CHAPTER 1

GENERAL INTRODUCTION
CHAPTER 1

Having multiple personality states: a participant’s story

“As a DID patient, I participated in the study investigating dissociative identity disorder (DID) using neuroimaging. It was exciting to get involved, because it is far from easy to ‘just’ bring another personality part of myself to the surface. No one with DID does so easily, unless under a state of threat. I believe there is much misunderstanding about a condition as DID anyway and therefore I am very grateful that with this thesis an attempt to give clarity and insight into the brain of DID patients is made and I’m thankful that I got the opportunity to be a small link in this. On the cover you see “Puzzle”, a painting I made before I was diagnosed with DID and before I knew that I consisted of multiple parts. At the time I painted this, I was hospitalized to cope with internal crisis and felt suicidal. Painting was a way to somehow stay ahead of the overwhelming emotions and in advance I did not know what I was going to make; often I was not even aware of who or what was painting. By painting, the parts in my head, which have their own life and age, communicated with the world and with the present time. When the painting was finished, and the emotion was translated to the canvas, generally it became clear what the story was about. However, sometimes it could take years for myself to understand what a painting depicted. I was not always ready to realize what an inner child wanted to make clear. Through painting, inner parts were communicating from the inside to the outside world. Sometimes it were the younger parts, inner children that tried to communicate, and sometimes other parts of the personality, such as defensive parts, or even parts that imitated perpetrators. My world inside was dark and cold, as if it were dark caves where the children were isolated, alone and withdrawn. All parts of our inner worlds were totally isolated and not in contact with each other until we began trauma therapy. We were on record as untreatable, constantly suicidal because of our defense system and we were terribly afraid to trust others.

After years of misdiagnoses and more than twenty hospitalizations, I started DID focused therapy and my fear and resistance were enormous. In the beginning I saw only an authoritarian perpetrator in my therapist. What contributed to overcome my resistance and fear was the psycho-education that helped me understand what was going on inside my head. I was so grateful that finally someone could explain my madness. It appeared that I was not crazy and

1 Translated from Dutch by the thesis’ author. The original statement can be found in Dutch on page 295 in appendix A of this thesis
that somehow my defenses were logical and understandable, although most complex. And the further therapy progressed, the more insight I gained into the functioning of my own brain. Gradually a picture unfolded to me of a complex personality with different identities, which seemed to have different functions, but were also often grouped around serious traumatic experiences. The constant intrusions, severe nightmares and numerous physical reactions captured me all those years and with that, I would not have lived long anymore. Now was the time to try to enter those horrors, to meet the different identity states and change the sharp emotions to memories that would not always overwhelm me. For that purpose I also took my paintings to therapy. The paintings articulate their own language and have their unique level of communication. Sometimes just observing them is enough.

Some time ago, I brought the Foundation Art from Violence (Stichting Kunst uit Geweld) to life. The aim is to provide a platform for survivors of domestic and sexual violence for sharing their art with each other and the world. The goal is to familiarize society with the effects of such violence and to make clear what the consequences are and try wherever possible to stop it.

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**Dissociative identity disorder**

Dissociative identity disorder (DID) is considered to be at the far end of the spectrum of trauma-related psychiatric disorders (Spiegel 1984, Van der Hart, Nijenhuis & Steele 2006). According to the DSM-5 (American Psychiatric Association 2013), DID is a psychiatric disorder that is, among others, characterized by the experience of two or more distinct personality states, recurrent gaps in the recall of everyday events or important personal information, and/or traumatic events that are inconsistent with ordinary forgetting, all of which should not be an outcome of substance abuse or general medication (American Psychiatric Association 2013). In addition to DSM-IV-TR criteria (American Psychiatric Association 2000), symptoms should cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. Furthermore, the disturbance is not a normal part of a broadly accepted cultural or religious practice (American Psychiatric Association 2013).
Personality states

DID is characterized by the development of different types of dissociative personality states. Such states have been classified as neutral personality states (NPS) or trauma-related personality states (TPS) (Reinders et al. 2003, Reinders et al. 2006, Reinders et al. 2012). In an NPS, DID patients concentrate on functioning in daily life. To that end, NPS has full or partial amnesia for traumatic memories, thereby disabling recognition of trauma-related information. In contrast, TPS does have conscious access to the traumatic memories. Personality states have previously also been referred to as neutral identity state (NIS) and trauma-related identity state (TIS) (Reinders et al. 2006, Reinders et al. 2012). The indicators NPS and TPS are derived from the terms “apparently normal part of the personality (ANP)” and “emotional part of the personality (EP)”, respectively, which are used in the Theory of Structural Dissociation of the Personality (TSDP) (Van der Hart, Nijenhuis & Steele 2006, Nijenhuis 2015). This theory defines dissociation as a division of personality into different types of subsystems, each with their own first-person perspective, that is, their own point of view as to who they are, what the world is like, and how they relate to that world (Nijenhuis 2015). Nijenhuis and Van de Hart (2011) outline a corporation metaphor, in which dissociation can be compared with a corporation that encompasses several departments and temporary projects. The corporation lacks a central management and is organized by interactions among all departments and employees. There is no hierarchically highest level dissociative part that guides lower level parts. The metaphor reflects the fact that no matter how dissociated and different parts of the personality may be, they are still linked and together they constitute a whole system (Braude 1995, Van der Hart, Nijenhuis & Steele 2006).

