

NEUROPSYCHOLOGICAL AND PET STUDY OF DEPERSONALIZATION AND DEREALIZATION:
A SINGLE CASE REPORT

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Abstract

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The present work depicts the case of a young man suffering from a depersonalization and derealization (DD) disorder, which mainly affects his own body. When the symptoms concern something else, they almost exclusively affect living beings. Neuropsychological and neuropsychiatric studies, as well as functional neuroanatomy studies, have led to hypothesize possible relationships among cognitive-neurofunctional alterations and symptoms of depersonalization and derealization. The present study suggests that a malfunction of the left frontal and prefrontal cortex causes deficits of working memory, producing some of the symptoms of DD.

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Introduction

Depersonalization and Derealization disorder (DD) is among the known disorders of perception both of body and extra body sensations.

DD is defined by DSM-5 as: “experiences of unreality, detachment, or being an outside observer with respect to one's thoughts, feelings, sensations, body, or actions (e.g., perceptual alterations, distorted sense of time, unreal or absent self, emotional and/or physical numbing)”; and “experiences of unreality or detachment with respect to surroundings (e.g., individuals or objects are experienced as unreal, dreamlike, foggy, lifeless, or visually distorted” (American Psychiatric Association, 2013).

The main experiential components of the disorder, according to Sierra and David (2011), are anomalous body experience, emotional numbing, anomalous subjective recall, and derealization.

Based on this definition, the diagnosis of DD is appropriate only if a series of characteristics manifest themselves. They are:

- 1) the patient must have a recurrent and abiding feeling of separation; if he usually depicts his own sensorial experience like “feeling of living in a dream”;
- 2) during the episode of depersonalization and/or derealization the patient preserves the ability to analyse reality;
- 3) the condition of depersonalization and/or derealization causes social, work and family difficulties;
- 4) depersonalization and/or derealization does not present itself with other psychiatric and/or neurological

disorders.

The prevailing view has been to conceive of DD as a psychological disturbance of self-awareness (Sierra & Berrios, 1997). Also, because DD was reported in affections of the central nervous system (CNS) and, in particular, in mild head trauma (Grigsby & Kaye, 1993) and temporal lobe epilepsy (Devinsky et al., 1991), it has been suggested that DD is due to a “biological damage” of the CNS (Sierra & Berrios, 1998).

Sierra and Berrios (1998) proposed a neurobiological model for DD in which right and left prefrontal cortex, amygdala, and anterior cingulate have been included. In this model, DD results from the combination of two mechanisms. The first one is an inhibitory mechanism mediated by the left prefrontal cortex (LPFC). LPFC would directly inhibit the amygdala and indirectly other structures, such as the anterior cingulate, causing a reduction of emotional response. The second mechanism is excitatory and is driven by uninhibited amygdala circuits, controlling both cholinergic and amino-aminergic ascending arousal systems. This lack of amygdala inhibition would lead to an activation of the right prefrontal cortex and to a consequent inhibition of the anterior cingulate.

A recent study (Büetiger et al., 2020) proposed, in a similar way, that there may be divergent pathophysiological mechanisms underlying DD. Investigating patients with DD, they found a decreased neuronal activity in the orbitofrontal cortex, but an increased activity within the caudate nucleus. These findings suggest that both top-down (orbitofrontal cortex) and bottom-up (caudate nucleus) mechanisms

could contribute to the emergence of DD.

The hypothesis of organic damage seems to have been confirmed by the presence of cognitive deficit, highlighted by neuropsychological evaluations.

Guralnik et al. (2000) found that patients suffering from DD perform poorly in attentional, short-term visual memory, verbal memory, and spatial reasoning tasks. Based on these results, they propose that DD involves alteration in the perceptual and attentional systems, which causes a malfunction of short-term memory. This alteration would be the cause of the deficits in the ability to process new information in the presence of an intact ability to conceptualize and manipulate previously encoded information.

The fact that DD patients also present memory deficits does not seem at all anomalous because a relationship may exist between consciousness and memory (Markowitsch, 1995). In addition, the cerebral cortex, particularly the prefrontal cortex, may be regarded as the main anatomical basis of consciousness (Markowitsch, 1995) and working memory (Courtney et al., 1998).

