NULL HYPOTHESIS CLASS OF EVIDENCE

Internet-based self-help randomized trial for motor functional neurologic disorder (SHIFT)

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Neurology® 2020;95:e1883-e1896. doi:10.1212/WNL.0000000000010381

Abstract

Objective

To determine whether self-rated health of patients with motor functional neurologic disorder (FND) can be improved by unguided Internet-based self-help and education.

Methods

In this nonblinded randomized controlled trial, patients were allocated 1:1 unbiased to an unguided education and self-help website in addition to usual care or usual care only. Patients over 17 years of age with a functional motor symptom that caused distress or disability were included. The primary outcome was self-rated health on the Clinical Global Improvement scale at 3 and 6 months. Secondary outcomes were severity of motor symptoms, other physical and psychiatric symptoms, physical functioning, quality of life, work and social adjustment, illness beliefs, and satisfaction with care.

Results

A total of 186 patients were randomized, with a follow-up rate of 87% at 6 months. There was no difference in improvement of self-rated health at 3 months (44% vs 40%, $p = 0.899$) or 6 months (42% vs 43%, $p = 0.435$). Secondary outcomes did not differ between groups, with a threshold of $p < 0.01$. Satisfaction was high, with 86% of patients recommending the website to other patients.

Conclusion

We found no significant effect of the intervention added to usual care on self-rated health or secondary outcome measures, despite high patient satisfaction with the intervention. These results suggest that online education and nonguided self-help could be valuable additions to stepped care for motor FND, but are not effective treatments as interventions in their own right.

Clinicaltrials.gov identifier

NCT02589886.

Classification of evidence

This study provides Class III evidence that for patients with motor FND, online education and self-help intervention does not significantly improve self-rated health.

MORE ONLINE

→ **Class of Evidence**
Criteria for rating therapeutic and diagnostic studies
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Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

This Null Hypothesis article is published as part of a collaborative effort between *Neurology* and CBMRT.

Glossary

CGI = Clinical Global Improvement; **DSM-5** = *Diagnostic and Statistical Manual of Mental Disorders, 5th edition*; **FND** = functional neurologic disorder; **IQR** = interquartile range; **OR** = odds ratio; **RAND36** = Dutch equivalent of Short Form–36 health-related quality of life; **RCT** = randomized controlled trial; **WHO-QoL** = a single question from the 1998 WHO Quality of Life scale; **WI** = Whitely Index; **WSAS** = Work and Social Adjustment Scale.

Education and self-help intervention are thought by many clinicians to be an important component of treatment for motor functional neurologic disorder (FND) but evidence of effectiveness is lacking.[1,2] Prognostic studies in FND and other functional disorders have shown a correlation between confidence in the diagnosis and good outcome[3–8] and satisfaction with care.[9,10] By contrast, patient groups have expressed concerns that information alone should not be a substitute for (multidisciplinary) treatment.

In patients with FND, a guided self-help study showed modest improvements in the intervention group and no harmful effects.[6] No studies of unguided self-help have been performed in FND.[11]

For this study, we developed a nonguided web-based program for motor FND aiming to improve patients' understanding of the disorder and encourage patients to take an active role in their treatment. Our model of motor FND was of involuntary motor symptoms arising from disordered nervous system functioning and a disorder at the interface between neurology and psychiatry. This includes changes in predictive processing,[12] occurring in the context of biological, psychological, or social factors that vary considerably between patients.[13]

We aimed to find out whether provision of this website added to usual care improved self-rated health status using clinical global improvement in patients with motor FND compared to usual care only. We also aimed to measure the impact of additional information on the severity of motor symptoms, other physical and psychiatric symptoms, physical functioning, quality of life, work and social adjustment, illness beliefs, and satisfaction with treatment.

Methods

Study design and procedures

This was a 2-group parallel superiority nonblinded randomized controlled trial (RCT) with patient-rated outcomes at 3 and 6 months. Between October 2015 and July 2017, neurologists from 31 neurology centers across the Netherlands referred eligible patients to the study.

Patients received information about the study procedures in the mail or via e-mail and gave written informed consent before they were enrolled in the study. The information they received stated the study consisted of a 2-group comparison in which one group would gain access to a website with information and self-help. They could contact the investigators for consultation about the study before enrollment but not afterwards.

After giving consent and completing the online baseline questionnaires, patients were randomized unbiased into 2 arms. The intervention group received access to the password-protected unguided education and self-help website as an addition to usual care. They were instructed to read the website at their own pace and preference. The control group received usual care only. "Usual care" in both groups was not standardized and included any treatment patients received during the trial. Patients were not allowed to discuss medical problems with the investigator (JMG) after randomization. This was not violated. All outcome measures were self-report, using online questionnaires at 3 and 6 months.

Standard protocol approvals, registrations, and patient consents

The SHIFT study (Self-Help and Education on the Internet for Functional Motor Disorders) was performed in accordance with the ethical and legal guidelines of the University Medical Center Groningen (METc 2015/141, M14.150920). All participants gave written consent. The trial was registered at clinicaltrials.gov (NCT02589886).

