

## Case Report

# Post-traumatic Stress Disorder Symptom Substitution as a Cause of Functional Neurological Disorder

Matthew J. Burke, M.D., Paulo Lizano, M.D., Ph.D.,<sup>†</sup> Claire Jacobs, M.D., Ph.D.,<sup>†</sup>  
Theodore A. Stern, M.D.

### Introduction

Functional neurological disorder (FND) is a complex diagnosis defined as the presence of myriad neurologic signs or symptoms that are inconsistent with recognized neurologic or medical diseases.<sup>1</sup> Presentations involve hypoactive states (such as paresis or blindness) or hyperactive states (such as tremors/jerks and psychogenic nonepileptic seizures [PNES]). Patients with FND are encountered commonly in clinical practice; their symptoms can be disabling, and the condition is challenging to manage.<sup>2</sup> Many psychological theories have been invoked to explain the etiology of FND, none more prominent than Sigmund Freud's model of "hysteria" that focused on the repression of painful/traumatic experiences and "conversion" into physical symptoms.<sup>3</sup>

More contemporary neuropsychiatric approaches to FND have moved away from psychodynamically-based frameworks because many patients with FND disavow a relationship with psychological factors and clinicians raise concerns that an undue emphasis on such factors can be counterproductive with regard to management.<sup>4</sup> Recent neuroimaging and neurophysiological studies suggest that patients with FND have disrupted brain networks that result in abnormal function of regions associated with their symptomatology (e.g., motor planning areas for functional movement disorders).<sup>5</sup> However, despite these advances, the overall pathophysiology of FND remains uncertain. In addition, trauma and adverse childhood experiences are risk factors for FND; however, many potential predisposing and precipitation factors exist, and evidence that implicates their specific role in the

pathogenesis of FND is controversial and remains a source of ongoing debate.<sup>6,7</sup> Similarly, comorbid psychological diagnoses such as post-traumatic stress disorder (PTSD), anxiety, and depression are commonly reported in those with FND, but their relationship to the development of FND has not been well established.<sup>1</sup> Finally, the potential substitution of a psychological symptom for a neurological symptom in the context of psychiatric treatment has also been poorly understood. The existence and nature of "symptom substitution" has been a source of ongoing debate by psychodynamic and behavioral theorists; although its importance as a concept has been fading from theoretical discourse and lacks empirical evidence.<sup>8</sup>

Here, we present a case of a 62-year-old man with FND whose functional neurological symptoms developed in the context of PTSD treatment.

### Case Vignette

Mr. T, a 62-year-old shipping worker with a long-standing history of PTSD, reported that at the age of

<sup>†</sup>These authors contributed equally to this manuscript.

Received January 15, 2019; revised March 3, 2019; accepted March 5, 2019. Division of Cognitive Neurology, Department of Neurology (M.J.B.) and Division of Cognitive Neurology, Department of Psychiatry (P.L.), Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA; Division of Epilepsy, Department of Neurology (C.J.) and Department of Psychiatry (T.A.S.), Massachusetts General Hospital, Harvard Medical School, Boston, MA. Send correspondence and reprint requests to Matthew J. Burke, MD, FRCPC, Beth Israel Deaconess Medical Center, KS-274, 330 Brookline Ave, Boston, MA 02215; e-mail: [mburke11@bidmc.harvard.edu](mailto:mburke11@bidmc.harvard.edu)

© 2019 Academy of Consultation-Liaison Psychiatry. Published by Elsevier Inc. All rights reserved.

## Case Report

19 years, he was sexually assaulted during his military training. Since that episode, he endorsed symptoms of PTSD (most notably flashbacks, hypervigilance, and avoidance of any military-related stimuli). He also developed depression, anxiety, and an alcohol-use disorder (now in remission). Throughout his adulthood, he avoided talking about his trauma and never received treatment for his PTSD. Nine months before the current assessment, his PTSD symptoms were triggered by a visit to a naval base. This prompted him to seek treatment. After entering an intensive psychotherapy/cognitive-behavioral treatment program, his PTSD symptoms quickly began to diminish. However, a few months later (in parallel to profound ongoing improvement in his PTSD), he developed FND and was admitted to a hospital for acute-onset right-sided weakness and difficulty in speaking. He was evaluated by the neurology team for the possibility of a stroke, and notes from their assessment indicated findings consistent with functional weakness (e.g., positive Hoover's sign, "give-way" weakness, and weakness that improved with distraction).<sup>1</sup> Extensive investigations were conducted (including a magnetic resonance imaging scan of his brain), which failed to show evidence of a new infarct or another relevant neurological disease. His neurological symptoms resolved spontaneously within 24 hours. However, similar subsequent functional attacks followed.

