Opposite brain emotion regulation patterns in identity states of dissociative identity disorder: A PET study and neurobiological model

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Abstract

In posttraumatic stress disorder (PTSD) imaging studies have shown differing neural network patterns between hypo-aroused/dissociative and hyper-aroused subtypes. Since dissociative identity disorder (DID) involves different emotional states this study tests whether DID fits aspects of the differing brain activation patterns in PTSD. While brain activation was monitored using positron emission tomography, DID individuals (n=11) and matched DID simulating healthy controls (n=16) underwent an autobiographic script-driven imagery paradigm in a hypo-aroused and hyper-aroused identity state. Results were consistent with those previously found in the two PTSD subtypes for the rostral/dorsal anterior cingulate, prefrontal cortex, and the amygdala and insula respectively. Furthermore, the dissociative identity state uniquely activated the posterior association areas and parahippocampal gyri whereas the hyper-aroused identity state uniquely activated the caudate nucleus. Therefore we propose an extended PTSD based neurobiological model for emotion modulation in DID: the hypo-aroused identity state activates the prefrontal cortex, cingulate, posterior association areas and the parahippocampal gyri, thereby overmodulating emotion regulation; the hyper-aroused identity state activates the amygdala and insula as well as the dorsal striatum, thereby undermodulating emotion regulation. This confirms the notion that DID is related to PTSD as hypo-aroused and hyper-arousal states in DID and PTSD are similar.
1. Introduction

In dissociative identity disorder (DID) different emotional states can be maintained between alternate identity states (Reinders et al., 2003, 2006, 2012; Schlumpf et al., 2013). A large body of data supports the conceptualization of DID as the most severe, chronic, complex, childhood onset posttraumatic disorder (Spiegel, 1984; Putnam, 1997; Van der Hart et al., 2006; Spiegel et al., 2011; Dalenberg et al., 2012; Reinders et al., 2012). In DID, repeated early traumatization may disrupt unification of identity through creation of behavioural and mental states associated with mitigating traumatic experiences and providing reparative experiences for the child (Putnam, 1997). Of note, the fantasy/sociocognitive model alternatively proposes that DID is an artefact mediated by high suggestibility, fantasy proneness and/or cognitive distortions (Lilienfeld et al., 1999; Kihlstrom, 2005; Giesbrecht et al., 2008; Lynn et al., 2012; Paris, 2012; Boysen and VanBergen, 2013). This controversy can be resolved by analysing the neurobiological basis of the different identity states in DID, especially in comparison with other stress related disorders such as post traumatic stress disorder (PTSD).

Recent research on PTSD has identified a dissociative subtype affecting about 12%-30% of the PTSD population (Lanius et al., 2010, 2012; Stein et al., 2012; Wolf et al., 2012b). When this subgroup is exposed to personal trauma scripts, subjects report high rates of dissociative symptoms, particularly depersonalization and derealization. The dissociative subtype is associated with a history of repeated childhood and adult interpersonal trauma, primarily sexual abuse (Wolf et al., 2012a, 2012b). The more common, hyper-aroused PTSD sub-type reports reexperiencing and hyper-arousal symptoms in response to personal trauma scripts (Lanius et al., 2010). Imaging studies have shown differing neural network patterns between the putative hypo-arousal/dissociative and hyper-aroused PTSD subtypes (Lange et al., 2005; Frewen and Lanius, 2006; Hopper et al., 2007; Felmingham et al., 2008; Lanius et al., 2010, 2012; Weniger et al., 2013). PTSD individuals with dissociative responses to trauma cues show hyper-activation of cortical brain areas involved in emotion regulation, including the rostral/dorsal anterior cingulate and the medial, middle and superior prefrontal cortex (Felmingham et al., 2008; Lanius et al., 2010). These cortical regions appear to inhibit subcortical areas, including amygdala, insula, and thalamic regions, that subserve posttraumatic emotional reactivity, and perception of aversive somatic and emotional states (Hopper et al., 2007; Lanius et al., 2010, 2012). This pattern is further characterized by autonomic hypo-arousal, as reflected in a decrease in heart rate and blood pressure during script-driven imagery for many subjects (Lanius et al., 2002). In contrast, PTSD individuals with the hyper-aroused subtype report subjective experiences of distressing intrusive trauma memories or flashbacks in response to trauma scripts. These subjects show decreased activation of frontal areas involved in emotion regulation, with failure to inhibit subcortical and limbic areas related to fear and perception of noxious stimuli. The latter pattern has been termed “undermodulation” of emotional response to trauma cues (Hopper et al., 2007; Felmingham et al.,
and is generally accompanied by hyper-arousal and increases in heart rate and blood pressure, consistent with the more classical “fight-flight” pattern (Van der Hart et al., 2006).

