden organic causes for the disease (stroke, multiple sclerosis, etc.).

Many different types of treatments are available, even though little evidence of efficacy is reported. In the usual therapy methods are included: psychotherapy, hypnosis, occupational therapy, physical therapy and medication for comorbidities (depression, anxiety).

1.3 History

Dissociation, as a well systematized concept, appears from the period Ellenberger called the “First Dynamic Psychiatry“ – medical and scientifical literature on Psychiatry, comprised from 1750 to 1900. French psychologist Pierre Janet (1859–1947) is considered to be the author of the concept, as he was “the first to show clearly and systematically how it is the most direct psychological defense against overwhelming traumatic experiences” (Hard and Horst, 1989). Pierre Janet developed the concept after several works on hysteria.

Soon, the “Second Dynamic Psychiatry” came along, with Freud and his followers, taking emphasis on psychanalysis (sex and aggression, dreams and repression), rather than in consciousness or mental states. This period coincides with a pause in the development of the concept of dissociation.

The Neodissociation Theory, Hilgard (1977), resumed the discussion. Posteriorly, theories from Carl Jung, Bowers (1990) and Woody and Sadler (1998) diverged from previous explanations and introduced the concept of dissociation as a natural operation of mental function. They also tried to provide a better understanding and explanation for the mental processes occurring in dissociation.

Lately, with development of imaging science and with the increase in studies related to dissociative disorders in general, the mechanisms involved in the dissociative process have been further sorted and systematized.

1.3.1 Evolution of the concept

Benjamin Rush (1812) was probably the first documented author to use the concept of dissociation, despite off using the term for patients who were, most likely, suffering from schizophrenia or mania.

The first dynamic psychiatrists (1750 to 1900) were interested in many kinds of matters, such as hypnosis, spiritism, psychogenic fugue, „magnetic diseases“ – cataplesy, sonambulism and lethargy (due to similarities to animal magnetism, precursor of hypnosis), multiple personality and hysterical conversion symptoms.

It was thought that diseases such as multiple personality disorder and hysteria were caused by a suggestion with origins in psychological trauma, unknown to the patients. This causes some experiences or thoughts to become separated from the control of the ego.

The philosopher Maine de Biran, Moreau de Tours (1845) – in his psychological studies on the effects of hashish, and Charles Richet (1884) – who stated “feeling, thinking, and acting become dissociated on somnambulistic state”, all used and contributed to the concept of dissociation.

By 1887, the concept of dissociation was being debated by Frederic Myers, in England, and by Charcot, Gilles de la Tourette and Pierre Janet, in France.

Myers studied the effects of dissociation in multiple personality disorder patients. Charcot, Gilles de la Tourette and Pierre Janet used the term dissociation in the same way, describing phenomena which characterized hysteria patients.

However, French philosopher and psychologist Pierre Janet (1859–1947) is considered to be the author of the concept of dissociation. He identified structures of the mental system called "psychological automatisms". According to Janet, all these automatism were bound together into a unique consciousness which, in certain circumstances, could be disaggregated or dissociated from the self-awareness and independent control. In spite of working on many hysteria cases following in traumatic experiences, Janet did not believe that dissociation was a psychological defense. Instead, he considered the trauma to be a stressor whose effects on “suggestive” individuals caused dissociative symptoms.

One of the famous patients that Janet described was Lucie. Her consciousness seemed to be composed of three parallel streams: “Lucie 1”, “Lucie 2”, and “Lucie 3” or “Adrienne”. Lucie 1 would be hypnotized and her stream would be interrupted in this state, then Lucie 2 would appear. Lucie 2 had memory of period when she predominated but also for everything Lucie 1 experienced. Adrienne would appear in the third stage, remembering experiences from all three personalities. For Janet, Adrienne is the complete total consciousness as she didn’t exhibit anesthesias nor unconscious actions. She even remembered a traumatic event which Janet afterwards described as the stressor which, in predisposed individuals, causes the dissociative disorder, as it happened to Lucie. The French philosopher later stated: "One cannot say that there was in Lucie an absence of consciousness, but rather the existence of two states of consciousness”

Janet’s thesis, “L’automatisme psychologique: Essai de psychologie expérimentale sur les formes inféreures de l’activité humaine”, published in 1889, can be regarded as history’s most important work on dissociation.

The interest on dissociation soon would disappear in Europe and around the world. Rapidly after the peak in interest in America, where William James, Boris Sidis, Morton Prince developed some work on dissociation, following Janet’s studies, the academic interest changed its focus. Psychoanalysis and behaviorism elaborated by Freud and his followers, the second dynamic psychiatrists, soon took over the interest of psychiatrists around the world. Freud avoided the dissociative phenomena. Zemach (1986) quoted him: “Depersonalization leads us to the extraordinary condition of double consciousness, which is more correctly described as split personality. But all of this is so obscure and had been so little mastered scientifically that I must refrain from talking about it anymore to you.”

For most of the twentieth century, there was little interest in dissociation. Discussion of dissociation only resumed when Ernest Hilgard published his Neodissociation Theory in the 1970s, after World War II.

The Neodissociation Theory states that the mind is organized as mental structures, each structure can receive and send information to the other structures. In normal situations, these mental structures are organized in a system, sharing information with the main central executive. These links, however, between a subordinate and the executive structures might be cut: some subordinate actions might, then, escape the control of the executive structure, becoming isolated from consciousness – dissociative process. According to Hilgard, the most important difference between Janet's dissociation and neodissociation is that Janet believed this process only occurred in hysteria patients, whilst Hilgard's view was that dissociative phenomena are universal experiences and not necessarily pathological.

Carl Jung, soon after, theorizes that dissociation manifestations as being special cases of the normal psyche. Jung was "unique in recognising that the 'dissociability of the psyche' is a fundamental process that extends along the continuum from 'normal' mental functioning to 'abnormal' states" (Noll R., 1989). With Jung, for the first time, dissociation is described as a normal process of the psyche and universal to every individual. Most of his work was related to multiple personality disorder.

Bowers, influenced by Hilgard, was one of the most important promotors of Neodissociation Theory. However, after some time he started criticizing this theory, reporting, for example, that amnesic barriers were an "implausible mechanism". If amnesic barriers could be created during hypnosis and hypnosis alters the hierarchy of the mental structures, then the patients experience would be resultant of a real change in control mechanisms, rather than an illusory effect of reduced self-awareness. In 1990, Bowers proposed that Neodissociation Theory should be branched into two separate streams: dissociated experience and dissociated control. Dissociated experience focus on how patients experience hypnosis – "the control being exercised is not consciously experimented". Dissociated control explains that hypnosis focus on how behavior is controlled: lower subsystems can be dissociated from the main central system.

Kirsch and Lynn (1998) described inconsistencies between the two different versions, creating a dead-lock. In response to the critics, Woody and Sadler (1998), proposed a reintegration

of both theories: “two complementary systems are responsible for initiation and control of action”. The first is the higher centralized system, which manages volitional, controlled acts. The second is a lower diverse system, which manages routine acts, more stimulus-driven.

Dissociation is, nowadays, a clinical feature growing in interest, due, namely, to studies on PTSD and DID, as well as, neuroimaging research and population studies. Further understanding and possibly different theories are bound to be unveiled in the years to come.

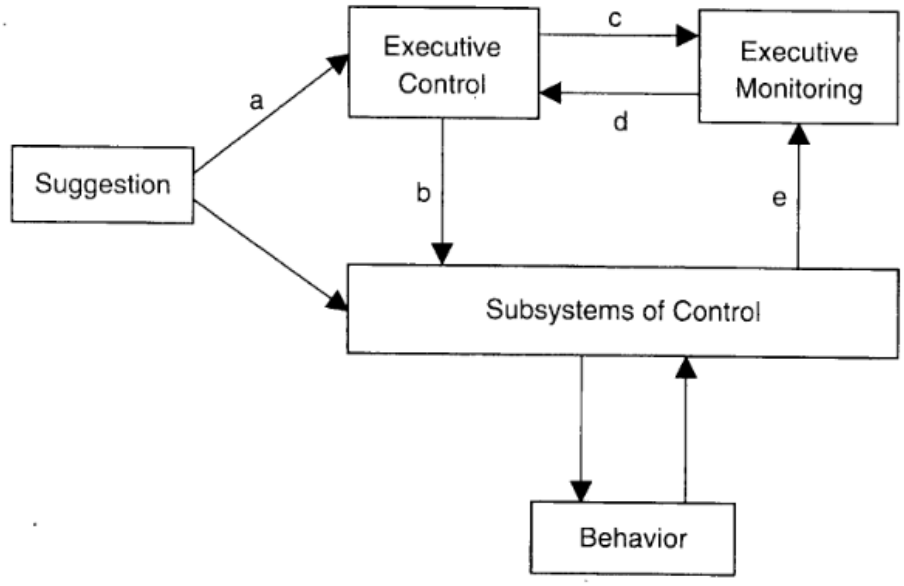

Figure 2 - Integrative model of dissociation theories of hypnosis (Nash and Barnier, 2008)

1.3.2 Evolution of the diagnosis

Dissociative disorders have had a troubled history in the Diagnostic and Statistical Manual (DSM), published by the APA. In the first edition, published in 1952, DD were part of psychoneurotic disorders. It included depersonalization, multiple personality disorder, stupor, fugue, amnesia, “dream states” and somnambulism. In this category, dissociation was associated to personality disorganization and conversion to symptoms of anesthesia, paralysis and dyskinesia. Previously, “conversion hysteria” was the group of conditions which included dissociative and conversion disorders. DSM-I was mostly relying on the psychoanalytic theory as reference.

A decade passed, and DSM-II was produced. In this manual, hysterical neurosis was divided in two types: dissociative type (alterations in consciousness and identity) and conversion type (alterations of the special senses or the voluntary nervous system).

In DSM-III (1980) and its revision, DSM-III-R (1987), the concepts neurosis and hysteria were abandoned. Dissociative disorders was a class composed by psychogenic amnesia, psychogenic fugue, multiple personality disorder, depersonalization disorder and atypical dissociative disorder. Conversion disorder was, then, for the first time, grouped with another category: somatoform disorders. In DSM-III-R, dissociative disorders had a central "disturbance in the normally integrative functions of identity, memory, or consciousness..." without evidence of organic brain disorder. Psychogenic fugue had the particularity of physical relocation and new identity formation. Still, information as interpersonal amnesia in multiple personality disorder was neglected, leading to mistakes and increased reports of MPD in 1980s and 1990s.

DSM-IV (1994), corrected the above mentioned mistake, including criteria of amnesia to the diagnostic of MPD, renamed dissociative identity disorder (DID). Cases similar to DID - but without episodes of amnesia, derealization without depersonalization and trance states were then added to a new category: dissociative disorder not otherwise specified" (DDNOS).

In the most recent version, DSM-V (2013), DD are divided in: dissociative amnesia (includes dissociative fugue), dissociative identity disorder, depersonalization disorder and dissociative disorders not otherwise specified - other specified dissociative disorder and unspecified dissociative disorder.

1.4 Etiology

Dissociation has been largely associated to psychological stress and trauma. Since Janet's studies on hysteria that some events are known for being responsible to affect predisposed individuals, originating dissociative phenomena. Further studies across time have linked the various types of dissociate disorders to several types of trauma, being them physical or psychological. Furthermore, recent studies on conditions such as DA, PTSD and DID have elucidated some of the mechanisms behind these dissociative processes. (Berntsen and Rubin, 2014; Huntjens et al., 2006).

Dissociation can also occur associated with organic mental disorder, a group of disturbances caused by brain dysfunction, which may resemble a psychiatric disorder but it is of somatic origin.

Last, but not least, dissociation may be originated by substance consumption, such as hallucinogens, cannabis or alcohol.

1.4.1 Relation to trauma

Dissociation has been correlated with history of trauma in several studies, especially childhood trauma, being it physical or psychological. It appears to have high specificity and low sensitivity towards history of trauma, meaning that dissociation is more common in traumatized patients but many traumatized patients never report dissociative symptoms.

The most important symptoms of dissociation described are depersonalization and amnesia regarding the abuse period. Dissociation may be considered a sort of defense mechanism in cases of trauma. Later on, victims of traumatic events may develop secondary symptoms such as anxiety, PTSD symptoms, somatization, depression, substance abuse or suicidal actions.

Personalization has been highly noted to occur in response to life-threatening danger. Similarly, dissociative amnesia and dissociative fugue have been noted in crime or disaster victims. In Putnam et al. (1985), 86% of the recent cases of DID reported history of sexual abuse, 75% reported physical abuse and 45% reported witnessing a violent death during childhood. Only 3% of the cases interviewed had no history of childhood trauma.

As most of these studies are retrospective, some authors consider them as being biased either by patients or clinicians. Furthermore, the definition of childhood trauma varies widely and, sometimes, extreme neglect and poverty were considered as such. In conclusion, the relation between childhood abuse and dissociative disorders should be considered as a hypothesis, not as an indisputable act. In the future, prospective studies containing groups of abused and non-abused children should be followed to determine the relation between childhood trauma and dissociative symptoms.

1.4.2 Organic Mental Disorder

Organic mental disorder (OMD), also known as organic brain syndrome or neurocognitive disorder, is a syndrome characterized by impaired mental function in the presence of organic (physiologic) brain disease, degeneration or damage. The primary causes include brain disease, degeneration or trauma; secondary causes are general medical conditions or substances. Some of the conditions related to OMD may be: concussion, epilepsy, encephalitis, hypoxia, meningitis, stroke, multiple sclerosis, Alzheimer's disease, vitamin B12 deficiency, alcohol abuse or drug abuse.

Symptoms may vary according to the general cause for the disease. These may include: confusion, dementia, delirium, impaired intellectual functions and agitation.

1.4.3 Psychoactive substances

Psychoactive substances may induce temporary states of dissociation. Among the most used, cannabis and alcohol may lead to dissociative states of depersonalization and derealization.

There is a particular group of drugs, called dissociatives – class of hallucinogens-, which are known to distort perceptions and produce dissociation symptoms. Some other effects of these dissociative drugs include: depressive symptoms, sedation, respiratory depression, analgesia, anesthesia, ataxia, amnesia and cognitive impairment.

Dissociatives are divided in two major groups:

- NMDA receptor antagonists – these include: Adamantanes (Amantadine, Memantadine); Arylcyclohexylamines (Ketamine, PCP, Tiletamine); Morphinans (Dextromethorphan, Methorphan); Diarylethylamines (Ephedine, Diphenidine); and others (Ibogaine, Nitroux Oxide, Chlorophorm)
- K-opioid receptor antagonists – Salvinorin A (from Salvia Divinorum); Ibogaine; Cyclazocine; Nalorphine; Pentazocine; Spiradoline; among others.

1.5 Diagnosis

Since Janet's studies on dissociation, even with some opposition from other investigators along the centuries, that dissociation is viewed as quantitative variable, present to a certain degree in everyone. Nowadays, it is quite a generalized opinion that dissociation ranges along a continuum from mild dissociative states to more pathological forms, represented by the DSM as dissociative disorders. Consistent with this generalized view, the Dissociative Experiences Scale (DES) was created by Bernstein and Putnam (1986), and, posteriorly, further "tuned" by Carlson and Putnam (1993). The DES is a diagnostic screening tool, the most widely used in the dissociative disorders field. Usage of this screening tool lead to the recognition of three core factors of dissociative disorders: absorption, derealization/depersonalization, and amnesia for dissociative states. The DES was created to answer to two important faults in the field: the need for a clinical screening instrument to detect dissociative disorders and the need to quantify dissociation in research studies.

