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### The traumatized brain

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**General Introduction**

**Chapter**

**I**



## Introduction

### **Dissociative identity disorder**

Dissociative identity disorder (DID), formerly known as multiple personality disorder, is a psychiatric disorder included in the DSM-IV (American Psychiatric Association, 1994). It is characterized by the presence of two or more distinct identities or personality states each with its own relatively enduring pattern of perceiving, relating to and thinking about the environment and self, with at least two of the identities or personality states recurrently taking control of the person's behavior. Another characteristic of this disorder is an inability to recall important personal information that is too extensive to be explained by ordinary forgetfulness, which is called dissociative amnesia (DA). These symptoms are not due to the physiological effects of a substance (e.g. blackouts or chaotic behavior during alcohol intoxication), a general medical condition (e.g. complex partial seizures) or imaginative play in children. In addition to these features, depersonalization, derealization, and sensori-motor dissociative symptoms are other characteristics features of this disorder.

### **The etiology of DID**

Despite the inclusion of DID in the DSM-IV (American Psychiatric Association, 1994), there is still no clear consensus regarding its diagnosis or treatment. There has been a considerable debate concerning the existence of DID as a mental disorder and some mental health professionals are still skeptical as to whether DID is a genuine psychiatric disorder (for reviews see Reinders, 2008, and Boysen and Vanbergen, 2013). The controversies surrounding this disorder, its etiology and disputed diagnosis can persist as long as limited neuroscientific evidence is available. Two etiological models for DID are: i) the trauma-related model and ii) the non-trauma-related model.

#### ***The trauma-related model***

The trauma-related model (Reinders et al., 2012), also known as the posttraumatic model (Gleaves, 1996) or trauma model (TM) (Dalenberg et al., 2012), states that

DID is causally related to a combination of factors that include disorganized attachment, lack of affect-regulation by caregivers, chronic emotional neglect, emotional, physical, and/or sexual abuse during early childhood (Boon and Draijer, 1993a, Chu and Dill, 1990, Nijenhuis and Den Boer, 2009, Van der Hart et al., 2006, Van der Hart et al., 2005). Based on these views, dissociation is a self-protecting mechanism that is used by the maltreated child to cope with overwhelming and inescapable abuse and neglect. This view is supported by the results of clinical research showing that 89%-97% of individuals with DID report exposure to either physical or sexual childhood abuse (Boon and Draijer, 1993c, Putnam, 1985, Ross, 1997). Proponents of this view propose that disorganized attachment between the child and caregivers leads to a disruption in the child's ability to integrate experiences (Freyd, 1996, International Society for the Study of Trauma and Dissociation, 2011). It has been proposed that eventually such circumstances can cause neurobiological changes that facilitate the development of distinct identity states each with differing consciousness of their experiences (Nijenhuis et al., 2002).

### ***The non-trauma-related model***

The non-trauma-related model (for a review see Reinders et al., 2012) includes views stating that DID is not related to antecedent trauma. This includes the iatrogenic, sociocognitive (Spanos, 1996) and fantasy model (FM) (Dalenberg et al., 2012). Proponents of these models believe that genuine cases of DID do not exist and assert that the symptoms of DID are either consciously or subconsciously enacted by the individual due to inappropriate psychotherapeutic techniques or due to socio-cultural influences (Giesbrecht et al., 2007, Lilienfeld et al., 1999, Merckelbach et al., 2002, Piper and Merskey, 2004). The iatrogenic model emphasizes the role of psychotherapeutic treatment in eliciting the symptoms associated with a diagnosis of DID. In this view, a close relationship between the therapist and patient can lead to a (sub-)conscious simulation of different identity states by the patient in order to please and satisfy the therapist. Proponents of the iatrogenic view also believe that false memories of child abuse may be fabricated

in suggestible individuals (Kampman, 1976, Spanos, 1996, Spanos et al., 1986). High suggestibility and fantasy proneness can be facilitating factors in the effectiveness of the construction of distinct identity states (Merskey, 1992). This view is supported by reports that many patients do not explicitly manifest alternate personality states until after the initiation of their therapy (Piper and Merskey, 2004).