Nijenhuis et al. (2002, 2009) and Reinders (2008) suggested that studies in DID need to recognize and assess various dissociative personality states. To date, a handful of studies investigated personality state differences (Reinders et al. 2003, Reinders et al. 2006, Hermans et al. 2006, Reinders et al. 2012, Huntjens, Verschuere & McNally 2012, Schlumpf et al. 2013, Schlumpf et al. 2014). The emphasis in this thesis will be, among others, on acknowledging the differences between personality states and the importance to study those states in order to reach more clarity about psychological and neurobiological correlates of DID.
Dorahy et al. (2004) recommended that studies in DID need to recognize and cognitively assess various dissociative personality states when studying working memory, since working memory performance may covary with different prototypical dissociative personality states. A cognitive architecture supporting vigilance and bias for threat stimuli is increasingly suggested by studies regarding attention and working memory in DID (Dorahy et al. 2014). The nature of this architecture may vary depending on the characteristics of the dissociative personality state that is assessed (Dale et al. 2008, Dorahy, Middleton & Irwin 2005, Hermans et al. 2006).

**Prevalence**

Prevalence rates for DID vary widely, which can be largely explained by the choice of diagnostic instrument and cultural differences in symptom interpretation (Friedl, Draijer & de Jonge 2000). The prevalence of DID appears to be highest in emergency psychiatric settings and affects approximately 1% of the general population (Dorahy et al. 2014). 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, Van der Hart, Nijenhuis 2009). Cross-cultural consistency of DID is suggested by similar reported symptom profiles in North America (Ross et al. 1990), The Netherlands (Boon, Draijer 1993b), Turkey (Sar, Yargic & Tutkun 1996, Akyuz et al. 1999) and Puerto Rico (Martinez-Taboas 1991).

**DID simulation**

In a review of studies comparing diagnosed DID with simulated DID (Boysen, VanBergen 2014) it was concluded that results provided more support for a sociocognitive model than for a trauma model (see below for further description of the models). Among others, inter-identity transfer of information was replicated various times using a variety of methods (Allen, Movius 2000, Kong, Allen & Glisky 2008, Huntjens et al. 2006, Huntjens, Verschuere & McNally 2012). This finding can support a skeptical view towards the accuracy of memory experiences among people diagnosed with DID (Boysen, VanBergen 2014). On the other hand, simulators and DID patients showed significant differences on some clinical measures and DID patients showed cognitive deficits in memory.
and performance speed (Boysen, VanBergen 2014). Differences between both DID patients and DID simulating healthy control groups have been reported more broadly, covering several measures (Reinders et al. 2012, Schlumpf et al. 2013, Schlumpf et al. 2014, Brand et al. 2006, Welburn et al. 2003, Hopper et al. 2002). Boysen and VanBergen (2014) noted that if systematic differences in brain functioning will be found between patients diagnosed with DID and DID simulators, this might provide supporting evidence for areas of the brain previously identified as related to DID, thereby contributing to the debate regarding factors of influence in this controversial psychiatric disorder.

Posttraumatic stress disorder

The trauma model posits that DID and posttraumatic stress disorder (PTSD) are etiologically and phenomenologically related disorders (Spiegel 1984, Van der Hart, Nijenhuis & Steele 2005, Bremner 1999). The link between dissociative symptoms and PTSD has been studied in various populations whereby dissociation has been shown to be a strong predictive factor for PTSD (Koopman, Classen & Spiegel 1994, Briere, Scott & Weathers 2005, Wabnitz, Gast & Catani 2013, Shalev et al. 1996, Bremner et al. 1992). Regarding the relationship between complex dissociative disorders and PTSD, one core assumption of the TSDP is that trauma-related disorders can be arranged on a continuum ranging from simple forms of PTSD and acute stress disorders to complex PTSD and DID (Van der Hart, Nijenhuis & Steele 2005).

According to DSM-5, the diagnostic criteria for PTSD include a history of exposure to a traumatic event that meets specific qualifications and symptoms from each of four symptom clusters: intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity (American Psychiatric Association 2013). The dissociative subtype of PTSD is new to DSM-5 (Lanius et al. 2010, Lanius et al. 2012). This subtype responds to trauma cues with a distinct pattern of neurobiological responses (Lanius et al. 2010) and may benefit differently from current treatments (Lanius et al. 2012) than PTSD patients with the more common undermodulated type, that involves a predominance of re-experiencing and hyperarousal symptoms (Lanius et al. 2010). Such important clinical implications highlight the need to further unravel the complex interplay of traumatic stress, dissociation, and related disorders.
Reinders et al. (2014) proposed an extended PTSD-based neurobiological model for emotion modulation in DID. It was found that hypo-aroused personality states activated the PFC, cingulate, posterior association areas and parahippocampal gyri, thereby overmodulating emotion regulation; hyper-aroused personality states activated the amygdala and insula as well as the dorsal striatum, thereby undermodulating emotion regulation. By including a PTSD group in studies of this thesis, and compare PTSD with DID, we are able to directly test the trauma model on both neuronal and psychological measures.

