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Original research

Characterising alexithymia in individuals with functional motor disorders: a cross-sectional analysis of the Italian Registry of Functional Motor Disorders

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ABSTRACT

Background Alexithymia, a personality trait characterised by difficulty in identifying and expressing emotions, may contribute to the onset and clinical presentation of functional motor disorders (FMDs), although this association remains underexplored.

Methods From the Italian Registry of FMDs, we selected individuals recruited between November 2011 and January 2023, diagnosed with FMD according to Gupta and Lang criteria and assessed for various neurological and psychological features with validated rating scales. The main statistical analysis included regression models using the Toronto Alexithymia Scale 20 items as an explanatory variable for a set of clinical measures, adjusting for sociodemographic factors and correcting for multiple testing.

Results In a cohort of 483 individuals, 20.7% had possible alexithymia and 31.5% had definite alexithymia. Higher levels of alexithymia were strongly associated with increased severity of depression (β=0.31, p<0.001), anxiety (β=0.32, p<0.001), general psychological distress (β=−0.27, p<0.001), fatigue (β=0.05, p<0.001) and pain (β=0.32, p<0.001) and moderately associated with a slower onset of FMD (β=0.02, p=0.003). Subscale analyses revealed that difficulties identifying feelings contributed most to these associations. No significant association was observed with motor symptom severity.

Conclusions Emotional processing difficulties of individuals with FMD and alexithymia might increase their vulnerability to mental health problems, pain and fatigue, possibly aggravating the overall prognosis. Further research is needed to elucidate the underlying mechanisms linking alexithymia to FMD and to explore the efficacy of interventions targeting emotional awareness and regulation in this population and to prevent long-term mental health burdens.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The psychological trait of alexithymia might contribute to the onset and characterisation of functional motor disorders (FMDs), but this association has been scarcely studied so far.

WHAT THIS STUDY ADDS

⇒ A relevant portion of individuals with FMD have a clinically significant level of alexithymia, which is strongly associated with depression, anxiety, general psychological distress, fatigue and pain.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings suggest that addressing emotional processing difficulties, such as alexithymia, could be crucial in managing functional movement disorders. Routine psychological assessments and psychological interventions focused on emotional awareness and regulation might play an essential role to improve the overall burden of disease in this population, warranting future experimental research.

INTRODUCTION

Functional motor disorders (FMDs) are defined as abnormal movements whose features are inconsistent over time, do not follow neuroanatomical pathways underpinning typical neurological diseases and might be significantly altered by distraction. They are characterised by a wide range of symptoms such as tremor, dystonia, paralysis, myoclonus, speech disorders, gait and coordination disturbances affecting different body parts.[1 2] The prognosis for functional neurological disorders is often unfavourable, with up to 40% of affected individuals showing no improvement after several

years of follow-up, high levels of interference of symptoms with daily functioning and poor quality of life.[3]

The diagnosis of FMD is mainly based on the neurological examination, which should be based on positive signs of variability, distractibility, suggestibility and exclude other neurological causes that unequivocally explain symptoms. Several 'rule-in signs', such as tremor entrainment, Hoover's sign and give-way weakness, are commonly used in clinical practice to support the diagnosis of FMD.[4] However, the diagnosis of FMD is often challenging and delayed due to the overlap with other neurological movement disorders (copresent in over 20% of individuals),[5] the lack of specific biomarkers and the lack of specific training for healthcare professionals.[6]

FMD may be underpinned by altered functionality of brain circuits involved in the planning, execution and monitoring of voluntary movements, modulated by placebo and nocebo effects.[7] Although etiopathogenic pathways are still unclear, they are likely based on a complex interaction between biological, physical, psychological and social factors.[1] According to the "Theory of Constructed Emotion", emotions are not prewired responses but are constructed through a dynamic process involving predictive brain activity, allostasis and interoception. In functional disorders, including FMD, disruptions in this process might be attributable to early-life adversity, chronic stress or trauma, which can lead to an 'inefficient emotion construction' and ultimately generate maladaptive symptoms.[8] Often, previously existing predisposing factors contribute to a state of vulnerability on which precipitating stressful events, such as trauma, illness or surgery, might trigger the onset and sustain the perpetuation of functional symptoms over time.[9] Among such predisposing factors, a prominent interest has been dedicated to the psychological construct of alexithymia, first described by Sifneos in the 1970s, defined as 'a state of deficiency in understanding, processing or describing emotions'.[10] Alexithymia is considered a psychological trait, indicating a stable and enduring characteristic of an individual's personality. High levels of alexithymia might hinder the transition from preverbal, somatic emotional states, to their mentalised, verbal (symbolic) correlates, preventing an effective process of self-regulation of somatic activation.[11] Alexithymia might represent a mediator between early life adversity, lower resilience[12] and the onset of psychopathology in adult life.[13]

Until now, relatively few and small studies have explored this construct in FMD, generally reporting a higher prevalence of alexithymia in individuals with FMD compared with healthy controls (see online supplemental table S1).[14–16] Notably, reports on the possible association between alexithymia and the severity of functional neurological symptoms are anecdotal, based on small and highly selected samples of individuals with FMD,[17] while the association with non-motor symptoms, such as pain and fatigue, and psychiatric comorbid symptoms, have never been explored.

Therefore, it is still unclear whether alexithymia may be associated with specific clinical features of FMD, such as its phenotype or coexisting motor and non-motor symptoms.

