



Special issue on the intersection between functional seizures and other functional neurological disorders



In the last decade, there has been an explosion of interest in functional neurological disorders (FNDs) from only a few publications available in the 1970's and 1980's to virtually hundreds of articles and books published in the last decade. This is driven by numerous and equally important factors that include:

- The lack of uniform, completely elucidated, and fully uncovered etiology of FNDs;
- The transcendent nature of FNDs and their occurrence amongst patients presenting across the spectrum of various neuropsychiatric conditions (e.g., movement or seizure disorders);
- Frequently clinically puzzling mixture of physical and psychological symptoms at presentation that escape standard clinical, electrophysiological and imaging localization measures;
- The growing evidence from neuroimaging studies for the existence of abnormal brain structure and connectivity;
- Difficulty in achieving a treatment success (i.e., freedom from the disabling symptoms); and
- The gradually developing recognition by clinicians of the increasing prevalence and importance of FNDs as a medical condition with education on the topic lagging behind.

The interest in FNDs is further fueled by the lack of a commonly acceptable name for the disorder – e.g., the most appropriate and acceptable by patients and clinicians name for functional seizures has evolved over time and a commonly acceptable term has not been agreed upon to date [1,2]. Further, there is an increasing recognition of functional symptoms outside of the fields of neurology and psychiatry as detailed by Dr. Benbadis and colleagues in this special issue of EBR [3]. The heightened interest in FNDs coincides with the recent founding of a Functional Neurological Disorders Society (www.fndsociety.org) of which many authors of articles included in this special issue are members and with growing community interest through societies such as the FND Hope (<https://fndhope.org/>) and other organizations. There is also continued interest in FNDs among major clinical and scientific societies, especially the American Epilepsy Society which has sponsored several symposia and special interest groups focusing on various aspects of FS care.

This special issue of Epilepsy and Behavior Reports titled “The intersection between functional seizures and other functional neurological disorders” focuses specifically on functional seizures (FS), frequently also called psychogenic non-epileptic seizures (PNES) or non-epileptic seizures (NES), and on the pathophysiological

overlap between FS and other FNDs [2,4]. The naming scheme used in this special issue does not reflect the preference of the editorial staff or the authors but rather is a way of providing a unifying term used across all publications in this issue to discuss common aspects of the disorders that fall under the name of FNDs (or functional neurological symptom disorder (FNSD) in DSM-5). It has been long recognized that there is a substantial overlap between various FNDs in their epidemiology, demographics of patients, certain aspects of clinical presentation, social and educational status, risk factors, psychiatric comorbidities, and occurrence of psychiatric and somatization disorders. In fact, some authorities have suggested a common/unifying pathophysiology with variable phenotypical manifestations [4,5]. These unifying arguments are the basis of this special issue in which authorities in this field discuss various aspects of diagnosis and care of patients with FNDs and, through detailed reviews of the literature, propose the next steps and how to move the field forward. While a detailed discussion of each of the articles included in this special issue is not possible or needed, I would like to highlight some of the important discussion points.

Drs. Raynor and Baslet provide a brief but detailed historical overview of the FNDs and a comparison of contemporary models of the disorder [6]. They highlight the historical approaches to the etiology of FNDs starting with ancient theories of FNDs originating in (or being caused by) the reproductive organs (i.e., hysteria), supernatural causes, and the more recent theories of conversion disorders and models embedded in cognitive and neuronal circuitry. Finally, they discuss the overlap and differences between the current theories and the importance of a flexible approach to the development of personalized treatment plans.

Several of the articles in this special issue discuss various aspects of managing patients with FNDs. Dr. Andrini and colleagues describe an odyssey of an adult patient with FS and highlight the common scenario many of the FND patients go through before they reach a clinician familiar with the disorder and its treatments [7]. Their case illustrates the common mistakes and misperceptions clinicians and caregivers may have about FNDs. Dr. Kozłowska and colleagues provide similar perspectives with focus on pediatric aspects of FND care [8]. These authors not only provide verbatim narratives from patients and clinicians, they also discuss in detail the specific aspects of those narratives that are incorrect and potentially harmful to patients and their therapeutic relationship with physicians. They also discuss in detail the preferred treatment approaches to patients with FNDs and the

differences between pediatric and adult FNDs. This article clearly articulates a framework for treatment approaches that may be more successful in pediatric FNDs and it discusses results of a recently completed randomized controlled trial of “retraining and control therapy (ReACT)” in children and adolescents in whom psychiatric comorbidities are less frequently observed than in adults [8,9]. This and another article in this special issue highlight the differences in etiologies, treatment targets, and therapeutic interventions between pediatric and adult FNDs [8,10]. Finally, Dr. Stager and colleagues provide needed data on the long-term outcome of ReACT for the treatment of pediatric and adolescent FS – a bottom-up, cognitive behaviorally based, mind–body intervention that targets novel mechanisms for pediatric FS including sense of control and catastrophic symptom expectations [11,12].