In the current study, we investigate whether neural activation patterns to script-driven imagery in different identities in DID, compared with simulating controls, are consistent with the neurobiological model proposed for the two subtypes of PTSD. To be able to examine the neurobiological model for hypo-aroused/dissociative and hyper-aroused PTSD in a sample of individuals with DID, we re-analyzed previously obtained brain imaging data from eleven individuals with DID (Reinders et al., 2003, 2006) in order to test specifically the hypothesis whether identity state dependent neural activation patterns in DID fit the neurobiological model of differing neural network patterns for hypo-aroused/dissociative and hyper-aroused PTSD subtypes. Moreover, we included a group of healthy controls that were instructed in order to simulate dissociative identity states. Following the conceptualization of Van der Hart et al. (Van der Hart et al., 2006) we studied regional cerebral blood flow (rCBF) in authentic and simulated Neutral Identity States (NIS) and Trauma-related Identity States (TIS). The terms NIS and TIS are derived from the Theory of Structural Dissociation of the Personality (TSDP) (Van der Hart et al., 2006; Nijenhuis and Van der Hart, 2011) and are analogous to that theory’s constructs, the “apparently normal part of the personality (ANP)” and “emotional part of the personality (EP)”, respectively. Patients and controls underwent a script-driven imagery paradigm while brain activation was being monitored and within-subject comparison of (simulated) hypo-aroused and hyper-aroused identity state dependent brain activation patterns were conducted.

The a priori hypotheses for the current study were, that in response to personal trauma scripts: (1) the DID patients’ NIS, the hypo-aroused identity state, will show hyper-activation in frontal areas and the rostral/dorsal cingulate, with hypo-activation in the amygdala and insula: the DID subjects’ NIS will consequently show psychophysiological hypo-arousal; (2) the DID patients’ TIS, the hyper-aroused identity state, will show hypo-activation in frontal areas and cingulate, with associated hyper-activation in the amygdala and insula: the DID subjects’ TIS will consequently show psychophysiological hyper-arousal.
2. Methods

2.1 Participants

Eleven patients with dissociative identity disorder (DID; all female, age: M = 41.0, SD = 6.1) diagnosed with the Structured Clinical Interview for DSM-IV Dissociative Disorders (SCID-D) (Steinberg, 1993) were compared to sixteen female healthy control subjects (CTRL; age: M = 41.1, SD = 10.7) without psychiatric or current or past trauma-related problems (evaluated with the Trauma Experience Checklist (TEC) (Nijenhuis et al., 2002) and the Somatoform Dissociation Questionnaire (SDQ-20) (Nijenhuis et al., 1996).

Individuals with DID included in the current study have been described previously (Reinders et al., 2003, 2006, 2012). In sum: Exclusion criteria were pregnancy, traumatic experiences in a hospital setting, systemic or neurological illness, and no command of the Dutch language. Treatment had progressed to Phase II (Brown et al., 1998), which involves therapeutic exposure to trauma-related memories. They had to be capable of self-initiated and self-controlled switching between identity states (for definitions see Supplemental Material) in an experimental situation with minimal guidance of their psychotherapist and had to have at least one TIS displaying signs of sympathetic nervous system activation when cued by trauma reminders and one NIS between which they could alternate if requested. Lanius et al. (Lanius et al., 2010) did not specifically relate their definitions for dissociation and hyper-arousal in PTSD subtypes to DID. Nevertheless, for the purpose of this study we will use the concepts of Lanius et al. in addition to the terminology for different identity states in DID based on the TSDP (Van der Hart et al., 2006; Nijenhuis and Den Boer, 2009).

Control data is a subset of a previously published sample (Reinders et al., 2012). Control subjects were recruited, included and instructed (see Supplemental Material) to simulate dissociative identity states as described previously (Reinders et al., 2012). Exclusion criteria were the presence of medical, neurological or psychiatric problems in the past or the present, the use of psychotropic medication 15 days prior to examination, participation in a positron emission tomography (PET) or other study that involved administration of radiation in the year prior to this study, and pregnancy. Two controls were found to be unable to maintain their roles during some of the study conditions: one listening as NIS to the trauma analogue script, and one listening as TIS to the neutral memory script. Data from these conditions were excluded from the analysis. Furthermore, the PET data of one control subject was lost due to storage failure at the PET centre, leaving 15 controls with PET data available and the HRV data for two control subjects could not be obtained, leaving 14 control subjects with HRV data.
2.2 PET Procedure and Data Processing