When Mr. T was assessed in the outpatient neuropsychiatry clinic several months later, his episodes had changed; they now involved bilateral weakness of his arms and legs, as well as involuntary eye closures (i.e., being unable to open his eyes despite being fully awake/cognitively intact). These episodes lasted approximately 15–30 minutes and occurred 3–6 times per day. Since their onset, these attacks steadily worsened in severity and frequency. He was unable to identify a clear trigger; however, he noted that minutes before each episode, he had a vague feeling that they were about to occur. No neurologic or systemic symptoms occurred outside of the attacks; nevertheless, he reported new episodes of nonspecific frontal headaches and worsening of chronic low back and right leg pain at other times. Overall, his FND was disabling, and it adversely affected his quality of life.

Mr. T's initial management focused on psychoeducation and counseling regarding the diagnosis of FND. We followed a stepwise explanatory approach that has been described in detail by Stone in 2009.<sup>1</sup> This

was accompanied by continuation of cognitive-behavioral treatment/psychotherapy (now geared toward FND in addition to pre-existing psychiatric comorbidities), pharmacological treatment of his pain (with gabapentin and nortriptyline), and physical therapy. After several months of this treatment regimen, his attacks of functional weakness improved (in frequency and severity); however, his chronic pain and headaches persisted. Mr. T's PTSD symptoms remain remitted. Finally, it is important to note that all of Mr. T's psychotherapy sessions were conducted by an external community provider. Thus, valuable and relevant information regarding specific details of these sessions is unfortunately not known.

### Discussion

FND lies at the interface between neurology and psychiatry and is arguably one of the most complex and poorly understood disorders in medicine. Over the past decade, new insights into the disorder's pathophysiology<sup>5</sup> have been gleaned from a growing body of functional neuroimaging studies (with both task-based<sup>9</sup> and resting-state<sup>10</sup> designs). Despite their diverse methodologies and specific FND subpopulations studied, several brain regions have been highlighted repeatedly, most notably, frontolimbic regions (such as the insula, amygdala, and anterior cingulate cortex) and the right temporal-parietal junction. The potential role that psychological factors (e.g., adverse childhood experiences, trauma) may have in creating dysfunctional networks has only recently been explored. One recent functional magnetic resonance imaging study assessed the recall of stressful life events in those with FND; it revealed abnormal activity in regions involved in emotion, memory control, and symptom-related motor planning/agency.<sup>11</sup> The authors suggested that their findings provided preliminary evidence that neural processing and recall of adverse events might be associated with physical symptoms in FND.

Another question raised by our case involves determining the circumstances surrounding the timing and onset of symptoms in those with FND because research on this topic is limited. The most comprehensive attempt to identify factors related to symptom onset was made on 107 patients with functional weakness in the United Kingdom.<sup>12</sup> They reported that symptom onset was often acute and possibly

precipitated by myriad events (e.g., physical injury, pain, migraines, fatigue, general anesthesia), and not just by psychologically-salient triggers (e.g., panic attacks). Theoretical models have suggested that such precipitants may activate an existing FND “scaffold” superimposed on short-term and long-term predisposing factors.<sup>13</sup>