In the present work, we describe a patient suffering from DD. An accurate examination of our patient, including a neuropsychological evaluation and PET (Positron Emission Tomography), has allowed us to assess the neuropsychological, neurometabolic and behavioural aspects characterizing DD disorder.

Case report

S.B. is a 26 years old man, right-handed, with 8 years of schooling, married, working as a bricklayer. In the anamnestic interview, S.B. reports that he leads a quiet life. He comes from a loving and supportive family and he describes the relationship with his parents as good both in the developmental and the current period. After finishing compulsory school, S.B. in fact decides to follow the path of his father, also working as a bricklayer in a private company.

S.B. reports that he has never suffered from any type of physical or psychological illness before, he also denies having suffered any kind of trauma in the recent period or in his childhood. S.B. has a normal social network and he formed a new family of his own, in fact he recently got married and now he lives with his wife.

He was submitted to a first psychiatric visit as a consequence of a sudden and transitory appearance of unreality and "strange feelings".

During the two months preceding the psychiatric visit, the patient had three episodes of about ten minutes, in which alteration of the perception of bodily feelings and alteration of the perception of the distances among the objects were present. After about a month from the last of these episodes, the symptoms appeared again and became permanent.

During the first interview, the patient reported not being able to perceive the somatosensorial stimuli and to perceive in "strange" way objects and people. More specifically, he complained that tactile stimuli evoked "distorted" feelings, while caloric and pain stimuli did not evoke any feelings.

The feeling of unreality was present with other people too. The patient suffered from the beginning of his illness problems in the experience of emotions, not only with unknown people or acquaintances but also with his own relatives, including his wife and son.

The patient reported having been forced to quit his job, both for difficulties in the appropriate use of the tools and for the appearance of slackening and motor

disturbances. Because of that, he reported spending the whole day at home mostly in bed or seated on the couch. He is not able to watch TV because of concentration problems. Also, he reported sleep disorders and a complete inability to distinguish sleep from wakefulness to the point of having a clear feeling never to sleep.

During the interview, the patient summarized his condition as "non-living", showing to be able to assess its absurdity and to have a serious concern for the presence and persistence of the disorder.

During the various interviews, the patient often reported having several times the very clear feeling of "not being physically present" and to "minding from the outside."

The symptomatology was not in any way changed by the various pharmacological therapies he was administered (**table 1**).

Table 1

Main Drug	Daily dose	Duration in days
CLOMIPRAMINE	200 mg	75
VENLAFAXINE	1500 mg	45
IMIPRAMINE	150 mg	50
PAROXETINE	20 mg	20
+		
DOSULEPINE	75 mg	20
SULPIRIDE	400 mg	20
PERICIAZINE	20 mg	20
TIORIDAZINE	400 mg	20
+		
CARBAMAZEPINE	600 mg	20
PERFENAZINE	6 mg	20
+		
AMITRIPTILINE	75 mg	20
RISPERIDONE	6 mg	20
CLOZAPINE	350 mg	30
Drug in combination		
LORAZEPAM	75 mg	
DIAZEPAM	10 mg	
CLONAZEPAM	6 mg	

Positron emission tomography

Magnetic nuclear resonance did not show any structural damage to the central nervous system. The patient was afterwards studied with PET (Positron Emission Tomography) using a Siemens (Ecat Exact 47) camera in 2-D mode.

