

# Diagnosis and management of functional neurological disorder

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## ABSTRACT

Functional neurological disorder (FND), previously regarded as a diagnosis of exclusion, is now a rule-in diagnosis with available treatments. This represents a major step toward destigmatizing the disorder, which was often doubted and deemed untreatable. FND is prevalent, generally affecting young and middle aged adults, and can cause severe disability in some individuals. An early diagnosis, with subsequent access to evidence based rehabilitative and/or psychological treatments, can promote recovery—albeit not all patients respond to currently available treatments. This review presents the latest advances in the use of validated rule-in examination signs to guide diagnosis, and the range of therapeutic approaches available to care for patients with FND. The article focuses on the two most frequently identified subtypes of FND: motor (weakness and/or movement disorders) and seizure type symptoms. Twenty two studies on motor and 27 studies on seizure type symptoms report high specificities of clinical signs (64-100%), and individual signs are reviewed. Rehabilitative interventions (physical and occupational therapy) are treatments of choice for functional motor symptoms, while psychotherapy is an emerging evidence based treatment across FND subtypes. The literature to date highlights heterogeneity in responses to treatment, underscoring that more research is needed to individualize treatments and develop novel interventions.

## Introduction

### Historical background

Functional neurological disorder (FND) is a prevalent, costly, and potentially disabling condition encountered by healthcare professionals in medical, clinical neuroscience, and rehabilitative specialties.<sup>1 2</sup> The condition has a complex narrative in the literature that has benefited from and been hampered by the interwoven history of neurology and psychiatry.<sup>3</sup> Labeled medicine's "silent epidemic," a "crisis" in neurology, and psychiatry's "blind spot,"<sup>4-6</sup> FND has inspired renewed clinical and research interest during the past several decades. Important breakthroughs have included new diagnostic and therapeutic approaches to FND, as well as parallel advances in its pathophysiology. Figure 1 gives a brief overview of the emerging neurobiology of FND<sup>7 8</sup>—depicting the condition as characterized by dysfunction within and across several brain networks.

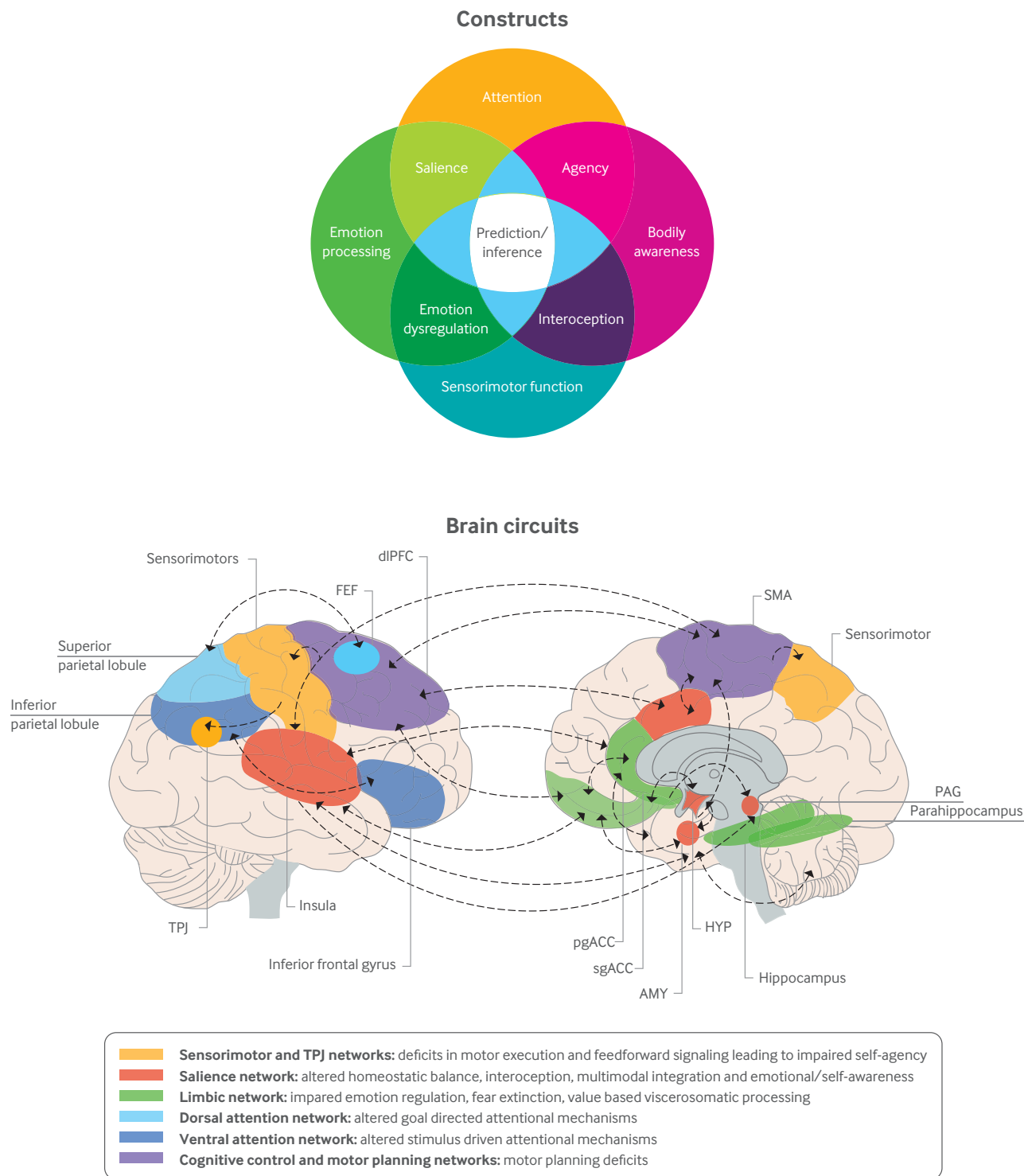
### Nosological classification

FND is classified as "conversion disorder/functional neurological symptom disorder" in the chapter "Somatic Symptom and Related disorders, code

F44.X" in the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5). In the ICD-11 (International Classification of Diseases), FND is classified as "dissociative neurological symptom disorder" in the chapter "Mental, Behavioural or Neurodevelopmental Disorders, code 6B60.X," as well as in the chapter "Diseases of the Nervous System, code 8A0X" under the term "movement disorder for parkinsonism, dystonia, and tremor" (see table 1 for details). This variability within and across classification systems is problematic, as it perpetuates a cartesian dualism and creates coding problems between mental health and neurological disorders that affect which clinical services will be reimbursed, or by which expert patients should be evaluated in medico-legal cases.

### Aims of this review

In 2013, a new set of diagnostic criteria for FND appeared in the DSM-5, and emphasized the importance of making a rule-in positive diagnosis based on physical examination and semiological features. In the DSM-IV, emphasis was given to making an exclusionary diagnosis (based on all available neurological tests being normal) and



**Fig 1 | Emerging pathophysiology of functional neurological disorder** In the left panel, core constructs implicated in FND are highlighted, including disturbances in attention, self-agency, prediction/inference, and emotion/threat processing. In the right panel, the brain circuits implicated in the pathophysiology of FND (and their interactions) are displayed. As depicted, FND is a multi-network disorder involving abnormalities within and across brain circuits implicated in sense of agency, emotion/threat processing, attention, homeostatic balance, interoception, multimodal integration, and cognitive/motor control, among other functions. Circuits are described by their related dysfunction in the pathophysiology of FND. Several areas cut across multiple networks; for example, the dorsal anterior insula is most strongly interconnected with the dorsal anterior cingulate cortex, while the posterior insula receives afferent projections from the lamina I spinothalamic pathway and somatosensory cortices. Similarly, the amygdala is part of both the saliency and limbic networks. Prefrontal brain regions are interconnected with striatal-thalamic areas (not shown), and these pathways should also be factored into the neural circuitry of FND. AMY=amygdala; dIPFC=dorsolateral prefrontal cortex; FEF=frontal eye fields; HYP=hypothalamus; PAG=periaqueductal gray; pgACC=perigenual anterior cingulate cortex; sgACC=subgenual anterior cingulate cortex; SMA=supplementary motor area; TPJ=temporoparietal junction. Figures reproduced with permission from Drane et al 2020 *CNS Spectrums*

**Table 1 | Nosological classification of functional neurological disorder (diagnostic entities include DSM-5, ICD-10, and ICD-11\*)**

DSM-5 (2013)	ICD-10 (2016)	ICD-11 (2019)
Somatic symptom and related disorders	Anxiety, dissociative, stress related, somatoform, and other non-psychotic mental disorders	06 mental, behavioral, or neurodevelopmental disorders
F44.X Conversion disorder (functional neurological symptom disorder)	Dissociative (conversion) disorders	6B60 dissociative neurological symptom disorder
F44.4: with motor symptoms (weakness or paralysis, abnormal movement, swallowing, speech)	F44.0 Dissociative amnesia	6B60.0 visual
F44.5: with attacks or seizures	F44.2 Dissociative stupor	6B60.1 auditory
F44.6: with sensory symptoms (anesthesia, sensory loss, visual/olfactory/hearing disturbance)	F44.4 Dissociative motor disorders	6B60.2 vertigo or dizziness
F44.7: with mixed symptoms	F44.5 Dissociative convulsions	6B60.3 sensory
Specify if: acute (<6 months) or persistent (>6 months)	F44.6 Dissociative anesthesia and sensory loss	6B60.4 non-epileptic seizures
Specify if: with or without psychological stressor	F44.7 Mixed dissociative (conversion) disorder	6B60.5 speech
	F44.8 Other dissociative (conversion) disorders	6B60.6 paresis or weakness
	F44.9 Dissociative (conversion) disorder, unspecified	6B60.7 gait
		6B60.8 movement
		6B60.9 cognitive
		08 Diseases of the nervous system
		8A00.3 Functional parkinsonism
		8A02.3 Functional dystonia or spasms
		8A04.4 Functional tremor

