Neuropsychiatric Associations With Gender, Illness Duration, Work Disability, and Motor Subtype in a U.S. Functional Neurological Disorders Clinic Population

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The assessment of functional neurological disorders (FND) requires an interdisciplinary approach. The authors retrospectively reviewed charts for 100 outpatients with FND and used univariate and regression analyses to investigate neuropsychiatric associations with gender, illness duration, and work disability; secondary analyses evaluated for differences across motor FND subtypes. Men reported higher rates of cognitive complaints and functional weakness, whereas women endorsed increased past physical/sexual trauma. Number of self-reported medication allergies/sensitivities positively correlated with illness duration. Individuals with functional weakness compared with other motor FND subtypes exhibited lower rates of past psychiatric hospitalization and head trauma. This study supports the feasibility of integrating FND research.

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Functional neurological disorder (FND)/conversion disorder (CD)—the modern-day equivalent of hysteria—presents with a wide variety of symptoms including seizures, abnormal movements, weakness, pain, fatigue, cognitive complaints, and affective dysregulation, among other symptoms. FND is exceedingly common,[1,2] and has been recognized since the emergence of modern neurology and psychiatry. However, the number of clinical programs focused on FND is surprisingly limited.

The most commonly reported form of FND, psychogenic nonepileptic seizures (PNES), accounts for 10% to 40% of epilepsy clinic referral visits.[3] Up to one in five individuals evaluated in movement disorder clinics are diagnosed with a functional movement disorder (FMD),[4] and patients exhibiting functional weakness may be as prevalent as those with multiple sclerosis.[2] Notably, many individuals with FND either exhibit mixed functional symptoms[5] or develop additional medically unexplained symptoms over the course of their illness.[6] Increased recognition of a clinical phenotypic overlap across patients with motor FND suggests the importance of integrating clinical and research efforts across FND subpopulations.[7]

Patients with FND endorse similar physical disability, emotional distress, and reduced health-related quality of life as other neurological disorders,[8,9] yet patients are frequently shuffled between providers, which delays diagnosis and treatment initiation. Psychiatrists often report feeling ill-equipped in the assessment of patients whose chief complaint is a neurological symptom, and neurologists lack a model framework for FND, which creates frustration.[10] While neurology subspecialties have traditionally placed individuals with PNES, FMD, and functional weakness into distinct diagnostic categories, many predisposing, precipitating, and perpetuating illness factors are shared across FND subtypes.[7,11] These observations underscore the need to integrate neurobehavioral and neuropsychiatric features of FND into a unified interdisciplinary clinical and research approach.

Women are two to three times more likely than men to be diagnosed with FND.[1] Studies focused on gender in FND indicate shared clinical sensory-motor symptoms across men and women, though etiological risk factors may vary. For example, women report higher rates of physical and sexual abuse, while symptom onset and diagnosis typically occur at an older age in men.[12] A study in individuals with PNES found few significant gender differences, with the exception of greater past sexual abuse and self-injurious behaviors in women and higher unemployment rates in men.[13] Other studies, however, have found similar unemployment rates across genders.[14,15] Men with FND may also display greater health anxiety, whereas women with FND more frequently reported environmental stress and family dysfunction in one study.[15] In a study comparing family functioning and quality of life in men and women with epilepsy or PNES, family dysfunction was reported in both those with epileptic

seizures and PNES, but greater family dysfunction was experienced by men in both groups.[16] Few studies have comprehensively investigated demographic and neuropsychiatric factors associated with gender, partially due to low sampling in men, which limits comparative analyses.