Based on the sociocognitive model (Spanos, 1996), socio-cultural factors such as widespread publicity of DID cases and frequent portrayal of this disorder in the media, films and novels can contribute to fabricating DID (Lilienfeld et al., 1999). In support of this concept is the finding that an increase in the representation of DID in Western media sources is correlated with the number of DID diagnoses (Merskey, 1992). Pope et al. (2006) tracked the scientific interest (based on the number of publication per year) in DA and DID from 1984 to 2003 and reported a sharp peak in the mid 1990's followed by a sharp decline by 2002 and 2003. This is while the publication rates for well-established diagnoses such as anorexia nervosa, alcohol abuse and schizophrenia remained constant or showed a steady rise during the same period of time. Based on these observations, Pope et al. (2006) claimed a decline of scientific interest in DA and DID diagnoses. However, this review was criticized by the proponents of the trauma-related model as suffering from several methodological deficits. For example, it missed several important papers providing evidence in favor of a trauma-related origin of DID (Dalenberg et al., 2007). Furthermore, a recent literature review article by Boysen and Vanbergen (2013) investigated the rate of publications on DID during the period of 2000 to 2010. This study reported a steady rate of the number of publications per year, although this was low when compared to other psychiatric disorders.

The role of fantasy proneness has recently been investigated in two independent papers: A recent literature review by Dalenberg et al. (2012) assessed the relationship between pathological dissociation, trauma and fantasy proneness. Dalenberg et al. (2012) aimed to investigate, based on existing literature, two

models for DID: the Trauma Model (TM) and the Fantasy Model (FM). They reported that the trauma-dissociation relationship appears reliably in both clinical and community samples and that it has a similar effect size in objective and self-report studies. Also, the trauma-dissociation relationship was found to be stable over the course of short periods in clinical populations unless treatment was offered. Furthermore, dissociation and childhood trauma were found to be correlated even when fantasy proneness was controlled, and dissociation is not reliably associated with suggestibility, which was expected based on the FM model. Dalenberg et al. (2012) also found that dissociation is related to objective fragmentation and is higher in dissociative disordered patients than in controls and that dissociation is positively related to a history of trauma memory recovery. Evidence from neurobiological studies was found to support the role of dissociation as a regulatory response to extreme psychological trauma. Relying on evidence from published literature, Dalenberg et al. (2012) found strong supports in favor of the TM. However, direct empirical evidence that proves that neurobiological abnormality in DID is related to childhood trauma is still lacking.

The second paper by Reinders et al. (2012) reported a neuroimaging study to test whether dissociative identity state-dependent psychobiological features in DID can be enacted by high or low level of fantasy prone individuals. Findings of this study revealed differences in psychobiological and neural activation patterns between DID patients and both high and low fantasy prone DID simulating groups. These findings indicate that DID is not due to suggestion, role-play or fantasy proneness and argue against the non-trauma-related views.

### **Diagnosing DID**

Individuals with DID are highly poly-symptomatic and the majority of them have co-morbid mental disorders (Boon and Draijer, 1993b, Ellason et al., 1996, Galbraith and Neubauer, 2000, Rodewald et al., 2011). These factors along with the skepticism or lack of knowledge by mental health professionals are the main reasons that DID is often missed and a more familiar psychiatric disorder is diagnosed such as affective disorders, personality disorders, anxiety disorders

and/or schizophrenia (Ross et al., 1989). An individual with DID usually receives a long and frequently ineffective and unsuccessful treatment for these other disorders before receiving an accurate diagnosis and appropriate treatment (Arbour, 1998, Ross et al., 1989).