It has been more than a century since the seminal work by Briquet<sup>14</sup> (1859; *Clinical and Therapeutic Treatise on Hysteria*) and Breuer and Freud<sup>15</sup> (1895; *Studies on Hysteria*) established the association between psychological stress and the onset of functional neurologic symptoms. Since then, a range of predisposing and precipitating factors, such as stressful life events and maltreatment, have been deemed crucial to the development of FND.<sup>16</sup> However, the evidence supporting this belief has been limited by poor study designs and insufficient qualitative syntheses. Nonetheless, a recent quantitative meta-analysis by Ludwig *et al.*<sup>6</sup> looked to overcome prior methodological limitations by examining the role of childhood and adult stressful life events and maltreatment on the development of broad functional neurologic phenotypes.<sup>6</sup> Ludwig showed that the frequency of childhood and adult stressful life events and maltreatment was increased in those with FNDs compared with controls, that these events preceded the onset of symptoms (odds ratio, 2.8), and that emotional neglect (cases, 49%; controls, 20%; odds ratio, 5.6) was more common than was the previously emphasized role of sexual (cases, 24%; controls, 10%; odds ratio, 3.3) or physical abuse (cases, 30%; controls, 12%; odds ratio, 3.9).<sup>6</sup>

Not only do PTSD and FND share predisposing and precipitating factors but also they are often comorbid.<sup>17</sup> Early FND structural neuroimaging studies have identified cortical atrophy in the dorsal anterior cingulate cortex<sup>18</sup> and increased cortical thickness in the insula,<sup>19</sup> whereas functional neuroimaging studies have revealed increased insular and anterior cingulate cortex activity during motor tasks<sup>20</sup> and increased cingulate gyrus activation during affectively valenced face processing.<sup>21</sup> Additionally, a brain voxel-based morphological study of patients with FND found that women (not in mixed gender analysis) have reduced insular volume with functional symptoms and childhood abuse, and this relationship was explained by the magnitude of reported childhood abuse.<sup>22</sup> These findings converge on stress-related neuroplasticity and may help explain the pathophysiology of functional neurologic symptoms.

Patients with FND often experience a wide range of symptoms, and episodes can occur in virtually any setting. As a result, patients with FND may present to and be treated in urgent care or emergency room settings, outpatient primary care or family care clinics, neurology or psychiatry clinics, or in the perioperative or peripartum settings.<sup>23</sup> For many, the first point of care for those with PNES or FND symptoms that mimic acute stroke may be (appropriately) the emergency department.<sup>24</sup> However, once a diagnosis of PNES or other FND is made, they may be instructed to follow up with their primary care physician, or with a neurologist, neurology subspecialist, neuropsychiatrist, or psychiatrist. Alternatively, they may be discharged without engaging in a thorough discussion of the diagnosis or follow-up plan and may go on to receive fractured care from multiple providers in different locations.<sup>25</sup> One of the difficulties faced by this patient population is finding a “medical home” with a multidisciplinary team (comprised of psychiatry, neurology, physical/occupational therapy, and psychotherapy) that is typically necessary to provide effective treatment.<sup>26</sup> The prognosis of FND is variable but is generally considered to be poor with symptoms that persist or worsen in roughly half of those with motor symptoms.<sup>27</sup> Many of the prognostic studies on FND come from the PNES literature; one long-term follow-up study reported that more than 70% of patients had ongoing PNES events four years after their diagnosis.<sup>28</sup>

The importance of timely and comprehensive management of PTSD and FND is clear. However, one concern associated with behavioral therapy for neuropsychiatric disorders has been the potential for “symptom substitution,” that is, treatment focused on one symptom in a cluster of related symptoms or responses is likely to affect those other related responses.<sup>29</sup> As was the case with our patient, Mr. T, the concern for symptom substitution was based on the belief that behavioral therapy did not adequately address the pathophysiologic underpinnings (psychodynamics of symptom formation underlying a behavior or symptom) and that treatment that targeted a behavior may have increased other symptoms linked with the underlying disorder. Studies of symptom substitution have been limited by several definitional challenges, including the ability to differentiate between the emergence of new symptoms associated with treatment, rather than expected symptom fluctuation or