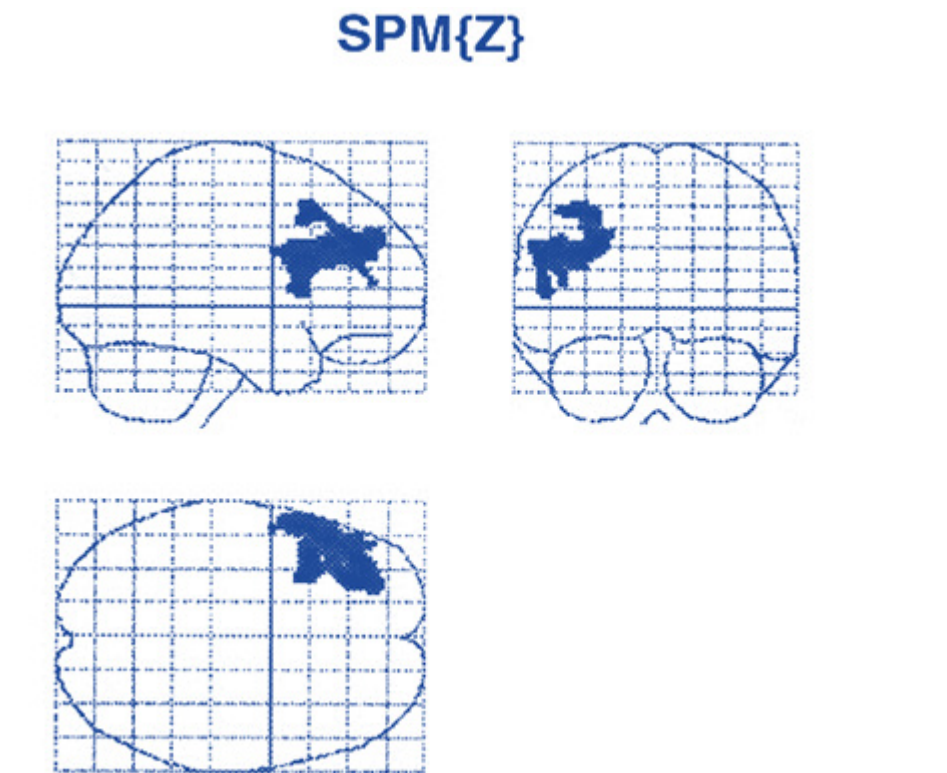
18F-FDG (18fluorine-fluorodeoxyglucose) PET scan was performed to assess brain metabolism. The patient was studied during DD state and 18F-FDG (270-340 MBq i.v.) was injected in resting condition (ear plugged and eyes closed). A transmission scan before 18F-FDG injection was acquired for 15 minutes, 45 minutes after 18F-FDG brain emission scan was performed and final data were reconstructed using statistical analysis performed by SPM96 (Friston et al., 1994) comparing the patient to a control group (10 age-matched healthy subjects).

The anatomical localization was assessed by reference to the standard stereotactic atlas of Talairach and Tournoux (1988).

SPM 96 analysis and the coordinates identified showed a glucose hypometabolism in Brodmann areas 8 and 9 i.e. in left Frontal Cortical (FC) and left Dorsolateral Prefrontal Cortical (DLPFC) regions (figure 1).

The patient showed a serious deficit of planning in the Tower of London test (Shallice, 1982). Planning might be defined as a hierarchic process that monitors the order in which a sequence of operations is performed (Miller et al., 1960). It requires that the subject is able to anticipate the outcome of intermediate operations.

Figure 1



voxel-level (Z)	Uncorrected k & Z	Side	x, y, z (mm)	Brodmann Area	Region
0.053 (4.47)	0.000	0.000	Left -26 38 34	9	PFC
0.074 (4.39)	0.000	0.000	Left -34 42 28	9	PFC
0.109 (4.28)	0.000	0.000	Left -38 18 50	8	FC

Coordinates (in standard stereotactic space as defined by Tailarach and Tournoux, 1988) refer to maximally activate foci indicated by the highest Z-score within an area of activation.

X= distance in mm to right (+) or left (-) of the interhemispheric line;

y= distance anterior (+) or posterior (-) to vertical plane;

z= distance above (+) or below (-) the intercommisural line;

FC = Frontal Cortex

PFC = Prefrontal Cortex

Neuropsychological examination

The patient was submitted to a range of neuropsychological tests in order to identify a cognitive profile. The main results are reported in Table 2.

Basic neuropsychological examination showed a deficit in tasks of long-term memory both for verbal and spatial material and a serious deficit in planning actions.

The selective remind technique (Buschke & Fuld, 1974) showed an intact short-memory and a deficit in long-term memory. Also, there was a deficit in retrieving learned information in a task of spatial learning (Capitani et al., 1980).