The incidence and prevalence of dissociative disorders was, for a long time, unknown and hard to estimate. It was only in 1996 that Steinberg and her colleagues produced the Structured Clinical Interview for Dissociative Disorders (SCID-D) according DSM-IV. Since then, diagnostic interviews, such as SCID-D, the DES, and the Composite International Diagnostic Interview (CIDI), have enabled more rigorous screening for dissociative disorders across the world. However, some authors insist that some sections of these screening tools are still incomplete or totally absent. While SCID-D and DES measure trait-like dispositions towards dissociation, the Clinician-Administered Dissociative States Scale (CADSS) (Bremner and Marmar, 1998) was created to measure episodic dissociative states and symptom changes. It appears, however, to be more focused on depersonalization/derealization symptoms instead of identity or memory impairment.

The prevalence of dissociative disorders in inpatient and outpatient psychiatric settings is estimated to be around 10%, with half of patients being diagnosed with DID. In one study, it was reported that "6.3% of the general population suffered from three or more frequently occurring dissociative symptoms possibly representing a dissociative disorder" (Sar, V; 2011).

2. Amnesia

The word Amnesia derives from the Greek: (a-), i.e. “without” and (mnesis), i.e. “memory”. Amnesia, also called amnesic syndrome, is the general term for conditions characterized by disturbances in memory formation or recall, in a magnitude surpassing the every day’s normal forgetfulness.

The two main types of amnesia are called anterograde amnesia and retrograde amnesia. Sometimes, both types of amnesia might occur at once – total global amnesia. There are several variants of amnesia, to be discussed further ahead.

Contrarily to the “common sense” provided by fiction, amnesia, generally, does not cause loss of self-identity. Albeit, the condition affects patients’ past and future in many cases. People suffering from retrograde amnesia might find it hard to imagine the future, because to imagine future scenarios we recall many facts from previous experiences.

Amnesia can result from organic (e.g. stroke, Alzheimer’s disease, drugs consumption) or psychogenic causes (PTSD, dissociative amnesia).

Several studies show that amnesia is associated to damaged areas of medial temporal lobe and hippocampus.

Fortunately, amnesia is in most cases temporary, lasting up to a few hours or days, depending on the severity of the case. However, there are some cases of longer duration and even chronic cases of amnesia.

The majority of amnesia cases resolve without treatment. The neurological mechanisms involved in memory formation and recall are yet to be fully understood. This is the reason for the lack of pharmacological therapy in the field. In some forms of amnesia, psychological therapy may help patients recall parts of lost information (Brandt and Van Gorp, 2006).

2.1 Definition

Amnesia, or memory loss, occurs when there is a problem with the way the brain stores or retrieves memories (Hardt, 2009).

Amnestic disorders, according DSM, are a group of disorders in which one of three factors is impaired:

- Loss of memories previously formed
- Loss of ability to create memories
- Loss of ability to learn new information

Amnesia results either from organic damage - as observed in physical injuries, general medical conditions (e.g. Alzheimer's disease, Parkinson's disease) or drugs/alcohol consumption (e.g. benzodiazepines) - or psychogenic causes - dissociative processes observed in conditions such as PTSD and dissociative amnesia, believed to be part of a psychological defense mechanism. An amnestic disorder whose cause cannot be definitely established may be given the diagnosis of amnestic disorder not otherwise specified

Amnesia is, sometimes, confused with dementia, but they involve are different phenomena (Mohs, 1988; Hirai, 2001). Dementias are associated with continuous decline and cognitive impairment, while amnesia impacts mostly memory processes and is often stable, if not associated with underlying progressive pathology. Amnesic patients can, in many cases, retain substantial intellectual, linguistic, and social skills (Cermak, 1984).

Memories of habits are usually better preserved than factual memories and the most distant memories are the best preserved, in most cases. When recovering, older memories are more commonly recalled first and the most recent ones are recovered last.

2.2 Classification of amnesia

Following, some of the most important classifications of amnesia will be shortly explained.

2.2.1 Anterograde

Anterograde amnesia is characterized by inability to produce new memories while long-term memories from before the traumatic event – in many cases head trauma – remain intact. The regions of the brain related to this condition are the medial temporal lobe and the medial diencephalon. Neuronal loss impossibilitates the cure of this condition.

2.2.2 Retrograde

Retrograde amnesia causes the patient to be prevented from remembering events which occurred before the traumatic incident, however, they remain capable of forming new memories and learning new information. In rare cases, anterograde and retrograde amnesia may occur simultaneously. Frequently, this type of amnesia occurs after lesions besides hippocampus; this part of the brain responsible for new memory formation. Following Ribot's law, discussed ahead, recent memories are less likely to be recalled than older memories. Retrograde amnesia is frequently temporary and can be treated in many cases.

2.2.3 Post-traumatic amnesia

Post-traumatic amnesia occurs after a severe head injury (e.g. car accident). This condition is often transient but may be permanent. Extent of the amnesia period is related to degree and extent of the injury. Patients affected by this condition usually experience loss of consciousness or even coma right after the injury.

2.2.4 Drug-induced amnesia

Drug-induced amnesia is intentionally induced by injection of an amnestic drug to cause patient to forget a medical procedure, especially those performed under full anesthesia. Such drugs are, commonly, benzodiazepines such as midazolam or flunitrazepam, however, other drugs such propofol or scopolamine may be used. Memories are permanently lost or substantially reduced during the period of drug usage. After the drug effects wear off, memory is no longer affected.

2.2.5 Childhood amnesia

Childhood or infantile amnesia is the common inability to remember events from childhood period, particularly early childhood. Sigmund Freud attributed this to sexual repression; nowadays, investigators relate it with brain and language development. Implicit memories cannot be recalled, contrarily to explicit memories, which can be partially recalled and described.

2.2.6 Transient global amnesia

Transient global amnesia is characterized by a temporary loss of all memory, it is more common in older adults with vascular diseases. It is a distinct form of amnesia, as abnormalities in the hippocampus can be observed with a diffusion-weighted imaging magnetic resonance. The cause is yet to be clearly assessed. Hypothesis of causes for the syndrome include transient reduced blood flow, seizures or atypical types of migraine. Symptoms typically last less than a day, then patient goes back to normal.

2.2.7 Dissociative amnesia

This type of amnesia will be discussed thoroughly on the next chapter. Post-hypnotic amnesia (amnesia after hypnosis) may be considered a subtype of dissociative amnesia.

2.3 History

It is unclear when the diagnosis of amnesia was first conceived. Probably, the condition itself was recognized since ancient times, as the outcome of traumatic accidents.

French psychologist Theodule-Armand Ribot was, probably, the first most relevant scientist to study amnesia. He postulated a law stating that there is a time gradient in retrograde amnesia: following the course of an amnesic disorder, the patients loses the most recent memories first, then personal memories, and finally intellectual memories. Ribot's Law of retrograde amnesia contributed to the stimulation of the studies on psychopathology of the condition. Even though a large percentage of studies support the predictions of Ribot's Law, it is not universally accepted, nowadays, as the most accurate model for memory consolidation and storage.

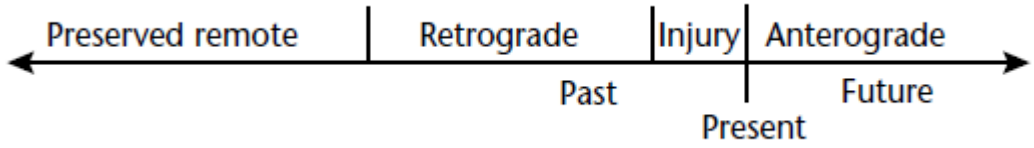

Figure 3 – Schematic representation of Ribot's Law (Budson and Price, 2001)

Case studies, along history, provided invaluable insight regarding pathophysiology of amnesia. Patient Henry Molaison (H.M), became a landmark in studies of memory and amnesia. W. Scoville and B. Milner, in 1957, reported the patient on their paper ""Loss of recent memory after bilateral hippocampal lesions". He suffered from severe epilepsy caused by a bicycle accident at the age of seven. Scoville, a neurosurgeon, decided to try brain surgery on the patient. He removed his medial temporal lobe bilaterally, which produced two separate opposite results: epilepsy did, indeed, improve and could now be managed by drugs; however, it also produced severe amnesia. H.M became to suffer from severe anterograde amnesia (which caused him to wake up every day, for the rest of his life, believing he was still in the 1950s) and retrograde amnesia for the eleven year period preceding his operation (predicted by Ribot's Law). He exhibited normal short-term memory but after a minute's time he would just totally forget the words. This was evidence that short-term and long-term memory imply different processes. Also, he could not remember doing some task, but he would improve at it after repeating it, showing that he was learning and remembering things unconsciously. In conclusion, he maintained his

procedural memory abilities, a common form of implicit memory. Scoville and Milner also noted that not all patients with temporal lobectomy developed amnesia, only if certain parts of the brain where removed. After analysis, they concluded that the removal of the hippocampus and/or amygdala was responsible for the amnesia. In the immediate years after, many researchers tried to link damage of the hippocampus with memory problems without much success.

Only in 1986, Zola-Morgan et al. published the first evidence paper linking selective damage of the hippocampus and amnesia. Patient R.B was a man diagnosed with angina and, after cardiac surgery, an ischemic episode occurred in the temporal lobe which left him with anterograde amnesia. The intriguing feature was that he only developed a very mild retrograde amnesia, with the exception of a couple of years before surgery. Postmortem analysis, by Zola-Morgan's group, demarcated a lesion in an area of hippocampus called the CA1 field. Subsequent reports, however, reported some inconsistencies concerning the presence and extent of anterograde and retrograde amnesia in lesions located in the hippocampus.

A study published in 1996, by Rempel-Clower et al. provides even further insight about the effects of hippocampal lesions on human memory. They evaluated data from patient R.B along with three other patients. One of them was G.D, a white male born in 1940 who served in the Navy. This patient, after a thyroid lobectomy procedure, developed cardiac problems. Only five days after release from the hospital, he showed signs of memory impairment without affection of any other cognitive processes. He also had a CA1 field lesion and the same clinical features as R.B. Two other patients, L.M and W.H, had more extensive damage to CA1, CA2, CA3, plus dentate gyrus and entorhinal cortex (W.H also had damage to the subiculum). Both patients had anterograde amnesia, which was more severe in W.H, and, simultaneously, a severe level of retrograde amnesia.

2.4 Memory formation

Memory system is the way in which the brain processes information that is available for use at a later time, with or without conscious awareness (Schacter and Tulving, 1994). Memory systems can be included in two major groups: declarative or explicit memory – events that can be consciously recalled –, and nondeclarative or implicit memory – expressed as a change in behavior, often unconscious.

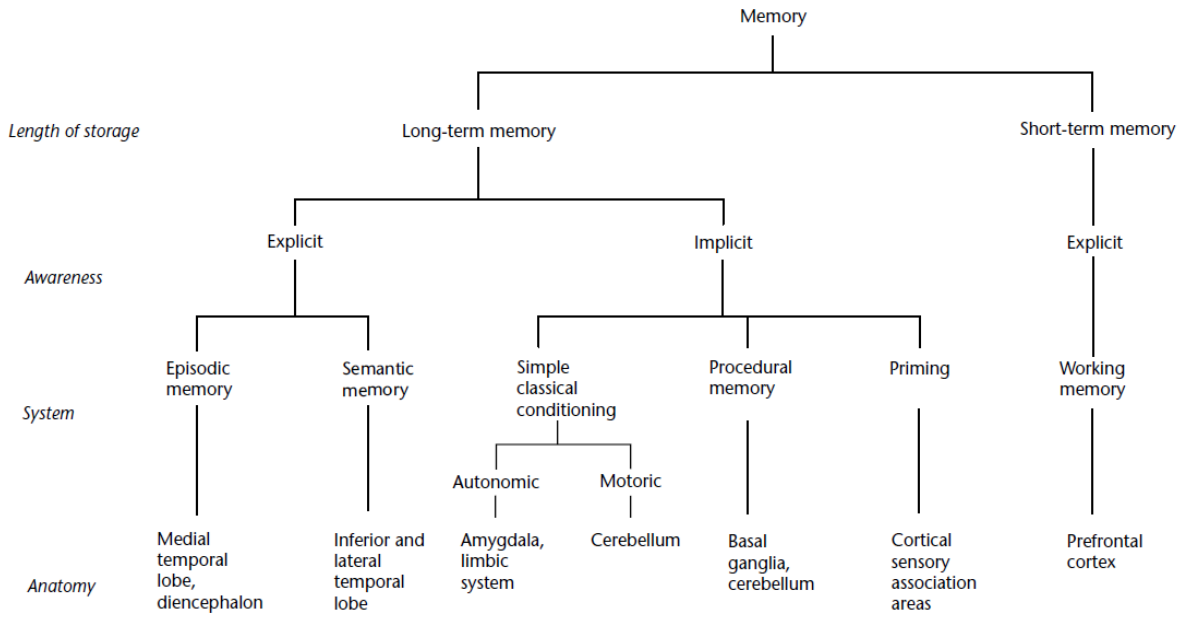

Figure 4 – Organization of memory systems (Budson and Price, 2001)

There are six separate and possibly dissociable memory systems:

- **Episodic memory** – personal, conscious recollection of our memories in our own context. Examples of related conditions include Alzheimer's disease, Korsakoff syndrome, transient global amnesia (TGA), herpes encephalitis, strokes, traumatic legions and vascular dementia.
- **Semantic memory –** factual knowledge, not related to any "specific" memory. It is declarative and conscious. For example, when we recall the first man who stepped on the moon, we immediately recognize Neil Armstrong as being the correct answer, even though we don't remember the context of when we learned it. This type of memory is relatively spared in conditions such as TGA, Korsakoff syndrome or trauma in medial temporal lobes. Examples of related conditions include Alzheimer's disease, encephalitis, traumatic legions, semantic dementia*.

  ***** This disorder has the particular feature of exhibiting "reverse Ribot" pattern, with anterograde memory and recent retrograde memory sparing but disrupted remote retrograde memory.
- **Simple classical conditioning –** involves pairing of two stimuli – an unconditioned stimulus and a conditioned stimulus. When the pairing exists, the response is elicited

by conditioned stimulus alone, no need for the unconditioned stimulus. This type of memory is unconscious and implicit. Such examples of this conditioning were those studied by Pavlov in animals. There are autonomic conditioned responses (e.g. fear) and motoric conditioned responses (e.g. eyeblink). Examples of related conditions include Alzheimer's disease, Korsakoff syndrome and degenerative diseases of cerebellum.

- **Procedural memory –** is the ability to learn behavioral and cognitive skills and algorithms that operate on an automatic, unconscious level. Some examples include riding a bicycle or swim. Diseases that affect basal ganglia or cerebellum can impair this type of memory. Examples of related conditions include Parkinson's disease, Huntington's disease, olivopontocerebellar degeneration and strokes.
- **Priming –** is when a particular previous encounter with an item changes how we respond to the current item. For example, if the subject is used to see a task being done in one way, it is normal to copy the same way when he does it, even though the task can be done in many different ways. This process occurs even without awareness of the subject, thus is an implicit type of memory. Two types of priming may occur: the perceptual priming (e.g. auditory, visual) or the conceptual priming. Any lesion of sensory association cortex may, in theory, be associated with defects of perceptual priming.
- **Working memory –** is the ability to maintain and manipulate information given in the moment towards an objective. For example, memorizing a phone number in order to call someone as soon as possible (phonological information) or giving someone directions following a mental route (visuospatial information), rely on working memory. Examples of related conditions include neurodegenerative diseases (PD, HD, AD), strokes and tumors (affecting frontal lobes and subcortical structures) and multiple sclerosis.

