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Systematic review

# Pain and functional neurological disorder: a systematic review and meta-analysis

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## ABSTRACT

**Background** Functional neurological disorder (FND) is characterised by neurological symptoms, such as seizures and abnormal movements. Despite its significance to patients, the clinical features of chronic pain in people with FND, and of FND in people with chronic pain, have not been comprehensively studied.

**Methods** We systematically reviewed PubMed, Embase and PsycINFO for studies of chronic pain in adults with FND and FND in patients with chronic pain. We described the proportions of patients reporting pain, pain rating and timing, pain-related diagnoses and responsiveness to treatment. We performed random effects meta-analyses of the proportions of patients with FND who reported pain or were diagnosed with pain-related disorders.

**Results** Seven hundred and fifteen articles were screened and 64 were included in the analysis. Eight case-control studies of 3476 patients described pain symptoms in a higher proportion of patients with FND than controls with other neurological disorders. A random effects model of 30 cohorts found that an estimated 55% (95% CI 46% to 64%) of 4272 patients with FND reported pain. Random effects models estimated diagnoses of complex regional pain syndrome in 22% (95% CI 6% to 39%) of patients, irritable bowel syndrome in 16% (95% CI 9% to 24%) and fibromyalgia in 10% (95% CI 8% to 13%). Five studies of FND diagnoses among 361 patients with chronic pain were identified. Most interventions for FND did not ameliorate pain, even when other symptoms improved.

**Conclusions** Pain symptoms and pain-related diagnoses are common in FND. Classification systems and treatments should routinely consider pain as a comorbidity in patients with FND.

## INTRODUCTION

Chronic pain affects many patients with functional neurological disorder (FND) and chronic pain disorders, such as complex regional pain syndrome (CRPS), irritable bowel syndrome (IBS) and fibromyalgia, are common comorbidities.<sup>1 2</sup> However, the pain symptoms and diagnoses of patients with FND are poorly characterised.

Therefore, we conducted a systematic review and meta-analysis of the chronic pain symptoms and pain-related diagnoses of patients with FND. We also evaluated studies which assessed the timing of pain symptoms in FND, their potential role in prognosis and their response to treatment. Finally,

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ In addition to core symptoms, such as seizures and abnormal movements, many patients with functional neurological disorder (FND) report pain or are diagnosed with pain-related conditions.

## WHAT THIS STUDY ADDS

⇒ This systematic review and meta-analysis quantifies the high pain comorbidity in FND. Chronic pain is more common in patients with FND than those with other neurological disorders and co-occurs at least as commonly as childhood maltreatment. Chronic pain can be present at the early stages of FND, may be associated with worse outcomes and is not ameliorated by standard treatments which improve other measures of quality of life.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This work challenges us to consider mechanistic and classification overlap between pain symptoms and FND and proposes the inclusion of pain-related treatments and outcome measures in clinical trials for patients with FND.

we analysed papers which described FND diagnoses in patients with chronic pain.

## METHODS

We searched the PubMed, Embase and PsycINFO databases for studies published between their start dates (1951, 1947 and 1967, respectively) and 18 February 2023 which described chronic pain in adults with a confirmed diagnosis of FND, and FND in adults with a diagnosis of chronic pain. Our search terms were (pain\* AND (functional neurological disorder OR functional movement/motor disorder OR functional seizures OR psychogenic non-epileptic seizures OR conversion disorder)). We also searched for relevant papers in reference lists and review articles.

We included studies with more than 10 patients which described data relevant to the pain symptoms or diagnoses of adults (aged >18 years) with FND. We included English language studies which used Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Classification of Diseases (ICD) diagnoses equivalent to FND or positive diagnoses of FND. We did not include



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studies which described headache syndromes, such as migraine, or DSM-IV diagnoses of somatisation disorder. Migraine in functional seizures was recently reviewed and we are aware of another review on migraine in FND currently under preparation.<sup>3</sup> In our quantitative analyses, we excluded studies which did not provide raw pain statistics. Two authors (MS and IM) independently screened studies and three assessed full-texts (MS, IM and IH). One author (MS) extracted data from studies using a predefined standardised protocol (online supplemental document 1). Two authors (MS and IM) independently appraised the risk of bias of studies for assessing pain in patients with FND or FND in patients with chronic pain using the Newcastle-Ottawa Scales for case-control and cohort studies (scored out of 9, where 9 is the lowest risk of bias).<sup>4</sup> Disputes of more than 2 points on the scale were resolved by discussion between authors. We averaged scores and classified risk of bias as 'low' (7–9 points), 'moderate' (4–6 points) or 'high' (0–3 points).

We collected data on pain reporting in FND versus other neurological disorders and in FND populations alone, the timing of pain in the FND disease course, comorbid pain diagnoses and the responsiveness of pain symptoms to treatment. We also specifically recorded diagnoses, when present, of CRPS, IBS and fibromyalgia, all of which have pain as a core and required symptom.

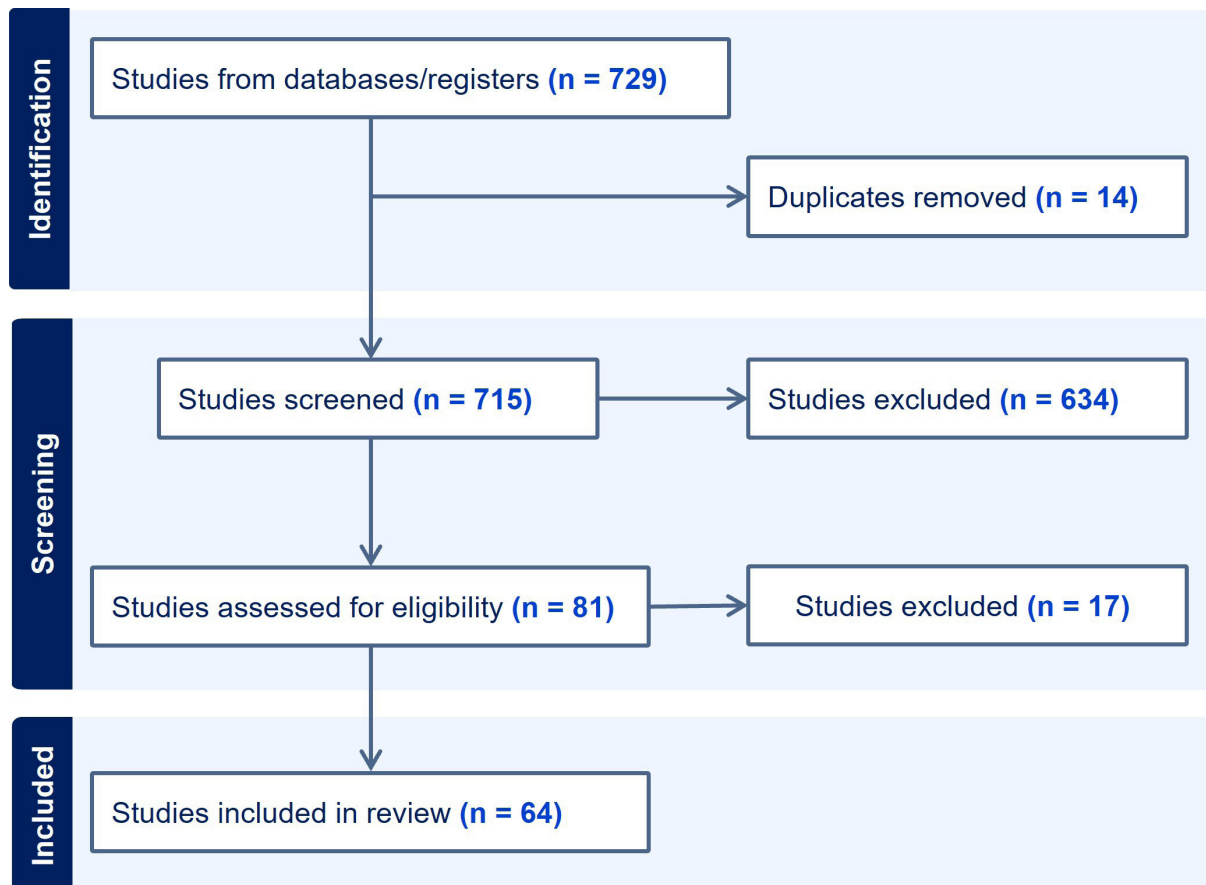
We described studies which compared pain characteristics between functional and other neurological disorders; quantified pain symptoms in subpopulations of FND cohorts and subtypes of FND; measured the timing of pain symptoms; assessed the relationship between pain and prognosis or evaluated pain treatment approaches in FND. We also described studies which