The following case study provides an illustration of the journey of a DID patient who participated in the studies presented in this thesis:

Mrs. IB was 55 years old when she participated in our study. Her first contact with mental healthcare was at the age of 27 because she was having symptoms of exhaustion, was anxious all the time, and was losing weight. At that time, she received a diagnosis of anorexia nervosa and received psychological therapy accordingly. IB felt that not only her therapy was unsuccessful, but that it was counterproductive. She remembered that the symptoms were present since she was in primary school and she felt sick all the time and needed to stay home. However, medical examinations did not show any sign of physical disease. After this initial diagnosis, over the years, IB has received many other diagnoses from different therapists such as adjustment disorder with depressive mood, personality disorder not-otherwise-specified (NOS), identity problems, problems due to negative sexual experiences, and borderline personality disorder. Finally, she came to realize that after being in therapy for all these diagnoses her symptoms persisted or even worsened.

She reported experiencing intense headaches that she described them “as if there is something in my head like a stone”. She also experienced episodes of derealization; as if her head and body were something separate. Furthermore, she complained about memory gaps (dissociative amnesia) several times a week and did not remember what she has been doing. It happened to her that she forgot everything about herself and her past (Dissociative Fugue). Additionally, sometimes she had the feeling that she was watching herself from a distance

(depersonalization). She has done several suicidal attempts, once consciously, but as she describes she was stopped by someone, something, like an angel. She is religious and believes that religion can support her.

IB read a book written by a DID patient and found a lot of similarities between her own symptoms and the ones reported in that book. She later read about our neuroimaging study in an internet advertisement and contacted us by phone to enquire about the objective of our study. At that time she was receiving therapy for negative sexual experiences but did not find it successful. She discussed the possibility of participating in this study with her therapist and her therapist agreed. After her initial phone call, our team member referred her to the DID expert Dr Ellert R.S. Nijenhuis for clinical assessment and diagnosis. Dr Nijenhuis conducted a SCID-D interview and established a DID diagnosis for her. Dr Nijenhuis also reported the new diagnosis to her therapist at the time. However, as her therapist was not experienced and trained enough regarding the course of treatment for this disorder, IB contacted several other therapists and eventually started appropriate treatment for DID. She reports that she feels good that finally her symptoms are recognized and acknowledged.

IB reported severe emotional neglect and abuse during her lifetime, starting in childhood. Her mom always told her what she did was wrong and threatened to hang her herself. She always felt like she should not exist. The sexual abuse could happen, because she never learned to stand up for herself and felt she had not developed a self-protecting mechanism. She could withdraw herself from her body during sexual abuse, but not from the emotional abuse; she says 'the emotional abuse happened in my head and I could not run from it; that is what made me all messed up'. She learned to be alone and felt always (and still does) very lonely with no one to care for her. 'And after all that happened, if

mental health care does not believe you and is unable or unwilling to provide the help needed, you're all alone once again', IB said.

At the time of participation in the studies for this thesis she reported having at least three dissociative identities besides her most prominent identity state: a 12-year old girl who is very depressed and prefers to die as she thinks she is "nobody". An 8-year-old girl who cries a lot but has no feelings. A 9-year old girl who cannot stay long and constantly switches to the other alters. She believes many more dissociative identities exist although she does not think of them as different people and thinks of them as a part of herself.

### **Prevalence of DID**

The international society for the study of trauma and dissociation (ISSTD) has reported that the prevalence of DID is between 1% and 3% in the general population, and between 1% and 5% in inpatient groups in Europe and North America (International Society for the Study of Trauma and Dissociation, 2011, Nijenhuis and Van der Hart, 2008). The proponents of the non-trauma-related views considered the geographically dependent prevalence of DID in North American and Western countries as evidence that this disorder is culture-bounded and not a universal response to early trauma, and hence DID is caused by iatrogenic and socio-cultural factors (Merskey, 1995). However, researchers have reported the appearance of DID in other countries and cultures (Coons et al., 1991) such as in Japan (Fujii et al., 1998, Okugawa et al., 2005), China (Xiao et al., 2006), the Philippines (Gingrich, 2009), India (Adityanjee et al., 1989), Turkey (Rhoades and Sar, 2006), South Africa (Savitz et al., 2004), Puerto Rico (Martinez-Taboas, 1991) and Australia (Irwin, 1994). For example, 2.3% of Chinese outpatients were diagnosed with full or partial forms of DID, although being from a community that has little public or cultural awareness of DID and is not familiar with any representation of the disorder in movies, novels or popular folklore. In China dissociative disorders are very rarely diagnosed by mental health professionals (Xiao et al., 2006). Furthermore, reports of similar symptom profiles in DID patients

in the North America (Ross et al., 1990), The Netherlands (Boon and Draijer, 1993c), Turkey (Akyuz et al., 1999, Sar et al., 1996) and Puerto Rico (Martinez-Taboas, 1991) suggest cross-cultural consistency of this disorder.

