Neurophysiological Evidence of Motor Network Reorganization in Myotonic Dystrophy Type 1: A Pilot Magnetoencephalographic Study

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Purpose: Myotonic dystrophy type 1 is the most common muscular dystrophy in adults. Although brain involvement is well recognized, the relationship between cortical motor control and voluntary movement has not been sufficiently explored. This study aims at assessing magnetoencephalographic (MEG) rhythms at oscillatory and connectivity levels to map central motor control.

Methods: Magnetoencephalographic data were acquired from healthy subjects and five myotonic dystrophy type 1 subjects during resting state and foot movement. Resting state EEG band power, event-related desynchronization/synchronization, functional connectivity, and network features (node strength and betweenness centrality) were estimated. A statistical comparison of these indexes between the two groups was run; a linear correlation between event-related desynchronization and motor performance was obtained.

Results: Myotonic dystrophy type 1 subjects showed higher theta power over central motor regions and lower beta power over frontal areas, with a decrease of beta node strength over the dominant hemisphere and an increase of betweenness centrality over the vertex. Foot movement in the most impaired myotonic dystrophy type 1 subjects was inefficient in evoking event-related desynchronization. In less severely impaired participants, dominant foot movement was related to a bilateral sensorimotor event-related desynchronization.

Conclusions: Results provide proof of a central dysfunction of movement. Identification of neurophysiological motor patterns in myotonic dystrophy type 1 could provide a guide for tailored therapy.

Key Words: MEG, Event-related synchronization/desynchronization, Coherence, Node strength, Betweenness centrality, Foot movement.

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Myotonic dystrophy type 1 (DM1), the most common form of adult muscular dystrophy, is caused by a trinucleotide (cytosine-thymine-guaine) expansion in the 3′ noncoding region of the myotonic dystrophy protein kinase gene on chromosome 19q13.3.[1] Expanded *myotonic dystrophy protein kinase* transcripts are toxic and are responsible for the wide range of DM1 clinical manifestations, as skeletal muscle and respiratory muscles involvement, cardiac conduction defects, and endocrine and gastrointestinal tract dysfunctions.[1–4] Brain involvement has been well described by clinical, neuropathological and neuroimaging studies. A wide range of structural brain abnormalities, such as white matter tracts alterations, gray matter cortical and subcortical atrophy, and abnormalities in cerebral metabolites, have been reported.[5,6]

The relationship between cortical motor control and voluntary movement has not been sufficiently explored in DM1. Mitsuoka et al.[7] evidenced a reduced amplitude of Bereitschaftspotential and negative slope suggesting that subclinical abnormality of central nervous system function was associated with movement preparation and execution, with no correlation to the clinical picture. A delayed central motor conduction time, abnormal sensorimotor (SM) plasticity independent of the primitive motor damage, and hyperexcitability in the sensory cortex have been demonstrated by transcranial magnetic stimulation and somatosensory-evoked potentials.[8–10] Functional magnetic resonance imaging evidenced changes in functional motor activity with advancing age and a marked frontal disconnection coupled with an increased parieto-cerebellar connectivity.[11,12]

A suppression of alpha and beta activity detected at the central region of the scalp has been shown to be associated with movements and motor imagery (for review, see[13]). These task-related changes, measured by EEG or magnetoencephalography (MEG), have been interpreted to be induced by the changes in synchrony of the underlying neuronal populations. They are usually termed event-related desynchronization (ERD) and event-related synchronization (ERS); ERD signals in alpha and beta band powers decrease over premotor and primary SM cortex during movement, and ERS indicates an increase in activity of the same EEG bands at movement conclusion.[14] Abnormalities of cortical activation related to movement execution, quantified by ERD/ERS, are a feature of different neurologic disorders as Parkinson disease[15] and stroke.[16,17] ERD can be interpreted as an electrophysiological correlate of activated cortical areas involved in processing sensory or cognitive information or in the production of a motor behavior. An increased or more widespread ERD could be the result of the involvement of a larger neural network in information processing.[13]

The identification of cerebral mechanisms involved in voluntary movement is essential in DM1, in light of the possible application of new rehabilitative techniques aimed to modulate noninvasively cerebral activity, as transcranial neuromodulation or neuromuscular electrical stimulation. In particular, recent

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studies[18,19] demonstrated that muscle strength improvement after short-term neuromuscular electrical stimulation is related to activity-dependent plasticity in supraspinal centers rather than changes at the muscular level. Neuromuscular electrical stimulation results in a multitude of neurally mediated responses that contribute substantially to force generation and may engender neural adaptations. Our recent study on short-term functional neuromuscular electrical stimulation in DM1[20] supports these findings, showing an improvement of muscle strength not accompanied by muscle variation at MRI.

