RESEARCH ARTICLE

Perception–Action Integration Is Altered in Functional Movement Disorders

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ABSTRACT: Background: Although functional neurological movement disorders (FMD) are characterized by motor symptoms, sensory processing has also been shown to be disturbed. However, how the integration of perception and motor processes, essential for the control of goal-directed behavior, is altered in patients with FMD is less clear. A detailed investigation of these processes is crucial to foster a better understanding of the pathophysiology of FMD and can systematically be achieved in the framework of the theory of event coding (TEC).

Objective: The aim was to investigate perception–action integration processes on a behavioral and neurophysiological level in patients with FMD.

Methods: A total of 21 patients and 21 controls were investigated with a TEC-related task, including concomitant electroencephalogram (EEG) recording. We focused on EEG correlates established to reflect perception–action integration processes. Temporal decomposition allowed to distinguish between EEG codes reflecting sensory (S-cluster), motor (R-cluster), and integrated sensory–motor processing (C-cluster). We also applied source localization analyses.

Results: Behaviorally, patients revealed stronger binding between perception and action, as evidenced by difficulties in reconfiguring previously established stimulus–response associations. Such hyperbinding was paralleled by a modulation of neuronal activity clusters, including reduced C-cluster modulations of the inferior parietal cortex and altered R-cluster modulations in the inferior frontal gyrus. Correlations of these modulations with symptom severity were also evident.

Conclusions: Our study shows that FMD is characterized by altered integration of sensory information with motor processes. Relations between clinical severity and both behavioral performance and neurophysiological abnormalities indicate that perception–action integration processes are central and a promising concept for the understanding of FMD. © 2023 The Authors. *Movement Disorders* published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society.

Key Words: functional neurological disorder; functional movement disorder; perception–action integration; theory of event coding; stimulus–response

Functional neurological movement disorders (FMD) are frequent and disabling.[1] Despite their heterogeneous phenomenology,[2] some common clinical and neurophysiological characteristics have been described, including variability and distractibility of clinical signs, impaired motor metacognition,[3] and altered sense of

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agency.[4,5] Although FMDs are per definition defined as a motor/movement disorder, evidence has accumulated that sensory processing and perception–motor integration are also disturbed.[6-8] For instance, in patients with functional tremor[9] and functional dystonia,[10] tactile temporal discrimination thresholds were increased compared to healthy controls[9] independent of the affected body side. These findings, suggesting altered processing of afferent sensory information in patients with FMD, were substantiated by results of a modeling approach based on sensory temporal discrimination data indicating altered quality and rate in the accumulation of sensory information in these patients.[6] Moreover, in patients with functional weakness the tonic vibration reflex and its perception were reduced, suggesting that attenuation of proprioception plays a role in abnormal movements/postures and presumably also an altered sense of agency in these patients.[11] In addition, in a force-matching paradigm, physiological sensory attenuation,[12] that is, the reduction in the perceived intensity of self-induced as compared to externally generated force, was reduced in patients with FMD.[13] This suggests that patients with FMD were more accurate in using sensory information to inform motor force compared to healthy controls.[13] Akin to this, there was a loss of the physiological reduction in the amplitude of sensory-evoked potentials at the onset of self-generated movements in patients with FMD.[14] Moreover, in an action–effect binding paradigm, FMD patients were more accurate than healthy controls in perceiving the actual time of a self-initiated key press and a subsequent tone, ie, showed less temporal compression.[7]

Physiological sensory attenuation and temporal compression appear to be relevant for perceiving movements as self-generated, and as a corollary, a lack of these phenomena is associated with defective agency for movement,[8,15] which has indeed been documented in patients with FMD.[16,17] Within the so-called "agency network," the temporoparietal junction is an important hub for aligning feedforward and feedback information, with abnormal activation during action authorship perception being documented in patients with FMD.[16,18]

Taking a conceptual view on these findings, a predictive coding framework proposed that in patients with FMD[19] there is a down-weighting of "bottom-up" sensory information in favor of "top-down" predictions (prior beliefs, feedforward information), reducing the quality and relevance of sensory information (feedback information) available to the individual.[6] This was also shown in a study investigating patients with FMD in a visual probabilistic reasoning task.[20] FMD patients used less visual information before making a decision.[20]

Crucially, whether altered sensory processing has a direct effect on higher-level cognitive functions involved in the control of goal-directed behavior in patients with FMD is unclear. Clarifying this point is of central importance not only for the understanding of goal-directed behavior in everyday situations[21] but also against the background that influential accounts on the interrelation of sensory and motor processes—such as ideomotor theory[22]—have long been stating a close connection between sensory and motor processes as a prerequisite of cognitive control. The theory of event coding (TEC)[23] and its recent extension in the form of the binding and retrieval in action control (BRAC) framework[24] specifying how perception is related to motor processes are relevant to better understand the interrelation of sensory and motor processes in FMD and thus add to the predictive coding model. Of note, the TEC framework has already been proven useful to provide a suitable conceptualization of Gilles de la Tourette syndrome.[25]

According to TEC and BRAC, sensory and motor processes affect each other because perceived stimulus features and motor processes are closely integrated (bound) with each other in so-called "event files."[26] An event file is reactivated if a particular feature of a stimulus is repeated. This can cause difficulties in executing the correct motor response if the response required is different from a response that was previously bound with the identical stimulus or if a different stimulus requires the same response. There are numerous studies observing this basic pattern across a wide range of different experimental paradigms[27-29] and the idea that the recent past shapes the current behavior routes in theories from the 1980s (Logan's instance theory[30]). Note further that predictive coding approaches and TEC/BRAC do not compete with each other. Instead, one could say that these frameworks complement each other, in that predictive coding models focus on how a sense of agency when generating movements can be achieved and on TEC/BRAC providing further detailed information on sensory–motor integration. TEC-inspired experimental approaches are, therefore, a stringent test to whether there is an altered perception–motor coupling in patients with FMD.