\*DSM-5=Diagnostic and Statistical Manual of Mental Disorders 5th edition, published 2013. ICD =International Classification of Diseases (ICD-10 is the 10th edition, 2016, and the ICD-11 the 11th, 2019)

linking symptom onset to a psychological trigger. The presence of a psychosocial stressor is now recorded as being present or absent as an adjunctive specifier, after a rule-in diagnosis of FND has been first confirmed. This implies that neurologists (and neuropsychiatrists) are first line in the diagnostic evaluation and immediate clinical management following diagnosis. Yet this is not implemented in clinical practice worldwide, as shown by a vote at the American Academy of Neurology during a 2018 plenary session: a majority of international neurologists expressed the opinion that it is not their role to be primarily involved in the management of FND.<sup>9</sup> Moreover, many neurologists still order additional tests, even if they are already convinced that the symptom is not caused by another condition<sup>10</sup>—reflecting that they do not rely on the clinical diagnosis as stated in the DSM-5.

In this review, we highlight literature that shows multidisciplinary and interdisciplinary approaches are important in the care of patients with FND.<sup>11</sup> In fact, international efforts are promoting such multidisciplinary collaborations: the American Neuropsychiatric Association Committee on Research has recently established practice recommendations<sup>12 13</sup> to guide the diagnostic process, integrating both neurological and psychiatric perspectives—an approach that not only informs diagnosis but also aids the development of a biopsychosocially informed, patient centered treatment plan. A new society, the international Functional Neurological Society ([www.fndsociety.org](http://www.fndsociety.org)) was established in 2019, open not only to neurologists, psychiatrists, and psychologists but also to all allied healthcare professionals (eg, physiotherapists, occupational therapists, speech and language pathologists, social workers, etc). Several patient associations ([fndhope.org/fndaction.org.uk](http://fndhope.org/fndaction.org.uk)) promote understanding and awareness of the disorder, develop support groups, and assist with access to appropriate medical care. Specialized FND clinics, focusing on diagnostic, therapeutic, and research aspects are being developed worldwide,<sup>14-16</sup>

modeled in part on a pioneering stepped care model developed in Scotland,<sup>17</sup> and with collaboration at its core.<sup>18</sup> Treatment facilities are also being developed and optimized across outpatient and inpatient settings.<sup>14 19-22</sup>

This clinical interest occurs in parallel with new research findings that show efficacy of specific therapeutic approaches,<sup>21 23 24</sup> and elucidate underlying neurobiological mechanisms<sup>25 26</sup> that open new routes into targeted treatment strategies.<sup>27-30</sup>

This article presents the evidence available to guide clinicians in the diagnosis and clinical management of patients with FND. We focus on motor (F44.4 and 6B60.3/6B60.5-8) and seizure type (F44.5 and 6B60.4) clinical presentations. We do not include the less frequent subtypes such as individuals with isolated somatosensory deficits (F44.6), cognitive symptoms (6B60.9), special sensory symptoms (visual 6B60.0, auditory 6B60.1), or dizziness and vertigo (6B60.2) that have been reviewed elsewhere.<sup>31 32</sup>

### **Incidence and prevalence of FND**

FND is a frequent<sup>33</sup> and disabling<sup>34 35</sup> condition affecting young people,<sup>36</sup> and has a poor prognosis in many patients.<sup>37</sup> The incidence rate of mixed FND is estimated at 4-12/100 000 population per year.<sup>38-41</sup> Motor FND (abnormal movements and weakness) is estimated at 4-5/100 000 per year, and seizure type FND (also known as psychogenic non-epileptic or dissociative seizures) at 1.5-4.9/100 000 per year.<sup>42-44</sup> Prevalence studies are scarce, but the reported rate of FND is around 50/100 000 in the population.<sup>36</sup> The prevalence of seizure type FND is estimated at 2-33/100 000.<sup>36 44</sup>

### **Sources and selection criteria**

We searched the Medline, PsycInfo, and Cochrane databases from inception to 1 November 2020 to find articles pertaining to motor FND (weakness and abnormal movements subtypes) and seizure type FND. Our search terms included “functional”,

**Table 2 | Validated positive motor signs for FND (positive signs evaluated in one or more validation studies with a control group, as well as specificities and sensitivities, and with relevant reference from articles reporting on these signs)**

Positive sign	How to test	Evidence/populations tested	Reference	Note
<b>General signs</b>				
Distractibility	Engage the patient in another motor or cognitive task and observe changes in the abnormal movement	In 19 functional stereotypies v 64 tardive dyskinesia; specificity 100%, sensitivity 58%	Baizabal-Carvalho 2017 <sup>45</sup>	Validated in stereotypies but can be seen in all FND subtypes
Variability	Observe changes during history taking/examination/arriving or leaving the examination room: periods of unexplained improvement/disappearance of symptom	In 19 functional stereotypies v 64 tardive dyskinesia; specificity 100%, sensitivity 84%	Baizabal-Carvalho 2017 <sup>45</sup>	Validated in stereotypies but can be seen in all FND subtypes
Convergence spasm	Instruct the patient to focus on your finger, 10 cm away from the face, at either extreme lateral gaze for 5 s. Move toward midline and observe the appearance of disconjugate gaze AND miosis	In 13 functional movement disorder, 11 “organic” controls, and 12 healthy: specificity 87%, sensitivity 15%. Good inter-rater reliability ( $\kappa$ 0.6)	Fekete 2012 <sup>46</sup>	
Eye movement abnormalities during examination	Systematically test for eye movements even in patients with no symptoms: a discordance between no visual complaint and abnormal findings can be seen (excessive blinking, effortful facial expression, increased latency, gaze deviation, limited range, absent frontalis contraction during upgaze)	In 101 FND patients 43% have abnormal examination	Teodoro 2019 <sup>47</sup>	No “organic” control group
Expressive behavior	Look for “expressive” behavior displaying disproportionate effort to the task during examination	In 20 FND v 20 “organic” controls, specificity 95%, sensitivity 55%. Good inter-rater reliability ( $\kappa$ 0.5)	Daum 2015 <sup>48</sup>	Can be observed throughout the examination
<b>Gait</b>				
Monoplegic leg dragging	The weak leg is “dragged” like a piece of wood/inanimate object, without spastic circumduction, usually along the floor surface	Validated in 2 studies; pooled specificity 100%, sensitivity 9%. Inter-rater reliability validated in 2 studies: Moderate to good inter-rater reliability ( $\kappa$ 0.4 to 0.7)	Daum 2015, <sup>48</sup> Stone 2010 <sup>49</sup>	
“Huffing and puffing” sign	Look for 6 behaviors; huffing, grunting, grimacing, breath holding, heavy breathing, crying. Rate each on severity 0 to 4 and duration 0 to 4	In 131 FND v 37 “organic” controls, when score $\geq 2$ : specificity 100%, sensitivity 44%. Moderate inter-rater reliability ( $\kappa$ 0.4)	Laub 2015 <sup>50</sup>	
Falls toward support	The patient tends to fall in the direction of support (wall, furniture)	In 20 FND v 20 “organic” controls; specificity 93%, sensitivity 19%. Excellent inter-rater reliability ( $\kappa$ 0.8)	Daum 2015 <sup>48</sup>	
Excessive slowness	Look for disproportionate slowness in gait (slow stepping movements contrasting with lack of limb bradykinesia)	In 20 FND v 20 “organic” controls; specificity 94%, sensitivity 32%. Moderate inter-rater reliability ( $\kappa$ 0.5)	Daum 2015 <sup>48</sup>	
Hesitation/caution	Look for disproportionate hesitation and caution in gait (contrasting with good balance, strength, sensation)	In 20 FND v. 20 “organic” controls; specificity 100%, sensitivity 37%. Good inter-rater reliability ( $\kappa$ 0.7)	Daum 2015 <sup>48</sup>	
Non-economic posture	Look for postures during gait that require good balance and strength such as flexed knees	In 20 FND v 20 “organic” controls; specificity 100%, sensitivity 21%. Moderate inter-rater reliability ( $\kappa$ 0.5)	Daum 2015 <sup>48</sup>	
Sudden knee buckling	Look for sudden buckling of the knee, usually with each step. Extreme cases will show knee touching the floor at each step	In 20 FND v 20 “organic” controls; specificity 95%, sensitivity 21%. Moderate inter-rater reliability ( $\kappa$ 0.5)	Daum 2015 <sup>48</sup>	
Chair test	In case of severe gait disorder, ask the patient to propel a chair with wheels; movements of the legs will be better than during gait	In 9 FND v 9 “organic” controls; specificity 100%, sensitivity 89%	Okun 2007 <sup>51</sup>	
<b>Axial</b>				
<b>Face</b>				
Hemifacial spasm	Lack of “other Babinski sign”	Observe eyebrow elevation: in “organic” cases ipsilateral to the spasm (= “other Babinski sign”), in FND absent or contralateral to the spasm	15 functional movement disorder v 37 hemifacial spasms: specificity 70%, sensitivity 100%	Baizabal-Carvalho 2017 <sup>52</sup>
	Long tonic contraction	Observe if tonic contractions are long ( $>3$ s)	Tonic contraction $>3$ s: specificity 97%, sensitivity 87%	Baizabal-Carvalho 2017 <sup>52</sup>
	Bilateral hemispasm	Observe if purely unilateral (“organic”) or also bilateral/alternating (functional)	Bilateral spasm: specificity 97%, sensitivity 40%	Baizabal-Carvalho 2017 <sup>52</sup>
	Isolated lower face spasm	Observe if isolated lower face involvement	Isolated lower spasm: specificity 97%, sensitivity 33%	Baizabal-Carvalho 2017 <sup>52</sup>
	Lip pulling	Observe if lower face involvement is a tonic deviation of the lower lip, often with ipsilateral platysma contraction	Lip pulling: specificity 100%, sensitivity 47%	Baizabal-Carvalho 2017 <sup>52</sup>
Oro-lingual dyskinesia	Lack of chewing movements	Observe if abnormal movement includes chewing	In 9 oro-lingual functional movement disorder v 50 oro-lingual tardive dyskinesia: lack of chewing movement: specificity 82%, sensitivity 78%	Baizabal-Carvalho 2017 <sup>45</sup>
	Lack of self biting	Observe if abnormal movement includes self-biting	Lack self-biting: specificity 64%, sensitivity 100%	Baizabal-Carvalho 2017 <sup>45</sup>
	Purely lingual movements	Observe if abnormal movement are both lingual and oral (“organic”) or purely lingual (functional)	Lingual without mouth movement: specificity 96%, sensitivity 44%	Baizabal-Carvalho 2017 <sup>45</sup>
	Oro-lingual and speech problem	Observe if speech is also affected	Accompanying abnormal speech: specificity 90%, sensitivity 44%	Baizabal-Carvalho 2017 <sup>45</sup>