The PET (Siemens/CTI ECAT HR+) procedure for the controls was close to identical to the patients (Reinders et al., 2003, 2006). In contrast to patients the controls did not habituate to the PET environment prior to the investigation as anxiety levels were expected to be low. No urine samples were obtained for the control groups, both medication and drugs use were verbally debriefed according to standard control research practice. For the controls one extra set of the four conditions was added to increase statistical power. The scanning sequence was therefore NISn, NISn, TISn, TiSt, TiSt, TISn, NiSt, NISt, TiSt, NiSt and NiSt. The last minor character (n or t) denotes the content of the memory script (MS: neutral or trauma-related). For patient comfort considerations, i.e. minimizing the number of identity state switches, a fixed condition order was used, which was also used for the controls to minimize methodological differences. Two minute heart rate variability (HRV) segments, post scan blood pressure (systolic and diastolic), and discrete heart rate frequency were measured.

Data reconstruction, attenuation correction, spatial transformation, spatial smoothing (isotropic Gaussian kernel of 12 mm), global normalization and statistical analysis of the data were performed as usual (Reinders et al., 2002, 2003, 2006, 2012) with SPM5 (www.fil.ion.ucl.ac.uk/spm). The subjective reactions and the autonomic reactions were included as usual as group specific covariates in the general linear model (GLM: three factor main effects (subject, condition and group), four conditions and the group by condition interaction) of SPM5 after PC analysis (Reinders et al., 2003, 2006, 2012), only the eigenvectors with an eigenvalue larger then one were included (DID: five, CTRL: nine). Global cerebral blood flow (CBF) was included as a nuisance covariate (AnCova by subject). Comparisons of interest included: between identity state effects and within identity state effects. Between identity state effects refer to differential processing of the trauma-related text and the neutral text between identity states. Within identity state effects refer to differential processing of the trauma-related and neutral text within the trauma-related or neutral identity state. All statistical analyses in SPM were ANOVAs.

The psychophysiological data was subjected to missing value, principal components (PC) data transformation and statistical analysis (SPSS-PC 15.0 (2006)). The within subject subtractions for the between and within identity state effects were submitted to one-way ANOVAs.

2.3 Statistical inference and reporting

Statistical parametric maps were thresholded using an uncorrected threshold of $p < 0.001$ (Friston et al., 1991) and explored for a priori hypothesized brain areas. Multiple comparisons correction was performed, using the false discovery rate statistics (Genovese et al., 2002) methodology included in SPM, for whole brain and for the a priori regions of interest (ROI). In the latter case a
small volume correction was applied using a sphere with radius of 9 mm (Reinders et al., 2005).

A priori hypothesized regions of interest (ROI) were the cingulate (mid and anterior), the pre-frontal cortex (medial, middle and superior prefrontal gyrus), the amygdala and the insula. These areas were derived from the review by Lanius et al. (Lanius et al., 2010) and publications concerning dissociative responses in posttraumatic stress disorder (Hopper et al., 2007; Felmingham et al., 2008). The coordinates were converted from MNI space to Talairach space (Brett, 2006) to be defined in Brodmann areas (BA) using both the Talairach atlas (Talairach and Tournoux, 1988) and Deamon (Lancaster et al., 1997, 2000). Activations in sulci was defined using Brain Tutor (Goebel, 2013). The location was anatomically compared to and described using a second brain atlas (Mai et al., 1997). Activation localization was performed as usual (Reinders et al., 2012). Only clusters larger than eight voxels are reported taking into account the spatial resolution of the PET camera. All peak voxels in clusters were explored and small volume correction was applied to the identified peaks as long as they were located within the a priori hypothesized regions.

For the psychophysiological data the $F$ and $p$ values are reported as well as the mean and standard deviation. Bonferroni correction was applied to correct for the number of tests within the subjective or autonomic categories. Values with a $p < 0.006$ for the subjective measures and values with a $p < 0.003$ for the objective measures were reported as significant after the correction for multiple comparisons.
3. Results

Significant differences in brain activation and psychophysiological measures between the DID patients and the controls are presented in Tables 1 and 2. The directionality of the neuronal responses and the most important brain areas are depicted in Figure 1.

