Medication prescriptions in 322 motor functional neurological disorder patients in a large UK mental health service: a case control study

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Abstract

Objective

This study describes medication prescribing patterns in patients with motor functional neurological disorder (mFND) treated in South London and Maudsley NHS Foundation Trust (SLaM), comparing outcomes to a control group of psychiatric patients from the same hospital trust.

Method

This is a retrospective case-control study using a psychiatric case register. Data were obtained from 322 mFND patients and 644 psychiatry controls between 1st January 2006 and 31st December 2016.

Results

A slightly lower proportion of mFND patients received medication compared to controls (76.6% v. 83.4%, OR: 0.59, CI: 0.39-0.89, $p < 0.05$). Of medication recipients, mFND patients were prescribed a higher number of agents (mean: 4.7 v 2.9, $p = 0.001$) and had higher prescription rates of antidepressants, anti-epileptics, analgesics, and certain non-psychotropic medications. Higher numbers of prescriptions were associated with co-morbid physical conditions, and previous psychiatric admissions.

Conclusions

This is the first study to describe medication prescriptions in a large cohort of mFND patients. Patients were prescribed a wide range of psychiatric and physical health medications, with higher rates of polypharmacy than controls. Psychotropic medication prescription is not necessarily the first line treatment for mFND, where physiotherapy and psychotherapy may be offered initially. There is however limited, early-phase evidence for pharmacological therapies for mFND. The benefit-to-risk ratio of prescribing in this complex and poorly understood disorder should be carefully assessed.

Keywords *Functional neurological disorder; Functional motor disorder; Psychosomatics; Conversion Disorder; Polypharmacy*

1. Introduction

In functional neurological disorder (FND), also known as conversion disorder, patients present with neurological symptoms with no known neurological cause (American Psychiatric Association, 2013). Symptoms commonly include seizures, sensory (e.g. numbness or visual impairment) and motor symptoms such as weakness, movement (e.g. tremor, paralysis and dystonia) and gait disorders. FND is common and associated with high rates of disability (Carson et al., 2011), lower quality of life (Anderson et al., 2007, Vroegop et al., 2013) and poor prognosis (Gelauff et al., 2014). FND has, until recently, fallen between the disciplines of Neurology and Psychiatry and has been under-researched. Consequently, there is a poor evidence base for treatment.

There is emerging evidence for the effectiveness of cognitive behavioural therapy (CBT) for psychogenic non-epileptic seizures (PNES), the seizure variant of FND, and specialist physiotherapy for motor FND (mFND) (Espay et al., 2018). There have been no large randomised controlled trials (RCTs) of pharmacological treatments and much of the evidence on pharmacotherapy comes from extrapolations from other functional disorders such as irritable bowel syndrome (IBS), fibromyalgia and multiple functional disorders, (American Psychiatric Association, 2013). A recent FND review states that it is inappropriate to prescribe medication for functional symptoms specifically, although comorbidities like pain and depression may be treated pharmacologically (Espay et al., 2018).

Of existing pharmacotherapy research in mFND, a small open-label study reported some effectiveness for the antidepressants citalopram and paroxetine (Voon and Lang, 2005), although all patients who improved had co-morbid anxiety or depression. A small, unblinded observational study of 18 functional patients, of whom nine had paralysis and two had ataxia, reported greater improvement in patients treated with sulpiride compared to haloperidol, although patients may have improved regardless of drug intervention (Rampello et al., 1996). There were beneficial responses to both benzodiazepines and placebo in a study of 26 patients with 'psychogenic paroxysmal movement' disorder (Ganos et al., 2014). In the seizure variant of FND, a pilot double-blind trial found sertraline reduced the frequency of non-epileptic seizures (LaFrance et al., 2010) and an open-label study of patients with PNES and anxious and depressive symptoms treated with venlafaxine also reported seizure reductions and improvements in co-morbid anxiety and depression (Pintor et al., 2010).

In other functional disorders, pharmacological guidelines differ but antidepressant use is common (Agger et al., 2018). Low-dose imipramine has been found to improve overall health in patients with multiple functional symptoms compared to placebo (Agger et al., 2017), and there is low-quality evidence for the efficacy of new-generation antidepressants in unexplained physical symptoms (Kleinstäuber et al., 2014). Within specific disorders, antidepressants have shown improvements in IBS (Ruepert et al., 2011, Ford et al., 2009), chronic pain (Kroenke et al., 2009) and somatoform pain disorder (Fishbain et al., 1998), with some evidence for their efficacy in patients without concomitant mood disorders (O'Malley et al., 1999, Agger et al., 2017). Most studies do not screen for comorbidities however, and the mechanisms of antidepressant effectiveness is poorly understood (Wessely, 1999).

Medication prescriptions rates are high across functional disorders. High prescription rates have been reported in patients with 'psychogenic jerky movement disorder' and in patients with unexplained pain, compared to Tourette's patients and those with pain disorders respectively (Heintz et al., 2013, Kouyanou et al., 1998). Opioid prescriptions varied between 28 and 36% in patients with unexplained gastrointestinal symptoms, fibromyalgia, and chronic fatigue (Sayuk et al., 2018, Fitzcharles et al., 2011, Vercoulen et al., 1996) and higher rates of benzodiazepines, gastric reflux medications, inhalers and blood pressure medications have been reported in PNES compared to epilepsy patients (Gazzola et al., 2012, Hantke et al., 2007). Patients with functional symptoms in primary care have been reported to have higher rates of both psychotropic and somatic medications compared to controls (olde Hartman et al., 2004).

The lack of pharmacotherapy evidence in mFND means prescribing patterns will vary and may be more likely to be influenced by a range of individual and systemic factors than prescriptions in non-FND patients. While psychiatrists will prescribe for common mFND comorbidities such as insomnia, pain, depression, anxiety and panic (Stone et al., 2010, Pareés et al., 2014), clinicians may also be influenced by patients' personal characteristics (Alexander et al., 1998), symptom severity and treatment preferences (Agger et al., 2018). Some GPs have described using prescriptions for patients with unexplained symptoms on a trial-and-error basis (Olde Hartman et al., 2009). The overall threshold for prescribing may be lower as a result of the fewer treatment options (Richardson et al., 2001). A lack of evidence may also lead some clinicians to prescribe placebos (Rommelfanger, 2013), with attendant complex ethics (Shamy, 2010). On a systemic level, functional patients have increased contact with and referrals within mental and physical health services (McGorm et al., 2010,

Barsky et al., 2005), which may lead to greater numbers of prescriptions and a cycle of medicalization may occur where patients require additional treatment to manage the side effects of a primary medication, for example requiring laxatives due to opioid analgesic prescriptions.

Given the potential for iatrogenic harm, there is a conspicuous lack of evidence on the type and number of medications mFND patients receive.

The aim of this study was to describe cross-sectional medication use in patients with mFND treated in a large secondary care mental health Trust,. Our objectives were to:

i) describe medication use and compare outcomes to a random sample of contemporaneous psychiatric patients treated in the same hospital trust;
ii) explore the socio-demographic variables and symptoms linked to polypharmacy in mFND; and
iii) examine the socio-demographic and symptom factors linked to prescriptions of opioid analgesics, antidepressants and anti-epileptic medications in mFND.

2. Methods

2.1. Design and source of clinical data

This was a retrospective case-control study which includes patients in contact with South London and Maudsley (SLaM) Foundation Trust, between 1st January 2006 and 31st December 2016.