Etiology debate

Dissociative identity disorder is controversial (Gillig 2009) and probably the most disputed psychiatric diagnosis (Reinders 2008). For decades the disorder has been officially recognized in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III (American Psychiatric Association 1980) (defined as Multiple Personality Disorder), DSM-IV (American Psychiatric Association 1994), DSM-5 (American Psychiatric Association 2013)), but many patients with DID share a history of years of misdiagnosis and various hospitalizations similar to Esther’s experience. Genuine DID patients present their dissociative symptoms with great reluctance. Because of the often mild phenomenology and the usually high shame threshold, symptoms have to be actively enquired after, as most patients do not report them spontaneously (Steinberg 1994). Only gradually, in a stable therapeutic environment, dissociative symptoms can be debriefed and explored, which has led skeptics to assume that DID has an iatrogenic origin. According to a survey among practitioners of patients with DID (Putnam et al. 1986), it took an average of seven years from the first contact with social workers to the time of adequate diagnosis, with nearly four prior other diagnoses. Under- and misdiagnosis may be related to unfamiliarity with the spectrum of dissociative disorders, disbelief that they exist, or lack of knowledge and appreciation of their epidemiology (Coons 1998, Brand et al. 2012). High comorbidity rates (Ellason, Ross 1997, Sar et al. 2004, Sar et al. 2006, Rodewald et al. 2011, Ross, Ferrell & Schroeder 2014, Bozkurt et al. 2014) complicate the diagnosis even further. To date, many clinicians and scientists still question the validity and even existence of DID (Merckelbach, Devilly & Rassin 2002, Piper, Merskey 2004a, Sar 2005, Coons 2005, Fraser 2005, Pope et al. 2006, Paris 2012, Lynn et al. 2014).
Trauma and fantasy models of DID

Supporters of the diametrically opposed trauma and fantasy models (Dalenberg et al. 2012) have engaged in a fierce debate regarding the etiology of DID. The fantasy model (Merckelbach, Muris 2001, Merckelbach, Devilly & Rassin 2002, Piper, Merskey 2004b, Pope et al. 2006, Piper, Merskey 2004a), also referred to as the sociocognitive/iatrogenic model (Spanos 1994, Spanos 1996, Lilienfeld et al. 1999) or non-trauma-related model (Reinders et al. 2012), regards DID as a simulation mediated by high suggestibility and/or fantasy proneness, suggestive psychotherapy and/or suggestive sociocultural influences (Giesbrecht et al. 2007, Rassin, Merckelbach & Spaan 2001, Giesbrecht, Merckelbach 2006, Giesbrecht et al. 2008, Lynn et al. 2012, Merckelbach, Rassin & Muris 2000, Merckelbach, Horseelenberg & Muris 2001). The sociocognitive view includes the idea that DID can be easily created in motivated suggestible individuals and that few suggestions would suffice to generate the symptoms of DID (Spanos 1996). Although fantasy proneness and suggestibility refer to different concepts, they are highly correlated (Merckelbach, Van de Ven 2001, Braffman, Kirsch 1999, Levin, Spei 2004) and dissociative symptoms correlate with fantasy proneness, heightened suggestibility, and susceptibility to pseudomemories in student samples (Merckelbach, Muris 2001, Rauschenberger, Lynn 1995). Opponents of the trauma model also suggested that mild cognitive impairment (Giesbrecht et al. 2008) or sleep disturbances (Van Heugten-van der Kloet et al. 2014) can be alternative mediating factors.

The trauma model postulates that DID is related to a combination of factors that include chronic emotional neglect and emotional, physical, and/or sexual abuse from early childhood, insufficient integrative capacity, attachment problems, and lack of affect-regulation by caretakers (Gleaves 1996, Spiegel 2006, Spiegel et al. 2011, Putnam 1992, Van der Hart, Nijenhuis & Steele 2006, Dell, O’neil 2009). Within the trauma-related view DID is thought to be a severe form of posttraumatic stress disorder, belonging at the far end of the spectrum of trauma-related psychiatric disorders (Spiegel 1984, Van der Hart, Nijenhuis & Steele 2005, Steele, Van der Hart & Nijenhuis 2009). Holders of the trauma-related view recognize that some features of dissociative personality states can be influenced by sociocultural factors (Van der Hart, Nijenhuis & Steele 2006), that false positive cases of DID have evolved in a treatment setting, and that some psychiatric patients imitate DID (Draijer,
Boon 1999). However, they also note that there are differences between genuine and imitated DID and that there is no evidence that DID can (sub-)consciously be created by sociocultural factors (Gleaves 1996). Even if DID symptoms can be created iatrogenically or enacted (Spanos 1994) this does not demonstrate that genuine trauma-related DID does not exist (Elzinga, Van Dyck & Spinhoven 1998).