Magnetoencephalography is an excellent technique for exploring the oscillatory dynamics of the brain. As EEG, it allows to investigate ERD/ERS during movement, but it has the advantages that the brain signals are unaffected by the conductivity differences of the brain and tissues, giving MEG a better spatial accuracy. Data from MEG on cortical oscillatory activity during movement and on functional connectivity are lacking in DM1. Magnetoencephalography, as other neurophysiologic techniques, allows to investigate functional connectivity between brain regions that describes the interactions between differently organized cortical regions, reflecting temporal synchrony among these regions. Coherence function is a measure of the synchronization between two signals at a given frequency. Graph-based methods can elucidate network structures, capturing the complexity and providing useful measures to characterize the topological proprieties and the functional organization of the networks. Among standard network indices, node strength (NS) and betweenness centrality (BC) represent measures of node centrality, which quantify the functional importance of each node with respect to the rest of the network, identifying nodes, which play a key role in functional integration, dubbed "hubs". These nodes could be more critical for information processing, and abnormal connectivity between hubs could cause more deficits compared with peripheral nodes.[21]

The aim of the study was two-fold: (1) to investigate resting-state brain oscillatory activity and functional connectivity, given the poor understanding of the neural mechanisms underlying these processes in DM1 and (2) to evaluate oscillatory activity changes during movement in light of the possible application of innovative rehabilitative techniques. To do so, MEG's resting-state relative powers, coherence as a measure of functional connectivity, and ERD/ERS during movement were extracted and correlated to motor deficits.

METHODS

Participants and Clinical Assessment

Five patients with a genetically proven diagnosis of DM1 (1 woman; mean age, 50.8 years ± SD 13.97) were recruited. Inclusion criteria were as follows: age $>$ 18 years; muscular impairment rating scale $>$ 2; presence of moderate to severe tibialis anterior muscle weakness (Medical Research Councils-cale $<$ 5); and ability to walk. Exclusion criterion was cardiac device implant.

Muscle strength was assessed by a trained physician using the Medical Research Council scale. Functional measures included the 6-minute walk test (6MWT) and the timed 10-meter walk test (10MWT) to evaluate endurance and gait speed, respectively. Neuropsychological evaluation[22] included an estimated intelligence quotient (brief intelligence test), selective attention and cognitive flexibility assessment (trail making tests [A and B]), automatic response inhibition test (stroop test), frontal and executive functions assessment (phonemic verbal fluency test, frontal assessment battery and modified Wisconsin Card Sorting Test), and spatial organization and visuo-constructional skills (Rey–Osterrieth Complex Figure). Participants' raw scores were corrected according to Italian normative values.[23]

Five healthy subjects (3 women; mean age, 39 years ± SD 5.85) served as the comparison group. All subjects were right handed[24] and right footed (Waterloo Handedness Questionnaire[25]). Informed consent was acquired from all the participants. The investigation and use of patients' data for research purposes was approved by the local research ethics committee in accordance with the Declaration of Helsinki.

MEG Data and Experimental Paradigm

The brain's magnetic field was recorded using a 275-channel MEG system (CTF Systems Inc, Vancouver, Canada) in a magnetically shielded room. To ensure continuous recordings of the head position relative to the MEG sensors during the measurement, localization coils were attached to the nasion and the preauricular points on each side of the head of the subject. Data were acquired at a rate of 600 Hz using a band-pass filter from 0.5 to 70 Hz. To remove low-frequency environmental magnetic noise in the magnetically shielded room, an adaptive software noise reduction technique (third-order synthetic gradiometer) was used.

Magnetoencephalography data were acquired during a resting-state condition with eyes closed for 5 minutes and during right cyclic ankle foot movements with a 1-Hz frequency, following a blocked design protocol. Eight runs of rest alternating with seven runs of execution were performed (each run lasting 15 s). The subjects were instructed to start and stop the motor task based on visual cues. Subjects were asked to lie supine on a bed and instructed to keep their eyes open and to look at a fixed point on the screen during the task.

MEG Data Analysis

The MATLAB (MathWorks, Natick, MA) package FieldTrip was used for data analysis (http://www.ru.nl/fcdonders/fieldtrip) together with custom-written routines. Magnetoencephalography data were band-pass filtered from 1 to 30 Hz, and trials contaminated by artifacts, such as eye-blinks and sensor jumps, were rejected. A fast Fourier transform was applied to non–overlapping epochs of 2 seconds and then averaged across epochs. The recordings were Hanning windowed to control for spectral leakage. Power spectra were estimated for all frequencies between 1 and 30 Hz, then the relative power (%) was calculated in the resting-state condition by dividing the power of each frequency bands (delta [1–4 Hz], theta [4.5–7.5 Hz], alpha [8–12 Hz], and beta [13–30 Hz]) with the power of 1 to 30 Hz. The non–parametric Mann-Whitney-Wilcoxon test was performed to

identify significant differences between controls and DM1 subjects (maps were thresholded at $P < 0.05$).