Of note, epidemiological studies in Turkey have reported an association between the severity of traumatization and pathological dissociation in the general population (Sar et al., 2007). Interestingly, this association remained significant after correction for possible iatrogenic factors, by removing individuals who received previous psychiatric treatments from the sample (Personal communication between Dr V. Sar and Dr A.A.T.S. Reinders).

### **Posttraumatic stress disorder**

Based on the trauma-related model DID develops in the context of severe trauma, therefore this model considers that DID and posttraumatic stress disorder (PTSD) are etiologically and phenomenologically related disorders (Bremner, 1999). According to the DMS-IV-TR (American Psychiatric Association, 1994), PTSD is characterized by: exposure to a traumatic event, followed by persistent re-experiencing of the traumatic event (flashbacks), persistent avoidance of stimuli associated with the event, symptoms of increased hyper-arousal not present before. Furthermore, the symptoms should last more than one month and cause significant impairment to an individual's life activities.

Recently, a subdivision among PTSD patients has been identified: a non-dissociative subtype and a dissociative subtype (Lanius et al., 2010, Lanius et al., 2012, Stein et al., 2013). The non-dissociative subtype has similar symptoms as listed above. The PTSD patients in this subtype respond to trauma cues with elevated level of autonomic activity (i.e. increased heart rate and blood pressure) resembling the “fight or flight” response in animals. In contrast, the dissociative subtype responds to trauma cues with a decreased or unchanged autonomic activity (Lanius et al., 2010). The latter response matches with “freezing” behavior of animals in response to threatening conditions when “fight or flight” is not possible (LeDoux, 1987, Nijenhuis et al., 1998). It should be noted that some PTSD patients may exhibit both types of responses to the reminders of traumatic events, either

simultaneously or at different time points (Lanius et al., 2010). However, it has been shown that prolonged traumatic experiences, for example chronic childhood abuse or combat trauma, are often associated with dissociative responses to trauma cues (Bremner et al., 1992, van der Kolk et al., 1996); whereas more acute traumatic experiences are associated with hyper-aroused and intrusive responses to trauma reminders (Lanius et al., 2010).

It has been reported that 60% of men and 51% of women experience at least one traumatic event in their lifetimes among whom 8% and 20%, respectively, develop PTSD (Davidson, 2000). The type of trauma most commonly associated with PTSD is combat exposure for men, and rape and sexual molestation among women (Kessler et al., 1995). While most individuals are able to cope with stressors and maintain or regain homeostasis, a minority of individuals fails to recover and develops PTSD. Evidence from twin and genetic studies indicates that vulnerability to PTSD is to some extent hereditary (Sarapas et al., 2011, True et al., 1993). Further research suggests that in addition to genetic influences, environmental factors such as early childhood experiences as well as interaction of genetic and environmental factors could increase vulnerability to develop PTSD in adulthood (Koenen et al., 2007, Koenen et al., 2009, Stein et al., 2002).

### **Effects of stress on the brain**

Stress is an inevitable part of daily life. The brain responds to stress by producing behavioral and physiological responses through stimulating the secretion and release of several hormones and neurotransmitters. Research from preclinical studies suggests that the hypothalamic-pituitary-adrenal (HPA) axis is a major neuro-endocrine component in the regulation of the stress response in mammals. Upon exposure to stress, neurons in the hypothalamic paraventricular nucleus (PVN) secrete corticotropin releasing factor (CRF) into the hypothalamo-hypophyseal portal circulation, in which CRF is transported to the anterior pituitary where it stimulates the production and release of adrenocorticotropin (ACTH). ACTH, in turn, stimulates the production and release of glucocorticoids (GCs) from the adrenal cortex. Several brain pathways modulate HPA axis activity. The

hippocampus and the prefrontal cortex inhibit the HPA axis whereas the amygdala stimulates the activity of PVN neurons (Tsigos and Chrousos, 2002).

