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One brain, two selves

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Abstract

Having a sense of self is an explicit and high level-functional specialization of the human brain. The anatomical localization of self-awareness and the brain mechanisms involved in consciousness were investigated by functional neuroimaging different emotional mental states of core consciousness in patients with multiple personality disorder, i.e. dissociative identity disorder (DID). We demonstrate specific changes in localized brain activity consistent with their ability to generate at least two distinct mental states of self-awareness, each with its own access to autobiographical trauma-related memory. Our findings reveal the existence of different regional cerebral blood flow patterns for different senses of self. We present evidence for the medial prefrontal cortex (MPFC) and the posterior associative cortices to have an integral role in conscious experience.

Introduction

The study of the cortical functional anatomy of human consciousness and sense of self-awareness is a point of intense research and debate. Functional brain imaging enables the functional localization of brain systems that are concerned with the mental states of the self. In general, normal subjects are tested when performing some kind of self-awareness task, e.g. self- versus non-self-referential information processing (Fink et al., 1996; Craik et al., 1999; Kelley et al., 2002; Kjaer et al., 2002). Here we approach the 'sense of self' in a brain with abnormalities in the perception of the self. Studying subjects with such a disturbed sense of self can provide valuable information about the brain areas and networks involved in a normal experience of the self (Frith et al., 1998; Blanke et al., 2002).

Dissociative identity disorder (DID) (American Psychiatric Association, 1994), formerly known as multiple personality disorder, challenges our basic notion of one continuous sense of self (Putnam, 1994; Damasio, 2000; Nijenhuis et al., 2002), as these patients recurrently switch from one personality state, i.e. sense of self, to another. Behavioral characteristics, sensations, perceptions, memories (Dorahy, 2001), bodily functions, and autobiographical sense of self (Damasio, 2000; Parvizi and Damasio, 2001) seem to depend on these personality states. DID usually develops in a context of severe childhood trauma and encompasses different types of dissociative personality states (Putnam, 1994, 1997), typically including 'traumatic' and 'neutral' personality states (TPS and NPS, respectively). Clinical data suggest that the TPS has access to autobiographical memories of traumatic experiences and reveals profound emotional response patterns to them (self-referential processing). Remaining in an NPS, DID patients claim a degree of amnesia for trauma memories, and/or respond as if these memories do not

pertain to them (non-self-referential processing). The majority view (Putnam, 1994; Damasio, 2000; Nijenhuis et al., 2002) is that DID patients have two or more distinct identities or personality states that recurrently take control of behavior and consciousness (Putnam, 1994; Damasio, 2000) and whose access to trauma-related autobiographical memory apparently depends on the personality state (Dorahy, 2001). These fluctuating states of consciousness and self-awareness within one human brain challenges the study of the self in the context of personality-state-dependent information processing. According to the minority view the existence of dissociative personality states is not proven.

Here, the functional anatomic representation of autobiographical self-awareness is uniquely investigated in patients with DID. We explored the possibility of one human brain to initiate (at least) two dissociative autobiographical selves, i.e. two dissociative personality states each with its own sense of self, using positron emission tomography (PET) and a script-driven imagery symptom provocation paradigm (Rauch et al., 1996). Our experimental procedure allows the comparison of four different conditions: exposure to a neutral and trauma memory script while remaining in a NPS or a TPS (see subjects and methods). If different cerebral activation patterns can indeed be distinguished, our results would not only be of importance for the conceptualization of DID, but would enrich our knowledge about the self in terms of autobiographical self-awareness and its functional neuroanatomical representation within the human brain as well.

Subjects and methods

Subjects

Eleven female subjects (age range 27-48 years), meeting the APA (American Psychiatric Association, 1994) (i.e. DSM-IV) and the SCID-D (Steinberg, 1993) criteria for dissociative identity disorder, participated in the investigation. All gave written informed consent according to procedures approved by the medical ethical committee of the Groningen university hospital. As a result of treatment the subjects had developed the ability to perform self-initiated and self-controlled switches between one of their neutral and one of their traumatic personality state (also described as the 'apparently normal parts of the personality' and 'emotional parts of the personality' (Nijenhuis et al., 2002)). The tested traumatic personality state (TPS) stored at least one traumatic memory and reported being emotionally affected by reactivation of this memory while the neutral personality state (NPS) reported to be emotionally unresponsive to the selected trauma memory and regarded itself as not having been exposed to the relevant traumatizing event.