In their review, Dr. Myers and colleagues focus on various aspects of adult FNDs care including specifics of various therapeutic approaches [13]. Specifically, these authors discuss the common psychopathologies that accompany FNDs and tailored approaches that concurrently target the symptoms of the FND and the comorbidities. These authors comment on the recent trials for the treatment of FS or functional movement disorders (FMDs) e.g., the CODES trial that failed to show improvement in FS but showed significant improvement in several secondary outcomes [14–16]. Based on the available data, the recommended psychotherapeutic approaches to include cognitive-behavioral therapy (CBT), third wave approaches, and psychodynamic psychotherapies as well as group therapeutic and psychoeducational interventions [13]. Dr. Litton, a clinician with vast clinical experience in treating patients with various FNDs summarizes the details of his self-developed / self-taught CBT-based therapeutic methods [17]. Three additional articles discuss important aspects of FND care. Dr. O’Neal and colleagues make an excellent case for engaging patients in their care as a potential avenue towards controlling their condition [18]. Dr. Revella and colleagues draw our attention to drop attacks as a relatively less characterized subtype of FND [19]. Drs. Freund and Tatum focus on a case of a patient whose generalized seizures were mistaken for FS because of the video recording provided by the family captured only the post-ictal behavior [20]. This article clearly illustrates the advantages and disadvantages of the smartphone videos for the diagnosis of FS. Finally, Drs. Lin and Espay bring all of these approaches into the realm of telehealth [21]. However, as eloquently pointed out in one of the research articles included in this special issue, all of these approaches are successful only if used by skilled and well-trained providers. The lack of FND education is one of the major roadblocks for the successful treatment of these patients [22]. Dr. Milligan and colleagues conducted a survey of neurology residency program directors and their recent graduates. The majority of the responders indicated they have not received specific FND treatment education. Both, the low response to the survey and the survey results themselves illustrate a significant curriculum gap in what neurology residents are taught about diagnosis and management of FNDs. These authors also provide specific recommendations for addressing these issues.

In another major effort, Drs. Kola and LaFaver discuss the overlap between FS and FMDs [23]. They indicate that while patients with FMDs often experience daily abnormal movements, FS are characterized by paroxysmal events. These authors further discuss that both patient populations share psychiatric and environmental comorbidities, but FS patients may experience higher levels of anxiety and neuroticism and a higher percentage of childhood trauma. Drs. Kola and LaFaver bring into the discussion the results of recent fMRI studies of patients with FNDs. Of importance is the network approach illustrated in some of the neuroimaging studies and the presence of various functional and structural differences between patients with FNDs and healthy or disease-specific controls [5,24]. As discussed in a recent white paper, the existing neu-

roimaging studies identified and provided extensive detail regarding the neural circuit models of FND in order to develop novel biologically and psychologically-informed treatments [24]. A paper by Sharma and Szaflarski illustrates a novel hypothesis and novel approach to studying FNDs – measurement of neuroinflammation using magnetic resonance spectroscopy and thermometry (MRS-t) [25]. This article discusses the evidence for neuroinflammation in various psychiatric conditions and then hypothesizes that early-life stressors cause neuroinflammatory and neuroendocrine changes that prime the brain for later development of FND following secondary trauma (e.g., psychological trauma) – a two hit theory.

Finally, Dr. Asadi-Pooya and colleagues discuss the negative impacts of FS on many aspects of a person’s life [26]. Rather than focusing on the diagnosis or treatment, they take a novel approach of analyzing the negative consequences of FS (i.e., psychiatric comorbidities, social consequences, costs that are associated with the condition, cognitive impairment in patients with FS, the quality of life of the people with FS, and the increased risk of mortality that is associated with FS). They make a sound case for the negative consequences of FS being comparable in their magnitude to those seen in patients with epilepsy. Highlighting these facts is extremely important as it should draw attention not only to the inadequate education of clinician and patient communities discussed by Milligan and colleagues in this special issue [22], but it should also nudge these communities towards taking specific clinical care and research steps that prioritize, facilitate, and expedite evidence-based diagnosis and treatment approaches. Dr. Adewusi and colleagues discuss the importance of validating the subjective complaints in patients with FNDs by correlating them with validated physiological measures [27]. This is vital because of the negative response bias on various tests observed in patients with FNDs [28]. To their dismay, they were able to identify only a handful of studies that took the approach of correlating subjective and objective data with only four reporting significant correlations between measures. This has important implications for the development of interventions for the treatment of FNDs and for measuring outcomes that should focus on objective rather than subjective metrics (e.g., objective seizure frequency rather than subjective cognitive or quality of life complaints [29]). To that end, Dr. Tolchin and colleagues discuss the importance of evidence-based guidelines in the diagnosis and treatment of FNDs [30]. These authors review clinical practice guidelines, their advantages and limitations, the reasons why evidence-based guidelines might be especially beneficial in the diagnosis and treatment of FNDs, and the steps that must be taken to create such guidelines for FNDs.

Conflict of interest

None to report.

Ethical statement

No human or animal data were used to write this introduction to the special issue on FNDs/FS.

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