Different dissociation and alexithymia domains specifically relate to patients with psychogenic non-epileptic seizures (PNES) and with PNES and comorbid epilepsy (PNES+EP)

Article · December 2021

DOI: 10.1016/j.jadr.2021.100296

CITATIONS
0

READS
35

7 authors, including:

Andrea Poli
Università di Pisa
36 PUBLICATIONS **695** CITATIONS
SEE PROFILE

Ciro Conversano
Università di Pisa
142 PUBLICATIONS **2,729** CITATIONS
SEE PROFILE

Angelo Gemignani
Università di Pisa
221 PUBLICATIONS **4,139** CITATIONS
SEE PROFILE

Mario Miccoli
Università di Pisa
156 PUBLICATIONS **2,393** CITATIONS
SEE PROFILE

Journal of Affective Disorders Reports 7 (2022) 100296

Contents lists available at ScienceDirect

Journal of Affective Disorders Reports

journal homepage: www.sciencedirect.com/journal/journal-of-affective-disorders-reports

Different dissociation and alexithymia domains specifically relate to patients with psychogenic non-epileptic seizures (PNES) and with PNES and comorbid epilepsy (PNES+EP)

Andrea Poli [a,b,*], Angelo Giovanni Icro Maremmani [c,d,e], Ciro Conversano [a], Giancarlo Muscas [f], Angelo Gemignani [a], Andrea Pozza [g], Mario Miccoli [b]

[a] Department of Surgical, Medical and Molecular Pathology and of Critical Care Medicine, University of Pisa, 56126, Pisa, Italy
[b] Department of Clinical and Experimental Medicine, University of Pisa, 56126, Pisa, Italy
[c] Department of Psychiatry, North-Western Tuscany Region NHS Local Health Unit, Versilia Zone, 55049 Viareggio, Italy
[d] Association for the Application of Neuroscientific Knowledge to Social Aims (AU-CNS), 55045 Pietrasanta, Lucca, Italy
[e] G. De Lisio Institute of Behavioral Sciences, 56100 Pisa, Italy
[f] Epilepsy Center, Department of Neurology, Careggi Hospital, 50134 Florence, Italy
[g] Department of Medical Sciences, Surgery and Neuroscience, University of Siena, 53100, Siena, Italy

ARTICLE INFO

Keywords:
Psychogenic non-epileptic seizures
Dissociation
Alexithymia
Depersonalization
Derealization
Difficulty describing feelings

ABSTRACT

Background: Several studies previously examined the role of dissociation and alexithymia in patients with psychogenic non-epileptic seizures (PNES). However, their relationship remains unclear.
Methods: We administered questionnaires for dissociation (DES-II), alexithymia (TAS-20), anxiety and depression to 57 subjects: 14 patients with PNES, 13 patients with comorbid PNES and epilepsy (PNES+EP), 14 patients with EP and 16 healthy controls. For between-group comparisons we applied Chi-square test, ANOVA and Kruskal-Wallis. The Spearman correlations, hierarchical regression analyses and path models, goodness-of-fit indices and maximum-likelihood estimates of model parameters were obtained through SPSS 27 and AMOS 27.
Results: Hierarchical regression analyses showed that nor DES-II neither TAS-20 total scores were able to predict TAS-20 and DES-II total scores, respectively, possibly due to subscale score pooling. Following modification indexes of AMOS 27, in PNES sample, we found that only Depersonalization/Derealization (Dep/Der) was fully mediated by Difficulty Identifying Feelings (DIF) and Absorption (Abs) in predicting Difficulty Describing Feelings (DDF), and a partial effect of DIF and Dep/Der implement DDF, while both DIF and DDF implement Abs. In PNES+EP group, Dep/Der was able to predict DDF, with a partial mediation of Abs that predicted Externally Oriented Thinking, while DDF was able to promote Abs, and DIF effect on Abs was fully mediated by Amnesia (Amn).
Limitations: Our study is cross-sectional, participants were self-selected and the data were derived from self-report measures. *Conclusions:* In PNES, Dep/Der and DIF may play a prominent role, while in PNES+EP, Dep/Der, Abs, DIF and Amn may be involved. Clinical implications are discussed.

1. Introduction

Psychogenic non-epileptic seizures (PNES) are paroxysmal time limited alterations in autonomic, sensory, motor, emotional and cognitive domains, similar to epileptic seizures (EP) but, unlike them, PNES are not associated with ictal epileptiform activity and are thought to have psychological underpinnings (Asadi-Pooya, 2020; Devinsky et al., 2011; LaFrance et al., 2013; Popkirov et al., 2017). PNES patients show greater emotional intensity (Roberts et al., 2012), in particular in response to angry faces (Bakvis et al., 2010), as well as emotion regulation difficulties (Roberts and Reuber, 2014). There is still growing evidence that experiencing overwhelming emotions, especially of traumatic nature, quenches central nervous system key hub regions with a prominent role in integrating sensorimotor output, regulating arousal

* Corresponding author at: Via Savi, 10, 56126, Pisa, Italy.
E-mail addresses: andrea.poli@med.unipi.it (A. Poli), angelo.maremmani@uslnordovest.toscana.it (A.G.I. Maremmani), ciro.conversano@unipi.it (C. Conversano), angelo.gemignani@unipi.it (A. Gemignani), andrea.pozza@unisi.it (A. Pozza), mario.miccoli@med.unipi.it (M. Miccoli).

https://doi.org/10.1016/j.jadr.2021.100296
Received 28 June 2021; Received in revised form 25 November 2021; Accepted 12 December 2021
Available online 14 December 2021

levels and translating experience in words (Clancy et al., 2017), and it has been shown that patients with PNES, especially those with active PTSD and childhood trauma, have lower clarity of their emotions and lower ability to adjust to emotional states than healthy individuals (Rosales et al., 2020). PNES patients are characterized for their inability to verbalize emotions when dealing with anxiety symptoms, therefore expressing them in a somatic dimension (Martino et al., 2018). Previous studies reported no overall differences in alexithymia scores between PNES and epileptic patients (Myers et al., 2013b), while Urbanek et al. (2014) reported that, in PNES patients, levels of alexithymia were positively associated with self-reported seizure severity. In order to define the difficulties related to the identification of emotions and to finding words for emotions, Sifneos introduced the term "alexithymia" [literal meaning "no words for emotions"] to identify "this specific difficulty which appears more likely to be due to a combination of neurophysiological and psychological defects rather than to purely psychological ones" (Goerlich, 2018; Sifneos, 1973). In accordance with this, research has highlighted an association between number of traumatic experiences and alexithymia, and the influence of emotional avoidance and numbing within this relationship. Furthermore, alexithymia retains the potential of being both a premorbid trait and a consequence of traumatization (Eichhorn et al., 2014). Higher levels of alexithymia post-treatment, indicating persistent alexithymia, correlated with an increased severity of the disorder post-treatment, and accordingly, with a lower response to treatment (Pinna et al., 2020). Thus, it is critical to investigate the role of alexithymia in PNES (Asadi-Pooya, 2015; Baslet, 2011).

However, alexithymia is not the only important psychological factor that deserves investigation in PNES. It has been shown that nearly one third of PNES patients reported an elevated use of emotion-focused coping strategies (i.e. self-oriented stress reduction approaches that include fantasizing, self-blame and angry outbursts) which is considered to be ineffective in resolving most stressful situations (Myers et al., 2013a). Although alexithymia has traditionally been associated with an incapacity to fantasize, enhanced fantasizing may also be related to dissociation (Elzinga et al., 2002). In accordance with this, recent research showed that difficulty fantasizing and low emotional reactivity are not components of the latent alexithymia construct (Preece et al., 2020), and people with high levels of alexithymia exhibited decreased anticipation of the occurrence of a negative emotional event (Starita et al., 2016), as it is for dissociation that stems from avoiding emotional information, especially negative emotion, to protect a fragile psyche (Oathes and Ray, 2008). Furthermore, dissociation score was significantly associated with a negative evolution of the number of seizures (Grenevald et al., 2021).

EP have been described as spontaneous paroxysmal electrical discharges from an epileptogenic brain substrate, usually causing transient physical manifestations. It has been shown that patients with PNES differed from those with epilepsy on a somatization scale but not on dissociation (Myers et al., 2019), while Reuber et al. (2003) found higher levels of dissociation in PNES compared to epileptic patients, in particular in patients with past traumatic experiences (Hingray et al., 2011). In accordance with this, PNES patients exhibited significantly higher rates of sexual and other trauma compared with those with intractable epilepsy. A history of psychological trauma was found to be the only condition found to discriminate between patients with PNES and those with epilepsy (Myers et al., 2019).