Clinical factors associated with work disability status and illness duration, both closely related to prognosis, have only been investigated within specific FND subtypes. In general, poor prognosis in FND has been linked to traumatic brain injury (TBI), psychiatric comorbidities, diagnostic delay, and longer duration of symptoms.[17,18] The presence of anxiety and mood disorders may also perpetuate disability and impede recovery.[19,20] European studies have linked medically unexplained physical symptoms, as well as mood disorders, with higher rates of absenteeism and work disability.[21,22]

This retrospective cohort study aimed to investigate neuropsychiatric variables associated with gender, work disability status, and illness duration in the first 100 consecutive patients with motor functional neurological symptoms evaluated in an integrated behavioral neurology-neuropsychiatry FND clinic. We previously conducted a preliminary study on clinical predictors of symptom burden and motor FND subtype in the first 49 patients with suspected functional neurological symptoms evaluated in the clinic.[5] Here, we build upon our preliminary findings to also secondarily investigate neuropsychiatric factors differentiating between motor FND subtypes. This cohort provides the opportunity to concurrently characterize associations across the motor FND spectrum, while also evaluating associations with specific FND subtypes. Based on prior research findings and our own clinical observations, we hypothesized that men would report lower rates of psychological trauma and affective symptoms than women, while concurrently endorsing more cognitive difficulties.[23] We also hypothesized that self-reported work disability status and illness duration would be independently predicted by neurological and psychiatric factors, including a history of head trauma and high acuity psychiatric presentations. In analyses investigating motor FND subtypes, we hypothesized that patients with PNES compared with other motor subtypes would exhibit greater high acuity psychiatric presentations (i.e., psychiatric hospitalizations).

METHODS

This cohort study reviewed the medical records of the first 100 consecutive outpatients evaluated in the FND Clinic at the Massachusetts General Hospital for suspected motor FND. Of the 100 patients who attended their initial consultation, 71 were referred from outpatient providers, 18 from inpatient services, and 11 from the emergency department. Referrals to the clinic are largely limited to PNES, FMD, and/or functional weakness; thus, patients with only somatic symptom disorders and/or isolated functional numbness were excluded.

As previously detailed,[5] patients who attended the initial consultation underwent a 1.5-hour semistructured clinical neuropsychiatric interview and physical examination by a dual-trained and board-certified neurologist-psychiatrist (DLP). Nineteen patients were evaluated in collaboration with a clinical fellow or resident supervised by DLP. Patients were systematically questioned on their history of medically unexplained motor and sensory symptoms, seizures, cognitive complaints, TBI, mental health, alcohol and drug use, and medical, family, and social histories (including work disability status). Neurological examinations evaluated for the presence of standardized "positive" functional neurological signs, including collapsing/give-way weakness, Hoover's sign, variable/distractible abnormal movements, tremor entrainment, astasia-abasia gait, and splitting of the midline nondermatomal sensory deficits.[24]

FND diagnoses were assigned in accord with established diagnostic criteria for PNES,[25] FMD,[4] and functional weakness.[26] Individuals with isolated functional gait were categorized as a FMD, whereas those with gait abnormalities in the context of functional leg weakness were categorized as having functional weakness. FND diagnoses were not mutually exclusive. For all individuals, we performed retrospective chart reviews to collect demographic, neuropsychiatric and psychosocial information. Coinvestigators uninvolved with patient care (NM, SSY, JNK) performed the chart reviews. We received institutional review board approval from the Partners Human Research Committee, the Institutional Review Board of Partners HealthCare. Individual informed consents were not required.

To identify variables associated with gender, work disability status, and illness duration (the dependent variables) at the baseline evaluation, we first performed univariate tests (chi-square tests or unpaired two-tailed t tests for normally distributed variables and Mann-Whitney U and Spearman's correlation tests for nonnormal variables). Independent variables demonstrating a statistically significant relationship with one of the three dependent variables ($p<0.05$) were included in second-level multivariate regression analyses. In addition, secondary univariate analyses were also performed to evaluate associations between motor FND subtypes and neuropsychiatric variables. We dichotomized dependent variables for motor FND subtypes and used logistic regression analyses following univariate tests to evaluate for factors associated with the presence or absence of PNES, functional weakness, or FMD. The percent variance explained by each regression model is presented using the Cox and Snell pseudo-R^2 values for logistic regression and R^2 values for linear regression.