3.1 Within identity state effects

We found, when the neutral state listened to the trauma-related text, as compared to the neutral text, bilateral activation in the superior frontal gyrus was found accompanied by activation in the right middle frontal gyrus and left medial frontal gyrus (see Figure 1, top). A trend was found for an increase in the subjective sensory perceptions, the heart rate frequency, and the systolic and diastolic blood pressure measurements (data not shown). No significant activations were found when the NIS listened to the neutral text, as compared to the trauma-related text. Furthermore, we found that when the TIS listened to trauma-related information the left insula (see Figure 1, bottom) and amygdala were activated. A concomitant significant increase in the subjective sensorimotor and emotional ratings, and of the objective heart rate frequency, systolic and diastolic blood pressure measurements was found, accompanied by a significant decrease in average HRV. No significant activations were found when the TIS listened to the neutral text, as compared to the trauma-related text.

3.2 Between identity states effects

We found that, when processing the trauma-related text, the NIS activated bilateral parahippocampal and cingulate gyri (see Figure 1: middle left) and additionally activated the posterior multimodal association areas: bilateral intraparietal sulcus, bilateral occipital areas (including (pre-)cuneus), accompanied by left lingual gyrus and right sided (occipito-)temporal and fusiform gyrus activation. The TIS activated the bilateral caudate nucleus (see Figure 1: middle right), the left amygdala, and the left insula. A concomitant significant increase in heart rate frequency, systolic blood pressure and subjective sensory perceptions was found. In addition, a trend was found for a decrease in HRV and for an increase in subjective emotional rating (data not shown). No significant differences were found in brain activation for the differential processing of the neutral text and none of the subjective ratings or autonomic reactions showed a difference between the TIS and NIS.
4. Discussion

We have two major findings. The first finding of this study is that, in response to personal trauma scripts, DID patients’ NIS and TIS alternate identities show opposite rCBF activation patterns, which are consistent with those previously found in the undermodulated (hyper-aroused) and overmodulated (dissociative) PTSD patient subtypes in separate individuals (Hopper et al., 2007; Felmingham et al., 2008; Lanius et al., 2010). The second finding is that important additional brain areas were revealed for identity state dependent emotion modulation in individuals with DID.

Our first finding concerns similarities between previously reported neural networks in PTSD involved in emotional undermodulation and overmodulation of affect and individuals with DID. In response to personal trauma scripts, and similar to individuals with the putative dissociative PTSD subtype (Felmingham et al., 2008), DID patients’ NIS, compared to patients’ TIS, on the within-identity state assessment, show autonomic hypo-arousal with increased activation of the right mid/anterior cingulate cortex, and bilateral superior frontal gyrus, right middle frontal gyrus and left medial frontal gyrus. The current findings are in line with the neurocorrelates of dissociative PTSD, characterized by emotional overmodulation in response to exposure to traumatic memories. In both DID and dissociative PTSD patients this is associated with hyper-activation of similar brain areas that suppress the arousal of the sympathetic nervous system, leading to hypo-responsiveness of the psychophysiological system. Remarkably, there seems to be an overlap between the cortical mechanisms in dissociative PTSD individuals and those of the DID patients’ NIS. These appear to control activation of subcortical systems related to fear, anguish, and nociception, as well as to dampen sympathetic responding to traumatic scripts (Nijenhuis and Den Boer, 2009). In contrast, in response to personal trauma scripts, the DID patients’ TIS activated subcortical brain areas including left amygdala, bilateral caudate, and left insula, but not in prefrontal cortex and cingulate regions. In addition, DID patients’ TIS showed significantly increased activation of the sympathetic nervous system, with increased heart rate and (systolic) blood pressure when listening to personal trauma scripts. Again, this shows a notable parallel to patterns found in individuals with hyper-aroused, undermodulated PTSD (Lanius et al., 2010, 2012).

Clinically, DID patients are similar to dissociative PTSD patients in having earlier and more severe childhood trauma experiences (Spiegel et al., 2011; Wolf et al., 2012b), as well as in treatment response (Van der Hart et al., 2006; Brand et al., 2012). However, there is still an ongoing debate in the literature about the conceptual status of DID, either as a posttraumatic disorder, or a disorder related to suggestibility and iatrogenesis (Dalenberg et al., 2012; Boysen and VanBergen, 2013). The current findings do not support the latter view and provides a first step in researching the shared neural substrate between DID and PTSD and can thus guide future studies by providing the a priori hypothesized regions as included in the neurobiological model for DID.
Our second finding concerns differing neurobiological markers between previously reported neural networks in PTSD and the current findings in DID. DID is the most symptomatically complex dissociative disorder (American Psychiatric Association, 2013). Accordingly, it is not surprising that the neurobiology of DID involves additional patterns of brain activation when compared to those of non-DID individuals with hyper-aroused or hypo-aroused symptoms. For example, the DID NIS showed neural network patterns consistent with clinical and non-clinical models of Dissociative Amnesia (DA) (Simeon et al., 2000; Sar et al., 2007). When comparing the brain response of the DID patients’ NIS to the patients’ TIS in response to personal trauma scripts, they activated bilateral parahippocampal gyri (Schlumpf et al., 2013) and the posterior multimodal association areas, e.g. bilateral intraparietal sulcus, occipital cortex and the bilateral (pre-)cuneus. The posterior association areas are thought to mediate the process of subjective disengagement from the emotional content of trauma-related information and/or inhibition of recognition of the self-relevance of this information (Reinders et al., 2003, 2012). Anderson et al. (Anderson et al., 2004) suggested that these networks are involved in top-down suppression of unwanted autobiographical memories, and propose these as a neurobiological model for DA, a criterion symptom for diagnosis of DID (American Psychiatric Association, 2013).