During the PET investigation, three patients were not free of medication which could influence the regional cerebral blood flow (rCBF). One patient used flu-

oxetine, one patient used paroxetine, and one patient used a combination of levopromazine, promethazine and flurazepam. In addition, in a small number of scans interference among personality states had been reported. Using the general linear model (GLM) (Friston et al., 1995b) as included in the statistical parametric mapping (SPM99) package (www.fil.ion.ucl.ac.uk/spm/), these interference and medication effects were tested. Extended models (see data analysis for the definitive model) were designed to test the interference and medication effects. Interference effects were set up as a covariate of interest and tested with an F test. Medication effects were tested on an individual level (excluding one subject from the group) and on a group level (medication versus no medication), with t tests. No significant rCBF effects were found when testing the interference effects, nor when testing effects of medication independently (data not shown). One patient's PET data were excluded from the analyses due to apparent neurological malformations. Due to head movements between scans, e.g. induced by a personality state switch, parts of the brain moved outside the field of view of the PET scanner. To maximize available brain volume for statistical testing, 11 scans with major non scanned brain parts were discarded after visual inspection by two independent observers. Three scans with observed head movement during the PET data collection and one scan suffering a procedural error were also excluded from the data analyses. A total of 15 scans needed to be excluded, leaving 65 scans to be statistically analyzed.

Scripts

Subjects listened to two autobiographical audio taped memory scripts involving a neutral and a trauma-related experience. The neutral memory script was regarded as a personal experience by both personality states. However, only the TPS experienced the trauma-related script as personally relevant. The duration of the scripts was 120 seconds. The patient offered the memories and the therapist cast them in terms of stimulus descriptions. To avoid effects of suggestion, i.e. to prevent the evocation of direct mood changes, memories were described in the third person singular and response descriptions were excluded. After approval of the scripts by one of the principal investigators, the therapist audio taped the scripts in a neutral tone of voice for playback during the PET investigation.

PET-symptom provocation

The complete scanning sequence was NPSn, NPSt, TPSn, TPSt, TPSn, TPSt, NPSn, and NPSt (four conditions, obtained twice). The minor character (n or t) indicates the content of the script (neutral or trauma related). Four scans involved NPS and four corresponded with the TPS. The two personality state switches were self-induced and supported by the patient's therapist. Synchronous with the bolus injection the audiotape was started while the heart rate variability (HRV)

measurement was marked (for HRV methods and analysis: see HRV guidelines (Malik, 1996)). Immediately following the end of the script blood pressure (systolic and diastolic) and discrete heart rate frequency were monitored, measuring the arousal of the autonomic nervous system in terms of cardiovascular state (objective measurements). Simultaneously, the therapist debriefed the emotional and sensorimotor subjective experiences of the subject regarding her subjective reactions to the scripts by use of a questionnaire using a ten point scale running from completely absent (0) to extremely intense (10). The six emotions pertained to fear, sorrow, sadness, anger, shame, and disgust, and the ten sensorimotor modalities visual, kinesthetic, auditory, olfactory, and gustatory reactions, as well as pain and physical numbness, body stiffening, paralysis and restlessness.

Image acquisition and data processing

Data acquisition, reconstruction, attenuation correction, spatial transformation, and spatial smoothing (Gaussian kernel of 12 mm) were performed as usual (Reinders et al., 2002, see chapter 4). In brief, all 120 seconds scans were obtained, after a bolus injection of 500 MBq of $H_2\,^{15}O$ for each scan, in 3D acquisition mode using a Siemens ecat exact HR+ PET scanner. The emission scans were reconstructed using standard filtered back reconstruction. Calculated attenuation correction was used as attenuation correction method (Reinders et al., 2002, see chapter 4). PET data were translated to Analyze data format. SPM99 was used for spatial transformation (Friston et al., 1995a; Talairach and Tournoux, 1988) and statistical analysis (Friston et al., 1995b) of the data. The origins were manually set at the anterior commissure, followed by realigning the PET time series to the mean. Hereafter, all the scans were spatially normalized to the MNI template (using heavy regularization). Data were smoothed with an isotropic Gaussian kernel of 12 mm FWHM (full width at half maximum).