Table 1

However, between 5% and 20% of outpatients with epilepsy have nonepileptic seizures as well, which can present a challenging scenario for both physicians and caregivers. Likewise, an estimated 10% (Benbadis et al., 2001; Widdess-Walsh et al., 2018) or 5% (Hamed et al., 2020) of patients with PNES have comorbid epilepsy. Failure to recognize either comorbidity can result in diagnostic delay and inappropriate treatment. Patients with comorbid PNES and EP (PNES+EP) were first described by Beau (1836), are highly heterogeneous and show many associated variables with respect to patients with EP: female gender predominated; they take a higher number of antiepileptic drugs than PNES alone; it has been shown an association with an earlier age of seizure onset; somatoform, conversion or cluster B personality disorders were more frequent (Baroni et al., 2016). With respect to PNES patients, PNES+EP patients showed lower scores of depression, anxiety and stress (Hamed et al., 2020). Unfortunately, Wilkins et al. (2018) pooled patients with PNES+EP with those with only PNES and found that 65% of patients with PNES, with respect to patients with EP showed depression, had higher mean depression scores and experienced significantly more fatigue. In addition, 70% of patients with PNES and 50% of patients with epilepsy reported sleep problems.

However, the specific relationship between alexithymia and dissociation in PNES is not known and excluding patients with PNES and comorbid epilepsy from investigation (Reuber et al., 2003) or including them in PNES group (Hingray et al., 2011; Wilkins et al., 2018) may have generated confounding effects. In addition, both dissociation and alexithymia are multifaceted dimensions that are characterized by different factors when using psychometric tools for their assessment. Dissociative Experiences Scale – II (DES-II; Carlson and Putnam, 1993) and Toronto Alexithymia Scale – 20 (TAS-20; Bagby, Parker, et al., 1994; Bagby, Taylor, et al., 1994) are gold standard assessment tools to assess

Table 1
Comparisons among the main demographic variables and study measures for PNES (n = 14), PNES+EP (*n* = 13), EP (*n* = 14) and HC (*n* =16) samples.

Variable	PNES	PNES+EP	EP	HC	χ2/F/H	*P*
1. Gender (F; n°/%)	11 (78.57%)	8 (61.54%)	10 (71.43%)	11 (68.75%)	5.115	=0.164
2. Age	43.64 (11.76)	41.77 (12.77)	41.64 (16.84)	44.69 (12.74)	0.086	=0.967
3. BDI-II	17.14 (8.83)	17.38 (7.64)	4.44 (3.61)	4.56 (4.26)	26.988	<0.001
4. STAI-S	49.07 (9.29)	46.85 (8.54)	36.78 (4.79)	36.94 (10.67)	16.539	<0.001
5. STAI-T	50.79 (6.24)	48.92 (8.22)	36.44 (6.73)	37.25 (10.04)	22.454	<0.001
6. TAS-20-Tot	63.71 (11.92)	59.00 (9.91)	36.44 (11.61)	38.69 (9.97)	28.856	<0.001
7. TAS-20-DIF	16.71 (6.21)	15.00 (5.16)	11.33 (5.61)	12.81 (5.74)	7.854	=0.049
8. TAS-20-DDF	21.86 (6,49)	18.08 (5,79)	10.22 (4.21)	11.13 (4.33)	23.883	<0.001
9. TAS-20-EOT	25.14 (3.48)	25.92 (5.39)	14.89 (2.42)	14.75 (2.67)	30.585	<0.001
10. DES-II-Tot	21.04 (13.02)	8.73 (5.97)	7.46 (5.85)	6.70 (4.29)	11.983	=0.007
11. DES-II-Abs	31.03 (15.58)	12.63 (11.56)	11.09 (7.77)	12.81 (9.98)	4.475	=0.009
12. DES-II-Amn	8.89 (10.97)	4.28 (10.62)	4.17 (5.90)	2.71 (2.87)	3.147	=0.369
13. DES-II-Dep/Der	12.13 (20.50)	3.88 (7.43)	1.11 (2.20)	0.94 (1.76)	2.007	=0.571

Note: *F*=Frequency and percentage of female subjects for each group; BDI-II=Deck Depression Inventory - II; STAI-*S* = State-Trait Anxiety Inventory - State; STAI-*T* = State-Trait Anxiety Inventory - Trait; TAS-20-Tot = Toronto Alexithymia Scale – 20 – Total Score; TAS-20-DIF = Toronto Alexithymia Scale – 20 – Difficulty Identifying Feelings; TAS-20-DDF = Toronto Alexithymia Scale – 20 – Difficulty Describing Feelings; TAS-20-EOT = Toronto Alexithymia Scale – 20 – Externally Oriented Thinking; DES-II-Tot = Dissociative Experiences Scale – II – Total score; DES-II-Tot = Dissociative Experiences Scale – II – Absorption; DES-II-Amn = Dissociative Experiences Scale – II – Amnesia; DES-II-Dep/Der = Dissociative Experiences Scale – II – Depersonalization/Derealization. Mean and standard deviation (in brackets) are shown, except for gender.

dissociation and alexithymia, respectively, that are used in our study. DES-II identifies absorption, derealization/depersonalization and dissociative amnesia as subscales, while TAS-20 identifies difficulty identifying feelings, difficulty describing feelings and externally-oriented thinking as subscales. Considering the specific and unique effect that each of the specific factors of DES-II and TAS-20 may play, total scores and specific subscale scores of these tools deserve careful investigation. Our study aims to investigate the role of dissociation and alexithymia in predicting PNES diagnosis by comparing four samples: a) PNES patients, b) PNES+EP patients, c) EP patients, and d) healthy controls (HC). The following were hypothesized: (1) alexithymia and dissociation would be major predictors of PNES and PNES+EP diagnosis over and beyond anxiety and depression; (2) dissociation dimensions would be a predictor of alexithymia dimensions in PNES over and beyond anxiety and depression; (3) alexithymia dimensions would be a predictor of dissociation dimensions in PNES+EP over and beyond anxiety and depression.

2. Materials and methods

2.1. Participants

The sample group of our study included 57, age and gender matched, subjects (14 PNES, 13 PNES+EP, 14 EP, 16 HC). Patients enrolled in the study met the following criteria: age between 18 and 65 years, they were admitted to our video-EEG (v-EEG) monitoring unit from 1 to 6 days and met proposed diagnostic level of certainty "documented PNES" for PNES group (LaFrance et al., 2013); patients with "documented PNES" and analyzed with stringent criteria for coexistent unequivocal epileptiform activity for PNES+EP group (Benbadis et al., 2001); patients with any form of epilepsy for EP group. Exclusion criteria were as follows: <2 seizures/month, drug or alcohol misuse, illiteracy, refusal to give informed consent. Patients with a history of traumatic brain injury or comorbid psychiatric disorders were not excluded. The diagnoses of EP and PNES were established by G.M.'s team of experienced epileptologists through V-EEG monitoring after both event types were captured, and other events such as syncope or migraine were excluded. The diagnosis of PNES was further supported by induction of a typical event through the use of suggestion techniques by a team psychiatrist or psychologist. All the subjects enrolled in the study provided their written informed consent. This study was conducted in accordance with the Helsinki Declaration as revised 1989.

2.2. Measures

Dissociative Experiences Scale - II (DES-II; Carlson and Putnam, 1993). The Dissociative Experiences Scale-Revised (DES-II) is a self-report scale that measures dissociative experiences in daily life related to depersonalization, derealization, amnesia, and absorption. The DES-II consists of 28 items. In the original DES, respondents were asked to indicate to what extent they experienced these symptoms (without being under the influence of alcohol or drugs) on 100-mm visual analogue scales. In the current DES-II, the analogue scales were replaced with a Likert-type scale ranging from 0%, meaning never, to 100%, meaning always (that is, containing 11 options at 10% increments). The total DES-II score is the mean of all 28 items scores. Research has shown that the DES-II has high reliability (test-retest = $0.79 < r < 0.84$; split-half = $0.83 < r < 0.93$; Cronbach's $\alpha = 0.95$) (Carlson and Putnam, 1993). Consistent with these findings, the Italian DES-II version (Bombi et al., 1996) was equally reliable (Cronbach's $\alpha = 0.91$; split-half: $r = 0.92$). In the present study, we used the Italian translation reported by Conti (2000), which showed excellent internal consistency (Cronbach's $\alpha = 0.95$) in previous research (Garofalo et al., 2015).

*Toronto Alexithymia Scale – 20 (TAS-20;*Bagby, Parker, et al., 1994; Bagby, Taylor, et al., 1994). The TAS-20 is a self-report scale used to measure alexithymia which is composed of 20 items that are rated on a 5-point scale, ranging from 1 (strongly agree) to 5 (strongly disagree). A score equal to or less than 51 represents non-alexithymia, whereas a score equal to or greater than 61 represents alexithymia. In-between scores of 52–60 represent possible alexithymia (Bagby et al., 1994b). This measure has demonstrated good internal consistency (Cronbach's alpha=0.81) and test–retest reliability (0.77, $p<.01$) and has also demonstrated adequate levels of convergent validity and concurrent validity (Bagby et al., 1994a). The Italian translation of the TAS-20 showed good internal consistency (Cronbach's alpha=0.82) (Bressi et al., 1996).

State-Trait Anxiety Inventory – Form Y (STAI-Y; Spielberger et al., 1983). The Italian version of the STAI-Y (Pedrabissi and Santinello, 1989) was used to measure the current level of anxiety. The questionnaire is composed of 20 items investigating the general feelings of respondents on a 1–4 Likert scale. Ten items are focused on negative feelings and 10 items are focused on positive feelings. Responses on the positive items were reversed, so that higher scores to the STAI correspond to a higher level of anxiety (range: from 1 to 80).