In addition, in this and related studies (Reinders et al., 2006, 2012), in response to personal trauma scripts, the DID TIS have consistently shown activation in the dorsal striatum, particularly the caudate nucleus. The dorsal striatum has been found to correlate negatively with trait dissociation during stress induced analgesia (Mickleborough et al., 2011), and to be involved in task switching and inhibition of irrelevant information (Yehene et al., 2005, 2008). We can speculate that the dorsal striatum is involved in dissociation (Mickleborough et al., 2011), particularly in switching between identity states (Tsai et al., 1999), as well as in maintaining state stability of a dissociative identity state (Reinders et al., 2006, 2012; Schlumpf et al., 2013). In a single subject functional MRI study, Savoy et al. (Savoy et al., 2012) reported the involvement of the ventral striatum (i.e. the accumbens area) during identity state switching. In addition, the dorsal striatum is involved in memory systems (Quirarte et al., 2009; Sánchez-Resendis et al., 2012). Stress impaired functioning of the hippocampal system coincides with higher activation of the dorsal striatum (Schwabe et al., 2008), leading to the hypothesizes that, in DID, a similar shift from hippocampal to striatal memory functioning takes place under certain stress-related conditions. Or, taking both the switching and memory hypotheses together, in DID the dorsal striatum may be involved in the regulation of memory access by modulating the presence of neutral or trauma-related identity states. However, further research is needed to replicate the current findings and to investigate this hypothesis about identity state switching and memory.

A limitation of the current study is that neither clinical nor psychometric assessment of PTSD was obtained on DID subjects. However, it is likely that the DID subjects met diagnostic
criteria for co-morbid PTSD, as do the large majority of DID patients, and given the TIS responses to personal trauma scripts, that included intense subjective distress and flashback like experiences (Reinders et al., 2003, 2006, 2012). One might argue that the current brief practice of DID simulation is insufficient to simulate the psychobiological profiles of NIS and TIS. Even if years of practice could generate these profiles, our findings are in line with our a priori hypotheses that similar, but extended, networks are involved in emotion regulation in DID and dissociative PTSD. This result has not been predicted by holders of the sociocognitive and fantasy based view. Other limitations are that the DID data only involves females, has been published previously, and that the neurobiological model for hypo-aroused/dissociative and hyper-aroused PTSD is based on literature rather than on the inclusion of PTSD subjects (Hopper et al., 2007; Felmingham et al., 2008; Lanius et al., 2010). However, we strongly believe that the current study provides important information on the similarities between DID and the putative PTSD subtypes, especially as empirical research into dissociative PTSD and DID in an early phase.

Although our results support and extend the model that DID is a severe, childhood onset posttraumatic disorder, some have conceptualized PTSD as fundamentally a dissociative process (Nijenhuis and Den Boer, 2009; Hart et al., 2006). Hence, the neurobiological similarity between DID identity states within a single human being, and the PTSD subtypes may be explained in both directions, and raises the question whether dissociative PTSD is a specific form of PTSD or, whether all forms of PTSD are fundamentally dissociative, as postulated by Nijenhuis and others (e.g., Nijenhuis and Den Boer, 2009; Hart et al., 2006). Indeed, DID may occur without co-morbid PTSD, and PTSD may occur without dissociative symptoms such as depersonalization, derealization, dissociative amnesia, and subjective self-division, albeit DSM-5 defines flashbacks as “dissociative reactions” (American Psychiatric Association, 2013). Also, 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. Future research to help resolve
this question will be needed on DID, PTSD, and, in particular, the dissociative PTSD subtype. DSM-5 has been developed to be an evolving structure that can be more rapidly amended than prior editions of the DSM. Thus, the current study opens avenues to further study of the conceptual status and nosological classification of both DID and PTSD.