On these grounds, we identified a large sample of individuals with FMD from an extensive national clinical registry to investigate the association between alexithymia as a dimensional trait construct and several motor and non-motor clinical characteristics of FMD.

METHODS

Data source

Data were extracted from the Italian Registry of Functional Motor Disorders (IRFMD), managed by the Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona and by the Italian Academy for the Study of Parkinson's Disease and Other Movement Disorders (LIMPE DISMOV Academy; RADAC project) and Fondazione LIMPE.[18] To be recorded in the IRFMD, a patient's medical history had to be documented by medical records or statements from informed relatives. Patient information was recorded using a web-based, encrypted and anonymised system on the website of the LIMPE DISMOV Academy, which complied with the General Data Protection Regulation.

Participants

Consecutive outpatients with FMDs were recruited by neurologists specialised in movement disorders from 21 tertiary movement disorders centres (10 in northern, 3 in central and 6 in southern Italy and 2 in Sardinia/Sicily) between 1 September 2019 and 5 January 2023 (the full list of coinvestigators is reported in online supplemental table S2). Participants fulfilled the following inclusion criteria: age ≥10 years, a clinically definite diagnosis of FMD (isolated or multiple) based on Gupta and Lang criteria with the presence of positive signs and distractibility manoeuvres[19]; the presence of one or more FMD phenotype including tremor, weakness, jerks, dystonia, gait disorders, parkinsonism, facial motor disorders; availability of an assessment of the psychological construct of alexithymia. Cognitive or physical impairment that precluded the provision of informed consent was considered an exclusion criterion. At each enrolling centre, a neurologist with clinical expertise in movement disorders evaluated participants in a single session, confirmed the diagnosis of FMD and performed a structured interview on several demographical and clinical variables, administering the following validated rating scales: the Simplified Functional Movement Disorders Rating Scale (S-FMDRS)[20] for the severity and duration of motor symptoms; the Short Form 12 items (SF-12)[21] for evaluating quality of life; the Beck Anxiety Inventory (BAI)[22] and the Beck Depression Inventory (BDI-II)[23] to evaluate anxiety and depression symptoms, respectively; the Brief Pain Inventory (BPI)[24] to evaluate the intensity and interference of pain during daily life; the Clinical Global Impression Severity (CGI-S)[25] to measure the intensity of motor symptoms; the Multidimensional Fatigue Inventory 20 items (MFI-20)[26] scale to measure fatigue and the Toronto Alexithymia Scale 20 items (TAS-20)[27] to evaluate the presence and severity of alexithymia.

Statistical analysis

We assessed alexithymia by using both a bivariate approach and a multivariate approach.

First, we identified three subpopulations based on the level of alexithymia, according to the commonly used clinical cut-offs of the TAS-20:[27] (a) individuals without alexithymia (score ≤51); (b) individuals with possible/borderline alexithymia (score between 52 and 60); (c) individuals with definite alexithymia (score ≥61). Differences in sociodemographic and clinical variables between these groups were examined using the χ^2 test for binary and the Kruskal-Wallis test for continuous variables. The resulting p values were corrected using the Benjamini-Hochberg adjustment.[28] A sensitivity analysis excluding people under 18 years of age was also performed.

Second, we used the TAS-20 total score as predictor for a set of clinical non-motor and motor measures, including BDI-II score; BAI score; BPI score; CGI-S score; MFI-20 score; number of motor symptoms; number of associated non-motor symptoms; SF-12 mental health score; S-FMDRS score; type of FMD

onset (acute vs slowly progressing); spontaneous remission of FMD symptoms. In case of continuous outcomes, we performed a Hausman test to decide whether including the recruiting centre as a random or fixed effect. In the case of binary outcomes, we performed logistic models by penalised maximum likelihood regression,[29] to address the issue of quasi-separation, by using a jack-knife estimator (meaning that the command was repeated once for each recruiting centre, leaving the associated cluster out of the calculations). All analyses were adjusted for recruiting centre; sex; age; years of education; childhood trauma; familiar history of neurological disorders; familiar history for psychiatric disorders; neurological comorbidities; medical comorbidities; SF-12 physical health; number of psychiatric comorbidities; number of precipitating factors; presence of physical trauma; presence of psychological trauma; current cognitive-behavioural treatment; number of psychotropic medications; number of current physical treatments. The resulting p values were corrected using the Benjamini-Hochberg adjustment, and CIs of the significant findings were derived accordingly. For each outcome, we assessed the strength of association according to the classification proposed by Ioannidis,[30] indicating three categories: 'moderate' ($0.005<p\leq0.05$), 'strong' ($0.001<p\leq0.005$) and 'very strong' ($p\leq0.001$).

Third, we assessed the possible differences in the impact of the three TAS-20 subscales (ie, difficulty in identifying feelings, difficulty in expressing feelings, and externally oriented thinking) on the measures that showed a significant association with overall TAS-20 score. We used the same models adopted for the main analyses, and again the Benjamini-Hochberg adjustment for p values.