Beck Depression Inventory-II (BDI-II; Beck et al., 1996). This 21-item self-report inventory is used to assess depressive symptoms over the preceding two weeks. Response choices are scored from 0 (absent) to 3 (severe) and total scores range from 0 to 63. The BDI-II has shown good psychometric properties and the Italian version of the BDI-II (Sica and Ghisi, 2007) has shown a one-factor structure, adequate internal consistency (α in the range 0.80–0.87), test-retest reliability ($r = 0.76$) and construct validity. Internal consistency was also excellent ($\alpha = 0.91$) in the current study.

2.3. Procedure

After signing the consent form, participants were given a short description of the study and were asked to complete a set of self-report questionnaires that included the aforementioned measures. Questionnaires were presented in a counterbalanced fashion to control for order and sequencing effects. Batteries were completed in 15 to 25 min. A research assistant waited until each participant had completed all of the questionnaires and provided assistance if the meaning of the question was not be understood. No external incentives were offered to participate in this study.

2.4. Statistical analysis

For between-group comparisons we applied Chi-square test ($\chi 2$), ANOVA and Kruskal-Wallis with Tukey's and Dunn's post-hoc test, respectively. The Spearman correlations between the DES-II and the TAS-20 total score and subscales and the BDI-II and STAI-Y were examined in order to test the hypothesized relationships. Correlations larger than 0.7 were considered as strong, correlations between 0.3 and 0.69 were considered as moderate and correlations between 0 and 0.29 were considered as weak. Hierarchical multivariate regression analyses (hierarchical generalized linear model) were then conducted to test the robustness of these associations and to determine whether dissociation and alexithymia contributed to the prediction of alexithymia and dissociation, above and beyond depression and anxiety, in PNES and PNES+EP.

Separate hierarchical multivariate regressions for PNES and PNES+EP were run using alexithymia and dissociation as dependent variables. In the first step of each regression model age and gender were entered as control variables. In the second step, total BDI-II, STAI-S and STAI-T scores were entered as additional control variables. In the third step, DES-II or TAS-20 total scores were entered to examine whether dissociation or alexithymia could independently account for a further proportion of variance in predicting TAS-20 or DES-II total scores, respectively.

Finally, the AMOS 27.0 and SPSS 27.0 statistical program were used to analyze the path models, obtain goodness-of-fit indices and

maximum-likelihood estimates of model parameters. The Variance Inflation Factor (VIF) was computed for each predictor and it always fell within the range (1.16 – 2.54) which is considered as evidence of a lack of substantial multicollinearity (Menard, 2002). Further examination of the data also indicated that the assumptions of linearity and homoscedasticity were met. Reported p values were two tailed, and p value <0.05 was considered significant. Associations of variables were analyzed before performing path analysis. In order to evaluate the model fit, $\chi 2$ and the root mean square error of approximation (RMSEA) were used as absolute fit indices; the comparative fit index (CFI) and the Tucker-Lewis index (TLI) were used as incremental fit indices in this study. A value of 0.90 or above for CFI and TLI, and the value of 0.06 or below for RMSEA were regarded as a "good fit". The $\chi 2$ values closer to zero indicate a better fit. $\chi 2$ was not recommended as a judgment of model fit because it is sensitive to the sample size used in the analysis of model fit (Park, 2018). Therefore, it was only reported but not used as a fit statistic in this study. Specifically, we used the following criteria for model fit (Marsh et al., 2004): TLI and CFI: values $\geq$ 0.90 indicated acceptable fit, values $\geq$ 0.95 indicated excellent fit; RMSEA: values $\leq$ 0.08 indicated acceptable fit, values $\leq$ 0.06 indicated excellent fit and we reported its 90% confidence interval (CI).

3. Results

3.1. Group comparisons

As a first step, we compared gender frequency and age among PNES, PNES+EP, EP and HC to evaluate gender and age homogeneity among groups. Gender frequency was not significantly different ($\chi^2(3) = 5.115$, $p = .164$), among all the four groups, as well as age ($F(3) = 0.086$, $p = .967$). Thus, PNES, PNES+EP, EP and HC groups were homogeneous regarding gender and age. Hence, we compared the scores shown by participants belonging to all the four groups regarding scales and subscales of the study measures. Regarding BDI-II, Kruskal-Wallis one way ANOVA (KW-ow-ANOVA) showed an overall significance ($H(3) = 26.988$, $p < .001$), and Dunn's post-hoc test revealed that both PNES and PNES+EP groups scored higher than EP and HC groups ($p < .05$ for both comparisons), while comparing PNES and PNES+EP groups and EP and HC groups there was not a significant difference ($p > .05$ for both comparisons). Comparison of scores among the four groups proved to be significant for STAI-S (KW-ow-ANOVA, $H(3) = 16.539$, $p < .001$) and STAI-T (KW-ow-ANOVA, $H(3) = 22.454$, $p <0.001$) and Dunn's post-hoc test showed that both PNES and PNES+EP groups scored significantly higher with respect to EP and HC for STAI-S ($p < .05$ for both comparisons) and STAI-T ($p < .05$ for both comparisons) as well. Post-hoc comparisons between PNES and PNES+EP and between EP and HC were found to be not significant ($p > .05$ for both comparisons). Comparisons related to TAS-20 total scores revealed an overall significant effect (KW-ow-ANOVA, $H(3) = 28.856$, $p < .001$) with Dunn's post-hoc test showing that both PNES and PNES+EP groups scored significantly higher with respect to EP and HC groups ($p < .05$ for both comparisons), while comparisons between PNES and PNES+EP and between EP and HC were found to be not significant ($p > .05$ for both comparisons). Regarding DES-II total scores, KW-ow-ANOVA revealed an overall significant effect ($H(3) = 11.983$, $p = .007$) with Dunn's post-hoc test showing that only PNES group scored significantly higher than PNES+EP, EP and HC groups ($p < .05$ for all comparisons), while comparisons among PNES+EP, EP and HC groups were not significantly different ($p > .05$ for all comparisons). To further specify the relationships between dissociation and alexithymia, we compared specific scores of TAS-20 and DES-II subscales. Regarding TAS-20-DIF subscale, KW-ow-ANOVA showed a marginal overall significance ($H(3) = 7.854$, $p = .049$); however, Dunn's post-hoc test revealed non-significant effects for all comparisons ($p > .05$). TAS-20-DDF comparisons revealed an overall significant effect (KW-ow-ANOVA, $H(3) = 23.883$, $p < .001$) and Dunn's post-hoc test showed that both PNES and PNES+EP groups scored significantly higher with respect to EP and HC groups ($p < .05$ for both comparisons), while comparisons between PNES and PNES+EP and between EP and HC were found to be not significant ($p > .05$ for both comparisons). Regarding TAS-20-EOT, the last TAS-20 subscale, a general significant effect was shown by KW-ow-ANOVA ($H(3) = 30.585$, $p < .001$), with Dunn's post-hoc test revealing that both PNES and PNES+EP groups scored significantly higher with respect to EP and HC groups ($p < .05$ for both comparisons), while comparisons between PNES and PNES+EP and between EP and HC were found to be not significant ($p > .05$ for both comparisons). In relation to DES-II subscales, we first analyzed comparisons regarding DES-II-Abs subscale. KW-ow-ANOVA showed an overall significant effect ($H(3) = 4.475$, $p = .009$), with Dunn's post-hoc test revealing that only PNES group scored significantly higher than PNES+EP, EP and HC groups ($p < .05$ for all comparisons), while comparisons among PNES+EP, EP and HC groups were not significantly different ($p > .05$ for all comparisons). DES-II-Amn and DES-II-Dep/Der subscale comparisons revealed a non-statistically significant difference (DES-II-Amn: $H(3) = 3.147$, $p = .369$; DES-II-Dep/Der: $H(3) = 2.007$, $p = .571$).

Zero-order correlations

Table 2 is related to the PNES group and shows the correlations of the scores of the DES-II and the TAS-20 scales and subscales with the other scales in this study. BDI-II scale showed very similar, moderate correlations with the STAI-T, DES-II-Tot and DES-II-Abs, suggesting that higher scores on depressive symptoms are associated with a higher tendency to show trait anxiety, overall dissociation and absorption. DES-II-Tot and TAS-20-Tot scores tended to be moderately, or strongly, correlated with their subscale scores (Dep/Der and Abs, and DIF, DDF and EOT, respectively), with the exception of DES-II-Tot and Amn subscale correlation that was found to be in the weak range. Notably, DIF and Dep/Der subscales were found to show a strong negative correlation suggesting that higher scores on difficulty identifying feelings are associated with a reduced tendency to depersonalization and derealization symptoms. Regarding PNES+EP group (supplementary table S1), BDI-II scale showed a strong correlation with the STAI-S, and STAI-S showed a strong correlation with the STAI-T, suggesting that higher scores on depressive symptoms are associated with a higher tendency to show state anxiety, and that higher scores on state anxiety are associated with a higher tendency to show trait anxiety as well. DES-II-Tot and TAS-20-Tot scores tended to be moderately, or strongly, correlated with their subscale scores (Abs, and DDF and EOT, respectively). DES-II subscale scores showed strong reciprocal positive correlations: Abs was found to be correlated with Amn and Dep/Der, while Amn was found to be correlated with Dep/Der suggesting that higher scores on absorption symptoms are associated with a higher tendency to show amnesia and depersonalization and derealization symptoms, and that higher scores on amnesia are associated with a higher tendency to show depersonalization and derealization symptoms. Notably, DDF and Abs subscales were found to show a strong positive correlation, suggesting that higher scores on difficulty describing feelings are associated with a higher tendency to absorption symptoms. Taken together, these results suggest a relationship between dissociation and alexithymia scores in both PNES and PNES+EP groups (see supplementary tables S2 and S3 for Spearman correlations among the study measures for EP and HC).