To date, the fantasy model has hardly been tested in studies involving DID patients (cf. (Van Heugten-van der Kloet et al. 2014)), and evidence that the complex phenomenology and psychobiology of DID can be created and sustained over time by these factors is lacking (Gleaves 1996, Brown, Frischholz & Schefin 1999, Xiao et al. 2006, Loewenstein 2007). The model mainly relies on studies with nonclinical samples regarding fantasy proneness, suggestibility, and memory, and cover only a small subset of the many studies on DID and traumatic dissociation (Loewenstein 2007). Despite this lack of empirical support, the fantasy model of DID is influential in contemporary psychiatry and there have been proposals to prevent the inclusion of DID in the DSM-5 (Gharaibeh, Merskey 2009). Although proponents of the model acknowledge that “most individuals with DID exhibit signs and symptoms of psychopathology and experience intense subjective distress” (Lilienfeld, Lynn 2003) (p.131), they believe these problems should be attributed to other disorders such as bipolar disorder, somatization disorder, and primarily, borderline and hysterical personality disorder (as described in Van der Hart, Nijenhuis 2009). Given these largely contradicting views, it seems to be of major importance to further study dissociative identity disorder, testing both models. In line with this, Brand et al. (2012) and, more recently Lanius (2015), specified the importance of conducting more neurobiological research.

This thesis aims to explore the etiology of DID in a design that acknowledges both the trauma and fantasy model. Moving beyond these positions, the hypothesis is tested whether DID has a unique pattern in brain structure and function when compared with control groups. Specifically, by identifying personality state differences in functional brain mechanisms as well as several psychological measures, results can further inform holders of both views about the etiology of DID and contribute to achieving consensus regarding diagnosis and treatment. In the past decades, research on the effects of trauma and mechanisms of recovery has evolved in various different directions. Despite these advances, countless individuals affected by traumatic stress still do
not receive optimal care, which is incredibly costly to the mental health care system (Coons 1998, Brand et al. 2012, Insel, Cuthbert 2015). Findings from (fundamental) research need to be better translated to clinical applications. This project has emerged from a neuroscientific interest with a translational aim and was set up in close collaboration with experts in the clinical field.

**Trauma, dissociation and attachment**

**Trauma**

In psychopathology trauma is regarded an unbearable and inescapable life-threatening experience in the face of which a person is powerless (Herman 1992, Farina, Liotti 2013, Van der Kolk 1996, Krystal 1988). It has been postulated that traumatic experiences overwhelm a person’s defense ability and take over the usual fight or flight defensive responses (Schore 2009). The activation of an archaic defense system causes a disconnection between the various functional levels of the mind, prevents the integration of the traumatic event in psychological life and causes the discontinuity and fragmentation of consciousness and memory (Schore 2009, Nijenhuis et al. 1998b, Putnam 1997).

Trauma can be seen as a psychological “wound” evolved in relation to a variety of associated psychological, biological, social, and other environmental factors (Nijenhuis, Van der Hart 2011). Psychobiological factors include limitations of the exposed individual’s integrative capacity as revealed in dissociative reactions, affect dysregulation, and persistent avoidance of traumatic memories. Several studies show that traumatic pathogenetic processes cause detached states and neurobiological damage, impair a person’s integrative capacity and cause the fragmentation of behavioral strategies, mental activities, autobiographic and procedural memories, as well as the sense of self (Schore 2009, Farina, Liotti 2013).

Early maltreatment has enduring negative effects on brain development (Teicher et al. 2002, Teicher et al. 2003, Teicher, Tomoda & Andersen 2006). Because children have limited coping and self-regulatory capability in early stages of development they are easily overwhelmed (Putnam 1997) and abuse during this time disrupts self-regulation of emotion as well as early organization of self-perception (Putnam 1997). Emotional dysregulation and
maltreatment during developmental years often co-occur and may be the precipitant of psychiatric treatment (Putnam 1997, Brand et al. 2012, Gentile, Dillon & Gillig 2013) and the neurobiological sequelae of early stress and maltreatment may play a significant role in the emergence of psychiatric disorders during development (Teicher et al. 2003). DID has been associated with prolonged, severe and early childhood trauma (Chu et al. 1999, Boon, Draijer 1993b, Putnam et al. 1986) and the vast majority of DID patients report severe forms of abuse.

Clinical and neurobiological studies show that childhood traumatic experiences typically affect the mental functions most heavily dependent on the development and functioning of large associative networks, such as the state of consciousness and self-consciousness, or from the integration of different brain areas, such as emotional control and autobiographic memory (Chu 2010, Lanius, Vermetten & Pain 2010, Teicher et al. 2010, Tononi, Koch 2008, Farina, Liotti 2013).

