



# Updates in Functional Movement Disorders: from Pathophysiology to Treatment Advances

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## Abstract

**Purpose of Review** This review discusses advances in functional movement disorders (FMD) over the past 3 years, with a focus on risk factors, diagnosis, pathophysiology, neuroimaging studies, and treatment.

**Recent Findings** The past decade has brought a revived interest in functional movement disorders, with a growing number of studies exploring pathophysiological mechanisms. Here, we review recent studies demonstrating changes in attention, emotional and sensorimotor function in FMD. Through international collaborative efforts, progress has been made in defining biomarkers and outcome measures, an important prerequisite towards standardization of diagnosis and reporting of outcomes in clinical trials. Of particular interest are neuroimaging studies demonstrating functional and structural changes in motor and emotional brain circuits, deepening our understanding of FMD as a neurocircuit disorder and potentially paving the way towards new treatments. Currently available treatment modalities have shown successful outcomes via outpatient, inpatient, and virtual delivery.

**Summary** The last 3 years have seen tremendous efforts to better understand, diagnose, and treat FMD. The disease model has been broadened to include a biopsychosocial formulation, and insights on the pathophysiology on FMD are informing treatment efforts. Several international multidisciplinary research collaborations are underway to define biomarkers and best outcome measures, highlighting the path towards improved standardization of future treatment trials. Additionally, the rise of telemedicine during the COVID-19 pandemic has reduced geographic barriers and paved the way for virtual therapy sessions and self-guided programs.

**Keywords** Functional movement disorders · Functional neurological disorders · Psychogenic · Conversion · Neuropsychiatry · Neuroimaging

## Introduction

Functional neurological disorder (FND) is a highly prevalent and disabling condition. It is now widely recognized that genetic, psychosocial, and neurobiological factors may have etiologic implications. Functional movement disorders (FMD) are one of the most common presentations of FND, manifesting as involuntary tremor, tics, myoclonus, dystonia, weakness, or gait abnormalities [1]. The last few years have seen remarkable advances in the field of FMD research. This review provides an update on research published over the last 3 years, with a focus on risk factors, diagnosis, pathophysiology, neuroimaging studies, and treatment.

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## Methods

For this narrative review, the PubMed search engine was utilized. The authors did independent literature reviews using the search terms of “functional movement disorders,” “functional neurological disorders,” and “conversion disorders.” Original research articles published within the last 3 years from 2019 to 2021 were included in the review, with special attention given to updates in pathophysiology, neuroimaging, and treatment approaches.

## Updates on Clinical Features

Several recent studies examined risk factors that can be relevant in the development of FMD. Kletenik et al. [48] reported on a multi-center case–control series with 199 FMD patients and 95 healthy controls that demonstrated an association between sexual abuse and prevalence of FMD in women but not men (OR 4.8,  $p < 0.0001$ ). This suggests that there is a higher chance that females who are sexually abused will develop FMD compared to their male counterparts. Williams et al. report on differentiating styles of attachment and their relation to other FMD risk factors [2]. Fearful attachment was linked to childhood trauma, alexithymia, and depression in FMD.

There has been a difference in opinions whether to “lump” or “split” patients with different functional neurological symptoms, which is important when examining pathophysiology and developing treatment plans. To better inform the clinical approach, Tinazzi et al. reported data on 176 patients with different FMD phenomenologies including tremor, gait disturbances, weakness, dystonia, and jerks [3]. Patients with tremor and gait disturbances were older at time of diagnosis. Those with weakness had a more acute onset, shorter lag time from symptom onset to diagnosis, and a higher frequency of functional sensory symptoms than other movement disorders. Other than these few differences, risk factors, psychiatric comorbidities, and associated FMD symptoms were comparable. Consistent with this study, Gelauff et al. [4] found no difference in demographics, onset, fatigue, depression, anxiety, or pain between patients with functional tremor, gait impairment, weakness, dystonia, or myoclonus in a study of similar sample size. These studies lend support to the hypothesis that different FMD phenomenologies share an underlying pathophysiology.

## Updates on Diagnosis

Rather than being considered a diagnosis of exclusion, making a “positive” diagnosis based on typical clinical features and findings on examination has been widely emphasized

over recent years. In Box 1, typical features of hypokinetic, hyperkinetic and axial FMDs are summarized [5].

