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Clinical differences between patients with psychogenic nonepileptic seizures and functional motor disorder

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ABSTRACT

Objectives: Why a patient might present with psychogenic nonepileptic seizures (PNES) as opposed to another functional neurological symptom is unknown. A recent review suggested that patients with PNES and functional motor disorders (FMD) differ on demographic and clinical factors of potential aetiological and mechanistic significance, arguing they might represent different disorders, though direct comparisons are limited. We sought to determine whether these factors differed in patients presenting with FMD and PNES at our clinic, as well as whether preceding medical complaints would differ between the two, particularly those affecting the limbs or head.
Methods: A retrospective chart review of all presentations with FMD or PNES patients to a functional neurology clinic, collecting demographic and clinical data, including medical and surgical history.
Results: Fifty-six patients with FMD and 52 with PNES were included. Significantly more patients with FMD had functional somatic syndromes (46% vs 27%, $p = 0.036$) and preceding medical events that affected their limbs than patients with PNES (34% vs 14%, $p = 0.013$); significantly more patients with PNES had dissociative symptoms (31% vs 4%, $p < 0.001$) and lifetime suicidal ideation (56% vs 32%, $p = 0.013$).
Significance: These results highlight the substantial comorbidities affecting FMD and PNES, but find clinical differences between the two groups that may be of aetiological or mechanistic significance.

1. Introduction

Functional neurological disorder is a condition characterized by neurological symptoms of voluntary motor or sensory function which cannot be explained by neurological disease or other medical conditions [1,2]. The two most common presentations are with functional motor symptoms and psychogenic nonepileptic seizures, however why a patient would present with one symptom rather than another is unclear. A number of studies have compared samples of patients with these presentations, and a review we conducted of these suggested there were differences between the two groups that may partly explain their presentations [3]. Patients with psychogenic nonepileptic seizures tended to be younger, and to present earlier, to have stronger histories of childhood adversity and adult psychological trauma, and to experience more dissociation. We argued these would support divergent aetiologies for PNES and functional motor disorders, though the studies reviewed were mainly small, and concerns remained about differing selection biases between the constituent PNES and FMD samples – for example being recruited from different clinics [4] or using different criteria [5].

Other factors which may contribute to symptom presentation come from the patient's medical history in several ways. It has long been argued that functional symptoms are dependent on the individual's *idea* of disease and by expectations of how the brain and body work [6–8], which may vary depending on their clinical history. An association of the patient's symptom with a pre-existing medical 'model' for it has been described, whether experienced in the patient themselves, or observed in someone close to them [9]. A medical complaint may focus the attention on the affected limb, galvanizing abnormal illness expectations [10]. Others suggest physical trauma or disease may trigger symptoms by impacting the stress pathways within the brain and body [11–14]. However, they might operate, such preceding medical events are

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certainly common in FMD and PNES. A systematic review found physical injuries at onset in 37% of a sample of 869 FMD patients [13], and organic disease has been reported in up to 60% [15]; while in patients with PNES, 10–15% have epilepsy [16,17] and 32% antecedent head injury [18]. However, whether these proportions differ between FMD and PNES is unknown.

The aim of the current study was to determine whether the demographic and clinical differences between samples of FMD and PNES that our review reported [3] would be found in a sample collected using the same method from the same source, and whether medical events that impact different parts of the body prior to symptom onset might also differ between FMD and PNES. We hypothesized that the differences reported in our review would be confirmed in this sample, and that patients with FMD would have a higher proportion of medical events related to their limbs, while patients with PNES would have a higher proportion of events related to their heads.

2. Methods

The medical records of consecutive patients presenting to Functional Neurology Clinic at the Austin Hospital located in Melbourne, Australia between 2017 and 2019 were included. Patients referred had all undergone a neurological assessment that concluded a probable diagnosis of functional neurological disorder, and the diagnosis of functional neurological disorder was confirmed by the clinic's neuropsychiatrist – a specialist in functional neurological disorder (RAK). Patients whose primary symptoms were pain or fatigue were not accepted by the clinic. Patients were included in the sample if they had a primary diagnosis of either FMD or PNES; they were excluded if they were under the age of 18 or had symptoms of both FMD and PNES.

