Movement Disorders
CLINICAL PRACTICE
RESEARCH ARTICLE

Elderly Onset of Functional Motor Disorders: Clinical Correlates from the Italian Registry

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Abstract: Background: Functional motor disorders (FMD) are a frequent neurological condition affecting patients with movement disorders. Commonly described in younger adults, their manifestation can be also associated to an elderly onset.

Objective: To assess the prevalence and describe the clinical manifestations of FMD with elderly and younger onset and their relationship with demographical and clinical variables.

Methods: We recruited patients with a "clinically definite" diagnosis of FMD from the Italian Registry of FMD. Patients underwent extensive clinical assessments. For elderly onset, we set a chronological cut-off at 65 years or older according to WHO definition. Multivariate regression models were implemented to estimate adjusted odds ratio of elderly FMD onset related to clinical characteristics.

Results: Among the 410 patients, 34 (8.2%) experienced elderly-onset FMD, with a mean age at onset of 70.9 years. The most common phenotype was tremor (47.1%), followed by gait disorders, weakness, and dystonia (29.4%, 23.5%, 14.7%, respectively). Eleven elderly patients had a combined phenomenology:

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Keywords: functional motor disorders, elderly onset, functional neurological disorders, functional parkinsonism, neurological comorbidities.

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Co-investigators of the IRFMDs are presented in the Appendix.

Received 11 July 2023; revised 6 October 2023; accepted 13 October 2023.
Published online 22 November 2023 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mdc3.13916

9 exhibited two phenotypes, 2 had three phenotypes. Weakness was isolated in 3/8 patients and combined with another phenotype in 5/8, manifesting as paraplegia ($n = 4$); upper limb diplegia ($n = 2$), hemiparesis/hemiplegia ($n = 1$), and tetraparesis/tetraplegia ($n = 1$). Non-motor and other functional neurological disorders occurred more frequently in the younger group (89.1%) than the elderly (73.5%). Neurological and non-neurological comorbidities were more prevalent in the elderly group (82.4%) as opposed to the younger (32.7%). In a multivariate regression analysis, elderly-onset FMD was significantly associated with neurological comorbidities, including parkinsonism (OR 6.73) and cerebrovascular diseases (OR 5.48).

Conclusions: These results highlight the importance of achieving an accurate diagnosis of FMD in the elderly, as it is crucial for effectively managing FMD symptoms and addressing neurological comorbidities.

Functional motor disorders (FMD) refer to clinically heterogeneous manifestations, characterized by involuntary (abnormal) movements that may be significantly reduced by distractive maneuvers and are inconsistent and incongruent with symptoms reported in neurological diseases.[1] They are a frequent neurological condition affecting between 2% and 20% of patients attending movement disorder clinics,[2] and may overlap with other neurological diseases,[3] leading to patients' disability and poor quality of life.[4] Younger adults are more commonly affected by FMD with a mean age at FMD onset ranging from 36.9 to 50 years old.[4–6] Few studies have dealt with FMD in the elderly pointing out that 10–21% of patients may have onset of their symptoms after the age of 60.[5–9] However, these studies may have not adequately addressed the presence of FMD in the elderly and how it differs from the younger age group with FMD. Indeed they may have overestimated the prevalence rates of FMD in the elderly[6–9] because patients were enrolled based on probable diagnosis of FMD rather than a clinical definite diagnosis.[6–8] Moreover, these studies have used 60 years old as the cut-off for defining the elderly population,[6,8,9] but due to the progressive increase of global life expectancy the World Health Organization has set the cut-off for defining the elderly population as 65 years.[10] Finally, many of these cohorts were retrospective studies[5,6,8,9] which may have introduced potential referral bias and lacked specific comparisons between the clinical and demographic characteristics of older individuals with FMD and those with an earlier onset.[5–7,9] Only one retrospective study[8] comparing patients with elderly FMD onset versus a cohort of younger FMD onset examined some clinical characteristics of FMD, however important features such as neurological comorbidities that may coexist in individuals with FMD in more than one third of patients[3,11] have been missed. Identifying FMD in older adults can be challenging because the presence of overlapping possible neurological comorbidities and missing the diagnosis can have important therapeutic implications for patients, such as the initiation of unnecessary and potentially harmful treatments.[12] In particular, the symptoms of FMD may mimic other neurological disorders, making it difficult to differentiate FMD from underlying neurological disease. To overcome these possible limits, we conducted a study using the Italian registry of FMD including FMD patients with a clinically definite diagnosis, 65 as the cut-off for defining the elderly population, and detailed description of several clinical features, to assess the prevalence in a large cohort and describe the clinical manifestations of FMD in individuals with elderly and younger onset and examine their relationship with demographical and clinical variables.