**Box 1** Positive clinical features of functional movement disorders

Functional hypokinetic movement disorder	Functional hyperkinetic movement disorders	Functional axial movement disorders
<b>General</b>	<b>Tremor and myoclonus</b>	<b>Gait</b>
Excessive slowness and fatigue	Variable frequency	Knee buckling
Giveaway weakness	Entrainment to different frequencies	Excessive slowness
Distractibility and variability	Suppression with contralateral movements	Dragging one leg
<b>Leg Weakness</b>	<b>Dystonia</b>	Resolution with change of pace or direction
Hoover sign*	Fixed at onset	Decreased swaying with distraction
Hip abductor sign**	Inconsistent resistance	Absent or controlled falls
Ability to stand on heels or toes despite supine plantar or dorsiflexion weakness	Lack of sensory trick	<b>Speech</b>
<b>Arm weakness</b>	Lack of overflow	Excessively effortful
Drift without pronation	<b>Tics</b>	Acute onset adult stuttering
Finger abductor sign***	Not stereotypical	Variable foreign accent
<b>Parkinsonism</b>	“Explosive” onset in adulthood of complex tics with lack of simple tics	<b>Swallowing</b>
Slow tapping without speed or amplitude decrement	Lack of premonitory urge	Globus sensation despite not swallowing anything
Inconsistent rigidity	Inability to suppress	

\*Pressure is felt under the paretic leg when the non-paretic leg is raised. No pressure is felt in the non-paretic leg when the paretic leg is being raised

\*\*Weakness of hip abduction in a paretic leg that resolves with contralateral hip abduction against resistance in the normal leg

\*\*\*Weakness of fingers abduction that resolves with contralateral finger abduction against resistance

There is agreement that an effective explanation of FMD is imperative to building patient confidence in the diagnosis and subsequent adherence to treatment. Nonetheless, many clinicians still struggle with delivering the diagnosis and this can be a barrier to successful management. In this vein, Stone and Hoeritzauer share a practical approach to provide

optimal delivery of a FMD diagnosis [6••]. Special attention is given to demonstrating positive physical signs, explaining the nature and mechanism of FMD, and showing possible reversibility of abnormal neuronal networks.

**Box 2** Approach to sharing the diagnosis of functional movement disorder

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Communicate diagnosis clearly to patient  
 Demonstrate positive features transparently  
 Explain the nature and mechanism of FMD  
 Explore and address unhealthy illness beliefs and behaviors  
 Ensure patients understand the potential of reversibility, use motivational interviewing techniques to enhance readiness for treatment  
 Foster independence and self-management  
 Involve families and caregivers in the diagnosis and treatment process

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Another essential tool in FMD diagnosis is the initial neuropsychiatric testing. Despite the use of this assessment for diagnostic and treatment purposes, evidence-based practices have not been established. In their expert opinion piece, Perez et al. [7••] advise that neuropsychiatric testing should obtain clinical, medical, psychiatric, and psychosocial histories, as well as illness perceptions, health care experiences, and physical exam signs.

## Updates on Pathophysiology

Recent studies aimed at elucidating the pathophysiology of FND focus on the two most common presentations, FMD and functional seizures. Huepe-Artigas et al. [8] demonstrated that compared to patients with functional seizures, those with FMD had significantly more comorbid functional somatic syndromes and preceding medical issues affecting their limbs. Conversely, patients with FMD had significantly less dissociative symptoms and lifelong suicidal ideation.

Attention plays an important role in FND as symptoms improve with distraction and worsen with attention. Huy et al. [9] reported that in a study comparing patients with FMD, organic movement disorders, and healthy control, FMD patients had impaired executive control of attention during conflict. This finding indicates that executive dysfunction is an important secondary feature of FMD, perhaps because excessive effort is placed on explicit motor control. Another study performed by Marotta et al. [10] revealed that patients with FMD have an attentional bias away from negative emotions, with specific attentional avoidance of sadness.

Van Wouwe et al. [11] investigated the ability of FMD patients to control their actions using choice-reaction, stop-signal, and Simon tasks compared to healthy controls.

Patients displayed impaired selective impulse inhibition and global action cancellation, suggesting two forms of abnormal inhibitory control in FMD.