Records were reviewed and data extracted by DHA and confirmed with SKM, with any discrepancies resolved by RAK. The following variables were collected: age, gender, employment status, education level, psychiatric history, traumatic events from childhood or adulthood, medical comorbidities, injuries, surgeries, date of functional symptom onset, and time from last preceding event to symptom onset. If any event not be confidently determined as preceding the onset of symptoms they were excluded. Injuries were considered to be events resulting in bodily trauma, occurring outside of surgery, with medical comorbidities the remaining physical diseases.

Events were attributed to the body parts they might be commonly thought to impact (head, trunk, limbs, back or whole body) by DHA, with resolution of uncertainty with RAK. Psychiatric and psychological disorders were included in "head". Events that affected internal organs (e.g. stomach, liver) were classified as "trunk", and those impacting the spine were grouped into "back". Events that might be attributed to more than one area were excluded. The classification of the medical events can be found in Supplementary Tables 1–6.

The collected data were coded and entered into Jamovi version 1.0.5, and analyzed using Mann–Whitney *U* for continuous variables, Chi-squared for categorical variables, or Fisher's Exact Test when the number of subjects in any of the cells of the contingency table were below 5 [19]. To correct for multiple comparisons, we adjusted the false discovery rate using the Benjamini-Hochberg method (adjusted *p*-values are in Supplementary Tables 8-9) [20,21].

The study was approved by the Human Research Ethics Committee of the Austin Hospital.

3. Results

3.1. Demographics

A total of 108 patients were included, 56 with FMD and 52 with PNES. The groups were demographically similar, however there was trend to a lower age at onset in PNES – see Table 1.

3.2. Medical events

Ninety three percent of patients reported a medical event before the onset of symptoms, which were classified into clinical (or medical) comorbid diseases (reported by 85%), surgeries (reported by 50%) and injuries (reported by 22%). As shown in Fig. 1, we found that FMD patients had a higher proportion of injuries occurring prior to symptom onset than PNES (30% compared to 14% respectively), X^2 (1, N = 24) = 4.45, p = 0.035 (table of adjusted *p*-values in Supplementary Table 8).

3.3. Medical events per body parts

In terms of body regions, medical events that impacted the limbs were significantly more common in FMD than PNES (34% and 14%, respectively, X^2 (1, N = 26) = 6.18, p = 0.013). See Fig. 2 for summary effects, with details relating to each specific body part provided in Supplementary 7.

3.4. Time between medical events and symptom onset

The data showed similarities between groups (Fig. 3). Twenty nine percent of all patients had a comorbidity, injury or surgery during the same day or week of symptom onset, while more than half (64%) had an event more than a week prior to functional symptom onset. Seven percent of patients were excluded from this analysis because their reported events had unclear dates of occurrence. There was a trend for more PNES than FMD to have had a clinical event the same day or week of their functional symptom onset (37% compared to 21%, X^2 (1, N = 31) = 3.01, p = 0.083).

Table 1
Demographics.

	FMD (%) n = 56	PNES n (%) n = 52	p value
Gender[a]			0.811
Female	41 (73%)	37 (71%)	
Male	15 (27%)	15 (29%)	
Age (years)[b]	48	43	0.113
Age at symptom onset (years)[b]	40	34	0.058
Employment[a]			0.448
Employed	16 (31%)	9 (18%)	
Unemployed	17 (33%)	17 (33%)	
Unemployed due to illness	16 (31%)	17 (33%)	
Retired[c]	2 (4%)	3 (6%)	–
Student[c]	1 (2%)	5 (10%)	–
Data unavailable	4	1	
Education[a]			0.292
≤Year 12	28 (57%)	18 (42%)	
Certificate I–IV or Diploma	10 (21%)	14 (33%)	
Bachelor's degree or above	11 (22%)	11 (26%)	
Data unavailable	7	9	

Percentages are of those with data available for that question.
* $p < 0.05$.
[a] Chi-square.
[b] Mann–Whitney *U*.
[c] Variables not included in the statistics because there were less than 5 cases.

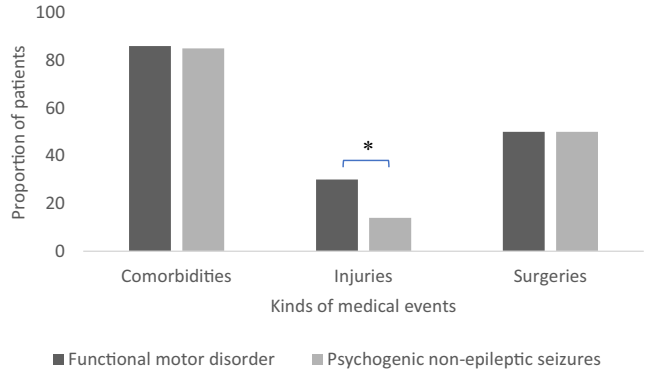

Fig. 1. Proportion of patients that reported different kinds of medical events before FND onset. * $p < 0.05$.