To study the functional connectivity differences among groups, coherence was computed using fast Fourier transform according to the equation:

$$\mathrm{Coh}_{xy}(f) = \frac{|S_{xy}(f)|^2}{S_x(f)S_y(f)} \quad (1)$$

where $S_x(f)$ and $S_y(f)$ are the power spectral densities of two MEG sensors x and y, respectively, $S_{xy}(f)$ is the cross power spectral density of x and y, and f is the reference frequency band. After averaging across epochs, the estimates of auto spectra and cross spectrum were obtained and then an estimate of the coherence was computed in the same frequency ranges (delta, theta, alpha, and beta).

Graph analysis was used for assessing the network model properties. The brain network was constructed based on the unthresholded spectral coherence values of the MEG sensors/nodes, using the coherence value as the weight of the edge connecting the two nodes (adjacency matrix). To characterize the network graph parameters, NS and BC were calculated using an open-source toolbox (Brain Connectivity Toolbox, https://sites.google.com/site/bctnet/Home) and in-house software (MATLAB). NS represents the sum of weights of links connected to the node—i.e., the number of connection that a given node has with any other node of the network. Nodes with the highest number of connections ("hubs") have a preeminent function in a given task or state. Betweenness centrality indicates the centrality of a node in a network and is considered equal to the number of shortest paths from all vertices to all others that pass through that node. A node with high BC has a large influence on the transfer of items through the network under the assumption that item transfer follows the shortest paths.

To obtain statistical inference regarding groups' differences in network parameters, a Mann-Whitney-Wilcoxon test ($P < 0.05$) was performed. Two-dimensional maps of each parameter were computed from the P values to detect the topographical distribution of the significance.

An ERD/ERS procedure was used to quantify the event-related changes in alpha and beta MEG power during foot movement.[14,26] A one-sample z-test was applied to compare the map of each patient with DM1 to the grand average of controls.[27] The statistical map defines the sensors in which ERD from an individual DM1 participant differs statistically from that of a reference population (control group).

A laterality index (LI), describing the contrast in the amount of activation (i.e., mean spectral power in alpha and beta bands) between the right and left hemisphere, was calculated as $(C - I)/(C + I)$ during the ankle movement task, where C is the mean spectral power of the sensors over the contralateral (left) primary SM area and I is the mean spectral power of the sensors over the ipsilateral (right) primary SM area. Laterality index can thus range from $+1$ (exclusively contralateral) to -1 (exclusively ipsilateral).

For all subjects, a linear regression (Statistical Toolbox, MATLAB) between the number of sensors with significant ERD values and motor clinical test (6 MWT and 10WMT), Medical Research Council and Muscular Impairment Rating Scale were calculated and a polynomial fitting with confidential intervals displayed. The Spearman rank correlation coefficient (nonparametric) was computed ($P < 0.05$ was considered statistically significant).

TABLE 1. Functional Assessments and Muscle Strength

	Participants				
Outcome Measures	**1**	**2**	**3**	**4**	**5**
MRC quadriceps (R/L)	5/5	5/5	5/5	5/5	5/5
MRC hamstrings (R/L)	4-/4-	4-/4-	4+/4	5/5	5/5
MRC tibialis anterior (R/L)	3+/3+	2/2	3+/4	4/4	3-/3-
MRC gastrocnemius (R/L)	5/5	4/4	5/5	5/5	5/5
6MWT (meters)	273	290	500	447	425
10MWT (seconds)	6.5	11	8	6	6

L, left; MRC, medical research council scale; 6MWT, six-minute walk test; 10MWT, 10-meter walk test; R, right.

RESULTS

Clinical Assessment

Results of neurologic examination and neuropsychological assessment are reported in Table 1 and 2. Participants were all within normal/high range intelligence score values. Neuropsychological testing scores were reported as equivalent values, a normalization procedure according to which values of 0 and 1 represent pathologic scores, whereas 2 to 4 indicate within the normal range values. Our subjects scored poorly on the frontal function tests (Wisconsin Card Sorting Test and Frontal Assessment Battery); only one subject displayed also a memory and attention deficit.

Resting State

A significant theta power increase that was observed over the bilateral SM area in DM1 associated with a significant beta

TABLE 2. Neuropsychological Assessment

	Participants				
Outcome Measures	**1**	**2**	**3**	**4**	**5**
Trail making test AB	4	1	4	4	2
STROOP time	3	0	3	2	3
STROOP error	3	2	3	4	2
FAS	4	2	4	4	4
FAB	3	3	0	2	4
WCST categories	1	1	1	4	4
WCST-perseverative errors	1	0	2	4	3
Rey Osterrieth Figure Copy	2	4	4	4	4
Rey Osterrieth Figure Memory	0	1	4	1	4
Brief intelligence test	109.07	114.42	107.18	115.21	115.95

FAS, phonemic verbal fluency test; FAB, frontal assessment battery; WCST, Wisconsin card sorting test.

power decrease in frontal regions in comparison to healthy controls (Fig. 1).