Lin et al. [12•] reported a dissociation between normal locomotive learning and the persistence of locomotive after-effects in patients with functional gait disorders. They showed that despite patients exhibiting slower gait velocity and larger truncal movements during the baseline explicit task of ambulating on a stationary walkway, patients had equivalent gait velocity and truncal sway during the implicit motor tasks of walking on a moving walkway. Interestingly, when tasked again with walking on a stationary walkway, patients took substantially longer to re-normalize their gait kinematics. This tendency to prolong learned motor programs has implications for the rehabilitation potential of patients with functional gait disorders.

There has been progress in identifying FMD biomarkers in the last few years. Teodoro et al. [13] studied contingent negative variation (CNV), a negative cortical wave related to motor preparation and anticipatory attention, that is absent in FMD patients at baseline. The group found that improvement of FMD following physiotherapy was associated with faster reaction times and normalization of CNV, suggesting that CNV could serve as a neurophysiological biomarker for poor attention in FMD. Similarly, Sadnicka et al. [14] discovered pathologically reduced drift rate in FMD, an entity that quantifies the quality and rate of information accumulation during a sensory task. Reduced drift rate again supports the finding of abnormal attention allocation in FMD and paves the way for future treatment strategies.

## Updates on Neuroimaging

The last two decades saw a renewed effort to elucidate the brain's structure–function relationship to help characterize FND's integrated biopsychosocial model. Fueled by this momentum, the new multidisciplinary FND Society was created to foster dissemination of knowledge in the field ([www.fndsociety.org](http://www.fndsociety.org)). The first International FND Neuroimaging Workgroup meeting took place virtually on June 17th, 2020, with the world's FND experts gathering to evaluate the state of field and to propose a neuroimaging research agenda. Perez et al. [15••] first shared their goals of summarizing what is known regarding FND's neuronal circuitry and pathophysiology from multimodal neuroimaging studies. The group then went on to outline several research barriers, including a wide range of symptoms over time, high rates of physical and psychiatric symptoms, and various etiologies such as adverse life events and physical or psychological stressors. They concluded that FND cohorts in neuroimaging studies require more detailed categorical and dimensional characterization. Proposed solutions consisted

of using patient controls to demarcate specificity of FND findings, ensuring study designs complement between-group and within-group analyses, and formulating longitudinal studies to investigate pathophysiology, prognostic biomarkers, and mechanisms of treatment response.

In a functional MRI (fMRI) study, Sojka et al. [16] reported that patients with FMD had increased activation of the post-central gyrus, precuneus, posterior cingulate cortex (PCC), and cerebellar vermis when viewing negative pictures. Extending on these findings, Piramide et al. [17] demonstrated that patients with functional dystonia also had altered functional connectivity of the motor circuit to areas involved in emotional processing.

Functional MRI has also been used to qualify improvement of FMD. Espay et al. [18•] showed that not only did cognitive behavioral therapy (CBT) significantly reduce functional tremor severity in 73.3% of patients, but it also reduced the excess activation of the anterior cingulate and paracingulate cortices found prior to treatment during a basic emotional processing task. Likewise, Faul et al. [19•] demonstrated that a brief motor retraining treatment program reduced FMD motor severity by 63.5% and increased connectivity between the premotor regions and bilateral amygdala, showing preliminary evidence of reorganization of motor and emotional pathways.

Although functional neuroimaging studies have dominated the FND literature in recent years, the Perez lab published two key structural imaging studies in 2021 that utilize diffusion tensor imaging (DTI) to shed light on white matter changes in FND. First, Diez et al. [20] identified microstructural differences in the limbic tracts involved in salience, defensive behaviors, and emotional regulation. Second, Sojka et al. [21] revealed that FMD patients had differences in interoceptive accuracy and trait prediction error that were associated with fiber bundle integrity originating from the insula, thalamus, putamen, and temporoparietal junction.