Table 2

Test	Score
Memory	
Buscke - Fuld (Recall from MLT)	z = -2.1
Buscke - Fuld (Non Random Recall)	z = -1.8
Spatial Supra-Span learning	z = -3.7
Planning	
Tower of London	z = -7.3

Results of the neuropsychological assessment. In this table are reported tests z values inferior to 1.6 corresponding to $\alpha \leq .05$

Behavioral analysis

We performed other tests in order to identify deficits that might characterize DD disorder.

ASSESSMENT OF SOMATIC AND VISUAL PERCEPTION

In the attempt of showing the difficulty to perceive bodily sensations, we administered tactile and caloric stimuli (with fingers and a test-tube filled with hot water) to various parts of the body (cheeks, back of the hands and the feet, forearms, shoulders, back, thighs). The patient was able both to detect the presence and to localize the position of each stimulus (to each zone of the body we presented 15 stimuli for each sensorial modality, tactile or caloric).

Even though the performance was excellent, the patient reported that the stimuli, though correctly detected and localized, were felt always "extraneous". In other words, the patient repeatedly reported that the stimuli seemed not to be localized on his own body and did not arouse any emotional response.

For what concerns visual perception, the assessment showed that the feeling of extraneousness concerned only some categories of stimuli. While the perception of inanimate objects (e.g. pens, pencils, computer, clock, sweater) is reported to be normal (regardless of object familiarity) the patient defined as strongly "altered" his perception of living beings (e.g. examiner, nurse, a cat, a bird).

For example, both the unfamiliar and familiar (for example his own dog) animals were described as "mechanic", "extraneous" or "strange". In the same way, people's salient features (e.g. face expressions, voice, and movements) were perceived as being "mechanic", "extraneous" independently of the fact that they belonged to strangers or relatives.

In brief, it is apparent an intact ability to recognize objects, people and animals, with a selective inability to perceive them as being "alive".

ASSESSMENT OF EMOTIONAL STATE

Regarding S.B.'s emotional states, during the interviews, he reported episodes characterized by an incongruity between experienced events and the corresponding emotional state. The incongruity consists of the patient inability to experience congruent emotions in specific situations. For example, S.B. reported an episode in which, although being threatened by a dog, he would not have experienced any emotion of fear or pulse to escape. Similarly, he reported total apathy after being accidentally injured in the hands and the left forearm.

At the end of the assessment, when asked to describe his actual emotional state, the patient stated that he did not feel depressed but that he noticed the presence of a state of general malaise that was not able to describe, apart from a strong tension at the throat and at the face accompanied by a mandatory push to cry.

From the assessment, it emerged an absence of emotions, as an inability to experience corresponding emotions at appropriate inducing conditions, both interior and external.

SEMANTIC KNOWLEDGE OF EMOTIONS

This third test aimed to assess what the patient knew about emotional states. S.B. was asked to describe 8 emotional states presented by the examiner (embarrassment, joy, sadness, worry, anger, fear, jealousy, envy). In this task the patient provided an excellent performance demonstrating his ability to define each emotion correctly and to possess good semantic knowledge.

CORRESPONDENCE BETWEEN SITUATION AND EMOTION.

A fourth test was administered to assess the ability of the patient to link some situations to the corresponding emotional states. S.B. was asked to define the emotional state that, given an event, a supposed protagonist of the story could have experienced. For example, given the story "Rita cries because she has lost her kitty", the subject must indicate the emotional state experienced by Rita.

The patient showed an accuracy equal to 100% (21 stories out of 21), demonstrating an intact ability to attribute the correct emotion to each story.

Discussion

The patient during the period of testing, which lasted about 12 months, always reported the presence of DD condition that includes bodily self-detachment, cognitive-emotional self-detachment, perceptual detachment, and detachment from reality.

S.B. reported the lack of "perception" of bodily sensations otherwise correctly identified and localized. Similar results were found in Michal et al. (2014) where DD patients reported an accurate self-correlated clearness of body perception despite out-of-body experiences. According to Tanaka (2018), it is not appropriate to consider these experiences totally disembodied. In fact, S.B. was able to move his own body in accordance with intended actions, but he felt as if his actions were automated.