3.5. Psychiatric aspects

Ninety four percent of the patients had experienced a psychiatric illness during their lifetime (Fig. 4, Supplementary table 10), with substantial majorities having previous diagnoses of depression and anxiety in particular. There was a significant difference between groups in *functional somatic syndromes* (which includes fibromyalgia, chronic pain syndrome, chronic fatigue syndrome and irritable bowel syndrome), with FMD having a higher rate than PNES (46% and 27% respectively), X^2 (1, $N = 40$) = 4.40, $p = 0.036$ (table of adjusted p-values in Supplementary Table 9)). By contrast, a history of *dissociative symptoms* (depersonalisation, derealisation) was significantly higher in PNES than FMD (31% and 4%, X^2 (1, $N = 18$) = 14.4, $p < 0.001$, Fisher's exact test). *Suicidal behavior* (which included suicide attempts) was also significantly more common in PNES (56% and 32%, respectively, X^2 (1, $N = 47$) = 6.12, $p = 0.013$).

3.6. Life events

Childhood trauma was found to be similar between groups (70% of FMD and 73% of PNES), as was adult psychological trauma (63% FMD and 69% of PNES). The groups had similar proportions of each type of events, with only a trend towards increased sexual abuse in adulthood in PNES – see Table 2.

4. Discussion

We examined the medical records of 56 FMD patients and 52 PNES patients sourced from the same clinic to determine whether there were differences in demographic and clinical factors between the two groups. Of the differences hypothesized, we confirmed that *dissociation* was more common in patients with PNES than with FMD, and that medical events impacting the *limbs* were more common preceding FMD than PNES. We also found that *injuries* in general and *functional somatic syndromes* were more common in FMD, while *suicidal behavior* was more common in PNES. None of the other hypothesized differences was confirmed, though all were in the expected direction, and some were close to statistical significance.

Overall, this is consistent with the proposed differences between PNES and FMD, though the support it provides is clearly limited by the number of negative findings. The number of hypotheses not confirmed does suggest that any differences are, at least, not as strong or as clear-cut. The differences we did identify are cross sectional in nature, and post-diagnosis, so cannot be seen as revealing etiology, but as they are all reported as preceding illness onset they do potentially provide support for pathophysiological differences to etiology and/or mechanism.

The higher prevalence of events affecting the *limbs* in FMD hypothesized has not been previously reported, though similarly high rates of events overall have been [13]. The 'functional overlay' commonly described might suggest a close spatial relationship between physical injury and functional impairment, though we are not aware of a demonstration of this beyond case reports [5]. The argument for an aetiological relationship, possible given the precedence of the physical injury, is strengthened by the temporal proximity of the events in our sample, by its relative frequency in FMD compared to PNES, and by the specificity of the body parts.

The confirmation of differing rates of dissociation was predicted, though our data were perhaps different than others. Dissociation is a complex concept, and not unitary: arguably different kinds of dissociation are involved in FMD and PNES [22]. The 'dissociation' that we employed was the presence of derealisation or depersonalisation, which are common clinical dissociative presentations, and which appeared much more common in PNES, though still only in a minority. It is of course possible that other dissociative symptoms, such as 'compartmentalisation', were more com-