measured FND diagnoses among patients with chronic pain. We used random effects models and 95% CIs to estimate the proportion of patients with FND who describe pain symptoms or are diagnosed with pain-related conditions. We measured heterogeneity in our meta-analyses using  $I^2$  and  $\tau^2$  values and indicate where subgroup analyses were performed, including between patients with different subtypes of FND. We performed these analyses using the meta package (V.4.9–6) in RStudio (RStudio Team, 2022).<sup>5</sup> We pooled studies which provided means and SDs of pain scores described by patients with FND and transformed these to scales ranging from 0 to 10, where 10 was the worst pain. We displayed the results of our analyses using forest and scatter plots. We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in the reporting of our study. This systematic review was preregistered and our protocol described analyses of both FND in pain clinics and pain among patients with FND. After identifying a limited number of papers describing FND in specialist pain settings, most of our results focus on pain symptoms and diagnoses among patients with FND.<sup>6</sup>

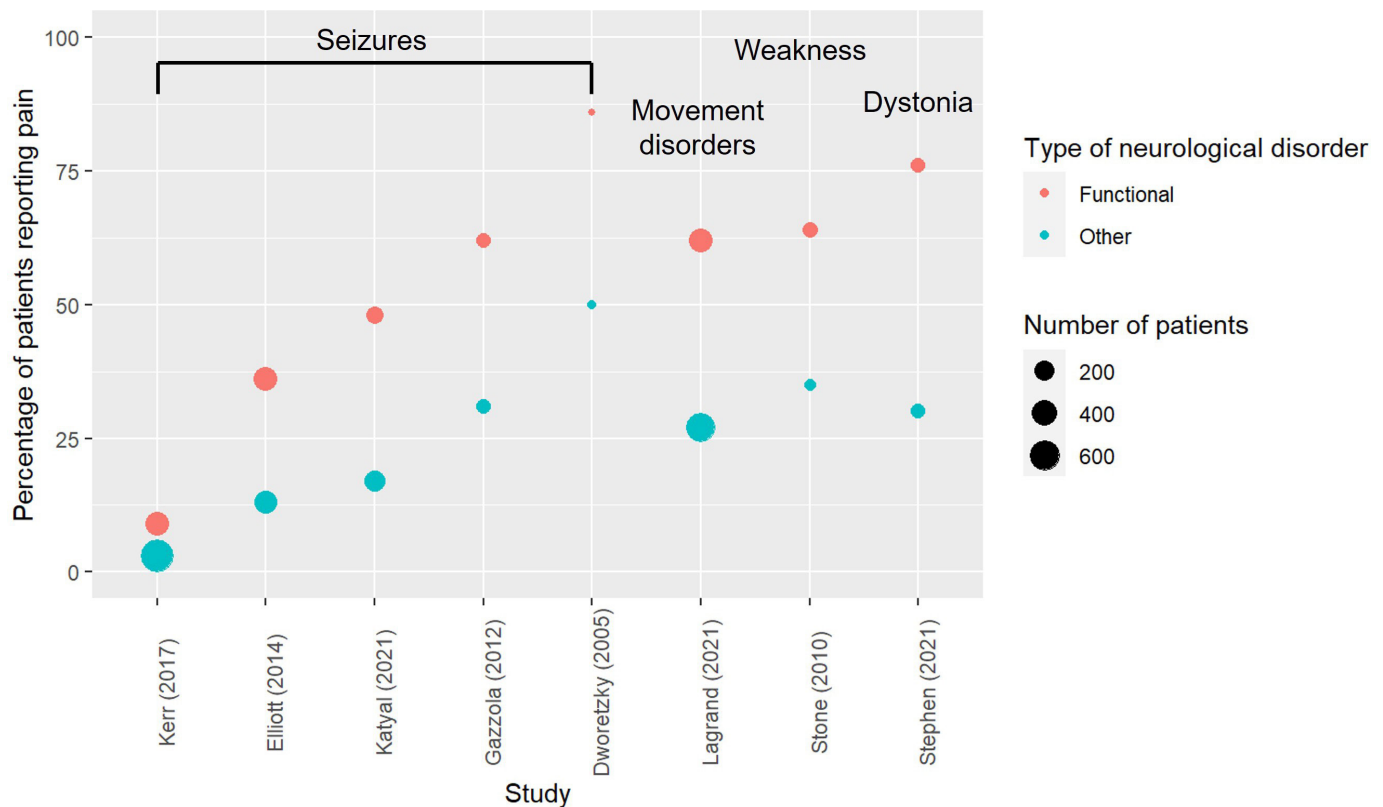
## RESULTS

### Included papers

Our search yielded 715 articles for screening, of which 81 full texts were assessed and 64 were included in the review (figure 1, online supplemental table 1). Papers were predominantly cohort (n=51) or case-control (n=11) studies, with one randomised controlled trial and one randomised feasibility study identified. Thirty studies included  $\geq 100$  patients with FND or chronic pain



**Figure 1** Flow diagram of study selection.



**Figure 2** Proportion of patients with FND reporting chronic pain compared with patients with other neurological conditions. FND, functional neurological disorder.

and 7 studies included  $\geq 300$  patients. Patients were identified from general and specialist neurology services ( $n=59$ ), such as epilepsy monitoring units and movement disorder services, or from specialist pain services ( $n=5$ ).

Fifty-nine studies described the clinical characteristics of patients with FND or specific FND subtypes (primarily seizures and movement disorders). Five studies measured FND diagnoses among patients with chronic pain. Seventeen studies compared pain symptoms among patients with FND to those with other neurological disorders, such as epilepsy, or healthy controls. Ten studies described the timing of pain symptoms in the FND disease course. Eight studies measured the effects of interventions, such as physiotherapy ( $n=4$ ), psychotherapy ( $n=3$ ) or follow-up with a neurologist ( $n=1$ ), on FND symptoms, including pain. Four studies described the use of analgesic medications, including opioids, among patients with FND.