Data analysis

To exclude contamination of the rCBF condition effects by self-suggestion or by the arousal of the cardiovascular system, two sets of covariates of interest were included in the PET-data analyses. To retain optimal statistical power of statistical parametric mapping (SPM), the 25 measurements (nine cardiovascular and 16 subjective ratings) were condensed to five (three versus two) covariates, using a principal component analysis (after missing value analysis; both performed in SPSS-PC 8.0, 1997), which were tested using two simple F contrasts. The resulting two F maps did not reveal any areas where a significant amount of variance could be explained by subjective ratings, i.e. measure of suggestibility effects, or cardiovascular measurements. The significance of task-related region-specific differences in rCBF was assessed using multiple univariate regression analyses

(Friston et al., 1995b). Condition-specific effects can be assessed by setting specific contrasts on the parameter estimates, testing against a null hypothesis, which states that there is no difference between conditions tested.

Our theory suggested statistically significant rCBF changes in this exploratory self-awareness study. However, no *a priori* areas were defined. Therefore, voxels surviving a $p < 0.001$ threshold (uncorrected for multiple comparisons (Friston et al., 1991)) were subjected to a cluster analysis. Consequently, the clusters reaching a statistical threshold of $p < 0.05$ (corrected for multiple comparisons) were included in the discussion, i.e. 'cluster level' (Friston et al., 1994)). In addition the presence of significant voxels, i.e. 'voxel-level' (corrected for multiple comparisons based on false discovery rate statistics as included in the SPM99 package (www.sph.umich.edu/~nichols/FDR/)), within these clusters was established. Significant effects are reported in table 5.1, in which the coordinates were converted from MNI space to Talairach space (www.mrc-cbu.cam.ac.uk/Imaging/) and their location is anatomically described (Mai et al., 1997) and also defined in Brodmann areas (BA) (Talairach and Tournoux, 1988).

Results

As these patients have different access to autobiographical affective memories we compared the rCBF patterns of the NPS to the rCBF patterns of the TPS, while they were listening to the trauma-related script, to find the neural correlates for their different autobiographical selves. NPS was hypothesized to process this script as non-self-referential, while TPS was considered to be aware of the self-referential nature of the information. Comparing this self-referential versus non-self-referential processing of the (identical) trauma-related script (subtraction NPSt - TPSt, for abbreviations see subjects and methods) showed a difference in activation pattern between the two selves.

The overall pattern of rCBF changes displayed a decrease in perfusion when TPS listened to the trauma-related script as compared to NPS (a typical example is depicted in figure 5.1.A). The areas involved are listed in table 5.1. Exploring the frontal brain region, a right sided unilateral finding was localized in the medial part of the superior prefrontal cortex, i.e. the MPFC (Brodmann area (BA) 10, figure 5.1.B) and rCBF changes in the ventral-medial part of the middle frontal gyrus (BA 6, parts C1 and C2 of figure 5.1) were found bilaterally. In the posterior association cortices we found our highest significant bilateral deactivation, which was located in the intra-parietal sulcus, i.e. the parietal integration areas (BA 7/40, see figure 5.1.D1 and 1.D2), in the transition from the superior to the inferior parietal lobe. Additionally, a decrease in perfusion in the visual association areas was found bilaterally in the parietal-occipital sulcus, in the transition of BA 18 to

Table 5.1: Group response to the autobiographical trauma-related script in neutral personality state (NPS) as compared to traumatic personality state (TPS).

Condition	brain area		L/R	cluster-level		voxel-level			
				p_{corr}	kE	$t_{[37]}$	x	y	z
NPSt - TPSt	Superior Frontal gyrus[c]	BA 10	R	0.016	388	4.53[a]	12	63	8
	Middle Frontal gyrus[d]	BA 6	R	0.008	459	4.52[a]	30	-11	47
	Middle Frontal gyrus[d]	BA 6	L	0.048	289	4.85[a]	-30	-4	46
	IPS (transition SPL/IPL)[d]	BA 7/40	R	0.032	323	5.20[a]	28	-37	42
	IPS (transition SPL/IPL)[d]	BA 7/40	L	0.010	432	5.19[a]	-24	-45	37
	Parietal-occipital sulcus[f]	BA 18/Pcu[e]	R	0.008	456	5.02[a]	26	-62	33
	Parietal-occipital sulcus	BA 18/Pcu[e]	L	0.001	690	4.95[a]	-8	-76	24
	Middle Occipital gyrus[g]	BA 19	L	0.047	290	5.14[a]	-44	-74	30
TPSt - NPSt	Parietal Operculum		L	0.000	789	5.94[a]	-48	-19	16
	Insula gyrus		L			4.56[b]	-26	-9	19