In conclusion, the current study shows similarities in neurobiological network patterns between patients with DID functioning as a NIS alternate identity, and PTSD patients with the dissociative or hypo-aroused subtype of PTSD. On the basis of the current results we propose an extended neurobiological model for emotion modulation in DID. For the hypo-aroused NIS we suggest the posterior association areas and parahippocampal gyri play a pivotal role in the suppression of unwanted (trauma-related) autobiographical memories. For the hyper-aroused TIS we propose the dorsal striatum to be crucial in the regulation of memory access by modulating the presence of different identity states. Finally, our study supports the notion that DID is closely related to posttraumatic stress disorder and not a disorder related to suggestibility.
Acknowledgements

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Table and figure legends

Table legend 1
Overview of brain areas in which statistically significant cerebral blood flow changes were found in the between or within identity state comparisons. T values and cluster sizes are given accompanied with the (x, y, z) coordinates in MNI space for the peak activation. The top section of the table presents the between identity state effects. These effects entail the comparison of the trauma-related state (TIS) to the neutral identity state (NIS) when processing of the trauma-related text (t) (DID(TIS_t vs. NIS_t) – CTRL(TIS_t vs. NIS_t)) and when processing the neutral text (n) (DID(TIS_n vs. NIS_n) – CTRL(TIS_n vs. NIS_n)), between DID patients and normal DID simulating controls. The bottom section of the table presents the within identity state effects. These effects concern the comparison of the differential processing of the neutral (n) and trauma-related (t) text within the trauma-related identity state (TIS) (DID(TIS_t vs. TIS_n) – CTRL(TIS_t vs. TIS_n)) or within the neutral identity state (NIS) (DID(NIS_t vs. NIS_n) – CTRL(NIS_t vs. NIS_n)), between DID patients and normal DID simulating controls.

Table legend 2
Results of the statistical analysis concerning subjective sensorimotor and emotional experiences, and of the cardiovascular responses. Results of the between and within identity state comparisons are presented. F and p values are given as well as the mean and standard deviations from both groups. Significant results are given in a bold font. The two columns with the heading “between identity state” present the statistical results of the comparison of the trauma-related state (TIS) to the neutral identity state (NIS) when processing of the trauma-related text (t) (first column: DID(TIS_t – NIS_t) > CTRL(TIS_t – NIS_t)) and when processing the neutral text (n) (second column: DID(TIS_n – NIS_n) > CTRL(TIS_n – NIS_n)), between DID patients and normal DID simulating controls. The two columns with the heading “within identity state” present the statistical results of the comparisons concerning the differential processing of the neutral (n) and trauma-related (t) text within the trauma-related identity state (TIS) (first column: DID(TIS_t vs. TIS_n) > CTRL(TIS_t – TIS_n)) or within the neutral identity state (NIS) (second column: DID(NIS_t vs. NIS_n) > CTRL(NIS_t vs. NIS_n)), between DID patients and normal DID simulating controls.

Figure legend
The artwork centralized in this figure is entitled “The Mask” and can be seen as depicting the neutral identity state (NIS) in the top part and the trauma-related identity state (TIS) in the bottom part, where the NIS “masks” the TIS and thereby the traumatic experiences (interpretation by:
AATSR). It is surrounded by the within and between identity state comparisons between the dissociative identity disorder (DID) patients and normal DID simulating controls. The within identity state comparisons at the top (NIS) and the bottom (TIS) are in alignment with the representations within the artwork. The bar-graphs show the directionality of effect and represent the average effect of the cluster. The first two bars represent the DID patients and the other two bars represent the healthy DID simulating controls. The red bars represent a more neutral condition, whereas the black bars represent a trauma-related condition (identity state or text). The picture of the brain in the top right of the figure shows the activation in the bilateral superior frontal gyrus and the activation in the left medial frontal gyrus. The latter activation is indicated with a blue arrow and coincides with the bar-graphs on the top left side. The bottom part of the figure shows the activation in the left insula and the magnitude of effects in the accompanying bar-graphs. The two graphical displays on the left show the activation in the left cingulate gyrus and the magnitude of effects in the bar-graphs. The activation, both location and magnitude, in the dorsal part of the left caudate nucleus is depicted in the middle right part of the figure.