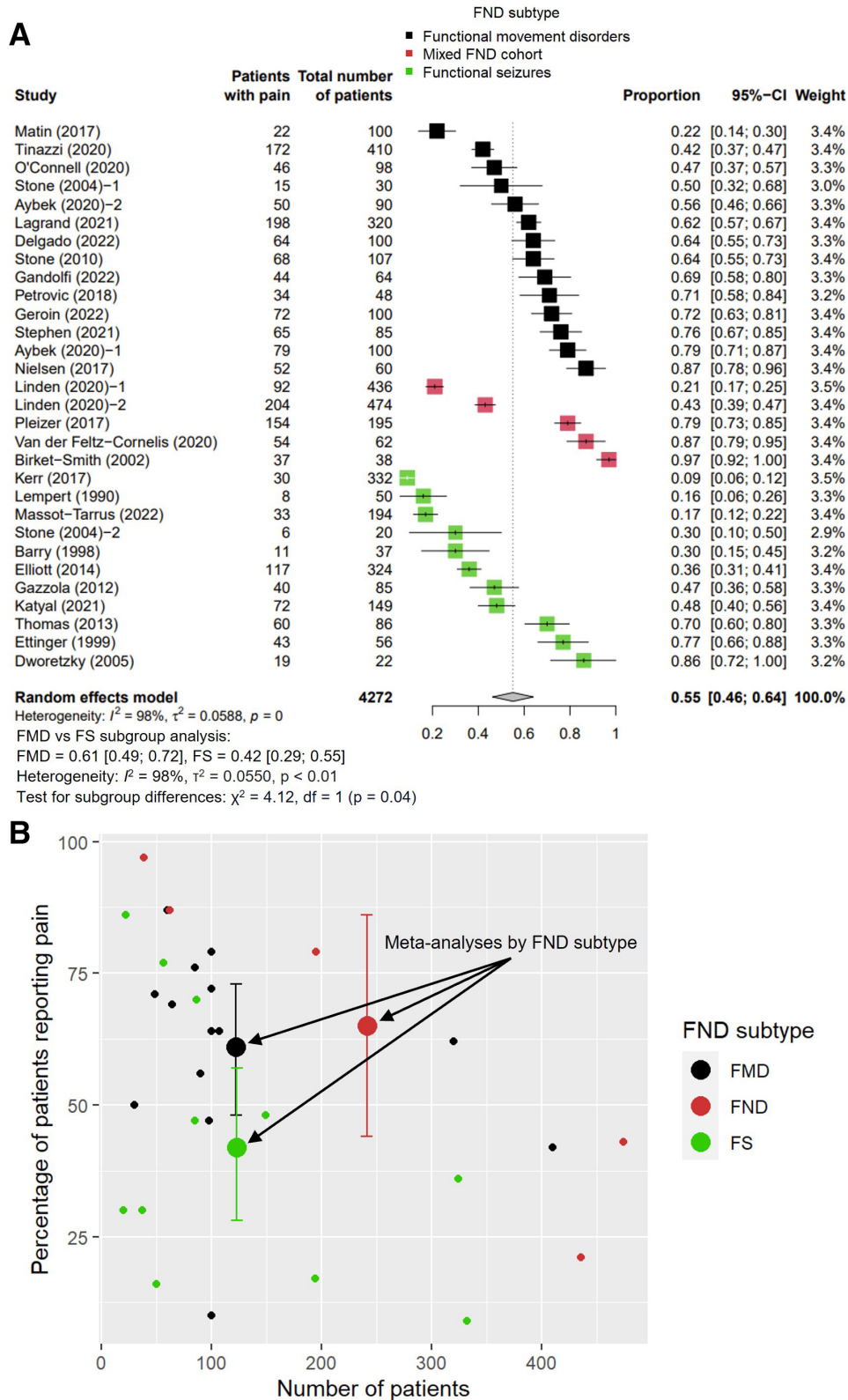
Thirty-three studies were retrospective and 31 were prospective. Twenty studies used formal pain rating scales, including Short Form-36 (SF-36) bodily pain, painDETECT and the Brief Pain Inventory. Fifteen studies quantified comorbid chronic pain diagnoses, such as fibromyalgia ( $n=10$ ), CRPS ( $n=7$ ) and IBS ( $n=6$ ), among patients with FND. Risk of bias assessments identified 29 (45%) studies at low risk of bias, 33 (52%) at moderate risk and two (3%) at high risk.

### Pain in FND compared with other neurological disorders

Seventeen studies compared pain in patients with FND to those with other neurological diagnoses, such as epilepsy and multiple sclerosis (figure 2). Cohort studies suggest that, among patients attending an epilepsy monitoring

unit, chronic pain is more common in patients with functional seizures than epilepsy and can aid in the differential diagnosis.<sup>7–11</sup> One of these studies described chronic pain symptoms in 30/332 (9%) patients with functional seizures, compared with 24/747 (3%) patients with epilepsy.<sup>7</sup> Using this and other clinical data, the authors developed a prospectively validated diagnostic score to differentiate between functional seizures and epilepsy, which placed a high weight on a patient's history of chronic pain as a distinguishing feature (log odds ratio difference=5.1).<sup>7</sup> Chronic pain was also often reported by patients with functional seizures who had comorbid epilepsy (23/84 (27%), 7/53 (13%) and 6/47 (13%)).<sup>7 8 12</sup>

Chronic pain symptoms were also more common in functional than other movement disorders. A 14-year case-control study found lower (worse) SF-36 bodily pain scores among patients with functional limb weakness (median=33/100, IQR=35) compared with controls with other neurological disorders (median=50/100, IQR=24).<sup>13</sup> The same cohort of patients more often reported pain in affected (68/107 (64%)) and unaffected (35/107 (33%)) limbs than controls with weakness due to other neurological conditions (35% and 20%, respectively).<sup>14</sup> Similar results were described in a large cohort study of patients with hyperkinetic functional (197/320 (62%)) and other movement disorders (150/554 (27%)).<sup>15</sup> A case-control study identified lower SF-36 bodily pain scores in 16 patients with functional jerks (median=49/100, IQR=52) than 23 patients with cortical myoclonus (median=80/100, IQR=33).<sup>16</sup> Notably, pain was the only health-related quality of life subdomain which differed between patients with functional jerks and cortical myoclonus.



**Figure 3** Pain reporting among patients with FND. (A) Random effects meta-analysis of the proportion of patients with FND reporting pain. (B) Random effects meta-analyses of the proportions of patients with different FND subtypes reporting pain. Small points represent individual studies. Large points represent subgroup meta-analyses by FND subtype. FMD, functional movement disorder; FND, functional neurological disorder; FS, functional seizures.

**Proportion of patients with FND reporting chronic pain**  
**Meta-analysis of chronic pain among patients with FND**

Fifty-one studies provided data on pain reporting and/or scoring in FND (figure 3A,B, tables 1 and 2). A random effects model of

pain reporting in 30 FND cohorts estimated that 55% (95% CI 46% to 64%) of patients with FND reported pain. This analysis identified significant heterogeneity between studies ( $I^2=98\%$ ,  $\tau^2=0.059$ ), which remained high following subanalysis by FND

