Abstract

Psychogenic non-epileptic seizures (PNES) and functional movement disorders (FMD) seem to represent the two ends of a continuum where different clinical phenotypes represent the manifestation of a common framework, involving dissociation. Aim of the present study was to assess dissociation and its subcomponents through the Mirror Gazing Test (MGT) in these functional neurological disorders. Eleven patients with PNES, 17 with FMD and 18 healthy controls (HC) underwent a 10 minutes MGT and completed the Strange Face Questionnaires (SFQ) and the Clinician-Administered Dissociative States Scale (CADSS). PNES, FMD and HC did not differ at the total score of the SFQ. PNES scored higher than HC at the SFQ-subscale *Dissociative Identity/Compartmentalization*. and at the CADSS-subscale *Dissociative Amnesia*, while FMD scored higher than HC at the CADSS total score and its subscale *Depersonalization*. FMD patients reported more sensations falling in the detachment facet of dissociation, while PNES patients in the compartmentalization facet. We hypothesized that both facets of dissociation might be significant pathophysiological processes for both PNES and FMD and that different instruments (self-report clinical scales VS experimental tasks) are able to detect different facets in different populations because they assess respectively "trait" and "state" facets of dissociation.

Keywords: Functional Neurological Disorder; Psychogenic Non-Epileptic Seizures; Functional Motor Disorder; Dissociation; Detachment; Compartmentalization.

Dissociation during mirror gazing test in Psychogenic Non-Epileptic Seizures and Functional Movement Disorders.

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Abstract

Psychogenic non-epileptic seizures (PNES) and functional movement disorders (FMD) seem to represent the two ends of a continuum where different clinical phenotypes represent the manifestation of a common framework, involving dissociation. Aim of the present study was to assess dissociation and its subcomponents through the Mirror Gazing Test (MGT) in these functional neurological disorders. Eleven patients with PNES, 17 with FMD and 18 healthy controls (HC) underwent a 10 minutes MGT and completed the Strange Face Questionnaires (SFQ) and the Clinician-Administered Dissociative States Scale (CADSS). PNES, FMD and HC did not differ at the total score of the SFQ. PNES scored higher than HC at the SFQsubscale Dissociative Identity/Compartmentalization. and at the CADSS-subscale Dissociative Amnesia, while FMD scored higher than HC at the CADSS total score and its subscale Depersonalization. FMD patients reported more sensations falling in the detachment facet of dissociation, while PNES patients in the compartmentalization facet. We hypothesized that both facets of dissociation might be significant pathophysiological processes for both PNES and FMD and that different instruments (self-report clinical scales VS experimental tasks) are able to detect different facets in different populations because they assess respectively "trait" and "state" facets of dissociation.

Keywords: Functional Neurological Disorder; Psychogenic Non-Epileptic Seizures; Functional Motor Disorder; Dissociation; Detachment; Compartmentalization

Declarations of interest: none.

1. Introduction

Psychogenic non-epileptic seizures (PNES) and functional movement disorders (FMD) are the two main clinical manifestations of functional neurological symptoms (FNS), neurological symptoms that are genuine and not feigned, but not due to an organic cause (DSM-5, A.P.A, 2015) (Hallett, et al., 2016). In the last decade, few studies have tried to define whether a common framework between these disorders may exist or whether they should be considered two separate entities (Kanaan, et al., 2017). Results, mainly obtained studying epidemiological and clinical features of the two disorders, have been quite contradictory: some studies highlighted the heterogeneity of the two disorders (Stone, et al., 2005; Reuber, 2008; Ekanayake, et al., 2017), some others showed more similarities suggesting that they should be considered under the same pathological umbrella (Driver-Dunckley, et al., 2011; Hopp, et al., 2012). A recent review by Erro et al. showed that there is a significant overlap between PNES and FMD, proposing that they would represent the two ends of a continuum (Erro, et al., 2016), where different clinical phenotypes (respectively non epileptic attacks and motor symptoms) represent the manifestation of a common pathophysiology. In line with this hypothesis, in a recent study of our group, we confirmed the traditional hypothesis according to which dissociation might have a central role in the pathophysiology of FNS, underlying how different facets of dissociation - detachment (an altered state of consciousness, characterized by a sense of separation from the self or world) and compartmentalization (a reversible loss of voluntary control over apparently intact processes and functions) - might be relevant respectively for PNES and FMD (Demartini, et al., 2016). Nevertheless, one of the main limitations of our previous study was the lack of an objective assessment of dissociation and its subcomponents, which were evaluated only through self-report scales and not by experimental tasks. In the last decades, several experimental techniques, such as dot staring, mirror staring, spiral staring, strobe light, hyperventilation, audio stimulation, and stimulus deprivation (Miller, et al., 1994;