Methods

We extracted data from the Italian Registry of Functional Motor Disorders (IRFMD), managed by the Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, and by the Italian Academy for the Study of Parkinson's Disease and Other Movement Disorders (Accademia LIMPE DISMOV RADAC project) and Fondazione LIMPE. The full methods of IRFMD have been detailed in a previous study.[4] Consecutive outpatients with FMD were recruited from 25 tertiary movement disorders centers, fulfilling the following inclusion criteria: age ≥10 years; a clinically definite diagnosis of FMD based on Gupta and Lang criteria with the presence of positive signs and distractibility maneuvers[13]; and the presence of one or more FMD phenotype including tremor, weakness, jerks, dystonia, gait disorders, parkinsonism, and facial motor disorders. Exclusion criteria considered a cognitive or physical impairment that precluded signing the informed consent form.[4] At each enrolling center, a neurologist expert in movement disorders evaluated patients in a single session, confirmed the diagnosis of FMD and performed a structured interview including several demographical and clinical variables.[4] Demographic data included age and gender (male/female). The clinical manifestations included the onset of FMD and its duration, presence of spontaneous remissions, FMD phenotypes, patients' self-reported nonmotor symptoms (anxiety, panic attacks, depersonalization/derealization, fatigue, pain, headache, insomnia), presence of other functional neurological disorders (FNDs) (functional seizures, sensory and visual functional symptoms), precipitating factors (physical and psychological trauma), the presence of neurological comorbidities (Parkinson's disease and/or parkinsonism, polyneuropathy, hyperkinetic movement disorder, multiple sclerosis, cerebrovascular diseases, migraine, epileptic seizures), the presence of psychiatric and non-neurological comorbidities, and the therapy (medications, physiotherapy and other modalities of intervention). We set the cut-off of elderly

TABLE 1 *Comparison of demographic and clinical features of patients with elderly and younger FMD onset*

Variable	Elderly FMD onset $N = 34$	Younger FMD onset $N = 376$	P value
Gender, *n* (%)			
Female	27 (79.4)	264 (70.2)	0.258
Age, y, mean (SD)	74.3 (5.2)	44.1 (13.9)	**<0.001**
Age at FMD onset, y, mean (SD)	70.9 (5.1)	38.4 (14.6)	**<0.001**
FMD duration, y, mean (SD)	3.4 (2.8)	5.8 (7.0)	0.211
FMD acute onset, *n* (%)	23 (67.6)	267 (71.0)	0.680
FMD spontaneous remission, *n* (%)	17 (50.0)	197 (52.4)	0.789
FMD isolated, *n* (%)	23 (67.6)	199 (52.9)	0.099
FMD combined, *n* (%)	11 (32.4)	177 (47.1)	0.099
FMD phenotype, *n* (%)			
Weakness	8 (23.5)	172 (45.7)	**0.012**
Tremor	16 (47.1)	151 (40.2)	0.433
Dystonia	5 (14.7)	114 (30.3)	0.055
Jerks	4 (11.8)	49 (13.0)	1.000
Facial motor disorders	1 (2.9)	46 (12.2)	0.156
Parkinsonism	3 (8.8)	21 (5.6)	0.437
Gait disorders	10 (29.4)	99 (26.3)	0.697
Nonmotor symptoms, *n* (%)			
Anxiety	18 (52.9)	196 (52.1)	0.928
Panic attacks	1 (2.9)	67 (17.8)	**0.026**
Depersonalization/ derealization	2 (5.9)	37 (9.8)	0.758
Fatigue	7 (20.6)	178 (47.3)	**0.003**
Pain	9 (26.5)	163 (43.4)	0.056
Headache	5 (14.7)	102 (27.1)	0.114
Insomnia	8 (23.5)	104 (27.7)	0.605
Other FNDs, *n* (%)	15 (44.1)	181 (48.1)	0.653
Functional seizures	3 (8.8)	53 (14.1)	0.601
Sensory functional symptoms	3 (8.8)	101 (26.9)	**0.021**
Visual functional symptoms	2 (5.9)	45 (12.0)	0.404
Precipitating factors, *n* (%)			
Physical trauma	1 (2.9)	49 (13.0)	0.102
Psychological trauma	7 (20.6)	107 (28.5)	0.327
Neurological comorbidities, *n* (%)			
Parkinsonism	4 (11.8)	9 (2.4)	**0.017**
Polyneuropathy	1 (2.9)	10 (2.7)	1.000
Hyperkinetic movement disorder	1 (2.9)	7 (1.9)	0.503
Multiple sclerosis	0 (0.0)	5 (1.3)	1.000
Cerebrovascular diseases	5 (14.7)	10 (2.7)	**0.005**
Migraine	1 (2.9)	25 (6.6)	0.712
Epileptic seizures	0 (0.0)	8 (2.1)	1.000
Psychiatric comorbidities, *n* (%)	10 (29.4)	155 (41.2)	0.179
Non-neurological comorbidities, *n* (%)			
Heart diseases	5 (14.7)	23 (6.1)	0.070
Hypertension	18 (52.9)	50 (13.3)	**<0.001**
Diabetes	4 (11.8)	15 (4.0)	0.062
Dyslipidemia	8 (23.5)	31 (8.2)	**0.009**
Oral medication, *n* (%)			
Antidepressant	9 (26.5)	126 (33.5)	0.403
Benzodiazepines	8 (23.5)	103 (27.4)	0.627
Antiepileptics	3 (8.8)	70 (18.6)	0.153
Antipsychotics	1 (2.9)	34 (9.0)	0.340
Painkillers, *n* (%)	5 (14.7)	144 (38.3)	**0.006**
NSAIDs	3 (8.8)	94 (25.0)	**0.034**
Physiotherapy, *n* (%)	7 (20.6)	109 (29.0)	0.298
Botulinum toxin injections, *n* (%)	3 (8.8)	49 (13.0)	0.600
Cognitive behavioral therapy, *n* (%)	1 (2.9)	41 (10.9)	0.233