Education was dichotomized for college graduation. Given the high co-occurrence of sexual and physical trauma in our sample, this metric was treated as one combined variable. History of suicidality included prior suicidal ideation and past suicide attempts. Lifetime depression or lifetime anxiety included any past or current diagnoses for these conditions. Patients applying for or on Social Security Disability Insurance, Supplemental Security Income, or another form of work disability were categorized as "on or applying for

TABLE 1. Demographic and Neuropsychiatric Characteristics of 100 Patients With Motor Functional Neurological Disorders[a]

Characteristic	Total Cohort (N=100) N (%) or Mean (±SD)	PNES (N=51) N (%) or Mean (±SD)	FW (N=41) N (%) or Mean (±SD)	FMD (N=38) N (%) or Mean (±SD)
Mean age at presentation (years)	39.6 (±12.4)	38.5 (±14.3)	39 (±12.6)	44.4 (±10)
Illness duration (years)	3.8 (±5.7)	3.9 (±6.1)	3.5 (±5.6)	3.1 (±3.7)
Gender	79 F/21 M	42 F/9 M	28 F/13 M	31 F/7 M
Race	79 W/21 NW	42 W/9 NW	31 W/10 NW	30 W/8 NW
Completed college (≥16 years)	46 (46%)	19 (37%)	22 (53%)	20 (52%)
Married	42 (42%)	18 (35%)	19 (46%)	22 (57%)
Unemployed (or not a full-time student)	66 (66%)	30 (58%)	26 (63%)	32 (84%)
On or applying for work disability	34 (34%)	22 (43%)	10 (24%)	12 (31%)
H/O physical/sexual trauma	41 (41%)	24 (47%)	15 (37%)	14 (37%)
H/O emotional/verbal abuse	30 (30%)	18 (35%)	11 (26%)	9 (23%)
H/O psychiatric hospitalization	32 (32%)	23 (45%)	8 (19%)	6 (15%)
H/O suicidality	31 (31%)	21 (41%)	10 (24%)	7 (18%)
Lifetime depression	66 (66%)	37 (72%)	26 (63%)	22 (57%)
Current major depressive disorder	26 (26%)	11 (21%)	14 (34%)	9 (23%)
Lifetime anxiety	77 (77%)	39 (76%)	32 (78%)	27 (71%)
Current generalized anxiety disorder	33 (33%)	19 (37%)	10 (24%)	10 (26%)
Current posttraumatic stress disorder	20 (20%)	15 (29%)	5 (12%)	5 (13%)
Family H/O psychiatric disease[b]	67 (67%)	37 (72%)	28 (68%)	24 (63%)
Family H/O neurologic disease[b]	46 (46%)	21 (41%)	23 (56%)	21 (55%)
Cognitive complaints	54 (54%)	32 (62%)	23 (56%)	21 (55%)
H/O head trauma	42 (42%)	26 (51%)	12 (29%)	14 (37%)
Comorbid epileptic seizures	6 (6%)	5 (10%)	1 (2%)	0 (0%)
H/O another functional syndrome	33 (33%)	15 (29%)	16 (39%)	15 (39%)
[H/O chronic pain]	22 (22%)	9 (17%)	8 (19%)	11 (28%)
[H/O fibromyalgia]	10 (10%)	5 (9%)	6 (14%)	4 (10%)
[H/O chronic fatigue]	3 (3%)	1 (2%)	3 (7%)	2 (5%)
Lifetime alcohol misuse	13 (13%)	8 (16%)	6 (15%)	4 (11%)
Lifetime drug misuse	25 (25%)	16 (31%)	9 (22%)	5 (13%)
Mean self-reported medication allergies/sensitivities at intake	1.3 (±1.7)	1.3 (±1.5)	1.1 (±1.4)	1.3 (±2.0)

[a] Variables listed in brackets are included for descriptive details but were not themselves included in statistical analyses. Diagnoses of psychogenic nonepileptic seizures (PNES), functional weakness (FW), and functional movement disorders (FMD) were not mutually exclusive, as 28 of 100 patients exhibited mixed motor functional neurological symptoms. F, female; H/O, history of; M, male; NW, nonwhite; SD, standard deviation; W, white.
[b] Data were missing for two patients.

disability." Given the high degree of co-occurrence of work disability and unemployment ($p<0.001$), unemployment status was not included for analyses investigating predictors of work disability. Independent variables with less than 20% variance across the entire 100 FND cohort (history of epileptic seizures, lifetime alcohol misuse) were excluded from analyses. All statistical analyses were performed in IBM SPSSv23 (Chicago).