Data were obtained from the SLaM Biomedical Research Centre's (BRC) Clinical Records Interactive Search (CRIS) database which contains anonymised electronic health records of over 250,000 individuals referred to SLaM services (Perera et al., 2016). SLaM provides inpatient and community services for a catchment of 1.5 million people living in southeast London. The trust also receives national referrals for FND patients.

We retrieved medication information from searches of the database's free clinical notes fields. As some patients had contact with SLaM over the course of years, the most contemporaneous medication information was collected from each participant, representing a cross-sectional snapshot at one timepoint, rather than a cumulative retrospective list of medications. In some cases, no information was available on medication at all.

This was marked, 'not known'. Given our data collection method and the necessary trade-off between capturing rich clinical information on a wide range of variables and increasing our sample size, we capped the number of medications we recorded per patient at 12. Strictly, this should be interpreted as "12 or more medications". We collected up to twelve prescriptions for each participant and calculated the total number of medications each participant was prescribed. We further categorised each drug based on their therapeutic properties, guided by the NICE British National Formulary (BNF) (Joint Formulary Committee, 2017). Our classification led to a total of 27 drug categories.

2.2. Study setting and participants

Cases were defined as any patient aged over-18 years with a primary or secondary diagnosis of 'Conversion disorder with motor symptom or deficit' (ICD-10 code: F44.4) who had contact with SLaM services. In addition, patients with any F44 diagnosis were included if there was additional evidence of functional motor symptoms in their unstructured case notes or correspondence (see "Supplementary Materials" for a comprehensive list of search strategies).

Our control group comprised contemporaneous SLaM patients who received any non-functional (i.e. non-F44) psychiatric diagnosis on the succeeding day the mFND patient received their diagnosis. Patients were included if they were aged over-18 years and had contact with SLaM services. Those with a neurodegenerative or intellectual disability (F70 – F79) diagnosis were excluded. We used a random number generator from the website, random.org to select controls from the returned search results and adopted a case-control ratio of 1:2.

2.3. Ethical approval

CRIS has received ethical approval from the Oxfordshire Research Ethics Committee C (08/H0606/71+5) as an anonymised dataset for mental health research. Ethical approval was granted in 2008 and renewed for a further five years in 2013. This study was approved by a patient-led NIHR BRC CRIS oversight committee (CRIS 14-101).

2.4. Statistical analysis

Descriptive statistics were used to describe socio-demographics and patients' prescriptions. Means, standard deviations, medians and interquartile ranges (IQR) were used to describe continuous data and proportions to

define categorical data. We employed odds ratios (OR) with 95% confidence intervals to compare the risk of medication prescription in both groups.

Univariate associations between prescription of five or more medications in mFND patients and patients' socio-demographics and symptoms were examined with "prescription of one to four medications" as the base outcome. Adjusting for all demographic and symptoms factors, a binary logistic regression model was conducted. We chose 'five or more medications' as five was the median number of medications in the mFND group and is a commonly applied definition of 'polypharmacy' (Haider et al., 2009, Hovstadius et al., 2010).

We conducted a univariate analysis of associations between socio-demographic and symptoms and prescriptions of opioid analgesic, antidepressant and anti-epileptic medications in mFND patients with "no prescriptions of these drugs" as the base outcome. In a binary logistic regression model, we adjusted for significant univariate socio-demographic variables and examined the associations between mFND symptoms and prescriptions of each drug.

SPSS for Windows (SPSS v21.0, Chicago, Illinois, USA), Microsoft Excel (Microsoft Office Professional Plus 2010, Version 14.0.7015.1000) and GraphPad Prism (Version 5.01, GraphPad Software, La Jolla California USA) were used to analyse data and create figures.

3. Results

Our search returned 322 mFND and 644 control patients. Socio-demographic characteristics of both groups are described in Table 4 (see 'Supplementary Materials'). The most frequent primary diagnosis in mFND was 'Neurotic, stress and somatoform disorders' of which 'Dissociative and Conversion Disorders' (F44) was the most common. In total 6.8% of mFND patients had a primary mood disorder diagnosis and the most common type was a single episode of major depression (F32). The most frequent secondary diagnosis, after neurotic stress and somatoform disorders were mood disorders, affecting 5.4% of the mFND group (see Table 4, in 'Supplementary Materials').

mFND patients were most commonly given their diagnosis in psychiatric and general hospital outpatient clinics (39.9%), neuropsychiatry liaison services in general hospital inpatient settings (17.7%) and liaison psychiatry in inpatient settings (12.6%).

The control group comprised patients with primary diagnoses of mood disorders (22.7%), mental and behavioural disorders due to psychoactive substances (17.4%), and schizophrenia, schizotypal and delusional disorders (14%). For a full description of control group diagnoses see O'Connell et al. (2019). Control participants received their diagnosis in liaison psychiatry services in inpatient settings (20.2%), A&E (14.9%), drug and alcohol services (11%) and assessment and liaison neighbourhood teams (11%).

The most commonly reported symptom was 'weakness' of any type accounting for 50.3% of all reported symptoms, followed by 'other' motor or sensory symptoms (37.9%) such as visual disturbances, facial droop, etc., and 'tremor' which includes 'tremor, spasms, jerks and tics' (33.9%).

3.1. Medication prescriptions

A lower proportion of mFND patients was prescribed at least one medication compared to the control group, although rates were high in both groups (76.7% vs 83.4% OR: 0.59, 95% CI: 0.39 – 0.89, $p < 0.02$). No information on medication was available for 28 mFND cases (8.7%) and 46 control group cases (7.1%).

We found no significant differences between proportions of mFND patients prescribed medication versus those prescribed no medications according to gender, marital status, pre-morbid employment status, co-morbid physical illness, experience of childhood sexual or physical abuse, or patients with a carer versus those without (p values > 0.05). There were significant differences between mFND patients in employment, 19.4% of whom were prescribed medication, versus unemployed mFND patients (42.6% were prescribed medication, $\chi^2 = 10.8$, $p = 0.001$). mFND patients who had a previous psychiatric inpatient admission were more frequently prescribed medication compared to mFND patients with no inpatient admission (40.5% versus 8.5%, $\chi^2 = 17.6$, $p = 0.001$). mFND patients with a carer were more likely to have a medication prescription compared to patients with no carer (36.8% versus 21.3%, $\chi^2 = 17.6$, $p < 0.001$).

In mFND patients, the mean number of prescribed medications was 4.77 (SD: 2.4), significantly higher than the 2.98 mean (SD: 2.7) in the control group (t (782) = 7.9, $p = 0.001$). The median prescription was 4 (IQR: 5) in mFND, compared with 2 (IQR: 2) in the control group. Figure 2 (Supplementary Material) displays a histogram showing the proportions of medications in both groups.

Amongst mFND patients, the most common prescriptions were antidepressants with 168 patients (68%) receiving one or more, anti-epileptics (34% prescribed one or more) and non-opioid painkillers (32.8% prescribed one or more). Opioid analgesics were the fourth most commonly prescribed medication (31.2% of patients were prescribed one or more). Table 1 outlines the proportion of medications in both groups.