(Continued)

Table 2 | Continued

	Positive sign	How to test	Evidence/populations tested	Reference	Note
Neck/trunk					
Weakness	Sterno-cleido-mastoid	Rotation of the head is weak (usually when turning toward the side of the limb weakness)	Validated in 2 studies; pooled specificity 93%, sensitivity 53%. Excellent inter-rater reliability ( $\kappa$ 0.83)	Daum 2015, <sup>48</sup> Horn 2017 <sup>53</sup>	
Lack of balance	Functional Romberg	Large disbalance display during Romberg task but no falls, usually gets better with distraction (drawing number in the back, cognitive task)	In 20 FND v 20 "organic" controls: specificity 100%, sensitivity 39% Moderate inter-rater reliability ( $\kappa$ 0.5)	Daum 2015 <sup>48</sup>	
Cataplexy	Absence of hypotonic facial phenomenon	Observe face during episode: absence of ptosis, mouth opening, and tongue protrusion in functional cataplexy	In 21 FND v 30 narcolepsy patients. Good to excellent inter-rater reliability ( $\kappa$ 0.74 to 0.86)	Pizza 2018 <sup>54</sup>	
	No abrupt facial change	Observe if smile and facial expression changes	Good inter-rater reliability ( $\kappa$ 0.63 to 0.78)	Pizza 2018 <sup>54</sup>	
	No facial jerks/grimaces	Observe if brief abnormal movement occurs	Good inter-rater reliability ( $\kappa$ 0.67 to 0.73)	Pizza 2018 <sup>54</sup>	
	No postural dyscontrol	Observe if head drops and trunk falls	Excellent inter-rater reliability ( $\kappa$ 0.83 to 0.86)	Pizza 2018 <sup>54</sup>	
	Persistence of reflexes	Test tendon reflexes during the episode; in cataplexy they disappear but in functional cases they persist	Good inter-rater reliability ( $\kappa$ 0.77)	Pizza 2018 <sup>54</sup>	
Limb					
Arm/leg weakness	Discordance/inconsistency	A movement cannot be done but the same muscle can be used later in another movement	In 15 FND v 40 controls: specificity 98%, sensitivity 13%	Chabrol <sup>55</sup>	
Arm/leg weakness	Give way weakness	When testing strength against resistance; initially good and then sudden loss of resistance from the patient	Validated in 3 studies: pooled specificity 97%, sensitivity 67% Good inter-rater reliability ( $\kappa$ 0.6)	Daum 2015, <sup>48</sup> Chabrol, <sup>55</sup> Stone 2010 <sup>49</sup>	
Arm/leg weakness	Co-contraction	When testing strength, no movement at the joint (elbow, for example) occurs because co-contraction of agonist and antagonist is observed	Validated in 2 studies; pooled specificity 100%, sensitivity 28% Good inter-rater reliability ( $\kappa$ 0.77)	Daum 2015, <sup>48</sup> Baker <sup>56</sup>	
Arm weakness	Drift without pronation	Arms stretched out, palms up in a full supination position, fingers adducted, eyes closed for 10 s: if a downward drift is seen, observe if a movement of pronation also occurs	Validated in 2 studies; pooled specificity 96%, sensitivity 78%. Good inter-rater reliability ( $\kappa$ 0.78)	Daum 2013, <sup>57</sup> Daum 2015 <sup>48</sup>	
Arm weakness	Abductor finger sign	In severe unilateral hand weakness, ask the patient to abduct the fingers of the healthy hand against resistance; observe if involuntary abduction of the 5th finger in the weak hand occurs (functional) or not ("organic")	In 10 FND v 11 "organic" controls; specificity 100% sensitivity 100%	Tinnazzi 2008 <sup>58</sup>	
Arm weakness	Flex-ext sign	Arms flexed at 30°, forearms held near the wrists by examiner. Ask patient to flex the healthy arm against resistance and observe/feel if increased extension of the weak arm occurs (functional) or not ("organic"). Then ask patient to flex weak arm and observe if extension of healthy arm occurs ("organic") or not (functional)	In 10 FND v 23 "organic" controls: specificity 100% sensitivity 100%	Lombardini <sup>59</sup>	
Leg weakness (unilateral)	Hoover sign	Ask to flex the healthy hip against resistance and observe/feel the strength of hip extension of the weak leg (if patient lying: examiner's hand under the heel, if sitting under the thigh). Compare with voluntary hip extension of the weak leg: if involuntary strength > voluntary strength, Hoover is positive	Validated in 5 studies: pooled specificity 99.5%, sensitivity 61%	Sonoo 2004, <sup>60</sup> Tinnazzi 2008, <sup>58</sup> Stone 2010, <sup>49</sup> Mcwirth 2011, <sup>61</sup> Daum 2015 <sup>48</sup>	
Leg weakness (unilateral)	Abductor sign	Ask to abduct both legs against resistance: observe/feel if involuntary abduction of the weak leg occurs (functional) or not ("organic")	In 16 FND v 17 "organic" controls; specificity 100%, sensitivity 100%	Sonoo 2004 <sup>60</sup>	
Leg weakness	Spinal injury center test	Passively put both legs in a flexed position, sole of feet touching the bed during a lying position; observe if the weak leg stays in this position (functional) or falls back on the bed ("organic")	Validated in 2 studies: pooled specificity 96%, sensitivity 47%	Daum 2015, <sup>48</sup> Yugue 2004 <sup>62</sup>	
Tremor	Distractibility	Pause during ballistic movement or during other motor/mental task or change in amplitude and frequency	In 50 FND tremor v 160 other tremors: specificity 92%, sensitivity 94%	Van der Stowe <sup>63</sup>	
	Increase in amplitude with weight	Wrap a weight (500 g) around the wrists and observe change in frequency and amplitude	In 50 FND tremor v 160 other tremors: specificity 92%, sensitivity 22%		
	Entrainment	Ask to imitate tapping motion with one hand and observe the change in tremor frequency on the other	In 50 FND tremor v 160 other tremors: specificity 91%, sensitivity 91%		
	Combination of the 3 features	Presence of at least 2 of these 3 tested in 50 FND and 160 other individuals with tremor	In 50 FND tremor v 160 other tremors; specificity 93%, sensitivity 100%		

**Table 3 | Validated positive signs for seizure type FND (positive signs evaluated in one or more validation studies with a control group, as well as specificities and sensitivities, and with relevant reference from articles reporting on these signs)**

