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Editorial

Is drug treatment of psychogenic nonepileptic seizures effective?

While significant advances have been made in diagnosis of psychogenic nonepileptic seizures (PNES) [1] and cross-cultural understanding [2], and growing treatment literature is available for PNES, implementing treatment at many sites around the world remains an issue [3]. At some sites, adherence to psychiatric treatment is scarce, with the attendance to psychiatric services dropping from 80% of subjects at the first outpatient visit to 42% at the second, 24% at the third, and only 14% at the fourth visit at one epilepsy center [4]. Dropouts may be associated with the acceptance of the psychiatric diagnosis and a low concern about own illness [4]. Dropouts may be a contributor to poor prognosis of this condition, as fewer than 40% of adults with PNES have been reported to be seizure-free within 5 years after diagnosis [5].

Outcomes for PNES could be improved by a multidisciplinary approach in the diagnosis and management of this disorder [6]. A Cochrane review [7] investigated the efficacy of psychotherapy in patients with PNES analyzing results of 12 studies (4 randomized controlled trials [RCTs]) for a total of 343 participants. Five studies were on psychotherapy, three on cognitive behavior therapy (CBT), two on hypnosis, one on paradoxical intention, and one on mixed interventions. The authors did not conduct a meta-analysis of the studies because of the heterogeneity of design and interventions. All the forms of psychotherapy showed promising results, but the authors noted cautious interpretation because of a paucity of RCTs in their review. A 2017 review of PNES treatments [8] was performed from studies of 346 participants, who were primarily female (85.5%) and aged between 16 and 60 years. A total sample of 228 participants was extracted and incorporated in the meta-analyses. The sample covered three CBT-informed interventions, four psychodynamic treatments, one paradoxical intention therapy, one mindfulness-based intervention, two psychoeducational interventions and two eclectic interventions. Forty-seven percent of people with PNES were seizure-free upon completion of a psychological intervention. An additional meta-analysis synthesized data from 10 studies with a total of 137 participants with PNES. This analysis found that 82% of people with PNES who completed psychological treatment experienced a reduction in seizures of at least 50%. The authors noted that fully powered trials with adequate samples of the various comorbidities had not yet been published.

Pharmacological interventions have been proposed for PNES; however, to date, no fully powered RCT has been conducted. Sertraline, in combination with CBT-informed psychotherapy, showed a significant reduction in seizures [9] In a pilot placebo-controlled study carried out al in an academic medical hospital [10,11] with outpatients with PNES, a 45% reduction in seizure rates from baseline to final visit ($p = 0.03$) in the sertraline arm vs an 8% increase in placebo ($p = 0.78$). Little is known about the efficacy of other selective serotonin reuptake inhibitors (SSRIs) or other psychotropic drugs.

Other explanations may contribute to lack of seizure reduction in PNES, including, secondary gain in a subset of patients with seizures, or because of diagnostic misclassification. In the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), symptoms are broken up to their individual phenotypes and deprived of their meaning into experience and history of the subject. Psychogenic nonepileptic seizures are thus included in the overall category "somatic symptoms and related disorders", and a number of papers describe psychiatric comorbidity in PNES, which has also been investigated in systematic reviews in the literature [12,13]. Some have proposed a consolidation of the various comorbidities [14], noting that patients with PNES may present a combination of mental disorders, including conversion disorder, somatization disorder or undifferentiated somatoform disorder, dissociative disorder not otherwise specified (NOS), and posttraumatic stress disorder. In contrast, we argued in our previous works [15,16] that PNES may not be a single psychiatric disorder but rather the phenotype of different psychiatric conditions, like the syncopes that emulate epileptic seizures but have a different cardiac etiology. The majority of patients with PNES are closely related to somatization and conversion disorders [17]. In these patients with PNES, in line with others who address somatoform disorders [18], antidepressants may impact this population, especially on somatic and the associated anxious and depressive symptoms. A clinical caveat may be; however, that in some patients with PNES, medication adverse effects could sometimes mitigate their clinical impact [9] from their condition. In contrast, some patients with PNES have a more regressive psychological functioning, linked to the inability to integrate pulses [17]. These patients are included in the borderline personality spectrum and, perhaps for this reason, none of the psychopharmacological interventions has been demonstrated efficacious for regressive symptoms [19], except for impulse control and emotional dysregulation. With these considerations of the population, developing a randomized controlled pharmacological trial in people with PNES can be challenging, as can be psychotherapy trials.

In conclusion, it is still premature to comment on treatment efficacy for PNES or to give definitive recommendations; fully powered treatment studies are necessary to confirm the current promising results of psychotherapy (regardless of the type of intervention). However, from the literature, we can speculate that integrated interventions (psychotherapy plus pharmacotherapy) could be used, and that a pharmacological intervention could focus on the psychiatric etiology. Future studies could identify responders' characteristics and specific treatment for the various subcategories of PNES.

Declarations of Competing Interest

None.

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Massimiliano Beghi
Department of Mental Health, AUSL Romagna, Ravenna, Italy
Corresponding author at: Mental Health Center, piazza della Magnolia 5, Ravenna, Italy.
E-mail address: Massimiliano.beghi@auslromagna.it

Cesare Maria Cornaggia
School of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy

Ettore Beghi
Department of Neurosciences, Mario Negri IRCSS, Milan, Italy

William Curt LaFranceJr
Alpert Medical School, Brown University, Director of Neuropsychiatry and Behavioral Neurology, Rhode Island Hospital, United States of America

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