Table 1 Use of prescription medications in mFND and control group patients

	Number and proportion of patients prescribed one or more medication[1]					Total prescriptions[2]				
	mFND n (%)	Control n (%)	OR	95% CI	*p* value	mFND n (%)	Control n (%)	Chi[2]	95 % CI	*p* value
Alcohol/drug treatment	7 (2.8)	37 (6.9)	0.4	0.2 – 0.9	**0.03**	7 (0.6)	40 (2.5)	14.6	0.9 – 2.8	**0.001**
Antidepressant	168 (68)	283 (52.7)	1.9	1.4 – 2.6	**0.001**	196 (16.8)	310 (19.3)	2.8	-0.4 – 5.40	0.09
Anti-epileptic	84 (34)	84 (15.6)	2.8	1.9 – 3.9	**0.001**	98 (8.4)	91 (5.7)	7.7	0.8 – 4.7	**0.005**
Anti-histamine[3]	27 (10.9)	33 (6.1)	1.9	1.1 – 3.2	**0.02**	27 (2.3)	33 (2.1)	0.28	-0.8 – 1.5	0.59
Sedating						4 (14.8)	21 (70)	16.5	29.5 – 71.3	**0.001**
Non-sedating						21 (77.8)	9 (30)			
Anti-inflammatory	24 (9.7)	9 (1.7)	6.3	2.9 – 13.8	**0.001**	24 (2.1)	9 (0.6)	12.5	0.6 – 2.5	**0.001**
Anti-manic	4 (1.6)	15 (2.8)	0.5	0.2 – 1.7	0.45	4 (0.3)	15 (0.9)	3.8	-0.02 – 1.2	0.052
Anti-microbial	18 (7.3)	20 (3.7)	2.0	1.1 – 3.9	**0.03**	22 (1.9)	24 (1.5)	0.7	-0.6 – 1.5	0.42
Anti-muscarinic	18 (7.3)	26 (4.8)	1.5	0.8 – 2.8	0.17	18 (1.5)	27 (1.7)	0.2	-0.8 – 1.1	0.68
Anti-nausea	15 (6.1)	11 (2.0)	3.1	1.4 – 6.8	**0.005**	16 (1.0)	12 (0.7)	0.7	-0.4 – 1.1	0.39
Antipsychotic	29 (11.7)	236 (43.9)	0.16	0.1 – 0.3	**0.001**	30 (2.6)	265 (16.5)	137	11.9 – 15.9	**0.001**
Anti-asthma	31 (12.6)	30 (5.6)	2.4	1.4 – 4.1	**0.001**	41 (3.5)	38 (2.4)	2.9	-0.2 – 2.5	0.09
Benzodiazepines	41 (16.6)	71 (13.2)	1.3	0.9 – 1.9	0.21	43 (3.7)	76 (4.7)	1.6	-0.6 – 2.5	0.19
Beta blocker	13 (5.3)	29 (5.4)	0.9	0.5 – 1.9	0.94	13 (1.1)	30 (1.9)	2.8	-0.2 – 1.7	0.09
Cardiac/hypertension	42 (17)	52 (9.7)	1.9	1.2 – 2.9	**0.004**	64 (5.5)	78 (4.9)	0.5	-1.0 – 2.3	0.48
CNS Stimulant	2 (0.8)	17 (3.2)	0.25	0.1 – 1.1	0.06	2 (0.2)	22 (1.4)	10.9	0.5 – 1.9	**0.001**
Corticosteroid	24 (9.7)	22 (4.1)	2.5	1.4 – 4.6	**0.003**	28 (2.5)	26 (1.6)	2.8	-0.2 – 2.1	0.09
Diabetes medication and insulin therapy	15 (6.1)	22 (4.1)	1.5	0.8 – 2.9	0.23	18 (1.5)	30 (1.9)	0.6	-0.6 – 1.4	0.43
Hormone replacement	30 (12.1)	26 (4.8)	2.7	1.6 – 4.7	**0.001**	35 (3)	27 (1.7)	5.2	0.2 – 2.6	**0.02**
Laxatives/bowel dysfunction	50 (20.2)	32 (6.0)	4.0	2.5 – 6.4	**0.001**	70 (6.0)	38 (2.4)	23.3	2 – 5.2	**0.001**
Nicotine replacement	3 (1.2)	5 (0.9)	1.3	0.3 – 5.5	0.71	5 (0.4)	5 (0.3)	0.2	-0.3 – 0.7	0.65
Nutrient	49 (19.8)	83 (15.5)	1.4	0.9 – 2.0	0.13	71 (6.1)	146 (9.1)	8.4	0.9 – 4.9	**0.004**
Opioid analgesic	77 (31.2)	28 (5.2)	8.3	5.2 – 13.1	**0.001**	89 (7.6)	35 (2.2)	46.1	3.8 – 7.1	**0.001**
Other	21 (8.6)	38 (7.2)	1.2	0.7 – 2.1	0.52	21 (1.8)	38 (2.4)	1.2	-0.5 – 1.6	0.28
Painkiller (non-opioid)	81 (32.8)	48 (8.9)	4.9	3.3 – 7.4	**0.001**	99 (8.3)	52 (3.2)	34.7	3.4 – 6.9	**0.001**
Proton pump inhibitors	58 (23.5)	48 (8.9)	3.1	2 – 4.7	**0.001**	58 (4.9)	49 (3.1)	5.9	0.3 – 3.4	**0.02**
Statin	35 (14.2)	41 (7.6)	1.9	1.2 – 3.2	**0.005**	36 (3.1)	43 (2.7)	0.4	-0.8 – 1.7	0.53
Muscle relaxant	15 (6.1)	3 (0.6)	11.5	3.3 – 40.1	**0.001**	15 (1.3)	3 (0.2)	12.4	0.5 – 1.9	**0.001**
Hypnotic	16 (5)	41 (6.4)	0.84	0.5 – 1.5	0.56	16 (1.4)	42 (2.6)	4.7	0.1 – 2.2	**0.03**
Total						1166 (100)	1604 (100)			

[1]Number and proportion of patients prescribed one or more medication: number and (%) of patients who received one or more of each drug class in both mFND and control groups. Denominator is the number of patients receiving medication. Odds ratio (OR) refers to risk of mFND receiving one or more prescriptions of that drug class compared to control participants

[2]Total prescriptions: number and (%) of all prescribed drugs according to drug class in both groups. Denominator is the total number of prescribed medications in each group. Chi[2] refers to the differences in frequencies of total prescribed medications

[3] Anti-histamines further classified according to whether they are sedating or non-sedating. 5 medications did not have enough information to classify as sedating or non-sedating

Compared to control patients, mFND patients had a higher likelihood of being prescribed antidepressants, cardiac and antihypertensive medications, statins, antihistamines (non-sedating), antimicrobials, anti-asthma medications, corticosteroids, anti-epileptics, opioid analgesics, hormone replacement therapies (including medications for hormone imbalance and female contraception), proton-pump inhibitors, medications for bowel

and urinary dysfunction, non-opioid analgesics, anti-inflammatories, anti-nauseas, nonsteroidal anti-inflammatory drugs (NSAIDs) and muscle relaxants.

Control patients were more likely to receive antipsychotic medication and treatment for drug and alcohol addiction. There were no differences in prescriptions of beta blockers, central nervous system stimulants, nicotine replacement therapies, nutrients, hypnotics, benzodiazepines, anti-manic or anti-muscarinic medications. The odds ratios and confidence intervals of medication prescription in mFND versus control group patients are displayed in Figure 1.

