

Functional neurologic disorder associated with SARS-CoV-2 vaccination

Annie Zhu MD, Matthew J. Burke MD

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A healthy 50-year-old woman developed involuntary movements of her legs about 4 days after her first dose of vaccine against SARS-CoV-2. These involuntary jerks progressed to involve the rest of her body. The movements occurred intermittently during the day, lasting for seconds, but they affected her gait so that she required a cane to walk. In addition, she described fatigue, headache and intermittent paresthesia and pain in different parts of her body.

She reported being stressed because of the pandemic and was initially hesitant to receive the SARS-CoV-2 vaccine, but had decided to get her first dose because she was employed in the education sector. She had no history of smoking, recreational drug use or substantial alcohol intake. She had no relevant medical history and no psychiatric history. During childhood, she had had psychological trauma that would be considered an adverse childhood experience. She reported no family history of any neurologic disorders. Her involuntary movements were pronounced during the physical examination, with “twitching” of her face during activation of her frontalis, and jerky movements of her arms during pronator drift. Her atypical movement patterns (with variability, distractibility and entrainment) were suggestive of a functional movement disorder.

The patient had been assessed previously at an emergency department, with consultation to general neurology to investigate potential causes of her acute-onset atypical movements. All laboratory investigations were normal. A computed tomography (CT) venogram and magnetic resonance imaging (MRI) scans of her brain and cervical spine with contrast ruled out structural lesions, including venous sinus thrombosis. A normal electroencephalogram (EEG) showed no evidence of epileptiform activity. She was referred to our functional neurologic disorders clinic for further assessment.

Given the clinical findings and normal investigations, the patient received a diagnosis of functional neurologic disorder (FND) following SARS-CoV-2 vaccination. We explained the diagnosis to her and offered FND-associated physiotherapy. In the following weeks, she noticed gradual improvement in her symptoms and no longer required a cane for ambulation. During the consultation she asked, “Is it safe for me to get the second shot?” as she was worried about developing worsening or new symptoms. Despite our encouragement that she do so, she decided not to receive any further vaccine doses.

Key points

- An increasing number of patients are presenting with functional neurologic disorders (FND) after SARS-CoV-2 vaccination.
- No evidence exists to suggest a direct causal relationship between specific constituents in the SARS-CoV-2 vaccine and FND; patients may develop FND after vaccination owing to a variety of complex and incompletely understood factors.
- Patients who develop new-onset FND after vaccination may be hesitant to receive subsequent doses of SARS-CoV-2 vaccine, and patients with pre-existing FND or related disorders may be hesitant to receive any doses of the vaccine.
- Treatment of FND includes appropriate delivery of the diagnosis, as well as patient education and multidisciplinary management.

Discussion

Formerly known as “conversion disorder,” FND is a complex neuropsychiatric condition in which patients experience neurologic symptoms due to a “functional” disruption of brain networks rather than a “structural” disorder of the nervous system.¹ For diagnosis, neurological symptoms need to be incongruent with recognized neurological or medical disease, not better explained by another condition and result in significant functional impairment.² Symptoms of FND are not voluntarily generated and should not be conflated with malingering or factitious disorders.¹ Recent work has expanded the diagnosis of FND from one primarily of exclusion, based on negative medical testing, to one that can be potentially ruled in by the presence of positive signs (Table 1).¹ This shift is not black and white and, in many cases — particularly with unusual symptoms or context — investigations to rule out other neurologic diseases are indicated. In this case, we had the benefit of extensive previous medical investigations, which were negative, before the patient’s clinic appointment. Many generalist clinicians do not have this information available upfront, and the decision about the extent of investigations is specific to each patient and remains an ongoing debate.

The etiology of FND is incompletely understood and involves multiple overlapping biopsychosocial aspects. These include

Table 1: Examples of positive diagnostic signs of functional neurologic disorder

FND subtype	Example of positive diagnostic signs*
Functional tremors	<ul style="list-style-type: none"> • Entrainment: When copying rhythmic movements with opposite hand, the tremor in the affected limb stops or is entrained to the same rhythm • Distractable: Abnormal movement stops when patient is focused on a different task
Functional weakness	<ul style="list-style-type: none"> • Inconsistent or “give-way” weakness (initially strong and then sudden loss of resistance) on power testing • Hoover sign: Ask the patient to voluntarily extend the hip of the weak leg and assess strength (if patient lying down, the examiner’s hand is placed under the heel). Then ask the patient to flex the healthy hip against resistance and again assess the strength of hip extension of the weak leg (this time it is involuntarily being extended). Compare voluntary to involuntary hip extension strength and if the latter is notably stronger, Hoover sign is positive
Functional seizures	<ul style="list-style-type: none"> • Long-duration waxing and waning episodes that may be accompanied by forced eye closure, tearfulness, side-to-side head-shaking or bilateral limb jerking with preserved consciousness

Note: FND = functional neurologic disorder.