RESULTS

The demographic and clinical characteristics of our 100 subjects (79 women, 21 men; mean age=39.6 [SD=12.4]) are summarized in Table 1. The cohort included 51 patients with PNES (32 video electroencephalogram documented, three clinically established, three probable, and 13 possible), 41 individuals with functional weakness (36 with "positive" examination findings, four with suspected paroxysmal symptoms, and one with complete bilateral lower extremity paralysis in the context of unremarkable brain and spine MRI and nerve conduction studies) and 38 patients with FMD (37 clinically established, one possible). Twenty-eight patients showed mixed motor functional neurological symptoms (PNES and FMD, N=5; PNES and functional weakness, N=9; FMD and functional weakness, N=11; three exhibited all three motor FND subtypes), and 19 subjects also had nondermatomal sensory deficits. Out of 42 total patients with a history of head trauma, 26 endorsed transient loss of consciousness, and only one patient had a severe TBI with abnormal brain MRI findings. Six subjects had comorbid epileptic seizures (five with PNES, one with functional weakness).

In our univariate analyses for gender, men were more likely to report cognitive complaints (χ^2=7.8; p=0.005), display functional weakness (χ^2=4.8; 0.028), and be married (χ^2=4.3; p=0.038) at the time of initial evaluation. Also, men demonstrated lower rates of sexual/physical trauma (χ^2=5.3; p=0.021) and lifetime anxiety (χ^2=5.9; p=0.015). In a logistic regression analysis including these independent variables, more frequent cognitive complaints (odds ratio [OR]=5.6; 95% confidence interval [CI]=1.5–20.3; p=0.009), lower rates of past sexual/physical trauma (OR=0.2; 95% CI=0.1–0.9; p=0.034) and a functional weakness diagnosis (OR=3.3; 95% CI=1.03–10.4; p=0.045) independently predicted male gender (Table 2). 22.9% of the data variance for gender was explained by this model. Given the association between

TABLE 2. Multivariate Regression Predictors of Gender, Work Disability Status, and Illness Duration in 100 Patients With Motor Functional Neurological Disorders

Outcome Variables	Significant Variables Identified by Univariate Screening	Odds Ratio	95% Confidence Interval	p[a]
Male (N=21) versus female (N=79)	History of physical/sexual trauma	0.2	0.1–0.9	**0.034**
	Lifetime anxiety	0.3	0.1–1.1	0.080
	Cognitive complaints	5.6	1.5–20.3	**0.009**
	Married	2.5	0.8–7.7	0.12
	Functional weakness diagnosis	3.3	1.03–10.4	**0.045**
Work disability (N=34) versus no work disability (N=66)	Past psychiatric hospitalization	2.4	0.9–6.7	0.095
	Family history of psychiatric disorder	2.4	0.8–7.4	0.14
	Current posttraumatic stress disorder	2.5	0.8–8.0	0.11
	Psychogenic nonepileptic seizure diagnosis	1.5	0.6–4.0	0.43
		Unstandardized beta	Standardized beta	
Illness duration (in years)	Number of medication allergies at intake	13.9	0.3	**0.001**

[a] Statistical significance is indicated in bold ($p<0.05$).

gender and cognitive complaints, we performed a post hoc analysis of available Montreal Cognitive Assessment (MoCA)[27] scores, though only 39 out of 79 female patients and 10 out of 21 male patients had MoCAs during their baseline evaluation. The mean MoCA scores in males and females were 24.50±3.69 and 23.62±3.11, respectively, which were not statistically different (p=0.50).

For work disability status, univariate analyses showed positive associations with a history of psychiatric hospitalization (χ^2=10.4; p=0.001), a family history of psychiatric disorders (χ^2=5.6; p=0.018), current posttraumatic stress disorder (PTSD) (χ^2=7.5; p=0.006), and a diagnosis of PNES (χ^2=3.9; p=0.049). There were no statistically significant independent predictors of disability status in a single logistic regression analysis.