Node strength and BC averaged across controls and DM1 subjects were computed to infer the network topology in a resting state (Fig. 2). Myotonic dystrophy type 1 subjects showed a high degree of NS over motor and frontal areas in delta and theta bands, a slight reduction in alpha frequencies over motor areas, and a marked, significant reduction of NS in beta over the left SM and frontal area. Betweenness centrality was primarily localized over the vertex with high degree in DM1 in all frequency ranges. Statistical comparison showed an increase of BC in subjects with DM1 compared with controls over the vertex in alpha and beta bands.

Motor Domain

As compared to healthy controls, patients presented greater and widespread ERD over the SM cortex during right foot movement.

Individual analysis highlighted two different patterns: (1) an almost absent ERD over the contralateral SM both in the alpha and beta bands in comparison to healthy controls during right-paced ankle flexion-extension, with a patchy activity over the ipsilateral SM (Fig. 3). This aspect was particularly evident in subjects nos. 1 and 2 who presented worst functional performances (mean six-minute walk test $<$ 300 m; mean 10MWT 8.75 s). (2) A bilateral ERD in the beta and a lesser extent in the alpha band, as shown in (Fig. 3) for subjects nos. 3, 4, and 5 who had a better functional performance (mean 6-minute walk test $>$ 400 m; mean 10MWT 6.6 s).

Laterality index confirmed beta band prevalence over the ipsilateral hemisphere and alpha rhythm over contralateral SM during right foot movement in better performing patients and an almost completely lateralized activity over the ipsilateral (right) hemisphere in poor performers (Fig. 4).

Correlation with Clinical Data

Spearman correlation identified a trend toward a coupling of better performance (measured by 6 MWT and 10MWT) and a larger cortical activated area, mainly for alpha desynchronization during movement (ERD vs. 10WMT, $R = -0.97$, $p = 0.03$) (Fig. 5).

No correlations were found between neurophysiological parameters and the degree of clinical impairment (measured by Medical Research Council and Muscular Impairment Rating Scale).

DISCUSSION

Our results provide evidence of brain oscillatory activity and connectivity abnormalities in subjects with DM1, related to functional impairment of the motor system, evident during performance of a simple motor task. Lower limb movement in the most functionally impaired subjects was inefficient in evoking desynchronization of oscillatory activity. In less functionally impaired subjects, a right foot movement was coupled to a bilateral SM ERD. In addition, DM1 subjects showed higher theta power over central motor regions and lower beta power over frontal regions, with a remarkable decrease of beta band node strength over the dominant (left) hemisphere and an increase of BC over the vertex.