*Included examples of FND-positive diagnostic signs focus on motor subtypes relevant to our patient. For a more detailed list of symptom subtypes and diagnostic signs, see Aybek and Perez’s recent review on this topic.¹

predisposing genetic and psychosocial factors (such as childhood adverse events), which may combine with a more acute triggering event. Such cases were previously attributed exclusively to psychological triggers; however, physical triggers such as injuries, illnesses or even vaccinations have been reported.¹ Functional neurological disorders have been estimated to comprise as many as one-third of referrals to medical subspecialty clinics such as neurology.³ The most common presentations include motor abnormalities (e.g., tremors, weakness) and seizure-like episodes.¹ Positive clinical signs for different presentations of FND are described in Table 1, but variability and inconsistency of symptoms are common across all subtypes.¹ For example, patients’ symptoms might become more pronounced in the presence of a physician or may fluctuate during an assessment as their attention shifts.

In addition to the growing validation of positive clinical signs, adjunctive diagnostic tests may help further confirm the diagnosis in cases of uncertainty. Electromyography (EMG) and EEG can be useful for diagnosing functional myoclonus and other motor abnormalities, and prolonged video EEG (vEEG) is the gold standard for the diagnosis of functional seizures.¹

The prognosis of FND is variable and, although these disorders are potentially reversible, prognosis is generally worse than clinicians may expect. Long-term follow-up studies of motor FND have reported that more than one-third of patients may have similar or worse symptoms years after diagnosis.¹ Factors associated with better outcomes include a short duration of symptoms before diagnosis (early diagnosis) and acceptance of and insight into the diagnosis of FND.¹

Reports of individuals developing FND after SARS-CoV-2 vaccination are increasing.⁴ This phenomenon has been seen with other vaccines, such as among adolescents in Korea who developed FND-spectrum illnesses after vaccination against H1N1.⁵ The Functional Neurological Disorders Society issued a press release on Jan. 19, 2021, noting that many social media videos suggesting major neurologic complications after vaccines against SARS-CoV-2 have findings consistent with FND.⁶ Worry-

ingly, without proper contextualization, such videos and stories may fuel more vaccine hesitancy. Documented examples of post-vaccine FND include patients with symptoms ranging from abnormal movements to seizure-like events.⁷⁻⁹

Clinicians are navigating challenging discussions about SARS-CoV-2-associated FND with limited evidence or guidance available for informing best practice. It is important to clearly communicate to patients that there is no evidence of a direct causal relationship between any vaccine constituents and FND. Instead, it is thought that the context surrounding SARS-CoV-2 vaccination — including threat-related hypervigilance, heightened attention to potential vaccine adverse effects (nocebo effects) and unconscious brain-based amplification of typically transient symptoms of immune activation — contribute to vaccine-triggered FND.⁷ Although neurologists are often involved in the care of patients with vaccine-triggered FND, many discussions on ongoing vaccine-related concerns occur in primary care. Generalists play a critical role in supporting patients with FND. Pragmatically, this involves education and guidance about vaccine-related FND, communicating the diagnosis and providing management strategies.

Delivery of the diagnosis is the first step in managing FND. It is critical to both clearly communicate the diagnosis and to validate patients’ concerns. Misconceptions regarding these disorders remain across medicine, and patients are frequently dismissed as “faking it.”¹⁰ It is important to name the diagnosis to patients rather than simply listing the other medical disorders that have been excluded. Using relatable language to describe FND can help patients gain a better understanding of their illness. Our patient noted that after feeling dismissed by previous physicians, a conversation that used these principles made her feel validated that her symptoms were not “made up.” Demonstrating and explaining positive signs to patients may also help them accept and understand how practitioners reached the diagnosis of FND. For example, “When your attention was focused on a different task, did you notice that your tremor stopped?”