**Table 1** Studies describing the proportion of patients with FND reporting pain.

Author (year)	Type(s) of FND	Patients with FND reporting pain	Patients in control/reference group reporting pain	Risk of bias (score on NOS)
Geroin (2022) <sup>67</sup>	FMD	72/100 (72%)	–	Low (7)
Mostile (2022) <sup>22</sup>	FMD	104/188 (55%)	–	Low (7)
Delgado (2022) <sup>68</sup>	FMD	64/100 (64%)	–	Moderate (4)
Massot-Tarrús (2022) <sup>12</sup>	FS	33/194 (17%)	FS and epilepsy=6/47 (13%)	Low (7)
Gray (2021) <sup>37</sup>	FD	29/29 (100%)	–	High (2)
Lagrand (2021) <sup>15</sup>	FMD	197/320 (62%)	Other hyperkinetic movement disorders=150/554 (27%)	Low (7)
Tinazzi (2021) <sup>18</sup>	FMD	FD=18/38 (47%); FW=22/58 (38%); FGD=5/17 (29%); FJ=5/23 (22%); FT=7/40 (18%)	–	Moderate (5)
Stephen (2021) <sup>40</sup>	FD	65/85 (76%)	Other dystonias=24/80 (30%)	Low (7)
Katyal (2021) <sup>10</sup>	FS	72/149 (48%)	Epilepsy=38/230 (17%)	Low (8)
O'Connell (2020) <sup>69</sup>	mFND	46/98 (47%)	–	Low (7)
Aybek (2020) <sup>70</sup>	FMD	UK=79/100 (79%); Canada=50/90 (56%)	–	Moderate (4)
Stone (2020) <sup>38</sup>	FW	Chronic back pain=43/107 (40%)	Patients with other neurological disease and healthy controls=14/85 (16%)	Moderate (6)
Linden (2020) <sup>27</sup>	FND	First World War soldiers=91/436 (21%); male civilians=47/153 (31%); female civilians=156/321 (49%)	–	Moderate (6)
Tomčić (2020) <sup>71</sup>	FMD	Affected body part=67/100 (67%); unaffected body part=50/100 (50%)	–	Low (8)
Tinazzi (2020) <sup>17</sup>	FMD	172/410 (42%)	–	Low (8)
Jimenez (2019) <sup>52</sup>	FND	Back=26/49 (53%); neck=15/49 (31%); joint=9/49 (19%); neuropathic=8/49 (16%); myofascial=6/49 (12%); abdominal=6/49 (12%)	–	Moderate (4)
Petrović (2018) <sup>20</sup>	FD	34/48 (71%)	–	Moderate (6)
Kerr (2017) <sup>7</sup>	FS	30/332 (9%)	FS and epilepsy=7/53 (13%); epilepsy=25/750 (3%)	Low (8)
Erba (2017) <sup>72</sup>	FS	Physical pain after seizure=10/17 (59%)	Epilepsy=1/11 (9%)	Moderate (6)
Matin (2017) <sup>73</sup>	FMD	22/100 (22%)	–	Low (8)
Perez (2016) <sup>74</sup>	FND	15/49 (31%)	–	Low (8)
Elliott (2014) <sup>8</sup>	FS	117/324 (36%)	FS and epilepsy=23/84 (27%); epilepsy=35/281 (13%)	Low (8)
Thomas (2013) <sup>26</sup>	FS	60/86 (70%)	–	Moderate (4)
Gazzola (2012) <sup>11</sup>	FS	40/85 (47%)	Idiopathic generalised epilepsy=10/85 (12%)	Moderate (6)
Ibrahim (2009) <sup>75</sup>	FD	3/35 (9%)	–	Moderate (5)
Dworetzky (2005) <sup>9</sup>	FS	19/22 (86%)	Epilepsy=13/26 (50%)	Moderate (6)
Schrag (2004) <sup>21</sup>	FD	38/41 (93%)	–	Moderate (5)
Stone (2004) <sup>24</sup>	FMS; FS	FMS=15/30 (50%); FS=6/20 (30%)	–	Moderate (6)
Birket-Smith (2002) <sup>76</sup>	FND	37/38 (97%)	–	Moderate (6)
Ettinger (1999) <sup>23</sup>	FS	43/56 (77%)	–	Moderate (4)
Barry (1998) <sup>77</sup>	FS	11/37 (30%)	–	Moderate (5)
Lempert (1990) <sup>78</sup>	FS	8/50 (16%)	–	Moderate (6)

FD, functional dystonia; FGD, functional gait disorder; FJ, functional jerks; FMD, functional movement disorder; FMS, functional movement symptoms; FND, functional neurological disorder; FS, functional seizures; FT, functional tremor; FW, functional weakness; mFND, motor FND; NOS, Newcastle-Ottawa Scale.

subtype (functional movement disorders=61% (95% CI 49% to 72%),  $I^2=97%$ ; functional seizures=42% (95% CI 29% to 55%),  $I^2=98%$ ).

In the two largest functional movement disorder cohorts, pain was reported by 172/410 (42%) and 197/320 (62%) patients.<sup>15 17</sup> In the largest study of patients with functional limb weakness, common distributions included back pain (38/107 (36%)), muscle pain (30/107 (28%)), joint pain (29/107 (27%)) and neck pain (20/107 (19%)).<sup>14</sup>

The prevalence and severity of pain symptoms and disorders are similar in most functional movement disorder subtypes, but chronic pain may be particularly common in patients with

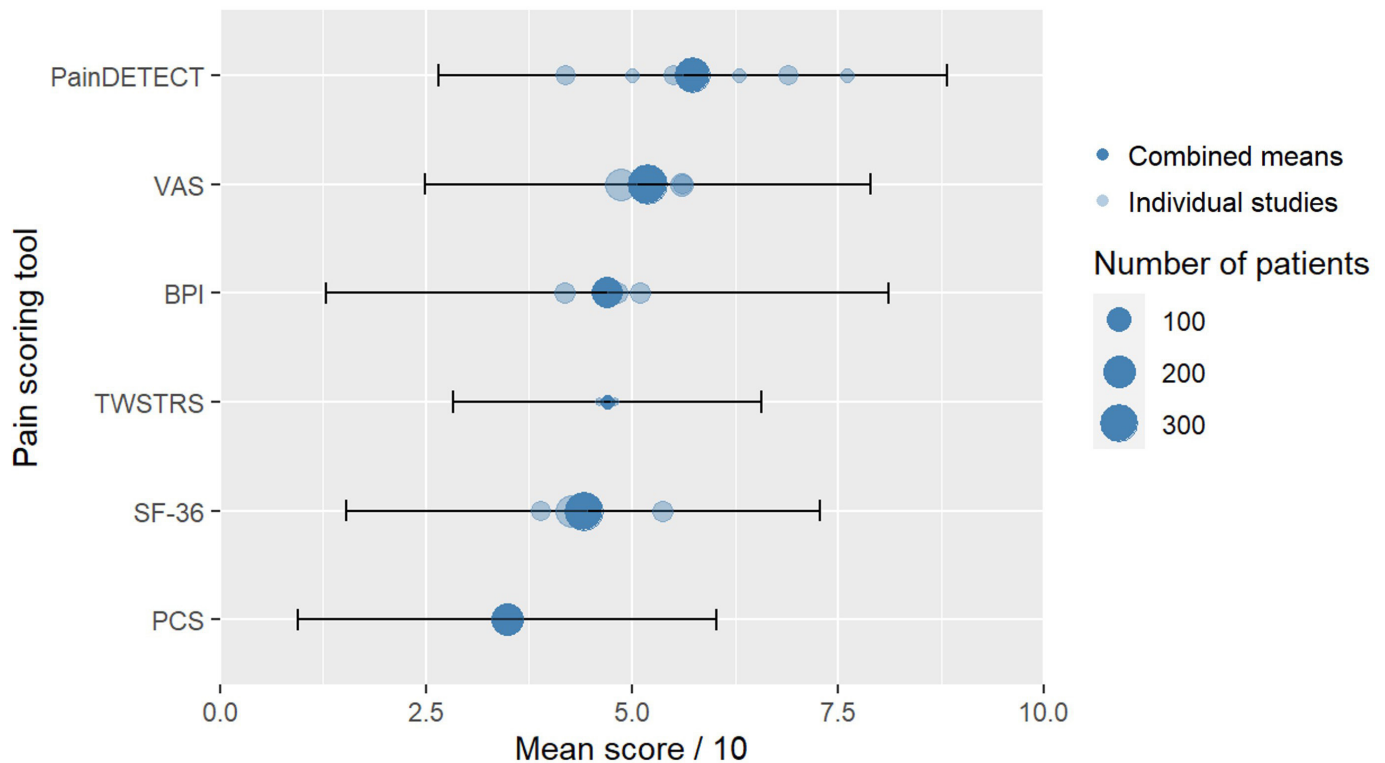
functional dystonia (18/38 (47%) and 10/23 (44%)).<sup>18–20</sup> In the largest prospective fixed dystonia cohort, 26/41 (63%) patients described painful spasms.<sup>21</sup> A phenotype analysis of 48 patients with functional dystonia found that pain symptoms and fixed dystonia diagnoses clustered together.<sup>20</sup> A similar analysis of 188 patients with functional movement disorders did not reproduce this finding.<sup>22</sup>