2.5 Etiology

A wide variety of conditions can produce memory impairment. These disturbances frequently occur after brain damage, but can be associated with psychopathologies as well. Amnesic disorders, the most severe form of memory impairment, has several types and associated conditions. Depending on the pathophysiology of the disease, different types of memory impairments might occur. Normal aging, depression and anxiety are commonly associated with memory difficulties. Many neurologic conditions and systemic illnesses can impair memory by affecting sensitive regions of the brain. Furthermore, some common medications can induce amnesia, even though mostly temporary.

A few causes and associated conditions of amnesia, considered important, are mentioned below:

- Psychiatric conditions – dissociative amnesia, which is discussed in detail in the third chapter, is one of the possible psychiatric causes of memory impairment. Conditions such as anxiety disorders, unipolar depression and schizophrenia can also impair concentration and attention, resulting in an inadequate processing of information by memory systems. In dissociative amnesia, dissociative fugue and dissociative identity disorder a patient may develop several deficiencies in retrograde memory by dissociative processes.
- Alzheimer's disease – is the most common neurodegenerative disease, affecting up to 20% of elders by the age of 80, causing evident impairment in the episodic memory system. Patients with AD develop dementia which may impair retrograde and anterograde memory systems.
- Frontotemporal dementia – disease in which frontal and temporal lobes are predominantly affected. In early stages, as frontal lobe is the most affected, personality changes are the most common feature but, as the temporal lobe involvement increases, memory deficits become clear.
- Parkinson's disease – is PD and other extrapyramidal disorders (Huntington's disease, Wilson's disease, etc.) may coincide with problems in memory registration and retrieval. In fact, several studies indicate that that memory impairment and other cognitive deficiencies develop several years before motor manifestations in HD. Cognitive impairment correlate strongly with extent of motor involvement in these conditions. In PD

substantia nigra degeneration of midbrain occurs, while in HD degeneration occurs mainly in caudate nucleus of the striatum.

- Multiple sclerosis – in MS, memory is one of the most consistently impaired cognitive functions. Long-term memory is particularly affected. The predominant memory function affected seems to be registration of memory.
- Cerebrovascular conditions – vascular dementia, strokes or any other cerebrovascular condition affecting normal cerebral blood flow may lead to amnestic syndromes. Lesions in the posterior cerebral artery, for example, which supplies the occipital and medial temporal lobes, may produce homonymous hemianopia as well as anterograde and retrograde amnesia. Infarctions in the thalamus can lead to anterograde amnesia, with special characteristics such as confusion and confabulation on patients. Infarctions in the subthalamic and mesencephalic regions may induce impaired attention and responsiveness, resulting in prominent deficits in concentration, registration and retrieval of memories.
- Epilepsy - complex partial seizures have been shown to cause deficits in memory, learning and attention. Verbal memory is particularly impaired when the dominant medial temporal lobe is involved and nonverbal memory when the nondominant side contains the primary seizure activity. Registration and short-term memory seem to be spared.
- Korsakoff syndrome – with the increased alcohol consumption registered in many countries, Korsakoff syndrome cases have increased. Chronic alcohol consumption may lead to poor nutrition and thiamine deficiency. Loss of neurons and myelinated nerve fibers damage several brain structures, in particular interrupting the Papez circuit, leading to profound anterograde amnesia and memory retrieval impairment for recent memories. Memory distortions and confabulations may occur.
- Head injuries – most common cognitive complaint after head injuries is memory impairment. Mostly recent memory- related tasks appear to be the most affected. Memory consolidation is related to areas of temporal lobes and orbitofrontal surface, which are very susceptible to contusion accidents.
- Herpes encephalitis – herpes simplex virus has predilection to damage limbic structures in cases of encephalitis. Medial temporal and orbitofrontal structures affected lead to an anterograde amnesia characterized by intact immediate memory and registration, but with impaired recent memory or consolidation.

- Tumors and abscesses – any space-occupying lesions of CNS may produce amnesia by two major mechanisms: local effects on various parts of limbic system or by exerting pressure on distant structures by increasing intracranial pressure and edemas.
- Hypoxia – severe and short hypoxia affects areas of the brain most vulnerable to an acute lack of oxygen, rending them permanently affected. Damage is greater on hippocampus leading to new learning and memory consolidation defects (anterograde amnesia). This may occur in drowning, strangulation, respiratory failure, or cardiopulmonary arrest. Chronic hypoxia results in more widespread impairment (e.g. chronic obstructive pulmonary disease)
- Drugs – anticholinergic agents such as scopolamine and atropine may mimic learning and memory deficits seen in neurodegenerative conditions in normal subjects. Benzodiazepines such as lorazepam and diazepam can create a direct amnestic effect, mostly on declarative memory system, sparing procedural memory. Contrarily, adrenocorticotropic hormone and vasopressin analogues improve memory and learning performance.

2.6 Pathophysiology

Amnesic disorders arise, mostly, after damage to important structures through which information passes before it is stored long-term, but can also occur after widespread cortical damage (Markowitsch and Staniloiu, 2012). However, some of these disorders occur even without evident brain damage detected on imaging methods. This type of disorders are associated with dissociative processes and psychiatric pathologies. In studies, such as Markowitsch's on mnestic block syndrome (2002), it was possible to identify that some changes affect regions with crucial roles in memory associated with these psychiatric pathologies. As the dissociative processes of memory impairment are similar in the various types of dissociative conditions (dissociative amnesia, dissociative fugue, dissociative identity disorder, depersonalization disorder and dissociative disorders not otherwise specified), the processes of disease formation for these conditions will be further discussed in the next chapter, concerning dissociative amnesia.

A hypothesis has been formed (Heichenbaum et al., 1996) that memory representations are set and maintained in the cortex and that hippocampal and parahippocampal regions contribute to

memory processing by modifying and organizing those cortical representations. However, not all modifications of cortical representations depend on hippocampal system. The role of hippocampus, thalamic nuclei and mammillary bodies is, then, to provide means to store and retrieve memories, particularly unconsolidated ones, being unlikely that these areas of the brain contain any specific memories. It is agreed that hippocampal region is critical specifically for declarative memory.

Other types of memory, as for example priming, seem to be intact following hippocampal damage. Recent studies, have focused the neural substrates involved in procedural (implicit) memory. This type of memory is complex and is likely to involve multiple CNS sites, although there is increased evidence of the critical role of the cerebellum in mediating many of these types of memory tasks. Immediate memory has been related to perisylvian cortex, surrounding sylvian fissure, an area essential for language repetition. Remote memories, evidence suggests, are stored diffusely in many CNS sites, including secondary and tertiary association cortex.

Amnesia can be described based on the place of brain damage: hippocampal or medial temporal lobe (MTL); diencephalic amnesia and basal forebrain amnesia. They have different features but share some others. Inside hippocampus itself, is thought to exist several stages of processing, being the outcome of integration of memories sent back to the parahippocampal region, which in turn sends its main outputs to the same tertiary region of cortex which provided the source of input. Several studies, such as Papanicolaou et al. (2007) show that severe amnesia can result from brain damage in the intersection of these areas, for example, after bilateral damage to fornix, projecting from the hippocampal formation (HF) to the mammillary bodies (part of diencephalon).

Also input from amygdala has been associated to social and emotional memory: neutral events are encoded in the memory system in a more simple way, contrarily to aversive events which have more complex encoding.

Scoville and Milner were essential to the understanding of several amnesia pathophysiological mechanisms, namely on the study of HM's case. MTL surgery lead to anterograde amnesia, impossibilitating formation of new memories, however semantic and procedural memories remained intact. Learning by conditioning and priming were still possible to the patient. Since then, hippocampal formation (hippocampus, dentate gyrus and subiculum) is thought to be essential in transmitting information from short to long terms. HF atrophy has been linked to early Alzheimer's disease but also occurs in non-demented elders.

Shimamura (2010) concluded that retrieval of Episodic-autobiographical memory (EAM) is a whole-brain process in which the hippocampus is the most important of MTL structures, even though it needs input from sensory and emotional information from other parts of the brain.

A special variant of MTL amnesia, developmental amnesia, is thought to be caused by damage to hippocampus, leading to reduction in bilateral volume. It may be caused by episodes of brain ischemia or hypoxia, occurring perinatally or in childhood. Children affected can still acquire and retrieve facts, but the learning process and retrieval of EAMs is severely impaired. These findings support the information that HF is a key structure in formation of EAMs. Wernicke-Korsakoff syndrome, characterized by anterograde and retrograde impairments of EAM, and sometimes semantic memory impairments and confabulations, is regarded as the "prototype" of diencephalic amnesia. Patients with this condition mainly suffer from degeneration from midline diencephalic structures but lesions can be more widespread (including middle cingulate gyrus lesions). Several reports have also given proof that bilateral damage to mammillary bodies or mammilothalamic tract is sufficient to cause amnesia. Thalamic damage is common after stroke due to the four arterial branches which vascularize different thalamic regions.

Basal forebrain is composed of 3 major nuclear complexes: basal nucleus of Meynert, diagonal band of Broca and septal nuclei. These nuclei project to HF and other areas of cortex. Medial septal region is connected to amygdaloid complex which enhances emotional relevance of information. Basal forebrain amnesia may occur after rupture or surgery of aneurysms of the anterior communicating artery, or tumours. In basal forebrain amnesia, executive dysfunctions are common, leading to problems recognizing information – if it extends to upper portions of frontal lobes, source amnesia (failure to remember where information came from) can occur. This type of amnesia also might occur with confabulations and false recognitions in procedural memory. Fornix is essential for memory consolidation and transfer of information from short to long-term because it connects all three major regions (MTL, diencephalon and basal forebrain).

2.6.1 Organic versus dissociative retrograde amnesia

In studies, such as Markowitsch's (1996), common features between psychogenic and organic amnesia were analyzed. Markowitsch's model postulates that stress may affect frontal executive systems, causing inhibition of autobiographic memories retrieval. If the stress is severe enough the inhibition may even affect personal believe systems resulting in a transient loss of personal identity or fugue. This model is consistent with knowledge of brain systems function known from organic amnesia.

Psychogenic amnesia can be either local or situation specific. The condition intertwines predisposing psychosocial factors and frontal lobe inhibitory mechanisms associated with systems related to normal memory and organic amnesia, more specifically retrograde amnesia.

Depending on the brain regional which was damaged, retrograde amnesia is a more variable condition than dissociative amnesia: right hemispheric temporo-frontal lesions lead to similar behavior from patients when compared with psychogenic amnesia; whereas patients with damage to diencephalic structures are more variable, even with partially preserved retrograde memories (following Ribot's gradient).

Several documents (Kopelman, 1987; Markowitsch, 1996a, 1996b, 2008; Reinhold et al., 2006; Serra et al., 2007) demonstrate that the same mechanisms influence both forms of retrograde amnesia (dissociative and organic) leading to a blockage or disruption in the way brain accesses stored memories. According "la belle indifférence" (Brand and Markowitsch, 2009; Markowitsch, 2009; Janet, 1907) – i.e "the beautiful indifference" - dissociation of emotion, self-sense and autobiographical memories may also contribute to retrograde amnesia.

Comparing patients with direct organic brain damage and with functional/dissociative amnesia, frequently dissociative amnesia patients manifest additional "somatizations" such as leg weaknesses, anomia, and palsies (Kritchevsky et al., 1997) and show a history of psychiatric illnesses.

	Organically caused isolated retrograde amnesia	Psychogenically caused isolated retrograde amnesia
Initiating event	Severe pathological event (stroke, trauma, etc.) Possibility of accompanying psychiatric symptoms (personality disorder)	(often) Mild head trauma Precipitating stress Possibility of accompanying psychiatric symptoms (personality disorder)
Brain alteration		
Structural	Bilateral brain damage in various regions, with a preponderance of right-hemispheric damage; most frequently in both temporopolar and inferolateral prefrontal areas	No (or just minor) structural brain alteration
Functional		Reduced brain metabolism, primarily in right inferolateral prefrontal regions and anterior temporal regions
Congruence of brain damage and severity of memory disorder	More likely given	Usually not given
Clinical appearance	Frequently no loss of self-identity knowledge (or at least fast recovery after onset) Insecure personality	Loss of self-identity knowledge Belle indifference Insecure personality and possibility of further psychiatric signs
Psychopathology	Usually no evidence of psychiatric disease or personality disorder	Possibility of premorbid psychiatric history or of subtle personality disorder
Neuropsychological profile		
Functions other than retrograde autobiographic memory	Intellectual functions partially disturbed, but large variance	Intellectual functions sometimes partially or temporarily disturbed, but frequently largely preserved
Retrograde autobiographic memory	Sometimes negative temporal gradient of retrograde autobiographical amnesia, sometimes total loss	Frequently homogeneous loss of retrograde autobiographical memory, sometimes just for certain life epochs or events

Table 1 - Similarities and differences between organic and psychogenic causes of retrograde amnesia (Reinold and Markowitsch, 2009)

2.7 Prognosis and management

Prognosis for amnesic disorders is highly dependent on the type of episode and lesions involved. In conditions such as transient global amnesia, patients recover completely, whereas in conditions involving bilateral damage to MTL, diencephalon or basal forebrain, the prognosis remains poor. Patients in risk of developing Wernicke-Korsakoff syndrome are given thiamine to prevent likelihood of disease or to prevent further damage – in some cases, lost memories can be even recovered.

Pharmacological treatment for amnesic disorders is somewhat insufficient and without high percentage of success. Some drugs used in the treatment of conditions which affect memory, such as Alzheimer's disease, have been investigated for their usefulness in the treatment of other conditions, namely: donepezil, rivastigmine, memantine and galantamine. Also, guafancine, used

in the treatment of attention deficit hyperactivity disorder (ADHD) has been proved to help working memory in humans (Jakala et al., 1999; Swartz et al., 2008). Piracetam, abundantly studied since 1960, a synthetic derivative of GABA, has been part of several case studies which demonstrate some potential in reducing neuronal damage and treating memory deficits. Yet, more studies are necessary to determine if this drug exerts meaningful benefits in the treatment of amnesia.

Sometimes treating or removing underlying conditions such as infections, tumors or medication side effects, might help to relieve or decrease degree of amnesia. However, evidence-based psychopharmacology does not provide definitively effective treatments to reverse memory impairments or deficits. It is thought that in the future, with further investigation and knowledge about biological memory brain processes, some drugs might be developed.

Electrical stimulation, such as deep brain stimulation (DBS), has been used to treat amnesia. Neuronal modulation occurs after these mild electrical currents are applied.

Changes in some hormonal levels may play a role in amnesia. Two neurosteroids in particular have been associated with memory disorders: pregnenolone and dehydroepiandrosterone (DHEA) (George et al., 2010). In animals, increasing age has been associated with lower levels of pregnenolone which was coincidental with memory impairment. Administration of this drug into the nervous system improved memory in model animals.

A very important part of the management of these patients should involve rehabilitation, which may address cognitive, emotional and psychosocial features of patient's functioning. It defines strategies that patients can use to compensate for the lost capacities of functioning either personally or in society. In severe cases of amnesia, procedural and priming tasks were used successfully as a "teaching" mechanism.

Psychotherapy is particularly useful in dissociative types of amnesia. Combined with sedating medications, it might help these patients to regain access to the lost memories (Brandt and van Gorp, 2006). People with other forms of amnesia can also benefit from psychotherapy – it can facilitate rehabilitation in patients with preserved insight, minimizing impact of memory loss on quality of life. Nowadays, mechanisms such as external memory aids and support, based on modern computer-based equipment are becoming more reliable and increasingly growing in importance for amnesic people.

3. Dissociative Amnesia

Dissociative amnesia is a very interesting psychiatric disorder. It is a condition related to severely impaired memory functions without an evident neurobiological cause in patients who have had one or more highly stressful life events in the past.