Educating patients is another important step in treatment by empowering them to better understand their diagnosis. Helpful resources include www.neurosymptoms.org and www.fndhope.org. A recent review discussed studies that showed that in functional seizure disorders, communication and acceptance of the diagnosis can lead to reduction of seizures as well as a reduction in emergency department visits and hospital admissions.¹

Interventions for FND often involve a multidisciplinary approach, which may include FND-informed physiotherapy, psychotherapy (e.g., cognitive behavioural therapy, psychodynamic therapy or both) and management of comorbid symptoms if present (e.g., pain, anxiety, depression).¹ Physiotherapy informed by FND is often the mainstay of treatment for patients who present with motor abnormalities. It uses the principle that FND symptoms improve with distraction (when patients are not paying attention to their body) and aims to retrain normal motor movements by attentional redirection.¹ Patients with motor abnormalities such as weakness have been shown to substantially improve their walking ability and quality of life, as well as physical and social functioning, after FND-informed physiotherapy.¹ A recent systematic review of psychotherapy concluded that both cognitive behavioural therapy and psychodynamic therapies may offer some benefit for FND, but results have been mixed and better-quality studies are needed.¹¹

Conclusion

Functional neurologic disorder associated with SARS-CoV-2 vaccination is increasingly recognized. As in all cases of FND, the key is to understand that the neurologic symptoms are a result of a “functional” disruption of brain networks rather than a recognized “structural” disorder of the nervous system. Symptoms are not voluntarily generated and should not be attributed to malingering or factitious disorders.

References

1. Aybek S, Perez DL. Diagnosis and management of functional neurological disorder. *BMJ* 2022;376:o64.
2. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. Fifth edition.* Arlington (VA): American Psychiatric Association Publishing; 2013.
3. Stone J, Carson A, Duncan R, et al. Who is referred to neurology clinics? — the diagnoses made in 3781 new patients. *Clin Neurol Neurosurg* 2010;112:747-51.
4. Favaro A, St. Philip E, Jones AM. Coronavirus News: What is functional neurological disorder and is it connected to COVID-19 vaccines? Experts explain. *CTV News* 2021 Aug. 22. Available: <https://www.ctvnews.ca/health/coronavirus/what-is-functional-neurological-disorder-and-is-it-connected-to-covid-19-vaccines-experts-explain-1.5557342> (accessed 2021 Nov. 23).
5. Yang TU, Kim HJ, Lee YK, et al. Psychogenic illness following vaccination: exploratory study of mass vaccination against pandemic influenza A (H1N1) in 2009 in South Korea. *Clin Exp Vaccine Res* 2017;6:31-7.

6. Press release from the Functional Neurological Disorders Society. Milwaukee (WI): Functional Neurological Disorders Society; 2021 Jan. 19. Available: <https://www.fndsociety.org/UserFiles/file/FNDSocietyPressReleaseCOVIDVaccines.pdf> (accessed 2021 Nov. 24).
7. Butler M, Tamborska A, Wood GK, et al. Considerations for causality assessment of neurological and neuropsychiatric complications of SARS-CoV-2 vaccines: from cerebral venous sinus thrombosis to functional neurological disorder. *J Neurol Neurosurg Psychiatry* 2021;92:1144-51.
8. Kim DD, Kung CS, Perez DL. Helping the public understand adverse events associated with COVID-19 vaccinations: lessons learned from functional neurological disorder. *JAMA Neurol* 2021;78:789-90.
9. Burke MJ, Del Rio C. Long COVID has exposed medicine’s blind-spot. *Lancet Infect Dis* 2021;21:1062-4.
10. Burke MJ. “It’s all in your head” — medicine’s silent epidemic. *JAMA Neuro* 2019; 76:1417-8.
11. Gutkin M, McLean L, Brown R, et al. Systematic review of psychotherapy for adults with functional neurological disorder. *J Neurol Neurosurg Psychiatry* 2020; 92:36-44.

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Affiliations: Division of Neurology, Department of Medicine (Zhu, Burke) and Neuropsychiatry Program, Department of Psychiatry (Burke), Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ont.; Division of Cognitive Neurology, Department of Neurology (Burke), Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Mass.

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Correspondence to: Matthew Burke, matthew.burke@sunnybrook.ca

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