Leonard, et al., 1999; Lickel, et al., 2008; Dorahy, et al., 2016) have been developed with the aim of inducing and investigating dissociation in the laboratory. Moreover, in the last years, a growing body of literature describing a dissociative phenomenon called "strange-face in the mirror illusion" emerged: if an observer steadily looks at his/her image reflected in a mirror, in a dimly lit room for eight/ten minutes – a procedure called Mirror Gazing Test (MGT) - several visual illusions occur, such as deformations of one's own face, a relative's face with some changed features or an unknown person's face; an archetypal face (i.e. a numinous child, a young androgyne, a very old woman, an ancestor or a shaman), an animal face and/or monstrous beings (Caputo, 2010a). This dissociative phenomenon physiologically occur in healthy subjects (Caputo, 2010a; 2010b); moreover, it has been shown to be stronger in a group of schizophrenic individuals (Caputo, et al., 2012) and reduced in depressed patients (Caputo, et al., 2014) when compared to healthy controls, suggesting a crucial role of specific psychopathological features in the subjective response to the MGT itself.

The aim of the present study was to assess dissociation and its subcomponents through the Mirror Gazing Test (MGT) in a group of patients with PNES, a group with FMD and a group of healthy controls.

2. Methods

2.1 Participants

Patients affected by PNES and FMD were recruited from the psychiatric outpatient clinic at San Paolo Hospital in Milano. Eleven consecutive patients affected by PNES took part in the study, and they were compared to seventeen patients affected by FMD and eighteen healthy controls (HC). The diagnosis of PNES was done on the basis of the consensus of at least two epilepsy specialists based on the clinical history and video-EEG monitoring. Typical nonepileptic attacks had been captured by video-EEG for all patients with PNES and PNES were therefore "documented" according to the diagnostic certainty levels described in LaFrance et al (2013). Panic attacks as an alternative explanation of the paroxysmal symptoms of PNES were excluded by psychiatric examination. Patients with FMD were included if they had "clinically established" FMD according to Fahn & Williams (Williams, et al., 1995) and Gupta & Lang (Gupta & Lang, 2009) criteria. The diagnosis was ascertained by a neurologist and psychiatrist on the basis of clinical presentation and appropriate investigations. The group of healthy controls was recruited from staff members, their friends and relatives. Psychiatric, neurological and medical disorders were excluded by means of a complete anamnestic questionnaire and a clinical interview. Participants of the three groups were Caucasian.

Exclusion criteria were as follows: (i) age less than 18 years, (ii) inability to understand the aim and the steps of the project, (iii) any other serious neurological (epilepsy included) or medical illnesses and (iv) overlay between functional and organic movement disorders.

One HC was excluded as outlier (performing two Standard Deviation above the average in the experimental variables). Every participant had the opportunity to ask for clarification and explanation during each stage of the study and was free to interrupt and leave the experiment at any moment. The study was approved and registered by the local ethics committee. Participants gave their informed written consent. The experiment was conducted in accordance with the Declaration of Helsinki.

2.2 Experimental Protocol

After the preliminary neurological and psychiatric assessment, participants completed in an experimental session lasting about 60 minutes during which they underwent the Mirror Gazing Test and a psychological assessment.

2.2.1 Mirror Gazing Test

MGT was conducted in a darkened room, 5 m×5 m, whose walls were grey-painted and the windows obscured. A large mirror (0.5 m×0.5 m) was mounted on a tripod in the centre of the room. Each subject seated at a distance of 0.4 m in front of the mirror and was instructed to keep staring into his/her own eyes for ten minutes. The room was lit only by a halogen light bulb (20 W), mounted on a spotlight placed 1.2 m behind the participant, on the floor (and therefore out of his/her visual field and out of the mirror reflection). Illumination of the face ('incident light') was about 1 lux (measured with TES-1330A luxmeter). For further details about the procedure see Caputo et al. (Caputo, et al., 2012). At the end of the session, participants completed the Strange Face Questionnaires (SFQ), an ad-hoc questionnaire assessing the sensations and perceptions they had looking in the mirror (Caputo, 2015) and the Clinician-Administered Dissociative States Scale (CADSS) (Bremner, et al., 1998).