In analyses of illness duration, number of self-reported medication allergies/sensitivities (Spearman's correlation coefficient=0.334; p=0.001) was a statistically significant positive predictor. A linear regression showed the same result (unstandardized beta regression coefficient=3.6; p=0.001), and 11.5% of the data variance was explained by the model.

In univariate analyses investigating subtype associations, a diagnosis of PNES compared with functional weakness and/or FMD was positively associated with a history of psychiatric hospitalization (χ^2=8.2; p=0.004), past suicidality (χ^2=5.0; p=0.025), higher rates of work disability (χ^2=3.9; p=0.049), and current PTSD (χ^2=5.8; p=0.016). (We previously reported a preliminary association between PNES and cognitive complaints; however, only positive associations that fell short of statistical significance (p=0.07) were observed in this larger cohort.[5]) In a single multivariate logistic regression analysis, there were no independent predictors of a PNES diagnosis (Table 3).

In univariate analyses investigating clinical variables associated with a functional weakness diagnosis compared with other subtypes, lower rates of past psychiatric hospitalization (χ^2=5.0; p=0.026) and head trauma (χ^2=4.6; p=0.032) were identified; as noted previously, male gender was also positively associated with a diagnosis of functional weakness. In a single multivariate logistic regression analysis, all three variables independently predicted a functional weakness diagnosis compared with other motor FND subtypes: male gender, OR=3.3; 95% CI=1.1–9.3; p=0.028; history of head trauma, OR=0.4; 95% CI=0.1–0.9; p=0.026; past psychiatric hospitalization, OR=0.5; 95% CI=0.1–0.9; p=0.048.

A diagnosis of FMD compared with other subtypes was negatively associated with a history of psychiatric hospitalization (χ^2=7.4; p=0.007), past suicidality (χ^2=4.5; p=0.033), and lifetime drug misuse (χ^2=4.6; p=0.032). Individuals with FMD were also more likely to be married (χ^2=6.4; p=0.012) and unemployed (χ^2=9.1; p=0.003). The multivariate logistic regression analysis with these variables showed that only unemployment (OR=4.5; 95% CI=1.5–13.2; p=0.007) independently predicted a diagnosis of FMD, with 19.8% of the data variance explained by the model.

DISCUSSION

In this study, men with FND demonstrated increased frequency of cognitive complaints and higher prevalence of functional weakness, while women more commonly reported past physical/sexual trauma. Across our cohort, illness duration at the baseline evaluation was positively associated with the number of self-reported medication allergies/sensitivities. While there were no independent predictors in regression analyses, univariate analyses showed that a history of psychiatric hospitalization, family history of psychiatric disorders, current PTSD, and a diagnosis of PNES were associated with individuals on or applying for work disability. In addition, patients with functional weakness compared with those with PNES and/or FMD demonstrated lower rates of past psychiatric hospitalization and head trauma; patients with FMD compared with other subtypes were more commonly unemployed.

The observation of increased cognitive complaints in men is a novel finding. Our post hoc analysis of MoCA scores,

TABLE 3. Logistic Regression Predictors of Motor Subtype in 100 Patients With Motor Functional Neurological Disorders[a]

Motor FND Subtype	Significant Variables Identified by Univariate Screening	Odds Ratio	95% Confidence Interval	p[b]
Psychogenic nonepileptic seizures (N=51) versus other motor FNDs (N=49)	Past psychiatric hospitalization	2.0	0.6–6.3	0.257
	History of suicidality	1.7	0.6–5.1	0.369
	Current post traumatic stress disorder	2.2	0.7–7.2	0.207
	On or applying for work disability	1.7	0.6–4.4	0.287
Functional weakness (N=41) versus other motor FNDs (N=59)	Past psychiatric hospitalization	0.4	0.1–0.9	**0.048**
	Male gender	3.3	1.1–9.3	**0.028**
	History of head trauma	0.4	0.1–0.9	**0.026**
Functional movement disorders (N=38) versus other motor FNDs (N=62)	Past psychiatric hospitalization	0.3	0.1–1.0	0.055
	History of suicidality	1.0	0.3–3.4	0.966
	Lifetime drug misuse	0.6	0.2–1.9	0.360
	Married	2.0	0.8–5.0	0.155
	Unemployed (or not a full-time student)	4.5	1.5–13.2	**0.007**