3.2. Regression analyses

In order to verify if DES-II or TAS-20 total scores were able to predict TAS-20 or DES-II total score, respectively, we carried out hierarchical multiple regression analyses. The VIF was computed for each predictor and it always fell within the range (1.16 – 2.54) which is considered as evidence of a lack of substantial multicollinearity (Menard, 2002). Further examination of the data also indicated that the assumptions of linearity and homoscedasticity were met. Results of the hierarchical multiple regression analyses predicting TAS-20 and DES-II total scores for PNES group and PNES+EP group are reported in supplementary

Table 2
Spearman correlations among the study measures for PNES sample ($n = 14$).

Measure	S	K	Range	1	2	3	4	5	6	7	8	9	10
1. BDI-II	−0.13	−0.60	2–31										
2. STAI-S	.01	.03	31–66	.32									
3. STAI-T	−0.08	−0.64	41–61	.61*	.63*								
4. TAS-20-Tot	−0.17	−0.65	43–84	.33	.28	.52							
5. TAS-20-DIF	−0.64	−1.37	6–24	−0.01	.00	.25	.71**						
6. TAS-20-DDF	−0.54	−0.62	11–32	.45	.29	.56*	.80**	.24					
7. TAS-20-EOT	−0.59	−0.57	19–30	.33	.43	.31	.65**	.19	.46				
8. DES-II-Tot	.11	−1.13	4.1–42.5	.60*	.08	.39	.25	−0.07	.51	.02			
9. DES-II-Abs	−0.20	−0.83	6.6–53.3	.67*	.46	.32	.20	−0.19	.55	.06	.80**		
10. DES-II-Amn	2.01	4.27	0.5–35	.12	.14	.59	.27	.28	.43	−0.25	.19	−0.01	
11. DES-II-Dep/Der	1.79	2.73	0–58.3	.51	.31	.25	−0.43	−0.77*	−0.01	−0.21	.80**	.60	−0.08

Note: *S*=Skewness; *K* = Kurtosis; BDI-II=Deck Depression Inventory - II; STAI-*S* = State-Trait Anxiety Inventory - State; STAI-*T* = State-Trait Anxiety Inventory - Trait; TAS-20-Tot = Toronto Alexithymia Scale – 20 – Total Score; TAS-20-DIF = Toronto Alexithymia Scale – 20 – Difficulty Identifying Feelings; TAS-20-DDF = Toronto Alexithymia Scale – 20 – Difficulty Describing Feelings; TAS-20-EOT = Toronto Alexithymia Scale – 20 – Externally Oriented Thinking; DES-II-Tot = Dissociative Experiences Scale – II – Total score; DES-II-Tot = Dissociative Experiences Scale – II – Absorption; DES-II-Amn = Dissociative Experiences Scale – II – Amnesia; DES-II-Dep/Der = Dissociative Experiences Scale – II – Depersonalization/Derealization.
*$p < .05$, ** $p < .01$.

tables S4 and S5, respectively.

Regarding PNES group, in the first step of the hierarchical multiple regression analysis predicting the TAS-20 total scores, age and gender did not explain a significant proportion of variance ($R^2 = 0.139$; $p > .05$). In the second step, entering the BDI-II, STAI-S and STAI-T scores did not significantly increase the variance explained (R^2 change = 0.234; $p > .05$). In the third step, entering the DES-II total scores did not significantly increase the variance explained (R^2 change = 0.004; $p > .05$). In this model, none of the considered variables emerged as significant individual predictors of the TAS-20 total scores. In the first step of the hierarchical multiple regression analysis predicting the DES-II total scores, age and gender did not explain a significant proportion of variance ($R^2 = 0.066$; $p > .05$). In the second step, entering the BDI-II, STAI-S and STAI-T scores did not significantly increase the variance explained (R^2 change = 0.346; $p > .05$). In the third step, entering the TAS-20 total scores did not significantly increase the variance explained (R^2 change = 0.004; $p > .05$). In this model, none of the considered variables emerged as significant individual predictors of the DES-II total scores as well.

Concerning PNES+EP group, in the first step of the hierarchical multiple regression analysis predicting the TAS-20 total scores, age and gender did not explain a significant proportion of variance ($R^2 = 0.31$; $p > .05$). In the second step, entering the BDI-II, STAI-S and STAI-T scores did not significantly increase the variance explained (R^2 change = 0.213; $p > .05$). In the third step, entering the DES-II total scores did not significantly increase the variance explained (R^2 change = 0.061; $p > .05$). In this model, none of the considered variables emerged as significant individual predictors of the TAS-20 total scores. In the first step of the hierarchical multiple regression analysis predicting the DES-II total scores, age and gender did not explain a significant proportion of variance ($R^2 = 0.403$; $p > .05$). In the second step, entering the BDI-II, STAI-S and STAI-T scores did not significantly increase the variance explained (R^2 change = 0.305; $p > .05$). In the third step, entering the TAS-20 total scores did not significantly increase the variance explained (R^2 change = 0.037; $p > .05$). In this model, none of the considered variables emerged as significant individual predictors of the DES-II total scores as well. Taken together, these results suggest that pooling the three subscales of both DES-II and TAS-20 may generate a masking effect of specific relationship that may be revealed at the subscale level.

3.3. Path analyses

In order to explore for possible specific relationship among DES-II and TAS-20 subscales, path analytic models were evaluated using AMOS 27 for both PNES and PNES+EP groups. Some variables analyzed showed slightly higher skewness and kurtosis: in PNES group, skewness ranged from −0.64 to 2.01, and kurtosis ranged from −1.37 to 4.27, while in PNES+EP group skewness ranged from −1.32 to 2.96, and kurtosis ranged from −1.84 to 8.82. Acceptable values of skewness fall between −3 and +3, and kurtosis is appropriate from a range of −10 to +10 when utilizing path analysis or structural equation modeling (SEM) (Brown, 2015; Griffin and Steinbrecher, 2013). Values that fall above or below these ranges are suspect, but path analysis and SEM are fairly robust analytical method, so small deviations may not represent major violations of assumptions (Griffin and Steinbrecher, 2013). The Maximum Likelihood (ML) estimator was used.

First, we evaluated if DES-II and TAS-20 subscales were able to predict TAS-20 and DES-II subscales, respectively, for both PNES and PNES-EP groups. In PNES group, Abs subscale was a unique significant predictor ($\beta = 0.951$, $p < .001$) of DDF subscale, and Dep/Der subscale was a unique significant predictor ($\beta = -1.053$, $p < .001$) of DDF subscale (Fig. 1). When inspecting if TAS-20 subscales were able to predict DES-II subscales, DIF and DDF were found to be significant predictors of Abs ($\beta = -0.546$, $p < .001$ for DIF; $\beta = 0.833$, $p < .001$ for DDF) and of Dep/Der ($\beta = -0.895$, $p < .001$ for DIF; $\beta = 0.510$, $p < .001$ for DDF) (Fig. 2).

In PNES+EP group, Abs subscale was a significant predictor ($\beta = 1$, $p < .001$) of DDF subscale and of EOT subscale ($\beta = 0.856$, $p < .01$). Amn subscale was a significant predictor ($\beta = -1.129$, $p < .05$) of EOT subscale, while Dep/Der was found to be a significant predictor of DDF ($\beta = -1.1221$, $p < .001$) (supplementary figure S1). Regarding TAS-20 subscales, DIF was found to be a significant predictor of both Abs ($\beta = -0.442$, $p < .05$) and Amn ($\beta = -0.586$, $p < .05$), while DDF was found

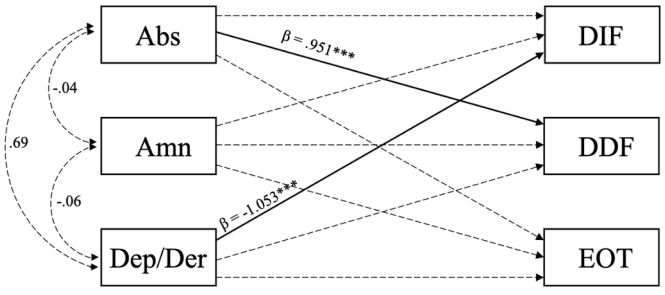

Fig. 1. Path analytic model related to DES-II subscales predicting TAS-20 subscales (PNES sample; $n = 14$).
Note: Dashed lines indicate non-significant relationships. Round boxes indicate errors. Abs = Absorption; Amn = Amnesia; Dep/Der = Depersonalization/Derealization; DIF = Difficulty Identifying Feelings; DDF = Difficulty Describing Feelings; EOT = Externally Oriented Thinking.
*$p < .05$, ** $p < .01$, ** $p < .001$, ***.