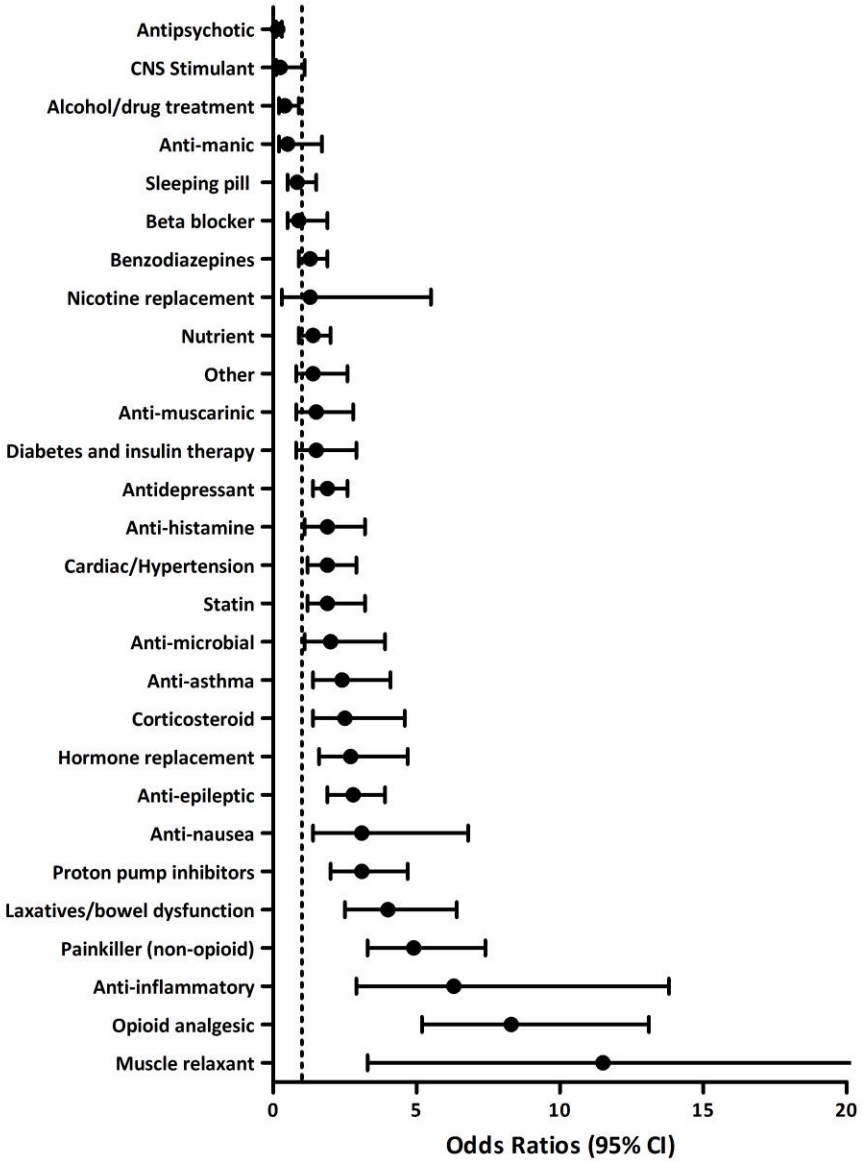

Figure 1 Forest plot showing odds of medication prescription in mFND patients compared to the control group

3.2. Associations between mFND patient characteristics and polypharmacy

Using the median number of medications, mFND patients were divided into those prescribed five or more medications and those prescribed one to four. We examined the socio-demographic and symptom variables associated with prescription of five or more medications.

108 (43.7%) mFND patients were prescribed five or more medications, compared to 18.2% in the control group. In mFND only, unadjusted comparisons showed an association between prescription of five or more medications and older age, being older at the time of symptom onset, receiving benefits, being unemployment, having previous psychiatric inpatient admission, a physical health condition, a lifetime history of using a walking aid, experiencing childhood sexual abuse, physical or sexual abuse in adulthood, and urinary or bowel dysfunction.

In a binary logistic regression, there was a strong association between polypharmacy and having a co-morbid physical health condition (OR: 6.1, 95% CI: 1.8 – 19.8, $p = 0.003$), a previous psychiatry admission (OR: 3.7, 95% CI: 1.3 – 10.7, $p = 0.02$), and not working as a health or social care worker (OR: 0.27, 95%: 0.08 – 0.9, $p = 0.04$). No symptoms or other socio-demographic factors were predictive in the adjusted model. Univariate and adjusted analyses are presented in Table 2.

Table 2 Logistic regression model examining factors associated with polypharmacy in mFND patients (compared to prescription of between one and four medications)

		Univariate OR	95% CI	*p* value	Adjusted OR	95% CI	*p* value
Demographics	Females versus males	1.60	0.9 – 2.9	0.12	2.1	0.7 – 6.2	0.19
	British versus other ethnicity	1.2	0.7-2.1	0.43	1.0	0.4 – 2.7	0.99
	Age at data collection	1.04	1.04 – 1.06	**0.001**	1.9	0.9 - 1.1	0.59
	Age at symptom onset	1.02	1.0 – 1.04	**0.04**	1.0	0.9 – 1.1	0.09
	Married versus unmarried	1.47	0.8 – 2.5	0.14	1.3	0.5 – 3.6	0.63
	Welfare recipient versus receiving no benefits	2.47	1.4 – 4.2	**0.001**	1.3	0.5 – 3.6	0.56
Employment	Employed versus unemployed	0.27	0.13 – 0.57	**0.001**	0.31	0.08 – 1.2	0.09
	Health or social care worker versus not employed in health or social care	0.88	0.45 – 1.7	0.72	0.27	0.08 – 0.9	**0.04**
Health	Psychiatric inpatient stay versus no stay	2.33	1.4 – 3.9	**0.001**	3.5	1.2 – 10.2	**0.02**
	Physical health condition versus no condition	3.18	1.6 – 6.1	**0.001**	7.5	2.1 – 26.7	**0.002**
	Lifetime prevalence of walking aid versus no aid	2.0	1.2 – 3.5	**0.01**	0.7	0.3 – 1.7	0.40
	Co-morbid non-motor functional symptoms versus no comorbid symptoms	1.15	0.7 – 1.9	0.60	0.7	0.3 – 1.8	0.43
Life events	Childhood sexual abuse versus no CSA	2.92	1.4 – 5.9	**0.003**	1.6	0.5 – 5.5	0.43
	Childhood physical abuse versus no CPA	1.74	0.9 – 3.4	0.10	1.8	0.5 – 6.7	0.39
	Physical or sexual abuse in adulthood versus no abuse in adulthood	2.16	1.1 – 4.1	**0.02**	2.5	0.7 – 8.7	0.16
Carers	Family carer versus not a family carer	0.64	0.3 – 1.6	0.34	0.48	0.1 – 2.3	0.37
	Patient has a carer versus has no carer	0.59	0.3 – 1.0	0.06	2.1	0.8 – 5.2	0.13
Symptoms	Tremor versus no tremor	1.2	0.7 – 1.9	0.55	1.9	0.6 – 5.9	0.25
	Weakness versus no weakness	1.3	0.8 – 2.1	0.36	2.2	0.9 – 5.9	0.10
	Back pain versus no back pain	1.0	0.5 – 2.1	0.91	1.8	0.4 – 7.3	0.39
	Other pain types versus no other pain types	1.5	0.8 – 2.5	0.15	1.3	0.5 – 3.4	0.57
	Numbness versus no numbness	1.1	0.6 – 1.9	0.79	2.5	0.9 – 7.1	0.08
	Urinary/bowel dysfunction versus no urinary or bowel dysfunction	3.8	1.4 – 10.1	**0.01**	3.5	0.7 – 16.8	0.12
	Paralysis versus no paralysis	0.8	0.4 – 1.7	0.62	0.44	0.13 – 1.4	0.18
	Gait disorders versus no gait disorders	1.7	0.9 – 3.0	0.10	1.4	0.5 – 4.3	0.55
	Depression present versus no depression present	1.2	0.7 – 1.9	0.51	1.4	0.5 – 3.5	0.52
	Anxiety present versus no anxiety present	0.9	0.5 – 1.7	0.69	0.41	0.1 – 1.7	0.22
	Fatigue present versus no fatigue present	0.8	0.3 – 2.1	0.66	1.9	0.3 – 13.0	0.51

CSA = childhood sexual abuse, CPA = childhood physical abuse

3.3. Associations between patient characteristics and opioid analgesic, antidepressant and antiepileptic prescriptions

Taking three commonly prescribed medications, we assessed characteristics associated with prescriptions of opioid analgesics, antidepressants and anti-epileptics, using mFND patients who weren't prescribed these medications as a reference group.