Abbreviations: FMD, functional motor disorders; FND, functional neurological disorders; NSAIDs, Non-steroidal anti-inflammatory drugs; SD, standard deviation; bold indicates significant values.

age ≥65 years[10] and stratified the total sample into two groups: elderly FMD onset group (age ≥65 years old) and younger FMD onset group (age < 65 years old). Age at FMD onset was considered as the year of the first clinical manifestation of FMD as reported by the patients during the interview.[4] In order to observe potential age-related differences in the clinical and demographical features, we further stratified the population into four groups: group 1, FMD with ages between 2 and 18 years old (pediatric); group 2, FMD with ages between 19 and 39 years old (adulthood); group 3, FMD with ages between 40 to 64 years old (late adulthood); and group 4, FMD with ages between 65 and 83 years old (elderly). The study was approved by the local ethics committee of the coordinator center (University of Verona, Azienda Ospedaliera Universitaria Integrata Verona, Prog. 1757CESC) and confirmed by the ethical committees of each participating center. All patients (or their guardians) were informed about the nature from the study and gave their written consent (consent for research). Patients were free to withdraw from the registry at any time.

Statistical Analysis

Data were expressed as mean ± standard deviation (SD) for continuous variables, frequencies for categorical variables. We compared groups (elderly FMD onset versus younger FMD onset) using the Mann–Whitney *U* test for continuous variables after checking for violations of normal distributions with the Shapiro–Wilk test and Chi-squared (χ^2) test or Fisher's exact test (in case of expected frequencies ≤5) for categorical variables. Logistic regression models were used to estimate the adjusted odds ratio (OR; 95% confidence interval [CI]) of elderly FMD onset (dependent variable) in relation to sociodemographic and clinical characteristics (independent variables). Statistical analyses were performed using SPSS statistical software (version 25; IBM-SPSS, Armonk, NY, USA).