Fourth, for exploratory aims, we performed cluster analysis on TAS-20 score and all outcomes by using the complete linkage method. The dissimilarity matrix was based on Gower's distance to allow us to consider continuous and binary measures simultaneously. We followed the Calinski/Harabasz pseudo-F criterion to select the number of clusters (all options between 2 and 10 were considered).[31]

RESULTS

From a total of 500 individuals included in the IRFMD, we identified 483 eligible participants, as for 17 of them data on alexithymia was not available. Sociodemographic and clinical characteristics are reported in table 1. About three over four participants were female, and the mean age was 45.3 (standard deviation (SD) 16.5). Of those included, 18.2% reported to have experienced childhood trauma, 27.5% had a family history of neurological disorders and 8.3% of psychiatric disorders. A relevant proportion of participants suffered from other medical comorbidities (41.2%), and the physical health was generally poor, as measured by the SF-12 physical health subscale (mean score 34.2, SD 11.5). Physical and psychological precipitating factor could be identified for 18.8% and 24.6% of the population, respectively. As for the characteristics of the FMD, most showed an acute onset of the condition (73.8%). The mean score on the S-FMDRS was 14.0 (SD 9.16). The most represented clinical manifestations were tremor (60.9%), weakness (56.7%), and gait disorders (42.0%) among motor symptoms, and fatigue (59.2%), pain (57.8%), and migraine (40.6%) among non-motor symptoms. Moreover, cognitive deficits (39.7%) and sensitive symptoms (35.2%) were also frequently reported. As for mental health, the population showed mild levels of depression (BDI-II mean score 13.7, SD 10.6) and moderate-to-high levels of anxiety (BAI mean score 20.1, SD 11.5). Nearly half of individuals (49.5%) were receiving some physical treatment for FMD when recruited, 17.0% were receiving some form of psychological treatment and 44.5% were taking a psychopharmacological treatment.

The overall population showed a mean score of 53.2 (SD 14.5) on the TAS-20, with 231 individuals (47.8%) without alexithymia, 100 individuals (20.7%) with possible/borderline alexithymia and 152 individuals (31.5%) with definite alexithymia.

The bivariate approach assessing differences in the distribution of sociodemographic and clinical variables across such categories, after the Benjamini-Hochberg correction, showed that individuals with definite alexithymia were older, received fewer years of education, had lower SF-12 mental health scores and higher CGI-S, BPI and MFI-20 scores.

The multivariate approach using the TAS-20 score as independent variable showed a significant association between alexithymia and 6 of the 12 clinical measures (table 2). The analysis showed a 'very strong' association between higher levels of alexithymia and worse scores on BDI-II, BAI, SF-12 mental health, MFI-20 and BPI. Further, a 'moderate' association emerged between higher levels of alexithymia and a slowly progressing onset of disease. Figure 1 shows predictive margins of the TAS-20 score for such measures. For the remaining measures, including the number of motor symptoms, the CGI-S score, the number of associated non-motor symptoms, and the S-FMDRS score, no association emerged. The sensitivity analysis excluding 14 participants under 18 years of age was largely comparable to the primary analysis in terms of point estimates, outcome of the Hausman tests and ranking of p values (see online supplemental table S3).

Regression models using TAS-20 subscales as independent variables found that higher scores on the subscale 'difficulty describing feelings' (DDF) were associated with worse scores on the BAI and BDI-II; higher scores on the subscale 'difficulty identifying feelings' (DIF) were associated with worse scores on the BAI, BDI-II, SF-12 mental health, MFI-20, and BPI (table 3); and lower scores in the subscale 'externally oriented thinking' (EOT) were associated with worse scores on the BAI (table 3). The test of equality of subscales parameters showed that the difference between the three subscales was significant for the BAI, BDI-II, SF-12 mental health, MFI-20, but not for the BPI.

The cluster analysis revealed three distinct subgroups of patients. The first cluster includes patients with acute onset and higher rates of spontaneous remission. This group exhibits the lowest alexithymia levels, mild anxiety and depression scores. FMD symptom severity is moderate, as are pain, fatigue and associated symptoms. The second cluster includes patients with mostly acute onset and intermediate rates of spontaneous remission. They show the highest alexithymia, anxiety and depression scores, alongside with severe FMD symptoms, pain and fatigue. The third cluster includes patients with slowly progressing onset and lower rates of spontaneous remission. This group shows intermediate levels of alexithymia, anxiety, depression, FMD symptom severity, pain and fatigue (see online supplemental table S4).

DISCUSSION

The present study found alexithymia to be highly prevalent in people with FMD and showed an association between alexithymia and increased psychological distress, fatigue and pain. To our knowledge, this is by far the largest study to examine the personality construct of alexithymia in individuals with FMD.