(a) = $p < 0.05$, corrected for multiple comparisons ; (b) = $p = 0.057$, corrected for multiple comparisons ; (c) = medial part of the gyrus (= medial pre-frontal cortex (MPFC)) ; (d) = ventral- medial part of the gyrus ; (e) = transition BA 18/precuneus ; (f) = lateral part of the sulcus ; (g) = superior part of the gyrus ; L/R = left or right hemisphere ; (x,y,z) = Talairach coordinates in mm ; kE = cluster size in voxels ; BA = Brodmann area ; IPS = intra - parietal sulcus ; SPL = superior parietal lobule ; IPL = inferior parietal lobule ; PCu = precuneus ; MPFC = medial prefrontal cortex ;
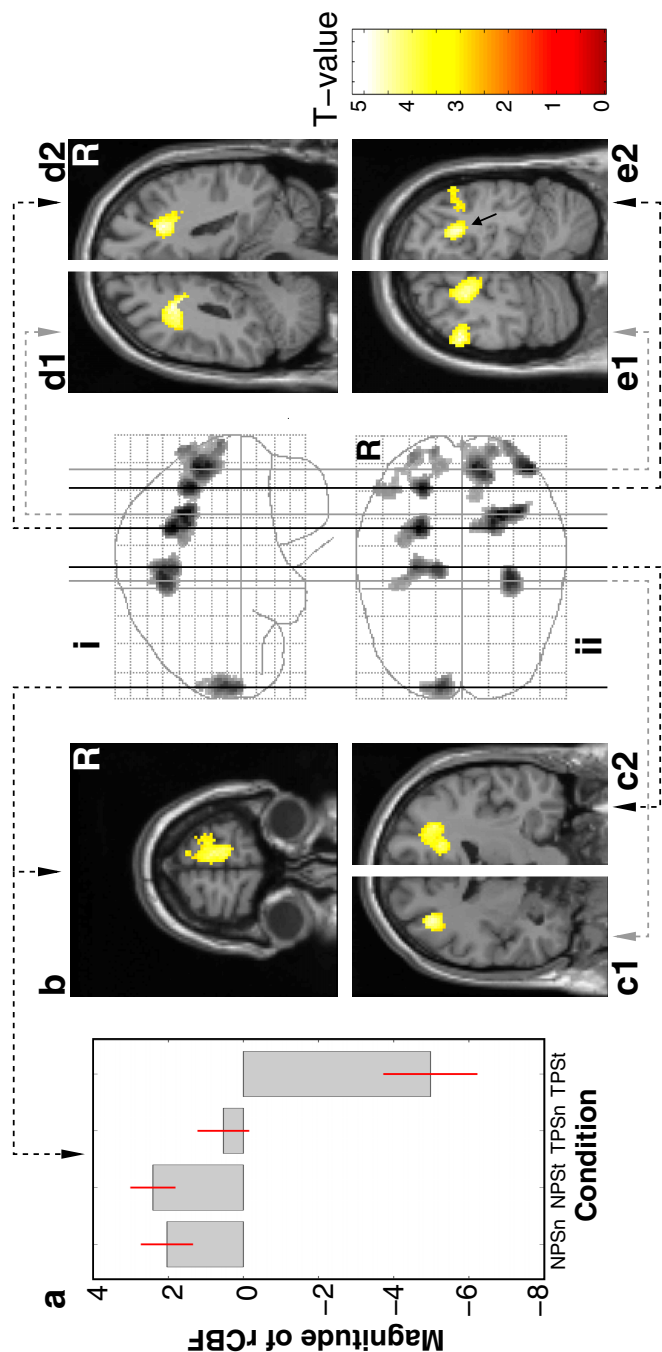
Figure 5.1: Caption on next page