This condition became an official diagnostic entity only after DSM-III. Before, it was considered a symptom of dissociative reaction, in DSM-I, and as hysterical neurosis, of the dissociative type, in the DSM-II. Being so controversial and with so disparate diagnostic methods, there are several case reports which mistake psychogenic amnesia with dissociative fugue (Akhtar, Lindsey, Khan, 1981; Gudjonsson and Haward, 1982; Lyon, 1985; Kaszniak, Berren, Santiago, 1988; Takahashi, 1988; Eisen, 1989) and some other disorders.

In the past years, the etiology and pathophysiology of condition has been subject of much debate and investigation. For such, the advances in memory research and neuroimaging methods have been essential.

The course of the disease and symptoms vary from patient to patient which suggests a possibly heterogeneous disorder. In most cases, dissociative amnesias are retrograde, mainly affecting autobiographical memory.

Nowadays, there is no evidence-based treatments available and the rehabilitation is mostly based on supportive psychotherapy, hypnosis and anxiolytic medication.

In the past few years, some important authors such as Markowitsch (2002) introduced a new concept called mnestic block syndrome. This syndrome has acute causes traced back to somatic illnesses, but the cognitive deteriorations go beyond the scope of amnesia for single events (e.g. posttraumatic stress disorder). Self-identity may be preserved, but social and other important aspects of life are usually impaired. This syndrome is mostly related to retrograde memory block due to psychic causes but, in rare cases, can also be related to anterograde memory block. Obviously, malingering and feigning should be excluded to conclude diagnostic.

Analysis of this concept is outside the scope of this thesis assignment, however its relation to dissociative amnesia is not clearly defined and it might prove to be important, in the future.

3.1 Definition

Dissociative amnesia is one of the first reported psychiatric phenomena, dating back from as soon as 1806 (General Assembly's Missionary Magazine) (Dell, 2013).

DA can be defined as a deterioration of memory function, precipitated, in most cases, by acutely stressful life events with absence of structural or biological brain damage. Primary symptom is typically retrograde amnesia, either comprising one or more specific episodes in the patient's life or the entire past memories. Memory for personal events is typically more impaired than memory for public events and there is little to none anterograde amnesia. Semantic memory, and cognitive capacities in general are commonly unaffected.

Dissociative amnesia, as a symptom, is:

a) A feature of dissociative amnesia, dissociative fugue and dissociative identity disorder
b) A common symptom of dissociative disorders not otherwise specified (DDNOS)
c) A symptom of PTSD, acute stress disorder and somatization disorder

Throughout the years, the group of amnesic disorders related to psychological mechanisms have been associated with various categories of diagnostic, sometimes having different theoretical bases and principles. The term dissociative amnesia is theoretically loaded as it is assumed that dissociation is the main or only pathological mechanism of memory deterioration. This theoretical load is different in both ICD-10 and DSM-V classifications. In ICD-10, diagnostic guidelines explicitly imply the need for associations between symptoms of the disorder and stressful life events. In contrast, DSM-5 does not explicit these associations as a diagnostic criterion, however it acknowledges their existence and likelihood.

To emphasize further the difference between these two classifications: in ICD-10, dissociative fugue is described as a separate entity from dissociative amnesia; whereas in DSM-V, dissociative fugue is encapsulated inside dissociative amnesia (clinical, neuropsychological and neuroimaging date support DSM's classification).

The last definition of DA in DSM-5 is closer to the original description by Janet and it narrows the gap between ICD-10 and previous DSM editions.

3.1.1 Nosological classification: DSM-V and ICD-10

- DSM-V diagnostic criteria for dissociative amnesia:

Code 300.12

"A. An inability to recall important autobiographic 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 (e.g., alcohol or other drug abuse, a medication) or a neurological or other medical condition (e.g., 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."

Specify if: Code 300.13 "With dissociative fugue: Apparently purposeful travel or bewildered wandering that is associated with amnesia for identity or other important autobiographical information."

- ICD-10 diagnostic criteria for dissociative amnesia:

Code F44.0

"The main feature is loss of memory, usually of important recent events, that is not due to organic mental disorder, and is too great to be explained by ordinary forgetfulness or fatigue. The amnesia is usually centered on traumatic events, such as accidents or unexpected bereavements, and is usually partial and selective. Complete and generalized amnesia is rare, and is usually part of a fugue (F44.1). If this is the case, the disorder should be classified as such. The diagnosis should not be made in the presence of organic brain disorders, intoxication, or excessive fatigue."

Exclude: alcohol or other psychoactive substance-induced amnesic disorder, amnesia not otherwise specified, anterograde amnesia, retrograde amnesia, non-alcoholic organic amnesic syndrome and postictal amnesia in epilepsy.

Note:

Currently there is a draft for a future ICD-11 under construction. In this draft, DA now clearly excludes causes such as traumatic brain injury and refers to stressful events to be a likely cause, in conjunction with traumatic events. These group of disorders have also been renamed to Dissociative Disorders rather than Conversion Disorders. These descriptions might, yet, be subject to changes.

3.1.2 Clinical-descriptive classification: Janet's four-fold

DSM-V describes DA close to Janet's four-fold classification of amnesia (localized, systematized, generalized and continuous). Janet's description is based on his studies on "hysteria" cases.

Localized amnesia is a common type, however it is infrequently diagnosed. In this type of amnesia the patient cannot recall events during a limited period of time, these periods can be of minutes, hours or days (e.g. sexual assault, car crash) but often comprise a period of years (e.g. chronic child abuse). There is a variant of localized amnesia, called selective amnesia where the patient can recall some events, but not all of them during a limited period of time. Thus, the patient might recall most of a traumatic event but neglect a particular aspect of it. This situation is quite common for clinicians who work with trauma.

Several experts consider systematized amnesia to be the most common form. This type of amnesia is characterized by a loss of all memories for certain categories such as family or a particular person. In this category, some patients might remember their entire childhood but forget about the episodes of their childhood sexual abuse.

Maybe the best known form of DA is generalized amnesia, in which these patients forget their entire lives and personal identities. This type of dissociative amnesia, despite being rare, is often associated with dissociative fugue. Often patients are found by police or taken into the

hospital's emergency room. It is thought that the fugue starts with the onset of memory loss and it stops when patients realize consciously that they have forgotten their own personality. Fugues are very common in DID.

3.1.3 Empirically-derived classification: Three dimensions of dissociative amnesia

In 2013, Dell proposed another type of classification based on Muldimensional Inventory of Dissociation (MID) as a diagnostic method. This classification's goal was to finally answer to the question: what are the dimensions of dissociative amnesia?

Dell's investigations lead him to the three dimensions of dissociative amnesia – "Gaps in Remote Memory", "Discovering Dissociated Actions" and "Lapses of Recent Memory and Skills". These dimensions are phenomenologically different from one another.

Gaps in Remote Memory fits conveniently with Janet's four-fold classification, particularly with localized amnesia. Discovering Dissociated Actions is classical process of DID and an example of generalized amnesia because dissociated actions are basically amnesias for a particular behavior (e.g. behavior of alter-egos). Lapses of Recent Memory are closely related to conversion or negative dissociative symptoms.

These three amnesia factors may constitute a dimension of increasing severity that begins with Gaps in Remote Memory, extends to Lapses of Recent Memory and Skills, and ends with Discovering Dissociated Actions (Dell, 2012). In Discovered Dissociated Actions, previously amnestic individuals are faced with the fact that they did something that they can't remember. Secondly, in Lapses of Recent Memory and Skills, individuals are suddenly faced with the fact that they are unable to do something that they usually did (e.g. they can't read, they can't remember the previous 5 hours or they can't use some device). Third, during Gaps in Remote Memory, the individuals are unaware of having holes in their memory and, as time passes, they may or may not become aware of this fact. Most of these individuals become aware of their memory gaps during clinical interviews and are usually hesitant in trying to remember these gap periods – intricate emotional response.

3.2 Dissociative Fugue

Dissociative fugue is recognized as a subtype of dissociative amnesia. During a fugue episode an individual may appear and act in a normal or purposeful way and it may last for days, weeks or longer. In this period, a sudden and unexpected travel away from usual places occurs in combination with retrograde amnesia and either loss of identity or assumption of an alter identity.

As the name suggests, psychological flight occurs in response to an overwhelming situation. Onset is sudden, triggered by a traumatic or stressful life event, however, history of traumatic events is commonly present in the individual's past. Dissociation, in these cases, is used as a primary psychological defense. The prevalence of this condition is estimated to be very low, 0.2% (Coons P.M. and Milstein V, 1999). Diagnosis of the DF depends on severe retrograde amnesia in the absence of anterograde amnesia or other cognitive impairments or evident neurological lesions.

- Diagnostic criteria in DSM-5:

Dissociative Amnesia + Code 300.13 "With dissociative fugue: Apparently purposeful travel or bewildered wandering that is associated with amnesia for identity or other important autobiographical information."

- Diagnostic criteria in ICD-10:

Code F44.1 "Dissociative fugue has all the features of dissociative amnesia, plus purposeful travel beyond the usual everyday range. Although there is amnesia for the period of the fugue, the patient's behavior during this time may appear completely normal to independent observers." Excludes postictal fugue in epilepsy

- ICD-11 draft diagnostic criteria:

Code 7B33.1 "Dissociative amnesia with dissociative fugue Dissociative amnesia with dissociative fugue is characterized by all of the features of dissociative amnesia, together with sudden, apparently purposeful, travel away from home, work, or significant others for an extended period of time (days or weeks), or with bewildered wandering. The amnesia is typically associated with confusion about one's identity, and presentation of a new identity may occur."

Alternate names: dissociative fugue and hysterical fugue

3.3 Brain mechanisms in disease formation

Freudian concept of repression has been used to explain the process by which dissociative amnesia appears. Highly stressful or traumatic situations are blocked or locked away by the conscious self. The ego becomes split or dissociated from the impulses or desires of the id. In spite of some studies attempting to prove the concept of repression, empirical support for it is limited and validity of claims of DA in trauma victims have been questioned (Pope et al., 1998).

Kopelman has developed a neurocognitive model to try to explain how psychosocial factors interact with brain to produce retrograde amnesia. The model proposes that severe stress on brain's executive control system, together with predisposing psycho-socio-biological factors, inhibit the retrieval of memories, namely autobiographical and episodic. When these pressing factors are severe enough they may even affect brain's personal belief system, resulting in loss of identity. In this model, the executive control system is independent from middle temporal/diencephalic memory system, which supports the formation of new memories. "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." (Staniloiu, Markowitsch; 2014).

Some neurochemical models emphasize that alterations in neuropeptides and neurotransmitters released during stress modulate formation and recall of memories of the trauma (Bremner et al., 1996; Markowitsch, 1999, 2003). The neurochemical model is supported by studies showing a dysregulation of the hypothalamic- pituitary/adrenal axis in dissociative amnesia. Also, autobiographical and semantic memories were affected in some patients following administration of glucocorticoids or psychosocial stressors. Changes in stress hormones and brain function arising from an interplay of genetic and environment factors can be used to explain likelihood of DA development, which is coherent with epigenetic models as well.

A new hypothesis based on cultural, societal, psychological and neurobiological factors was formulated. The two-hit hypothesis assumes a synergistic interaction between psychological and physical events to explain some cases of DA following mild traumatic brain injury,

electrocution or general anesthesia. In particular, mild traumatic brain injury cases are interesting given that microstructural changes in the white matter after trauma correlated to worse performances on executive tasks.

Recent fMRI studies have provided some insight concerning neural mechanisms involved in memory suppression, in particular prefrontal cortex involvement. Anderson el al. (2004) reported increased activity of bilateral dorsolateral prefrontal cortex (DLPFC) and decreased hipoccampal activity were involved in exclusion of unwanted memories. Depue et al. (2007) postulated that emotional memory is suppressed by two pathways, right inferior frontal gyrus and right middle frontal gyrus, which controls memory representations in hippocampus and amygdala.

There were produced PET studies reporting: reduced activity in the right hemisphere (Markowitsch, Fink, Thone, Kessler, Heiss, 1997), reduced activity in the right frontal and temporal regions (Markowitsch, Calabrese, et al., 1997), and reduced activity of the hippocampus with increased activity of the anterior medial-temporal lobe (MTL) including the amygdala (Yasuno et al., 2000) during memory retrieval tasks. Also, some fMRI experiments showed dysfunction of the MTL in patients with DA (Yang et al., 2005). The reason for this MTL deactivation occurring in areas for memory processing has not been clarified.

A recent study, by Kikuchi et al. (2009), pointed out increased activity in prefrontal cortex and decreased activity in the hippocampus in association with DA. In this study, after treatment for retrograde amnesia, these activations disappeared in one of the patients who recovered his memories, whereas they remained unchanged in the other patient, to who the treatment was unsuccessful. This indicates that the changes in activation were specific to the patient's deficit in memory retrieval. Albeit, there might be another explanation for the prefrontal activation and hippocampal deactivation. Some unknown mechanism causes hippocampal deactivation and inhibition of memory retrieval and then prefrontal cortex activates signaling the strong effort to retrieve those memories. In fact, there is no clear causal relationship that prefrontal activation induces hippocampal deactivation, only speculation about the process. Further and more sophisticated studies are needed in the future in order to fully understand this process.

3.4 Patterns of memory loss and cognitive changes

Dissociative amnesia is a very heterogeneous condition, in terms of clinical and neuropsychological presentation. The disease might have variable courses, causes, mechanisms and underlying ideologies.

Some cases might involve loss of all autobiographical information, while other cases may involve some particular aspect of a traumatic event and be only partially blocked from the patient's awareness. In some cases, patients might have amnesia for an entire traumatic event such as childhood sexual abuse, while maintaining normal autobiographical memory for other aspects of their childhood. This type of memory block are considered by many authors as recoverable, thus the diagnosis of this form of DA remains lacking of empirical support, controversial and debatable.

Memory impairment is most frequently retrograde and is mostly limited to episodic-autobiographical type, delimited or generalized in time. It may or may not follow Ribot's law of memory preservation. Variable impairments of old semantic memory have been reported as well.

Autobiographical-semantic memory is usually preserved in milder cases of DA. Loss of personal identity occurs in more severe cases and in cases of dissociative fugue. Components of autobiographical-semantic memory can be impaired in organic causes of amnesia, which provides ground for differential diagnosis. Abrupt loss of autobiographical memory and identity is strongly suggestive of dissociative amnesia. Perceptual memory has not been formally assessed in DA patients, as well as procedural memory. However, impairments in executive function and complex attention tasks and changes in perception, social cognition and behavior have been described. Although, the results are not uniform. Priming is typically preserved.

Memory acquisition of new information is often spared but concomitant decreased performance in anterograde memory tasks can occur. DA with anterograde memory impairments in the absence of retrograde amnesia (continuous amnesia) is diagnosed rarely. The underlying mechanism of this process are deficits in conscious acquisition of new information with or without a memory retrieval block.

Intelligence is usually preserved, even if there is history of pseudodementic presentations on record. Language is spared, but semantic memory and executive function deficits may influence the performance of patients. Absence of concern for symptoms ("la belle indifference") may or may not occur in DA.

Many patients, however, report some distress related to their amnesic symptoms. There is a hypothesis that dissociation prompts individuals to create confabulations and feigning symptoms but there is no strong empirical support. DA can occur suddenly, but a lag time may exist between the traumatic event and the onset of amnesia.

3.5 Etiology

Dissociative amnesia may be encountered by specialists in several departments, being psychiatric, neurological or other. A significant part of these patients, however, have a sudden onset of symptoms following a traumatic event, thus, it is quite common to be found in emergency situations. Models that propose that trauma can cause dissociative reactions are well documented by retrospective and prospective studies of peritraumatic psychological dissociation (Nijenhuis et al., 2001).