Table 1 Sociodemographic and clinical characteristics of participants

Variables	Overall (n=483)	No alexithymia (n=231)	Possible alexithymia (n=100)	Alexithymia (n=152)	P value
Female participants, n (%)	363 (75.2)	183 (79.2)	65 (65.0)	115 (75.7)	0.057
Age, mean (SD)	45.3 (16.5)	42.9 (15.6)	45.5 (19.3)	48.9 (15.3)	**0.001***
Years of education, mean (SD)	12.1 (3.6)	12.7 (3.3)	11.7 (3.6)	11.4 (3.8)	**0.005***
Presence of childhood trauma, n (%)	88 (18.2)	43 (18.6)	17 (17.0)	28 (18.4)	0.963
Family history of neurological disorders, n (%)	133 (27.5)	63 (27.3)	28 (28.0)	42 (27.6)	0.990
Family history of psychiatric disorders, n (%)	40 (8.3)	16 (6.9)	7 (7.0)	17 (11.2)	0.322
Presence of medical comorbidities, n (%)	199 (41.2)	88 (38.1)	38 (38.0)	73 (48.0)	0.112
SF-12 physical health, mean (SD)	34.2 (11.5)	35.6 (12.5)	32.6 (10.2)	33.1 (10.4)	0.116
Presence of neurological comorbidities, n (%)	155 (32.1)	71 (30.7)	32 (32.0)	53 (34.9)	0.692
Presence of psychiatric comorbidity, n (%)	184 (38.1)	69 (29.9)	38 (38.0)	77 (50.7)	**<0.001***
SF-12 mental health, mean (SD)	41.9 (12.2)	45.7 (12.0)	40.7 (11.4)	37.0 (11.1)	**<0.001***
BDI-II score, mean (SD)	13.7 (10.6)	9.1 (7.3)	14.7 (9.2)	20.2 (12.0)	**<0.001***
BAI score, mean (SD)	20.1 (11.5)	16.0 (10.1)	21.0 (10.5)	25.8 (11.8)	**<0.001***
CGI-S score, mean (SD)	2.6 (1.6)	2.3 (1.6)	2.5 (1.6)	3.0 (1.7)	**<0.001***
TAS-20 score, mean (SD)	53.2 (14.5)	40.9 (7.6)	56.1 (2.7)	70.1 (7.4)	–
Presence of physical precipitating factors, n (%)	91 (18.8)	40 (17.3)	23 (23.0)	28 (18.4)	0.589
Presence of psychological precipitating factors, n (%)	119 (24.6)	45 (19.5)	26 (26.0)	48 (31.6)	**0.030**
Acute onset of FMD (vs slowly progressing), n (%)	349 (73.8)	177 (78.0)	66 (66.0)	106 (69.7)	0.185
Number of different types of motor symptoms, mean (SD)	2.3 (1.4)	2.2 (1.4)	2.2 (1.1)	2.4 (1.5)	0.566
Type of motor symptom/disorder†					
Tremor, n (%)	294 (60.9)	32 (32.9)	42 (42.0)	71 (46.7)	**0.035**
Weakness, n (%)	274 (56.7)	145 (62.8)	56 (56.0)	73 (48.0)	**0.017**
Gait disorders, n (%)	203 (42.0)	88 (38.1)	43 (43.0)	72 (47.4)	0.190
Dystonia, n (%)	117 (24.2)	58 (25.1)	25 (25.0)	34 (22.4)	0.738
Speech disorders, n (%)	89 (18.4)	40 (17.3)	12 (12.0)	37 (24.3)	**0.023**
Facial movement disorders, n (%)	74 (15.3)	34 (14.7)	13 (13.0)	27 (17.8)	0.417
Non-epileptic seizures, n (%)	69 (14.3)	28 (12.1)	12 (12.0)	29 (19.1)	0.148
S-FMDRS total score, mean (SD)	14.0 (9.16)	13.7 (9.0)	13.2 (8.5)	15.0 (9.8)	0.437
Number of co-occurrent non-motor symptoms, mean (SD)	3.0 (2.0)	2.9 (2.0)	3.1 (2.0)	5.0 (1.8)	0.456
Type of non-motor symptoms†					
Fatigue, n (%)	286 (59.2)	130 (56.3)	64 (64.0)	92 (60.5)	0.376
Pain, n (%)	279 (57.8)	131 (56.7)	60 (60.0)	88 (57.9)	0.861
Migraine, n (%)	196 (40.6)	96 (41.6)	39 (39.0)	61 (40.1)	0.915
Cognitive deficits, n (%)	192 (39.7)	78 (33.8)	47 (47.0)	67 (44.1)	**0.028**
Sensitive symptoms, n (%)	170 (35.2)	90 (39.0)	37 (37.0)	43 (28.3)	0.071
Visual symptoms, n (%)	80 (16.6)	32 (13.8)	19 (19.0)	29 (19.1)	0.306
BPI total score, mean (SD)	38.4 (30.4)	32.3 (29.5)	39.3 (31.5)	47.0 (28.9)	**<0.001***
MFI-20 global score, mean (SD)	14.4 (4.4)	13.4 (4.6)	15.3 (3.7)	15.3 (4.3)	**<0.001***
Any physical treatment for FMD, n (%)	239 (49.5)	117 (50.6)	54 (54.0)	68 (44.7)	0.391
Any psychological treatment, n (%)	82 (17.0)	43 (18.6)	9 (9.0)	30 (19.7)	0.069
Psychopharmacological treatment, n (%)	215 (44.5)	95 (41.1)	47 (47.0)	73 (48.0)	0.356
Spontaneous remission of motor symptoms, n (%)	213 (49.2)	106 (51.0)	41 (46.6)	66 (48.2)	0.679

Missing values: years of education (n=10); acute onset (n=4); S-FMDRS total score (n=9); CGI-S score (n=14); BPI score (n=1); MFI-20 score (n=1); spontaneous remission of motor symptoms (n=15).
Values in bold indicate statistically significant results (i.e., $p < 0.05$).
*Significant after the Benjamini-Hochberg correction.
†Only symptoms/disorders recurring in 15% or more of the overall population are reported.
BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; BPI, Brief Pain Inventory; CGI-S, Clinical Global Impression-Severity; FMD, Functional Motor Disorder; MFI-20, Multidimensional Fatigue Inventory 20 items; SF-12, Short Form 12 items; S-FMDRS, Simplified Functional Movement Disorders Rating Scale; TAS-20, Toronto Alexithymia Scale 20 items.