Positive sign	How to test	Evidence /populations tested	Reference	Note
<b>General signs</b>				
Long duration	Observe if >2 minutes	In 341 FND v 441 epilepsy patients: specificity 93% sensitivity 65%	Seneviratne 2017 <sup>64</sup>	Other studies: Syed 2011, <sup>65</sup> Bazil, <sup>66</sup> Jedrzejczak 1999, <sup>67</sup> De Paola 2016, <sup>68</sup> Slater 1995, <sup>69</sup> Azar 2008, <sup>70</sup> Vogrig 2018, <sup>71</sup> Bazil 1997, <sup>66</sup> CAVEAT: duration can be short in frontal lobe epilepsy, Saygi 1992. <sup>72</sup> Note: status epilepticus should also be considered on the differential diagnosis
Waxing and waning/ fluctuating	Observe seizure course: a decrease/ increase of motor events and/or pauses in the seizure course is suggestive of FND course	In 50 FND v 20 epilepsy patients: specificity 100% sensitivity 94%	De Paola 2016 <sup>68</sup>	Other studies: Syed 2011, <sup>65</sup> Vogrig 2018, <sup>71</sup> Chen 2008 <sup>73</sup>
<b>Clues that the patient has preserved awareness</b>				
External influence on attack course	Observe if others can intensify or alleviate the symptoms	In 12 FND v 23 epilepsy patients: specificity 99% sensitivity 83%	Syed 2011 <sup>65</sup>	
Eye contact	Observe if eyes respond to environment and stimuli	In 12 FND v 23 epilepsy patients: specificity 77% sensitivity 79%	Syed 2011 <sup>65</sup>	
Responsiveness	Observe if patient can respond during an attack	In 50 FND v 20 epilepsy patients: specificity 100% sensitivity 36%	De Paola 2016 <sup>68</sup>	
Shaking without loss of consciousness	Observe if semiology looks like generalized seizure (shaking of limbs) but with NO loss of consciousness	In 20 FND v 20 epilepsy patients: specificity 100% sensitivity 20%	Devinsky 1996 <sup>74</sup>	
Recall of event	Ask the patient if she/he recalls the event	In 50 FND v 20 epilepsy patients: specificity 100% sensitivity 60%	De Paola 2016 <sup>68</sup>	
Recall of a named item	During the attack, name a color, object, or phrase and ask the patient afterwards if he/ she can recall it; if yes suggestive of FND	In 20 FND v 20 epilepsy patients: specificity 85% sensitivity 90%	Devinsky 1996 <sup>74</sup>	Other study: Bell 1998 <sup>75</sup>
<b>Motor behavior</b>				
Closed eyes	Observe if eyes are closed and/or resist attempted opening by examiner, and or eyelids flutter during seizure	In 52 FND v 156 epilepsy patients: specificity 98% sensitivity 96%	Chung 1996 <sup>76</sup>	Other studies: Syed 2011, <sup>65</sup> Chen 2008, <sup>73</sup> De Paola 2016, <sup>68</sup> Gates 1985, <sup>77</sup> Devinsky 1996, <sup>74</sup> Detoleado 1996, <sup>78</sup> Azar 2008 <sup>70</sup>
Asynchronous limb movements	Observe if arm or leg movements are synchronous: if not, suggestive of FND	In 50 FND v 20 epilepsy patients: specificity 100% sensitivity 84%	De Paola 2016 <sup>68</sup>	Other studies: Syed 2011, <sup>65</sup> Chen 2008, <sup>73</sup> Azar 2008, <sup>70</sup> Gates 1985, <sup>77</sup> CAVEAT: can be seen in frontal lobe seizures
Pelvis thrusting	Observe if rhythmical movements of pelvis occur	In 12 FND v 23 epilepsy patients: specificity 99% sensitivity 8%	Syed 2011 <sup>65</sup>	Other studies: De Paola 2016, <sup>68</sup> Chen 2008, <sup>73</sup> Azar 2008, <sup>70</sup> Gates 1985, <sup>77</sup> Geyer 2000, <sup>79</sup> Saygi 1992 <sup>72</sup>
Side-to-side head movements	Observe if head (or body) has side-to-side lateral movements	In 50 FND v 20 epilepsy patients: specificity 100% sensitivity 66%	De Paola 2016 <sup>68</sup>	Other studies: Syed 2011, <sup>65</sup> Chen 2008, <sup>73</sup> Azar 2008, <sup>70</sup> Gates 1985, <sup>77</sup> Saygi 1992 <sup>72</sup>
Arching back ("Arc de cercle")	Observe if the patient arches back in opisthotonos-like posture	In 50 FND v 20 epilepsy patients: specificity 100% sensitivity 38%	De Paola 2011 <sup>68</sup>	Other study: Syed 2011 <sup>65</sup>
Rotation in bed	Observe if the patient rotates/changes position in bed	In 50 FND v 20 epilepsy patients: specificity 100% sensitivity 26%	De Paola 2016 <sup>68</sup>	Other study: Azar 2008, <sup>70</sup> CAVEAT: can be seen in frontal lobe seizures, Saygi 1992 <sup>72</sup>
<b>Accompanying behavior</b>				
Ictal crying	Observe if the patient cries during seizure	In 12 FND v 23 epilepsy patients: specificity 98% sensitivity 8%	Syed 2011 <sup>65</sup>	Other studies: De Paola 2016, <sup>68</sup> Devinsky 1996, <sup>74</sup> Chen 2008, <sup>73</sup> Slater 1995, <sup>69</sup> Walczak 1996, <sup>80</sup> Asadi-Pooya, 2016 <sup>81</sup>
Ictal whispering	If the patient talks, observe if whispering	In 12 FND v 23 epilepsy patients: specificity 91% sensitivity 49%	Syed 2011 <sup>65</sup>	
Ictal stuttering	If the patient talks, observe if stuttering	In 117 FND v 113 epilepsy patients: specificity 100% sensitivity 9%	Vossler 2004 <sup>82</sup>	
Ictal hyperventilation	Observe if patients hyperventilates throughout the seizure	In 50 FND v 20 epilepsy patients: specificity 100% sensitivity 14%	De Paola 2016 <sup>68</sup>	Other studies: Devinsky 1996 <sup>74</sup>
<b>Post-ictal behavior</b>				
Short, irregular, shallow breathing pattern	Observe breathing pattern: in FND often irregular, rapid, and shallow (hyperventilation pattern), no snoring, not loud and shorter duration	In 24 FND v 23 generalized epilepsy and 20 frontal lobe epilepsy patients: Mean duration in FND 94 ±55 seconds, in generalized epilepsy 347 ±118 seconds and in frontal lobe epilepsy 64 ±26 (P<0.001)	Azar 2008 <sup>70</sup>	Other studies: Chen 2008 <sup>73</sup>
Rapid recovery	Observe if patient has immediate recovery	In 12 FND v 23 epilepsy patients: specificity 85% sensitivity 73%	Syed 2011 <sup>65</sup>	Other studies: Izadyar 2018 <sup>83</sup> CAVEAT: rapid recovery also occurs in frontal lobe epilepsy, Saygi 1992, <sup>72</sup> Azar2008 <sup>70</sup>
No confusion	Observe if patient has confusion or disorientation; if not suggestive of FND	In 24 FND v 23 epilepsy patients (generalized); specificity 100% sensitivity 88%	Azar 2008 <sup>70</sup>	Slater 1995 <sup>69</sup> CAVEAT: no confusion also occurs in frontal lobe epilepsy, Saygi 1992 <sup>72</sup>
Abrupt signs of recovery	Observe 3 specific behaviors: 1. Blink or brief head shaking after the event. 2. Looking around, 3. Question "what happened?"	In 64 FND v 42 epilepsy patients: if at least one of the 3 behaviors: specificity 100% sensitivity 45%	Izadyar 2018 <sup>83</sup>	

(Continued)

Table 3 | Continued

Positive sign	How to test	Evidence /populations tested	Reference	Note
Additional clues				
Teddy Bear sign	Observe if a stuffed animal is brought by the patient during vEEG monitoring: when yes, suggestive of FND	In 104 FND v 147 epilepsy patients: specificity 88% sensitivity 13%	Cervenka <sup>84</sup>	Not a semiology sign per se
Signs suggestive of epilepsy				
Occurrence from physiological sleep	During video-EEG monitoring, assess if events occur during physiological sleep	In 280 non-epileptic events v 622 epileptic events: specificity 100% sensitivity 31%	Bazil 1997 <sup>66</sup>	Other study: De Paola 2016, <sup>68</sup> If present, is specific for epilepsy. Requires video EEG, not a bedside test. Apparent clinical sleep but without EEG sleep pattern (pseudosleep) occurs in FND (100% specificity, 56% sensitivity) Benbadis 1996 <sup>85</sup>
Vocalization during attack	Observe if brief vocalization occurs during the seizure (epileptic cry)	In 25 FND v 25 epilepsy patients: specificity 100% sensitivity 60%	Gates 1985 <sup>77</sup>	If present is specific for epilepsy. In FND, vocalization such as groaning, moaning can occur before the seizure Other study: De Paola 2016 <sup>68</sup>
Oral (lateral tongue) laceration	Observe if lateral tongue laceration occurred during the event	In 18 FND vs. 66 epilepsy patients: specificity 100% sensitivity 26%	Oliva 2008 <sup>86</sup>	If present is specific for epilepsy. Tested in inpatient setting with objective evaluation by staff. Other study: Dufresne 2019. <sup>87</sup> Of note, REPORTED tongue laceration (not objectively assessed) has been reported equally frequently in epilepsy and FND (around 25%) <sup>88,89</sup>
Self-injury	Observe if event caused injury	In 32 FND v 42 epilepsy patients: specificity 97% sensitivity 19%	Slater 1995 <sup>69</sup>	If present is specific for epilepsy. Of note, reported injuries are less frequent in FND but can occur (found in up to 40% of cases in Peguero 1995 <sup>88</sup> )
Post-ictal Babinski sign	Test for plantar reflex within 5 minutes of the event	In 13 FND v 40 patients with epilepsy: specificity 100%, sensitivity 43%	Walczak 1994 <sup>90</sup>	If Babinski sign, specific for epilepsy

“psychogenic”, “conversion”, “dissociative”, and “hysterical.” More comprehensive details on search terms are available in the supplementary file.