The Strange Face Questionnaire, in its new version used in the present study, is composed by a total of 28 items, describing sensations or perceptions possibly occurred during the MGT. Participants had to evaluate, on a Likert 5-point scale, how often they experienced the perception described (where 0 meant "never" and 4 meant "almost always"). Item 19 is a response control: therefore, the questionnaire has been considered valid only if the answer was 0, never. Firstly, number of answers "never" and number of answers ranging from 1 to 4 were counted, as an index of how many different apparitions and sensations occurred during the MGT to each participant. Secondly, a total score, ranging from 0 to 108, has been calculated. Finally, three subscales have been calculated and analysed: (i) *Depersonalization* (summing items: 14, 17, 18, 20, 22, 23, 24; total score ranging from 0 to 28); (iii) *Dissociative Identity/Compartmentalization* (summing items: 2, 7, 9, 12, 13, 21, 25, 26, 27; total score ranging from 0 to 36).

The CADSS is composed by 19 items, to be replied on the same 5-point Likert scale (0 being "never" and 4 being "almost always"). An overall total score, ranging from 0 to 76, has been calculated by summing the answers of each item; in addition, the three following subscales have been calculated and analysed: (i) *Derealisation* (summing items: 29, 30, 36, 37, 38, 39, 40, 41, 44, 45, 46, 47; total score ranging from 0 to 48); (ii) *Depersonalization* (summing items: 31, 32, 33, 34, 35; total score ranging from 0 to 20); (iii) *Dissociative Amnesia* (summing items: total score ranging from 0 to 8).

2.2.2 Psychometric Assessment

Participants have been assessed by a psychiatrist for their levels of depressive and anxiety symptoms, respectively through the Hamilton Depression Rating Scale (HAM-D) and the Hamilton Anxiety Rating Scale (HAM-A).

2.3 Data Analysis

Data have been analysed with the software SPSS (Statistical Package for Social Science), Version 25.

Univariate ANOVA has been run to assess whether the three groups (PNES, FMD and HC) were different with respect to demographical, experimental and psychometric variables; when a questionnaire presented more than one subscale, multivariate ANOVA (MANOVA) has been used, with the subscales as dependent variables (and *Groups* as factor); in both cases, Bonferroni post-hoc analysis was used to verify specific differences between two of the three groups. Categorical variables have been analysed via Pearson Chi Square (χ^2) test.

Additionally, Pearson's correlational analysis has been used to assess correlations between the variables assessed.

3. Results

3.1 Demographic Data

The three samples were sex-(χ (2)=2.737, p=0.255) and age-(F(2, 43)=0.891, p=0.418) matched. They differed for psychiatric comorbidities (χ (2) = 7.926, p=0.019), but not for psychiatric familiarity (χ (2) = 0.126, p=0.939).

Average years of illness for PNES was 3.2 years (S.D.=2.64), while for FMD was 4.35 years (S.D.=4.26); duration of illness was comparable between the two groups of patients (t(26)=0.797, p=0.433 - with Levene's F=2.223, p=0.148).

Demographic, experimental and psychometric values are reported in table 1.

3.2 Mirror Gazing Test

PNES, FMD and HC did not differ at the total score of the Strange Face Questionnaire (F(2, 43)=2.378, p=0.105). Neither the number of times they had misperceptions by looking in the mirror (F(2, 43)=1.501, p=0.234) differed between the three groups. A difference between the three groups emerged at the subscale *Dissociative Identity/Compartmentalization* (F(2, 43)=3.88, p=0.028), with PNES scoring higher than HC (p=0.024) but not than FMD (p=0.424); no differences between FMD and HC (p=0.44) were detected. Furthermore, no differences between the three groups emerged at the two other subscales (*Derealisation*: F(2, 43)=1.335, p=0.274; *Depersonalization*: F(2, 43)=0.92, p=0.406).

Groups also differed at the CADSS total score (F(2, 43)=3.933, p=0.027), with PNES having higher values than HC (p=0.029) but not than FMD (p=0.841); no differences between FMD and HC (p=0.208) were detected. Specifically, differences emerged at the CADSS subscales *Depersonalization* (F(2, 43)=3.509, p=.039), with FMD presenting higher values than HC (p=0.043), and *Dissociative Amnesia* (F(2, 43)=4.057, p=0.024), with PNES presenting higher

values than HC (p=0.025). No differences between the three groups at the subscale *Derealisation* emerged (F(2, 43)= 1.978, p=0.151).

3.3 Psychometric Assessment

HAM-D and HAM-A.

Groups were different for their levels of anxiety (F(2, 43)=10.933, p<0.001), with FMD being more anxious than HC (p<0.001) and PNES (p=0.005), and depression F(2, 43)=8.169, p=0.001), again with FMD being more depressed than HC (p=0.001) and PNES (p=0.028).