The association between higher levels of alexithymia and an increased severity of depressive and anxiety symptoms is consistent with previous observations in the general population and in other functional medical conditions.[32–34] Such association is supported by a strong theoretical rationale, as individuals with alexithymia might experience difficulties in identifying and expressing emotions, leading to emotional suppression, maladaptive coping strategies, and ultimately interpersonal challenges and social isolation, which further exacerbate psychological distress. Further, cognitive biases may contribute to negative interpretations of experiences, reinforcing feelings of worthlessness and hopelessness.[35 36]

The association between higher levels of alexithymia and increased fatigue and pain levels expands previous research

Table 2 Results of regression models with the TAS-20 total score as explanatory variable for a set of clinical outcomes

Outcomes	Coef.	Std. coef.	P value*	Benjamini-Hochberg corrected p value	Strength of association
BDI-II score	0.311	0.428	**1.03×10^{-26}**	**1.13×10^{-25}**	Very strong
BAI score	0.321	0.405	**1.02×10^{-17}**	**5.26×10^{-17}**	Very strong
SF-12 mental health	−0.274	−0.327	**1.57×10^{-9}**	**5.74×10^{-9}**	Very strong
MFI-20 score	0.053	0.174	**5.79×10^{-5}**	**1.59×10^{-4}**	Very strong
BPI total score	0.323	0.154	**8.61×10^{-5}**	**1.89×10^{-4}**	Very strong
Acute vs slowly progressing onset	0.019	0.142	**0.013**	**0.024**	Moderate
CGI-S score	0.008	0.068	**0.043**	0.068	No association
Number of motor symptoms	0.009	0.089	0.050	0.068	No association
Number of associated non-motor symptoms	0.010	0.071	0.080	0.098	No association
S-FMDRS score	0.020	0.031	0.514	0.554	No association
FMD spontaneous remission	−0.004	−0.033	0.554	0.554	No association

Values in bold indicate statistically significant results (i.e., $p < 0.05$).
*The model is adjusted for recruiting centre; sex; age; years of education; childhood trauma; familiar history of neurological disorders; familiar history for psychiatric disorders; neurological comorbidities; medical comorbidities; SF-12 physical health; number of psychiatric comorbidities; number of precipitating factors; presence of physical trauma; presence of psychological trauma; current cognitive-behavioural treatment; number of psychotropic medications; number of current physical treatments.
BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BPI, Brief Pain Inventory; CGI, Clinical Global Impression; FMD, Functional Movement Disorder; MFI, Multidimensional Fatigue Inventory; SF-12, Short Form 12-items; S-FMDRS, Simplified Functional Movement Disorders Rating Scale; TAS-20, Toronto Alexithymia Scale 20 items.

suggesting a transdiagnostic link between alexithymia and the burden of somatic symptoms. Meta-research data showed that alexithymia is associated with increased pain intensity and physical interference in people with chronic pain,[34] somatic symptoms disorder[37] and fibromyalgia,[38] while an association with fatigue has been observed in individuals with multiple sclerosis,[39] fibromyalgia[40] and cancer.[41] However, available studies have mostly been conducted in the general medically ill population and in people with functional medical disorders, but not in individuals with FMD. In general, individuals with alexithymia may exhibit heightened sensitivity to physical sensations, fatigue and pain due to lacking self-regulatory feedback, dysregulated stress responses and chronic central sensitisation processes.[42] Higher levels of anxiety and depression, along with dysfunctional self-regulating behaviours, might further exacerbate the symptomatology.

The moderate association between higher levels of alexithymia and slower progression to FMD has not been previously described. In the general population, alexithymia has been repeatedly associated with the phenomenon of delay in seeking medical attention and obtaining an accurate diagnosis due to its influence on the perception and interpretation of early physical manifestations.[33] Understanding this association could provide valuable insights into the psychological factors influencing the onset of FMD and potentially guide targeted approaches aimed at addressing both the physical and emotional aspects of the disorder. Moreover, other factors such as personality traits could also be implicated within this relation,[43] and further investigation is needed.

Interestingly, when analysing TAS-20 subscales separately, we found that most of the observed effect was attributable to higher scores on the DIF subscale and, to a lesser extent, to the DDF subscale, while higher scores on the EOT subscale did not predict any of the clinical outcomes. Some previous studies have shown that higher DIF and DDF scores are associated with more severe clinical manifestations of FMD, although details of specific clinical correlates were not provided (see online supplemental table S1).[14–16] The TAS-20 subscale DIF specifically reflects challenges