We reviewed titles and abstracts of studies that provided sufficient information on clinical diagnosis and treatment. We excluded case reports, studies not available in English, French, or German, and articles focusing on mechanistic related research questions. In addition, we reviewed the reference lists of selected articles and included other relevant articles. We prioritized original articles but also included noteworthy systematic reviews, narrative reviews, and expert opinions. For the review of positive signs, we summarized in table 2 and table 3 those which had some form of validation (controlled designs to test for specificity and sensitivity or data on inter-rater reliability). To this end, we selected 22 studies<sup>45-63 91-93</sup> reporting on 37 bedside clinical tests or groups of tests for motor FND (functional weakness and functional movement disorder) as well as 27 studies<sup>64-87 90 94 95</sup> reporting on 23 bedside clinical tests or group of tests for seizure type FND. In addition, we also discuss important case series or reviews that highlight relevant bedside clinical tests. We excluded studies that had a primary focus on laboratory tests, as our aim was to provide evidence informing the use of clinical neurological examination findings at the bedside.

#### Diagnosis of FND

Criterion A of the DSM-5 requires “One or more symptoms of altered voluntary motor or sensory function.”<sup>96</sup> This means that patients present with neurological symptoms, and when these concern motor function (F44.4) they can be divided into two broad categories: negative symptoms (lack of movement, weakness) or positive symptoms

(abnormal movement such as tremor, jerks, dystonia, etc). Symptoms can also occur in brief episodes and resemble an epileptic seizure, encompassing the functional seizure (F44.5) diagnosis. To frame subtypes under the overarching diagnostic category of FND, this article refers to functional seizures as seizure type FND.

Criterion B of the DSM-5 requires that “Clinical findings provide evidence of incompatibility between the symptom and recognized neurological or medical conditions.” Demonstrating this incompatibility (eg, noting that subacute arm or leg weakness is distinct from lesional cortico-spinal tract disruptions as might be present in multiple sclerosis or ischemic stroke) is achieved through evaluating for positive signs during the physical examination. The presence of these signs, such as a give-way pattern of weakness when performing confrontation strength testing, or appreciation of tremor entrainment (ie, the rhythmicity of the tremor can be modulated by performance of paced volitional movements performed in a different body part) confirms criterion B and enables a physician to make a positive rule-in diagnosis. This approach is fundamentally different from an exclusionary process and helps not only to make the diagnosis but also to initiate treatment. Indeed, showing or explaining to the patient how diagnosis was reached—by appreciating positive physical examination signs—has been suggested by expert opinion to help individuals understand their disorder and not feel as though “everything is normal in my tests” so the doctor is jumping to the conclusion that “it is functional.”

Most of these clinical bedside positive signs were described a century ago by Jean-Martin Charcot,<sup>97</sup> Charles Hoover,<sup>98</sup> and Joseph Babinski.<sup>99</sup> In the era of evidence based medicine, recent studies have looked

at the sensitivity and specificity of these signs, and a few tested their inter-rater reliability. Below, we detail the current evidence on the formal validation of these rule-in signs.

#### Positive diagnosis of motor FND (F44.4)

Our search found 37 bedside clinical tests or groups of tests for motor FND (functional weakness and functional movement disorder) that had some formal validation (table 2). Sample size varied between 8 and 107 patients with FND. Most investigations of positive signs were conducted in a single study or a small number of studies (maximum five for the Hoover sign), allowing for the calculation of pooled specificity and sensitivity by merging data from different studies. Five studies reported on the inter-rater reliability of positive signs.

Overall, the specificities of validated signs are high, ranging from 64% to 100%; however, the sensitivities are lower, ranging from 9% to 100%. Inter-rater reliability of these signs is overall good to excellent (defined as  $\kappa$  values: <0.2 poor/0.21-0.4 fair/0.41-0.6 moderate/0.61-0.8 good/>0.8 excellent).

#### *What to look for at the bedside*

General signs common to all FND presentations are: variability of the symptom, which can be observed during history taking and examination, and effortful or grimacing expression while following the examiner's instructions during examination. If suspecting a functional movement disorder, test oculomotor function to show abnormal eye movements and in particular convergence spasm,<sup>100</sup> even if the patient did not endorse this as a concern during history taking.

When assessing gait, look for typical positive signs such as monoplegic leg dragging, excessive visible effort ("huffing and puffing" sign),<sup>50</sup> falling toward support (chair nearby, table, wall), excessive slowness, hesitation or caution, non-economic posture (for example knee flexed), and knee buckling (sudden loss of tone at each step).<sup>101</sup> Asking a patient with severe gait disorder to propel a chair while sitting on it will show improvement in FND.<sup>51</sup>

When assessing hemifacial spasm, look for typical signs such as long contraction of more than three seconds, lip pulling (tonic deviation of the lip, often the lower one) sometimes with platysma contraction, and lack of "other Babinski sign" for hemifacial spasm (other Babinski sign=eyebrow elevation on the side of the spasm).<sup>102</sup> Positive signs for functional orofacial movements in comparison with tardive dyskinesia are: lack of chewing movements, lack of self-biting, lingual movements without mouth movements, and abnormal speech.<sup>45</sup> A large case series (61 patients) that focused on facial functional movement<sup>103</sup> reported involvement of the lip as the most frequent (60.7%, with the lip pulling feature).

When assessing movements of the trunk, look for the typical positive sign of asymmetry in strength of the sterno-cleido-mastoid muscle.<sup>53</sup> A "functional

Romberg" sign is described as large movements of imbalance with sudden steps and no falls and improvement with cognitive distraction or numbers drawn on the back.<sup>48</sup>

When assessing episodes of cataplexy (brief, symmetrical loss of muscle tone with retained consciousness precipitated by strong emotions) look for positive signs<sup>54</sup> such as lack of sudden facial expression change, facial jerks or grimaces, postural dyscontrol (head drop, trunk fall), in addition to preserved tendon reflexes (which typically disappear during cataplexy associated with narcolepsy).

When assessing upper arm weakness, look for discordance or inconsistency in strength (at different instances during the examination), as well as a give-way/collapsing pattern, drift without pronation, and/or co-contractions of agonist and antagonist muscles preventing movement of the tested joint. As a cautionary note, give-way/collapsing pattern of weakness is common in patients with pain limited weakness (and pain limited weakness should not be mistaken for functional limb weakness).<sup>104</sup> In cases of complete hand plegia, involuntary abduction of the fifth finger can be seen when the patient is asked to do a forced abduction against the examiner's resistance on the healthy hand.<sup>58</sup> The flex-ext sign, which is the equivalent of the Hoover sign,<sup>105</sup> can be elicited as follows: the involuntary flexion of the arm at the elbow that occurs when the patient focuses on extending the healthy elbow against the examiner's resistance is better than the voluntary flexion.<sup>59</sup>

When assessing lower limb weakness, also look for discordance/inconsistency, give-way/collapsing weakness, co-contractions, and the Hoover sign.<sup>61</sup> The classical way to describe a positive Hoover sign is when the involuntary hip extension (when the patient focuses on flexing the healthy leg against the examiner's resistance) is stronger than the voluntary hip extension. A similar pattern can be found during leg abduction<sup>60</sup>: when the patient is asked to do a forced abduction with both legs against the examiner's resistance, the weak leg will have a stronger involuntary abduction than when the voluntary abduction is tested. In patients with severe unilateral leg weakness, positioning passively the leg in flexion with the soles on the bed (spinal injury test)<sup>62</sup> shows a discordance in strength as the weak leg will not fall on the side, as expected in complete weakness.

When assessing tremor, typical signs are distractibility, entrainment, and increase in amplitude with weight load on the wrists. In addition, look for variability in amplitude, frequency, and direction of tremor.<sup>63</sup> A "whack a mole" sign can be seen<sup>106</sup>: when the limb affected by tremor is immobilized by the examiner, the tremor appears in another body segment (head, trunk, other arm, or legs).

No validated clinical signs are available for assessing dystonia, but a pattern of adult sudden onset fixed dystonia (typically clenched fist sparing thumb and index finger<sup>107</sup>) or equinovarus foot is



suggestive of functional dystonia.<sup>108</sup> Associated prominent pain and other FND signs can help support the diagnosis.<sup>109</sup>

When assessing tics, no validated signs are available but clinical clues can help identify functional tics<sup>110 111</sup>: lack of premonitory urge and inability to suppress the movement, female preponderance, additional FND symptoms, lack of response to anti-tic medication, and absence of family history. In functional tics, the cranial region is less affected, the type of tic is often “blocking” (ie, interferes with voluntary action) and palin, echo, and copro phenomenon are less common.