**Dissociation**

Many divergent experiences have been described as dissociative, ranging from normal failures in attention to the breakdown of memory processes as seen in dissociative disorders. There is no consensus on the meaning of the term dissociation and the term is, in psychopathology, essentially used to define three different yet related concepts (Farina, Liotti 2013): 1) a diagnostic category, Dissociative Disorders (DD) of the ICD-10 and DSM-5; 2) a group of symptoms, dissociative in nature such as amnesia or derealization; 3) some pathogenic processes caused by traumatic experiences interfering with the integration of mental functions. Both retrospective and prospective studies and clinical observation suggest that dissociation is the central pathogenic mechanism rather than a peripheral feature of trauma related disorders (Sar 2011). Dissociative symptoms can disrupt every area of psychological functioning and are usually divided into two types (Spiegel et al. 2013): first there are unbidden intrusions into awareness and behavior, with accompanying deficits in continuity of subjective experience, labeled “positive” dissociative symptoms, and second, there is an inability to access information or to control mental functions, called “negative” dissociative symptoms (Spiegel et al. 2013).
Clinicians and researchers seem to agree that dissociation is the loss of the ability of the mind to integrate some of its higher functions (Dutra et al. 2009, Waller, Putnam & Carlson 1996, Farina, Liotti 2013). Dissociation can be broadly defined as a structured separation of mental processes that are normally integrated (Spiegel, Cardena 1991), such as memory, consciousness and identity (Liotti 2004). Dissociation in DID appears to serve as an automatic defense mechanism which reduces the impact of highly aversive or traumatic events (Van IJzendoorn, Schuengel 1996). Boon and Draijer (1993a) note that the assumption of a dissociative continuum, ranging from ‘normal’ forms of dissociation² to pathological dissociation such as found in DID (Hilgard 1977, Ludwig 1983, Bernstein, Putnam 1986, Putnam 1989), is in contrast with Janet’s original ideas (Janet 1907) in which dissociative states are regarded as discrete pathological states and dissociation is defined as a lack of integration among two or more different ‘systems of ideas and functions that constitute personality’ (p332) (Nijenhuis, Van der Hart 2011). The term dissociation was used by Janet to indicate a disorder of the integrative capacity leading to a mental fragmentation over several levels: from a deficit in the field of consciousness to an impairment of the unity of the subject’s personality (Van der Hart, Nijenhuis & Steele 2006). The disconnection of the normally overlapping and integrated functional levels of the mental functions is induced by the violent emotions caused by traumatic experiences (Van der Hart, Dorahy 2006). The development of a structured clinical interview for diagnosing dissociative disorders, which examines the quality and seriousness of five dissociative symptom classes (SCID-D) (Steinberg 1993) has contributed to the phenomenological knowledge of the various forms of dissociation.

In line with Cardena (1994) and Allen (2001), Brown (2006) and Holmes (2005) proposed a different classification of dissociative phenomena. They proposed two distinct forms of dissociation, namely detachment and compartmentalization. Detachment consists of depersonalization, derealization, and related phenomena, like out-of-body experiences. These experiences are typically triggered by overwhelming emotions caused by life-threatening experiences (Lanius et al. 2010). Compartmentalization, in contrast, encompasses dissociative amnesia, somatoform dissociation, surfacing of traumatic memories and distorted emotional and identity unity control (alternation of multiple personalities) (Nijenhuis, Van der Hart 2011, Holmes

² Such as daydreaming or losing oneself in a good book
et al. 2005, Nijenhuis et al. 1998a) and stem from the compartmentalization of normally integrated functions. Compartmentalization symptoms are typically a consequence of traumatic development and seem to modify the very structure of the personality (Lanius et al. 2010, Chu 2010, Classen et al. 2006), whereas detachment symptoms are experienced by everybody in extreme situations.

Putnam (1997) proposed a trauma-related developmental pathway to complex dissociative disorders such as DID via repetitive evocation of "discrete behavioral states" in the traumatized infant or young child (Van der Hart, Nijenhuis 2009). These states are precursors to a normally cohesive personality. Recurrent traumatization of the child compromises developmental psychobiological processes and involves a lack of integration among behavioral states and, eventually, dissociative parts of the personality (Putnam 1997).

Psychodynamic views regard dissociation as a psychological defense that emerges when an individual lacks the capacity, skills, motivation, or social support to integrate extremely stressful events or resolve intrapsychic conflict (Howell 2005, Kluft 1985). Recent psychodynamic views on dissociative disorders have integrated object relations, ego and self-psychology, intersubjectivity, and affect and attachment theories to further the understanding and treatment of these complex disorders (Howell 2005, Kluft, Foote 1999).

**Attachment**

Attachment theory is a psychological model that attempts to describe the dynamics of long-term interpersonal relationships between individuals and is often integrated with a psychodynamic perspective. This theory relates DID to highly disturbed attachment patterns between caretakers and their children (Lyons-Ruth et al. 2006, Barach 1991). This pattern involves the caretaker's extreme emotional unavailability and unduly frightened and frightening behaviors toward the child, resulting in a disorganized attachment style (Van der Hart, Nijenhuis 2009). Fear without solution, caused by the interaction with a seriously neglectful, maltreating, dissociated or simply frightened parent, prevents children from coherently organize their normal attachment behaviors (Main, Hesse 1990, Farina, Liotti 2013). Results of a prospective
study indicate that neglect and verbal violence in childhood are the traumatic experiences most closely associated with the development of dissociative disorders and symptoms in adulthood (Dutra et al. 2009). Disorganized attachment plays a central role in trauma-related disorders. It has been suggested that the propensity to react to traumatic events with dissociation is related to disorganization of early attachment and its developmental sequelae (Liotti 2004). It is hypothesized that early disorganized attachment is the first step in many developmental pathways that lead to increased vulnerability to dissociative disorders and dissociative reactions to later traumas in the face of traumatic experiences during childhood and adolescence (Liotti 1992).