3.4 Correlational Analysis

Considering the whole sample, a positive correlation emerged between the years of illness and the CADSS, both at the total score (r=0.334, p=0.025) and at its subscales derealisation (r=0.325, p=0.029) and dissociative amnesia (r=0.399, p=0.007). Focusing on the correlations within each group, only a positive correlation between the years of illness of FMD patients and the CADSS subscale *Dissociative Amnesia* (r=0.556 p=0.020) emerged.

Additionally, within PNES group, a negative correlation emerged between levels of anxiety (HAM-A) and CADSS subscale *Dissociative Amnesia* (r=-0.692, p=0.018). Values of depression (HAM-D) did not correlate with any of the MGT questionnaires in any group.

4. Discussion

The aim of the present study was to assess dissociation and its subcomponents through the Mirror Gazing Test in a group of patients with PNES, a group with FMD and a group of healthy controls. Our results showed that patients with PNES, patients with FMD and HC reported, at the SFQ, to have had misperceptions during the ten minutes of mirror gazing, whose frequency was not different amongst the groups. Previous results on different populations of patients

showed that schizophrenic patients reported more apparitions than HC at the MGT (Caputo, et al., 2012) and, on the contrary, depressed patients experienced less apparitions than both HC and schizophrenic patients (Caputo, et al., 2014). Authors hypothesized that the lower number of apparitions experienced by depressed patients was explained by the well-known deficits in emotional facial recognition and expression typical of these patients (Caputo, et al., 2014). On the other hand, it has been speculated that one of the crucial differences between healthy controls' and schizophrenic patients' answers at the MGT questionnaires lied in the feeling of reality of the apparitions (Caputo, et al., 2012). In other words, schizophrenic patients tended to identify themselves with the apparitions in the mirror, contrarily to healthy individuals who predominantly felt dissociative experiences during the MGT (Caputo, 2010b). In the present study both patients with PNES and patients with FMD reported a similar number of misperceptions during the MGT to the one reported by healthy controls. This confirms that the MGT is a good instrument to induce typical dissociative symptoms also in clinical populations where a psychotic trait is not present and whose depressive symptomatology, occurring in comorbidity, does not alter MGT results (as attested by the absence of correlation between MGT questionnaires and HAM-D values).

Moreover, our results showed patients with PNES to score significantly higher than HC at the SFQ subscale assessing *Dissociative Identity/Compartmentalization*. This difference was corroborated by the CADSS results, with PNES patients reporting higher scores at the *Dissociative Amnesia* subscale, since dissociative identity is usually associated with dissociative amnesia (Holmes, et al., 2005). On the other hand, patients with FMD reported higher values at the *Depersonalization* CADSS subscale than HC. In other words, patients with FMD reported more sensations (such as "feeling like they were looking at things from outside their own body", "feeling like being in a dream" or even "feeling like looking at the things as through a fog") that would fall in the detachment facet of dissociation, while patients

with PNES reported more sensations (such as "recognizing in the mirror another personality that he/she would not have expected" or "feeling like wandering with their own thoughts and/or losing track of what was happening") falling in the compartmentalization facet.

These results apparently seem not to confirm our previous finding, obtained by self- report questionnaires, according to which PNES patients presented higher levels of detachment and FMD patients of compartmentalization than HC (Demartini, et al., 2016). But, as anticipated before, a strong limitation of our previous study was the use of subjective instruments for the assessment of dissociation, namely self-report questionnaires. In addition, previous studies showed that both the facets of dissociation (detachment and compartmentalization) might be relevant from a pathophysiological angle for all the clinical manifestations of Functional Neurological Symptoms, including PNES and FMD. Kuyk and colleagues (1999) showed that 17 out of 20 patients with PNES, when hypnotized, were able to recall seizure memories usually unavailable to consciousness, contrarily than a control group with organic epileptic attacks; authors argued that in PNES, unlike in epilepsy, there is no permanent memory loss due to a encoding deficit occurred during the attack, but a retrieval deficit due to dissociation (or, more specifically, compartmentalization) of the ictal memories (Brown & Reuber, 2016). Given that these non-epileptic attacks have been interpreted also as a dissociative response to autonomic arousal aimed to reduce intense anxiety (Goldstein & Mellers, 2006), this is also in line with our results, showing that, only in PNES patients, the higher the levels of anxiety at the HAM-A, the higher the score at the Dissociative Amnesia CADSS subscale. Patients with PNES and patients with epilepsy have also been compared on self-report questionnaires about dissociations, with inconsistent findings: Alper and colleagues (1997) found that PNES patients scored higher than patients with epilepsy on the DES subscales measuring depersonalizationderealization, but this was attributed by the authors to a higher prevalence of childhood abuse in the PNES group; furthermore, Lawton, Baker, and Brown (2008) found a difference between

PNES and epilepsy patients only at the compartmentalization subscale of the DES (for a review, see Brown, 2016).