Patients with functional movement disorders who experience additional FND symptoms, such as functional seizures or sensory and visual symptoms, may be more likely to report pain. In the largest study of this type, 104/188 (55%) patients with combined functional movement disorders described pain

**Table 2** Studies describing pain scoring among patients with FND.

Author (year)	Type(s) of FND	Patients with FND reporting/scoring pain	Patients in reference/control group reporting/scoring pain	Risk of bias (score on NOS)
Gelauff (2020) <sup>19</sup>	FMD	Proportion reporting pain=46/179 (26%) Median SF-36 (lower=worse) pain=46/100 (IQR=22–80)	–	Moderate (6)
Pleizier (2017) <sup>28</sup>	FNS	Proportion reporting pain=154/195 (79%) Mean SF-36 (lower=worse) pain=42.6/100 (SD=29.0); mean VAS pain=48.6/100 (SD=25.1); mean PCS=18.1/52 (SD=13.2)	–	Low (8)
Nielsen (2017) <sup>29</sup>	FMS	Proportion reporting slight to moderate pain=24/60 (40%); severe to extreme=28/60 (47%) Mean SF-36 (lower=worse) pain=38.9/100 (SD=30.2)	–	Low (8)
Stone (2010) <sup>14</sup>	FW	Proportion reporting pain (other than affected limb)=68/107 (64%); back=39/107 (36%); affected limb=35/107 (33%); muscle=30/107 (28%); joint=29/107 (27%); neck=20/107 (19%) Median SF-36 (lower=worse) pain=33/100 (IQR=22–44)	Other neurological weakness: other than affected limb=16/46 (35%); back=8/46 (17%); affected limb=9/46 (20%); muscle=6/46 (13%); joint=4/46 (9%); neck=1/46 (2%)	Moderate (6)
Reuber (2007) <sup>30</sup>	FNS	Proportion reporting pain=19/91 (>20%) Mean SF-36 (lower=worse) pain=5.9/11 (SD=2.7)	–	Moderate (6)
Gandolfi (2022) <sup>35</sup>	FMD	Proportion reporting pain=44/64 (69%) Mean BPI=19.3/40 (SD=13.5) intensity; 29.3/70 (SD=24.4) interference	–	Moderate (6)
Gandolfi (2021) <sup>36</sup>	FMD	Proportion reporting pain=26/33 (79%) Mean BPI=19.21/40 (SD=11.92) intensity; 33.58/70 (SD=24.89) interference	–	Low (7)
Van der Feltz-Cornelis (2020) <sup>34</sup>	FND	Proportion reporting pain=54/62 (87%) Patients with BPI≥3 ('pain of clinical significance') = 52/62 (84%)	–	Moderate (6)
Serranová (2019) <sup>79</sup>	FMD	Proportion reporting lower limb pain=56/90 (62%) Mean VAS pain in past 4 weeks=5.6/10 (SD=3)	Healthy controls=9/76 (12%)	Low (7)
Sandri (2022) <sup>80</sup>	FMD	Proportion reporting moderate or severe pain=18/60 (30%) Mean pain score=2.81/5 (SD=1.37)	–	Moderate (5)
Gelauff (2019) <sup>13</sup>	FMD	Median SF-36 (lower=worse) pain (107 patients): Baseline=33/100 (IQR=35) Follow-up (mean 14 years)=20/100 (IQR=20)	Median SF-36 (lower=worse) pain (neurological controls): Baseline (38 patients)=50/100 (IQR=24) Follow-up (23 patients)=20/100 (IQR=20)	Low (8)
Gelauff (2018) <sup>81</sup>	FMD	Median SF-36 (lower=worse) pain (181 patients)=46/100 (IQR=57)	–	Moderate (5)
Zutt (2017) <sup>16</sup>	FJ	Median SF-36 (lower=worse) pain (16 patients)=49/100 (IQR=52)	Median SF-36 (lower=worse) pain (23 patients with cortical myoclonus)=80/100 (IQR=33)	Moderate (6)
Kuyk (2008) <sup>31</sup>	FS	Mean SF-36 (lower=worse) pain (22 patients)=58.5/100	–	Moderate (6)
Teodoro (2022) <sup>82</sup>	FCD	Median PainDETECT (19 patients)=6/38 (IQR=2–11)	Median PainDETECT (23 healthy controls)=1/38 (IQR=0–5)	Moderate (6)
Forejtová (2022) <sup>83</sup>	mFND	Median PainDETECT (152 patients)=~6/10 (IQR=~4–8)	–	Low (8)
Hanzlíková (2019) <sup>32</sup>	FMD	Mean pain scores (22 patients): Current=5.0/10 (SD=2.9); average=6.3/10 (SD=2.4); maximal=7.6/10 (SD=2.4)	Mean pain scores (22 healthy controls): Current=0.1/10 (SD=0.3); average=1.9/10 (SD=2.0); maximal=1.0/10 (SD=1.1)	Low (7)
Věchetová (2018) <sup>33</sup>	FMD	Mean pain scores (61 patients): Current=4.2/10 (SD=3); average=5.5/10 (SD=3); maximal=6.9/10 (SD=3)	Mean pain scores (61 healthy controls): Current=0.9/10 (SD=1); average=1.4/10 (SD=2); maximal=2.7/10 (SD=3)	Low (8)
Morgante (2018) <sup>84</sup>	FD	Mean pain scores (12 patients): Severity=4.8/10 (SD=2.0); duration=3 years (SD=1.3); disability=2.3/5 (SD=0.9)	Mean pain scores (10 patients with idiopathic cervical dystonia): Severity=7.2/10 (SD=3.3); duration=3.9 years (SD=2.9 years); disability=2.6/5 (SD=1.6)	Low (7)

BPI, Brief Pain Inventory; FD, functional dystonia; FJ, functional jerks; FMD, functional movement disorder; FMS, functional movement symptoms; FND, functional neurological disorder; FNS, functional neurological symptoms; FS, functional seizures; FW, functional weakness; mFND, motor FND; NOS, Newcastle-Ottawa Scale; PCS, Pain Catastrophising Scale; SF-36, 36-Item Short Form Survey; VAS, Visual Analogue Scale.