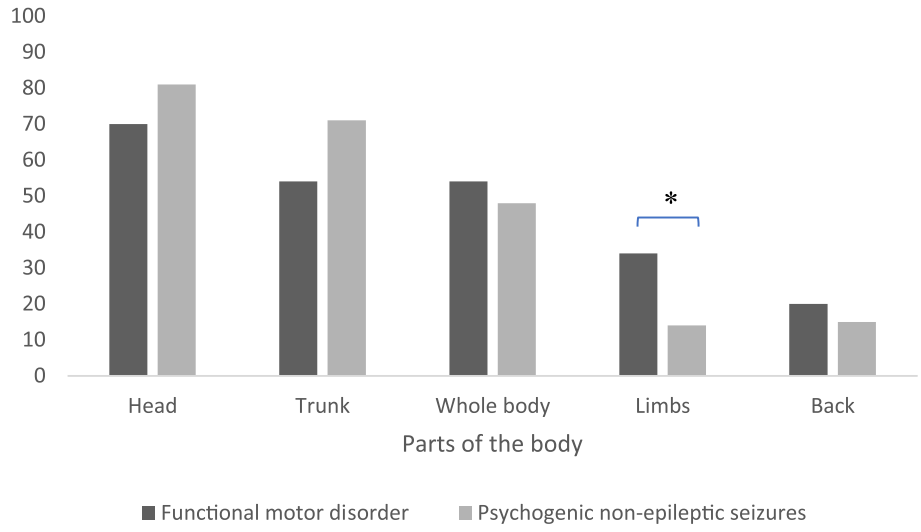

Fig. 2. Proportion of patients that reported comorbidities, injuries or surgeries affecting different parts of the body before the onset of functional symptoms. * $p < 0.05$.

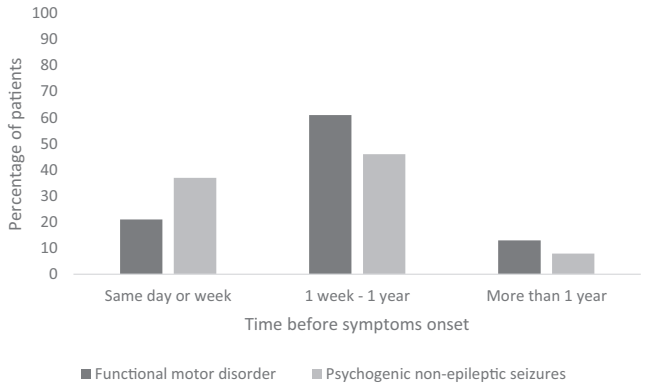

Fig. 3. Proportion of patients that reported any kind of medical event prior to the symptom onset. Only the last event of every patient was considered.

mon in FMD. A tendency to dissociation is a common response to developmental trauma [23] and it is possible that this difference in rates represents differences in rates of developmental trauma between our groups – though we did not confirm any such differences developmental trauma in our sample. These may represent discrete dissociative disorders in our sample, though it is also likely that in many patients their dissociative symptoms occurred in the context of their neurological symptoms. This provides some support for the idea that the seizures themselves – their phenomenology, at least, and possibly their mechanism – are dissociative, and that they differ from FMD in this respect.

The differences in *functional somatic syndromes* and *suicidal behavior* were not expected. Though comorbid functional somatic syndromes are common in functional neurological disorders [24], a difference between sub-types has not been reported previously. As these were lifetime syndromes (and not necessarily antecedent), the nature of the relationship with the functional neurological symptom is less clear. But bodily pain or fatigue experienced in a functional somatic syndrome might conceivably to lead to bodily neurological symptoms by any of the same mechanisms as for bodily injuries. The increased rate of suicidal behavior is unexpected given the lack of an obvious difference in the psychopathologies commonly associated with it, and perhaps suggests a differential association with other psychopathologies not assessed in this study, such as personality disorder. It is clearly of considerable clinical significance given the recognition of the substantially increased mortality in PNES [25].

5. Limitations

There are many limitations of a study such as this. The main limitation is its retrospective nature, based on medical reports. These will impose a degree of subjectivity in their reporting and our interpretation. Recall bias is likely, and events are only likely to be recorded when both the patient and the doctor thought them important. The categorisation of events by type, by time, and by body part affected are also complex and subjective assessments. We have attempted to be conservative – excluding when decisions were not clear – but this may introduce another source of bias, as well as suggesting lower rates than would otherwise be found. Another critical issue is that, though the clinic was a single source, it does not preclude differences in pathways to the clinic, which might introduce additional biases. For example, the relative availability of video-EEG suites (there are 4 public hospitals offering this in Melbourne) may lead to more rapid and more definitive

Table 2
Traumatic life events.