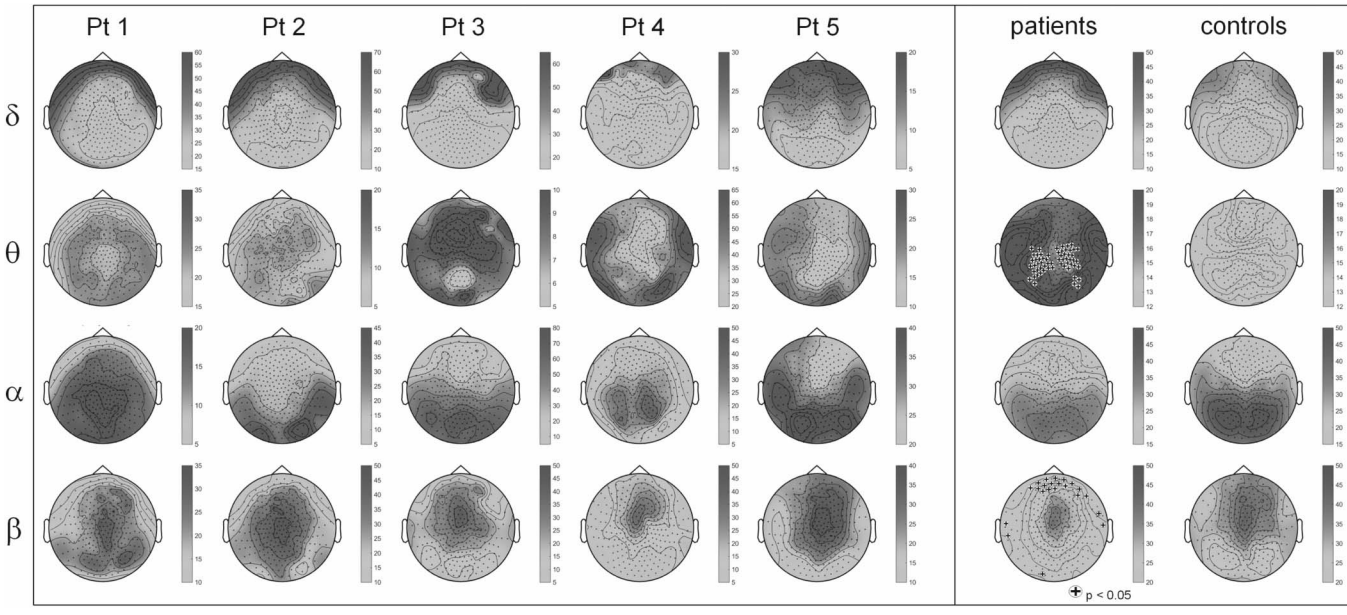

FIG. 1. Resting state MEG data. Relative power maps (%) for each patient with DM1 and grand average map for patients and controls in delta (1–4 Hz), theta (4.5–7.5 Hz), alpha (8–12 Hz), and beta (13–30 Hz) bands. Red coding indicates maximal relative power. A Mann-Whitney-Wilcoxon test was performed to compare the relative powers of the two groups. Legend: $P < 0.05$ indicated by (+). DM1, myotonic dystrophy type 1; MEG, magnetoencephalography.

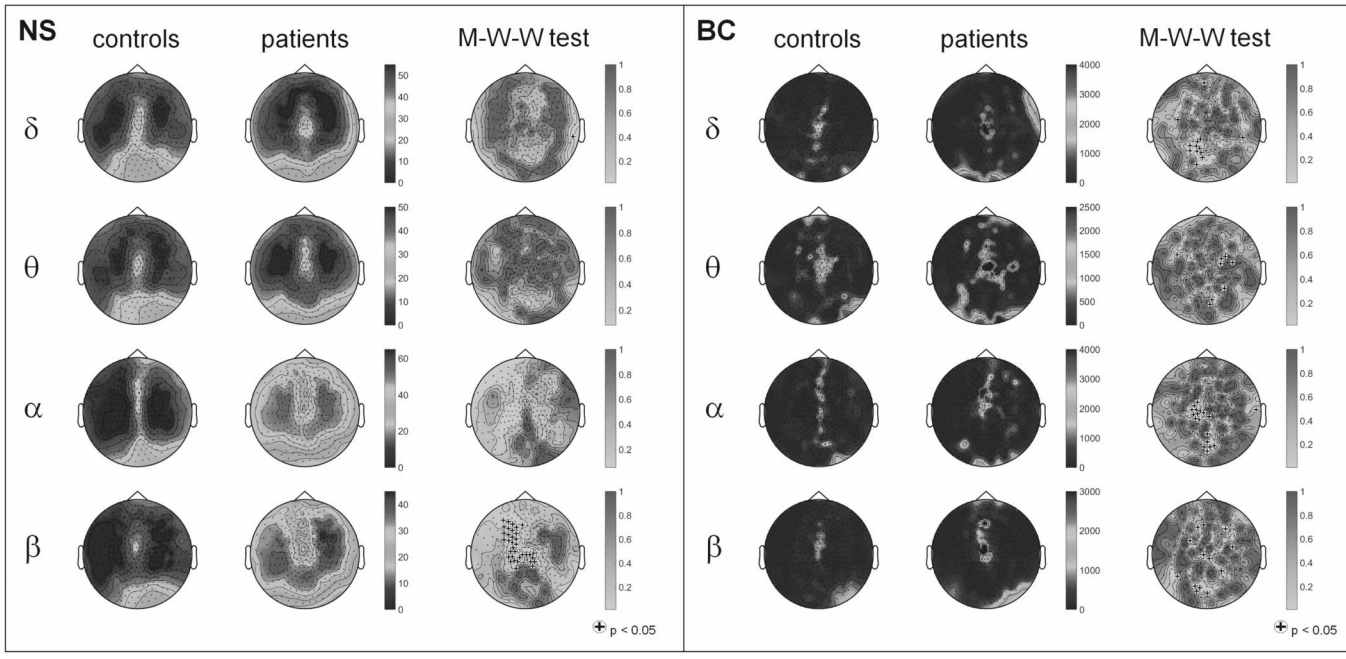

FIG. 2. Network parameters. Controls' and patients' grand average node strength (NS) and betweenness centrality (BC) in delta (1–4 Hz), theta (4.5–7.5 Hz), alpha (8–12 Hz), and beta (13–30 Hz) bands. P-maps, derived from Mann-Whitney-Wilcoxon test (M-W-W test) (controls vs. patients), of network parameters, thresholded at $P < 0.05$ (+).