Results

From a total of 410 patients with FMD, 34 (8.2%) were included in the elderly FMD onset group. Of these patients, 79.4% were female, with mean age of 74.3 ± 5.2 years and mean age at FMD onset of 70.9 ± 5.1 years (Table 1). The most frequent phenotype was tremor (47.1%), followed by gait disorders, weakness, and dystonia (29.4%, 23.5%, and 14.7%, respectively). In the elderly, 11 patients had a combined phenomenology: 9 patients had two phenotypes while 2 patients had three phenotypes. Weakness in the elderly was present in 8/34 (23.5%) patients in different forms: in 3/8 patients it was isolated, while in 5/8 patients weakness was combined with another phenotype. In the combined form, weakness was present with the following other phenotypes tremor ($n = 1$), facial motor disorders ($n = 1$), gait disorders ($n = 1$), tremor and jerks ($n = 1$), dystonia and gait disorders ($n = 1$). The body distribution of weakness in the 8 patients was: paraplegia ($n = 4$); upper limb diplegia ($n = 2$); hemiparesis/hemiplegia ($n = 1$); tetraparesis/tetraplegia ($n = 1$). When compared with the younger FMD onset group, elderly FMD patients reported less weakness ($P = 0.012$), panic attacks ($P = 0.026$), fatigue ($P = 0.003$), sensory functional symptoms ($P = 0.021$). Moreover, elderly FMD onset patients reported more neurological and non-neurological comorbidities like parkinsonism ($P = 0.017$), cerebrovascular diseases ($P= 0.005$), hypertension ($P = 0.001$), dyslipidaemia ($P = 0.009$) than younger FMD onset. When considering the pooled symptoms of "non-motor + other FNDs," it was observed that these symptoms occurred more frequently in the younger group (335/376, 89.1%) compared to elderly group (25/34, 73.5%) ($P = 0.024$). Additionally, upon combining "neurological + non neurological comorbidities", it was evident that these comorbidities were more prevalent in the elderly (28/34, 82.4%) as opposed to the younger group (123/376, 32.7%) ($P < 0.001$). Elderly FMD onset reported less use of painkillers ($P = 0.006$) and non-steroidal anti-inflammatory drugs (NSAIDs) ($P = 0.034$) than patients with younger FMD onset (Table 1). After mutually adjusting for the variables reported in Table 1, the multivariate logistic regression model confirmed the association between elderly age at FMD onset and the following variables: fatigue (adjusted OR, 0.27; 95% CI, 0.11–0.68), parkinsonism (adjusted OR, 6.73; 95% CI, 1.63–27.73), cerebrovascular diseases (adjusted OR, 5.48; 95% CI, 1.48–20.25), and hypertension (adjusted OR, 6.79; 95% CI, 3.12–14.80) (Table 2). In the elderly, FMD appeared after the diagnosis of parkinsonism (100%, $n = 4$, mean latency 1.7 ± 2.4 years) and cerebrovascular diseases (100%, $n = 5$, mean latency 1.2 years±0.8 years). In the explorative analysis when

TABLE 2 *Clinical variables associated with elderly FMD onset*

Independent variable	Total sample	OR	95% CI Lower–Upper	*P* value
Patients, *n*	410			
Fatigue, yes vs. no[a]		0.27	0.11–0.68	**0.005**
Parkinsonism, yes vs. no[a]		6.73	1.63–27.73	**0.008**
Cerebrovascular diseases, yes vs. no[a]		5.48	1.48–20.25	**0.011**
Hypertension, yes vs. no[a]		6.79	3.12–14.80	**<0.001**

[a]Reference category. Bold indicates significant values; significant associations at $P < 0.05$.
Abbreviations: CI, confidence interval; FMDs, functional motor disorders; OR, odds ratio.

stratified by four different groups of age, elderly FMD patients showed several age-related comorbidities, including Parkinsonism, cerebrovascular diseases, hypertension and dyslipidaemia. Interestingly, weakness as a functional symptom was less frequent in older patients while the other functional symptoms were equally distributed in the various age groups (Table S1.).

Discussion

In this large multicentre study, we found that 8.2% of FMD patients presented their first FMD symptom onset at the age of 65 or higher. On multivariate regression analysis, parkinsonism, cerebrovascular diseases and hypertension were commonly associated with elderly FMD onset, while fatigue was commonly associated with younger FMD onset. When compared with our sample, the higher prevalence rates reported in the previous literature (10–21%) may be due to the fact that in these cohorts some patients were enrolled based on probable diagnosis of FMD rather than a clinical definite diagnosis[6–8] and many studies have used 60 years old as the cut-off for defining the elderly population.[6,8,9] Therefore, all these studies may have not captured the real frequency of FMD in the elderly.