## Case Report

progression of the disorder.<sup>8,29</sup> Another issue has been the identification of a temporal relationship that links the therapeutic intervention with reduction in one symptom and emergence of a new, related symptom. Interestingly, a 2013 study of comprehensive behavioral intervention for tics found no evidence of tic substitution or tic worsening with comprehensive behavioral intervention for tics treatment and instead found that fluctuations in tic severity was within the range expected for the disorder.<sup>30</sup> Previous work investigating symptom substitution in patient populations with FND has been very limited. One study looked to evaluate whether in patients whose PNES symptoms resolve, these symptoms get substituted for other medically unexplained symptoms.<sup>31</sup> Their findings did not support this hypothesis but did reveal high comorbidity of PNES with other medically unexplained symptoms.<sup>31</sup> To our knowledge, no studies have examined symptom substitution in the context of PTSD treatment to FND. However, we speculate that maladaptive plasticity and abnormal functional connectivity associated with chronic PTSD (e.g., in amygdala and frontolimbic networks),<sup>32,33</sup> when treated with behavioral strategies, could lead to changes in these networks<sup>34</sup> which potentially unmask FND symptoms. This model is theoretical and underscores the need for further studies to empirically evaluate such

mechanisms. Finally, in our case (Mr. T), it remains unclear whether the emergence of FND after apparently successful psychiatric treatment of PTSD was part of the natural history of his trauma and long-standing PTSD (possibly exacerbated by therapy bringing traumatic memories to the forefront) or, as was suggested by the temporal sequence between engaging in intensive psychotherapy/cognitive-behavioral treatment, an improvement in his symptoms of PTSD, and new-onset FND, a case of symptom substitution. Although helpful strategies have been established, the evaluation and management of FND remains a clinical challenge.<sup>4</sup> Future research is also needed to assess the potential value of preventative approaches to reduce the risk of FND development in the patient population with PTSD.

*Funding: M.J.B. is supported by the Sidney R. Baer, Jr. Foundation. P.L. is supported by the Sidney R. Baer, Jr. Foundation and the Harvard Medical School Dupont Warren Fellowship. C.J. is supported by a NIH/NINDS R25 NS065743 grant. Disclosures: M.J.B., P.L., and C.J. have nothing to disclose. T.A.S. is an employee of the Academy of Consultation-Liaison Psychiatry (as Editor-in-Chief of Psychosomatics), and he receives royalties from the Massachusetts General Hospital Psychiatry Academy for editing textbooks on psychiatry.*

## References

1. Stone J: Functional symptoms in neurology: the bare essentials. *Pract Neurol* 2009; 9:179–189
2. Lehn A, Gelauff J, Hoeritzauer I, et al: Functional neurological disorders: mechanisms and treatment. *J Neurol* 2016; 263:611–620
3. Kanaan RA: Freud's hysteria and its legacy. *Handb Clin Neurol* 2016; 139:37–44
4. McKee K, Glass S, Adams C, et al: The inpatient assessment and management of motor functional neurological disorders: an interdisciplinary perspective. *Psychosomatics* 2018; 59:358–368
5. Voon V, Cavanna AE, Coburn K, et al: Functional neuroanatomy and neurophysiology of functional neurological disorders (conversion disorder). *J Neuropsychiatry Clin Neurosci* 2016; 28:168–190
6. Ludwig L, Pasman JA, Nicholson T, et al: Stressful life events and maltreatment in conversion (functional neurological) disorder: systematic review and meta-analysis of case-control studies. *Lancet Psychiatry* 2018; 5:307–320
7. Reuber M, Howlett S, Khan A, et al: Non-epileptic seizures and other functional neurological symptoms: predisposing, precipitating, and perpetuating factors. *Psychosomatics* 2007; 48:230–238
8. Tryon WW: Whatever happened to symptom substitution? *Clin Psychol Rev* 2008; 28:963–968
9. Burke MJ, Ghaffar O, Staines WR, et al: Functional neuroimaging of conversion disorder: the role of ancillary activation. *Neuroimage Clin* 2014; 6:333–339
10. Maurer CW, LaFaver K, Ameli R, et al: Impaired self-agency in functional movement disorders: a resting-state fMRI study. *Neurology* 2016; 10:212
11. Aybek S, Nicholson TR, Zelaya F, et al: Neural correlates of recall of life events in conversion disorder. *JAMA Psychiatry* 2014; 71:52–60
12. Stone J, Warlow C, Sharpe M: Functional weakness: clues to mechanism from the nature of onset. *J Neurol Neurosurg Psychiatry* 2012; 83:67–69
13. Brown RJ, Reuber M: Towards an integrative theory of psychogenic non-epileptic seizures (PNES). *Clin Psychol Rev* 2016; 47:55–70
14. Briquet P: *Traité clinique et thérapeutique de l'hystérie*. VII. Paris, France: J-B Baillière et Fils; 1859 (in French)
15. Breuer J, Freud S: *Studies on hysteria*. London, UK: Hogarth Press; 1895