Some of the traumatic events may be childhood abuse, adult rape, accidents, attempted suicide, criminal acts or witnessing violent deaths (Arrigo and Pezdek, 1997). People under psychiatric treatment after physical or psychological abuse are susceptible for developing DA. A considerable number of people admitted into a psychiatric hospital have elevated Dissociative Experiences Scale (DES), according reports.

People who had had histories of sexual or physical abuse, and those who had witnessed violence between parents, are the largest groups with high DES scores. Dissociative amnesia in military hospitals, after experiencing combat horror, has early been noted as common (Sargant and Slater, 1941). Many of these patients satisfying criteria for PTSD.

Genetic influences on dissociative amnesia and dissociative disorders in general are unknown. However, some quantitative genetic studies reported heritability rates for dissociation of 50-60% (Staniloiu and Markowitsch, 2014).

3.5.1 Childhood abuse

Memories recovered from childhood abuse has been accepted by many clinicians, however, there is still a considerable number of investigator questioning the validity of recovered memories of childhood abuse and proposing that, in some cases, clinicians may be cooperating in the creation of pseudomemories.

Recent studies have demonstrated that memories can be inaccurate. The role of suggestion in alteration of memories has been well established and documented. Based on Piaget's studies, it is known that patients can create pseudomemories of events that never occurred, especially if introduced to them in "fragile" states by trusted individuals.

Clinical research has generally accepted the influence of childhood abuse as a cause for DA. Self-reports of childhood abuse in clinical populations treated for trauma-related conditions reached values as high as 62% in some studies.

Childhood abuse were related to higher levels of dissociation, although not invariably so. There was noted also an inverse proportionality between age and levels of dissociation – the earlier the age of onset, the higher will be the levels of dissociation. Chronic abuse, hence, stimulates dissociative mechanisms which persist to adulthood. A recent analysis by Putnam et al. (1996) introduces subsets on population of high dissociators and low dissociators, people with more or less likelihood to develop dissociative symptoms. This differential susceptibility may explain the large deviations on DES found on several studies.

3.5.2 Pregnancy

Dissociative experiences during pregnancy and childbirth have been reported. The prevalence of such situations is not known.

In an article by Hema Tharoor et al. (2007), a curious case of DA following pregnancy is reported. The predominant disturbance in this patient was an inability to recall important personal information.

After delivering her sixth child, some of her family members noticed that didn't acknowledge her new born or recall her pregnancy. She didn't deny the pregnancy itself but had

no memory of any personal information or the pregnancy. She continued to breast feed the baby and took an active interest in his care, forming ordinary mother-infant bonding. Organic etiology was ruled out by a series of examinations. The patient admitted to childhood abuse in one interview with psychiatrists. There was no evidence of post-partum depression nor psychosis. The patient fulfilled all the criteria for DA.

After an interview in which she was given thiopentone intravenously, the admitted that the current pregnancy was seen as a major stressor, that she was exhausted physically and that she had a verbal conflict with her spouse regarding termination of the pregnancy during the first trimester. Following hypnosis, she improved even further in recollection of her memories. A combination of hypnosis and memory enhancing tasks were useful in facilitating the recovery.

3.5.3 Other causes

Mayumi Ishida et al. (2015) described what seems to be the first reported case of DA following death of a loved one by cancer, as a response to unbearable grief.

The patient was a housewife who had no history of psychiatry illnesses or substance abuse. She had spent the last year of her life nursing her husband, dying of pancreatic cancer, while taking care of their three children. During her childhood, she experienced traumatic violence from her father, an alcoholic. After marriage, she developed a kind, cooperative character. However, she tended to be dependent on her husband.

After studying and interviews, clinicians assumed that her husband's death explained the development of DA partially, although not completely. Three other factors were involved: a) "denial" coping mechanisms (she refused to take recommendation and requested further treatment for her husband); b) her dependency on her husband, and posteriorly, to her children; c) her life history, because she experienced violence during her childhood, classified as a risk factor for developing psychiatric symptoms.

In summary, psychiatric intervention may be needed soon after the death of loved ones in some at-risk patients.

Several studies have, also, related war trauma as an induction method of DA. Data collected in the end of World War I (WWI), provided considerable relation between combat trauma and PTSD/dissociative symptoms (van der Hart, Brown, Graafland, 1999).

Historical data supports modern studies of military trauma. Military, as civilian trauma, manifests syndromes of PTSD, characterized by either partial or complete amnesia, or hypermnesia. These historical findings might be the key on the debate over childhood trauma and if traumatic memories can be lost and recovered, spontaneously or therapeutically. It became clear on these studies that peritraumatic dissociation led to acute memory loss, even partially or of the entire experience. These memories could be recovered, either by flashbacks or under hypnosis.

3.6 Epidemiology

Epidemiological studies in several countries resulted in inaccurate estimates of prevalence of DA because different terminologies, definitions, assessment methods and experiment settings were adopted.

Brandt and van Gorp, in 2006, mentioned that "all the dissociative disorders are extremely rare". For some authors, some dissociative disorders do not even exist in their countries (Takahashi, 1991) and for others it results from a myth or cultural contamination (Pope, Poliakoff, Parker, Boynes, Hudson, 2007). Albeit, recent date suggests that DD are widespread across many cultures and is based on the same etiological link, psychological stress.

Prevalence for DA has been rated between 0.2 to 7.3% among several studies (Staniloiu and Markowitsch, 2014). Data for DF is insufficient, at best. In one study of 628 women in Turkey, only one participant satisfied the criteria for DF. Diagnostic interviews assessing general psychiatric disorders (e.g. Structured Clinical Interview and Composite Diagnostic Interview), were lacking sections suitable to screen for DD, which affects all reliability of the studies assessing epidemiological data.

Dissociative symptoms, besides constituting a category - dissociative disorders -, also take part in other psychiatric disorders, such as borderline personality disorder, conversion disorder and obsessive-compulsive disorder. The most common personality traits and symptoms associated with DA were borderline, dependent and histrionic, in a study by Coons and Millstein, in 1989.

"Data collected in diverse geographic locations such as North America, Puerto Rico, Western Europe, Turkey, and Australia underline the consistency in clinical symptoms of dissociative disorders" (Sar, 2011). In these studies, patients reported high frequencies of childhood psychological trauma.

Some studies reported high levels of dissociative symptoms and disorders in psychiatric inpatients. However, the overall prevalence of DD in inpatient and outpatient psychiatric settings appears to be around 10%, with half of the cases representing DID (Sar, 2011). Substance abusers and exotic dancers or prostitutes usually report highly traumatic childhood backgrounds, and are also known to be at risk for developing dissociative symptoms.

"The prevalence of the symptoms of DA in the general population is much higher than the estimates for the disorder of DA" (Staniloiu and Markowitsch, 2014). DA and DF are often diagnosed in young age, from 20 to 40 years old, although some cases in children and older adults have been reported.

"The prevalence in both sexes of DA is similar between sexes" (Staniloiu and Markowitsch, 2014). Recurrence rates cannot be assessed accurately because there aren't enough longitudinal studies, and even these have insufficient sample sizes.

There has been introduced data suggesting that DD pose high risk for suicide, as well. (Foote B, Smolin Y, Neft D.I, Lipschitz D., 2008).

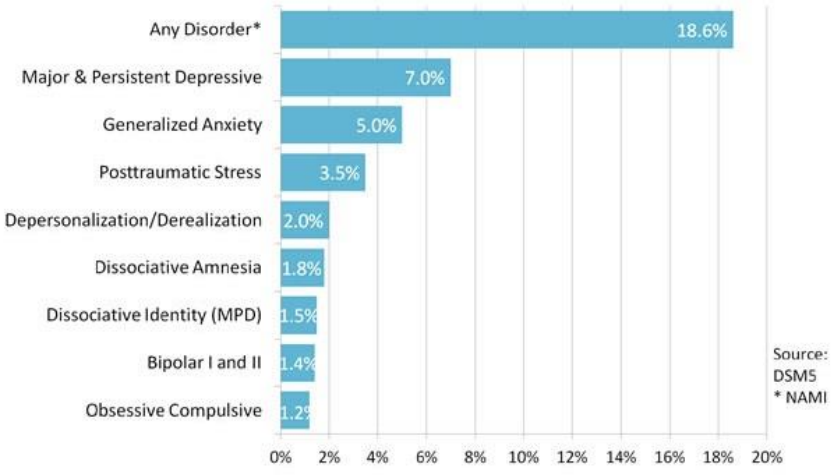

Figure 5 – Annual prevalence of dissociative disorders. Source: DSM-V (Trauma and Stressor-related Disorders. Retrieved March 24, 2017 from http://traumadissociation.com/information)

3.7 Diagnosis

A patient presenting with loss of memory for one or more life events, without neurological cause and, possibly, with emotional/traumatic ties towards that event, should be referred to psychiatrist under possibility of DA.

Diagnosis of DA includes: a) psychiatric, physical and neurological examination; b) laboratory investigation (toxicology, neuroimaging and electroencephalography); c) neuropsychological evaluation; d) psychiatric questionnaires (Staniloiu and Markowitsch, 2014).

Probably the most important step is for the patient to be evaluated for organic causes for the amnestic episodes, especially based on neuroimaging methods and toxicology screening. If all the examinations come back negative or cannot account for the clinical presentation, then all the symptoms are assumed to be of psychiatric origin.

It is possible that DA appears after traumatic brain injury or any other type of brain damage, yet, in this case, the extent and nature of amnesia does not reflect the affected location or the severity of the brain lesion. Trauma or intense stress present in history of the patient and loss of personal identity increase the likelihood of the diagnosis.

A special consideration should be taken by the clinicians regarding feigning or malingering behavior, especially if the patient has something to gain or any motivation in faking complaints (e.g. avoiding prosecution, monetary restitution during personal injury case, etc.). Clinicians should not accept nor reject blindly patient's reports as being truthful. Evidences of absurd symptoms, interview inconsistencies and/or signs of malingering on psychological tests should be considered. Assessment of malingering through memory tasks can prove challenging: as the patients might quickly relearn their past through semantic memory system, which causes complications in distinguishing relearned from remembered personal information.

The revised Structured Clinical Interview for Dissociative Disorders (SCID-D-R) is considered the gold standard diagnostic instrument for DD.

The diagnosis of DA is reinforced in case of indicative scores of the disorder on dimensional and classificatory scales (e.g. Autobiographical Memory Interview; Autobiographical Interview; Autobiographical Memory Test; Famous Faces Test; Dead/Alive Test, etc.). Some of these tests, although, present some "unfair" or fallacious assumptions: that the patient is embedded in

mainstream culture and that he/she registers these events normally. Determination of veracity of autobiographical information may represent a challenge, especially if there is no one else – i.e. friends or family – who can confirm the given information.

To determine patient's mental disorders or feigning, a neuropsychological examination, such as the Personality Assessment Inventory (PAI) or the Minnesota Multiphase Personality Inventory 2 (MMPI-2), should be used. These two tests have the advantage of possessing validity scales, which can help physicians to determine if the patient is answering consistently or if he is attempting to appear more symptomatic.

Structured Interview of Reported Symptoms (SIRS), might be used as a diagnostic tool, as well. Usage of this tool can help to reveal inconsistencies in self-report and implausible, extreme or feigned symptoms. Also, Test of Memory Malingering (TOMM) and Validity Indicator Profile (VIP) may be used for the same purpose. These tests assume that if the patient is exaggerating or fabricating problems during these cognitive tests, then he/she is probably exaggerating or fabricating the retrograde amnesia as well.

In cases of physical or sexual abuse, especially during childhood, patient should be approached carefully by the physician, as encouraging such "memories" to vulnerable or suggestive patients may cause worsening.

Patients with DA, normally, score average or higher on tests of general intelligence, like Weschsler Intelligence Scales. However, some patients might possess semantic memory impairment, scoring low on verbal subtests (e.g. Information and Vocabulary). Performance in these tests is almost never impaired in patients with organic amnestic syndromes ()

Very low scores on tests of new learning and memory (e.g. Hopkins Verbal Learning; Wechsler Memory Scale- III; Recognition Memory Test, etc.) are characteristic of organic amnestic syndromes.

Based on Muldimensional Inventory of Dissociation (MID), Dell (2012) presented what he considered to be more clinically useful guidelines for frontline clinicians: "Gaps in Remote Memory", "Discovering Dissociated Actions" and "Lapses of Recent Memory and Skills".

Presence of:	Absence or exclusion 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)	• 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

Table 2 – Suggestive criteria for the diagnosis of dissociative amnesia (Staniloiu and Markowitsch, 2014)

3.8 Differential Diagnosis

Differential diagnosis of DA comprises amnesic disorders caused by general medical conditions (e.g. transient epileptic amnesia), substance abuse-related disorders, other dissociative disorders in which dissociative amnesia is a symptom, borderline personality disorder (BPD) and mood/anxiety disorders.

"Pseudodementic presentations should be distinguished from neurodegenerative dementias, especially in elderly people" (Staniloiu and Markowitsch, 2014).

It is important to note that chronic retrograde amnesia after neurological insults has been reported.

Dissociative fugues are a rare condition and many times are rediagnosed as DID. In children, a relatively common error of diagnosis is to mistake DF for disruptive disorders.

In PTSD, the memory impairments are usually comprised to period and aspects of the traumatic event. In DA, the memory impairments are usually more widespread.

Substance abuse-related amnesia may occur after alcohol and/or benzodiazepines intoxication. In these cases both short and long term memories may be affected, causing the individual to have blackouts.

In the range symptoms of BPD we encounter dissociative symptoms, one of them being dissociative amnesia. Under severely stressful situations, patients with BPD may dissociate and reached altered states of consciousness and maybe amnesia follows.

Differential diagnosis of amnesia true challenge, as has been debated, is to distinguish true amnesia from cases of feigning or malingering. In some cases, both situations can coexist, even in cases of severe organic brain damage.

3.9 Treatment and management

Presently, there are no effective evidence-based treatment options for DA. Almost all information about treatment of the condition is based on case reports, each of them with different concepts and methodologies. In many cases, treatment studies consist of insufficient sample sizes and non-randomized designs.

"Many patients appear to recover spontaneously or with only supportive and suggestive psychotherapy. The retrograde amnesia appears to shrink, with memory for more remote events returning before memory for events more proximal to the onset of amnesia." (Brandt and Van Gorp, 2006) Memory recovery appears to follow Ribot's law.

Medical examinations of the patients should be controlled in terms of frequency and intensity in order to not "reinforce illness beliefs" (Staniloiu and Markowitsch, 2014). There is a risk that the patients gain conviction of a primary neurological condition and reduce connection between memory and emotional problems.

Historically, treatment of DD was mostly based on extended psychoanalysis sections in which repressed memories are "brought back" to conscious awareness. In some cases, patients would abreact during this process, enabling them to recover partially and completely these hidden memories. Abreaction was defined by Jackson (1994) as the "liberation by revival and expression of the emotions associated with forgotten or repressed ideas of the event that first caused it".

Abreaction therapy was particularly popular during Second World War (WWII), but lately has been falling from grace among psychiatrists (Lipton, 1950; Putnam, 1992). Both hypnosis and pharmacological methods can be used for abreaction. This method may still be used with good results in forensic practice (Vattakatuchery and Chesterman, 2007)

Notwithstanding, in sensitive or suggestive patients, this process would do more harm than good. Psychoanalysis also has the potential to create false memories, especially if the clinicians are creating conditions for such.

Systematic relaxation therapy and imagery-guided therapy/desensitization have been used lately to decrease sensibility of the patients towards menacing memories and emotions.