The diagnosis in older adults can be challenging due to the presence of possible overlapping neurological comorbidities.[3] The diagnosis of FMD may coexist with other neurological disorders up to 22% of patients,[3,11] in particular with parkinsonism and cerebrovascular disease.[3] In the majority of these patients, FMD manifested after the diagnosis of a neurological disease. However, in case of parkinsonism, functional symptoms often predated the parkinsonism diagnosis.[3] We found that parkinsonism and cerebrovascular diseases were commonly associated with FMD in elderly population and were observed to occur following their diagnosis. The elderly are themselves at an increased risk for cerebrovascular disease such as stroke when compared to the general population and its risk factors include among others age and hypertension.[14] In our sample, we found that hypertension was present at the onset of FMD in the elderly patients. Therefore the presence of comorbid neurological diseases seem to affect in particular older patients. A recent survey conducted by the International Movement Disorder Society revealed that neurologists consider the extremes of age (75 years) as "very influential" in leading to diagnoses other than FMD.[15] Consequently, FMD may be underdiagnosed in older adults. The less frequent diagnosis of weakness in our older patients may be in line with this view.

Neurologists treating elderly patients with movement disorders need to be aware regarding the possibility that FMD may be the main cause of disability. Functional tremor and gait disorders were the most commonly reported clinical manifestations in patients with elderly FMD onset.[5,8,9] Consistent with previous studies, tremor (47.1%) and gait disorders (29.4%) were also the most frequently reported symptoms in our cohort of patients with elderly FMD onset. A previous study indicated that functional gait phenotype was significantly more prevalent in individual with elderly FMD onset than in the younger population.[8] However, authors did not find any significant differences in other features such as the other types of phenotype, presence of precipitating factors or psychiatric comorbidities.[8] In our sample, we did not identify a distinct phenotype or risk factor for a specific group of FMD, suggesting that the clinical signs may not differ significantly across lifespan.[6] Therefore, our findings support the importance of establishing a comprehensive diagnosis in elderly people with FMD, rather than relying solely on phenotype or other clinical characteristics.[6] Our explorative analysis suggests that patients with elderly FMD onset may have a shorter disease duration likely due to delayed diagnosis, and confirm the presence of additional neurological comorbidities.

Among the non-motor symptoms, fatigue appears to be more characteristic of the younger FMD group. Generally, fatigue affects 45% up to 82% of FMD patients,[4,16,17] and in our sample, it was predominant in the younger FMD group (47.3%) and less common in the elderly FMD group (20.6%). These findings align with a previous large international survey ($n = 1048$) that reported fatigue as a symptom in up to 93% of patients with functional neurological disorders, with only 2% ($n = 23$) of those being individuals aged ≥65 years old.[18] In our study, the lower occurrence of fatigue among older FMD may be related to a smaller sample size in the elderly FMD or the challenges associated with diagnosing this symptom in older age, especially when it coexists with other neurological comorbidities. A significant number of FMD patients experience fatigue, even when compared to individuals with organic neurological disorders.[17] Fatigue plays a crucial role in FMD and is significantly associated with reduced quality of life and lower self-rated health in these patients, regardless of the severity of the FMD. Therefore, the role of fatigue in FMD should be acknowledged in clinical practice and addressed with tailored intervention.[17]

The main limitation of our study is the lack of a control group, as well as the cross-sectional design and the reliance on clinical records and patient self-reports which may introduce recall bias. Additionally, we were unable to assess the severity of recorded symptoms due to the absence of rating instrument for them, as well as evaluate the effects of treatments (ie, botulinum toxin or physiotherapy, others). However, the main strength of our work lies in the large multicenter sample of patients with FMD, which is representative of the entire Italian national territory. The standardized collection of clinical data across all centers allowed us to provide novel insights into the presence of FMD in the elderly population using a definite diagnosis of FMD confirmed by a neurologist expert in movement disorders, 65 years old as the cuff-off for defining FMD onset in the elderly population, and including a detailed description of neurological comorbidities. These findings emphasize the importance of accurate diagnosis in the elderly individuals with FMD, as it can aid effectively managing FMD symptoms and addressing associated neurological comorbidities. Collaboration between geriatricians and neurologists specialized in movement disorders is encouraged to develop and implement efficient and timely diagnostic and treatment approaches.[7] In the elderly, a missed or incorrect diagnosis can have serious consequences, including the initiation of unnecessary and potentially harmful therapies for an alternative neurological diagnosis. Longitudinal studies are needed to investigate

the long-term outcome of elderly FMD onset, including its impact in terms of disease severity, functional disability and therapeutical interventions.

Appendix

Coinvestigators. Italian Registry of Functional Motor Disorders Study Group.

Authors Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the first draft, B. Review and Critique.