Primary research question

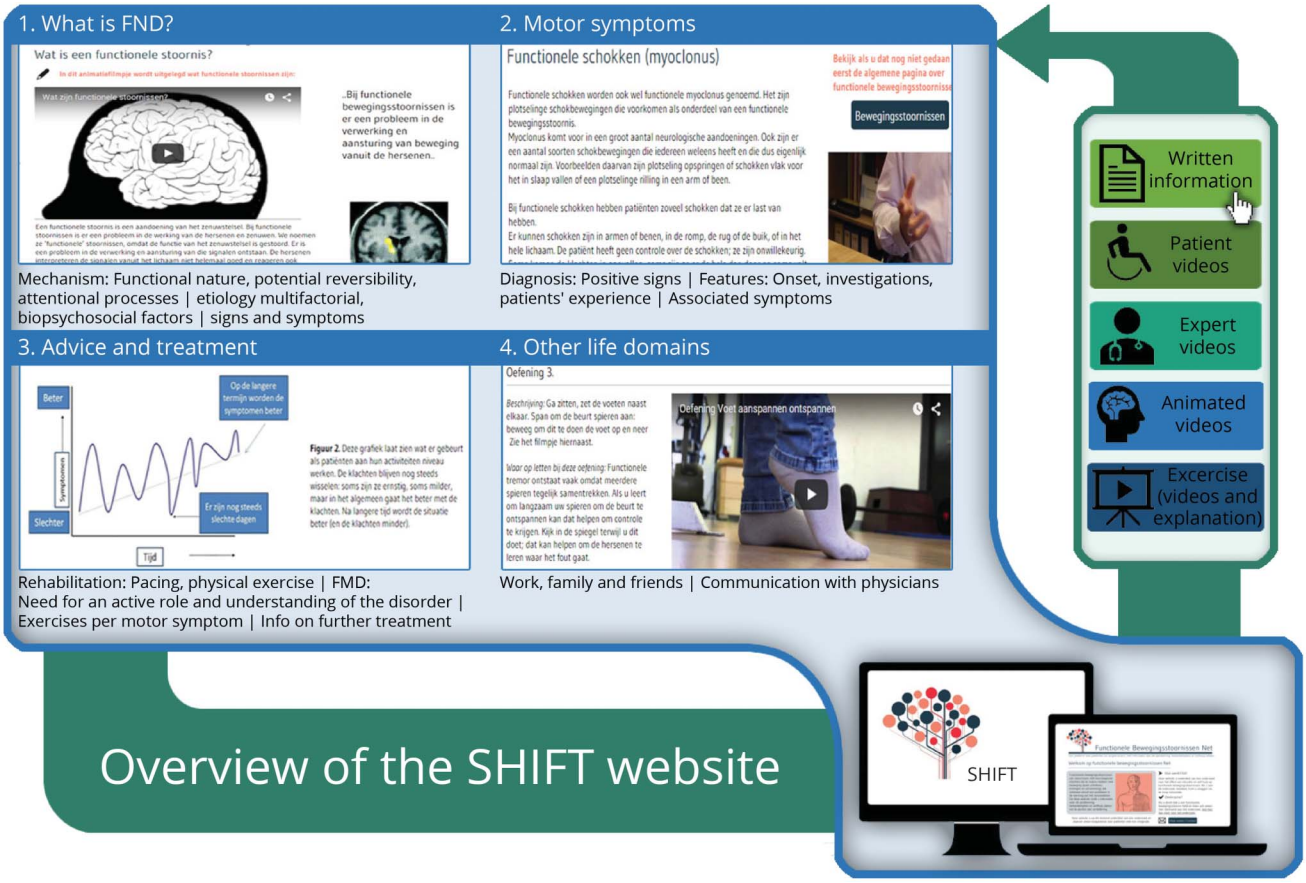
Does provision of a self-help and education website added to usual care improve the self-rated health status in patients with motor FND compared to usual care only at 3 and 6 months follow-up?

Our study provides Class III evidence to answer this question.

Participants

Inclusion criteria were (1) 18 years of age or older; (2) functional motor symptom (limb weakness or movement disorder) diagnosed by a neurologist; (3) symptoms causing distress or impairment in social, occupational, or other important areas of functioning or that warrant medical evaluation (definition according to DSM-5); (4) able to read the Dutch language; and (5) access to a computer with an Internet connection on a regular basis. We excluded (1) patients who were unable to provide informed consent; (2) patients with other (functional) complaints, in whom the motor symptom was an accidental finding in neurologic investigation (i.e., where

Figure 1 Overview of the nonguided self-help website



The left panel shows examples of pages and descriptions of the content of the 4 blocks on general functional neurologic disorder (FND) (1); specific motor symptoms that patients could choose (2); and rehabilitation advice, exercises, and information on treatment possibilities (3) and on the influence of FND on daily life (4). The right panel shows the different media that were used to provide information, which were mostly newly developed for this study.

motor symptoms were not an impairing symptom), which was assessed by the referring neurologist; and (3) patients who were known visitors of the (previously available, but during the study offline) translated (Dutch) version of a website by J.S. (see below). This was assessed in the baseline questionnaire. Patients with comorbid (neurologic) disease were not excluded from the study.

Intervention

The tested intervention was a newly developed educational website in Dutch, which included self-help elements. A pdf version of the website can be found as supplementary material. The content was in line with the explanatory model described by Stone et al.[14] It combined elements of a website developed by J.S., neurosymptoms.org, a self-help workbook developed for functional neurologic symptoms,[6] and expert opinion of J.S., M.A.J.T., J.G.M.R., A.C., and G.N.

The website consisted of 4 blocks focusing on different domains, and included several different sources of information (figure 1). The website also included exercises adapted from physiotherapy recommendations from Nielsen et al.[15] It was piloted and altered based on the feedback of 12 patients and their family members for intelligibility, clearness, relevance, and applicability. Readability scored level B1, with a moderate Douma readability score of 64 out of 100 (based on the English Flesh-Kincaid test), corresponding with a reading age of 13/14 (adjusted for "functional" and "disorder").

Outcome measures

The main outcome was self-rated health, measured on the Clinical Global Improvement (CGI) scale, a 7-point Likert scale (high scores correspond to poor health) at 3 and 6 months.

Secondary outcome measures were severity of all individual motor symptoms (self-rated change in presenting symptom scale [range 0–7]), fatigue (Checklist Individual Strength, fatigue severity subscale [range 7–56]), pain (RAND36, the Dutch equivalent of the Short Form–36, subscale [range 0–100]), depressive symptoms (Patient Health Questionnaire–9 [range 0–27]), anxiety (Generalized Anxiety Disorder questionnaire [scores 0–14]), health

Table 1 Baseline data by treatment arm

	Intervention group (n = 93)	Control group (n = 93)
Demographics		
Age, y, mean (SD)	48 (15)	49 (15)
Sex, % female	73	70
Not in work	78	70
For nonmedical reasons	20	16
On health-related benefits <2 years	21	16
On health-related benefits >2 years	37	38
Referring center (% academic hospital)	55	55
Symptoms		
Duration of motor symptoms, mo, mean (SD)	70 (108)	66 (105)
Severity of all presenting motor symptoms (CPS) (% moderately severe/severe/very severe)	81	82
Main motor symptom according to the referring neurologist		
Tremor	18	15
Myoclonus	23	26
Dystonia	14	11
Paresis	13	18
Gait disorder	15	18
Mixed/unclear	17	12
Pain (RAND36), median (IQR)	45 (55)	57 (47)
Fatigue (CIS severity), median (IQR)	44 (16)	46 (17)
Depression (PHQ-9), median (IQR)	9 (9)	7 (7)
Anxiety (GAD-7), median (IQR)	6 (10)	5 (9)
Health anxiety (WI), median (IQR)	3 (2)	3 (2)
Self-rated health, quality of life, and functioning		
Self-rated health (CGI), % moderately bad and bad and very bad	43	39
Quality of life (WHO-QoL), % good and very good	32	29
Physical functioning (RAND36), median (IQR)	40 (45)	40 (50)
Work and social adjustment (WSAS), median (IQR)	26 (18)	26 (15)
Illness beliefs and satisfaction with care, % agree and strongly agree		
I am confident that the diagnosis functional disorder is correct.	63	61
I am afraid that something (e.g., a possible serious diagnosis) has been missed when making the diagnosis.	15	17
My symptoms are caused by stress/worry or psychiatric problems in the past.	19	25
FND are disorders of the nervous system.	56	51
My disorder is a mystery to me (IPQ).	56	48
What I do determines the outcome of my disorder (IPQ).	54	63
My disorder is permanent rather than temporary (IPQ).	51	48
I think physiotherapy will improve my symptoms.	37	33