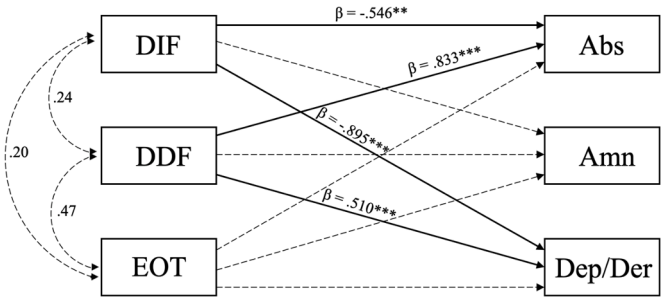

Fig. 2. Path analytic model related to TAS-20 subscales predicting DES-II subscales (PNES sample; $n = 14$).
Note: Dashed lines indicate non-significant relationships. Round boxes indicate errors. Abs = Absorption; Amn = Amnesia; Dep/Der = Depersonalization/Derealization; DIF = Difficulty Identifying Feelings; DDF = Difficulty Describing Feelings; EOT = Externally Oriented Thinking.
*$p < .05$, ** $p < .01$, ** $p < .001$, ***.

to be a significant predictor of Abs (β = 0.53, $p < .01$) (supplementary figure S2). Considering the values of < 0.90 or lower for CFI and NFI, and the value of 0.08 or higher for RMSEA, these models, though informative, were not regarded as a "good fit" for DES-II and TAS-20 subscales relationship. Hence, we further specified additional models among these variables that could represent a "good fit" following modification indices suggested by AMOS 27.

In PNES group among DES-II subscales, we found that Dep/Der was able to significantly predict both DIF (β = −0.79, $p < .001$, SE = 0.054) and Abs (β = 0.681, $p = .004$, SE = 0.187), but not DDF (β = 0.316, $p = .428$, SE = 0.112) . Finally, DDF was found to be significantly predicted by DIF (β = 0.814, $p = .013$, SE = 0.315) and by Abs (β = 0.765, $p = .006$, SE = 0.097). Overall, Dep/Der was found to be the unique DES-II variable to be fully mediated by both DIF and Abs in predicting DDF (Fig. 3) ($\chi 2$ (1) = 2.565, $p = .109$; CFI = 0.969, TLI = 0.961, RMSEA = 0.027 [.024; 0.030]). Among TAS-20 subscales, we found that DIF was able to significantly predict both Dep/Der (β = −0.802, $p < .001$, SE = 0.651), Abs (β = −0.555, $p = .005$, SE = 0.538), and DDF (β = 1.151, $p = .001$, SE = 0.37) as well. Finally, DDF was found to be significantly predicted by Dep/Der (β = 1.132, $p = .001$, SE = 0.104) and by Abs (β = 0.755, $p < .001$, SE = 0.515). Overall, DIF was found to be the unique TAS-20 variable to be partially mediated by both Dep/Der and Abs in predicting DDF (Fig. 4) ($\chi 2$ (1) = 0.137, $p = .934$; CFI = 0.942, TLI = 0.933, RMSEA = 0.035 [.032; 0.038]).

In PNES+EP group among DES-II subscales, we found that Dep/Der was able to significantly predict both Abs (β = 0.69, $p = .004$, SE = 0.351) and DDF (β = −0.708, $p = .006$, SE = 0.207). In addition, Abs was found to be a significant predict of DDF (β = 1.126, $p < .001$, SE = 0.135) and EOT (β = 0.562, $p = .027$, SE = 0.129). Overall, Dep/Der was found to be the unique DES-II variable to be partially mediated by Abs in predicting DDF. Abs was also found to be an independent variable in predicting EOT (supplementary figure S3) ($\chi 2$ (1) = 0.978, $p = 1.367$; CFI = 0.957, TLI = 0.948, RMSEA = 0.031 [0.028; 0.034]). Among TAS-20 subscales, we found that DIF was able to significantly predict Amn (β = −0.598, $p = .027$, SE = 0.564) but not Abs (β = −0.254, $p = .222$, SE = 0.428), while DDF was able to significantly predict Abs (β = 582, $p <$ 001, SE = 0.305). Finally, Abs was found to be significantly predicted by Amn (β = 0.467, $p = .025$, SE = 0.205). Overall, DIF was found to be the unique TAS-20 variable to be fully mediated by both Amn in predicting Abs. Abs was also found to be predicted by DDF (supplementary figure S4) (χ^2 (1) = 1.251, $p = .263$; CFI = 0.957, TLI = 0.948, RMSEA = 0.031 [.028; 0.034]).

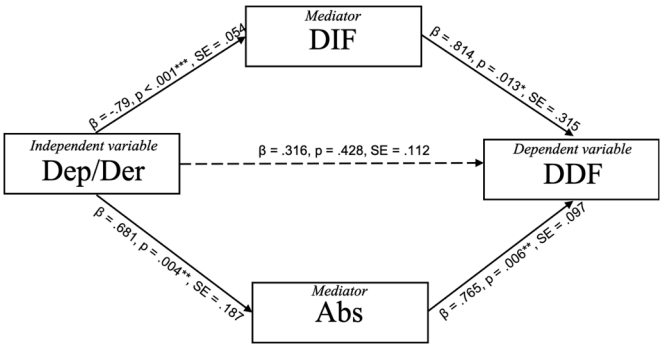

Fig. 3. Path analytic model showing Dep/Der as unique DES-II independent variable fully mediated by DIF and Abs in predicting DDF (PNES sample; $n = 14$).
Note: Dashed lines indicate non-significant relationships. Abs = Absorption; Dep/Der = Depersonalization/Derealization; DIF = Difficulty Identifying Feelings; DDF = Difficulty Describing Feelings.
*$p < .05$, ** $p < .01$, ** $p < .001$, ***.

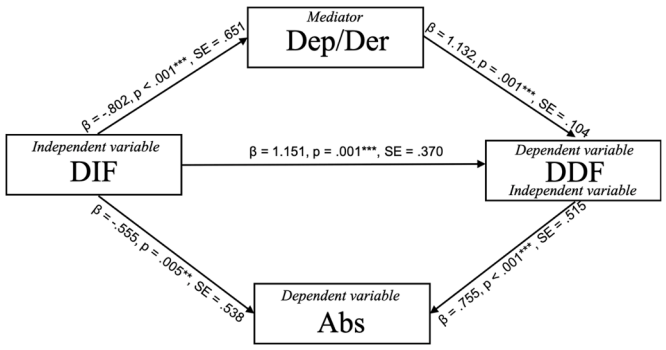

Fig. 4. Path analytic model showing DIF as unique TAS-20 independent variable partially mediated by Dep/Der in predicting DDF and predicting Abs along with DDF (PNES sample; $n = 14$).
Note: Dashed lines indicate non-significant relationships. Abs = Absorption; Dep/Der = Depersonalization/Derealization; DIF = Difficulty Identifying Feelings; DDF = Difficulty Describing Feelings.
*$p < .05$, ** $p < .01$, ** $p < .001$, ***.

4. Discussion

Between groups comparisons demonstrate that only PNES patients show higher levels of dissociation, in particular Abs and Dep/Der, even if the latter is not significant at the level of between groups comparisons. Interestingly, considering the dissociative qualities of detachment (defined as the subjective experience of an altered state of consciousness, characterized by a sense of separation from certain aspects of everyday experience, be it the body, the sense of self, or the external world) and compartmentalization (defined as the ability to deliberately control processes or actions that would normally be amenable to such control) (Brown, 2006; Holmes et al., 2005), both Abs and Dep/Der have been found to be related to the domain of detachment (Mazzotti et al., 2016). Conversely, both PNES and PNES+EP patients show higher levels of alexithymia and comorbid depressive and anxious symptomatology, suggesting that the difficulties related to identifying and describing feelings may play an important role in both PNES and PNES+EP patients. However, the interaction between dissociation and alexithymia is unclear and may be bidirectional in nature. An investigation of DES-II and TAS-20 subscales may promote a deeper understanding of this relationship. Accordingly, In PNES group, Spearman correlations revealed that Dep/Der and DIF showed a strong negative significant correlation, while in PNES+EP sample, DDF and Abs, and EOT and Abs showed a strong positive significant correlation, confirming the presence of specific, subscale level, relationships.