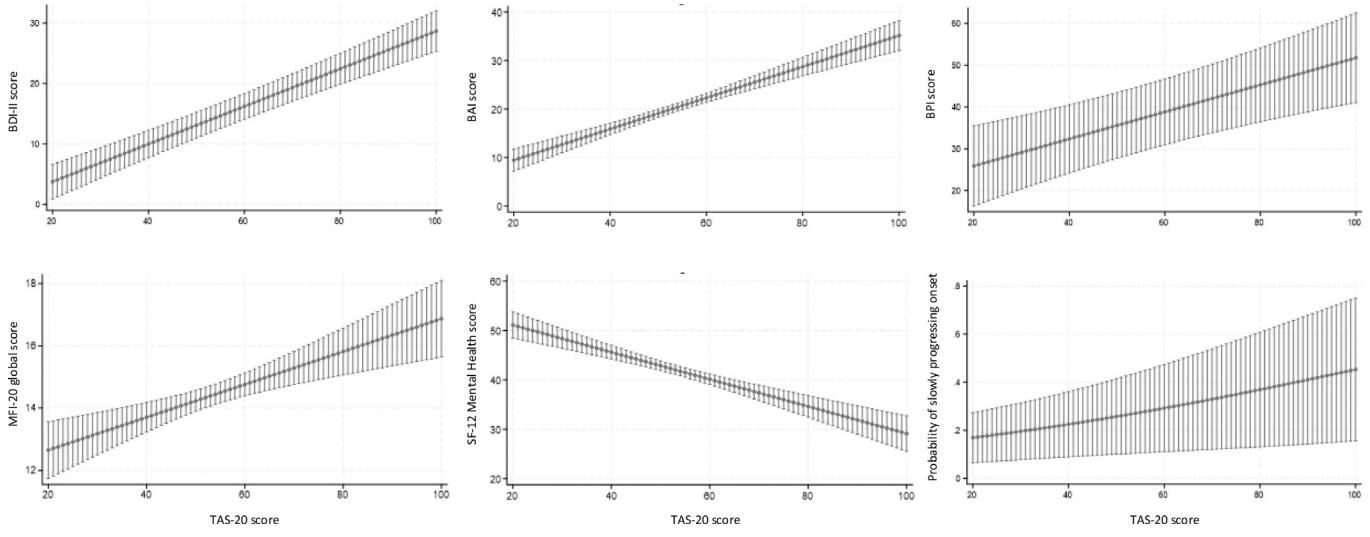

Figure 1 Predictive margins of the TAS-20 with their 95% CI for the six variables significantly associated with alexithymia. BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; BPI, Brief Pain Inventory; MFI-20, Multidimensional Fatigue Inventory; SF-12, Short Form 12-items; TAS-20, Toronto Alexithymia Scale 20 items.

Table 3 Results of regression models with the TAS-20 subscales as explanatory variables

	Difficulty describing feelings		Difficulty identifying feelings		Externally oriented thinking		
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value	P value*
BAI score	0.377 (0.141 to 0.614)	**0.002**	0.647 (0.494 to 0.800)	**<0.001**	−0.199 (−0.352 to −0.046)	**0.011**	**4.45×10^{-12}**
BDI-II score	0.277 (0.056 to 0.497)	**0.014**	0.620 (0.482 to 0.758)	**<0.001**	−0.074 (−0.203 to 0.054)	0.258	**4.38×10^{-11}**
SF-12 mental health	−0.113 (−0.392 to 0.167)	0.429	−0.659 (−0.840 to −0.477)	**<0.001**	0.128 (−0.053 to 0.309)	0.165	**1.90×10^{-7}**
MFI-20 score	0.042 (−0.057 to 0.141)	0.405	0.116 (0.052 to 0.180)	**<0.001**	−0.029 (−0.093 to 0.036)	0.388	**0.016**
BPI total score	0.372 (−0.276 to 1.020)	0.261	0.570 (0.164 to 0.975)	**0.006**	0.001 (−0.375 to 0.378)	0.995	0.150
Acute vs slowly progressing onset	0.066 (−0.019 to 0.152)	0.121	−0.015 (−0.076 to 0.046)	0.616	0.025 (−0.019 to 0.069)	0.253	0.489

Values in bold indicate statistically significant results (i.e., $p < 0.05$).
*Test of equality of subscale parameters.
BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; BPI, Brief Pain Inventory; MFI-20, Multidimensional Fatigue Inventory 20 items; SF-12, Short Form 12 items; TAS-20, Toronto Alexithymia Scale 20 items.

in recognising and verbalising emotions, which could impact how individuals perceive and cope with pain, fatigue and mental distress associated with FMD.

Several limitations should be considered when interpreting the results of this study. First, the cross-sectional design of the study prevents drawing conclusions on a possible causal relationship between alexithymia and clinical characteristics of FMDs, and results should be therefore regarded as merely exploratory. However, alexithymia is a psychological construct that becomes increasingly evident as a personality trait throughout neurodevelopment, and which remains relatively stable over time, and is therefore thought to precede the onset of motor and non-motor clinical manifestations of FMD. Second, we assessed alexithymia with the TAS-20, which is a valuable tool to measure 'subjective alexithymia', although it relies on the individual's self-awareness and ability to accurately report emotional experiences, and responses to the questionnaire might also be biased by social desirability and adherence to cultural norms. Alternative investigational approaches, such as the performance-based 'Levels of Emotional Awareness Scale' can provide a more objective evaluation of emotional processing abilities.[44] Future studies aiming at integrating such complementary constructs could offer a more nuanced understanding of the emotional dysregulation processes underlying FMD. Third, although the regression model included several sociodemographic and clinical potential confounders, some of them might have been imprecisely measured. For instance, simply assessing the presence or absence of a significant childhood trauma cannot be as accurate as administering a validated trauma scale, such as the short form of the Childhood Trauma Questionnaire.[45] Fourth, although individuals were recruited from the age of 10, the setting of recruitment was primarily dedicated to adults, and children and teenagers were relatively few. Therefore, results might be not applicable to this population subgroup. Finally, the psychological construct of alexithymia is complex and deeply interlaced with other constructs for which no assessment was performed, such as childhood adverse events,[46] attachment style,[47] personality traits/dimensions,[48] coping styles[49] and dissociative experiences.[50]

Despite these limitations, results from this study can provide further insights into the mechanisms underlying FMDs, allowing to draw implications for both research and clinical practice. From a research perspective, findings from this study highlight the importance of considering psychological factors, such as alexithymia, in understanding the heterogeneity of FMD presentations and their impact on participants' clinical outcomes. Future research should, therefore, explore the underlying mechanisms linking alexithymia to FMD, and longitudinally assess whether higher levels of alexithymia might predict a poorer prognosis and a weakened response to common rehabilitation programmes, as well as pharmacological and psychological treatments.