Continued

Table 1 Baseline data by treatment arm *(continued)*

	Intervention group (n = 93)	Control group (n = 93)
I think psychotherapy will improve my symptoms.	19	17
I have confidence in my neurologist.	65	58
My neurologist and I agree on the nature of my symptoms.	61	52
I would recommend the care I received to other patients.	27	31
Communication with doctors (PSQ)	3 (1)	3 (1)
Interpersonal relation doctors (PSQ)	4 (1)	4 (1)
Technical quality of doctors (PSQ)	3 (1)	3 (1)

Abbreviations: CGI = Clinical Global Improvement; CIS = Checklist Individual Strength; CPS = change in presenting symptoms scale; FND = functional neurologic disorder; GAD-7 = Generalized Anxiety Disorder Questionnaire, health anxiety; IPQ = Illness Perception Questionnaire; IQR = interquartile range; PHQ-9 = Patient Health questionnaire; PSQ = patient satisfaction questionnaire; RAND36 = Dutch equivalent of Short Form–36 health-related quality of life; WHO-QoL = a single question from the 1998 WHO Quality of Life scale; WI = Whitely Index; WSAS = Work and Social Adjustment Scale (see tables 1 and 2). Higher scores represent poor outcome in CGI, CPS, CIS, PHQ, GAD, WI, and WSAS; higher scores represent good outcome in RAND36. All statements on illness and satisfaction agreement were measured on a 5-point Likert scale (1 = totally disagree, 2 = disagree, 3 = neither agree nor disagree, 4 = agree, 5 = totally agree), percentages are displayed for readability, and statistics were performed on the whole scale. Values are presented as percentages unless indicated otherwise.

anxiety (Whiteley Index [range 0–7]), health-related quality of life and functioning (RAND36) and quality of life (using a single question from the 1998 WHO Quality of Life scale: "How would you rate your quality of life?") (5-point Likert scale, 5 representing good quality of life), and work and social adjustment (Work and Social Adjustment Scale [WSAS] [range 0–40]). Illness perception, satisfaction with care, and confidence in physiotherapy and psychotherapy were assessed by the level of agreement on a 5-point scale on several statements, partly derived from the Illness Perception Questionnaire (tables 1 and 2) and the patient satisfaction questionnaire. Hospitalizations, visits to other websites on FNS, and other treatments were recorded. Open fields were available for additional comments, including comments on improvement if that occurred.

A combination of patients' self-report and the number of times they logged on to the website was used to record use of the website. Evaluation of the intervention website was carried out by agreement on a series of statements on a 5-point scale (not at all–strongly agree) (table 3). If patients did not fill out the online questionnaires, they were contacted by phone at 6 months to assess the main outcome, change in presenting symptoms, quality of life, and agreement with the statements "I would recommend this website to other patients" and "The website helped me a lot."

Baseline data from this study were used in another publication on fatigue severity.[16]

Sample size

Sample size calculation, using Fisher exact proportions for independent groups test in G-power version 3.1.7 software, was based on the expected percentage of patients showing any improvement on the CGI self-rated health scale (all scores below 4 "no change"). Based on a previous RCT on self-help,[6] our prognosis review,[3] and a pilot study of 10 patients in which 40% of patients improved, we estimated that 20% of patients would improve in both groups and an additional 20% in the intervention group. With an alpha of 0.05 and a power of 0.80, a 2-tailed calculation resulted in a sample size of 90 patients per group. To anticipate drop out, we aimed for 100 patients per group. No interim analyses were performed.

Randomization and blinding

Block randomization with stratification, with a ratio of 1:1 into the intervention and control group, was performed by an online randomization tool, ALEA, programmed by the Clinical Research Desk of the University Medical Center Groningen. Stratification factors were having limb weakness as a main motor symptom and duration of symptoms >1 year. The investigators were unaware of the trial group assignments during randomization.

Patients were not blinded to the intervention allocation, because of the obvious difference between the 2 groups (with and without access to the website). Investigators were not blinded: outcome measures were collected remotely via an online form (with equal procedures in both groups), without interference of the investigator. All research data were anonymized before analysis.

Statistical analysis

An intention-to-treat analysis was performed at 3 and 6 months after randomization. A between × within design was used, by subtracting outcome and baseline values and comparing the differences between groups. Mann-Whitney *U* tests (using the whole scale) and χ^2 tests were used for non-parametric and *t* tests for normally distributed variables.

Table 2 Outcome measures at 3 and 6 months in the intervention and control group (intention-to-treat)