Hypnosis and hypnotherapy may be used, but evidence data has provided a wide range of success rates (McKay and Kopelman, 2009)

Drug-assisted interviews, with usage of hypnotics or benzodiazepines may help the patients to relax, thus assisting them in the process of memory recovery (Perry JC, Jacobs D, 1982). However, "so far, no randomized placebo-controlled trials have been done of pharmacologically assisted interview in dissociative amnesia" (Staniloiu and Markowitsch, 2014). Antidepressants can be used in the treatment of comorbid depression.

Electroconvulsive therapy, single case reports provided different results (Staniloiu and Markowitsch, 2014).

Treatment by psychotherapy should follow a judicious approach: first, stabilization of the patient and symptoms reduction; secondly, addressing the traumatic and emotional events; third and final step is to ensure patient's motivation to continue with psychotherapy and reeducation. Reeducation of the patient consists in reeducating the patient about his autobiographical memories, which in many cases can be learned effortlessly. One example of successful treatment of DA was reported, recently, by Cassel and Humphreys (2015). In this case, "Ben" was treated using cognitive behavioral therapy (CBT) and acceptance and commitment therapy (ACT). After 12 therapy sessions, Ben's retrograde and anterograde memory impairments improved and were maintained at follow-up. Evidence was provided that DA can effectively be treated with a short therapeutic intervention, serving as a solid base for future research.

3.10 Prognosis

There are not enough follow-up studies, and not enough information in those available, to provide a definitive answer concerning prognosis. By clinical experience, clinicians know that the outcome of DA may vary. In some cases, memories are recovered spontaneously or after treatment, in others symptoms and severity may even increase and the patient status can become worse.

Some patients may even end up for being re-diagnosed with PTSD (Spiegel D, Loewenstein RJ, Lewis-Fernandet R, et al., 2011). There is an argument that some patients have lesser forms of the disease or better outcomes and are missed by follow-up studies.

The definitive variables influencing prognosis have not been properly studied. However, short duration of symptoms and presence of comorbid depression is considered to be a good prognostic factor. In any event, longer disease duration does not impossibilitate successful therapy.

4. Diagnostic status and scientific validity of dissociative amnesia

Dissociative disorders, such as DA, have been linked to psychological trauma and stress. Many clinicians believe that DA patients use dissociation as a defensive coping mechanism to protect them of extremely stressful or traumatic event. The progression and sophistication of imaging methods are providing further understanding of the neurobiological bases for these conditions, however, problems with conceptualization and diagnostic status/validity persist.

Up to date, the underlying mechanisms of DA are unclear, at best. Such lack of knowledge, mostly concerning memory mechanisms, leads to skepticism and intense debate. Previously, in this thesis assignment, it was shown that memory is seen, currently, as a collection of systems, rather than a singular one and that memory formation and recovery are related but unique operations. This could explain the singularity of each case of memory loss in DA.

Even among board-certified American psychiatrists, there is little consensus regarding the diagnostic status and scientific validity of DA and DID.

The processes being trauma victims loss of memory remains one of the most intense debates in literature. Most experts defend that the traumatic events are remembered very well, but some other theorists disagree. The latter defend that these memories are available, although they are stored and dissociated/repressed from awareness.

Brown, Scheflin and Whitfield (1999) are keen defenders of the theory of memory repression in traumatic events and that these memories can be accurately recovered posteriorly. Contrarily, as seen in an article from Jr. Piper A. Jr. Pope H.G. and J.J. Borowiecki III, in 2000, the arguments detailed by Brown, Scheflin and Whitfield were accused of having “unsupported assertions, misleading quotations of the authors, and inaccurate reporting of evidence”.

In a recent article, Pope, Poliakoff, Parkers, Boynes and Hudson (2007), introduced a controversial hypothesis that if individuals could forget trauma, then the phenomenon would be in literature prior to 1800. Based on their conclusions they defend that dissociative amnesia is a “culture-bound syndrome”. As seen before in this debate, some authors (Goldsmith, Cheit, Wood, 2009) disputed the validity of such assumptions, providing “examples of forgetting trauma from literature written before 1800”, summarizing “extensive cognitive and neurological data that Pope et al. did not consider” and explaining the “several misrepresentations of the state of the science

regarding memory for trauma". "If a psychological condition can be culture-bound, the denial of a phenomenon may certainly be culture-bound as well" (Goldsmith, Cheit, Wood, 2009). Dissociative amnesia could serve as an adaptation of the individuals to function in society because family or culture denies the form of trauma that the individual experienced. (Goldsmith, Cheit, Wood, 2009). This view is consistent with Freyd's (1996) betrayal trauma theory – abuse experiences are separated from consciousness to prevent cognitive dissonance and cause problems with caregivers or close others, which are necessary for survival. This would explain why victims abused by caregivers are more likely to develop dissociative amnesia than victims abused by others.

It is important to take in consideration that is it practical to consider dissociative amnesia "a rare form of illness-simulating behavior" because the difficulties in distinguishing DD from malingering is typically hard for clinicians. Kopelman, in 1987, introduced an article showing that in forensic settings, many homicide defendants claim amnesia as a defense method.

4.1 Problems with conceptualization and diagnosis

The first problem related to dissociative amnesia, as a disease entity, comes related to its terminology. There has been some debate considering the correct terminology for this condition. It is, often, mistaken in literature with psychogenic amnesia or functional amnesia. All three terms, although, have slightly different meanings and theoretical bases.

Some sources, such as DSM-IV, classify psychogenic amnesia as the older terminology for dissociative amnesia. The most accepted terminology is that psychogenic amnesia defines a broader term than dissociative amnesia, being the latter incorporated in the former. Psychogenic amnesia links amnesia to a wide range of psychological mechanisms: dissociation, suppression, avoidance, exaggeration of symptoms, etc.

Functional amnesia, on the other hand, is defined as a "more suitable term to classify patients whose memory disorders cannot be traced back to organic or psychological causes" (de Renzi et al., 1997).

Of course, these three terms have been disputed and discussed. But, in here, they are introduced as defined by Staniloiu and Markowitsch. In their article, from 2014, "Dissociative amnesia", they provide invaluable insight concerning conceptualization of the condition.

Another problem of DA consisted, for many years at least, before development of advanced neuroimaging methods, in differentiating it from organic causes. Differentiation between organic causes and dissociative amnesia is not always easy and, sometimes, elements of both may be combined. There are several related cases of dissociative which result from traumatic brain injury, however, these injuries are not significant enough to produce such type or intensity of amnesia. Many times, even with the usage of neuroimaging methods, circumstances of the amnesia, as well as clinical and neuropsychological features are essential to distinguish between organic and psychogenic causes. In transient organic amnesia, repetitive questioning is a characteristic feature, even though personal identity is rarely lost. In dissociative fugue, contrarily, repetitive questioning is rare but loss of personal identity is common. Pattern of deficits and preserved function in transient organic amnesia are classical of amnesic syndromes and varies between patients, whilst in dissociative amnesia, central loss involves autobiographical memory, either global or situation specific. Semantic and procedural memory integrity varies in DA patients.

The third, and probably, the greatest problem of DA is its diagnostic status and validity. The conceptualization problems lead to difficulties establishing reliable inclusion or exclusion guidelines for several studies. This, in itself, further complicated the standardization of clinical trials.

Nowadays, it is possible to find an amalgam of studies which are not uniform in terms of methods, hence the difficulties in estimating prevalence and even qualify/quantify features of the disease in different patients. Most studies are retrospective, which may lead to bias and "memory implantation" by over-eager clinicians. On the other hand, asking people about their traumatic experience might represent "over-cueing", reducing possibilities of detecting dissociative amnesia. There are not enough prospective studies concerning DA, especially because the succession of events leading to the disease are unclear and many traumatic events occur in early childhood (e.g. childhood abuse). The ideal situation to detect DA would be in cases of well-documented abuse, in which patients would be interviewed and then followed. These patients must be older than 6 years-old and free of organic causes for dissociative symptoms (Pope et al., 1998).

Most studies also encompass an insufficient number of people in the study group and no control groups. It has been argued that some types of trauma are too "shallow" or benign to be investigated for DA. However, both intact memories and amnesia have been found in people, whether in response to mild or severe traumas.

In a study from Pope et al. (1999), a questionnaire was mailed to 367 board-certified American psychiatrists. With a rate of 82% of answers (301 clinicians), only one-third of them replied that DA and DID should be included without reservations in DSM-IV. Most board members answered that they should be included only as proposed diagnoses. As little as one-fourth of the inquired considered that there was strong evidence of validity of DA. A mathematical regression, using likelihood ratio test, provided insufficient statistical relation between acceptance of DA or DID and gender, age, principal activity (patient care or other) or publications. This study shed some light about the lack of consensus concerning scientific validity of DA and DID.

Question and Diagnosis	N	%	95% CI	N	%	95% CI	N	%	95% CI	N	%	95% CI
	Should not be included at all			*Should be included only with reservations*[a]			*Should be included without reservations*			*No opinion*		
If DSM-IV were to be revised today, how should it treat the diagnosis of												
Dissociative amnesia	27	9	6–12	143	48	42–53	104	35	29–40	27	9	6–12
Dissociative identity disorder[b]	45	15	11–19	128	43	37–48	106	35	30–41	22	7	4–10
	Little or no evidence of validity			*Partial evidence of validity*			*Strong evidence of validity*			*No opinion*		
In your opinion, what is the status of scientific evidence regarding the validity of												
Dissociative amnesia	56	19	14–23	145	48	43–54	69	23	18–28	31	10	7–14
Dissociative identity disorder	59	20	15–24	153	51	45–56	62	21	16–25	27	9	6–12

[a] The full text of this response option was, "Should be included only with reservations (e.g., only as a 'proposed diagnosis')."
[b] The full text of the first response option here was, "Should not be included at all (or included only as an 'iatrogenic' phenomenon)."

Table 3 - Answers of 301 board-certified American psychiatrics concerning diagnosis of dissociative amnesia and dissociative identity disorder (Pope et al., 1999)

4.2 Advanced neuroimaging methods

Besides the neuropsychological variability in dissociative amnesia and fugue, it is still unclear whether some organic brain abnormalities occur in these conditions (Reinhold et al., 2006).

Typically, symptoms appear to occur in absence of brain damage, at least as far as conventional brain imaging techniques go. However, some authors reported task-specific functional brain changes, especially in limbic and prefrontal regions - particularly in the right hemisphere. (Markowitsch, Fink et al., 1997b; Yasuno et al., 2000; Fujiwara et al., 2008). When some brain damage does exist, as a result of traumatic brain injuries, for example, the extent of amnesia is not proportional to degree or locus of brain damage (Piolino et al., 2005).

In the past years, functional brain imaging studies of DD have been increasing in frequency and depth, in particular positron emission tomographies (PET) scans. Studies using glucose PET scans were used to try to disclose any organic abnormalities related to memory impairments, mostly in persistent retrograde dissociative amnesia. In a paper from Markowitsch, Fink et al. (1997b) using water-PET in a retrograde amnesic patient showed different activations (while recalling memories of their past) in comparison to that of a control patient. Control patient had predominant right temporo-frontal activation while amnesic patient had left-hemispheric activation of the same regions. The results were interpreted as suggestive of the patient perceiving his own autobiographical episodes as belonging to a third person.

Kopelman, in 2002 demonstrated EEG abnormalities in right frontal and temporal regions in a patient with fugue.

Markowitsch, Kessler, Van der Ven, Weber-Luxenburger and Heiss (1998) detected, in patient A.M.N, significant reductions in glucose metabolism all over the brain, but particularly in memory processing areas such as medial temporal lobe and diencephalon. The interesting features of this case were that A.M.N, a 23 year-old, woke up the morning after a traumatic incident thinking he was 17 years old and did not remember any personal information beyond this age. He developed the condition after witnessing a fire in his house. Organic causes were ruled out. It was later known that he remembered witnessing a car crash with another car in flames when he was only 4 years old. The same memory was confirmed by his mother. Authors hypothesized that the traumatic event at the age of 4 elicited subtle organic changes in his brain and that during the second traumatic event triggered a magnified biological response which covered his last 6 years of life.

In a subsequent paper, in 2000, the authors demonstrated that combined psycho-pharmaceutical (antidepressants) and psychotherapeutic interventions, lead to memory recovery and normal values of brain's glucose level. Also, Piolino et al (2005) introduced a case of a patient

with dissociative retrograde amnesia who had hypometabolic right ventrolateral/inferolateral prefrontal cortex in a resting state PET of his brain.

Brand et al. (2009) introduced a [18F] fluorodeoxyglucose PET (FDG-PET) study in which 14 patients with DA and severe autobiographical deficits were analyzed in comparison with a control group. It was considered to be the first study with a relatively large sample group showing functional brain changes in DA patients. In this study, hypometabolism of right inferior prefrontal cortex (essential structure for triggering self and autobiographical memories) was observed. It was suggested that in patients with DA, consistent malfunction of this brain region indicates stress or trauma-related experiences, thereby inactivating "trigger signals that are necessary for synchronizing limbic and neocortical structures for reinstating engrams of personal relevance". These findings have important therapeutic implications because "if the brain regions

of the right temporo-frontal cortex, which are interconnected by the uncinate fascicle, were brought to normal metabolic activity via environmental manipulations, the patients' ability to recollect personal events from the past might be reinstated" (Staniloiu, Vitcu, and Markowitsch, 2012).

Tramoni et al. (2009), found in a patient with DA evidence of significant metabolic changes and structural alterations in the right prefrontal region, as well, but this time by using magnetization transfer ratio measurement and magnetic resonance spectroscopy. In other articles, single photon emission computed tomography (SPECT) and/or fMRI have been used (Anderson et al.,2004; Hennig-Fast et al., 2008; Yang et al., 2006; Piolino et al., 2005; Yasuno et al., 2000; Thomas-Antérion, Guedj, Decousous, and Laurent, 2010; Kikuchi et al., 2010). In the majority of cases some metabolic and functional changes were also found.

In a study from Kitamura, Yasuno et al. (2014), it was found that "5-HT_{1A} receptor bindings of the patients in right superior frontal cortex, left inferior cortex, left orbitofrontal cortex and bilateral inferior temporal at the post-amnesic state were significantly higher than those of HC by PET analysis". The increase of these receptors postynaptically on pyramidal neurons in the frontal and temporal regions were related to a recovery from DA. This opens the possibility of creating drugs working as agonists of postsynaptic 5-HT_{1A} receptors to improve dissociative symptoms, although there is a risk of hippocampal function suppression (Yasuno et al., 2003).

4.3 Discussion

In my opinion, the diagnostic status and scientific validity of DA is a grey area. Many authors and clinicians are delaying the validation of DA until some irrefutable proof or, in this case, method is able to clearly define the disease, its pathophysiology and its course. It is understandable. A quote from Andrew Smith - “People fear what they don't understand and hate what they can't conquer” – appears to be accurate to describe this situation.

In light of the study review presented in this thesis assignment, it is impossible, in my opinion, to refute the existence of the condition. However, one must tread lightly when considering the disease in judicial terms because: 1) the possibility of feigning and malingering exists, especially if it benefits the guilty person; 2) with the available resources, at present, it is impossible to clearly define if a patient suffers from memory impairments or not. The available methods to detect feigning and malingering are not one hundred per cent effective, at best.

Another important area of future focus is the necessity to clearly define and further clarify terms related to DA, such as mnestic block syndrome, psychogenic amnesia and functional amnesia. Some efforts have been done concerning this matter. The approximation of concepts and guidelines proposed for DD in ICD-11 and DSM-V, demonstrates that clinicians and authors around the world are getting close to reaching a consensus.