In our univariate analysis the characteristics associated with opioid analgesic prescription were unemployment, receipt of welfare benefits, lifetime use of walking aids, having a carer, functional weakness, back pain, other pain, urinary and bowel dysfunction, and depression. Adjusting for these in a logistic regression analysis we assessed the functional motor symptoms associated with opioid analgesic prescription. In this model, weakness (OR: 4.5, 95% CI: 1.7 – 11.7, p = 0.002) and pain (excluding back pain) (OR: 4.5, 95% CI: 1.8 – 11.1, p = 0.001) were associated with opioid analgesic prescription.

In a univariate analysis, antidepressant prescriptions were associated with lifetime use of walking aids, and experiences of depression and anxiety. Accounting for these factors in an adjusted analysis of the mFND symptoms linked to antidepressant use, we found having no paralysis (OR: 0.45, 95% CI: 0.2 – 0.99, $p = 0.05$) and experiencing anxiety (OR: 2.9, 95% CI: 1.1 – 7.6, $p = 0.03$) were significantly predictive of antidepressant prescription.

A univariate analysis of factors found being male, British, married and experiencing childhood abuse were associated with anti-epileptic medication. In an adjusted analysis we found no associations between mFND symptoms and anti-epileptic prescriptions. The binary logistic regression results are outlined in Table 3.

Table 3 Logistic regression of functional symptoms that predict opioid analgesic, antidepressant and antiepileptic use in mFND

		Opioid analgesics						Antidepressants						Anti-epileptics					
		Univariate analysis			Adjusted model			Univariate analysis			Adjusted model			Univariate analysis			Adjusted model		
		OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value
Demographics	Female versus male	1.1	0.6 – 2.1	0.70				0.9	0.5 – 1.7	0.80				**0.43**	**0.2 – 0.8**	**0.005**			
	British versus other ethnicity	1.1	0.6 – 1.9	0.79				0.81	0.4 – 1.4	0.45				**1.95**	**1.1 – 3.4**	**0.02**			
	Age[a]	1.0	0.9 – 1.0	0.94				0.99	0.9 – 1.0	0.54				0.98	0.9 – 1.0	0.06			
	Married versus single	0.74	0.4 – 1.3	0.27				1.6	0.9 – 2.7	0.10				**1.4**	**0.8 – 2.3**	**0.25**			
Employment	Employed versus unemployed	**0.11**	**0.03 – 0.4**	**0.001**				0.58	0.3 – 1.1	0.10				0.50	0.2 – 1.0	0.07			
	Welfare benefits v no welfare	**2.1**	**1.2 – 3.8**	**0.01**				1.5	0.9 – 2.7	0.14				1.6	0.9 – 2.7	0.11			
	Health or social care worker versus not a health or social care worker	0.65	0.3 – 1.4	0.28				0.8	0.4 – 1.7	0.63				0.6	0.3 – 1.3	0.20			
Illness	Psychiatric inpatient stay versus no inpatient stay	1.6	0.9 – 2.7	0.10				1.4	0.8 – 2.4	0.27				0.83	0.5 – 1.4	0.49			
	Walking aid use versus no walking aid use	**2.5**	**1.3 – 4.5**	**0.004**				**2.3**	**1.3 – 4.0**	**0.005**				1.3	0.7 – 2.2	0.41			
	Physical illness versus no physical illness	0.84	0.5 – 1.6	0.58				0.98	0.5 – 1.8	0.94				1.1	0.6 – 2.0	0.81			
	Co-morbid non-motor functional symptoms versus no such symptoms	1.08	0.6 – 1.9	0.80				1.3	0.7 – 2.2	0.42				1.5	0.8 – 2.5	0.18			
Abuse	Childhood sexual abuse versus no childhood sexual abuse	1.9	0.9 – 3.8	0.06				1.4	0.7 – 2.9	0.39				**1.9**	**0.9 – 3.9**	**0.05**			
	Childhood physical abuse versus no childhood physical abuse	1.5	0.7 – 2.9	0.26				1.01	0.5 – 2.0	0.98				1.4	0.7 – 2.7	0.38			
	Adult physical or sexual abuse versus no abuse in adulthood	0.85	0.4 – 1.7	0.64				0.96	0.5 – 1.9	0.91				0.9	0.4 – 1.7	0.63			
	Age of psychiatric symptom onset[a]	0.99	0.9 – 1.0	0.15				0.99	0.9 – 1.0	0.34				0.9	0.9 – 1.0	0.45			
Caring	Patient has a carer versus patient has no carer	**2.3**	**1.3 – 4.1**	**0.01**				1.4	0.8 – 2.5	0.26				0.96	0.5 – 1.7	0.89			
	Carer to family versus not a carer to family	0.7	0.3 – 2.1	0.54				2.03	0.7 – 6.3	0.22				0.62	0.2 – 1.8	0.37			
Symptoms	Tremor versus no tremor	0.9	0.5 – 1.6	0.79	0.65	0.20 – 1.9	0.42	0.9	0.5 – 1.6	0.69	0.80	0.4 – 1.7	0.54	0.85	0.5 – 1.5	0.57	1.9	0.9 – 4.2	0.10
	Weakness versus no weakness	**2.8**	**1.6 – 4.9**	**0.001**	**4.5**	**1.7 – 11.7**	**0.002**	1.5	0.9 – 2.7	0.11	1.3	0.7 – 2.6	0.43	1.01	0.6 – 1.7	0.97	0.8	0.4 – 1.7	0.63
	Back pain versus no back pain	**2.6**	**1.3 – 5.2**	**0.01**	0.46	0.2 – 1.4	0.16	1.0	0.5 – 2.2	0.94	0.98	0.4 – 2.4	0.96	1.34	0.7 – 2.7	0.42	1.1	0.5 – 2.9	0.77
	Other pain types versus no other pain types	**4.1**	**2.3 – 7.2**	**0.001**	**4.5**	**1.8 – 11.1**	**0.001**	0.7	0.4 – 1.3	0.28	0.73	0.4 – 1.4	0.35	1.64	0.9 – 2.8	0.08	1.7	0.8 – 3.5	0.15
	Numbness versus no numbness	1.1	0.6 – 2.0	0.76	0.90	0.4 – 2.3	0.83	1.06	0.6 – 1.9	0.86	0.9	0.4 – 1.9	0.81	1.4	0.8 – 2.5	0.29	1.1	0.5 – 2.2	0.85
	Urinary/bowel dysfunction versus no urinary or bowel dysfunction	**4.5**	**1.8 – 11.2**	**0.001**	4.5	0.9 – 21.4	0.06	1.02	0.4 – 2.6	0.98	1.02	0.3 – 3.0	0.97	1.4	0.6 – 3.4	0.46	1.5	0.5 – 4.5	0.44
	Paralysis versus no paralysis	1.1	0.6 – 2.3	0.76	0.37	0.1 – 1.2	0.11	0.64	0.3 – 1.3	0.21	**0.45**	**0.2 – 0.99**	**0.05**	0.75	0.4 – 1.6	0.44	0.53	0.2 – 1.3	0.15
	Gait disorders versus no gait disorders	0.9	0.5 – 1.8	0.86	0.7	0.3 – 2.1	0.55	0.90	0.5 – 1.7	0.74	0.68	0.3 – 1.4	0.30	0.82	0.4 – 1.6	0.54	0.73	0.3 – 1.6	0.43
	Depression present versus no depression present	**1.7**	**0.9 – 2.9**	**0.05**	1.4	0.6 – 3.2	0.48	**2.4**	**1.3 – 4.3**	**0.003**	1.8	0.9 – 3.4	0.09	1.04	0.6 – 1.8	0.87	1.2	0.6 – 2.4	0.60
	Anxiety present versus no anxiety present	0.84	0.4 – 1.7	0.62	0.54	0.15 – 1.9	0.36	**2.6**	**1.2 – 5.9**	**0.02**	**2.9**	**1.1 – 7.6**	**0.03**	1.2	0.6 – 2.3	0.61	0.9	0.4 – 2.3	0.83
	Fatigue present versus no fatigue present	1.1	0.4 – 3.1	0.85	1.4	0.2 – 9.3	0.70	0.73	0.3 – 1.9	0.52	0.7	0.2 – 2.2	0.53	0.98	0.4 – 2.7	0.97	1.01	0.3 – 3.6	0.98