[a] FND, functional neurological disorder.
[b] Statistical significance is indicated in bold ($p<0.05$).

which did not demonstrate an objective difference in cognitive performance, suggests that this gender difference may relate to subjective complaints. While cognitive symptoms are common in FND,[23] few studies have focused on cognition across the entire FND spectrum. Our findings support the importance of assessing cognitive symptoms and objective task performance in FND and suggest potential gender differences in the frequency of reported cognitive complaints. The endorsement of cognitive symptoms may, in part, overlap with the extended spectrum of functional neurological symptoms, including dissociation.[23] Functional cognitive symptoms, like functional motor symptoms, are frequently variable, amplify when attended to, and are often initially detected by patients themselves rather than outside observers.[23] Impairments in attention-concentration and executive functions are well described in some patients with FND, particularly those with PNES; however, cognitive profiles may not necessarily distinguish patients with FND compared with other neurological populations.[3] Additionally, many individuals with FND fail performance validity measures acquired during neuropsychological testing, suggesting that an unintentional lack of motivation may also contribute to poor cognitive task completion.[28] Some studies have also appreciated the relative absence of cognitive deficits in FND subpopulations, particularly those with FMD.[29]

Psychiatric comorbidities are also associated with cognitive symptoms in FND. Affective disturbances are linked to cognitive symptoms, and depression and anxiety are frequently co-occurring in patients with FND.[23] In our study, men were less frequently diagnosed with anxiety, a finding consistent with research noting a higher prevalence of anxiety in women with FND.[30] It is thus notable that men more commonly endorsed cognitive symptoms while reporting lower lifetime anxiety, suggesting a possible disconnect between anxiety and cognitive symptoms in men with FND. These observations support that cognitive complaints should be screened for as part of the assessment of FND, and that cognitive complaints may require consideration when developing individualized treatment plans for patients.[23,31,32] Apart from cognitive complaints, we found lower levels of physical/sexual trauma in men, which is consistent with prior literature.[15]

Number of self-reported medication allergies/sensitivities was a positive predictor of greater illness duration as reported during an initial outpatient evaluation, which highlights potential relationships between somatization tendencies and reported medication allergies.[33] Previous studies have characterized idiopathic environmental intolerance, in which patients present with multiple somatic symptoms and hypersensitivity to chemical substances, as a form of a somatic symptom disorder[33,34] A retrospective study of patients in an epilepsy monitoring unit observed that reported polyallergy distinguished patients with PNES from those with epilepsy.[35] Another retrospective study replicated this observation, theorizing that patients with PNES may inaccurately interpret and report allergies as a means of externalizing psychological distress.[36] Our finding extends these observations to include links between number of self-reported medication allergies/sensitivities and illness duration at the time of initial outpatient evaluation across the spectrum of FND.

In univariate–but not multivariate–analyses, several mental health factors were positively associated with work disability status, including a history of psychiatric hospitalization, family history of psychiatric disease, current PTSD, and a diagnosis of PNES. In the entire cohort, 34% were on or applying for disability, and 65% of these individuals were diagnosed with PNES. We have previously reported preliminary positive associations between individuals with PNES and past psychiatric hospitalizations.[5] More severe psychiatric comorbidities may worsen overall prognosis and lead to increased disability claims. Our univariate findings are consistent with a systematic review of studies across discrete FND subtypes denoting that patients with psychiatric comorbidities have worse prognoses compared with individuals with less prominent psychiatric difficulties.[17] Concurrent mood and anxiety disorders further increase medical disability across neurology outpatients irrespective of diagnoses.[19] Interestingly, associations between current PTSD and disability status may relate in part to recognized

associations between adverse life events and illness severity in FND.[37]