**Figure 4** Pain scoring by patients with FND. Pain scores were transformed to 0–10 (10=worst). All studies using the SF-36 specifically reported pain subdomain scores. Error bars denote combined SD across studies. BPI, Brief Pain Inventory; FND, functional neurological disorder; PCS, Pain Catastrophising Scale; SF-36, 36 Item Short Form Survey; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale; VAS, Visual Analogue Scale.

symptoms, compared with 68/222 (31%) patients with an isolated disorder.<sup>17</sup>

The two largest studies of patients with functional seizures described pain in 30/332 (9%) and 117/324 (36%) patients.<sup>7,8</sup> Smaller studies described a wide variation (33/194 (17%) to 19/22 (86%)).<sup>9,12</sup> One study described the range of pain symptoms experienced by patients with functional seizures, including ‘multiple sites and symptoms’ (29/56 (52%)), back pain (15/56 (27%)), neck pain (13/56 (23%)) and ‘other pain’ (11/56 (20%)).<sup>23</sup>

Two studies identified comparable reporting of pain or a chronic pain disorder in patients with functional movement disorders (pain, n=15/30 (50%), pain disorder, n=11/38 (29%)) and functional seizures (pain, n=6/20 (30%); pain disorder, n=9/51 (18%)).<sup>24,25</sup>

Female patients with FND may be more likely to report pain symptoms than males. This was found in a cohort of patients with functional seizures (pain in females, n=50/59 (85%); males, n=10/27 (37%)) and a study of functional disorders among civilians following the First World War (pain in females, n=156/321 (49%); males, n=47/153 (31%)).<sup>26,27</sup> Two phenotype analyses also found that pain symptoms were more likely to be reported by clusters which had a younger onset of FND.<sup>20,22</sup> Together, these studies indicate that patients with FND, including functional movement disorders and seizures, often report pain symptoms.

### Pain rating in FND

Twenty studies used a pain scoring tool to describe pain symptoms among patients with FND at baseline and/or at follow-up (figure 4). Follow-up studies included routine review and patients

undergoing specified management, such as psychotherapy or physiotherapy.

Four studies reported mean SF-36 bodily pain scores ranging from 39–59/100, where lower scores denote more significant symptoms.<sup>28–31</sup> The longest follow-up study of patients with functional weakness identified worsening SF-36 pain scores (median=33/100 (IQR=35) to 20/100 (IQR=20)) over a period of 14 years.<sup>13</sup> On the painDETECT scale, patients in two studies reported mean current pain of 4.2–5.0/10 (SD=3), mean average pain of 5.5–6.3/10 (SD=2.7) and mean maximal pain of 6.9–7.6/10 (SD=2.7).<sup>32,33</sup>

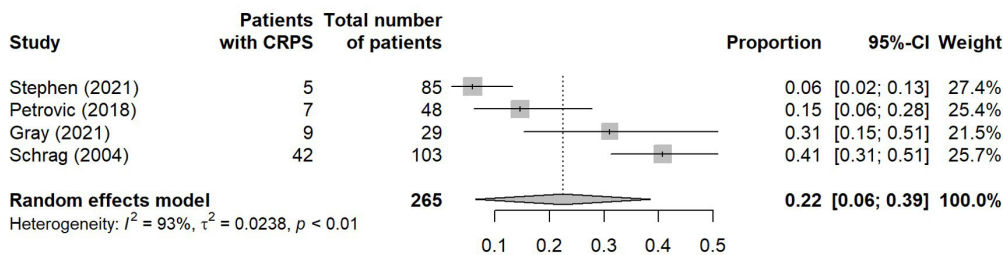
Three studies measured pain intensity and interference using the Brief Pain Inventory. In one cohort, 52/62 (87%) patients with FND reported a mean Brief Pain Inventory score of  $\geq 3/10$  across all sections, which denotes ‘pain of clinical significance’.<sup>34</sup> In 64 patients with functional movement disorders, mean pain intensity values were 18–21/40 (SD=13) and mean pain interference scores ranged from 27–31/70 (SD=25).<sup>35,36</sup>

### Comorbid CRPS, IBS and fibromyalgia in FND Meta-analyses of comorbid pain-related diagnoses in FND

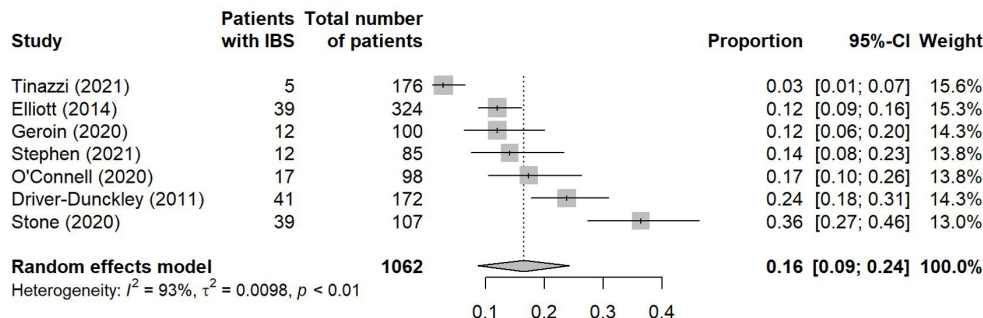
Fifteen studies reported data on comorbid pain-related diagnoses among patients with FND, most commonly CRPS, IBS and fibromyalgia (figure 5). Random effects models of CRPS, IBS and fibromyalgia diagnoses estimated prevalences of 22% (95% CI 6% to 39%), 16% (95% CI 9% to 24%) and 10% (95% CI 8% to 13%), respectively. These analyses identified significant heterogeneity between studies (CRPS:  $I^2=93\%$ ,  $\tau^2=0.0238$ ; IBS:  $I^2=93\%$ ,  $\tau^2=0.0098$ ; fibromyalgia:  $I^2=50\%$ ,  $\tau^2=0.0007$ ).

CRPS was most common among patients with fixed dystonia (42/103 (41%)) and patients referred to orthopaedic surgery for

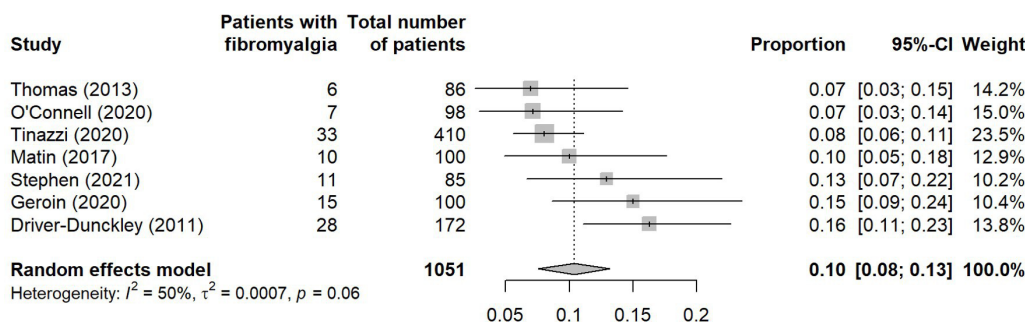
## Complex regional pain syndrome



## Irritable bowel syndrome



## Fibromyalgia



**Figure 5** Meta-analyses of comorbid complex regional pain syndrome (CRPS), irritable bowel syndrome (IBS) and fibromyalgia diagnoses among patients with FND. Error bars denote 95% CIs. FND, functional neurological disorder.

functional dystonia of the foot or ankle (9/29 (31%)).<sup>21 37</sup> IBS diagnoses ranged from 40/324 (12%) to 40/116 (35%) patients with functional seizures and from 6/176 (3%) to 39/107 (36%) patients with functional movement disorders.<sup>8 18 38 39</sup> Fibromyalgia diagnoses varied from 7/176 (4%) patients in one functional movement disorder cohort to 21/116 (18%) patients in a group with functional seizures.<sup>18 39</sup> In one study, patients with functional seizures reported more than one pain diagnosis (35/116 (31%)) more often than patients with functional movement disorders (1/56 (2%)).<sup>39</sup> Other studies found that CRPS, IBS and fibromyalgia were more common among patients with FND than either healthy controls or patients with other neurological disorders.<sup>8 38 40 41</sup>

## Timing of pain symptoms in FND

Ten studies described pain as a symptom identified prior to the diagnosis of FND or as a primary cause of a patient's acute presentation.