In terms of clinical practice, the study underscores the importance of characterising alexithymia in participants with FMD, as it may have implications for prognosis and treatment planning. Alexithymia may be used to identify a subgroup of patients with FMD who are at increased risk of developing mental health problems and who may be the target of indicated preventive interventions. Healthcare professionals should consider incorporating assessments of alexithymia into routine clinical evaluations of individuals with FMD. Additionally, our findings suggest the potential utility of interventions targeting alexithymia in the management of FMD in order to prevent the development of mental health conditions, such as psychotherapy approaches aimed at enhancing emotional awareness and regulation skills.[51] By addressing psychological factors such as alexithymia, clinicians may be able to improve outcomes and quality of life for individuals with FMD and a further step in the research agenda should include the design of randomised-controlled studies to assess the effectiveness of psychosocial interventions specifically targeting alexithymia in people with FMD.

Overall, results from this study contribute to our understanding of the complex interplay between psychological factors and FMD and highlight the importance of integrating psychological assessments and interventions into the multidisciplinary care of individuals with FMD. Further research is needed to elucidate the underlying mechanisms and optimal management strategies for addressing alexithymia in the context of FMD.

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REFERENCES

1 Thenganatt MA, Jankovic J. Psychogenic (Functional) Movement Disorders. *Continuum (Minneap Minn)* 2019;25:1121–40.
2 Ercoli T, Tinazzi M, Geroin C, *et al*. Do demographic and clinical features and comorbidities affect the risk of spread to an additional body site in functional motor disorders? *J Neural Transm (Vienna)* 2022;129:1271–6.
3 Gelauff J, Stone J. Prognosis of functional neurologic disorders. *Handb Clin Neurol* 2016;139:523–41.
4 Espay AJ, Aybek S, Carson A, *et al*. Current Concepts in Diagnosis and Treatment of Functional Neurological Disorders. *JAMA Neurol* 2018;75:1132–41.
5 Tinazzi M, Geroin C, Erro R, *et al*. Functional motor disorders associated with other neurological diseases: Beyond the boundaries of "organic" neurology. *Eur J Neurol* 2021;28:1752–8.
6 Walzl D, Carson AJ, Stone J. The misdiagnosis of functional disorders as other neurological conditions. *J Neurol* 2019;266:2018–26.
7 Fiorio M, Braga M, Marotta A, *et al*. Functional neurological disorder and placebo and nocebo effects: shared mechanisms. *Nat Rev Neurol* 2022;18:624–35.
8 Jungilligens J, Paredes-Echeverri S, Popkirov S, *et al*. A new science of emotion: implications for functional neurological disorder. *Brain (Bacau)* 2022;145:2648–63.
9 Fobian AD, Elliott L. A review of functional neurological symptom disorder etiology and the integrated etiological summary model. *J Psychiatry Neurosci* 2019;44:8–18.
10 Sifneos PE. Alexithymia: past and present. *Am J Psychiatry* 1996;153:137–42.
11 Bucci W. Symptoms and symbols: A multiple code theory of Somatization. *Psychoanal Inq* 1997;17:151–72.
12 Jalilianhasanpour R, Williams B, Gilman I, *et al*. Resilience linked to personality dimensions, alexithymia and affective symptoms in motor functional neurological disorders. *J Psychosom Res* 2018;107:55–61.
13 Kick L, Schleicher D, Ecker A, *et al*. Alexithymia as a mediator between adverse childhood events and the development of psychopathology: a meta-analysis. *Front Psychiatry* 2024;15:1412229.
14 Demartini B, Petrochilos P, Ricciardi L, *et al*. The role of alexithymia in the development of functional motor symptoms (conversion disorder). *J Neurol Neurosurg Psychiatry* 2014;85:1132–7.
15 Gulpek D, Kelemence Kaplan F, Kesebir S, *et al*. Alexithymia in patients with conversion disorder. *Nord J Psychiatry* 2014;68:300–5.
16 Ricciardi L, Nisticò V, Andrenelli E, *et al*. Exploring three levels of interoception in people with functional motor disorders. *Parkinsonism Relat Disord* 2021;86:15–8.
17 Steffen A, Fiess J, Schmidt R, *et al*. "That pulled the rug out from under my feet!" - adverse experiences and altered emotion processing in patients with functional neurological symptoms compared to healthy comparison subjects. *BMC Psychiatry* 2015;15:133.
18 Tinazzi M, Morgante F, Marcuzzo E, *et al*. Clinical Correlates of Functional Motor Disorders: An Italian Multicenter Study. *Mov Disord Clin Pract* 2020;7:920–9.
19 Gupta A, Lang AE. Psychogenic movement disorders. *Curr Opin Neurol* 2009;22:430–6.
20 Nielsen G, Ricciardi L, Meppelink AM, *et al*. A Simplified Version of the Psychogenic Movement Disorders Rating Scale: The Simplified Functional Movement Disorders Rating Scale (S-FMDRS). *Mov Disord Clin Pract* 2017;4:710–6.
21 Ware J, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220–33.
22 Beck AT, Epstein N, Brown G, *et al*. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol* 1988;56:893–7.
23 Beck AT, Steer RA, Ball R, *et al*. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. *J Pers Assess* 1996;67:588–97.
24 Keller S, Bann CM, Dodd SL, *et al*. Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. *Clin J Pain* 2004;20:309–18.
25 Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry (Edgmont)* 2007;4:28–37.
26 Smets EM, Garssen B, Bonke B, *et al*. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *J Psychosom Res* 1995;39:315–25.