The attachment system, although more often active during infancy and childhood, is operant throughout an individual’s life and powerfully activated during and after any experience of fear and of physical or psychological pain (Liotti 2004). A need to cope with a traumatic stressor activates the attachment system. Disorganization of attachment closely mimics the collapse of the integrative functions of consciousness that characterize any dissociative experience, and may be the first instance of dissociative reactions during life (Liotti 2004). Treatment of dissociative patients with developmental trauma disorders is complex and must be based on a multi-phase program, where the first goal is to overcome relational and arousal modulation difficulties (Cloitre et al. 2011, Courtois, Ford 2009).

**Closely related concepts**

Traumatic experiences, attachment dynamics and dissociative reactions seem to be intertwined, like three threads woven into a single strand (Liotti 2004). This strand may extend into developmental pathways leading, in the presence of later traumas, to complex forms of posttraumatic stress disorder, dissociative disorders and borderline personality disorder. Early childhood trauma-related consequences and to neglect or attachment related problems often co-exist (Draijer 2003, Courtois, Ford 2009). Traumatic experiences in children are often inflicted by people they depend on and who should protect them. Not only do children develop posttraumatic stress symptoms accordingly, also severe problems in affect regulation and social relationships might emerge (Draijer, Langeland 2009). It has been indicated that dissociation, although trauma-related, is neglect-related as well (Draijer, Langeland 1999). In particular, maternal dysfunction was found to be related to
the level of dissociation (Draijer, Langeland 1999). This implies the importance of object relations and attachment in the diagnosis and treatment of patients with dissociative disorders. Secure attachment rests on the basis of emotion regulation and insecure, especially disorganized, attachment, together with trauma, may profoundly disturb affect regulation.

DSM-5 did not include dissociative disorders (DD) under the Trauma- and Stressor-Related Disorders, as the diagnostic criteria for dissociative disorders do not include a stressor criterion (Criterion A), although the DDs in DSM-5 were deliberately placed just after the Trauma- and Stressor-Related Disorders group to indicate that most DD are associated with traumatic experiences (Reinders et al. 2014, Spiegel et al. 2013).

Since 2009, attempts to introduce the diagnosis of complex posttraumatic stress disorder for adults in the DSM-5 have been made, defined as Developmental Trauma Disorder among the disorders with onset in childhood and adolescence (Sar 2011). Complex PTSD presents with clinical features of full or partial PTSD together with symptoms from three additional clusters, namely problems in emotional regulation, negative self-concept, and problems in interpersonal relations (Marinova, Maercker 2015). Complex PTSD is proposed as a new diagnostic entity in ICD-11 and typically occurs after prolonged and complex trauma.

Effects on the brain

Carlson et al. (2010) regard learning as the process by which experiences change the nervous system and behavior accordingly. Learning is crucial to human survival. If we could not form memories as infants, we could not learn to do anything or benefit from experience. Early stress signals the nascent brain to develop along an alternative pathway adapting itself to survive and reproduce in a malevolent stress-filled world (Teicher, Tomoda & Andersen 2006). In psychotrauma, protection against the overwhelming exposure of threatening stimuli may be realized by inhibiting information processing. The DSM-5 definition (Spiegel et al. 2013, American Psychiatric Association 2013) of dissociation along with the general clinical assumption (Van der Hart, Nijenhuis & Steele 2006) suggest that individuals who experience high levels of dissociation, will show information processing dysfunction, such as disturbances in attention and memory, provoked by the implied defensive
Stress has effects on brain areas that play a critical role in learning and memory, including the hippocampus and prefrontal cortex (PFC) (Bremner et al. 2004, McEwen, Nasca & Gray 2015). It has been well documented that stress hormones 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 glucocorticoids. Early-life chronic exposure to stress and glucocorticoids could result in the suppression of neurogenesis, a reduction in dendritic branching or neuronal atrophy or neural loss in the hippocampus (McEwen 1999, Sapolsky 1993), which is involved in memory processes. Childhood maltreatment is considered to be a severe life stressor and 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 (Andersen et al. 2008). Studies examining the neuroanatomical correlates of childhood maltreatment in adults found decreased gray matter volume in the hippocampus (Vythilingam et al. 2002, Kitayama et al. 2005) and changes in the PFC (Teicher et al. 2003, Van Harmelen et al. 2010).