Unfortunately, predictor variables that are not significantly related to outcome variables are often eliminated at the bivariate level. Bivariate results, such as zero-order correlation coefficients, provide only

partial information about the relationship between a predictor and an outcome variable, and are an improper method for selecting variables for a multiple regression model. Some variables may act as suppressor variables, in particular when these variables are theoretically related (i.e., different subscales of the same dissociation or alexithymia construct). A suppressor variable correlates with other potential independent variables, and accounts for, or suppresses, some outcome-irrelevant variation or errors in one or more other predictors, and improves the overall predictive power of a model even when they are uncorrelated with outcome variables in zero-order correlation (Pandey and Elliott, 2010). Nevertheless, researchers often prematurely eliminate these variables during their variable selection process based on the variable's very low bivariate correlation with the dependent variable (Shieh, 2006; Velicer, 1978). However, eliminating these uncorrelated variables will cause the researcher to underestimate some of the parameters, will undermine the predictive power of the model, and may yield regression equations which are overly sample-specific. Therefore, to accurately assess the contribution of each independent variable to the dependent variable, all theoretically relevant independent variables must be retained, including those variables that may not be correlated with the dependent variable at the bivariate level. Parsimonious use of a number of independent variables in regression models increases statistical power of tests (Cohen, 2013; Tabachnick and Fidell, 2013), but elimination of theoretically relevant variables may result in underestimation of parameters (Pandey and Elliott, 2010; Tonidandel and LeBreton, 2011).

For these reasons, we performed hierarchical regression analyses including DES-II and TAS-20 total scores, to retain all the subscales. Controlling for demographic variables and depression and anxiety scores, we found that nor DES-II neither TAS-20 total scores were able to significantly predict TAS-20 and DES-II total scores, respectively, possibly due to reciprocal suppressor variable effects, due to the subscale score pooling.

Following modification indexes of AMOS 27, in PNES group we found that Dep/Der were fully mediated by DIF and Abs in predicting DDF. Considering the negative strong correlation between Dep/Der and DIF, it can be hypothesized that Dep/Der and DIF symptoms emerge as consecutive self-protection mechanisms aimed at avoiding the re-emergence of traumatic memories. Since dissociation involves a change of one's sense of self, whereas alexithymia reflects a cognitive state of externally oriented thinking with an inability to identify and report discrete emotions (Wise et al., 2000), dissociative symptoms (in particular, Dep/Der and Amn symptoms) may be more disruptive than alexithymic symptoms. Thus, to avoid the emergence of dissociative Dep/Der symptoms, DIF symptoms could be preferentially shown and promoted. Accordingly, investigating depersonalization disorder, it has been shown that the ascertained brain regions for TAS-20 subscales subserve interoception, and that alexithymia plays a substantial role in emotional dysregulation in depersonalization disorder, presumably based on restrictions in interoception (Lemche et al., 2013), and, thus, by increasing the levels of DIF and DDF. Simultaneously, to implement DIF symptoms, at the alexithymia level, Abs may be required on the dissociation level. Finally, DIF and Abs together may generate the final outcome of DDF. Similarly, when investigating TAS-20 subscales predicting DES-II subscales, DIF is able to predict Dep/Der. Thus, when low levels of DIF are present, Dep/Der levels are increased and, simultaneously, Abs is needed, possibly to alleviate Dep/Der effects. Overall, Dep/Der and a partial effect of DIF, implement DDF, while both DIF and DDF implement Abs, possibly to alleviate Dep/Der effects.

In PNES+EP group, in accordance with PNES group, we found that Dep/Der was able to directly predict DDF, with a partial mediation of Abs. It can be hypothesized that Abs facilitates the implementation of DDF promoting EOT symptoms. When investigating if TAS-20 subscales were able to predict DES-II subscales in PNES+EP group, DDF was able to reciprocally promote Abs, and DIF effect on Abs was fully mediated by Amn. Considering that also in the case of PNES+EP group, the relationship between DIF and Amn has shown a negative β, it can be hypothesized that in case of a reduction of DIF symptoms, the emergence of Amn symptoms would be required. DIF symptoms have been shown in case of dissociative amnesia (Krause-Utz et al., 2017), and dissociation has been shown that can occur as a result of trauma, epilepsy or dissociative drug use (American Psychiatric Association, 2013; Krystal, 1994). Thus, regarding PNES+EP group, it could hypothesized that the co-occurrence of actual EP events may impact on a dissociative mind and be perceived as overwhelming and uncontrollable by the patients, so that Abs and EOT may be favored in order to promote an externally oriented thinking to rely on the activity of brain regions related to the salience network and the central executive network, avoiding the activity of brain regions related to the default mode network that are related to the self and to autobiographical memories (Menon, 2011; Menon and Uddin, 2010;). In addition, as in PNES group, DIF may be promoted to avoid the emergence of Amn symptoms, that are related to the compartmentalization quality of dissociation (Mazzotti et al., 2016).

Accordingly, in mice it has been shown that, after administration of the precisely-dosed dissociative agents ketamine or phencyclidine, large-scale imaging of neural activity revealed that these agents elicited a 1–3-Hz rhythm in layer 5 neurons of the retrosplenial cortex, and, testing for causal significance, it was found that rhythmic optogenetic activation of retrosplenial cortex layer 5 neurons recapitulated dissociation-like behavioral effects. Similarly, in a patient with focal epilepsy, simultaneous intracranial stereoencephalography recordings from across the brain revealed a similarly localized rhythm in the homologous deep posteromedial cortex that was temporally correlated with pre-seizure self-reported dissociation, and local brief electrical stimulation of this region elicited dissociative experiences (Vesuna et al., 2020). Taken together, these results suggest that dissociation and alexithymia show a complex differential interplay in PNES and PNES-EP. In PNES, Dep/Der and DIF may play a prominent role. Promoting DIF improvement may unmask Dep/Der symptoms, as a subsequent protection from a possible excessively rapid re-emergence of past traumatic memories (Grenevald et al., 2021). Thus, both DIF and Dep/Der dimensions need to be taken into account and treatment of DIF symptoms should be carefully administered. In PNES+EP, Dep/Der, Abs, DIF and Amn may play a prominent complex role. Similarly to what has been observed in PNES group, promoting DIF may unmask Amn symptoms as a subsequent protection from the re-emergence of past traumatic memories. Thus, in both PNES and PNES+EP groups, psychotherapeutical intervention should simultaneously take into account DIF, Dep/Der and Amn symptoms, as well as the possible re-emergence of traumatic memories, to address the treatment of psychological symptoms of PNES and PNES+EP patients.

The following limitations should however be considered. 1) Our study is cross-sectional and the specific temporal order of the variables cannot be defined; alternative orders have not been ruled out and it is possible that these relationships are bi-directional in nature. Longitudinal studies are essential in order to draw conclusions about changes occurring within the individual over time. 2) Participants were self-selected; this might limit the generalizability of our conclusions. 3) All of the data was derived from self-report measures; relying exclusively on self-report data tends to inflate associations among variables. 4) The samples of patients are relatively small. 5) We conducted may statistical analyses and additional research with wider samples of patients will be needed to confirm our results.

Considering our findings, PNES patients show symptoms related to the detachment quality of dissociation, while patients with PNES+EP show symptoms related to both detachment and compartmentalization qualities of dissociation. Thus, PNES patients may benefit from grounding techniques, modulation of arousal, and prevention of detachment triggers (Ogden, 2015; Ogden et al., 2006), while PNES+EP patients, in addition to grounding techniques, modulation of arousal, and prevention of detachment triggers, may also benefit from treatment based on integration of functions and contents (i.e., parts of personalities, body representation, and control) (Steele et al., 2017; van der Hart

et al., 2006) and from Eye Movement Desensitization and Reprocessing (EMDR), in order to process, and to stimulate the re-emergence, of dissociated traumatic memories (Shapiro, 2018). However, we can't exclude that, also in PNES group, compartmentalization symptoms may be present, but protected by Dep/Der and DIF symptoms, thus the recommendation is to consider EMDR and other integrative treatments for these patients as well.

Author contributions

Conceptualization, Andrea Poli; methodology, Andrea Poli. and M. M.; validation, Andrea Poli, A.G.I.M. and M.M.; formal analysis, Andrea Poli; investigation, Andrea Poli. and M.M.; resources, A.G.I.M., C.C., G. M., A.G., Andrea Pozza; data curation, Andrea Poli and M.M.; writing—original draft preparation, Andrea Poli; writing—review and editing, Andrea Poli, Andrea Pozza and M.M.; supervision, M.M.; project administration, Andrea Poli and M.M.; All authors have read and agreed to the published version of the manuscript.

Role of funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Conflicts of interest/Competing interests

The authors declare that they have no conflict of interest

Acknowledgements

None

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jadr.2021.100296.

References

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Publishing, Book, Arlington, VA.

Asadi-Pooya, A.A., 2020. International multicenter studies on psychogenic nonepileptic seizures: a systematic review. Psychiatry Res. 285, 112812 https://doi.org/10.1016/j.psychres.2020.112812.

Asadi-Pooya, A.A., 2015. Neurobiological origin of psychogenic nonepileptic seizures: a review of imaging studies. Epilepsy Behav. 52, 256–259. https://doi.org/10.1016/j.yebeh.2015.09.020.

Bagby, R.M., Parker, J.D.A., Taylor, G.J., 1994a. The twenty-item Toronto Alexithymia scale—I. Item selection and cross-validation of the factor structure. J. Psychosom. Res. 38, 23–32. https://doi.org/10.1016/0022-3999(94)90005-1.