Similarly, there always was a denial of the presence of emotional experiences of situations that would have caused them, although the patient demonstrated to have correct semantic information. Despite this subjectively "anomalous" experience, the patient always demonstrated having a preserved awareness of the "absurdity" of his condition.

Moreover, S.B. reported extrabodily feelings exclusively for living beings demonstrating a specific perceptual detachment for this category.

The anatomical localization of the changes in metabolic brain values, assessed by reference to the standard stereotactic atlas of Talairach and Tournoux (1988) and by SPM 96 analysis, showed a glucose hypometabolism in Brodmann Areas 8 and 9, that is in left FC and left DLPFC regions.

The neuropsychological assessment showed a deficit in planning actions and long-term memory. In particular, difficulties were shown in the recall of formerly learned information. This deficit in the absence of a real long-term memory (semantic or episodic) deficit might be interpreted as due to a working memory deficit (Atkinson & Shiffrin, 1971; Baddeley, 1986).

In the Atkinson and Shiffrin model (Atkinson & Shiffrin, 1971), working memory was identified with consciousness. The thoughts and the visual, auditory and tactile information of which we are aware at a given moment are part of the working memory content (Paivio, 1978; Tulving, 1983; Squire, 1986; Warrington & McCarthy, 1986). "Damages" in working memory processes cause problems in the processing of visual and tactile stimuli and body sensations.

S.B. was also unable to anticipate a sequence of operations to obtain a goal. The poor performance in the planning task might be due to the absence of a suitable strategy, to the presence of perseveration and of violation of the task rules, as Milner's (1963) frontal patients. Shallice (1992), using the Tower of London, demonstrated the sensitivity of the test to anterior lesions, especially on the left, and located the function

of programming or planning in the prefrontal cortex.

A relationship between consciousness, working memory and prefrontal areas was suggested by Courtney et al. (1998). They proposed that working memory enables us to hold in our “mind’s eye” the contents of our conscious awareness, even in the absence of sensory input, by maintaining an active representation of information for a brief period of time. In this case, prefrontal areas are brought into play during the monitoring and manipulation of information in working memory, in addition to those engaged during the maintenance of this information.

According to this interpretation, Frith and Dolan (1996) speculate that the higher cognitive functions, working memory, mental imagery, and willed action are all intimately associated with consciousness. The common process underlying all these functions is that information is “held in mind” for a period of time. From the neuroanatomical point of view, Frith and Dolan underline that brain imaging studies show that “holding something in mind” is associated with activity in an extended system that involves both the prefrontal cortex and more posterior areas whose location is determined by the nature of the information being held in mind. In another work, Markowitsch (1995) proposed that the cerebral cortex and in particular its frontal areas, the prefrontal cortex, was regarded as the principal anatomical basis of consciousness. Also, he proposed a dependence of consciousness on memory processes and on the ability to order the processes in time.

For what concerns the DD syndrome specifically cognitive deficits due to DD (Guralnik et al., 2000) were shown: attention, visual and verbal short-term memory and spatial reasoning problems. A PET study of Hollander et al. (1992) reporting clinical and biological correlates in a patient with DD found a left hemispheric frontotemporal activation and decreased left caudate perfusion.

In accord with Sierra and Berrios (1998) and the results of the present and previous studies, we believe that a “biological damage” to the CNS, determining a deficit at various levels of information processing, might cause DD disorder. Furthermore, it seems possible to hypothesize that DD disorder is correlated to a working memory deficit attributable to insufficient functionality of the left frontal and prefrontal cortex.

Finally, we believe it is important to mention the study of Maquet et al. (1996). They discovered a negative correlation between rapid eye movement (REM) sleep and cerebral flow, in particular, a decreased activity in the left and right dorsolateral prefrontal cortex, right and left parietal cortex, precuneus and posterior cingulate cortex, and increased activity in right and left amygdaloid complex; left thalamus anterior, cingulate cortex, right parietal operculum and pons had correlated with an increase of the REM sleep. Therefore, it seems to exist a crucial role of the PFC involved in the experience of “living a dream” while sleeping and in the experience of “living like in a dream” in DD.

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