**Brain structure**

Structural magnetic resonance imaging (sMRI) studies found in general a smaller volume of the hippocampus in PTSD patients and childhood-maltreated individuals as compared with traumatized and healthy controls (Karl et al. 2006, Kuhn, Gallinat 2013). For DID, some studies reported smaller volume of the hippocampus (Ehling, Nijenhuis & Krikke 2008, Irle et al. 2009, Tsai et al. 1999, Vermetten et al. 2006) as compared with healthy controls. As hippocampal volume loss has been linked to elevated levels of glucocorticoids secretion during stress, these results suggest a trauma-related nature of DID (McEwen 1999, Sapolsky 1993). To date, no studies have compared hippocampus morphology in DID with a trauma-related disorder such as PTSD to test for similarities of these disorders. In order to directly test the trauma model’s hypothesis, we will include both PTSD and healthy controls as control groups for DID and compare hippocampus shape and volume. As the prefrontal cortex matures, response to stress becomes more restrictive (Lyss et al. 1999) due to the inhibitory influence of the prefrontal
cortex on other regions (Brake et al. 2000). It has been hypothesized however that early stress activates the developing PFC, altering its development and producing precocious maturation but stunted final capacity (Teicher et al. 1996, Teicher et al. 2003).

**Working memory**

Memory, and especially working memory is vulnerable to stress (Arnsten 1998), which appears to impair performance during tasks that require prefrontal cortex (PFC) operations (Arnsten 2009). Working memory (WM) has been defined as a limited capacity system that provides temporary maintenance and manipulation of information necessary to execute complex tasks (Baddeley 1996, Baddeley 2003). One of these tasks can be the exclusion of unwanted or irrelevant material from consciousness (Brewin, Smart 2005). Meta-analyses (Owen et al. 2005, Rottschy et al. 2012) have shown the involvement of the prefrontal-parietal network (PPN) during working memory processes in healthy participants. Cole et al (2014) suggest a critical role for the frontoparietal control system in promoting and maintaining mental health. They proposed that this system implements feedback control to regulate symptoms and named it the “immune system of the mind”. They noted the frontoparietal control system as an important target for future research. Okon-Singer et al. (2015) described research that demonstrates that stress, anxiety, and other kinds of emotion can profoundly influence key elements of cognition, including selective attention, working memory, and cognitive control. Circuits involved in attention, executive control, and working memory contribute, in turn, to the regulation of emotion.

There is compelling evidence that brain regions and psychological processes commonly associated with cognition, such as the dorsolateral prefrontal cortex and working memory, play a central role in emotion (Okon-Singer et al. 2015). In a recent meta-analysis (Scott et al. 2015) it was suggested that PTSD patients show hypoactivation of regions involved in attention and working memory. In PTSD, several brain imaging studies have demonstrated working memory deficits associated with altered prefrontal activation (Galletly et al. 2001, Clark et al. 2003, Elzinga et al. 2007, Moores et al. 2008, Weber et al. 2005). Patel et al., (2012) described lower activation in dLPFC and lateral parietal cortex in PTSD patients coupled with higher precuneus activation. These authors proposed that the loss of top-down inhibition is one of the
main components underlying impaired extinction or under-modulation of affect. A review (Aupperle et al. 2012) reported subtle impairments in response inhibition and attention regulation in PTSD that may be exacerbated within emotional or trauma-related contexts, and may relate to dorsal prefrontal dysfunction. Rolls (2013) reviews evidence suggesting that the maintenance of a regulatory goal in emotion regulation highly depends on working memory (Okon-Singer et al. 2015). Research examining working memory and attentional mechanisms has attempted to build a cognitive profile of several other psychiatric conditions (Nigg 2000), but results regarding the relation between dissociation and working memory have been ambiguous. Inconsistent results regarding dissociation and working memory require clarification (Giesbrecht et al. 2008).

One multi-subject functional magnetic resonance imaging (fMRI) study has been conducted in dissociative disorders (Elzinga et al. 2007). This study assessed working memory performance in patients with dissociative disorders (DID and DD-NOS) as compared with healthy controls. Dissociative patients showed enhanced working memory performance together with greater activation in the left anterior PFC, dorsolateral PFC and parietal cortex compared with controls. Unfortunately, it remains unclear which type of personality state (NPS or TPS) was tested. Since it is known from previous studies that different types of personality states display distinct patterns of neural activation (for example (Reinders et al. 2003, Reinders et al. 2006)), personality state differences (NPS/TPS) need to be examined for working memory functioning as compared with multiple control groups, testing both the trauma and fantasy model.

**Neuroimaging DID**

Over the past few decades a variety of methods have been developed to study the brain (Matthews, Jezzard 2004). Neuroimaging includes the use of various techniques to either directly or indirectly image the structure, pharmacology or function of the brain. Structural MRI is a neuroimaging technique for performing volumetric measurements of the brain tissue classes, with a spatial resolution on a millimeter scale. Tissue classes include white matter, gray matter and cerebrospinal fluid. Pathological conditions related to trauma may affect the gray and white matter of the brain (Bremner et al. 1997, Carrion
et al. 2001) and by the use of sMRI, potential neuroanatomical abnormalities in DID and PTSD patients can be studied.