Pain is a common reason for emergency presentations among patients with FND. In one study, 5/42 (12%) patients who presented to the emergency department and were subsequently

diagnosed with FND had initially described pain as their primary complaint.<sup>42</sup> Another study found that patients with functional seizures were more likely to present to the emergency department for pain-related symptoms (10/28 (36%)) than those with epilepsy (4/31 (13%)).<sup>43</sup> In the same cohort, on average, patients with functional seizures presented to the emergency department for pain-related symptoms 2.5 and 2.4 times in the 3 years pre- and post-diagnosis, respectively.

Pain is also reported by patients in non-emergency settings prior to the diagnosis of FND. In a large study of the onset of functional movement disorders, 43/107 (40%) patients with functional limb weakness reported chronic back pain prior to diagnosis, compared with 14/85 (18%) patients with limb weakness attributed to another neurological disorder and healthy individuals.<sup>38</sup> Pain can also precipitate episodes of functional motor symptoms, with reports ranging from 4/50 (8%) to 46/179 (26%) patients in two cohort studies.<sup>19 44</sup>

Pain reporting may remain unchanged before and after a diagnosis of FND. A national registry study of functional seizures identified 'rheumatism-related pain' in 19/455 (4%) and 26/472 (6%) patients before and after diagnosis, respectively.<sup>45</sup>



Together, these findings suggest that pain is common prior to and following the diagnosis of FND, and in both emergency and non-emergency settings.

### Role of pain in FND prognosis

Ten studies assessed the role of pain or pain diagnoses in the prognosis of patients with FND. In a 14-year case-control study of patients with functional limb weakness, individuals reporting pain at baseline were less likely to show functional improvement at follow-up and pain correlated with weakness severity.<sup>13</sup> In a study of 16 patients admitted to a psychotherapeutic unit with functional seizures, those who were seizure-free 6 months following admission also reported less significant pain symptoms.<sup>31</sup> Similarly, among 56 patients with functional seizures who were receiving care from a psychotherapist or psychiatrist, those episode-free at follow-up were less likely to report moderate or severe pain.<sup>23</sup>

In a study of 81 patients with FND, those with a chronic pain disorder were less likely to show overall clinical improvement at 7-month follow-up (12% improved compared with 34% without a pain diagnosis).<sup>25</sup> A cluster analysis of 48 patients with functional dystonia found that patients who were more likely to experience progressive deterioration also more often had a CRPS diagnosis or described prominent pain.<sup>20</sup>

### FND among patients with chronic pain

Only five studies described FND diagnoses among patients attending specialist chronic pain services. Studies from the 1980s described 'conversion disorder' in 1/43 (2%), 108/283 (38%) and 15/35 (43%) patients with chronic pain.<sup>46-48</sup> Non-dermatomal sensory abnormalities, which are FND-related sensory disturbances, were also common among patients attending chronic pain services (74/283 (26%) and 100/247 (40%)).<sup>49 50</sup>

### Pain treatment approaches in FND

Eleven studies described treatment approaches, such as analgesic medications and rehabilitative therapy, which could potentially improve pain symptoms in patients with FND (table 3). Patients with functional seizures were commonly prescribed opiates/opioids (12/85 (14%) and 55/170 (32%)), as were patients with functional dystonia (25/85 (29%)) and a mixed FND cohort (12/64 (19%)).<sup>11 34 40 51</sup>

Other treatment paradigms included physiotherapy, psychotherapy and an interdisciplinary chronic pain rehabilitation programme. Patients with functional movement disorders (n=64) who received home-based physical exercises from a physiotherapist did not show improvements in the Brief Pain Inventory compared with those in the self-management group.<sup>35</sup> A randomised feasibility study of physiotherapy for patients with functional motor disorders (n=57) found no significant changes in SF-36 bodily pain, despite improvements in physical and social function.<sup>29</sup> Likewise, a pilot study of tailored psychotherapy for 63 patients with functional neurological symptoms identified global improvements in the SF-36 but not in bodily pain.<sup>30</sup> Two further rehabilitation programmes focusing on psychotherapy, symptom exploration and patient education in patients with FND (n=26) and functional motor disorders (n=33) did not find changes in Brief Pain Inventory scores.<sup>34 36</sup>

A randomised trial comparing two follow-up appointments with a neurologist after FND diagnosis (n=195) to immediate referral to a general practitioner identified global improvements in several pain measures at 12 months but these did not differ between the intervention groups.<sup>28</sup> Finally, one uncontrolled

cohort study of 49 patients with FND and comorbid pain described improvements on the Pain Disability Index following enrolment in an outpatient interdisciplinary chronic pain rehabilitation programme for 3-4 weeks (mean=46/70 to 21/70).<sup>52</sup> Improvements in scores relating to depression, anxiety and stress were also found. This programme consisted of medication management, psychotherapy, education, biofeedback techniques and physical therapy.

Overall, pain medication use, including opioids, is common among patients with FND and treatment paradigms, such as psychotherapy and physiotherapy, often do not alleviate pain symptoms, despite improvements in social and physical function. Conversely, interdisciplinary pain management programmes may be effective for pain symptoms among patients with FND.

### DISCUSSION

In this systematic review and meta-analysis, we found that patients with FND commonly describe chronic pain symptoms which contribute to their acute and chronic presentations and can be associated with comorbid pain-related diagnoses, in particular CRPS, IBS and fibromyalgia. In addition, pain appears to have prognostic relevance and be resistant to several treatment approaches in FND, even when patients report improvements in other symptoms.

Some of these results, such as the overlap of CRPS and functional movement disorders, were expected. The motor and sensory features of CRPS, such as weakness, dystonia, tremor and numbness, which form part of the diagnosis in many patients, are indistinguishable from those seen in FND without pain.<sup>1</sup> However, CRPS overlap data make up only a small proportion of the 4272 patients included in our meta-analysis and comorbid pain is common across all subtypes of FND. This makes pain at least as common as risk factors for developing FND, such as childhood maltreatment, and comorbidity with other neurological disorders.<sup>53 54</sup>

This review brings focus to important questions on the overlap of FND and pain, which are currently separated in classification frameworks. First, further work is required to better understand the mechanisms which drive chronic pain symptoms in FND. Both nociplastic pain and FND can be modelled from Bayesian perspectives which link aberrant predictive processing with emotional regulation, allostasis and interoception.<sup>2 55-57</sup> Key risk factors are shared between FND and chronic pain, including adverse childhood experiences, gender and physical triggering events.<sup>2 55</sup> There are also commonalities in their neural correlates, including salience, multimodal integration and attention networks, which together are involved in the overall perception of self.<sup>58 59</sup> This mechanistic overlap raises questions relating to whether pain should be included in the diagnostic criteria for FND and the extent to which nociplastic pain can be considered a functional sensory symptom. Maggio *et al* recently proposed an amendment to the DSM-5 criteria which would allow clinicians to add a 'pain specifier' to an FND diagnosis.<sup>60</sup> Similarly, although ICD-11 improves on ICD-10 in the classification of primary pain disorders and aids in the classification of pain in CRPS, IBS and fibromyalgia, there is still no overt link with nociplastic pain in patients with FND. Improving the ability of classification criteria to handle pain symptoms in FND would improve research studies, especially those relating to treatment, and help assess how FND symptoms map onto our current models of nociplastic, nociceptive and neuropathic pain. Integrating pain into the diagnosis

**Table 3** Studies describing the prognostic relationship between pain and FND, and pain-related treatment paradigms for FND.