Bagby, R.M., Taylor, G.J., Parker, J.D.A., 1994b. The twenty-item Toronto Alexithymia scale—II. Convergent, discriminant, and concurrent validity. J. Psychosom. Res. 38, 33–40. https://doi.org/10.1016/0022-3999(94)90006-X.

Bakvis, P., Spinhoven, P., Putman, P., Zitman, F.G., Roelofs, K., 2010. The effect of stress induction on working memory in patients with psychogenic nonepileptic seizures. Epilepsy Behav. 19, 448–454. https://doi.org/10.1016/j.yebeh.2010.08.026.

Baroni, G., Piccinini, V., Martins, W.A., de Paola, L., Paglioli, E., Margis, R., Palmini, A., 2016. Variables associated with co-existing epileptic and psychogenic nonepileptic seizures: a systematic review. Seizure 37, 35–40. https://doi.org/10.1016/j.seizure.2016.02.003.

Baslet, G., 2011. Psychogenic non-epileptic seizures: a model of their pathogenic mechanism. Seizure 20, 1–13. https://doi.org/10.1016/j.seizure.2010.10.032.

Beau, M., 1836. Recherches statistiques pour servir al'histoire de l'épilepsie et de l'hystérie. Arch Gen Med 328–352.

Beck, A.T., Steer, R.A., Brown, G., 1996. Manual For the Beck Depression Inventory-II. Psychological Corporation, San Antonio, TX.

Benbadis, S.R., Agrawal, V., Tatum, W.O., 2001. How many patients with psychogenic nonepileptic seizures also have epilepsy? Neurology 57, 915–917. https://doi.org/10.1212/WNL.57.5.915.

Bombi, A.F., Bertin, I., Cristante, F., Colombo, G., 1996. Un contributo alla standardizzazione della Dissociative Experiences Scale (DES) di Bernstein e Putnam [A contribution to the standardization of the Dissociative Experiences Scale (DES) of Bernstein and Putnam]. Giunti Organizzazioni Speciali 219, 39–46.

Bressi, C., Taylor, G., Parker, J., Bressi, S., Brambilla, V., Aguglia, E., Allegranti, I., Bongiorno, A., Giberti, F., Bucca, M., Todarello, O., Callegari, C., Vender, S., Gala, C., Invernizzi, G., 1996. Cross validation of the factor structure of the 20-item Toronto Alexithymia Scale: an Italian multicenter study. J. Psychosom. Res. 41, 551–559. https://doi.org/10.1016/S0022-3999(96)00228-0.

Brown, R.J., 2006. Different Types of "Dissociation" Have Different Psychological Mechanisms. J. Trauma Dissociation 7, 7–28. https://doi.org/10.1300/J229v07n04_02.

Brown, T.A., 2015. Confirmatory factor analysis for applied research. ed, Methodology in the Social Sciences, 2nd edition. The Guilford Press, New York London.

Carlson, E.B., Putnam, F.W., 1993. An update on the Dissociative Experiences Scale. Dissociation 6, 16–27.

Clancy, K., Ding, M., Bernat, E., Schmidt, N.B., Li, W., 2017. Restless 'rest': intrinsic sensory hyperactivity and disinhibition in post-traumatic stress disorder. Brain 140, 2041–2050. https://doi.org/10.1093/brain/awx116.

Cohen, 2013. Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences, 3rd ed. Routledge. https://doi.org/10.4324/9780203774441.

Conti, L., 2000. Handbook of Clinical Rating Scales and Assessment in Psychiatry. SEE, Firenze, Florence.

Devinsky, O., Gazzola, D., LaFrance, W.C., 2011. Differentiating between nonepileptic and epileptic seizures. Nat. Rev. Neurol. 7, 210–220. https://doi.org/10.1038/nrneurol.2011.24.

Eichhorn, S., Brähler, E., Franz, M., Friedrich, M., Glaesmer, H., 2014. Traumatic experiences, alexithymia, and posttraumatic symptomatology: a cross-sectional population-based study in Germany. Eur. J. Psychotraumatol. 5, 23870. https://doi.org/10.3402/ejpt.v5.23870.

Elzinga, B.M., Bermond, B., van Dyck, R., 2002. The Relationship between Dissociative Proneness and Alexithymia. Psychother. Psychosom. 71, 104–111. https://doi.org/10.1159/000049353.

Garofalo, C., Velotti, P., Zavattini, G.C., Tommasi, M., Romanelli, R., Espirito-Santo, H., Saggino, A., 2015. On the factor structure of the Dissociative Experiences Scale: contribution with an Italian version of the DES-II. Psychiatria I Psychologia Kliniczna 15, 4–12. https://doi.org/10.15557/PiPK.2015.0001.

Goerlich, K.S., 2018. The Multifaceted Nature of Alexithymia – A Neuroscientific Perspective. Front. Psychol. 9, 1614. https://doi.org/10.3389/fpsyg.2018.01614.

Grenevald, L., Gagny, M., Maillard, L., Chrusciel, J., Sanche, S., Schwan, R., Klemina, I., Biberon, J., de Toffol, B., Thiriaux, A., Visseaux, J.F., Martin, M.L., Meyer, M., Hage, W.E., Hingray, C., 2021. Post-traumatic factors are involved in the evolution of the number of seizures in patients with PNES. Epilepsy Behav. 115, 107544 https://doi.org/10.1016/j.yebeh.2020.107544.

Griffin, M.M., Steinbrecher, T.D., 2013. Large-Scale Datasets in Special Education Research. Int. Rev. Res. Dev. Disabil. 155–183. https://doi.org/10.1016/B978-0-12-407760-7.00004-9.

Hamed, S.A., Attiah, F.A., Fawzy, M., 2020. Psychogenic nonepileptic seizures in adults with epilepsy: a tertiary hospital-based study. Int. J. Neurosci. 130, 522–532. https://doi.org/10.1080/00207454.2019.1698566.

Hingray, C., Maillard, L., Hubsch, C., Vignal, J.-P., Bourgognon, F., Laprevote, V., Lerond, J., Vespignani, H., Schwan, R., 2011. Psychogenic nonepileptic seizures: characterization of two distinct patient profiles on the basis of trauma history. Epilepsy Behav. 22, 532–536. https://doi.org/10.1016/j.yebeh.2011.08.015.

Holmes, E., Brown, R., Mansell, W., Fearon, R., Hunter, E., Frasquilho, F., Oakley, D., 2005. Are there two qualitatively distinct forms of dissociation? A review and some clinical implications. Clin. Psychol. Rev. 25, 1–23. https://doi.org/10.1016/j.cpr.2004.08.006.

Krause-Utz, A., Frost, R., Winter, D., Elzinga, B.M., 2017. Dissociation and Alterations in Brain Function and Structure: implications for Borderline Personality Disorder. Curr. Psychiatry Rep. 19, 6. https://doi.org/10.1007/s11920-017-0757-y.

Krystal, J.H., 1994. Subanesthetic Effects of the Noncompetitive NMDA Antagonist, Ketamine, in Humans: psychotomimetic, Perceptual, Cognitive, and Neuroendocrine Responses. Arch. Gen. Psychiatry 51, 199. https://doi.org/10.1001/archpsyc.1994.03950030035004.

LaFrance, W.C., Baker, G.A., Duncan, R., Goldstein, L.H., Reuber, M., 2013. Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: a staged approach: a report from the International League Against Epilepsy Nonepileptic Seizures Task Force. Epilepsia 54, 2005–2018. https://doi.org/10.1111/epi.12356.

Lemche, E., Brammer, M.J., David, A.S., Surguladze, S.A., Phillips, M.L., Sierra, M., Williams, S.C.R., Giampietro, V.P., 2013. Interoceptive–reflective regions differentiate alexithymia traits in depersonalization disorder. Psychiatry Res.g 214, 66–72. https://doi.org/10.1016/j.pscychresns.2013.05.006.

Marsh, H.W., Hau, K.-T., Wen, Z., 2004. Search of Golden Rules: comment on Hypothesis-Testing Approaches to Setting Cutoff Values for Fit Indexes and Dangers in Overgeneralizing Hu and Bentler's (1999) Findings. Struct.l Equ. Model. 11, 320–341. https://doi.org/10.1207/s15328007sem1103_2.

Martino, I., Bruni, A., Labate, A., Vasta, R., Cerasa, A., Borzì, G., De Fazio, P., Gambardella, A., 2018. Psychopathological constellation in patients with PNES: a new hypothesis. Epilepsy Behav. 78, 297–301. https://doi.org/10.1016/j.yebeh.2017.09.025.

Mazzotti, E., Farina, B., Imperatori, Claudio, Mansutti, F., Prunetti, E., Speranza, A.M., Barbaranelli, C., 2016. Is the Dissociative Experiences Scale able to identify detachment and compartmentalization symptoms? Factor Structure of the Dissociative Experiences Scale in a Large Sample of Psychiatric and Nonpsychiatric subjects. NDT 1295 https://doi.org/10.2147/NDT.S105110.

Menard, S., 2002. Applied Logistic Regression Analysis. SAGE Publications, Inc., 2455 Teller Road, Thousand Oaks California 91320. United States of America. https://doi.org/10.4135/9781412983433.