Functional magnetic resonance imaging (fMRI) is a procedure that measures brain activity by detecting associated changes in blood flow. This technique relies on the fact that cerebral blood flow and neuronal activation are coupled (that is, when an area of the brain is in use, blood flow to that region also increases). Blood oxygenation level dependent (BOLD) fMRI is a powerful approach to define activity in the human brain (Matthews, Jezzard 2004).

Despite the fact that imaging neuroscience has been around for more than 20 years and is by now the predominant technique in behavior and cognitive neuroscience (Friston 2009), few neuroimaging studies have been conducted in patients with DID (Dorahy et al. 2014, Dalenberg et al. 2012, Reinders 2008). In contrast, numerous functional neuroimaging studies have studied the neural mechanism underlying PTSD. Although imaging studies have elucidated neurophysiological markers of the dissociative response in patients with a range of DD and PTSD, studies performed specifically in DID patients are more limited (Dorahy et al. 2014), even though prevalence estimates are similar to for example schizophrenia, a disorder that many neuroimaging studies were devoted to. Dorahy et al. (2014) reviewed psychobiological findings and suggested a unique neurophysiological profile in DID.

Switching processes in DID are characterized by activation and inhibition of various brain areas and the exact patterning of these may be related to the psychobiological characteristics of the dissociative personality states involved (Dorahy et al. 2014). During a personality state switch, Tsai et al. (1999) observed brain activity in hippocampal areas, as well as the parahippocampus, medial temporal structures, substantia nigra, and global pallidus, as well as right hippocampal activation when the participant was returning to her original identity (Dorahy et al. 2014). Savoy et al. (2012) demonstrated involvement of the dorsolateral prefrontal cortex, the anterior prefrontal cortex, and orbitofrontal cortex, as well as bilateral activation in the nucleus accumbens during switching in a DID patient.

Reinders et al. (2003) conducted a PET study in DID and found two distinct states of self-awareness, each with its own access to autobiographical trauma-related memory with involvement of the medial prefrontal cortex.
and the posterior associative cortices in the representation of these different states of consciousness. In another study (Reinders et al. 2006), the different personality states were associated with different brain activation patterns when confronted with trauma-related cues. The cortical multimodal posterior association areas (PAA), the subcortical amygdala and subparts of the dorsal striatum were described to be involved in the psychopathology of DID. Their findings were unrelated to fantasy proneness (Reinders et al. 2012), since neither high nor low fantasy prone mentally healthy simulating controls were able to enact the psychophysiological and neural activation patterns of the authentic dissociative personality states.

In response to subliminally presented neutral and angry faces, Schlumpf et al. (2013) found abnormal reaction times for EP (equivalent of TPS), but not for ANP (equivalent of NPS), and EP activated different brain areas including in the parahippocampal gyrus, the brainstem, face-sensitive regions, and motor-related areas. Furthermore, Schlumpf et al. (2014) compared ANP and EP on resting state measures and found that ANP showed elevated perfusion in bilateral thalamus. Compared with ANP, EP had increased perfusion in the dorsomedial prefrontal cortex, primary somatosensory cortex, and motor-related areas. In both studies, patterns could not be mimicked by ANP and EP simulating healthy controls. Others (Mathew, Jack & West 1985) found hyperperfusion in the right temporal cortex in a single case study in a DID patient. Two uncontrolled resting state studies also found the involvement of the temporal lobe of the brain in DID (Saxe et al. 1992, Sheehan, Thurber & Sewall 2006) and two controlled studies, that included the largest sample of 21 DID patients in studies into DID using brain imaging techniques to date (Sar et al. 2001, Sar, Unal & Ozturk 2007) found bilateral frontal perfusion differences between patients and controls. The latter results are consistent with a neurodevelopmental model for DID proposed by Forrest (2001), underlining deficient functionality of the orbitofrontal region in the brain. The orbitofrontal lobe has been hypothesized to be affected by early trauma (Dorahy et al. 2014).

Findings from the majority of the above described studies have indicated the involvement of the frontal, parietal and temporal cortices and the hippocampus and striatum in the neuropsychopathology of DID.
Thesis outline

As described in previous paragraphs, neuroimaging studies in DID are limited and the disorder remains controversial. In order to add insight to the etiology debate regarding DID, further research is needed to elucidate the neural and psychological substrates of this disorder.

The aim of this thesis is to provide more knowledge about DID. A group of DID simulating healthy controls was included in studies of this thesis to investigate the degree to which DID can be simulated on both neural and psychological measures, allowing a direct test of the fantasy model. A global overview of thesis related topics is provided above in the general introduction. Chapter 2 discusses a range of psychological measures in DID and several control groups, covering both the trauma and fantasy model. Chapter 3 focuses on investigating differences in morphology of the hippocampus between DID, PTSD and HC in relation to childhood maltreatment. Chapter 4 and 5 focus on working memory functioning and test the trauma and fantasy model respectively, including both PTSD and DID simulating healthy controls as control groups. Finally, a general discussion follows, with a reference to implications for clinical practice and suggestions for future research. In sum, this thesis focuses on the etiology discussion of dissociative identity disorder in a broad sense and more specifically the importance of assessing personality state differences.
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CHAPTER 1


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CHAPTER 1