It has been well documented that although stress hormones are protective and beneficial for survival in the short run, they may damage the brain when secretion is excessive or unnecessarily prolonged (McEwen, 2002). The hippocampus, in particular, is a major target for stress hormones due to the abundant presence of receptors for GCs. Early-life chronic exposure to stress or GCs could result in the suppression of neurogenesis, a reduction in dendritic branching or neuronal atrophy or neural loss in this brain structure (McEwen, 1999, Sapolsky, 1993).

Childhood maltreatment, which includes emotional and physical neglect and (sexual) abuse, is considered to be a severe life stressor. Teicher et al. (2003) suggested that early adversity could produce a cascade of physiological and neuro-hormonal responses, leading to long-lasting alterations in the patterns of brain development. Specific effects of maltreatment may depend on the age at the time of the maltreatment, and severity, frequency and duration of the maltreatment and the identity of the abuser (e.g., caregiver or other adult) (Andersen et al., 2008). However, since brain maturation continues throughout the lifespan, the effects of stress are not specific to childhood and can still influence the brain during the adulthood.

### **Neuroimaging**

The advent of neuroimaging techniques made it possible to explore several aspects of brain function and structure in vivo (Hurley and Taber, 2008). In particular, these techniques have greatly advanced our understanding of neural processes underlying several neurological diseases and psychiatric disorders (Rauch and Renshaw, 1995).

#### ***Functional neuroimaging***

Functional neuroimaging techniques including functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and single photon emission computed tomography (SPECT) are used to investigate the metabolic activity in

brain during a specific task compared to a baseline condition. Thus far, only a limited number of functional neuroimaging studies have investigated the neural correlates of DID. These studies have either assessed the neural activity during an identity state switch (Savoy et al., 2012, Tsai et al., 1999) or they have compared the activity across various identity states in DID (Hughes et al., 1990, Reinders et al., 2003, Reinders et al., 2006, Saxe et al., 1992, Sheehan et al., 2006) or between DID and controls (Elzinga et al., 2007, Reinders et al., 2012, Sar et al., 2001, Sar et al., 2007). Findings from the majority of these studies have indicated the involvement of the frontal, parietal and temporal cortices and the hippocampus and striatum (including pallidum and nucleus accumbens) in the neuropsychopathology of DID.

Numerous functional neuroimaging studies have studied the neural mechanism underlying PTSD. Although the findings of these studies, research designs, methodologies, and techniques vary to a great extent, the majority of these studies have consistently reported involvement of the limbic system in the pathophysiology of PTSD (for reviews see Francati et al., 2007 and Patel et al., 2012). It has been shown that different PTSD subtypes show unique and distinctive patterns of neural activity in response to trauma cues. The non-dissociative subtype shows decreased activation of the frontal areas involved in emotion regulation, along with failure of inhibition of the limbic areas related to fear extinction, i.e. the amygdala. In contrast, the dissociative PTSD subtype shows hyper-activation of cortical brain areas involved in emotion regulation, including the anterior cingulate and the medial prefrontal cortex (Lanius et al., 2010), which leads to a greater inhibition of the limbic emotional networks including the amygdala, insula, and thalamic regions (Hopper et al., 2007, Lanius et al., 2010, Lanius et al., 2012).

### ***Structural neuroimaging***

Structural neuroimaging techniques include anatomical MRI and diffusion tensor imaging (DTI) which can provide morphological information about white matter (WM) and gray matter (GM) of the brain.

### Gray matter imaging in DID and PTSD

Anatomical MRI, or structural MRI (sMRI), allows us to look at the brain with a spatial resolution to the millimeter scale. Using this technique, volumetric measurements of the brain tissue classes, i.e. WM, GM and cerebrospinal fluid (CSF), can be obtained. Pathological conditions related to childhood and adult trauma have detrimental effects on the gray and white matter of the brain (Bremner et al., 1997, Carrion et al., 2001). Using sMRI, possible neuroanatomical abnormalities in DID and PTSD patients can be studied.