	3 months					6 months				
	Intervention		Control			Intervention		Control		
	N	%	N	%	Group comparison	N	%	N	%	Group comparison
Self-rated health (CGI), % improved	70	44	65	40	U = 2,247; p = 0.899	84	42	79	43	p = 0.435
Symptoms, median (IQR)/% improved										
Severity all motor symptoms, % improved	70	53	65	38	U = 2,247; p = 0.899	84	42	79	44	U = 3,087; p = 0.435
% Of totally remitted motor symptoms	70	5	65	0	—	84	6	79	4	—
Pain (RAND36)	69	55 (68)	65	57 (44)	U = 2,239; p = 0.989	79	55 (68)	69	57 (40)	U = 2,563; p = 0.533
Fatigue (CIS severity)	—	—	—	—	—	71	42 (20)	66	44 (23)	U = 2,180; p = 0.674
Depression (PHQ-9)	69	6 (7)	65	7 (6)	U = 1756; p = 0.040	79	6 (8)	69	6 (8)	U = 2,170; p = 0.056
Anxiety (GAD-7)	70	5 (9)	65	4 (8)	U = 2,250; p = 0.912	79	5 (9)	69	5 (8)	U = 2,704; p = 0.933
Health anxiety (WI)	—	—	—	—	—	74	2 (4)	68	2 (2)	U = 2,419; p = 0.689
Quality of life and functioning, median (IQR)										
Quality of life (WHO-QoL), % good, very good	70	41%	65	29	U = 2,232; p = 0.838	84	40	79	42	U = 3,290; p = 0.863
Physical functioning (RAND36)	70	50 (61)	65	40 (53)	U = 2,274; p = 0.996	79	40 (65)	69	45 (58)	U = 2,407; p = 0.217
Work and social adjustment (WSAS)	70	21 (19)	65	25 (14)	U = 2,170; p = 0.643	81	25 (18)	69	24 (18)	U = 2,757; p = 0.887
Illness beliefs and satisfaction with care, % agree/strongly agree										
I am confident that the diagnosis functional disorder is correct.	73	62	66	47	U = 1863; p = 0.014	76	58	70	56	U = 2,346; p = 0.193
I am afraid that something (e.g., possible serious diagnosis) has been missed.	72	18	66	17	U = 2,104; p = 0.220	79	20	69	19	U = 2,347; p = 0.718
Symptoms are caused by stress/worry or psychiatric problems in the past.	73	19	66	23	U = 2,277; p = 0.548	76	21	69	20	U = 2,502; p = 0.610
Functional movement disorders are disorders of the nervous system.	73	60	66	52	U = 2,329; p = 0.719	76	39	69	48	U = 2,561; p = 0.801
My disorder is a mystery to me (IPQ).	73	41	66	47	U = 2,112; p = 0.246	76	34	69	46	U = 2,286; p = 0.211
What I do determines the outcome of my disorder (IPQ).	73	59	66	65	U = 2047; p = 0.116	76	45	69	57	U = 2,319; p = 0.217
My disorder is permanent rather than temporary (IPQ).	73	48	66	55	U = 2,197; p = 0.344	77	58	69	65	U = 2,448; p = 0.389
Exercise worsens my symptoms.	73	51	66	56	U = 1,989; p = 0.072	76	49	69	64	U = 2,161; p = 0.035
I think physiotherapy will improve my symptoms.	73	41	66	36	U = 2,020; p = 0.089	76	41	69	26	U = 2,148; p = 0.052
I think psychotherapy will improve my symptoms.	73	27	66	20	U = 2,004; p = 0.101	76	20	69	19	U = 2,576; p = 0.962

Continued

Table 2 Outcome measures at 3 and 6 months in the intervention and control group (intention-to-treat) *(continued)*

	3 months					6 months				
	Intervention		Control		Group comparison	Intervention		Control		Group comparison
	N	%	N	%		N	%	N	%	
I would recommend the care I received.	76	54	66	36	U = 2,112; p = 0.095	81	47	69	38	U = 2,725; p = 0.659

Abbreviations: CGI = Clinical Global Improvement; CIS = Checklist Individual Strength; GAD-7 = Generalized Anxiety Disorder Questionnaire, health anxiety; IPQ = Illness Perception Questionnaire; IQR = interquartile range; PHQ-9 = Patient Health Questionnaire-9; RAND36 = Dutch equivalent of Short Form–36 health-related quality of life; WHO-QoL = a single question from the 1998 WHO Quality of Life questionnaire; WI = Whitely Index; WSAS = Work and Social Adjustment Scale.
Absolute numbers at follow-up are displayed as well as Mann-Whitney *U* tests on the difference between follow-up and baseline. Higher scores represent poor outcome in CGI, change in presenting symptoms scale, CIS, PHQ, GAD, WI, and WSAS; higher scores represent good outcome in RAND36. For all statements on illness and satisfaction, agreement was measured on a 5-point Likert scale (1 = totally disagree, 2 = disagree, 3 = neither agree nor disagree, 4 = agree, 5 = totally agree), percentages are displayed for readability, and statistics were performed on the whole scale.

For the main outcome, missing data were imputed, by means of multiple imputation methods using linear regression in SPSS (version 23). We imputed missing data based on all baseline and follow-up variables, generating 5 new datasets. These were used for a sensitivity analysis (to explore the effect of dropout). In the data displayed in the tables and outcomes, data without imputation are provided.

An additional per protocol analysis was planned, excluding patients who never logged on to the website from the intervention group, to investigate whether the website itself has a beneficial effect, but would need promotion.

Post hoc we analyzed the effect of change between baseline and follow-up on agreement with the statements "I am confident that the diagnosis functional disorder is correct," "My disorder is a mystery to me," and "What I do determines the outcome of my disorder" on the main outcome. Furthermore, we investigated a limited number of possible prognostic factors (baseline factors that influence outcome): duration of symptoms, type of referring center (academic vs nonacademic), age, sex, and the same illness perception statements as listed above. For these correlations, we used univariable ordinal regression models, first in the entire cohort, and second with randomization group added to the model, to investigate associations between groups.

Due to multiple comparisons, secondary outcome measures were interpreted conservatively with p values of greater than 0.01 treated with caution.

Data availability

Data are available on request from the authors.

Results

Participants

A total of 355 patients were screened for eligibility, of whom 186 participated in the study. Randomization resulted in 93 patients for each group at baseline. The flowchart (figure 2) summarizes reasons for exclusion and loss to follow-up.

Reasons for not visiting the website varied. At 3 months, some patients reported forgetting about it (n = 4), believing (n = 2) or being concerned (n = 2) about undesirable content, alleviated symptoms (n = 1), skepticism regarding diagnosis (n = 1), and various additional reasons. Between 3 and 6 months, most patients (n = 44) ceased further website visits, primarily due to improved symptoms (n = 7), having fully read the website (n = 8), being focused on a different treatment (n = 5), and severe symptoms or impaired concentration (n = 5). Two patients disagreed with the content, citing dislike of the term "disorder" and uninformative content; another 2 "did not feel like" visiting the site.