Overall, the evidence for rule-in motor signs shows very high specificity, which advocates for their routine use in clinical practice. A range of educational pictorial and video libraries illustrate many of these signs.<sup>2 101 102 112 113</sup> Too much emphasis on a single sign, however, can lead to false positives. In a cohort of 190 patients diagnosed with a neurological disorder, 37 (20%) had at least one positive functional neurological sign.<sup>91</sup> Interestingly, regression analysis showed that this 20% of the cohort had typical risk factors known in patients with FND, suggesting that the presence of positive signs in this subgroup could either be false positives or indicate the presence of an FND comorbidity. Keep in mind the possibility that the patient has both FND and another neurological disorder: recent reports describe functional neurological signs in a subset of patients with Parkinson’s disease<sup>114 115</sup> or multiple sclerosis.<sup>116</sup> Overall, data from a systematic review and a prospective study underscore that rates of misdiagnosis in FND since 1970 (once confirmed) are low, and between 1% and 4%.<sup>117 118</sup>

Recently, efforts have been made to integrate additional clinical features in the process of diagnosis, such as, for example, abrupt onset, fluctuations of the motor symptom, comorbid pain, and fatigue.<sup>119</sup> The presence of these features should raise the index of suspicion and prompt a more systematic search of signs positive for FND.

#### Positive diagnosis of seizure type FND (F44.5)

Our search highlighted 23 bedside clinical tests or groups of tests for seizure type FND that had some formal validation (table 3). Sample size varied between 11 and 341 patients with seizure type FND. Most positive signs were investigated in multiple studies with different control groups, so we decided not to calculate pooled specificities and sensitivities. We report in table 3 data from the main study (usually the largest cohort) of the corresponding sign but added citations of all others that tested the same sign. Four studies looked at inter-rater reliability of the signs.<sup>65 79 94 95</sup>

Overall, the specificities of validated signs are high, ranging from 77% to 100%. Sensitivities are lower, ranging from 9% to 96%. The inter-rater agreement of two independent raters was excellent ( $\kappa > 0.87$ ) for 40 signs.<sup>65</sup>

#### What to look for at the bedside

Duration is an important feature helping to differentiate seizure type FND from epileptic seizures: a duration of more than two minutes is highly specific for FND (although caution should be taken not to miss status epilepticus in emergent situations). A pattern of waxing and waning, irregular course, or pauses in the event are also typical.

Preserved consciousness can be shown when patients recall the event or are able to encode a memory (it is useful to ask the patient to memorize items during the event and ask afterwards if that information can be recalled). Indirect evidence of preserved awareness includes patients responding to eye contact, exploring the room visually, or having their event influenced by other people (alleviating or aggravating it).

Specific behaviors can be observed, such as closed eyes or even resistance to passive opening attempts by the examiner, asynchronous limb movements (can also occur in frontal lobe seizures), pelvis thrusting, side-to-side head movements, and arching back.

Vocalization or abnormal speech can take the form of moaning or groaning (usually before the event), crying or weeping, whispering, or stuttering. Vocalization in the form of a sudden cry during the seizure is suggestive of epileptic seizures (during the tonic phase).

After the event, rapid recovery is typical in seizure type FND with no post-ictal confusion. Motor signs indicating an abrupt stop of the event can be observed, such as blinking or brief head shaking indicating the end, looking around, asking “what happened?” Breathing is different from epileptic stertorous breathing (low pitch sound during inspiration) and takes the form of regular hyperventilation.

Features that suggest epileptic seizures include: occurrence from physiological sleep and post-ictal Babinski sign. Note that urinary incontinence<sup>120</sup> and self-injury<sup>88</sup> can occur in individuals with epileptic seizures and in those with the seizure type of FND. Also, an oral tongue laceration (usually lateral part) documented by medical staff is specific for epilepsy; reports of tongue laceration by the patient are less specific, as it has been reported in up to 21% of non-epileptic events compared with 27% of epileptic seizures.<sup>89</sup>

Overall, the evidence for positive signs of seizure type FND also shows very high specificity, which advocates for their routine use clinically. Along with these clinical signs, electroencephalographic (EEG) recording of the event can help differentiate FND from epilepsy as the event will not be accompanied by the typical electrographic features on EEG. The gold standard for diagnosis is thus to capture a typical event with video EEG (if needed with specific provocation techniques<sup>121</sup>). Video EEG is not always available, therefore the International League Against Epilepsy has developed staged criteria to make a diagnosis of seizure type FND, including possible, probable, clinically established, and documented criteria.<sup>122</sup> A diagnosis is “possible” when the history

and description from a witness is suggestive of FND and an interictal EEG is normal. The diagnosis reaches the level of “probable” when a clinician with experience diagnosing seizure disorders observes the positive signs either by witnessing an event or a video recording and an interictal EEG is normal. Thus, it is helpful to ask patients to obtain home videos of typical events when possible.<sup>123</sup>

The diagnosis is “clinically established” when these semiological features are observed (in person or on video) and an ambulatory ictal EEG of a typical event is normal (separated in time). It is “documented” when a typical event is concurrently captured on video and EEG. Keep in mind the possibility that a patient has both FND and epilepsy, as around 20% of patients with seizure type FND also have epileptic seizures.<sup>124 125</sup>

The experience of the clinician assessing the presence and interpretation of these positive signs is also important. A study<sup>126</sup> showed that emergency department staff (physicians or nurses) without specific neurology training only recognized 44-58% of functional neurological events, while neurology-trained staff recognized 70-73%, and epileptologists 88% of seizure type FND events. These observations underscore the need for increased educational efforts pertaining to the recognition of highly specific signs for seizure type FND.

Recent efforts have been made to integrate self-reported subjective features in the diagnosis process, such as, for example, amnesia of the event, mind-body-world disconnection, or sensory experiences.<sup>127</sup> The presence of these features can help raise the index of suspicion for a given diagnosis, prompting diagnostic confirmation based on semiological features and EEG data. Emerging research also looks at how to optimally combine self-report and objective signs to support the clinical diagnosis, such as, for example, history of migraine and female sex associated with long duration and eye closure being strongly suggestive of FND.<sup>128</sup> Before good clinical scales with precise cut-off scores are available, subjective reports should be regarded cautiously, and objective assessment through video EEG remains the gold standard.

#### Role of exclusion (alternative diagnoses) in making the diagnosis

Criterion C of the DSM-5 requires that “the symptom or deficit is not better explained by another medical or mental (health) disorder.” This should not be mistakenly interpreted to represent that a patient cannot have FND AND a comorbid neurological condition. In instances of diagnostic uncertainty, the diagnosis for a subset of patients with functional movement symptoms can benefit from the use of an electromyogram, an accelerometer, or an EEG (to seek Bereitschaft potential in cases of jerky movements, for example) to help make a laboratory assisted diagnosis of FND (for a review of adjunctive diagnostic tests in FND, see<sup>129</sup>). In particular, validated criteria for tremor (which can capture

features of entrainment or pauses that may not be readily appreciable through visual inspection) are now available to help reach a “laboratory supported” level of certainty about diagnosis.<sup>130-132</sup> Similarly, for patients with seizure of diagnostic uncertainty, using adjunctive diagnostic tests,<sup>133</sup> such as nuclear medicine brain imaging approaches, may help provide additional diagnostic clarification.<sup>13</sup>

#### Impact on daily activities and quality of life

Criterion D of the DSM-5 requires that “the symptom or deficit causes clinically significant distress or impairment in social, occupational, or other important areas of functioning or warrants medical evaluation.” In clinical practice, the fact that patients seek medical attention helps support this criterion, as their symptoms often have a significant impact on their daily activities. Across both motor and seizure type FND, health related quality of life (HRQoL) is comparable with, if not worse than, that observed in other major neurological disorders. The most robust literature is found in those with seizure type FND, where this population has consistently reported lower HRQoL than populations with epilepsy.<sup>134 135</sup> In a 20 year retrospective study, patients with seizure type FND also showed a standardized mortality ratio 2.5 times above that of the general population—rates comparable with people observed in treatment for refractory epilepsy.<sup>136</sup> Notably, frequency of seizures has not been found to have a dose dependent relationship with HRQoL in patients with seizure type FND; achieving complete resolution of seizures, however, does positively correlate with improvements in HRQoL.<sup>137 138</sup> As detailed in a systematic review, a range of psychiatric and psychosocial factors influence HRQoL in patient with seizure type FND.<sup>139</sup> These factors include depression, dissociation, other somatic (bodily) symptoms, escape-avoidance coping, negative illness perceptions, medication side effects, family functioning, and perceived stigma regarding a diagnosis of seizure type FND.<sup>134 135 140-147</sup>

Patients with motor FND reported similar HRQoL to patients with Parkinson’s disease,<sup>148 149</sup> and worse HRQoL compared with individuals with primary dystonia.<sup>149</sup> Non-motor symptoms were closely related to HRQoL in patients with motor FND—most notably fatigue, cognitive complaints, and anxiety.<sup>150 151</sup> A study of 107 patients with motor FND reported them to have similarly impaired HRQoL to patients with other neurological causes for limb weakness.<sup>49</sup> Two separate long term follow-up studies showed that HRQoL remained impaired in patients with motor FND at levels comparable with patients who had other neurological conditions (eg, multiple sclerosis).<sup>117 152</sup> In one 14 year follow-up study, patients with motor FND showed a 1.48 standardized mortality ratio.<sup>117</sup> Lastly, in a study of mixed FND, positive associations were observed between social network size and physical and mental HRQoL, underscoring the importance of the biopsychosocial formulation in determinants of health status in patients with FND.<sup>153</sup>