16. Roelofs K, Spinhoven P: Trauma and medically unexplained symptoms towards an integration of cognitive and neurobiological accounts. *Clin Psychol Rev* 2007; 27:798–820
17. Sar V, Akyuz G, Kundakci T, et al: Childhood trauma, dissociation, and psychiatric comorbidity in patients with conversion disorder. *Am J Psychiatry* 2004; 161:2271–2276
18. Labate A, Cerasa A, Mula M, et al: Neuroanatomic correlates of psychogenic nonepileptic seizures: a cortical thickness and VBM study. *Epilepsia* 2011; 53:377–385
19. Ristic AJ, Dakovic M, Kerr M, et al: Cortical thickness, surface area and folding in patients with psychogenic nonepileptic seizures. *Epilepsy Res* 2015; 112:84–91
20. Voon V, Brezing C, Gallea C, et al: Aberrant supplementary motor complex and limbic activity during motor preparation in motor conversion disorder. *Mov Disord* 2011; 26:2396–2403
21. Aybek S, Nicholson TR, O'Daly O, et al: Emotion-motion interactions in conversion disorder: an fMRI study. *PLoS One* 2015; 10:e0123273
22. Perez DL, Matin N, Barsky A, et al: Cingulo-insular structural alterations associated with psychogenic symptoms, childhood abuse and PTSD in functional neurological disorders. *J Neurol Neurosurg Psychiatry* 2017; 88:491–497
23. Carson A, Lehn A: Epidemiology. *Handb Clin Neurol* 2016; 139:47–60
24. Dworetzky BA, Weisholtz DS, Perez DL, Baslet G: A clinically oriented perspective on psychogenic nonepileptic seizure-related emergencies. *Clin EEG Neurosci* 2015; 46:26–33
25. Rommelfanger KS, Factor SA, LaRoche S, et al: Distinguishing stigma from functional neurological disorders: conference report and roadmap for the future. *Front Neurol* 2017; 8:1–7
26. Espay AJ, Aybek S, Carson A, et al: Current concepts in diagnosis and treatment of functional neurological disorders. *JAMA Neurol* 2018; 75:1132–1141
27. Gelauff J, Stone J, Edwards M, et al: The prognosis of functional (psychogenic) motor symptoms: a systematic review. *J Neurol Neurosurg Psychiatry* 2014; 85:220–226
28. Reuber M, Pukrop R, Bauer J, et al: Outcome in psychogenic nonepileptic seizures: 1 to 10-year follow-up in 164 patients. *Ann Neurol* 2003; 53:305–331
29. Kazdin AE: Symptom substitution, generalization, and response covariation: implications for psychotherapy outcome. *Psychol Bull* 1982; 91:349–365
30. Seahill L, Woods DW, Himle MB, et al: Current controversies on the role of behavior therapy in Tourette syndrome. *Mov Disord* 2013; 28:1179–1183
31. McKenzie PS, Oto M, Graham CD, et al: Do patients whose psychogenic non-epileptic seizures resolve, 'replace' them with other medically unexplained symptoms? Medically unexplained symptoms arising after a diagnosis of psychogenic non-epileptic seizures. *J Neurol Neurosurg Psychiatry* 2011; 82:967–969
32. Gilboa A, Shalev AY, Laor L, et al: Functional connectivity of the prefrontal cortex and the amygdala in posttraumatic stress disorder. *Biol Psychiatry* 2004; 55:263–272
33. Moguel-Cobos G, Maroney Z, Erickson JM, et al: Psychogenic movement disorders and dopamine transporter scans: still a clinical diagnosis? *Psychosomatics* 2017; 58:83–89
34. Shou H, Yang Z, Satterthwaite TD, et al: Cognitive behavioral therapy increases amygdala connectivity with the cognitive control network in both MDD and PTSD. *Neuroimage Clin* 2017; 14:464–470