**Figure subscript**

NISt = neutral identity state exposed to the trauma-related memory script

NISn = neutral identity state exposed to the neutral memory script

TIS = trauma-related identity state exposed to the trauma-related memory script

TISn = trauma-related identity state exposed to the neutral memory script

R = Right hemisphere

L = Left hemisphere

DID = dissociative identity disorder patients

CTRL = normal DID simulating healthy controls
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subtype. Archives of General Psychiatry 69, 698–705.
Within identity state

Neutral identity state: differential processing of the neutral and trauma-related text

DID(NISn – NISn) – CTRL(NISn – NISn)

<table>
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<th>R/L</th>
<th>Brain region</th>
<th>Brodmann area</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>kE</th>
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DID(NISn – NISn) – CTRL(NISn – NISn)

n.s.

Trauma-related identity state: differential processing of the neutral and trauma-related text

DID(TISn – TISn) – CTRL(TISn – TISn)

<table>
<thead>
<tr>
<th>R/L</th>
<th>Brain region</th>
<th>Brodmann area</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>kE</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>Insula</td>
<td>BA 13</td>
<td>-38</td>
<td>-14</td>
<td>11</td>
<td>4.25</td>
<td>4.25</td>
</tr>
<tr>
<td>L</td>
<td>Amygdala</td>
<td></td>
<td>-10</td>
<td>-4</td>
<td>126</td>
<td>3.87</td>
<td>3.87</td>
</tr>
</tbody>
</table>

DID(TISn – TISn) – CTRL(TISn – TISn)

n.s.

Between identity states

Processing of the trauma-related text

DID(TISn – TISn) – CTRL(TISn – TISn)

<table>
<thead>
<tr>
<th>R/L</th>
<th>Brain region</th>
<th>Brodmann area</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>kE</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>IPS (transition SPL/IPL)</td>
<td>BA 7/40</td>
<td>30</td>
<td>-38</td>
<td>49</td>
<td>298</td>
<td>4.30</td>
</tr>
<tr>
<td>L</td>
<td>IPS (transition SPL/IPL)</td>
<td>BA 7/40</td>
<td>-34</td>
<td>-50</td>
<td>49</td>
<td>3.96</td>
<td>3.96</td>
</tr>
<tr>
<td>R</td>
<td>Cingulate sulcus/S.Frontal sulcus</td>
<td>BA 4/6/24</td>
<td>16</td>
<td>-12</td>
<td>44</td>
<td>272</td>
<td>4.24</td>
</tr>
<tr>
<td>R</td>
<td>Cingulate gyrus</td>
<td>BA 32</td>
<td>6</td>
<td>16</td>
<td>100</td>
<td>3.95</td>
<td>3.95</td>
</tr>
<tr>
<td>R</td>
<td>Parahippocampal gyrus</td>
<td>BA 36</td>
<td>20</td>
<td>-52</td>
<td>79</td>
<td>3.87</td>
<td>3.87</td>
</tr>
<tr>
<td>L</td>
<td>Parahippocampal gyrus</td>
<td>BA 35</td>
<td>-40</td>
<td>-46</td>
<td>77</td>
<td>4.12</td>
<td>4.12</td>
</tr>
<tr>
<td>L</td>
<td>Parahippocampal gyrus</td>
<td>BA 35</td>
<td>-24</td>
<td>-26</td>
<td>11</td>
<td>3.52</td>
<td>3.52</td>
</tr>
<tr>
<td>R</td>
<td>M. Temporal gyrus</td>
<td>BA 21</td>
<td>62</td>
<td>-14</td>
<td>25</td>
<td>3.75</td>
<td>3.75</td>
</tr>
<tr>
<td>R</td>
<td>Occipitotemporal sulcus</td>
<td>BA 20/37</td>
<td>48</td>
<td>-6</td>
<td>124</td>
<td>4.63</td>
<td>4.63</td>
</tr>
<tr>
<td>R</td>
<td>Fusiform gyrus</td>
<td>BA 19/37</td>
<td>38</td>
<td>-62</td>
<td>32</td>
<td>3.60</td>
<td>3.60</td>
</tr>
<tr>
<td>L</td>
<td>Lingual gyrus</td>
<td>BA 18</td>
<td>-8</td>
<td>-90</td>
<td>96</td>
<td>3.51</td>
<td>3.51</td>
</tr>
<tr>
<td>R</td>
<td>S. Parietal lobule/Precuneus/Angular gyrus</td>
<td>BA 7/39</td>
<td>24</td>
<td>-64</td>
<td>564</td>
<td>4.53</td>
<td>4.53</td>
</tr>
<tr>
<td>L</td>
<td>(Pre-) Cuneus</td>
<td>BA 7/31/18/19</td>
<td>-10</td>
<td>-64</td>
<td>38</td>
<td>4.48</td>
<td>4.48</td>
</tr>
<tr>
<td>R</td>
<td>S. Occipital sulcus/Cuneus</td>
<td>BA 18/19</td>
<td>18</td>
<td>-90</td>
<td>411</td>
<td>4.45</td>
<td>4.45</td>
</tr>
<tr>
<td>L</td>
<td>S. Occipital gyrus/Angular gyrus</td>
<td>BA 19/39</td>
<td>-38</td>
<td>-82</td>
<td>176</td>
<td>4.33</td>
<td>4.33</td>
</tr>
</tbody>
</table>