So far, there have been only four multi-subject studies (Ehling et al., 2008, Irle et al., 2009, Vermetten et al., 2006, Weniger et al., 2008) and one single-subject study (Tsai et al., 1999) investigating neuroanatomical abnormalities in DID patients, using region of interest (ROI)-based approaches. Comparing DID patients with comorbid PTSD to healthy controls, some of these studies reported smaller volume of the hippocampus (Ehling et al., 2008, Irle et al., 2009, Tsai et al., 1999, Vermetten et al., 2006), amygdala (Ehling et al., 2008, Irle et al., 2009, Vermetten et al., 2006), and parahippocampal cortex (Ehling et al., 2008) in DID patients. These findings can be indicative of a trauma-related nature of DID, as hippocampal volume loss has been linked to elevated levels of GC secretion during stress (McEwen, 1999, Sapolsky, 1993). However, the bilateral hippocampal volume reduction in the study of Vermetten et al. (2006) has been criticized by proponents of non-trauma-related models as being age-dependent rather than genuine findings (Smeets et al., 2006, Spiegel, 2006). In addition, one of the volumetric studies in DID (Weniger et al., 2008) reported preserved hippocampal and amygdalar volumes in a sample of combined DID and dissociative amnesia patients without comorbid PTSD compared to healthy controls. Studies by Tsai et al. (1999), Vermetten et al. (2006) and Ehling et al. (2008) compared volumetric measurements in individuals with DID to those of healthy controls to investigate the differences in regional volumes, but none of these studies compared the volumetric measurements in DID to a trauma-related disorder such as PTSD to test for similarities in neuropsychopathology of these disorders, which would be expected

on the basis of the trauma-related model. Furthermore, the volumetric studies by Weniger et al. (2008) and Irle et al. (2009), comparing hippocampal and amygdalar volumes between DID, PTSD and healthy controls, are clearly underpowered as they included only four and two actual DID patients, respectively.

Several sMRI studies have investigated volumetric changes of brain structures in PTSD patients or individuals with a history of childhood trauma without PTSD, as compared to traumatized controls or to healthy controls. The most consistent finding among these studies is a smaller volume of the hippocampus in PTSD patients and childhood-maltreated individuals (Karl et al., 2006, Kuhn and Gallinat, 2013). Furthermore, in traumatized individuals a reduction of gray matter volume has been reported for whole-brain cortical gray matter (Carrion et al., 2001, De Bellis et al., 1999, De Bellis et al., 2002, Woodward et al., 2009), the anterior cingulate (Chen et al., 2006, Corbo et al., 2005, Kasai et al., 2008, Kitayama et al., 2006, Woodward et al., 2006, Yamasue et al., 2003), insula (Chen et al., 2006, Corbo et al., 2005, Kasai et al., 2008), frontal (Eckart et al., 2011, Geuze et al., 2008, Liu et al., 2012, Woodward et al., 2009) and temporal (De Bellis et al., 2002, Geuze et al., 2008, Woodward et al., 2009) cortices. Regarding the amygdala, volumetric findings in traumatized individuals have been inconsistent and some studies have reported smaller amygdalar volume in PTSD patients (Rogers et al., 2009, Weniger et al., 2008), others have observed preserved amygdalar volume in PTSD (Gurvits et al., 1996, Kuo et al., 2012) and adult victims of childhood maltreatment (Cohen et al., 2006). Interestingly, there is also a report of larger amygdalar volume in combat veterans with PTSD as compared to non-PTSD veterans (Kuo et al., 2012).