[a] For a 1-year increase in age, and one additional functional symptom

Adjusted model accounts for factors significant in the univariate analysis

4. Discussion

The purpose of this study was to provide a cross-sectional description of the medication patterns of mFND patients treated in a psychiatric setting, and the socio-demographic factors and mFND symptoms associated with polypharmacy and certain prescriptions.

Physicians prescribed a total of 1166 medications to 247 mFND patients. A slightly lower proportion of mFND patients received medication compared to controls but rates in both groups were high. High rates in the psychiatric disorder control group are perhaps to be expected but given the lack of evidence for the efficacy of medications in FND, the high prescription rate in the mFND group was surprising. Of patients with a prescription, mFND patients were given a higher proportion and greater variety of medications. This heterogeneity has been reported previously in patients with multiple functional symptoms in secondary care (Agger et al., 2018), and in fibromyalgia patients (Robinson et al., 2012). Polypharmacy in mFND patients was linked to co-morbid physical illness and previous psychiatric inpatient admission. Rates of co-morbid physical illness in FND is often high (Pareés et al., 2014), and while it might partly account for polypharmacy, when we assessed patients with no co-morbid organic conditions, mFND patients still had higher proportions of prescribed medications, with a similar pattern in patients with no history of psychiatric admission.

mFND patients were significantly more likely to have a prescription of one or more antihistamines, and the results indicated the drug was more frequently prescribed to mFND patients as an anti-allergy and as a sedative to control patients. Previous studies have reported higher rates of self-reported allergies in PNES patients compared to epileptic patients (Robbins et al., 2016), as well as heightened sensitivities and side effects to medications (Park et al., 2014, Nassim Matin et al., 2017). The presence of increased allergy and non-specific medication side-effects in mFND deserves further examination and highlights the importance of a considered and collaborative prescription strategy (Barsky et al., 2002).

Beyond psychological and physical health comorbidities, a variety of factors that we could not measure may contribute to these high rates of somatic and psychotropic medication in FND. Diagnosing mFND can be complex, challenging and a time-consuming process for patients, particularly if presentation is atypical and there isn't access to sufficiently trained or experienced clinicians to consider FND, confirm it, and perhaps most

importantly, explain it in a way that the patient understands and accepts. During this process, patients likely accrue medications as they are referred within and between medical and psychiatric specialities. One suggestion is that there is a disproportionate reliance on pharmacological solutions as clinicians often feel obligated to try to do something to help a clearly distressed and disabled patient, an option that might be preferred by both clinicians and patients (Jackson and Kroenke, 2006). This argument gains credence in the context of overstretched medical settings where medication prescriptions may be seen as a preferable passive form of treatment (Netherlands Institute of Mental Health and Addiction, 2010). There have been recent recommendations for clinicians to utilise a reduction of medications which lack a clear clinical indication in the therapeutic process itself (McCormack et al., 2014, Stone, 2016), where it may help shift patients' external locus of control to an internal one, although deprescribing can be a difficult and complex process (Salisbury, 2019).

4.1 Antidepressants

We found a significantly higher proportion of mFND patients were prescribed at least one antidepressant (68%) compared to psychiatric controls, similar to previous findings in patients with chronic functional symptoms in primary care (olde Hartman et al., 2004). This is perhaps surprising given that only 6.8% of mFND patients have a primary mood disorder diagnosis and 5.4% have a secondary mood disorder diagnosis, compared to 22.7% and 25.1% with these diagnoses in the control group. In our analysis of unstructured free text, we found 34% of mFND patients had previous reports of low mood or depression, significantly lower than the 44.7% in the control group. There were anxiety rates of 17.4% and 15.2% in the mFND and control groups respectively, with no significant difference.

Our rate is higher than previously reported rates, varying between 22 and 56%, in patients with unexplained visual loss, PNES patients, somatoform disorder patients in primary care, mFND patients in a neurology and tertiary movement disorders clinic, and patients with multiple functional symptoms in secondary care (Duncan et al., 2014, Noyes et al., 1998, Kranick et al., 2011, de Waal et al., 2008, O'Leary et al., 2016, Agger et al., 2018). Our higher rate partly reflects the specialist psychiatric setting from which the sample is drawn where patients will receive treatment for psychiatric co-morbidities, but compared to psychiatric patients from the same Trust, antidepressant use is nonetheless high.

The current guidance to prescribe only for co-morbidities in FND is borne out in our adjusted findings as patients with a lifetime history of anxiety were nearly three times more likely to be prescribed antidepressants. Antidepressants may have multiple actions, including possible central analgesic effects (Lynch, 2001), and reductions in affective arousal and sleep dysfunction (Clouse et al., 1994). The relationship between antidepressant treatment and mFND prognosis remains complicated by the presence of co-morbid depression and anxiety, as well as other factors such as attachment traits (Jalilianhasanpour et al., 2018), emotional regulation (Sojka et al., 2018), attentional dysregulation (Edwards et al., 2012), health anxiety and illness belief (Bakvis et al., 2009), and phobic avoidance (Stone et al., 2012). As it stands, the effectiveness or otherwise of antidepressants in this group and their mechanism of action remain poorly understood.

4.2 Opioid Analgesics

Opioid analgesics were more commonly prescribed in mFND patients than controls and the prescription was strongly associated with weakness, non-back related pain, and linked to urinary and bowel dysfunction (although the association was not significant). While opioids are most commonly prescribed to treat pain, the associations with urinary and bowel dysfunction may be due to the opioid medication itself (Panchal et al., 2007). It is perhaps surprising that weakness, a lack of motor function, was associated with these drugs. This may be because pain inhibits patients from increasing physical activity as part of their rehabilitation, leading to increased prescribing to relieve the impasse. However, it is likely the relationship is bidirectional with pain and lack of activity reinforcing each other. In a case control study of functional weakness Stone et al. (2010) found widespread pain to be a common complaint in mFND, not just pain linked to the affected limb.

Of patients on medication, 31% in our study received at least one opioid analgesic, a rate similar to reports in fibromyalgia (Fitzcharles et al., 2011) and unexplained gastrointestinal symptoms (Sayuk et al., 2018). Like our antidepressant results, it is difficult to ascertain whether patients are prescribed these drugs to treat co-morbidities, to treat mFND directly or to alleviate secondary pain arising from motor symptoms, like pain due to spasms, cramps and stiffness. Of note however, we did not find an association between opioid analgesics and the presence of co-morbid physical health conditions or co-morbid functional disorders like somatoform pain disorder, IBS or fibromyalgia.