Baseline

The majority of patients were female (72%) and many were out of work (74%), mainly for medical reasons. Mean

Table 3 Per protocol analysis

	3 months					6 months				
	Intervention		Controls			Controls		Intervention		
	N	%	N	%	Group comparison	N	%	N	%	Group comparison
Self-rated health (CGI), % improved	58	45	65	40	U = 1,879; p = 0.975	78	42	79	43	U = 2,851; p = 0.412
Symptoms, median (IQR)/% improved										
Severity all motor symptoms (CPS)	63	51	66	38	U = 1,982; p = 0.641	79	51	79	44	U = 3,002; p = 0.581
Pain (RAND36)	57	45 (58)	65	57 (43)	U = 1,816; p = 0.851	73	45 (68)	69	57 (40)	U = 2,370; p = 0.543
Fatigue (CIS severity)		NA		NA		66	43 (21)	65	44 (13)	U = 2,023; p = 0.574
Depression (PHQ-9)	57	7 (8)	65	7 (5)	U = 1,517; p = 0.084	71	8 (9)	69	6 (8)	U = 2,041; p = 0.088
Anxiety (GAD-7)	58	6 (10)	65	4 (8)	U = 1,863; p = 0.909	73	5 (9)	69	5 (8)	U = 2,485; p = 0.887
Health anxiety (WI)		NA		NA		70	2 (3)	68	2 (2)	U = 2,293; p = 0.705
Quality of life and functioning, median (IQR)/% good										
Quality of life (WHO-QoL), % good/very good	58	67	65	29	U = 1,833; p = 0.776	78	37	79	41	U = 2,909; p = 0.531
Physical functioning (RAND36)	58	48 (67)	65	40 (52)	U = 1,870; p = 0.937	73	40 (65)	69	45 (58)	U = 2,477; p = 0.865
Work and social adjustment (WSAS)	58	22 (18)	65	25 (13)	U = 1,779; p = 0.588	75	26 (19)	69	24 (18)	U = 2,380; p = 0.405
Illness beliefs and satisfaction with care, median (IQR)										
I am confident that the functional disorder diagnosis is correct.	59	61	66	47	U = 1,487; p = 0.014	70	58	70	56	U = 2,114; p = 0.138
I am afraid that something (e.g., possible serious diagnosis) has been missed.	58	14	66	17	U = 1,667; p = 0.189	70	23	69	19	U = 2,214; p = 0.373
Symptoms are caused by stress/worry or psychiatric problems in the past.	59	19	66	23	U = 1,883; p =0.731	70	20	69	20	U = 2,234; p = 0.409
Functional movement disorders are disorders of the nervous system.	59	59	66	52	U = 1,860; p = 0.649	70	59	69	48	U = 2,396; p = 0.933
My disorder is a mystery to me (IPQ).	58	40	66	47	U = 1,603; p = 0.108	69	31	69	46	U = 2,042; p = 0.134
What I do determines the outcome of my disorder (IPQ).	59	63	66	65	U = 1,759; p = 0.335	70	46	69	57	U = 2,152; p = 0.252
My disorder is permanent rather than temporary (IPQ).	59	46	66	55	U = 1,644; p = 0.111	71	59	69	65	U = 2,225; p = 0.323
Exercise worsens my symptoms.	59	51	66	59	U = 1,579; p = 0.065	70	55	71	62	U = 2,003; p = 0.044
I think physiotherapy will improve my symptoms.	59	44	66	36	U = 1,491; p = 0.019	70	41	69	26	U = 1,881; p = 0.019
I think psychotherapy will improve my symptoms.	59	29	66	20	U = 1,592; p = 0.069	69	21	69	19	U = 2,373; p = 0.972

Continued

Table 3 Per protocol analysis *(continued)*

	3 months					6 months				
	Intervention		Controls			Controls		Intervention		
	N	%	N	%	Group comparison	N	%	N	%	Group comparison
I would recommend the care I received.	63	62	66	36	U = 1,866; p = 0.301	74	48	71	37	U = 2,566; p = 0.802

Abbreviations: CGI = Clinical Global Improvement; CIS = Checklist Individual Strength; CPS = change in presenting symptoms scale; GAD-7 = Generalized Anxiety Disorder Questionnaire, health anxiety; IPQ = Illness Perception Questionnaire; IQR = interquartile range; PHQ-9 = Patient Health Questionnaire; RAND36 = Dutch equivalent of Short Form–36 health-related quality of life; WHO-QoL = a single question from the 1998 WHO Quality of Life questionnaire; WI = Whitely Index; WSAS = Work and Social Adjustment Scale.
Data are displayed at follow-up; tests are performed on the change between follow-up and baseline. Absolute numbers at follow-up are displayed, as are Mann-Whitney *U* tests on the difference between follow-up and baseline. Higher scores represent poor outcome in CGI, CPS, CIS, PHQ, GAD, WI, and WSAS; higher scores represent good outcome in RAND36. For all statements on illness and satisfaction, agreement was measured on 5-point Likert scale (1 = totally disagree, 2 = disagree, 3 = neither agree nor disagree, 4 = agree, 5 = totally agree), percentages are displayed for readability, and statistics were performed on the whole scale.

duration of symptoms was 5.7 years. Self-rated severity of motor symptoms was moderately severe to very severe in 82% of cases. A majority of patients reported confidence that the diagnosis of a functional movement disorder was correct (62%), but 54% felt the disorder was a mystery to them. Patients reported poor quality of life (only 30% had good or very good quality of life) and physical function impairment (median 40 out of 100 [100 corresponding to unimpaired functioning] and 26 out of 40 on the WSAS [40 corresponding to poor functioning]).

Outcome

Main outcome

At 3 months, 44% (n = 31) of patients in the intervention group reported improvement of their general health ("minimally," "much," or "very much" improved), compared to 40% (n = 26) of the controls on the CGI, which was not significantly different. At 6 months, 42% (n = 35) of patients in the intervention group reported to have improved, compared to 43% (n = 34) in the control group. Figure 2 shows the CGI scale for both groups.

The sensitivity analysis with imputed data did not result in a different main outcome.

To investigate potential harm, the number of patients with worse general health on the CGI was compared between groups. At 3 months, 20 (29%) patients in the intervention group reported worse general health, compared to 18 controls (28%) (U = 2,255, p = 0.910). At 6 months, 30 patients in the intervention group (36%) had worse outcome, compared to 21 controls (27%) (U = 3,015, p = 0.210).

The per protocol analysis (where patients who never logged on to the website were excluded from the intervention group) did not show a significant difference between groups (table 3).