Involvement of the central nervous system is an emerging datum in DM1. A central involvement of motor control has been suggested by functional magnetic resonance imaging[11] and is further supported by our neurophysiological results (ERD/ERS), describing greater activation over SM areas after movement compared with controls. The main finding of our study is a marked neurophysiological alteration related to lower limb movements, with a suggestive coupling of ambulation function with central activations, even in the absence of a correlation with clinical scales. An almost absent ERD was detected in participants with poor functional performance at walking tests, suggesting the inability of the motor cortex to transfer a command through the corticospinal tract to the final effectors.

Subjects with DM1 with a better performance showed a bilateral activation of SM areas, as if a compensatory mechanism was taking place:[28] The ipsilateral motor areas vicariate the loss of function of the cortex, which should generate the movement. A similar compensatory mechanism has been

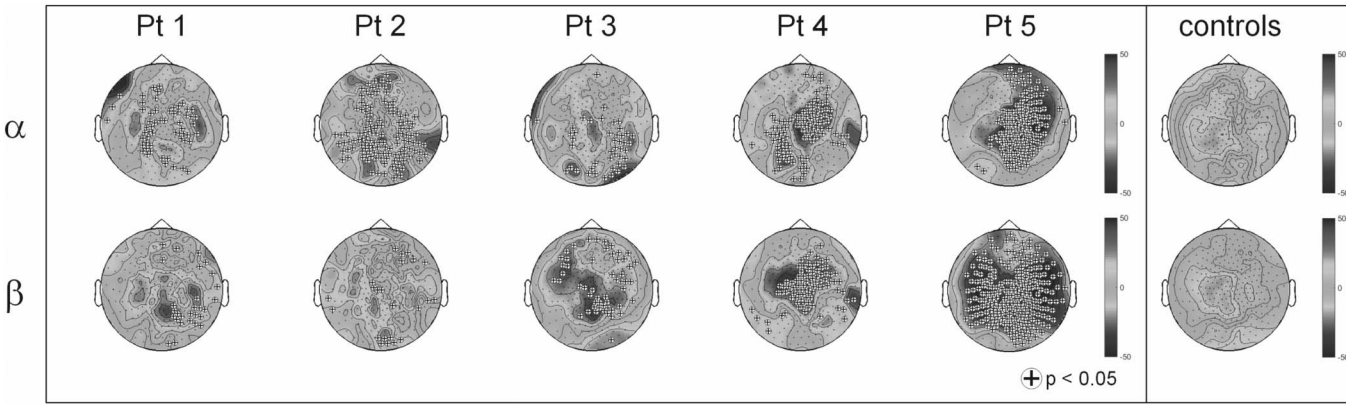

FIG. 3. MEG data during foot movement. ERD/ERS values in DM1 subjects during right foot movement. Negative values of event-related power percentage changes represented the event-related desynchronization ERD (blue color), whereas positive values indicated the event-related synchronization ERS (red color). The z-test was applied to compare the ERD/ERS map of each patient to the mean ERD/ERS map of the controls (on the right). Legend: $P < 0.05$ indicated by (+).DM1, myotonic dystrophy type 1; ERD, event-related desynchronization; ERS, event-related synchronization; MEG, magnetoencephalography.

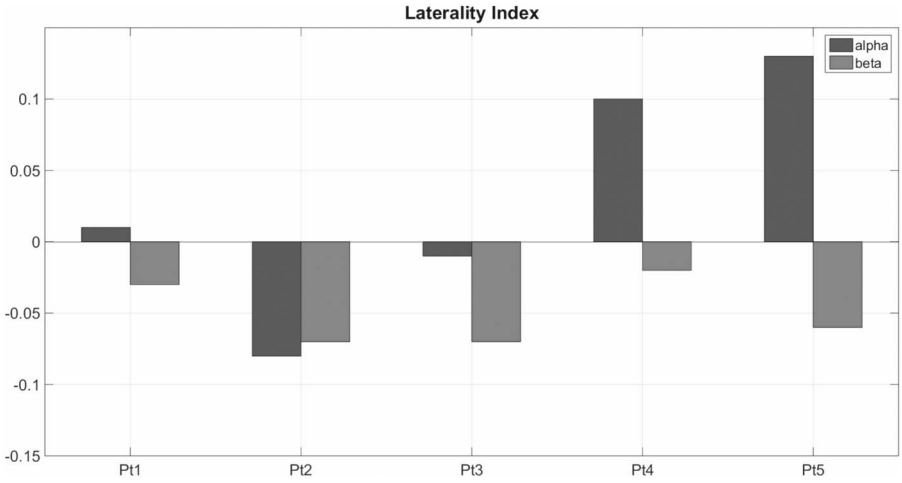

FIG. 4. Laterality index (LI) in alpha and beta bands during right foot movement. LI was calculated as (C−I)/(C + I), where C is the mean spectral power over the contralateral (left) SM area and I is the mean spectral power over the ipsilateral (right) SM area.

observed in SM lesions, e.g., stroke[29–31]: the less effective the motor recovery, the larger the cortical area, which is recruited when performing a movement, with an almost linear correlation between motor performance and extension of activated cortical areas. A correlation, albeit not significantly, between the extension of the desynchronizing cortex (i.e., which activates to generate the movement) and gait performance was also detected in our data set.