Studies, such as Piolino et al. (2005), Brand et al. (2009), Tramoni et al. (2009), Kikuchi et al. (2010) and Kitamura, Yasuno et al. (2014), have provided invaluable insight concerning metabolic and organic changes occurring in the brain during dissociative amnesia. The development of new imaging methods and improvement of the existing ones will for sure, in the future, further scrutinize the pathophysiology of the disease. Clinical settings of investigation should be improved. Creating more standardized methods and guidelines for inclusion and exclusion of patients will provide better insight on DA and other DD. It is also important to perform trials with increased sample sizes and control groups. Methodology of prospective studies is hard to implement, thus, probably we will not see many examples of it in the future.

New studies and trials, particularly those involving usage of advanced imaging methods, will, without a doubt, provide a definitive answer about the scientific validity of the disease and offer new and effective therapeutic methods for the patients suffering from this psychiatric condition.

Conclusion

Dissociative amnesia continues to be in the center of a lot of debate among scientists and clinicians around the world. In spite of developments in neuroimaging methods and increased number of studies, the diagnostic status and scientific validity is not uniformly accepted.

The concepts and diagnostic guidelines appear to be aligning between the two most prominent authorities in the matter: the World Health Organization and the American Psychiatric Association (APA). In the new ICD-11 and DSM-5, dissociative amnesia and other dissociative disorders are recognized as diagnostic entities and there appears to be a common ground according concepts and features of the disease.

Neuroimaging methods, mostly since the start of the 21st century, have shed some light concerning memory mechanisms, pathophysiology of memory impairments and organic changes in the brain occurring in dissociative amnesia. In the future, it is expected more progress in this matter.

The condition remains without evidence-based treatment. However, there are reports of successful treatment in some cases and new investigations are opening up the range of available options.

List of sources employed

AGGLETON J.P. Understanding anterograde amnesia: Disconnections and hidden lesions. The Quarterly Journal of Experimental Psychology, 2008; 61(10): 1441-1471

AKHTAR S., LINDSEY B., KHAN F.L Sudden amnesia for personal identity. Pensylvania Medicine, 1981; 84, 46-48

AMINOFF M.J. et al. Clinical Neurology. 8th Ed. New York, N.Y.: The McGraw-Hill Companies, 2012

ANDERSON M.C., OCHSNER K.N., KUHL B., et al. Neural systems underlying the suppression of unwanted memories. Science, 2004; 303:232–235

ARRIGO, J.M. and PEZDEK, K. Lessons from the study of psychogenic amnesia. Current Directions in Psychological Science 1997; 6, 148-152.

BARNIER A. J. and NASH M. R. Introduction: a roadmap for explanation, a working definition. In M. R. Nash and A. J. Barnier (eds). The Oxford Handbook of Hypnosis: Theory, Research and Practice, 2008. Oxford: Oxford University Press

BARTSCH T. and DEUSCHI G. Transient global amnesia: functional anatomy and clinical implications. Lancet neurology, 2010; 9: 205-214

BECK B.J. and TOMPKINS K.J. Mental disorders due to another medical condition. In Stern T.A., Fava M., Wilens T.E., Rosenbaum J.F., eds. Massachusetts General Hospital Comprehensive Clinical Psychiatry, 2016; chap 21. 2nd ed. Philadelphia, PA: Elsevier

BERNSTEIN E. M. and PUTNAM F. W. Development, reliability and validity of a dissociation scale. Journal of Nervous and Mental Disease, 1986; vol. 174, 12; 727–735.

BERNTSEN D. and RUBIN D.C. Clin Psychol Sci, 2014 March 1; 2(2): 174–186. doi:10.1177/2167702613496241

BOWERS K.S. Unconscious influences and hypnosis. In J.L Singer (Ed.), Repression and dissociation: Implications for personality theory, psychopathology and health, 1990; 143-179. Chicago: University of Chicago Press

BRAND B. and LOWENSTEIN RJ. Dissociative Disorders: An Overview of Assessment,

Phenomenology and Treatment. Psychiatric Times, 2010: 62-69

BRAND M. and MARKOWITSCH H.J. Environmental influences on autobiographical memory: The mnestic block syndrome. In L. Backman and L. Nyberg (Eds.), Memory, aging, and brain, 2009. New York: Psychology Press.

BRAND M., EGGERS C., REINHOLD N., et al. Functional brain imaging in fourteen patients with dissociative amnesia reveals right inferolateral prefrontal hypometabolism. Psychiatry Research: Neuroimaging Section, 2009; 174, 32-39

BRANDT J. and VAN DER GORP W.G. Functional "Psychogenic" Amnesia. Semin Neurol 2006; 26(3): 331-340 doi: 10.1055/s-2006-945519

BREMNER J.D. and MARMAR C.R. (Eds.). Trauma, memory, and dissociation, 1998. Washington, D.C.: American Psychiatric Association

BREMNER J.D., KRYSTAL J.H., CHARNEY D.S., SOUTHWICK S.M. Neural mechanisms in dissociative amnesia for childhood abuse: relevance to the current controversy surrounding the ''false memory syndrome.'' Am J Psychiatry, 1996; 153:71–82

BRESSERT S. Depersonalization / Derealization Disorder Symptoms. Psych Central, 2016. Retrieved on March 18, 2017, from https://psychcentral.com/disorders/depersonalization-derealization-disorder-symptoms/

BROWN D., SCHEFLIN A.W., WHITFIELD C.L. Recovered memories: The current weight of the evidence in science and in the courts. Journal of Psychiatry and Law, 1999; 27, 5–156

BUDSON A.E. and PRICE B.H. Memory: Clinical Disorders. ENCYCLOPEDIA OF LIFE SCIENCES, 2001. Macmillan Publishers Ltd, Nature Publishing Group

CARLSON E. B., PUTNAM F. W., ROSS C. A. et al. Validity of the dissociative experiences scale in screening for multiple personality disorder: a multicenter study. American Journal of Psychiatry, 1993; vol. 150, no. 7, 1030–1036

CASSEL A. and HUMPHREYS K. Psychological therapy for psychogenic amnesia: Successful treatment in a single case study, Neuropsychological Rehabilitation: An International Journal, 2005. doi: 10.1080/09602011.2015.1033431

CERMAK L.S. The episodic-semantic distinction in amnesia. New York: Guilford Press, 1984;

CHU J.A., FREY L.M., GANZEL B.L., MATTHEWS J.A. Memories of Childhood Abuse: Dissociation, Amnesia, and Corroboration. Am J Psychiatry, 1999; 156:749–755

COONS P.M. and MILSTEIN V. Psychogenic amnesia: a clinical investigation of 25 cases. Dissociation, 1992; Vol. V, 2

COTTENCIN O. Conversion disorders: Psychiatric and psychotherapeutic aspects. Neurophysiol Clin, 2014; 44(4):405-10. doi: 10.1016/j.neucli.2013.09.005

D. BAKER, E. HUNTER, E. LAWRENCE, et al. Depersonalization disorder: clinical features of 204 cases. Br J Psychiatry, 2003; 182:428.

DAMASIO H., GRABOWSKI T.J., TRANEL D., HICHWA R.D., DAMASIO A.R.A neural basis for lexical retrieval. Nature, 1996; 380: 499–505

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.

DELL P.F. Three Dimensions of Dissociative Amnesia, Journal of Trauma and Dissociation, 2013; 14:1, 25-39. doi: 10.1080/15299732.2012.724762

DRAAISMA D. Neuroscience: Losing the past. Nature, 2013; 497 (7449): 313. doi: 10.1038/497313a

EISEN M.R. Return of me repressed: Hypnoanalysis of a case of total amnesia. International Journal of Clinical and Experimental Hypnosis, 1989; 37, 107-119

ELLENBERGER H.F. The discovery of the unconscious: The history and evolution of dynamic psychiatry. New York: Basic Books, 1970

ERICKSON K.R. Amnestic disorders - Pathophysiology and patterns of memory dysfunction. West J Med, 1990; 152:159-166

FOOTE B., SMOLIN Y., NEFT D.I., LIPSCHITZ D. Dissociative disorders and suicidality in psychiatric outpatients. J Nerv Ment Dis, 2008; 196: 29–36

FRANKEL F.H. Dissociation in hysteria and hypnosis: A concept aggrandized. In S.J. Lynn and J.W. Rhue (Eds.), Dissociation: Clinical and theoretical perspectives, 1994; 80-93 New York: Guilford Press

FREYD J. J. Betrayal trauma: The logic of forgetting childhood abuse. Cambridge, MA: Harvard University Press, 1996

FUJIWARA, E., BRAND M., KRACHT L., et al. Functional retrograde amnesia: a multiple case study. Cortex, 2008; 44, 29-45

GEORGE O., VALLEE M. et al. Low Brain Allopregnanolone Levels Mediate Flattened Circadian Activity Associated with Memory Impairments in Aged Rats. Biological Psychiatry, 2010; 68: 956-963

GOLDSMITH R.E., CHEIT R.E., WOOD M.E. Evidence of Dissociative Amnesia in Science and Literature: Culture-Bound Approaches to Trauma in Pope, Poliakoff, Parker, Boynes, and Hudson (2007). Journal of Trauma and Dissociation, 2009; 10:3, 237-253, doi: 10.1080/15299730902956572

GUDJONSSON G.H. and HAWARD L.R.C. Case report – hysterical amnesia as an alternative to suicide. Medicine Science and the Law, 1982; 22, 68-72

HEICHENBAUM H., SCHOENBAUM G., YOUNG B., BUNSEY M. Functional organization of the hippocampal memory system. Proc. Natl. Acad. Sci. USA, 1996; Vol. 93, 13500–13507

HEMA T. DINESH N, ASHUTOSH C., ANOOP M., PODILA S.V.N.S. Dissociative Amnesia Related to Pregnancy. German J Psychiatry, 2007; 10: 119-121

HIRAI S. Distinction between Dementia and Memory Decline. Journal of the Medical Association of Japan, 2001; 44 (60): 274-278

HUNTJENS R.J.C., PETERS M.L., WOERTMAN L., VAN DER HART O., POSTMA A., Memory transfer for emotionally valenced words between identities in dissociative identity disorder. Behaviour Research and Therapy 45, 2007; 775–789

ISHIDA M. et al. Missing memories of death: Dissociative amnesia in the bereaved the day after a cancer death. Palliative and Supportive Care, 2015; 13, 1787–1790. Cambridge University Press

JACKSON S. Catharsis and abreaction in the history of psychological healing. Psychiatric. Clinics of North America, 1994; 17, 471–490

JAKALA P., RIEKKINEN M., SIRVIO J., et al. Guanfacine, but not clonidine, improves planning and working memory performance in humans. Neuropsychopharmacology, 1999; 20:460–470

JANET P. The major symptoms of hysteria: Fifteen lectures given in the Medical School of Harvard University, 1997. New York: Macmillan.

KASZNIAK A.W., BERREN M.R., SANTIAGO J. Amnesia as a consequence of male rape: A case report. Journal of Abnormal Psychology, 1988; 97, 100-104

KIHLSTROM J. F. Dissociative Disorders. In H.E. Adams and P.B. Sutker (Eds.) Comprehensive Handbook of Psychopathology, 2001, 3rd Ed.; 259-276. New York: Plenum.

KIHLSTROM J.F. Dissociative and conversion disorders. In D.J. Stein and J. Young (Eds.), Cognitive science and clinical disorders, 1992; 247-270. San Diego: Academic

KIHLSTROM J.F. One hundred years of hysteria. In S.J. Lynn and J.W. Rhue (Eds.), Dissociation: Theoretical, Clinical, and Research Perspectives, 1994; 365-394 New York: Guilford

KIHLSTROM J.F., TATARYN D.J., HOYT I.P. Dissociative disorders. In P.J. Sutker and H.E. Adams (Eds.), Comprehensive handbook of psychopathology, 2nd Ed, 1993; 203-234. New York: Plenum.

KIKUCHI H., FUJII T., ABE N., et al. Memory Repression: Brain Mechanisms underlying Dissociative Amnesia. Journal of Cognitive Neuroscience, 2009; 22:3, 602–613. Massachusetts Institute of Technology

KIRSCH I. and LYNN S.J. Dissociation theories of hypnosis. Psychological Bulletin, 1998; 123, 100-115

KITAMURA S., YASUNO F., INOUE M., KOSAKA J., KIUCHI K., MATSUOKA K., KISHIMOTO T., SUHARA T. Increasedbindingof5-HT1A receptors in a dissociative amnesic patient after the recovery process. Psychiatry Research: Neuroimaging, 224, 2014; 67–71

KLEIN R.M. and DOANE B.K. Psychological concepts and dissociative disorders. Hillsdale, N.J.: Erlbaum, 1994

KOPELMAN M.D. Disorders of memory. Brain, 2002; 125, 2152-2190

KOPELMAN, M. D. Amnesia: Organic and psychogenic. British Journal of Psychiatry, 1987:150, 428–442.

KRITCHEVSKY M., ZOUZOUNIS J., SQUIRE L.R. Transient global amnesia and functional retrograde amnesia: contrasting examples of episodic memory loss. Philos. Trans. R. Soc. London B Biol. Sci, 1997; 352, 1747–1754

LEONG S., WAITS W., DIEBOLD C. Dissociative Amnesia and DSM-IV-TR Cluster C Personality Traits. Psychiatry (Edgmont), 2006; 3(1): 51–55

LIPTON E. The Amytal Interview; a review. American Practitioner and Digest of Treatment, 1950; 1, 148–163

LOEWENSTEIN R.J. Dissociative amnesia and dissociative fugue. In L.K. Michelson and W.J. Ray (Eds.), Handbook of dissociation: Theoretical, empirical, and clinical perspectives, 1996; 307-336. New York: Plenum

LUCCHELLI F., SPINNLER H. The ‘‘psychogenic’’ versus “organic” conundrum of pure retrograde amnesia: is it still worth pursuing? Cortex, 2002; 38:665–669

LUDWIG A.M. The psychobiological functions of dissociation. Am. J. Clin. Hypn, 1983; 26: 93 -99.

LYON L.S. Facilitating telephone number recall in a case of psychogenic amnesia. Journal of Behavioral, Therapeutic and Experimental Psychiatry, 1985; 16, 147-149

MACDONALD K. and MACDONALD T. Peas, Please: A Case Report and Neuroscientific Review of Dissociative Amnesia and Fugue, Journal of Trauma and Dissociation, 2009; 10:4, 420-435. doi: 10.1080/15299730903143618

MARKOWITSCH H. J., KESSLER J., VAN DER VEN C., et al. Psychic trauma causing grossly reduced brain metabolism and cognitive deterioration. Neuropsychologia, 1998; 36, 77-82

MARKOWITSCH H.J and STANILOIU A. Amnesic disorders. Lancet, 2012; 380: 1429–40 doi: 10.1016/S0140-6736(11)61304-4

MARKOWITSCH H.J. Functional neuroimaging correlates of functional amnesia. Memory, 1999; 7:561–583

MARKOWITSCH H.J. Psychogenic amnesia. Neuroimage, 2003; 20:S132–S138

MARKOWITSCH H.J. Functional retrograde amnesia – mnestic block syndrome. Cortex, 2002; 38: 651–54

MARKOWITSCH H.J. Gedachtnis und Brain Imaging. Fortschritte der Neurologie Psychiatrie, 2008; 76(Suppl. 1), S1–S6

MARKOWITSCH H.J. Organic and psychogenic retrograde amnesia: Two sides of the same coin? Neurocase, 1996a; 2, 357–371

MARKOWITSCH H.J. Retrograde amnesia: Similarities between organic and psychogenic forms. Neurology, Psychiatry and Brain Research, 1996b; 4, 1–8

MARKOWITSCH H.J., CALABRESE P., FINK G.R., et al. Impaired episodic memory retrieval in a case of probable psychogenic amnesia Psychiatry Research: Imaging, 74, 1997a; 119–126

MARKOWITSCH H.J., FINK G.R., THONE A., KESSLER A., HEISS W.D.A. PET study of persistent psychogenic amnesia covering the whole life span. Cognitive Neuropsychiatry, 1997b; 2:135–58

MCKAY G. C. M. and KOPELMAN M. D. Psychogenic amnesia: When memory complaints are medically unexplained. Advances in Psychiatric Treatment, 2009;15, 152–158.