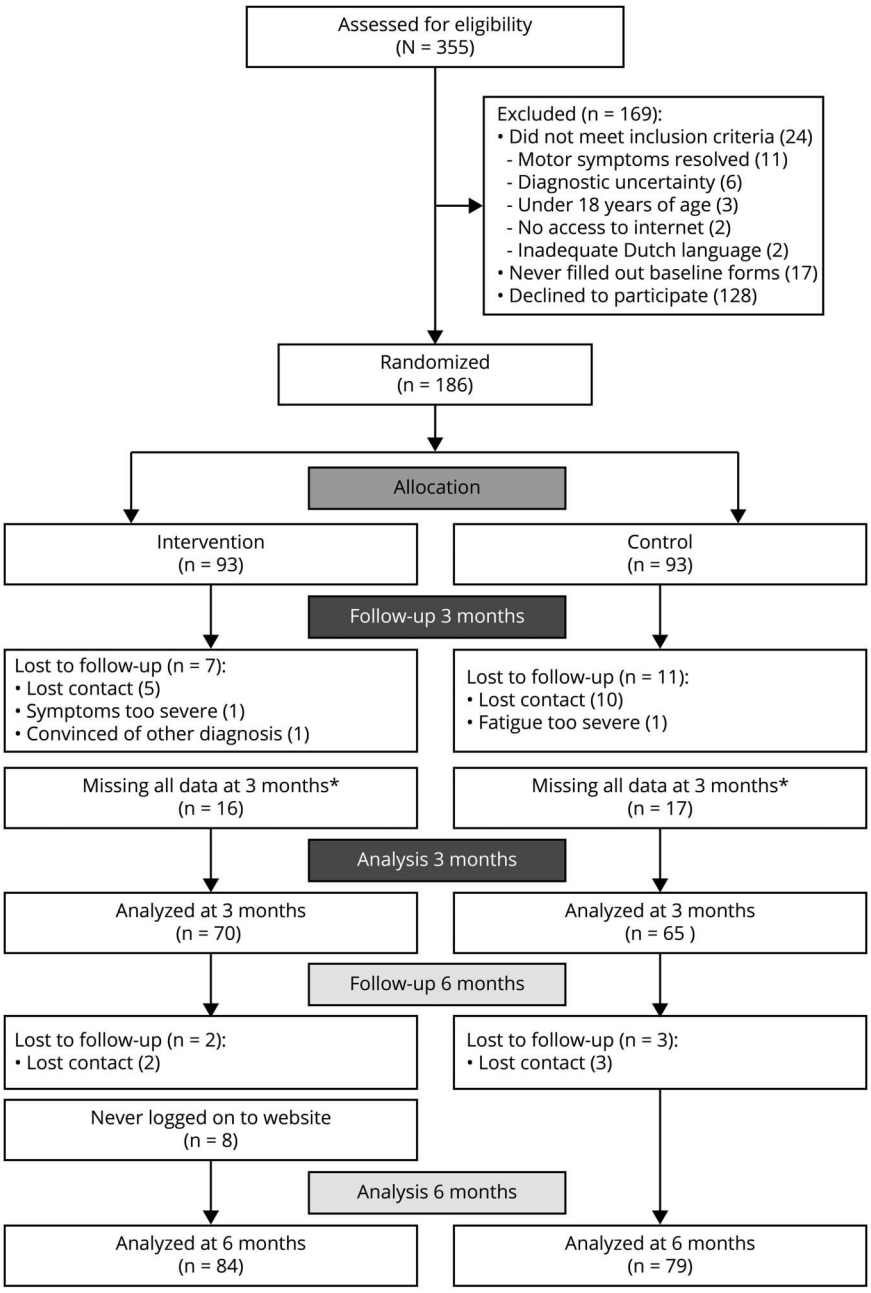
A post hoc comparison showed that patients with paresis as the main motor symptom might have benefitted less from the intervention than patients with other motor symptoms. Numbers were too small to perform statistical tests, but at 6 months, 45% of patients with paresis improved in the intervention group, vs 41% with other motor symptoms, while in the control group, this was 69% vs 38%, respectively (figure 3).

Secondary outcomes

There were no differences between groups on any of the outcome measures at 3 and 6 months follow-up, using a cutoff for statistical significance of $p < 0.01$.

Symptom severity of all functional motor symptoms improved in less than half of the patients (between 40% and 44%) at 3 and 6 months in both groups compared to baseline. Depression scores were significantly higher in the intervention

Figure 2 Flow diagram (adapted from CONSORT [Consolidated Standards of Reporting Trials])



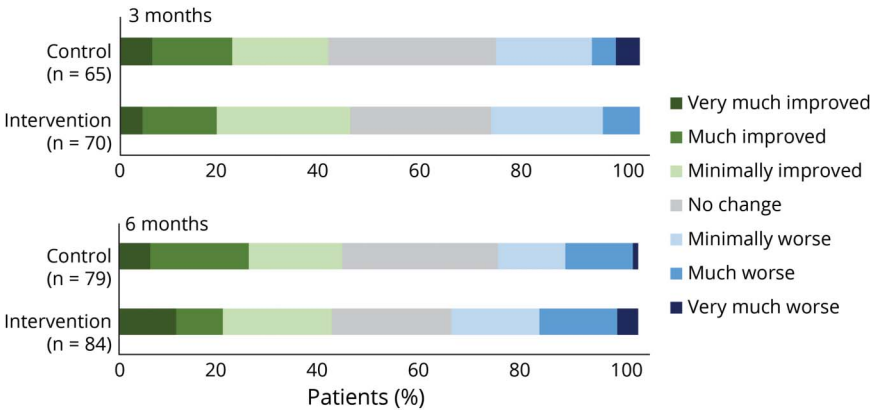
*Data missing at 3 months, but present at 6 months (and therefore these participants were not lost to follow-up).

group than in the control group at baseline, while at 3 and 6 months this equalized. Anxiety and health anxiety remained stable over time in both groups, as well as pain, fatigue, physical functioning, quality of life, and work and social adjustment.

There were no significant differences between groups on the illness perception questions. Agreement with the statement "I am confident that the diagnosis of a functional disorder is correct" was higher in the intervention group (62%) than in the control group (47%) at 3 months, but this did not reach significance ($p = 0.014$). Fewer than half of the patients (36% of controls vs 41% of patients in the intervention group at 3 months, and 26% vs 41% at 6 months) believed physiotherapy would improve their symptoms, and an even smaller number believed psychotherapy would improve their symptoms (20% of controls, 27% of patients in the intervention group at 3 months, 19% vs 20% at 6 months); neither changed significantly over time. Overall satisfaction with their clinical care (i.e., care other than the website) increased slightly over time in both groups.

There were no statistically different outcomes from the per protocol analysis (table 3).