27 Bagby RM, Parker JD, Taylor GJ. The twenty-item Toronto Alexithymia Scale--I. Item selection and cross-validation of the factor structure. *J Psychosom Res* 1994;38:23–32.
28 Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society Series B* 1995;57:289–300.
29 Firth D. Bias reduction of maximum likelihood estimates. *Biometrika* 1993;80:27–38.
30 Ioannidis JPA. The Proposal to Lower P Value Thresholds to .005. *JAMA* 2018;319:1429–30.
31 Everitt B. *Cluster Analysis*. Chichester, West Sussex, UK: Wiley, 2011.
32 Bamonti PM, Heisel MJ, Topciu RA, *et al*. Association of alexithymia and depression symptom severity in adults aged 50 years and older. *Am J Geriatr Psychiatry* 2010;18:51–6.
33 Porcelli P, De Carne M, Leandro G. Alexithymia and gastrointestinal-specific anxiety in moderate to severe irritable bowel syndrome. *Compr Psychiatry* 2014;55:1647–53.
34 Aaron RV, Fisher EA, de la Vega R, *et al*. Alexithymia in individuals with chronic pain and its relation to pain intensity, physical interference, depression, and anxiety: a systematic review and meta-analysis. *Pain* 2019;160:994–1006.
35 Preece DA, Mehta A, Petrova K, *et al*. Alexithymia profiles and depression, anxiety, and stress. *J Affect Disord* 2024;357:116–25.
36 Lane RD, Schwartz GE. Levels of emotional awareness: a cognitive-developmental theory and its application to psychopathology. *Am J Psychiatry* 1987;144:133–43.
37 Smakowski A, Hüsing P, Völcker S, *et al*. Psychological risk factors of somatic symptom disorder: A systematic review and meta-analysis of cross-sectional and longitudinal studies. *J Psychosom Res* 2024;181:111608.
38 Habibi Asgarabad M, Salehi Yegaei P, Jafari F, *et al*. The relationship of alexithymia to pain and other symptoms in fibromyalgia: A systematic review and meta-analysis. *Eur J Pain* 2023;27:321–37.
39 Chalah MA, Ayache SS. Alexithymia in multiple sclerosis: A systematic review of literature. *Neuropsychologia* 2017;104:31–47.
40 Montoro CI, Reyes del Paso GA, Duschek S. Alexithymia in fibromyalgia syndrome. *Pers Individ Dif* 2016;102:170–9.
41 Gritti P, Lombardi S, Nobile B, *et al*. Alexithymia and cancer-related fatigue: a controlled cross-sectional study. *Tumori* 2010;96:131–7.
42 Preece DA, Mehta A, Petrova K, *et al*. Alexithymia and emotion regulation. *J Affect Disord* 2023;324:232–8.
43 Perez DL, Aybek S, Popkirov S, *et al*. A Review and Expert Opinion on the Neuropsychiatric Assessment of Motor Functional Neurological Disorders. *J Neuropsychiatry Clin Neurosci* 2021;33:14–26.
44 Lane RD, Smith R. Levels of Emotional Awareness: Theory and Measurement of a Socio-Emotional Skill. *J Intell* 2021;9:42.
45 Badenes-Ribera L, Georgieva S, Tomás JM, *et al*. Internal consistency and test-retest reliability: A reliability generalization meta-analysis of the Childhood Trauma Questionnaire – Short Form (CTQ-SF). *Child Abuse & Neglect* 2024;154:106941.
46 Cerqueira A, Almeida TC. Adverse Childhood Experiences: Relationship with Empathy and Alexithymia. *J Child Adolesc Trauma* 2023;16:559–68.
47 Kajanoja J, Karukivi M, Scheinin NM, *et al*. Early-life adversities and adult attachment in depression and alexithymia. *Dev Psychopathol* 2021;33:1428–36.
48 Grabe HJ, Spitzer C, Freyberger HJ. Alexithymia and personality in relation to dimensions of psychopathology. *Am J Psychiatry* 2004;161:1299–301.
49 Di Tella M, Tesio V, Ghiggia A, *et al*. Coping strategies and perceived social support in fibromyalgia syndrome: Relationship with alexithymia. *Scand J Psychol* 2018;59:167–76.
50 Majohr K-L, Leenen K, Grabe HJ, *et al*. Alexithymia and its relationship to dissociation in patients with panic disorder. *J Nerv Ment Dis* 2011;199:773–7.
51 Iwakabe S, Nakamura K, Thoma NC. Enhancing emotion regulation. *Psychother Res* 2023;33:918–45.