The neurophysiological significance of this finding can be speculated building on previous reports on stroke. We know that lesioned cortex, even after recovery, bears a scar of the ischemic event, which translates in an increase of lower rhythms and an overall slowing of EEG activity.[32,33] It is likely that the dominant SM cortex, which bears a higher functional request, incurs in a phenomenon that we could describe as "overexaustion", as it happens in the very early stages of stroke recovery.[34] The

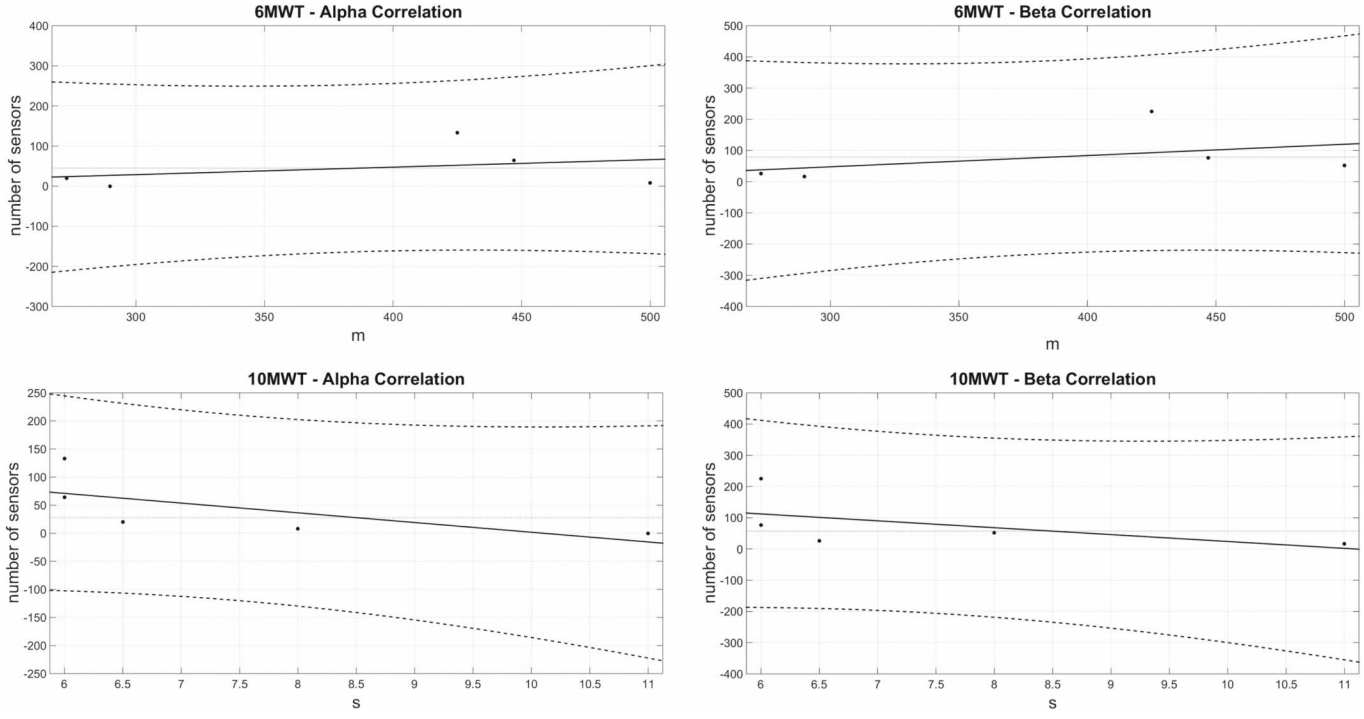

FIG. 5. Correlation between brain activity and gait performance. Regression of the number of sensors with ERD-significant values and meters/seconds (6MWT/10MWT) in alpha and beta band (non–parametric Spearman test). ERD showed a positive correlation with 6MWT in alpha ($R = 0.1$, $P = 0.95$) and beta ($R = 0.5$, $P = 0.45$). ERD showed also a negative correlation with 10MWT in alpha ($R = -0.97$, $P = 0.03$) and beta ($R = -0.87$, $P = 0.1$).ERD, event-related desynchronization; 6MWT, 6-meter walk test; 10-MWT, 10-meter walk test.

contralateral cortex intervenes to "vicariate" the deficient motor area activity.