In our univariate analysis, two associations with opioid analgesics emerged; severity (i.e. using a walking aid and having a carer) and socio-economic position (those unemployed and receiving welfare benefits), similar to previous findings in patients with multiple functional symptoms and fibromyalgia (Agger et al., 2018, Fitzcharles et al., 2013). Such associations may not be specific to mFND as opioid prescription is higher in people with mental health disorders (Sullivan et al., 2006) and in those with a lower socio-economic status in the general population (Zhou et al., 2018, Ruscitto et al., 2015).

A future study quantifying mFND severity in a more fine-grained way would be helpful as previous research on somatisation reported that it was only patients with severe symptoms that engaged in opioid overuse (Trafton et al., 2011). Opioids were ranked as the most helpful medication amongst fibromyalgia patients (Bennett et al., 2007) although the evidence for their effectiveness is weak (Clauw, 2014) and they have significant clinical risks, not least pharmacological tolerance and dependence, bowel and bladder dysfunction, cognitive impairment, hormonal changes, and even immune modulation.

4.3 Anti-Epileptics

34% of mFND patients were prescribed one or more anti-epileptics. Prescriptions were associated with being male, British, married and having experienced sexual abuse in childhood. Previous evidence on anti-epileptics in mFND found 27% of functional movement disorder patients were prescribed anti-epileptics (Ganos et al., 2014), and anti-epileptics were commonly prescribed in children with mFND (Ferrara and Jankovic, 2008).

Anti-epileptics' multiple indications makes it difficult to draw conclusions on their usage. A previous study reported that anti-epileptics were prescribed by psychiatrists most frequently to treat bipolar disorder and anxiety, while neurologists tended to prescribe them to treat seizures, migraine and pain (Cascade et al., 2008). In our sample, anti-epileptics may have been prescribed to modify pain and reduce anxiety (Mula et al., 2007) and to manage co-morbid seizures (epileptic and or undiagnosed PNES), although no specific symptoms associations or links with co-morbid physical illness were observed. In an additional analysis, not reported above, we found no significant difference in the rates of anti-epileptic prescriptions between mFND patients with co-morbid non-epileptic seizures and those without. Another possible explanation for their high prescription rate may be that the motor symptoms are themselves a result of the administration of anti-epileptics (Zadikoff et al.,

2007), although this is unlikely in this tertiary psychiatric setting where the functional diagnosis is often well-established.

4.4 Strengths and Limitations

This study is the first to describe detailed medication usage in a large sample of mFND patients. The use of routine clinical records allows for a naturalistic study without the selection biases common to trials or studies requiring patient recruitment, increasing the representativeness of our results. Access to anonymous health records allowed us to compile detailed socio-demographic and health information on mFND patients, and the use of a contemporaneous control group enabled us to report the specific risk of medication prescriptions in mFND patients.

The use of electronic health records brings certain limitations. While we can assess patterns in prescriptions, we cannot report their adherence, effectiveness or side effects. For drugs with multiple clinical indications, such as anti-epileptics and antidepressants, we do not know the primary reason for their prescription or where and by whom medication was initiated. For each patient, we recorded contemporaneous medication information from their clinical notes, so we cannot report treatment duration or discontinuation. In addition, we cannot account for any data entry errors made in health records, and it is possible that there may be under-reporting of medications, particularly as we capped the number of medications at 12, although this is unlikely to cause systematic bias. Our method will only capture self-prescriptions if this has been disclosed to the clinician. Our control group included patients with psychotic spectrum disorders and addictions which will likely accentuate differences in antipsychotic medication and drug and alcohol treatment risks. This retrospective study included patients treated over a ten-year period so it is possible more recently treated patients will have been prescribed drugs not developed in 2006. In addition, prescribing patterns themselves may have shifted due to changes in DSM-5 criteria and advances in the education and training of new clinicians, something we are unable to account for in our analysis. We established the drug categorisations based on the collected data and therapeutic usage but given the multi-action nature of certain drugs and the many sub-classifications, it is possible that our definitions and use of a miscellaneous category missed some meaningful associations. Finally, this study was set in a large psychiatric NHS Trust. The Trust receives referrals as a tertiary neuropsychiatry service, which limits our ability to generalise to services without neuropsychiatry input or to other healthcare systems.

4.5 Conclusions

This is the first study to describe medication patterns in mFND patients. These patients are prescribed an extensive range of psychiatric and physical health medication, most commonly anti-depressants, anti-epileptics and analgesics. This polypharmacy may be partially explained by higher rates of physical co-morbidities but may also reflect functional symptoms in other bodily systems, higher symptom reporting combined with a lack of therapeutic options for clinicians managing patients with complex functional and 'organic' conditions and chronic pain. As there are no evidence-based pharmacological therapies, it is important to carefully assess the benefit to risk ratio of prescribing in this complex and poorly understood disorder.

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6. Declaration of interests

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9. Figure Legend

10. Table Legend

11. Supplementary Material

Table 4 Socio-demographic, health characteristics and primary and secondary diagnoses of mFND and control group patients