Figure 5.1: Brain regions showing a significant response on the autobiographical trauma-related script in neutral personality state (NPS) as compared to traumatic personality state (TPS). (A) Mean regional cerebral blood flow (rCBF) changes at the voxel of maximum activation (x = 12, y = 63, z = 8) in the right medial prefrontal cortex (MPFC, Brodmann area (BA) 10) for the four conditions of our study, that is exposure to a neutral (minor character n) and trauma (minor character t) memory script while remaining in NPS or TPS. Bars represent standard errors. The response shown is typical for the areas depicted in parts B through E. (B, C, D, E) Coronal slices of the brain regions involved in the functional neural network of autobiographical self-awareness representation. Slices are shown at the level of the most significant activation: part B (Right BA 10; x = 12, y = 63, z = 8), C1 (Left BA 6; x = -30, y = -4, z = 46), C2 (Right BA6; x = 30, y = -11, z = 47), D1 (Left BA 7/40; x = -24, y = -45, z = 37), D2 (Right BA 7/40; x = 28, y = -37, z = 42), E1 (Left BA18/precuneus; x = -8, y = -76, z = 24 and BA19; x = -44, y = -76, z = 30) and E2 (Right BA18/precuneus; x = 26, y = -62, z = 33 (as indicated with the small black arrow)). See also table 1. (I and II) Parts I (sagittal view) and II (transaxial view) show the statistical parametric maps (the glass-brains) of significant areas. Black and gray lines represent the various brain levels, where the activations depicted in parts B through E of the figure have their peak significance value. Black lines are used for clusters located in the right hemisphere, while gray lines are used for clusters in the left hemisphere. The letter R indicates the right side of the brain.

the precuneus (see figure 5.1.E1 and 5.1.E2). These two bilateral rCBF changes were accompanied by a single left-sided middle occipital gyrus deactivation in BA 19 (see also figure 5.1.E1).

The area with the most significant increase (when testing the contrast TPSt - NPSt) of activation is the parietal operculum (PO). This cluster includes the insular gyrus (IG). Both PO and IG are related to the high emotional mental state in which TPS remains.

As a unique characteristic of DID, NPS should process the trauma-related memory script in a similar (presumably non emotional) way as the neutral memory script. This was tested by comparing NPSn with NPSt. No significant changes in rCBF were found, as expected. Finally, we tested whether NPS and TPS process the neutral memory script in a similar autobiographical (non emotional) way by comparing TPSn with NPSn. Consistent with our hypothesis, no significant voxels or clusters could be found.

Discussion

Damasio and co-workers (Damasio, 2000; Parvizi and Damasio, 2001) distinguish between a core self and an autobiographical self. The generation of the core self is based upon the continuing cerebral representation of one's momentary body state. This self has a highly constrained organization and emerges from core

consciousness, which is a simple biological phenomenon. The core self lacks a sense of the past, i.e. memory, and imagined future, features required for a sense of autobiographical self. The autobiographical self, which is connected to autobiographical memories, is more vulnerable to environmental influences. According to Damasio, DID patients must draw from the same biological resources, and thus have one core self. However, because autobiographical memories are subject to distorting environmental influences, they can have different autobiographical selves. Our findings are consistent with the theory of Damasio and co-workers (Damasio, 2000; Parvizi and Damasio, 2001), that DID patients have different autobiographical selves.

When comparing the self-referential versus non-self-referential processing of the trauma-related script (subtraction NPSt - TPSt), we found a network of deactivated brain areas including the right MPFC, the bilateral middle frontal gyrus (BA 6), the visual association (BA 18/19), and the bilateral parietal integration (BA7/40) areas (see figure 5.1). Interestingly, this deactivation pattern is consistent with earlier functional imaging reports in normal subjects (Fink et al., 1996; Craik et al., 1999) exploring autobiographical versus non autobiographical, i.e. self versus non-self, episodic memory retrieval. This confirms the non-autobiographical manner in which NPS processes the trauma-related script, supporting the concept of a different sense of autobiographical self for NPS and TPS within one brain.