	FMD (%) $n = 54$[a]	PNES n (%) $n = 52$	p value [b]
Childhood			
Physical abuse	27.8%	34.6%	0.477
Emotional abuse	38.9%	42.3%	0.72
Sexual abuse	13.0%	23.1%	0.175
Verbal abuse	14.8%	9.6%	0.415
Bullying	29.6%	44.2%	0.119
Academic difficulty	38.9%	26.9%	0.19
Parent separation	14.8%	21.2%	0.395
Adulthood			
Domestic violence	3.7%	7.7%	0.433
Sexual abuse	5.6%	17.3%	0.07
Bullying work/university	9.3%	5.8%	0.716
Disease/death relative/friend	37%	38.5%	0.88
Accident/disease	9.3%	13.5%	0.495
Others	10.9%	17.3%	0.341

[a] Data unavailable $n = 2$.
[b] Chi-square.

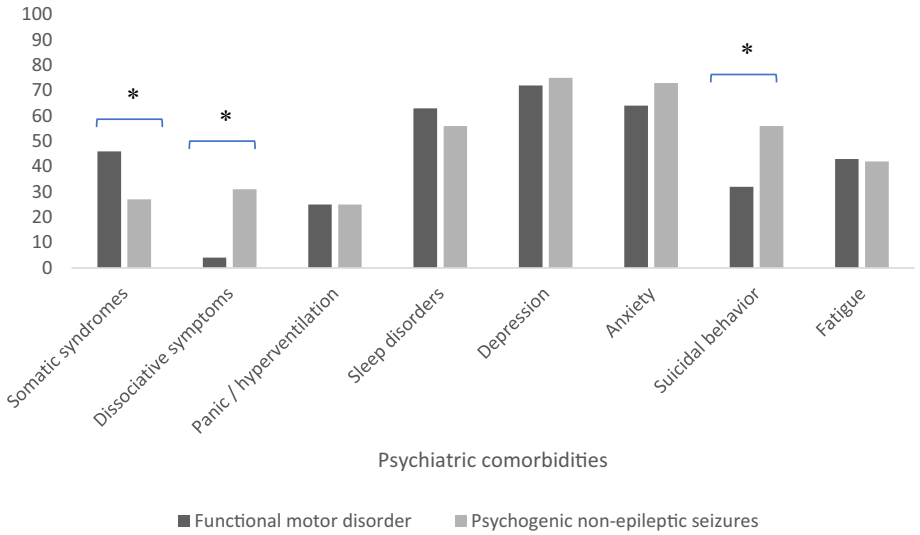

Fig. 4. Main psychiatric and related comorbidities reported by patients. * $p < 0.05$.

diagnoses in PNES, and so to a younger presentation to our clinic. Finally, the sample, though relatively large for such studies, is still only moderate, and it is possible that some of the negative findings reflect type 2 error.

6. Conclusion and future directions

In summary, FMD had a higher rate of preceding clinical events that impacted the *limbs*, with *injuries* being the most common, and a higher prevalence of *functional somatic syndromes*, while PNES showed higher prevalence of *suicidal behavior* and *dissociative symptoms*. These provide further support for the idea that symptomatic presentation can be differentially influenced by previous clinical events, and that the pathophysiology may differ between PNES and FMD. Larger, perhaps multi-center, studies will be needed to confirm these findings.

Conflicts of Interest and Source of Funding

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None.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm this report is consistent with those guidelines.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2020.107577.