		mFND n (%) (n=322)	Control n (%) (n=644)	OR	95% CI	*p* value
Demographics	Mean age	46.1 (13.4)	47.6 (16.2)			n.s
	Mean age at psychiatric symptom onset	33.2 (14.6)	32.5 (17.8)			n.s
	Female gender	238 (73.9)	341 (53)	2.5	1.9 – 3.4	0.001
	British	195 (60.6)	328 (50.9)	1.5	1.1 – 1.9	0.005
	Any other ethnicity	127 (39.4)	316 (49.1)			
	Married, civil partner or cohabiting	141 (43.4)	111 (17.7)	4	2.9 – 5.4	0.001
	Single, divorced, separated or widowed	163 (53.6)	515 (82.3)			
Employment	Employed	73 (24.5)	104 (17.4)	1.5	1.1 – 2.2	0.01
	Unemployed	225 (75.5)	492 (82.6)			
	Receives benefits	143 (47.8)	337 (55.7)	0.73	0.6 – 0.9	0.03
Health	Physical health condition	219 (74.5)	326 (59.6)	1.9	1.4 – 2.7	0.001
	Psychiatric inpatient stay	107 (33.2)	280 (43.5)	0.65	0.5 – 0.9	0.002
	Lifetime history of depression or low mood	112 (34.8)	288 (44.7)	0.64	0.5 – 0.9	0.002
	Lifetime history of anxiety	56 (17.4)	98 (15.2)	1.16	0.8 – 1.7	0.41
	Lifetime walking aid use*	163 (58.2)	-			
	Comorbid functional symptoms (e.g. IBS, chronic pain)	106 (33.8)	12 (1.9)	25.9	14 – 48.2	0.001
	Mean HoNOS score[1] *t*-test	12.7 (6.2)	12.1 (6.2)			n.s
	Mean PHQ-9 score[2] *t*-test	13.1 (7.4)	20 (6.3)			0.04
Primary Diagnosis	(F00-F09) Organic mental disorders	7 (2.2)	5 (0.8)			
	(F10-F19) Mental & behavioural disorders due to psychoactive substances	3 (0.9)	112 (17.4)			
	(F20 – F29) Schizophrenia, schizotypal and delusional disorders	4 (1.2)	90 (14)			
	(F30 – F39) Mood disorders	22 (6.8)	146 (22.7)			
	(F30, F31, F33, F34, F38 & F39) Manic episode, bipolar disorder, recurrent depressive disorder, persistent mood disorders, other mood disorders, unspecified mood disorder	4 (18.2)	56 (38.4)			
	(F32) Major depressive disorder, single episode	18 (81.8)	90 (61.6)			
	(F40 – F48) Neurotic, stress & somatoform disorders	185 (57.5)	70 (10.9)			
	(F40, F41, F42, F43, F45, F48) Phobic anxiety disorders, other anxiety disorders, obsessive compulsive disorder, reaction to severe stress, and adjustment disorders, somatoform disorders, & other nonpsychotic mental disorders	18 (9.7)	70 (100)			
	(F44) Dissociative and conversion disorders	167 (90.3)	0 (0)			
	(F50 – F98)[3]	6 (1.9)	46 (7.1)			
	(F99) Unspecified mental disorder	41 (12.7)	73 (11.3)			
	(Z00 – Z99) Factors influencing health status and contact in health services	38 (11.8)	89 (13.8)			
	Other diagnoses[4]	16 (4.9)	13 (2)			
	Total primary diagnoses	322 (100)	644 (100)			
Secondary Diagnosis	(F00-F09) Organic mental disorders	5 (2.7)	15 (2.9)			
	(F10-F19) Mental & behavioural disorders due to psychoactive substances	2 (1.1)	92 (17.8)			
	(F20 – F29) Schizophrenia, schizotypal and delusional disorders	3 (1.6)	95 (18.3)			
	(F30 – F39) Mood disorders	10 (5.4)	130 (25.1)			
	(F30, F31, F33, F34, F38, F39) Manic episode, bipolar disorder, major depressive disorder, recurrent, persistent mood disorder, recurrent depressive disorder, other mood disorders, unspecified mood disorder	2 (20)	70 (53.8)			
	(F32) Major depressive disorder, single episode	8 (80)	60 (46.2)			
	(F40 – F48) Neurotic, stress & somatoform disorders	139 (75.5)	62 (12)			
	(F40, F41, F42, F43, F45, F48) Phobic anxiety disorders, other anxiety disorders, obsessive compulsive disorder, reaction to severe stress, somatoform disorders, other nonpsychotic mental disorders	21 (15.1)	61 (98.4)			
	(F44) Dissociative and conversion disorders	118 (84.9)	1 (1.6)			
	(F50 – F98)[3]	7 (3.8)	48 (9.3)			
	(F99) Unspecified mental disorder	7 (3.8)	37 (7.1)			
	(Z00 – Z99) Factors influencing health status and contact in health services	3 (1.6)	31 (6)			
	Other diagnoses[4]	8 (4.3)	8 (1.5)			
	Total secondary diagnoses	184 (57.1)	518 (80.4)			

* Data collected only for mFND group; [1] Data available for 121 mFND and 400 control patients; 2 Data available for 39 mFND and 6 control patients

[3]Category includes 'Behavioural syndromes associated with physiological disturbances'; 'Disorders of adult personality and behaviour'; 'Intellectual disabilities'; 'Disorders of psychological development'; and 'Behavioural and emotional disorders with onset in in childhood and adolescence' and other diagnoses

[4]'Other' includes 'Mental, behavioural and neurodevelopmental disorders', 'Diseases of the nervous system', 'Diseases of musculoskeletal system', 'HIV' and 'Intentional self-harm'

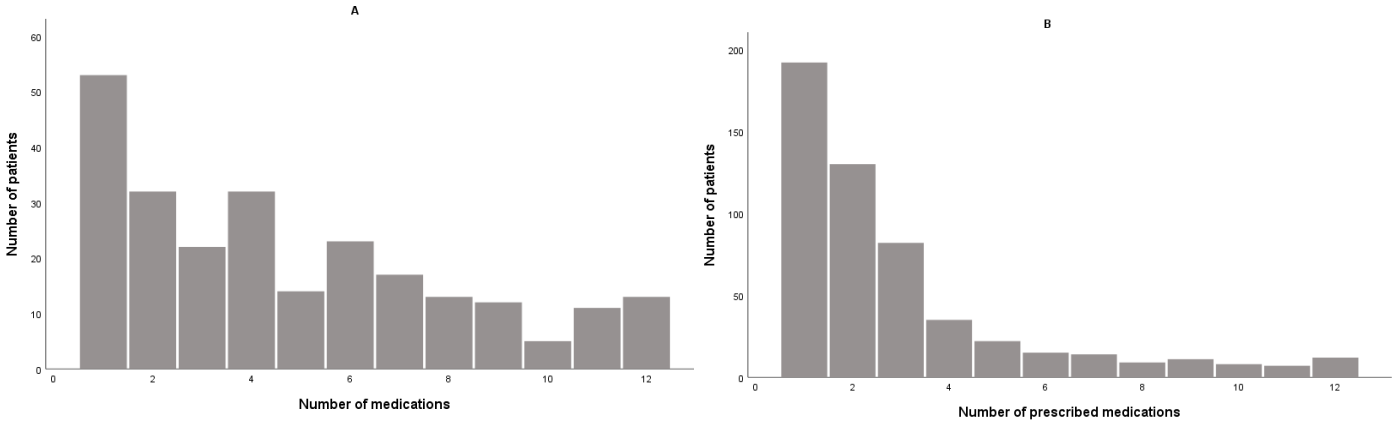

Figure 1 Histograms showing the proportion of medications in mFND patients (Figure A) and in control group participants (Figure B)

Comprehensive list of CRIS search terms

First search: F44.4 in primary diagnosis yielding 176 results.

CRIS code: (Assmnts.Diagnosis.Primary_Diag="F44.4 - Dissociative motor disorders")

Second search: “Functional Motor”, “Dissociative Motor”, “Psychogenic Motor”: free text search in ‘Events and Correspondence’ yielding 167 results.

CRIS code: (Events.Event.Comments=""Dissociative motor"") OR
(Events.Event.Comments=""Functional motor"") OR
(Events.Event.Comments=""Psychogenic motor"") OR
(Correspondence.Attachment.Attachment_Text=""Psychogenic motor"") OR
(Correspondence.Attachment.Attachment_Text=""Functional motor"") OR
(Correspondence.Attachment.Attachment_Text=""Dissociative motor"")

Third search: F44.7 AND ((“motor” in events) OR (“motor” in correspondence)) yielding 60 results

CRIS code: (Assmnts.Diagnosis.Primary_Diag="F44.7 - Mixed dissociative [conversion] disorders") AND ((Events.Event.Comments="Motor") OR (Correspondence.Attachment.Attachment_Text="Motor"))

Fourth search: F44.4 in secondary diagnosis, yielding 12 results.

CRIS code: (Assmnts.Diagnosis.Secondary_Diag_1="F44.4")

Fifth search: F44.7 in secondary diagnosis AND ((“motor” in events) OR (“motor” in correspondence)), yielding 9 results

CRIS code: (Assmnts.Diagnosis.Secondary_Diag_1="F44.7") AND ((Events.Event.Comments="Motor") OR (Correspondence.Attachment.Attachment_Text="Motor"))

Sixth search: Free-text search of “motor conversion disorder” yielding 10 results

Seventh search: Free-text search of “motor conversion” yielding 13 results

Eight search: Search of “F44” in primary diagnosis and free-text search of “motor” in events, yielding 77 results

CRIS code: Assmnts.Diagnosis.Primary_Diag="F44 - Dissociative [conversion] disorders") AND (Events.Event.Comments="Motor")

Ninth search: Search of “F44” in primary diagnosis field and free-text search of “weak” in events”, yielding 155 results

CRIS code: (Assmnts.Diagnosis.Primary_Diag="F44 - Dissociative [conversion] disorders") AND (Events.Event.Comments="weak")