### How to explain the diagnosis

Central to delivering a diagnosis of FND is the language used—a topic that has been debated for decades. Pejorative terms such as “hysteria” or “pseudoseizures” are no longer acceptable.<sup>154 155</sup> However, debate continues regarding use of “functional” versus “psychogenic.” Support for the term “functional” includes: (1) it is a neutral framing that embraces the causes and mechanistic heterogeneity of this condition within the biopsychosocial model; (2) it parallels the transient reversibility of symptoms reflected in diagnostic criteria; (3) it aids acceptance given the lack of overt connotations to a mental health condition; and (4) it avoids mind-body dualism.<sup>156-159</sup> Arguments in favor of “psychogenic” include: (1) it is a term that closely couples the condition with psychiatric or psychological care; (2) the term “functional” has a complicated history itself—and patients experience their symptoms as “dysfunctional”; and (3) “functional” can contribute to a sometimes unhelpful function-versus-structure dualism (replacing one misguided dualistic framing with another).<sup>160-162</sup>

Practitioners in movement disorders have shifted from “psychogenic” to “functional movement disorders,” while epileptologists continue to debate “functional seizures” versus “dissociative seizures” versus “psychogenic nonepileptic seizures” versus other terms (eg, non-epileptic attack disorder).<sup>163-165</sup> Another complicating factor is lack of agreement regarding use of “seizure” for paroxysmal FND versus “events” or “attacks.”<sup>166 167</sup>

We support “functional neurological disorder” as the overarching diagnostic category, and thus our opinion is that FND subtypes should carry the qualifier “functional.” This should not be interpreted, however, as invalidating that FND remains at the intersection of neurology and psychiatry, and research suggests that the language used around the diagnosis is also important in framing the condition.<sup>168</sup> Lastly, the “organic” versus “non-organic” label is falsely dualistic of brain and mind, and calls for its removal are well founded.<sup>169</sup>

Efforts have been made to operationalize the communication of a FND diagnosis—framing this as the first step in treatment.<sup>170</sup> Early strategies to conceptualize the diagnosis as “good news” have fallen out of favor as this can be perceived as invalidating.<sup>170</sup> In the literature, communication approaches recommended by Hall-Patch and colleagues include: (1) validating symptoms as genuine and common; (2) naming the condition; (3) providing a brief mechanistic explanation (eg, “brain becomes overloaded and shuts down”); (4) addressing effective and ineffective treatments; and (5) fostering a hopeful sentiment of improvement (eg, pointing out that treatments are available).<sup>171</sup>

Describing FND as akin to a “software rather than a hardware problem” and symptoms occurring when the “computer crashes” is another helpful mechanistic explanation.<sup>172 173</sup> Showing patients their “rule-in” signs and referring back to those

features when discussing the diagnosis is an expert recommendation that has been widely adopted<sup>174</sup>; similarly, focusing on the “what” of diagnosis rather than the “why” can help avoid overly simplistic attempts to link FND symptoms to stress.<sup>175</sup> High yield “how to” articles written by FND experts have further contributed to the dissemination of good clinical practices regarding communication approaches<sup>172 176 177</sup> (an illustration on how to deliver a diagnosis is provided in video 1, supplementary file 1). Additionally, providing patients with written materials (eg, [www.neurosymptoms.org](http://www.neurosymptoms.org)) can further enhance their understanding.<sup>156</sup> Improved education for physicians is needed around delivery of the diagnosis,<sup>178</sup> given that neurologists find FND a challenging condition to discuss with patients and to document within the medical records.<sup>179-182</sup> A clinical practice survey in 2018 from the International Parkinson and Movement Disorder Society, however, showed that members were more likely to communicate a FND diagnosis without ordering unnecessary tests compared with 10 years prior.<sup>183</sup>

### Treatments

Therapeutic options range from explanation alone to complex multidisciplinary rehabilitation. Triaging patients in the appropriate pathway is important and should, when possible, be individualized to specific clinical characteristics (an illustrated guide on triaging managing decisions is presented in video 2, supplementary file 2).

### Communicating the diagnosis as the first step

In patients with seizure type FND, delivery of the diagnosis has been shown in a small minority of patients to result in cessation of seizures or decreased seizure frequency.<sup>184-189</sup> For example, in 54 patients with seizure type FND, 27% achieved seizure remission in the week following communication of the diagnosis.<sup>185</sup> Studies have also shown that post diagnosis, emergency department visits and inpatient hospitalizations decrease,<sup>43</sup> with a shift toward increased use of outpatient psychiatric services.<sup>190</sup> However, it remains unclear if fewer patients overall are utilizing healthcare.<sup>191</sup> The long term benefit of communicating a diagnosis of seizure type FND, if used in isolation, also remains unclear.<sup>192</sup> More research is needed on the immediate impact of the delivery of a diagnosis of FND in other subtypes.

### Psychoeducation

Several studies have investigated the efficacy of augmented educational interventions.<sup>193-197</sup> One RCT evaluated the benefit of three monthly psychoeducation sessions (n=34) versus routine follow-up (n=30) in patients with seizure type FND.<sup>194</sup> No differences in frequency of seizures were recorded at a group level; however, the intervention group reported significantly improved psychosocial functioning at three and six months. In a mixed FND cohort (n=193) and their relatives (n=152)

attending a single 105 minute multidisciplinary education session, significant increases in diagnostic understanding, acceptance, belief of treatability, and hopefulness were observed across all in attendance.<sup>196</sup> A large RCT in 186 patients with functional motor symptoms investigated the efficacy of online education and self-help interventions (n=93) compared with usual care alone (n=93), and showed no incremental benefits in terms of health status.<sup>197</sup> Thus, while patient satisfaction is generally high for educational initiatives, their use in isolation does not appear to positively affect recovery from FND.

#### *Physiotherapy and other rehabilitation*

Physiotherapy is a first line treatment for patients with motor FND, although more research is needed to optimize and personalize its use. A major advance was the publication of the 2015 consensus recommendations for physiotherapy for functional motor symptoms.<sup>198</sup> General components of physiotherapy for motor FND as outlined in this article include: education on FND, creating a positive expectation of improvement, open and consistent communication between the multidisciplinary team and patient, limited hands-on interventions, encouraging early weight bearing, focusing on task completion and automatic movements, avoiding use of adaptive equipment where possible, and physiotherapy should be psychologically informed, including recognizing and exploring unhelpful thoughts and behaviors. In terms of rehabilitation strategies, an important principle of physiotherapy for motor FND is emphasis on motor retraining in the context of diverted attention (leveraging observations that functional neurological symptoms improve with distraction and worsen when attention is drawn toward the body).

Two RCTs have shown the efficacy of physiotherapy for motor FND to date.<sup>199 200</sup> In the first, 60 patients with a functional gait disorder were randomized to a three week inpatient multidisciplinary rehabilitation (n=31) versus a wait list control (n=29).<sup>199</sup> The intervention, performed by a multidisciplinary rehabilitation team, consisted of “adapted physical activity with an educational and cognitive behavioral frame of reference.” Core treatments included symptom explanation and actively reinforcing normal movements. The intervention was associated with a significant improvement in walking ability and quality of life, with gait improvements sustained at one month and one year post treatment. In the second study, 60 patients with motor FND were randomized to five consecutive days in a day hospital for specialized neurophysiotherapy (eight 45-90 minute sessions; n=30) versus referral to non-specialist local neurophysiotherapy (n=30).<sup>200</sup> At six months, 72% in the intervention group rated their symptoms as improved (versus 18% in controls). Significant improvements in physical and social functioning were also reported in patients assigned to specialized neurophysiotherapy.

Additionally, a 2013 systematic review reported on 29 cohort studies that also underscored the efficacy of physiotherapy in most patients treated.<sup>201</sup> Nonetheless, unanswered questions remain, including optimal and cost effective treatment settings (eg, inpatient versus day hospital versus outpatient versus tele-physiotherapy) as well as the optimal frequency and intensity.<sup>19 202 203</sup> More research is needed regarding the management of commonly present non-motor symptoms, such as pain and fatigue.<sup>204</sup> A large scale RCT for physiotherapy for motor FND currently under way will likely help clarify some of these questions.<sup>205</sup>

Another rehabilitative treatment that requires more research is occupational therapy. Recently published consensus recommendations for occupational therapy<sup>206</sup> will help standardize interventions in this area. While beyond the scope of this article, speech and language interventions for functional speech/voice disorders may also be helpful in patients with FND—with consensus recommendations published in 2021.<sup>207</sup> Additionally, given the phenotypic heterogeneity found in FND, published consensus recommendations to standardize outcomes measures for clinical trials across core FND symptoms, other physical and mental health symptoms, life impact, healthcare economics, and adverse event reporting, will positively influence research on FND in future.<sup>208 209</sup>