Author (year)	Treatment paradigm / follow-up	Pain measurement	Risk of bias (score on NOS)
Gelauff (2019) <sup>13</sup>	Follow-up	Median SF-36 bodily pain (107 patients with FMD): Baseline=33/100 (IQR=35) Follow-up (mean 14 years)=20/100 (IQR=20)	Low (8)
Jennum (2019) <sup>45</sup>	Follow-up	Rheumatism-related pain in patients with FS: In 3 years prediagnosis=19/455 (4%) In 3 years postdiagnosis=26/472 (6%)	Low (8)
Pleizier (2017) <sup>28</sup>	Follow-up with neurologist vs GP	Pain scores at 12 months in immediate GP management group (100 patients with FNS): Mean VAS pain=42.22/100 (SD=26.56); mean PCS=13.61/52 (SD=12.86); mean SF-36 bodily pain=50.14/100 (SD=25.40) Pain scores at 12 months in initial neurologist management group (95 patients with FNS): Mean VAS pain 48.17/100 (SD=25.98); mean PCS=14.81/52 (SD=12.51); mean SF-36 bodily pain=49.55/100 (SD=27.64)	Low (8)
Stephen (2021) <sup>40</sup>	Pain medication	Opiate/opioid use in patients with FD=25/85 (29%)	Low (7)
Gazzola (2012) <sup>11</sup>	Pain medication	Prescription pain medication use in patients with FS=20/85 (24%); opiates=12/85 (14%)	Moderate (6)
Hantke (2007) <sup>51</sup>	Pain medication	Analgesic use in patients with FS=79/170 (47%); 'narcotic analgesics'=55/170 (32%)	Low (8)
Gandolfi (2022) <sup>35</sup>	Physiotherapy	Mean BPI in telemedicine group (32 patients with FMD): Before 5-day programme=20.69/40 (SD=14.8) intensity; 31.13/70 (SD=24.21) interference After 12-week telemedicine programme=15.44/40 (SD=13.30) intensity; 20.84/70 (SD=20.76) interference Mean BPI in self-management group (32 patients with FMD): Before 5-day programme=17.91/40 (SD=12.04) intensity; 27.47/70 (SD=24.82) interference After 12-week self-management programme=18.63/40 (SD=13.11) intensity; 27.88/70 (SD=24.57) interference	Moderate (6)
Gray (2021) <sup>37</sup>	Physiotherapy	Patients with FD receiving physiotherapy without improvement in pain=22/29 (76%) Patients with FD and worsening pain following surgery=6/12 (50%)	High (2)
Nielsen (2017) <sup>29</sup>	Physiotherapy	Mean SF-36 bodily pain in intervention group (30 patients with FMS): Baseline=45.6/100 (SD=33.5) At 6 months=47.4/100 (SD=33.1) Mean SF-36 bodily pain in control group (30 patients with FMS): Baseline=32.1/100 (SD=25.3) At 6 months=33.9/100 (SD=27.4)	Low (8)
Van der Feltz-Cornelis (2020) <sup>34</sup>	Psychotherapy	38 patients with FND who completed treatment and BPI: Mean BPI at baseline=5.68/10 (SD=2.60); post-treatment=5.58/10 (SD=2.51) Patients with pain medication use (except opiates) = 24/64 (38%); opiates=12/64 (19%)	Moderate (6)
Reuber (2007) <sup>30</sup>	Psychotherapy	63 patients with FNS: Mean SF-36 bodily pain pretherapy=5.9/11 (SD=2.7); post-therapy=6.0/11 (SD=2.8)	Moderate (6)
Gandolfi (2021) <sup>36</sup>	Psychotherapy and physiotherapy	Mean BPI of 33 patients with FMD: On admission=19.21/40 (SD=11.92) intensity; 33.58/70 (SD=24.89) interference At 5 day discharge=17.61/40 (SD=11.89) intensity; 27.70/70 (SD=24.16) interference At 3-month follow-up=20.15/40 (SD=12.01) intensity; 33.61/70 (SD=23.16) interference	Low (7)
Jimenez (2019) <sup>52</sup>	Multidisciplinary pain programme	Mean PDI of 49 patients with FND: preintervention=46.4/70; postintervention=20.9/70	Moderate (4)

BPI, Brief Pain Inventory; FD, functional dystonia; FMD, functional movement disorder; FMS, functional movement symptoms; FND, functional neurological disorder; FNS, functional neurological symptoms; FS, functional seizures; GP, general practitioner; NOS, Newcastle-Ottawa Scale; PCS, Pain Catastrophising Scale; PDI, Pain Disability Index; SF-36, 36-Item Short Form Survey; VAS, Visual Analogue Scale.

and management of FND may help reconcile contrasting and dualistic viewpoints on the distinction between nociplastic pain and FND which fail to recognise overlapping risk factors and mechanisms.<sup>61–63</sup>

It is important that effective pharmacological and non-pharmacological pain treatment approaches are identified for patients with FND. Clinical trials for people with FND could include treatments and outcomes focused on pain and other comorbidities, rather than focusing entirely on conventional FND symptoms. This could also involve validation of pain scoring tools in order to standardise their use. In particular, further evidence is needed to establish the effectiveness of specialised interdisciplinary pain programmes for patients with FND.

More generally, there is a lack of high-quality literature on the role of multidisciplinary care for patients with pain

and FND. In addition to studies which described the pain characteristics of patients with FND, we identified a small number of papers from 1986 to 2003 which quantified diagnoses of FND and non-dermatomal sensory abnormalities in specialised pain clinics.<sup>46–50</sup> A recent study from our own group, which was published after our search was conducted, described FND diagnoses in 17% of 190 patients attending a regional chronic pain service and undiagnosed neurological symptoms in a further 6%.<sup>64</sup> In addition, patients with comorbid FND were more likely to have a chronic primary pain disorder, such as fibromyalgia. These data suggest there is a significant overlap between the FND and chronic pain populations and indicate a potential role for the integration of pain management techniques and services in the treatment of certain patients with FND.

## Limitations

There are both limitations in the evidence base and our own methodology. Most included studies described relatively small single-centre cohort studies which retrospectively identified consecutive patients diagnosed with FND and analysed their clinical characteristics using data from health records. These studies were generally at moderate or low risk of bias, but for symptoms such as pain, data from health records are limited by the completeness of clinicians' history-taking and documentation and are subject to reporting biases. These limitations are partially addressed by our inclusion of case-control studies which compared pain symptoms reported by patients with FND and those with other neurological disorders, and our analysis of pain scoring tools. We also included studies published over a long time period and the diagnostic criteria for FND have changed over time.<sup>65 66</sup> These factors will have contributed to the heterogeneity we identified in the reporting of pain symptoms and diagnoses. Most interventional studies we identified were unrandomised and uncontrolled, and therefore, do not provide robust evidence on the effectiveness of specific pain treatments in FND. In terms of our methodology, searching specifically for studies reporting pain symptoms and diagnoses among patients with FND may have introduced selection and publication biases. This may have overestimated the prevalence of pain symptoms or diagnoses among patients with FND or selected for studies reporting an association between pain and the diagnosis or prognosis of FND.

## CONCLUSION

Chronic pain is a common comorbidity in FND. It is likely at least as common as aetiological risk factors, such as childhood maltreatment. Chronic pain is also likely more common in patients with FND than those with other neurological disorders and comorbid pain-related diagnoses are prevalent. Pain needs to be more integrated into the classification, assessment and treatment of people with FND.

## DATA AVAILABILITY STATEMENT

We have shared the items included in our data extraction tool. We have provided the raw data (online supplemental table 2) and code (online supplemental document 2) we used to conduct the meta-analyses and produce the figures as online supplemental material. The data extracted from included studies are summarised in [tables 1 and 2](#) and online supplemental table 1.

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