C.G.: 1A, 1B, 1C; 2A, 2C; 3A, 3B
M.P.: 1A, 1B, 1C; 2A, 2C; 3A, 3B
S.D.T.: 1C, 2B, 2C, 3B
E.M.: 1C, 2C, 3B
R.E.: 1C, 2C, 3B
S.C.: 1C, 2C, 3B
R.C.: 1C, 2C, 3B
S.M.: 1C, 2C, 3B
A.P.: 1C, 2C, 3B
A.P.: 1C, 2C, 3B
L.M.R.: 1C, 2C, 3B
R.E.: 1C, 2C, 3B
M.Z.: 1C, 2C, 3B
A.N.: 1C, 2C, 3B
C.D.: 1C, 2C, 3B
C.A.: 1C, 2C, 3B
F.B.: 1C, 2C, 3B
V.L.: 1C, 2C, 3B
B.D.: 1C, 2C, 3B
O.G.: 1C, 2C, 3B
N.M.: 1C, 2C, 3B
E.O.: 1C, 2C, 3B
L.B.: 1C, 2C, 3B
A.A.: 1C, 2C, 3B
G.F.: 1C, 2C, 3B
A.T.: 1C, 2C, 3B
L.L.: 1C, 2C, 3B
G.C.B.: 1C, 2C, 3B
F.M.: 1C, 2C, 3B
M.E.: 1C, 2C, 3B
A.P.: 1C, 2C, 3B
P.M.: 1C, 2C, 3B
L.T.: 1C, 2C, 3B
F.T.: 1C, 2C, 3B
S.C.: 1C, 2C, 3B
T.E.: 1C, 2C, 3B
F.S.: 1C, 2C, 3B
M.C.M.: 1C, 2C, 3B
G.D.: 1A, 1B, 1C; 2A, 2C; 3A, 3B
M.T.: 1A, 1B, 1C; 2A, 2C; 3A, 3B

Disclosures

Ethical Compliance Statement: Approval was obtained by the Institutional Ethics Committee of the Coordinator Centre (University of Verona, Azienda Ospedaliera Universitaria Integrata Verona, Project Number. 1757CESC) and confirmed by the committees of each participating center. All patients (or their guardians) were informed about the nature of the study and gave their written consent to participate (consent for research). Participants were free to withdraw from the registry at any time. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Funding Sources and Conflicts of Interest: The authors declare that there are no conflicts of interest to report.

Financial Disclosures for the Previous 12 Months: Francesca Morgante reports receiving speaking fees from Abbvie, Medtronic, Zambon, Bial, Merz; travel grants from the International Parkinson's Disease and Movement Disorder Society; advisory board fees from Merz; consultancy fees from Merz and Bial; research support from Boston Scientific, Merz, and Global Kynetic; royalties for the book entitled Disorders of Movement, Springer Verlag; is a member of the editorial board of Movement Disorders, Movement Disorders Clinical Practice, and European Journal of Neurology. Roberto Erro reports receiving honoraria from UCB, Bial, the International Society for Parkinson's Disease and Movement Disorders and the American Academy of Neurology. Andrea Pilotto has served on the advisory board of Z-cube (technology division of Zambon Pharmaceuticals); he received honoraria from Z-cube s.r.l., Biomarin, Zambon, Nutricia, and Chiesi Pharmaceuticals. He received grant funding from the Ministry of Health and H2020 calls and independent research support from Vitaflo Germany and Zambon Italy. Alessandro Padovani is a consultant and has served on the scientific advisory board of GE Healthcare, Eli Lilly, and Actelion Ltd Pharmaceuticals; he has received speaker fees from Nutricia, PIAM (PIAM Pharma & Integrative Care), Lansgstone Technol- ogy, GE Healthcare, Eli Lilly, UCB Pharma, and Chiesi Pharmaceuticals; and grants from the Ministry of the University, H2020, JPND (EU Joint Programme—Neurodegenerative Disease Research), CARIPLO restricted grants; and independent research support from Zambon, Italy. Fabrizio Stocchi reports receiving research/grant support from Zambon; he has received honoraria/consulting fees/compensation for advisory boards from Bial, Chiesi, Neuroderm, Britannia, Sunovion Pharmaceuticals Inc., Lundbeck, Zambon, Cynapsus, Biogen, and Kyowa. All other authors have no disclosures to report. ■

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Supporting Information

Supporting information may be found in the online version of this article.

Supplementary Table S1. Comparison of demographic and clinical features of patients with different FMD age of onset.