In this study, several noteworthy clinical differences across FND subtypes were also characterized; specifically, patients with functional weakness compared with those with PNES and/or FMD were less likely to endorse past psychiatric hospitalizations and prior head trauma events. These findings extend our preliminary observations that patients with PNES compared with those with other functional neurological symptoms more commonly reported past psychiatric hospitalizations[5]; this is also consistent with the literature showing that patients with PNES compared with those with functional weakness exhibit higher rates of borderline personality disorder.[38] More broadly, we observed in univariate analyses that those with PNES also more frequently endorsed past suicidality. A study of 100 inpatients with FND reported that suicidality was positively associated with past childhood trauma and psychiatric hospitalizations; while not statistically significant, it was observed that 51% of FND patients with suicidality had PNES, while only 44% without suicidality had PNES.[39] These collective findings raise the possibility that high acuity psychiatric presentations may be a distinguishing characteristic of patients with PNES compared with other motor FND subtypes. In our cohort, similarities across motor FND subtypes include comparable rates of lifetime depression, anxiety, and the frequency of previously endorsed sexual/physical trauma.

Clinicians and researchers are increasingly embracing an interdisciplinary (trans-diagnostic) approach to FND.[6,7,38,40] The results of our study, however, should be contextualized within the existing literature, which suggests many similarities and some differences across FND subpopulations. Prior work has demonstrated that PNES and other motor FNDs share similar psychosocial profiles, health-related quality of life, predisposition for comorbid psychiatric and somatoform disorders, and presence of alexithymia.[3,41,42] Furthermore, from a clinical perspective, FND subpopulations often share similar phenotypes or exhibit mixed symptomatology. For example, full-body, high-amplitude abnormal movements with preserved consciousness in FMD often resemble PNES events, and many patients with functional tremor also exhibit collapsing/give-way weakness in the same limb.

Some clinical differences have also been previously noted between FND subtypes. Studies have found significantly lower age of onset, as well as greater childhood abuse, in PNES populations[15,39,43]; sampling biases in the inquiry of past childhood abuse may potentially explain observed differences in abuse frequencies between PNES and FMD.[43] Dissociation may be more common in PNES patients, whereas other somatic symptoms may be more commonly reported in FMD.[41,44] Our observations here suggest that endorsement of past head trauma may be less common in patients with functional weakness compared with those with other motor FND subtypes, further suggesting that some predisposing and precipitating factors may vary across motor FND subpopulations. TBI events have been previously associated with PNES, with one study noting that mild TBI was more strongly associated with nonepileptic seizures than epileptic seizures.[31] These findings suggest that clinicians should consider the many shared and overlapping characteristics of FNDs, while also addressing some important differences across motor FND subtypes.

Limitations of this research include the retrospective nature of the study, which is prone to potential selection bias. Our cohort included 100 patients with motor functional neurological symptoms, though diagnostic certainty ranged from possible to documented, suggesting that this clinical population may be somewhat heterogeneous. Analyses investigating gender differences were limited by the low number of male subjects. Our ability to further quantify associations between male gender and cognitive symptoms through the use of post hoc comparisons of MoCA scores was also limited by missing data. Future efforts should use prospective neuropsychological testing to quantitatively investigate gender differences in cognitive profiles, along with the concurrent use of performance validity measures. Self-report, particularly for illness duration and prior head trauma, may be prone to biased reporting. Future research should characterize associations between objective markers of physical impairment, neuropsychiatric variables, and longitudinal prognosis. It will also be important to investigate the generalizability of our neuropsychiatric relationships in comparison to patients seen in other integrated FND clinics.

In conclusion, this study used a trans-diagnostic approach to investigate neuropsychiatric variables associated with gender, work disability status, illness duration, and motor subtype in patients with motor FNDs. Associations between male gender and cognitive complaints, work disability status and psychiatric comorbidities, and baseline illness duration and number of self-reported medication allergies/sensitivities underscore the importance of an integrated neuropsychiatric approach to the assessment of FND. There were also some important differences across FND subtypes, including emerging observations that patients with PNES may be more prone to high acuity psychiatric presentations. Future prospective research should investigate if patients across the motor FND spectrum have similar clinical predictors of prognosis and treatment responses.

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