The areas found in the posterior association cortices (see also results, figure 5.1.D, figure 5.1.E and table 5.1) are involved in the integration of visual information and somatosensory information reflecting the visualization and physical discomfort when reliving the trauma. Changed perfusion in BA 7/40 was previously found to be related to differences in sense of self in patients with depersonalization disorder (Simeon et al., 2000). In addition, the posterior regions (BA 7/40 and the precuneus) have been suggested to supply information for conscious processing (Mazoyer et al., 2001; Kjaer et al., 2002). The rCBF changes in the visual association areas (BA 18 and precuneus) and middle occipital gyrus (BA 19) reflect an inability of NPS to integrate visual and somatosensory information. This 'blocking' of trauma related information prevents further emotional processing, which reflects the defense system, as applied by DID patients, to enable them to function in daily life (Nijenhuis et al., 2002). Thus, the NPS, as compared to TPS, shows disturbances of parietal and occipital blood flow, suggesting a relatively low level of somatosensory awareness and integration (Simeon et al., 2000), by suppression of the (re-)activation of these areas. These results match the clinical depersonalized features of NPS (Nijenhuis et al., 2002) as well as their subjective responses in the current experiment.

The MPFC is known to be involved in conscious experiences, self-referential mental activity (Gusnard et al., 2001) and is involved in the explicit representation of states of the selves (Frith and Frith, 1999). Especially, the right medial prefrontal

cortex is indicated to play a crucial rule in the representation of the self-concept (Craik et al., 1999; Kelley et al., 2002). Our results confirm this self-related functional specialization of the right prefrontal cortex when comparing brain activity in the NPSt and TPSt conditions. Our unilateral finding in the right prefrontal cortex (see table 5.1; BA10: medial superior prefrontal cortex; and figure 5.1.B) reflects differences in autobiographical self-referential information processing (Wheeler et al., 1997; Craik et al., 1999) particularly during TPS (figure 5.1.A). Additional responses in the frontal cortex were found bilaterally, as deactivation of the ventral-medial part of the middle frontal gyrus (BA 6, see figure 5.1.C1 and 5.1.C2 and table 5.1) (Fink et al., 1996; Craik et al., 1999).

With the contrast TPSt - NPSt we were able to explore the interaction of the personality state of mind and the emotional impact of the autobiographical memory. The area with the most significant increase of activation is the PO, including the IG, both of which play a role in regulating emotional and behavioral reaction to pain (Sawamoto et al., 2000) and other somatosensory cues of distressing nature (Reiman, 1997). Activation of these areas in TPS as compared to NPS, in reaction to the trauma related script, thus shows emotional and behavioral dissociation in DID patients. Insula activation for TPS during autobiographical memory retrieval may also be attributed to the high emotional impact of the task (Fink et al., 1996).

This conceptual analysis reveals areas which are previously reported to be involved in neural correlates of human consciousness as involved in resting state (Mazoyer et al., 2001), sleep (Maquet, 2000), general anesthesia (Fiset et al., 1999), and recovery from coma after vegetative state (Laureys et al., 1999) and therefore confirms the involvement of the posterior associative cortices (including the parietal areas), the neural correlates of conscious awareness (Gusnard and Raichle, 2001). Our data confirm the emergence of conscious (TPSt) versus unconscious (NPSt) experience in the neural network (Fiset et al., 1999; Laureys et al., 1999; Maquet, 2000; Gusnard and Raichle, 2001) of superior and inferior parietal lobule, left occipital cortex, precuneus, and frontal brain areas including BA 6 and BA 10.

The few attempts to find cerebral correlates of dissociative disorders in specific brain areas have generated a wide diversity of results (see for reviews, Nijenhuis et al. (2002) and Dorahy (2001)). None of these attempts, however, exploited the unique opportunity to directly compare responses to trauma-related stimuli in a single patient who can exhibit different, dissociative, personality states. We have shown that these patients have state-dependent access to autobiographical affective memories and thus different autobiographical selves. Although it could be argued that DID patients voluntarily trigger or simulate different (cognitive) states, this would not be consistent with literature on both the diagnosis and the treatment of these patients, including the DSM-IV (American Psychiatric Association, 1994) and the SCID-D (Steinberg, 1993). Even so, whatever the underlying mechanism, the DID patients exhibited significantly different state-dependent

rCBF patterns which closely match current literature on the sense of self and on (autobiographical) self-awareness. In this context, we conclude that DID patients are able to remain in two different (personality) states and the observed relation between different states in DID patients and self holds.

In conclusion, the functional anatomic representation of autobiographical self-awareness was uniquely explored in patients with dissociative identity disorder. Our results indicate the possibility of one human brain to generate at least two distinct states of self-awareness, each with its own access to autobiographical trauma-related memory, with explicit roles for the MPFC and the posterior associative cortices in the representation of these different states of consciousness.

Acknowledgements

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