#### *Psychotherapy*

RCTs have examined the efficacy of cognitive behavioral therapy (CBT) in treating patients with seizure type FND.<sup>210</sup> A 2010 pilot RCT performed in seizure type FND (n=66) compared 12 weekly conventional CBT sessions plus standard medical care (SMC) (n=33) versus SMC alone (n=33).<sup>211</sup> This study showed that at three months the CBT group exhibited a reduced frequency of seizures compared with controls (CBT group: monthly seizure frequency at end of treatment 2.0 (interquartile range (IQR) 6.0) versus 6.75 (IRQ 38.63) in the SMC group. However, at six months this effect did not remain significant. A four arm pilot RCT compared 12 session, weekly CBT informed psychotherapy (n=9) versus CBT plus sertraline (n=9) versus sertraline (n=9) versus standard care (n=7), identifying significant seizure frequency reductions (>50%) in both CBT alone (post-treatment/pre-treatment seizure ratio, mean=0.49; standard error (SE)=0.1; 95% confidence interval (CI) 0.28 to 0.84) and CBT plus sertraline (post-treatment/pre-treatment seizure ratio, mean=0.41 (SE=0.1); 95% CI 0.21 to 0.79).<sup>212</sup> Patient and psychotherapist manuals for the 2014 study have been published.<sup>213</sup>

The largest published RCT to date, the cognitive behavioral therapy versus standardized medical care for adults with dissociative non-epileptic seizures trial, compared 186 patients receiving 12 session, weekly conventional CBT plus standardized medical care versus 182 patients receiving standardized medical care alone. At 12 months post randomization,

no significant differences in four week seizure frequency (CBT plus standardized medical care: median four seizures (IQR 0-20) versus standardized medical care: median seven seizures (IQR 1-35)) were observed across treatment arms—albeit both groups improved from baseline. Additionally, nine of 16 secondary outcomes (eg, somatic symptoms, psychosocial functioning) improved differentially in the CBT plus standardized medical care treatment group. In a separate pilot RCT of 60 patients with seizure type FND, the addition of motivational interviewing to CBT (versus CBT alone) improved treatment adherence and decreased frequency of seizures.<sup>214</sup>

CBT has also been evaluated in RCTs across several other FND populations. In a mixed cohort, 127 patients were randomized to self-guided CBT plus usual care (n=64) versus usual care alone (n=63), with a significant (but modest) increased proportion of individuals in the CBT arm reporting being “better” or “much better” at three months<sup>215</sup> (adjusted common odds ratio for an improved outcome with CBT plus usual care of 2.36 (95% CI 1.17 to 4.74). Health anxiety and somatic symptom burden also improved in the CBT arm; the self-guided CBT manual used in this study has been published.<sup>216</sup> A pilot 12 week RCT in motor FND compared CBT (n=14) with CBT plus adjunctive physical activity (n=15) with SMC (n=8), and showed significant improvements in FND severity, as well as secondary measures (ie, depression, anxiety, somatic symptom scales) in the CBT alone and CBT plus activity groups compared with SMC.<sup>217</sup>

A systematic review of prospective psychotherapy clinical trials published in FND to date was published in 2020.<sup>218</sup>

#### *Psychopharmacology*

Several studies have investigated the efficacy of serotonergic based medications in the treatment of patients with FND.<sup>219-221</sup> In general, selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors (or other indicated psychotropic medications) are used to manage concurrent mental health symptoms, but are not themselves indicated for the direct treatment of FND.<sup>222</sup>

#### **Emerging treatments**

Studies have set out to evaluate the efficacy of mindfulness based therapy,<sup>223</sup> prolonged exposure,<sup>224</sup> psychodynamic psychotherapy,<sup>225</sup> and group psychotherapy (including dialectical behavioral therapy)<sup>226-228</sup> in patients with FND. Additionally, hypnosis has been studied in RCTs across inpatient<sup>229</sup> and outpatient settings,<sup>230</sup> with data supporting that outpatients with functional motor symptoms receiving hypnosis improved relative to baseline and a wait list control.<sup>230</sup> Telepsychotherapy also appears to be a viable option in patients with FND.<sup>231</sup> Given the mixed psychotherapy results observed in the FND field to date, it remains to

be determined if guiding treatment selection based on clinical (biopsychosocial) formulations may yield more efficacious and consistent results.<sup>232</sup>

In addition to psychotherapy, evidence from RCTs supports using botulinum neurotoxin in the management of functional motor symptoms, although the mechanism of action may be related to placebo effects.<sup>233 234</sup> Emerging evidence, yet limited, supports transcranial magnetic stimulation, although it remains unclear if potential efficacy is owing to circuit-specific neuromodulation or placebo response.<sup>29 235-238</sup> More research is needed to identify potential therapeutic roles for therapeutic sedation, botulinum neurotoxin treatment, placebo, hypnosis, and virtual reality interventions among other promising management strategies.<sup>234 239-243</sup>

In addition to targeting functional motor and seizure symptoms, many patients with FND experience mental health concerns (depression, anxiety, post-traumatic stress disorder, etc) and/or non-motor symptoms (pain, fatigue, dizziness, cognitive symptoms, etc) that require active consideration in the development of patient-centered treatment plans. Additionally, while only a subset of patients with FND reports adverse life experiences (eg, childhood maltreatment),<sup>244</sup> these factors can be linked to increased severity of symptoms and higher rates of psychiatric comorbidities.<sup>245</sup> More work is needed regarding how to optimally consider concurrently present mental health factors and non-motor physical symptoms in the treatment of patients with FND.

#### **Guidelines**

The American Neuropsychiatric Association's Committee on Research has established expert opinion statements regarding the diagnostic approach to motor FND<sup>12</sup> and seizure type FND,<sup>13</sup> integrating both neurological and psychiatric aspects. However, these articles do not offer guidelines regarding how to optimally manage prominent mental health problems and/or pain, fatigue, and cognitive symptoms when present. A task force from the International League Against Epilepsy proposed in 2013 minimum requirements for the diagnosis of seizure type FND,<sup>122</sup> yet a need persists to better integrate neurological and psychiatric diagnostic criteria for FND. It is anticipated that the FND Society will be working to further operationalize the diagnostic and therapeutic approach to FND.

#### **Conclusion**

The diagnosis of the two most frequent presentations of functional neurological disorder (motor and seizure type) is now a rule-in approach where the careful use of positive clinical signs and neurological expertise is mandatory. A thorough physical examination is necessary and the diagnosis should not rely solely on medical record review and/or a history of associated risk factors (eg, a traumatic life event) that is non-specific for the diagnosis. The use of adjunctive electrophysiological tests such as movement

recordings for tremor or EEG for seizure type FND help ascertain the diagnosis in diagnostically challenging cases; capturing a typical seizure event on video EEG and appreciating the absence of an electrographic correlate helps make a diagnosis of documented seizure type FND. Other neurological tests are not required for the diagnosis but may help if an underlying coexisting neurological disorder is suspected. A dual diagnosis of FND and another neurological disorder should always be considered. Once the diagnosis is made, a clear explanation should be provided to the patient, avoiding the term “medically unexplained.” Educational materials in the form of written or web based information can help patients understand the disorder, build social supports, and achieve diagnostic understanding through collaboration with patient support groups if desired. Early treatment should be based on the patient’s physical symptoms and informed by the biopsychosocial model, taking into consideration relevant mental health and sociocultural factors. First line treatments for both motor FND and seizure type FND include education and psychotherapy; physiotherapy is also first line treatment for motor FND. Many patients benefit from a multidisciplinary approach that incorporates neuropsychiatric and rehabilitation perspectives. Neurological follow-up should be routinely scheduled, as new symptoms can arise that require clinical triage. Lastly, research efforts are under way to aid the development of novel, biologically informed treatments.

#### QUESTIONS FOR FUTURE RESEARCH

- Given that individual positive signs vary in their sensitivities and specificities, what would be the added value to combine signs in a score and what cut off could bring the best positive predictive value to improve the diagnosis of FND?
- Other than additional comorbidities (eg, fatigue, pain, anxiety, and depression) can we identify prognostic markers that can help clinicians and patients choose the optimal treatment path for a given patient?
- In addition to physiotherapy, psychotherapy, and multidisciplinary treatments, can we refine neuromodulation protocols (informed by neural circuit models of FND) to obtain a clinically significant therapeutic effect?

#### PATIENT INVOLVEMENT

The CEO and founder of a charity dedicated to patients with FND (FND Hope) reviewed a draft of this manuscript and made suggestions and edits on the content and presentation; the main suggestions concerned avoiding a lengthy historical background section which we agreed with and general feedback on the terminology used for FND.

Contributors: SA drafted the outline of the draft, designed collection of data, collected and analyzed data, critically appraised data, and wrote and edited the final manuscript. She is guarantor.

DLP drafted the outline of the draft, designed collection of data, collected and analyzed data, critically appraised data, and wrote and edited the final manuscript. He is guarantor.

Both SA and DLP selected the relevant articles, reviewed critically the literature, and wrote the manuscript.

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**Supplementary file 1: Search terms**

**Supplementary file 2: Video 1** How to explain the diagnosis of FND. Key elements that can be discussed with patients when delivering a diagnosis of FND. Video made using Doodly software version 2.6.13

**Supplementary file 3: Video 2** Triaging initial treatment recommendations in patients with FND. Key elements that warrant consideration when providing initial treatment recommendations to patients with FND. Video made using Doodly software version 2.6.13

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