Menon, V., 2011. Large-scale brain networks and psychopathology: a unifying triple network model. Trends Cogn. Sci. (Regul. Ed.) 15, 483–506. https://doi.org/10.1016/j.tics.2011.08.003.
Menon, V., Uddin, L.Q., 2010. Saliency, switching, attention and control: a network model of insula function. Brain Structure and Function 214, 655–667. https://doi.org/10.1007/s00429-010-0262-0.
Myers, L., Fleming, M., Lancman, Martin, Perrine, K., Lancman, Marcelo, 2013a. Stress coping strategies in patients with psychogenic non-epileptic seizures and how they relate to trauma symptoms, alexithymia, anger and mood. Seizure 22, 634–639. https://doi.org/10.1016/j.seizure.2013.04.018.
Myers, L., Matzner, B., Lancman, Martin, Perrine, K., Lancman, Marcelo, 2013b. Prevalence of alexithymia in patients with psychogenic non-epileptic seizures and epileptic seizures and predictors in psychogenic non-epileptic seizures. Epilepsy Behav. 26, 153–157. https://doi.org/10.1016/j.yebeh.2012.11.054.
Myers, L., Trobliger, R., Bortnik, K., Zeng, R., Saal, E., Lancman, M., 2019. Psychological trauma, somatization, dissociation, and psychiatric comorbidities in patients with psychogenic nonepileptic seizures compared with those in patients with intractable partial epilepsy. Epilepsy Behav. 92, 108–113. https://doi.org/10.1016/j.yebeh.2018.12.027.
Oathes, D.J., Ray, W.J., 2008. Dissociative tendencies and facilitated emotional processing. Emotion 8, 653–661. https://doi.org/10.1037/a0013442.
Ogden, P., 2015. Sensorimotor psychotherapy: interventions for trauma and attachment. Norton Series On Interpersonal Neurobiology, 1st edition. W.W. Norton & Company, New York.
Ogden, P., Minton, K., Pain, C., 2006. Trauma and the body: a Sensorimotor Approach to Psychotherapy, 1st ed. W.W. Norton, New York. The Norton series on interpersonal neurobiology.
Pandey, S., Elliott, W., 2010. Suppressor Variables in Social Work Research: ways to Identify in Multiple Regression Models. J Soc Social Work Res 1, 28–40. https://doi.org/10.5243/jsswr.2010.2.
Park, E.-Y., 2018. Path analysis of strength, spasticity, gross motor function, and health-related quality of life in children with spastic cerebral palsy. Health Qual. Life Outcomes 16, 70. https://doi.org/10.1186/s12955-018-0891-1.
Pedrabissi, L., Santinello, M., 1989. Verifica Della Validità Dello STAI Forma Y di Spielberger. [Verification of the Validity of the STAI-Y]. Giunti Organizzazioni Speciali, Firenze, Italy.
Pinna, F., Manchia, M., Paribello, P., Carpiniello, B., 2020. The Impact of Alexithymia on Treatment Response in Psychiatric Disorders: a Systematic Review. Front. Psychiatry 11, 311. https://doi.org/10.3389/fpsyt.2020.00311.
Popkirov, S., Jungilligens, J., Grönheit, W., Wellmer, J., 2017. Diagnosing psychogenic nonepileptic seizures: video-EEG monitoring, suggestive seizure induction and diagnostic certainty. Epilepsy Behav. 73, 54–58. https://doi.org/10.1016/j.yebeh.2017.05.027.
Preece, D.A., Becerra, R., Robinson, K., Allan, A., Boyes, M., Chen, W., Hasking, P., Gross, J.J., 2020. What is alexithymia? Using factor analysis to establish its latent structure and relationship with fantasizing and emotional reactivity. J. Pers. 88, 1162–1176. https://doi.org/10.1111/jopy.12563.
Reuber, M., House, A.O., Pukrop, R., Bauer, J., Elger, C.E., 2003. Somatization, dissociation and general psychopathology in patients with psychogenic non-epileptic seizures. Epilepsy Res. 57, 159–167. https://doi.org/10.1016/j.eplepsyres.2003.11.004.
Roberts, N.A., Burleson, M.H., Weber, D.J., Larson, A., Sergeant, K., Devine, M.J., Vincelette, T.M., Wang, N.C., 2012. Emotion in psychogenic nonepileptic seizures: responses to affective pictures. Epilepsy Behav. 24, 107–115. https://doi.org/10.1016/j.yebeh.2012.03.018.
Roberts, N.A., Reuber, M., 2014. Alterations of consciousness in psychogenic nonepileptic seizures: emotion, emotion regulation and dissociation. Epilepsy Behav. 30, 43–49. https://doi.org/10.1016/j.yebeh.2013.09.035.
Rosales, R., Dworetzky, B., Baslet, G., 2020. Cognitive-emotion processing in psychogenic nonepileptic seizures. Epilepsy Behav. 102, 106639 https://doi.org/10.1016/j.yebeh.2019.106639.
Shapiro, F., 2018. Eye Movement Desensitization and Reprocessing (EDMR) therapy: Basic principles, protocols, and procedures, Third edition. The Guilford Press, New York.
Shieh, G., 2006. Suppression Situations in Multiple Linear Regression. Educ. Psychol. Meas. 66, 435–447. https://doi.org/10.1177/0013164405278584.
Sica, C., Ghisi, M., 2007. The Italian versions of the Beck Anxiety Inventory and the Beck Depression Inventory-II: psychometric properties and discriminant power. In: Lange, M.A. (Ed.), Leading-Edge Psychological Tests and Testing Research. Nova Science Publisher, Inc., pp. 27–50
Sifneos, P.E., 1973. The Prevalence of 'Alexithymic' Characteristics in Psychosomatic Patients. Psychother. Psychosom. 22, 255–262. https://doi.org/10.1159/000286529.
Spielberger, C.D., Gorsuch, R.L., Lushene, R., Vagg, P.R., Jacobs, G.A., 1983. Manual For the State-Trait Anxiety Inventory. Consulting Psychologists Press, Palo Alto, CA.
Starita, F., Làdavas, E., di Pellegrino, G., 2016. Reduced anticipation of negative emotional events in alexithymia. Sci. Rep. 6, 27664. https://doi.org/10.1038/srep27664.
Steele, K., Boon, S., Hart, O.van der, 2017. Treating Trauma-Related dissociation: a practical, Integrative approach, A Norton Professional Book. W. W. Norton & Company, New York London.
Tabachnick, B.G., Fidell, L.S., 2013. Using multivariate statistics, 6th ed. Pearson, Boston, MA.
Tonidandel, S., LeBreton, J.M., 2011. Relative importance analysis: a useful supplement to regression analysis. J. Bus. Psychol. 26, 1–9. https://doi.org/10.1007/s10869-010-9204-3.
Urbanek, M., Harvey, M., McGowan, J., Agrawal, N., 2014. Regulation of emotions in psychogenic nonepileptic seizures. Epilepsy Behav. 37, 110–115. https://doi.org/10.1016/j.yebeh.2014.06.004.
van der Hart, O., Nijenhuis, E.R.S., Steele, K., 2006. The haunted self: structural dissociation and the treatment of chronic traumatization. The Norton series On Interpersonal Neurobiology, 1st ed. W.W. Norton, New York.
Velicer, W.F., 1978. Suppressor Variables and the Semipartial Correlation Coefficient. Educ. Psychol. Meas. 38, 953–958. https://doi.org/10.1177/001316447803800415.
Vesuna, S., Kauvar, I.V., Richman, E., Gore, F., Oskotsky, T., Sava-Segal, C., Luo, L., Malenka, R.C., Henderson, J.M., Nuyujukian, P., Parvizi, J., Deisseroth, K., 2020. Deep posteromedial cortical rhythm in dissociation. Nature 586, 87–94. https://doi.org/10.1038/s41586-020-2731-9.
Widdess-Walsh, P., Nadkarni, S., Devinsky, O., 2018. Comorbidity of Epileptic and Psychogenic Nonepileptic Seizures: diagnostic Considerations. In: LaFrance Jr, W.C., Schachter, S.C. (Eds.), Gates and Rowan's Nonepileptic Seizures. Cambridge University Press, pp. 58–70. https://doi.org/10.1017/9781316275450.006.
Wilkins, S.S., Mesraoua, B., Palomo, G.A., Al Hail, H., Salam, A., Melikyan, G., Azar, N., Haddad, N., Uthman, B., Siddiqi, M., Elsheikh, L., Ali, M., Alrabi, A., Shuaib, A., Deleu, D., Asadi-Pooya, A.A., 2018. Characteristics of patients with confirmed epilepsy and psychogenic nonepileptic seizures in Qatar. Epilepsy Behav. 85, 218–221. https://doi.org/10.1016/j.yebeh.2018.06.014.
Wise, T.N., Mann, L.S., Sheridan, M.J., 2000. Relationship between Alexithymia, Dissociation and Personality in Psychiatric Outpatients. Psychother. Psychosom. 69, 123–127. https://doi.org/10.1159/000012379.