DID(TISn – TISn) – CTRL(TISn – TISn)

n.s.

Processing of the neutral text

DID(TISn – TISn) – CTRL(TISn – NISn)

n.s.

DID(NISn – TISn) – CTRL(NISn – TISn)

n.s.

DID = dissociative identity disorder patients
CTRL = normal DID simulating healthy controls
TIS = trauma-related identity state exposed to the trauma-related memory script
NIS = neutral identity state exposed to the trauma-related memory script
TISn = trauma-related identity state exposed to the neutral memory script
NISn = neutral identity state exposed to the neutral memory script

L/R = Left/Right
*p < 0.05, corrected for multiple comparisons
region of interest, corrected for multiple comparisons using small volume correction (SVC)
IPS = intraparietal sulcus
SPL = superior parietal lobule
IPL = inferior parietal lobule
S. = superior

Page 1
**Table 2**

<table>
<thead>
<tr>
<th>Subjective ratings</th>
<th>Between identity state</th>
<th>Within identity state</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>sensory rating</strong></td>
<td>CTRL(M = 0.79, SD = 0.64)</td>
<td>DID(M = 4.10, SD = 2.38)</td>
</tr>
<tr>
<td></td>
<td>F(1,26) = 28.55, P &lt; 0.001 **</td>
<td>F(1,26) = 51.78, P &lt; 0.001 **</td>
</tr>
<tr>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>emotional rating</strong></td>
<td>CTRL(M = 0.50, SD = 0.64)</td>
<td>DID(M = 0.30, SD = 0.64)</td>
</tr>
<tr>
<td></td>
<td>F(1,26) = 24.79, P &lt; 0.001 **</td>
<td>F(1,26) = 51.78, P &lt; 0.001 **</td>
</tr>
<tr>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Autonomic reactions</strong></td>
<td>CTRL(M = 0.22, SD = 0.44)</td>
<td>DID(M = 4.39, SD = 2.04)</td>
</tr>
<tr>
<td></td>
<td>F(1,26) = 18.67, P &lt; 0.001 **</td>
<td>F(1,26) = 36.85, P &lt; 0.001 **</td>
</tr>
<tr>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>CTRL(M = 0.50, SD = 1.24)</td>
<td>DID(M = 0.60, SD = 1.24)</td>
</tr>
<tr>
<td></td>
<td>F(1,26) = 11.97, P = 0.002 **</td>
<td>F(1,26) = 14.34, P = 0.001 **</td>
</tr>
<tr>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>CTRL(M = -0.7, SD = 0.24)</td>
<td>DID(M = 1.32, SD = 1.74)</td>
</tr>
<tr>
<td></td>
<td>F(1,26) = 14.87, P = 0.001 **</td>
<td>F(1,26) = 11.97, P = 0.002 **</td>
</tr>
<tr>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

**Note:**
- CTRL = normal DID simulating healthy controls
- DID = dissociative identity disorder patients
- TISt = trauma-related identity state exposed to the trauma-related memory script
- NISt = trauma-related identity state exposed to the neutral memory script
- TISn = trauma-related identity state exposed to the trauma-related memory script
- NISn = trauma-related identity state exposed to the neutral memory script
- CTRL = normal DID simulating healthy controls
- DISt = dissociative identity disorder patients
- ** = corrected for multiple comparisons
- ** = corrected for multiple comparisons
- M = mean
- SD = standard deviation
- n.s. = not significant

**Legend:**
- Between identity state: differential processing of the neutral and trauma-related text
- Within identity state: differential processing of the neutral and trauma-related text
- **Processing of the trauma-related text**
- *Processing of the neutral text*
Trauma identity state (TIS)

NISt – NISn: L Medial Frontal Gyrus

Neutral identity state (NIS)

TISt – NISn: L Medial Frontal Gyrus

Trauma identity state (TIS)

TISt – TISn: L Caudate

TISt – TISn: L Insula