Figure 3 Main outcome: change in self-rated general health at 3 and 6 months compared to baseline in both groups



Other websites and other treatments

During the study, 4 patients in the intervention group and 3 patients in the control group reported to have read information on the English website neurosymptoms.org. Twelve percent of patients in the intervention group and 20% in the control group (χ^2 2.5, $p = 0.111$) visited one or more other related websites.

In the first 3 months, 69% of the patients in the intervention group received physiotherapy and 68% in the control group. Respectively 33% and 37% received some form of psychotherapy. A total of 19% of the intervention group and 15% of controls reported to have received no therapy at all. Between 3 and 6 months, 49% of the intervention group and 50% of controls received physiotherapy, 23% and 26% respectively received psychotherapy, and 17% and 18% respectively reported to have received no therapy.

Hospital admissions

Twelve patients in the intervention group (14%) were admitted to the hospital during the 6 months follow-up period; this was related to motor FND in 6 cases, unrelated in 4, and there was missing information in 2 cases. Twelve controls (15%) were admitted to the hospital during the 6 months follow-up period: related to motor FND (n = 7), unrelated (n = 4), or missing information (n = 1).

Post hoc correlations

Correlation between baseline variables and outcome

Duration of symptoms of more than 6 months at baseline (mean duration at baseline was 5.7 years) was associated with poor general health outcome at 6 months in a univariable logistic regression model (odds ratio [OR] 2.80 [1.45–5.42], $p = 0.002$). Fifty-nine percent of patients with short duration improved, compared to 37% with long (>6 months) duration of symptoms. This relationship was stronger in the intervention group (interaction group × duration of symptoms, OR 1.84 [1.05–3.20], $p = 0.033$), although not significantly. Outcome was worse in men (28% of patients were men) (OR 2.94 [1.58–5.48], $p = 0.001$), which was not significantly different between groups. A number of variables were not significantly associated with outcome in the entire cohort or in the groups separately: the referring center (55% of patients were referred from an academic center) (OR 1.49 [0.86–2.60], $p = 0.158$), older age at onset (OR 1.02 [1.00–1.04], $p = 0.026$), "I am confident that the diagnosis functional disorder is correct" (62% agreed) (OR 1.14 [0.84–1.55], $p = 0.405$), "My disorder is a mystery to me" (52% agreed) (OR 1.07 [0.86–1.33], $p = 0.533$), and "What I do determines the outcome of my disorder" (58% agreed) (OR 0.98 [0.77–1.24], $p = 0.877$).

Correlation between change in illness perceptions and outcome

The effect of change in understanding the diagnosis (measured on a change on 3 illness perception questions) on the main outcome at 6 months (general health on the CGI) was investigated by univariable ordinal regression. An increase in agreement from baseline to 6 months with "I am confident that the diagnosis functional disorder is correct" provided an OR of 1.43 (1.12–1.83; $p = 0.004$) with good general health (CGI) at 6 months in the entire cohort. When the randomization group was added as an interaction term, the OR was 1.42 (1.01–2.00; $p = 0.044$), indicating there was a trend towards a bigger effect in the intervention group. A decrease in agreement with "My disorder is a mystery to me" (OR 1.30 [1.02–1.63], $p = 0.033$), and an increase in agreement with "What I do determines the outcome of my disorder" (OR 1.13 [0.93–1.36], $p = 0.234$), were not significantly associated with outcome.

Evaluation of the education and self-help website

Sixty-three patients in the intervention group (74% of the 85 who viewed the website at least once) filled out the evaluation. Eighty-six percent of patients reported they would recommend the website to other patients, 68% of patients found the

website very useful, and 67% performed the exercises provided on the website at some point during the 6 months follow-up.

A smaller number of patients answered more detailed questions evaluating the website (n = 55). Seventy-eight percent agreed with the explanation of their symptoms that was provided on the website, 89% found the information on the website was easy to understand, 22% perceived difficulty in taking in the information, 49% agreed the information on the website matched the explanation given by the neurologist they had seen for their symptoms, and 75% reported they would want to keep on using the website in the future. Of them, 9% reported they felt angry or misunderstood (for divergent and sometimes multiple) reasons: the website was patronizing (n = 2), too negative (n = 1), a specific symptom the patient had was not mentioned (n = 1), the website created a stronger focus on the symptoms, which was unhelpful (n = 1), physical exercises made the symptoms worse (n = 1), and there was a discrepancy between the opinion of health care providers in reality and the information on the website (n = 1).

In additional comments, patients mentioned they experienced health care providers seemed to lack knowledge on FND (n = 10), which either impeded treatment generally or made the website less helpful because of the lack of connection with their experience of health care (some felt this was highly frustrating). Others remarked the website was helpful to educate their health care providers or explain the disorder to relatives and friends. Several patients (n = 10) mentioned they felt heard after reading the website and felt it validated their experiences, or they were relieved to see other patients had similar symptoms and impairments. Three patients asked for an overview of health care providers with experience in this field or a patient forum.

Discussion

In this RCT, there was no difference in self-rated general health on the CGI scale at 3 or 6 months between motor patients with FND who were directed towards an education and self-help website in addition to usual care and patients who received only usual care. Nor were there significant differences on the secondary outcomes (severity of motor symptoms, other physical and psychiatric symptoms, physical functioning, quality of life, work and social adjustment, or illness beliefs [including beliefs of the effect of physiotherapy/psychotherapy and satisfaction with care]). Patient satisfaction with the website was high. The per protocol analysis results were similar to the primary intention-to-treat analysis. We also showed that the intervention did no harm. Poor outcomes and hospitalizations were similar in both arms.

Our results suggest nonguided online self-help is not effective as a sole addition to usual care for motor FND. There are no studies of unguided self-help and education for motor FND to compare our data with. A meta-analysis of self-help in the broader group of functional syndromes (chronic pain, chronic fatigue, and irritable bowel syndrome) showed improvement of quality of life or symptom reduction of both guided and unguided self-help, although outcome measures were heterogeneous and there were only 5 unguided studies.[11] A recent meta-analysis of treatment modalities in depression also showed unguided self-help therapy was not more effective than care as usual, while guided self-help was.[17] Our findings support patient group concerns, for example expressed by individual patients and patient organizations that an unguided self-help website should not be regarded as all that is needed to manage motor FND. Motor symptoms improved in roughly 2 out of 5 patients spontaneously. This suggests that neurologists should follow patients with FND after diagnosis to monitor early improvement and to direct the remaining 3 out of 5 patients to further treatment, and not rely on the provision of information alone as treatment.