## Updates on Prognosis and Treatment

Because FMD symptoms are not a result of irreversible structural damage, patients have the potential to make full recoveries. For treatment to be successful, however, the diagnosis must be communicated clearly (Box 2). Several recent studies have sought to determine the optimal treatment setting paradigms and meaningful outcome measures for FMD. Schmidt et al. [22] demonstrated a significant improvement in the psychogenic movement disorder rating scale (PMDRS) based on blinded videos and self-rated assessments after individualized, interdisciplinary, inpatient psycho- and physiotherapies. Patients completed 20–60-min sessions about 10–15 times/week

for a median duration of 21 days. While Hebert et al. [23] also found that multidisciplinary inpatient rehabilitation improved function, mood, and somatic symptoms, 1-year follow-up failed to show sustained improvement or decreased debility. In a retrospective cohort study by Maggio et al. [24], an outpatient physical therapy program was associated with clinical improvement. Petrochilos et al. [25] supported this finding with their study showing that outpatient multidisciplinary, team-based therapy led to sustained improvement in health and social functioning, depression, anxiety, and somatic symptoms. Complementing the positive findings of in person multidisciplinary rehabilitation, Demartini et al. [26] demonstrated the success of weekly virtual physical therapy sessions for 21 weeks for patients with FMD, resulting in significant improvement in PMDRS scores six months post-intervention. Perez [27] also published a case report of a functional tremor patient successfully treated with a mix of local physical and psychotherapy, self-guided cognitive behavioral therapy workbook, and virtual neurological follow-ups (Box 3). These are especially crucial findings since the COVID-19 pandemic has often restricted already scarce treatment resources.

### Box 3 Principles of treatment for functional movement disorders

General	Physical rehabilitation
Establish diagnosis prior to starting treatment	Start motor retraining by establishing elementary movements (weight-shifting) before adding more complex movements
Communicate treatment goal of relearning normal motor control	Visual feedback such as mirrors or video can be helpful during motor retraining
<b>Cognitive behavioral therapy</b>	Emphasize quality of movements over quantity
Help patient become aware of their triggers and find alternate responses	Avoid excessive attention to abnormal movements
Teach relaxation techniques (deep breathing, meditation, and grounding methods)	Treatment adjuncts may enhance motor retraining (treadmill, electrical stimulation, electromyography biofeedback, and transcranial magnetic stimulation)

In the realm of drug therapies, there has been interest to explore a potential role of psychedelics in the treatment of FMD. In a review of nine studies, Butler et al. [28] reported that 69% of FMD patients had an improvement in symptoms following use of psychedelics with only mild side effects. However, most studies included in the review lacked control groups and valid outcome measures, and further randomized-controlled studies are needed to determine the value of this approach. Stewart et al. [29]

also conducted a review and discussed the pros and cons of psilocybin. The group recommended that patients with non-paroxysmal FMD serve as the target population while studying the effects of psilocybin in conjunction with physical and psychotherapy on pre- and post-fMRI as next steps.

Neuromodulatory therapies have also been garnering attention in recent years. In a randomized controlled trial, Taib et al. [30] determined that repetitive transcranial magnetic stimulation significantly reduced functional tremor ( $n=18$ ,  $p<0.001$ ) based on the PMDRS at 1-, 2-, 6-, and 12-months post-intervention. In a proof-of-concept study, Spagnolo et al. [31] found that intermittent theta burst stimulation decreased fronto-amygdalar connectivity and influenced amygdala reactivity to emotional stimuli. This change in neurocircuitry was associated with a marked reduction in the severity of functional tremor, dystonia, gait, and speech disorders.

Despite advances in FMD therapies, well-validated outcomes to assess treatment success have not been established. Nicholson et al. [32] explain the barriers to identifying outcome measures, including the high variability in FMD core features and associated symptoms. They propose that long-term assessments are more beneficial than momentary evaluations, and that subjective feedback from patients are equally important as objective measures. In a systematic review, Pick et al. [33••] identify the most common measurement domains in prior treatment studies of various FND symptoms. Of all available FMD clinician-rated scales, the authors favor the Simplified Functional Movement Disorders Rating Scale (S-FMDRS) over the PMDRS due to its simplicity and ability to be administered by clinicians without expertise in movement disorders. They also prefer assessing FND impact by including quality of life, disability, and psychological measures.