References

[1] American Psychiatric Association (2013). Diagnostic and statistical manual of mental disorders: DSM-5. American Psychiatric Association. Washington, DC..
[2] Hallett, M. (2011). Psychogenic movement disorders and other conversion disorders (Cambridge). Cambridge, UK.
[3] Kanaan RAA, Duncan R, Goldstein LH, Jankovic J, Cavanna AE. Are psychogenic non-epileptic seizures just another symptom of conversion disorder? J Neurol Neurosurg Psychiatry 2017;88:425–9. https://doi.org/10.1136/jnnp-2017-315639.
[4] Ludwig L, Whitehead K, Sharpe M, Reuber M, Stone J. Differences in illness perceptions between patients with non-epileptic seizures and functional limb weakness. J Psychosom Res 2015;79:246–9.
[5] Demartini B, Goeta D, Barbieri V, Ricciardi L, Canevini MP, Turner K, et al. Psychogenic non-epileptic seizures and functional motor symptoms: A common phenomenology? J Neurol Sci 2016;368:49–54. https://doi.org/10.1016/j.jns.2016.06.045.
[6] Edwards MJ, Fotopoulou A, Pareés I. Neurobiology of functional (psychogenic) movement disorders. Curr Opin Neurol 2013;26:442–7. https://doi.org/10.1097/WCO.0b013e3283633953.
[7] Parees I, Saifee TA, Kassavetis P, Kojovic M, Rubio-Agusti I, Rothwell JC, et al. Believing is perceiving: mismatch between self-report and actigraphy in psychogenic tremor. Brain 2012;135:117–23. https://doi.org/10.1093/brain/awr292.
[8] Stone J, Mutch J, Giannokous D, Hoeritzauer I, Carson A. Hurst revisited: Are symptoms and signs of functional motor and sensory disorders "dependent on idea"? J Neurol Sci 2017;381:188–91. https://doi.org/10.1016/j.jns.2017.08.3248.
[9] Raskin M, Talbott JA, Meyerson AT. Diagnosis of conversion reactions. Predictive value of psychiatric criteria. JAMA 1966;197:530–4.
[10] Edwards MJ, Adams RA, Brown H, Parees I, Friston KJ. A Bayesian account of 'hysteria'. Brain 2012;135:3495–512. https://doi.org/10.1093/brain/aws129.
[11] Apazoglou K, Mazzola V, Wegrzyk J, Frasca Polara G, Aybek S. Biological and perceived stress in motor functional neurological disorders. Psychoneuroendocrinology 2017;85:142–50. https://doi.org/10.1016/j.psyneuen.2017.08.023.
[12] Pareés I, Kojovic M, Pires C, Rubio-Agusti I, Saifee TA, Sadnicka A, et al. Physical precipitating factors in functional movement disorders. J Neurol Sci 2014;338:174–7. https://doi.org/10.1016/j.jns.2013.12.046.
[13] Stone J, Carson A, Aditya H, Prescott R, Zaubi M, Warlow C, et al. The role of physical injury in motor and sensory conversion symptoms: A systematic and narrative review. J Psychosom Res 2009;66:383–90. https://doi.org/10.1016/j.jpsychores.2008.07.010.
[14] Stone J, Warlow C, Sharpe M. Functional weakness: clues to mechanism from the nature of onset. J Neurol Neurosurg Psychiatry 2012;83:67–9. https://doi.org/10.1136/jnnp-2011-300125.
[15] Folks DG, Ford CV, Regan WM. Conversion symptoms in a general hospital. Psychosomatics 1984;25:285–95. https://doi.org/10.1016/S0033-3182(84)73046-5.
[16] Alper K, Devinsky O, Perrine K, Luciano D, Vazquez B, Pacia S, et al. Dissociation in epilepsy and conversion nonepileptic seizures. Epilepsia 1997;38:991–7. https://doi.org/10.1111/j.1528-1157.1997.tb01481.x.
[17] Benbadis SR, Agrawal V, Tatum WO. How many patients with psychogenic nonepileptic seizures also have epilepsy? Neurology 2001;57:915–7. https://doi.org/10.1212/WNL.57.5.915.
[18] Westbrook LE, Devinsky O, Geocadin R. Nonepileptic seizures after head injury. Epilepsia 1998;39:978–82. https://doi.org/10.1111/j.1528-1157.1998.tb01447.x.
[19] Larntz K. Small-sample comparisons of exact levels for chi-squared goodness-of-fit statistics. J Am Stat Assoc 1978;73:253–63. https://doi.org/10.1080/01621459.1978.10481567.
[20] Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J Roy Stat Soc: Ser B (Methodol) 1995;57:289–300. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x.
[21] SIMES RJ. An improved Bonferroni procedure for multiple tests of significance. Biometrika 1986;73:751–4. https://doi.org/10.1093/biomet/73.3.751.
[22] Brown RJ. Different types of "dissociation" have different psychological mechanisms. J Trauma Dissoc 2006;7:7–28. https://doi.org/10.1300/J229v07n04_02.
[23] Loewenstein RJ. Dissociation debates: everything you know is wrong. Dialogues Clin Neurosci 2018;20:229–42.
[24] Oconnell N, Nicholson TR, Wessely S, David AS. Characteristics of patients with motor functional neurological disorder in a large UK mental health service: a case-control study. Psychol Med 2020;50:446–55.
[25] Nightscales R, McCartney L, Auvrez C, Tao G, Barnard S, Malpas CB, et al. Mortality in patients with psychogenic nonepileptic seizures. Neurology 2020;95. https://doi.org/10.1212/WNL.0000000000009855. e643 LP-e652.