A similar finding—a shift of power spectrum to slower alpha rhythm—has been reported in a previous EEG study on subjects with myotonic dystrophy.[35] The authors noted a high coherence in the alpha band, suggesting a considerable degree of bilateral synchrony in posterior and anterior cortical areas. They concluded that, in these population, a smaller number of neurons per unit area take part in the generation of alpha rhythms than is normally the case. This may be regarded as being compatible with the general degenerative nature of the disease.

Whether the motor cortex involvement is a primary or secondary phenomenon dependent on ineffective end organs (both muscles and nerves, as a neuropathy is a common trait in DM1[36]) is unknown. Following the compensatory hypothesis, SM should be hyperactive to try to overcome muscle inefficiency; a self-standing central dysfunction thus seems more likely. Indeed, the central dysfunction hypothesis seems verified by the prevalence of theta rhythms in a resting state over motor areas and our results during movement task.

The inefficiency of the contralateral SM to support movement generation, implying recruitment of ipsilateral and distant cortices, is also confirmed by graph analysis findings in the resting state. Functional connectivity shows a clear-cut alteration in DM1 subjects compared with controls. Beta band NS decrease over the dominant (left) hemisphere signals the reduced role of SM during movement, as previously discussed and detected by ERD distribution and laterality index. Increased BC over the vertex bears a similar neurophysiological significance, pointing to a depletion of the lower limb motor network, the activity of which clusters in DM1 over the lower limb cortical representation instead of over a more articulated network. BC derived from functional magnetic resonance imaging data detected comparable results, with an additional increased connectivity in the supplementary motor area and in the right cerebellum.[37]

In our cohort, executive dysfunctions were the main neuropsychological impairment. Given the prevalent role in the executive network of frontal nodes, a link between decreased beta power over the anterior regions and reduced beta NS is suggestive. Persistence of beta band oscillations has been related to the maintenance of the status quo,[38] both in the cognitive[39,40] and in the motor domain.[41] Executive functions deficits, which encompass selective attention and attentional shifts, rely on beta oscillatory activity. Our subjects show a reduction of frontal beta coupled with a reduced left frontal node strength.

A potential confounder could have been the slightly younger age of the control group. We know that the peak frequency of the mu wave increases during infancy and childhood until maturation into adulthood, when it reaches its final and stable frequency of 8 to 13 Hz.[42] An MEG study in resting-state condition showed a significant power decrease in low-frequency bands (i.e., delta and theta) and a significant increase in high bands (mainly beta-1 and beta-2) from childhood to adolescence.[43] This trend was observed until the sixth decade of life, though only slight changes were found. In addition, healthy aging was characterized by a power increase in low-frequency bands mainly localized over frontal regions, but no significant differences were found between the two groups (group IV 30–39 years, group VI 50–59 years). The main differences observed between our subjects were localized over motor areas in the theta band and over the frontal area in the beta range; the location was not significantly affected by age changes. In light of this literature, we are quite confident that the results we report are related to real dysfunctions over the motor areas and not to minor modifications due to aging, which would indeed be more represented over the frontal and not motor areas.

The main limitation of our study is the small sample size partially explained by the relative low incidence of DM1. Ankle torque force during MEG acquisition was not recorded, but a correlation, albeit not significantly, between altered brain activity and timed walking tests (significant ERD values vs. gait performance) emerged. This is an indirect correlation but suggests that DM1 subjects with comparable functional capacity show a similar cortical activation and supports the hypothesis of central dysfunction. Another limitation derives from the fact that we evaluated brain oscillations and connectivity at the sensor level. Magnetic field spread can induce spurious correlations between MEG sensors, and an analysis at the source level could enhance the spatial resolution. However, parameters from a normative population were compared with the same indexes in DM1 subjects; in fact, the difference between the two populations points to a real different neurophysiological functioning. Possible errors caused by magnetic field spread would have affected data in both populations, thus substantially limiting this type of bias. In the source space analysis, the magnetic field can localize the sources of the activity within the brain (inverse problem); source locations are subsequently superimposed on anatomical images (MRI) to provide information both on the structure and function of the brain. In this research work, we focused on ERD/ERS, which are mainly investigated at the scalp level and provide an immediate insight into oscillatory brain rhythms during movement. Source analysis could be implemented in future studies, increasing the sample size, to deepen our understanding of anatomical brain networks once we have established that an alteration in respect to normal motor function is detectable in DM1 at the central nervous system level.

We observed a clear-cut abnormal pattern of oscillatory activity and functional connectivity in people with DM1 prevalent over SM regions, supporting the existence of a deficit of the motor network both in the resting-state condition and during voluntary movement. These findings from the present pilot study provide evidence of a central dysfunction of movement execution correlated with ambulation function and not influenced by peripheral muscle weakness or muscle fatigability, as already reported in literature,[7–9] where no correlations were found between neurophysiological/neuroimaging data and the degree of clinical impairment. Further studies are needed to clarify whether these cortical abnormalities lead to fatigue or are an attempt to compensate for it.

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