### **White matter imaging in DID and PTSD**

Diffusion tensor imaging (DTI) provides information about the magnitude and direction of water diffusion within the white matter of the brain (Basser and Pierpaoli, 1996). The white matter of the brain consists mostly of myelinated axons that transmit signals from one region of the cerebrum to another and between the cerebrum and lower brain regions. Almost 70% of the white matter of the brain is

water. Water diffusion in the white matter of the brain is dependent on the physical environment and is restricted by the myelin sheaths and axonal membranes, facilitating diffusion of water along fiber tracts but not across them, a situation known as anisotropic diffusion. It has been reported that pathological conditions such as multiple sclerosis (Senda et al., 2012) and Alzheimer's disease (Stepan-Buksakowska et al., 2012) or psychiatric disorders such as schizophrenia (Lee et al., 2013) and major depressive disorder (Cole et al., 2012) change the anisotropic diffusion by either a destruction or reduplication of membranous elements or by a change in cellularity. Therefore, examining the anisotropy parameters in white matter tracts can provide information about the quality and integrity of brain anatomical connectivity in pathological conditions.

To the best of our knowledge, no DTI study has yet examined the quality of brain anatomical connectivity in DID patients. Regarding PTSD patients and individuals with a history of childhood trauma, only a few DTI studies have investigated the anatomical connectivity in these groups. Although the results of these DTI studies have been heterogeneous, the majority of these studies have indicated a lower WM integrity in traumatized individuals (see Daniels et al. (2013) for a review). In these studies lower WM integrity has been reported in several white matter tracts including in the corpus callosum, superior longitudinal fasciculus, cingulum, internal capsule and fornix (Choi et al., 2009, Eluvathingal et al., 2006, Fani et al., 2012, Huang et al., 2012, Jackowski et al., 2008, Kim et al., 2005, Schuff et al., 2011). These findings indicate that trauma is associated with abnormalities of the integrity of brain connectivity in several major white matter tracts in traumatized individuals.

### **Conception of the thesis**

As reviewed above, neuroimaging studies in DID are very limited and insufficient knowledge concerning the neurobiological correlates of DID is one of the major factors explaining the controversy regarding the etiology of DID. Therefore, in order to resolve the controversies between the proponents of the trauma-related and non-trauma-related models further research is needed to elucidate the neural

substrates of this disorder. The aim of this thesis is to provide more neuroscientific knowledge about DID and to study its relation to antecedent trauma using structural brain imaging techniques.

Considering that stress in general, and childhood stress in particular, has been associated with regional brain gray and white matter abnormalities, investigating neuroanatomical changes in DID as compared to healthy controls may provide neuroimaging evidence in favor of either models as to whether DID is a genuine neurobiological disorder. Findings which indicate that DID, compared to healthy controls, is associated with brain morphological abnormalities can support the trauma-related model, whereas findings presenting no morphological difference between DID patients and healthy controls may provide evidence in favor of the non-trauma-related model.

Furthermore, volumetric studies in PTSD and other traumatized individuals have indicated the involvement of a wide range of brain regions in the psychopathology of trauma, whereas thus far morphological studies in DID have only focused on a limited number of a priori hypothesized brain regions. With the etiology discussion of DID in mind, it would be of interest to investigate (dis-)similarities in the neuroanatomy between individuals with DID and individuals with a trauma-related disorder, e.g. PTSD. It is hypothesized that if the trauma-related model is correct morphological similarities should be present between DID and for example PTSD. On the other hand, if the claim of proponents of the non-trauma-related views holds DID should have little or no morphological similarities with trauma-related disorders.

It has been shown that the majority of DID patients (80-98%) have co-morbid PTSD (Rodewald et al., 2011). All the DID patients recruited in the studies presented in this thesis (chapters 4, 5 and 6) had either current co-morbid PTSD or had PTSD in remission. Therefore, dissimilarities in neuroanatomical abnormalities between DID patients with co-morbid PTSD and PTSD patients without DID may manifest disorder-specific abnormalities. Nevertheless, future studies in patients with DID but without a co-morbid PTSS are of great interest as well.

## Chapter 1

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In sum, the studies in this thesis aim to investigate the neuroanatomy of the DID patients and to compare it to that of gender-, age-, education-matched PTSD patients and healthy controls. To this end, both gray and white matter structural neuroimaging techniques are applied in the same sample of DID patients (n=17) and PTSD patients (n=16) and HC (n=32) in the studies presented in this thesis.

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