Providing patients with reliable and accessible information does not need to resolve or even improve symptoms in order to be justifiable. Explanation and education remain, in our view, an essential element of stepped care for motor FND. Improved confidence that the diagnosis was correct correlated with improvement in health across the whole cohort, and to a greater extent in the intervention group, although the latter did not reach the predetermined threshold ($p < 0.01$) for significance. Nonetheless this suggests the right direction of travel in terms of improving understanding. Treatment studies of motor FND using a comparable educational model, either as a guided self-help intervention[6] or combined with physical and cognitive behavioral interventions in inpatient[18–20] or outpatient[21,22] settings, have shown favorable outcomes. In practice, patients often experience lack of availability of expert knowledge, as reflected in patients' written comments and the finding that only half the patients (49%) agreed that the information from the website matched the explanation of the neurologist. This is a problem recognized by physicians in the field[2] and emphasizes the need for consistency between health professionals caring for the same patient.

The type and content of an optimal educational intervention for motor FND, in which much remains unknown about pathophysiology and treatment, can be debated. We chose a conceptual model, based on our clinical experience and our interpretation of contemporary scientific findings, that we think is the best fit between accurate mechanistic descriptions and patient acceptability. However, there are many unknowns in this condition and this is an inherent problem with any model. We described FND as a problem in nervous system functioning but also did not ignore the importance of psychological factors. The model aimed to promote self-efficacy and to help patients see how they could take part in their own rehabilitation. There was less emphasis on potential etiologic

factors, partly as these vary between individuals and are difficult to address via self-help. This model has been criticized as "depsychologizing" the condition and potentially causing iatrogenic harm by suggesting that it is all a "brain" condition and nothing therefore directing the patient away from tackling psychological problems in their lives. Whereas we reject this notion as dualistic and misunderstanding of our model, we nonetheless accept that it is a valid criticism and a more explicitly psychological model may have led to improved outcomes. In this regard, we note that there have been a number of trials of the reattribution model, which is more explicitly psychological, in so-called medically unexplained symptoms that paradoxically showed poorer patient outcomes.[23] There is a separate theoretical concern that any form of education may ask patients to spend too long reading or thinking about their disorder and could have an amplifying effect on symptomatology.

The study had several additional possible limitations. Patients in our study had a long duration of symptoms (mean of 5.6 years), which may have negatively influenced outcomes, as we found that symptom duration correlated to worse outcome. Prognostic studies[3] in general have found that a longer duration of symptoms correlates with poorer prognosis. Early educational intervention seems beneficial in some conditions commonly comorbid with motor FND.[24,25]

The fact that we employed liberal inclusion criteria and advertised the study broadly (with good result: 31 centers, both academic and nonspecialized, referred patients) improved generalizability. This is to date the largest RCT in any FND. The overall improvement of motor symptoms in 40%–44% of patients is comparable to other cohorts.[26,27] However, selection bias most likely occurred at patient level (patients who did not believe the diagnosis were less likely to enroll) and physician level (neurologists with an interest in FND would be more likely to refer into the study). A large number of patients (n = 128) refused to take part. In addition, 17 patients never completed the baseline questionnaires and many patients only viewed the website a few times. There may have been issues with accessibility and readability although we did not receive negative feedback regarding these from patient evaluation.

Outcomes might also have been influenced because the study was not blinded and a nocebo effect in the control group could have occurred. However, this effect is likely to be small in this low-intensity study. Use of alternative websites like neurosymptoms.org was low and equal between groups. Furthermore, the study website was different from neurosymptoms.org, in that it provided a program of information to work through, and numerous videos and examples not available elsewhere. Our patient cohort might have been too small to capture subtle differences in secondary outcomes. The follow-up period was relatively short and therefore long-term effects, for example on compliance with or effect of further treatments, might have been missed. The fact that the study was Internet-based, compared to on paper, did not appear to cause problems in inclusion or follow-up in the large majority of patients.

Measuring outcome in (motor) FND is complicated by the heterogeneity of the population and the symptoms themselves. We chose a self-rated general health scale (CGI) as the main outcome because this is the most clinically relevant for a complex heterogeneous and variable disorder and is less susceptible to floor and ceiling effects than other scales. Self-rated measures are ultimately subjective, although a recent international collaboration concluded that this was preferable to objective measures for this particular disorder.[28] Physician-rated and objective measures would have provided a complementary and useful perspective but can be problematic in a variable fluctuating disorder.

In this first randomized controlled trial of an online education and self-help program for motor FND, we found it was well received but it did not lead to improvements in self-rated general health on the CGI scale at 3 or 6 months, nor did it lead to any harmful effects.

Nonetheless, provision of information is a core part of clinician–patient interaction, and this trial shows it can be done safely in FND. Patients with FND have the same rights as other patients to be informed of the nature of their condition, but the provision of such information is insufficient on its own to alter clinically relevant outcomes in motor FND compared to usual care.

Acknowledgment

The authors thank the neurologists who referred patients to this study from the 31 centers in the Netherlands.

Study funding

This study was funded by Stichting MIND (previously Fonds Psychische Gezondheid) with an unrestricted grant. J.S. is supported by an NHS Scotland NRS Clinical Fellowship. The pilot study that preceded this randomized controlled trial was supported by an unrestricted healthy aging pilot project grant from the University of Groningen. G.N. receives research funding from the National Institute for Health Research.

Disclosure

J.M. Gelauff, J.G. Rosmalen, A. Carson, J.M. Dijk, M. Ekkel, and G. Nielsen report no disclosures relevant to the manuscript. J. Stone has run a self-help website for functional neurologic disorder, neurosymptoms.org, which is free and carries no advertising, since 2009. M.A.J. Tijssen reports no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Publication history

Received by *Neurology* September 23, 2019. Accepted in final form April 7, 2020.

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Martijn Ekkel, MD	Department of Neurology, University Medical Center Groningen, University of Groningen, the Netherlands	Major role in acquisition, analysis, and interpretation of the data
Glenn Nielsen, PhD	Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, UK	Design and conceptualization of the study, interpretation of the data, revising the manuscript for intellectual content
Jon Stone, MB, ChB, FRCP, PhD	Centre for Clinical Brain Sciences, University of Edinburgh, UK	Design and conceptualization of the study, major role in analysis and interpretation of the data, drafting and revising the manuscript for intellectual content
Marina A.J. Tijssen, MD, PhD	Department of Neurology, University Medical Center Groningen, University of Groningen, the Netherlands	Design and conceptualization of the study, major role in acquisition and interpretation of the data, revising the manuscript for intellectual content

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