## FMD During the COVID-19 Pandemic

Since beginning of the COVID-19 pandemic, clinicians have seen an increase in FMD cases. Hull et al. [34] shared that from March 1–October 30, 2020, their movement disorders center diagnosed 8.2% of newly referred patients with FMD. This represented a 60.1% increase when compared to the identical timeframe in 2019 before the pandemic. The emergence of many new onset tic-like movements during the COVID-19 pandemic deserves special attention. Hull and Parnes [35] illustrate how in some cases, the increased use of social media during the pandemic may have led to the dissemination of FMD virtually. The authors describe six teenage girls who developed an explosive onset of tic-like movements after witnessing the same social media personality on TikTok. Olvera et al. [36] corroborated this

finding and further differentiated the rising “TikTok tics” from conventional tic disorders. Patients with “TikTok tics” were mostly women with a mean age of 18.18 years old. Tic phenomenology was distinct from Tourette’s syndrome because the arms were the most frequently affected and there were a significant number of tics per minute, coprolalia, self-injurious behavior, and disability. In an international study, Pringsheim et al. [37•] reinforced that social media was a likely contributing factor that triggered tic-like movements in susceptible patients who experienced increased psychosocial stress factors due to the pandemic. Though the pandemic has caused a rise of FMD, it has also stipulated the use of telemedicine and allowed clinicians to treat more FMD patients who may not be able to undergo in-person therapies.

## Future Directions

Although the last decade has led to a better understanding and development of treatments, we are still only beginning to understand the pathophysiology, individual risk factors, and best treatments for patients with FMD. More work needs to be done to reach a similar degree of understanding, accessible treatments, and resources that are available to patients with comparable neurological conditions. Spagnolo et al. [38] suggests that adopting a multidimensional, neuroscience-based approach could elucidate disease mechanisms and classify disorder subtypes. Rommelfanger and Rapaport [39••] highlighted a 4-paper series published in *CNS Spectrums* in a remarkable multidisciplinary effort to summarize what is known about FND and proposed a research agenda to promote necessary changes in the field. The first article by MacDuffie et al. [40] draws attention to the high prevalence of stigma associated with FND from clinicians and patients and share ways to combat it. Second, Drane et al. [41] explore the pathophysiology and encourage a brain circuit-oriented research approach. The third article by Lidstone et al. [42] recommends using a diagnostic triad by identifying non-motor diagnostic features, understanding neuropsychiatric phenotypes, and designing patient-centered treatment programs tailored to FND symptoms and etiologies. Lastly, LaFaver et al. [43] emphasize utilizing multidisciplinary treatment approaches and suggest a research agenda towards better treatment studies.

To better understand remaining challenges in the field, LaFaver et al. [44•] examined how attitudes regarding FMD have changed over the last 10 years. More physicians preferred the term “functional” over “psychogenic,” felt comfortable diagnosing FMD without ordering additional tests, and believed that their role was to diagnose and coordinate management. Treatment barriers consisted

of lack of knowledge, training, and management. International studies also shed light on the need for increased global awareness of FMD. A Chinese study by Xie et al. [45] determined that more than 80% of survey respondents thought that atypical movements, numerous somatizations, and psychiatric disturbances were essential for an FMD diagnosis. In a similar Italian survey, Tinazzi et al. [46] reported that respondents favored explaining symptomology based on abnormal nervous system functioning and omitted discussing mental illness. They referred patients to psychologists rather than psychiatrists and thought physical and psychiatric therapies were not useful. The Chinese and Italian studies call for increased dissemination of knowledge to ensure the best clinical practices for patients with FND. Of note, education on FND is needed across specialty lines, as highlighted by international survey of psychiatrists in Australia and the United Kingdom. In the study, Dent et al. [47] found that psychiatrists used predominantly psychosocial models for the explanation of conversion disorder and believed that there was an element of feigning. They also felt that psychiatrists were crucial to diagnosis FND but did not support a diagnosis without a psychiatric basis. The study highlights how neurologists and psychiatrists may view FND differently, and the importance of ongoing international and multidisciplinary collaborations.

## Conclusion

The last 3 years have brought important advances to the field of FMD. International collaborations have yielded new findings in the pathophysiology of FMD and begun efforts towards development of biomarkers and standardized outcome measures to facilitate large scale clinical studies. The COVID-19 pandemic has furthermore highlighted previously existing challenges in FMD and led to innovation in treatment delivery, promising better access to care in the future.

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## Declarations

**Conflict of Interest** SK and KL have no conflict of interests.

**Human and Animal Rights** This article does not contain any studies with human or animal subjects performed by any of the authors.

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