MEDFORD N., BRIERLEY B., BRAMMER M., et al. Emotional memory in depersonalization disorder: A functional MRI study. Psychiatry Research: Neuroimaging, 2016; 148 (2–3): 93102 doi: 10.1016/js.pscychresns.2006.05.007 PMID 17085021

MEDFORD N., SIERRA M., BAKER D., DAVID A. Understanding and treating depersonalisation disorder. Advances in Psychiatric Treatment. Royal College of Psychiatrists, 2005; 11 (2): 92–100. doi:10.1192/apt.11.2.92

MILLER P., BRAMBLE D., Buxton N. Case study: Ganser syndrome in children and adolescents. Journal of the American Academy of Child and Adolescent Psychiatry. 36 (1): 112–5. PMID 9000788. doi:10.1097/00004583-199701000-00024

MOHS R.C. Memory impairment in amnesia and dementia: implications for the use of animal models. Neurobiology of Aging, 1988; 9(5-6):465-468

NEMIAH J.C. Dissociative disorders (hysterical neuroses, dissociative type). In Kaplan H.I. and Sadock B.J. (Eds.), Comprehensive textbook of psychiatry, 1989, 5th ed.; Vol. 1, 1028-1044). Baltimore, Md.: Williams & Wilkins

NIJENHUIS E., VAN ENGEN A., KUSTERS I., VAN DER HART O. Peritraumatic Somatoform and Psychological Dissociation in Relation to Recall of Childhood Sexual Abuse, Journal of Trauma and Dissociation, 2001; 2:3, 47-66. doi: 10.1300/J229v02n03_04

NOLL R. Multiple personality, dissociation, and C.G. Jung's complex theory. J Anal Psychol, 1989 Oct; 34(4):353-70

PAPANICOLAOU A.C., HASAN K.M., BOAKE C., ELUVATHINGAL T.J., KRAMER L. Disruption of limbic pathways in a case of profound amnesia. Neurocase, 2007; 13: 226–28

PARKIN A.J. Human memory: The hippocampus is the key, 1996; vol 6, 1583-1585. Philadelphia, PA: Elsevier doi: 10.1016/S0960-9822(02)70778-1

PERRY J.C., JACOBS D. Am J Psychiatry, 1982; 139(5):552-9.PMID:7072839

PIOLINO P., HANNEQUIN D., DESGRANGES B., GIRARD C., BEAUNIEUX H., GITTARD, B., et al. Right ventral frontal hypometabolism and abnormal sense of self in a case of disproportionate retrograde amnesia. Cognitive Neuropsychology, 2005; 22, 1005-1034

PIPER A. What the science says -- and doesn't say -- about repressed memories: A critique of Scheflin and Brown. Journal of Psychiatry & Law, 1997; 25, 614-639.

PIPER A. and MERSKEY H. The persistence of folly: Critical examination of dissociative identity disorder. Part II. The defense and decline of multiple personality or dissociative identity disorder. Canadian Journal of Psychiatry, 2004; 49 (10): 678–683. PMID 15560314

PIPER A., POPE H. R., BOROWIECKI J.J. Custer’s last stand: Brown, Scheflin’ and Whitfield’s latest attempt to salvage “dissociative amnesia”. Journal of Psychiatry and Law 28, 2000

POPE H.G., HUDSON J., BODKIN J.A., OLIVA P. Questionable validity of ‘‘dissociative amnesia’’ in trauma victims: evidence from prospective studies. Br J Psychiatry, 1998; 172:210–215

POPE H.G., OLIVA P.S., HUDSON J.I., J., BODKIN J.A, M.D., GRUBER A.J. Attitudes Toward DSM-IV Dissociative Disorders Diagnoses Among Board-Certified American Psychiatrists. Am J Psychiatry, 1999; Volume 156, Issue 2, 321-323

POPE H.G., POLIAKOFF M.B., PARKER M.P., BOYNES M., HUDSON J.I. Is dissociative amnesia a culture-bound syndrome? Findings from a survey of historical literature. Psychol Med, 2007; 37: 225–33

PUTNAM F. W. Using hypnosis for therapeutic abreactions. Psychiatric Medicine, 1992; 10, 51–65.

PUTNAM F.W. Dissociation as a response to extreme trauma. In R.P. Kluft (Ed.), Childhood antecedents of multiple personality, 1985; 65-97 Washington, D.C.: American Psychiatric Press

PUTNAM F.W. Dissociation in children and adolescents: A developmental perspective. New York: Guilford, 1997

PUTNAM F.W., CARLSON E.B., ROSS C.A., et al. Patterns of dissociation in clinical and nonclinical samples. J Nerv Ment Dis, 1996; 184:673–679

REINHOLD N., KÜHNEL S., BRAND M., MARKOWITSCH, H. J. Functional neuroimaging in memory and memory disturbances. Current Medical Imaging Reviews, 2006; 2, 35-57

REINOLD N. and MARKOWITSCH H.J. Retrograde episodic memory and emotion: A perspective from patients with dissociative amnesia. Neuropsychologia 47, 2009; 2197–2206

REMPEL-CLOWER N.L. ZOLA-MORGAN S., SQUIRE L.R. AMARAL D.G. Three cases of enduring memory impairment after bilateral damage limited to the hippocampal formation. The Journal of Neuroscience, 1996 (16): 5233–5255. PMID 8756452

RIBOT, T. Diseases of Memory: An essay in the positive psychology. London: D. Appleton and company, 1882

RICHARD J. MCNALLY, PHD Dispelling Confusion about Traumatic Dissociative Amnesia. Mayo Clin Proc. 2007; 82(9):1083-1087

ROSS C.A. Epidemiology of multiple personality disorder and dissociation. Psychiatric Clinics of North America, 1991; 14 (3): 503–17. PMID 1946021

ROSS, C.A Dissociative identity disorder: Diagnosis, clinical features, and treatment of multiple personality. New York: Wiley, 1997

ROSS, et al. Prevalence, Reliability and Validity of Dissociative Disorders in an Inpatient Setting. Journal of Trauma and Dissociation, 2002; 7–17. doi:10.1300/J229v03n01_02

SADOCK B.J., SADOCK V.A. Dissociative disorders — Dissociative identity disorder. Kaplan & Sadock's synopsis of psychiatry: behavioral sciences/clinical psychiatry, 2007, 10th ed. Philadelphia: Lippincott Williams & Wilkins. pp. 671–6. ISBN 978-0-7817-7327-0

SANG-SHIN L., SINHYUNG P., SI-SUNG P. Use of Lorazepam in Drug-Assisted Interviews: Two Cases of Dissociative Amnesia. Psychiatry Investig, 2011; 8(4):377-380

SAR V. Epidemiology of Dissociative Disorders: An Overview. Hindawi Publishing Corporation. Epidemiology Research International, 2011. doi:10.1155/2011/404538

SCHACTER D.L. and TULVING E. What are the memory systems of 1994? In Schacter DL and Tulving E (eds) Memory Systems, 1994; 1–38. Cambridge, Massachusetts: MIT Press

SCOVILLE W.B and MILNER B. Loss of recent memory after bilateral hippocampal lesions. Journal of Neurology, Neurosurgery and Psychiatry, 1957; 20 (1): 11–21. PMC 497229. PMID 13406589. doi:10.1136/jnnp.20.1.11

SERRA L., FADDA L., BUCCIONE I., CALTAGIRONE C., CARLESIMO G. A. Psychogenic and organic amnesia. A multidimensional assessment of clinical, neuroradiological, neuropsychological and psychopathological features. Behavioral Neurology, 2007; 18: 53 - 64. doi:10.1155/2007/193140

SHARMA P., GUIRGUIS M., NELSON J., MCMAHON T. A case of Dissociative Amnesia with Dissociative Fugue and treatment with psychotherapy. Prim Care Companion CNS Disord, 2015; 17(3). doi:10.4088/PCC.14l01763

SHIMAMURA A.P. Hierarchical relational binding in the medial temporal lobe: the strong get stronger. Hippocampus, 2010; 20: 1206–16

SHOBE K.K. and KIHLSTROM J.F. Is traumatic memory special? Current Directions in Psychological Science, 1997; 6, 70-74

SIERRA M. Depersonalization disorder: pharmacological approaches. Expert Review of Neurotherapeutics, 2008; 8 (1): 19- 26 PMID:18088198

SIMEON D., GURALNIK O., KNUTELSKA M., HOLLANDER E., SCHMEIDLER J. Hypothalamic-pituitary-adrenal axis dysregulation in depersonalization disorder. Neuropsychopharmacology, 2001; 25 (5): 793–5. doi:10.1016/S0893-133X(01)00288-3. PMID 11682263

SIMEON D., GURALNIK O., SCHMEIDLER J., SIROF B., KNUTELSKA M. The role of childhood interpersonal trauma in depersonalization disorder. The American Journal of Psychiatry, 2001; 158 (7): 1027–33. doi:10.1176/appi.ajp.158.7.1027. PMID 11431223

SPIEGEL D., LOEWENSTEIN R.J., LEWIS-FERNANDET R., et al. Dissociative disorders in DSM-5. Depress Anxiety, 2011; 28: 824–52.

STANILOIU A. and MARKOWITSCH H.J. Dissociative amnesia. Lancet Psychiatry, 2014; 1: 226–41 doi: 10.1016/ S2215-0366(14)70279-2

STANILOIU A., VITCU I., MARKOWITSCH H.J. Neuroimaging and Dissociative Disorders, Advances in Brain Imaging. Dr. Vikas Chaudhary (Ed.), 2012. ISBN: 978-953-307-955-4

STEINBERG M. Handbook for the assessment of dissociation: A clinical guide, 1995. Washington, DC: American Psychiatric Press

STEINER H., CARRION V., PLATTNER B., KOOPMAN C. Dissociative symptoms in posttraumatic stress disorder: diagnosis and treatment. Child and Adolescent Psychiatric Clinics North America, 2002; 12: 231–249. doi:10.1016/s1056-4993(02)00103-7

STONE J., CARSON A., SHARPE M. Functional symptoms and signs in neurology: assessment and diagnosis. J. Neurol. Neurosurg. Psychiatr., 2005; 76 Suppl 1: i2–12

SWARTZ B.E., MCDONALD C.R., PATEL A., TORGESEN D. The effects of guanfacine on working memory performance in patients with localization-related epilepsy and healthy controls. Clinical neuropharmacology, 2008b; 31:251–260

TAKAHASHI Y. Aokigahara-jukai: Suicide and amnesia in Mt. Fugi's Black Forest. Suicide and Life-threatening Behavior; 1988; 18, 164-174

TAKAHASHI Y. Is multiple personality really rare in Japan? Dissociation, 1991; 3, 57–59

TARTER R.E., AMMERMAN R.T., OTT P.J. Handbook of Substance Abuse: Neurobehavioral Pharmacology, 1998; 265 NY: Plenum Press

THOMAS-ANTÉRION C., DUBAS F., DECOUSUS M., JEANGUILLAUME C., GUEDJ E. Clinical characteristics and brain PET findings in 3 cases of dissociative amnesia: Disproportionate retrograde deficit and posterior middle temporal gyrus hypometabolism. Neurophysiologie Clinique/Clinical Neurophysiology, 2014; 44, 355—362

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

TOLLISON C. D, SATTERTHWAITE J. R., TOLLISON J. W. Practical Pain Management. Lippincott Williams & Wilkins, 2002 ISBN 9780781731607

TRAMONI E., AUBERT-KHALFA S., GUYE M., RANJEVA J. P., FELICIAN O., CECCALDI M. Hypo-retrieval and hyper-suppression mechanisms in functional amnesia. Neuropsychologia, 2009; 47, 611-624

VAN DER HART O. and HORST R. The Dissociation Theory of Pierre Janet. Journal of Traumatic Stress, 1989; Vol. 2, No. 4

VAN DER HART O. and NIJENHUIS E. Generalized dissociative amnesia: episodic, semantic and procedural memories lost and found. Australian and New Zealand Journal of Psychiatry 2001; 35:589-600

VAN DER HART O., BROWN P., GRAAFLAND M. Trauma-induced dissociative amnesia in World War I combat soldiers. Australian and New Zealand Journal of Psychiatry, 1999; 33:37-46

VATTAKATUCHERY J.J and CHESTERMAN P. The use of abreaction to recover memories in psychogenic amnesia: A case report, The Journal of Forensic Psychiatry and Psychology, 2006; 17:4, 647-653, doi: 10.1080/14789940600965938

WALLER N.G., PUTNAM F.W., CARLSON E.B. Types of Dissociation and Dissociative Types: A Taxometric Analysis of Dissociative Experiences. Psychological Methods, 1996; Vol.1, No.3, 300-321

WOODY E. and SADLER P. Dissociation in hypnosis: theoretical frameworks and psychotherapeutic implications. In S. J. Lynn, J.W. Rhue and I. Kirsch (Eds.), Handbook of clinical hypnosis, 2010. Washington, D.C: APA

WOODY E. and SADLER P. Dissociation theories of hypnosis. In M.R. Nash and A.J. Barnier (Eds.), Oxford handbook of hypnosis, 2008; 81-110. Oxford, England: Oxford University Press

WOODY E. and SADLER, P. On reintegrating dissociated theories: Commentary on Kirsch & Lynn (1998). Psychological Bulletin, 1998; 123, 192-197

YANG J. C., JEONG G. W., LEE M. S., KANG H. K., EUN S. J.,Kim Y. K., et al. Functional MR imaging of psychogenic amnesia: A case report. Korean Journal of Radiology, 2005; 6, 196–199

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.

YASUNO F., NISHIKAWA T., NAKAGAWA Y., IKEJIRI Y., TOKUNAGA H., MIZUTA I., et al. Functional anatomical study of psychogenic amnesia. Psychiatry Research, 2000; 99, 43–57

YASUNO F., SUHARA T., NAKAYAMA T., et al. Inhibitory effect of hippocampal l5-HT1A receptors on human explicit memory. American Journal of Psychiatry, 2003; 160, 334–340.

ZOLA-MORGAN S., SQUIRE L.R. AMARAL D.G. Human amnesia and the medial temporal region: Enduring memory impairment following a bilateral lesion limited to field CA1 of the hippocampus. The Journal of Neuroscience, 1986; 6 (10): 2950–2967. PMID 3760943

ASSOCIATIONS:

Dissociative Amnesia and Fugue. Traumadissociation.com, Retrieved March 24, 2017 from http://traumadissociation.com/dissociativeamnesia

Trauma and Stressor-related Disorders. Traumadissociation.com. Retrieved March 24, 2017 from http://traumadissociation.com/information

American Academy of Child and Adolescent Psychiatry. P. O. Box 96106, Washington, D.C. 20090. (800) 333-7636. <www.aacap.org>. Tish Davidson, A.M.

World Health Organization. (2017) Classification of Diseases (ICD). Retrieved February 16, 2014, from http://www.who.int/classifications/icd/revision/en/

AMERICAN PSYCHIATRIC ASSOCIATION. Diagnostic and statistical manual of mental disorders: DSM-5. (5. Ed.), 2013