On the other hand, recent studies suggested that detachment might have a specific role also in patients with FMD: Stone et al. (2012) for example, found that 39% of their patients with functional weakness reported depersonalization or derealization 24 hours prior the onset of the symptom. With regard to the processes underpinning compartmentalization, there is some evidence that FMD patients have difficulties when actions are explicitly initiated, but not when they are evoked implicitly, which is consistent with the dissociated control account (Roelofs, et al., 2001).

In this view, we hypothesized that both the facets of dissociation (detachment and compartmentalization) might be significant pathophysiological processes for both PNES and FMD and that different instruments (self-report clinical scales VS experimental tasks) are able to detect different facets in different populations because they assess respectively "trait" and "state" facets of dissociation. In fact, self-report questionnaires commonly used to assess dissociation in FND, such as the Dissociative Experience Scale or the Somatoform Dissociation Questionnaire, explore a set of symptoms (trait dissociation) and not a process; on the other hand, experimental tasks such as the MGT directly explore a process, namely induced dissociative experiences (state dissociation).

It seems, furthermore, that both aspects of dissociation are strictly linked to the duration of illness in the whole sample, suggesting a predominant role of both detachment (CADSS *Derealization* subscale) and compartmentization (CADSS *Dissociative Amnesia* subscale) in the maintenance of the symptomatology. In conclusion, our data corroborate the hypothesis according to which both detachment and compartmentalization are important for understanding the mechanism underlying both PNES and FMD: we might hypothesize that (i) PNES are primarily a detachment phenomenon (measured by a "trait" dissociation instrument such as the

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Dissociative Experience Scale) and the compartmentalization (measured by a "state" dissociation instrument such as the MGT) represent a state dissociative epiphenomenon, in terms of loss of executive control of mental processes; (ii) FMD are primarily a compartmentalization phenomenon (measured by a trait dissociation instrument such as the Somatoform Dissociation Questionnaire) and detachment (measured by a "state" dissociation instrument such as the MGT) is often part of the ongoing clinical picture and may contribute to the development and maintenance of FMD (Figure 1).

We acknowledge the limitation of our study. Firstly, the limited sample size, although in line with other experimental studies on similar topics. Secondly, the absence of self-report clinical questionnaires on this same cohort of patients does not allow us to draw definitive conclusions on our hypothesis about the different tests' sensibility to the facets of dissociation. Finally, although the paradigm used is gaining more and more evidences of reliability in different clinical populations, our data would be stronger if confirmed by other experimental paradigms aimed to assess the process of dissociation.

Future researches should expand our preliminary results, evaluating FMD and PNES patients with both state and trait dissociation instruments.

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	FMD	PNES	НС	Р
Sex [M/F]	4/14	1/13	3/14	0.255
Age [Average (S.D.)]	43.6 (16.1)	36.1 (16.8)	38.1 (13.8)	0.418
Psychiatric familiarity [(Y/N)]	6/12	4/6	6/11	0.939
Psychiatric comorbidities [(Y/N)]	11/7	8/3	4/13	0.019
Years of illness	4,4 (4,3)	3,2 (2,647)	NA	NA
SFQ – Total Score	12.6 (11.8)	20 (14.4)	11.06 (6.9)	0.105
% of misperception (SFQ)	22%	32%	21%	0.234
SFQ – Derealization	3.3 (4.1)	5.2 (4.5)	2.8 (3)	0.274
SFQ – Depersonalization	2.8 (3.1)	4.5 (4.6)	3.1 (2.8)	0.406
SFQ - Dissociative Identity - Compartmentalization	2.6 (2.9)	4.3 (4.6)	1.1 (1.3)	0.028
CADSS-Total Score	15 (12.9)	19.7 (12.6)	7.8 (8.2)	0.027
CADSS-Derealization	9.4 (7.7)	10.9 (6.3)	6.2 (5)	0.151
CADSS-Depersonalization	6.9 (7.3)	5.9 (6.1)	1.9 (3.3)	0.039
CADSS-Dissociative Amnesia	2.1 (2.3)	2.9 (2.0)	0.9 (1.1)	0.024
HAM-A	14.6 (10)	5.5 (4.3)	4.1 (4.1)	<0.001
HAM-D	11.2 (7.8)	5 (4)	3.4 (4.4)	0.001

Table 1 – Values for demographical, psychometric and experimental variables.

Figure 1 - A dissociation model for FNS.