In the present study, we combined a TEC paradigm with concomitant electroencephalogram (EEG) recording and analysis using novel EEG signal decomposition (ie, residue iteration decomposition [RIDE][31]) to examine whether sensory–motor integration processes and their neurophysiological basis are altered in FMD. Of note, in response to selection tasks, the event-related component P3 has been suggested to reflect processes mediating stimulus evaluation and response selection,[32-35] and the same has been shown to be the case for the RIDE-decomposed data.[36-38] The TEC framework, and the event file concept in particular, addresses these stimulus–response association processes in the "binding" concept. Therefore, the P3 is a suitable marker of stimulus–response translation processes referred to as event files in the TEC framework. Moreover, previous studies have shown that only after

applying EEG signal decomposition with the goal to distinguish between codes in the EEG signal reflecting purely sensory (S-cluster), purely motor (R-cluster), and integrated sensory–motor codes (C-cluster) is a reliable examination of perception–motor integration possible.[36] We also used source localization methods to examine which functional neuroanatomical structures are associated with FMD-associated changes in perception–motor integration.

In view of the aforementioned results suggesting increased sensory processing in patients with FMD,[13,14,20] and given the close interrelations of sensory and motor processes in ideomotor theory and TEC, we hypothesized that perception–action binding is altered in patients with FMD compared to healthy controls, reflected in difficulties to reconfigure previously established perception–action connections. Based on findings in healthy participants on the neurophysiological and functional neuroanatomical implementation of perception–action bindings,[36,37,39,40] we expected these changes in FMD to be reflected by atypical processing in the C-cluster in the RIDE analysis with different patterns of activation within the temporoparietal junction.

Patients and Methods

Participants and Clinical Assessment

Twenty-one patients with FMD (N = 14 women, mean age: 39 years, age range: 16–63 years) were recruited from the outpatient clinics of the Center for Rare Diseases and the Department of Neurology at the University Medical Center Schleswig-Holstein, Lübeck, and the Department of Neurology at the University Medical Center Hamburg Eppendorf, Germany. Patients were clinically diagnosed according to published diagnostic criteria.[41] Twenty-one age- and sex pairwise-matched (±6 years) healthy controls (N = 14 women, mean age: 40 years, age range: 16–59 years) were recruited through an announcement at the billboard of the University Medical Center Schleswig-Holstein, Lübeck, Germany. Written informed consent was obtained from all participants. The study was approved by the local ethics committee of the University of Lübeck, Germany (20–136). All patients were examined according to a standardized video-recorded and video-instructed protocol based on the Simplified Functional Movement Disorders Rating Scale (S-FMDRS).[42] Videos were rated by A.W. using the S-FMDRS.[42] Detailed clinical data are presented in Table S1.

Behavioral Task

A modified version of a stimulus–response paradigm was used as described before.[43] During the stimulus–response paradigm, participants faced a computer screen (Asus VG248QE, 24″, refresh rate: 144 Hz).

Each trial of the stimulus–response paradigm entailed *two* subsequent responses, R1 and R2. At the start of each trial, a rectangle comprising three vertically aligned squares was displayed, with the middle square comprising a leftward- or a rightward-pointing arrowhead (Cue), which indicated the first response R1 (ie, left or right button press depending on the orientation of the arrowhead). The Cue was shown for 1500 ms. Participants were instructed not to respond immediately to the Cue but to carry out R1 as soon as the stimulus S1 occurred. S1 was shown for 500 ms, depicting a bar that varied between trials in position (top or bottom square), orientation (vertical or horizontal), and color (red or green). These features of S1 were not directly relevant for R1 (which was defined by the Cue) but, according to TEC, served to create an association ("binding" according to TEC) between S1 and R1. After a 2000 ms interstimulus interval, S2 was shown, which again depicted a bar that varied between trials in position (top or bottom square), orientation (vertical or horizontal), and color (red or green). In contrast to R1, the second response (R2) was specified by the orientation of the bar in S2. Participants were instructed to press the left control key if the orientation of the bar was horizontal and to press the right control key if the orientation of the bar was vertical. Participants were instructed to respond as fast and accurately as possible (Fig. 1).

Trials differed with stimuli (S1 and S2) being repeated or alternated and responses (R1 and R2) being repeated or alternated. There was either full (same position, orientation, and color of S1 and S2) or zero feature overlap (different position, orientation, and color) between S1 and S2, that is, stimulus repetition (full overlap) or alternation (zero overlap). In addition, there was either response repetition or alternation within trials. TEC assumes that S1 and R1 are integrated into an event file. Thus, if only one of the two dimensions, ie, stimulus or response information, was repeated within a trial but the other changed (stimulus repetition with response alternation, or vice versa, stimulus alternation with response repetition; referred to incompatible conditions in the following), responding correctly to S2 requires unbinding/reconfiguration of the previously established event file, ie, the S1–R1 association. Unbinding is computationally costly and therefore impairs performance (ie, partial repetition costs: lower accuracy and longer response time). In contrast, in conditions where correctly responding to S2 does not require unbinding (stimulus repetition with response repetition or stimulus alternation with response alternation; referred to as compatible conditions in the following), performance is relatively superior (ie, full repetition or full alternation, leading to relatively higher accuracy and shorter response times).

After participants received instructions and a short practice block (12 trials), they performed the main

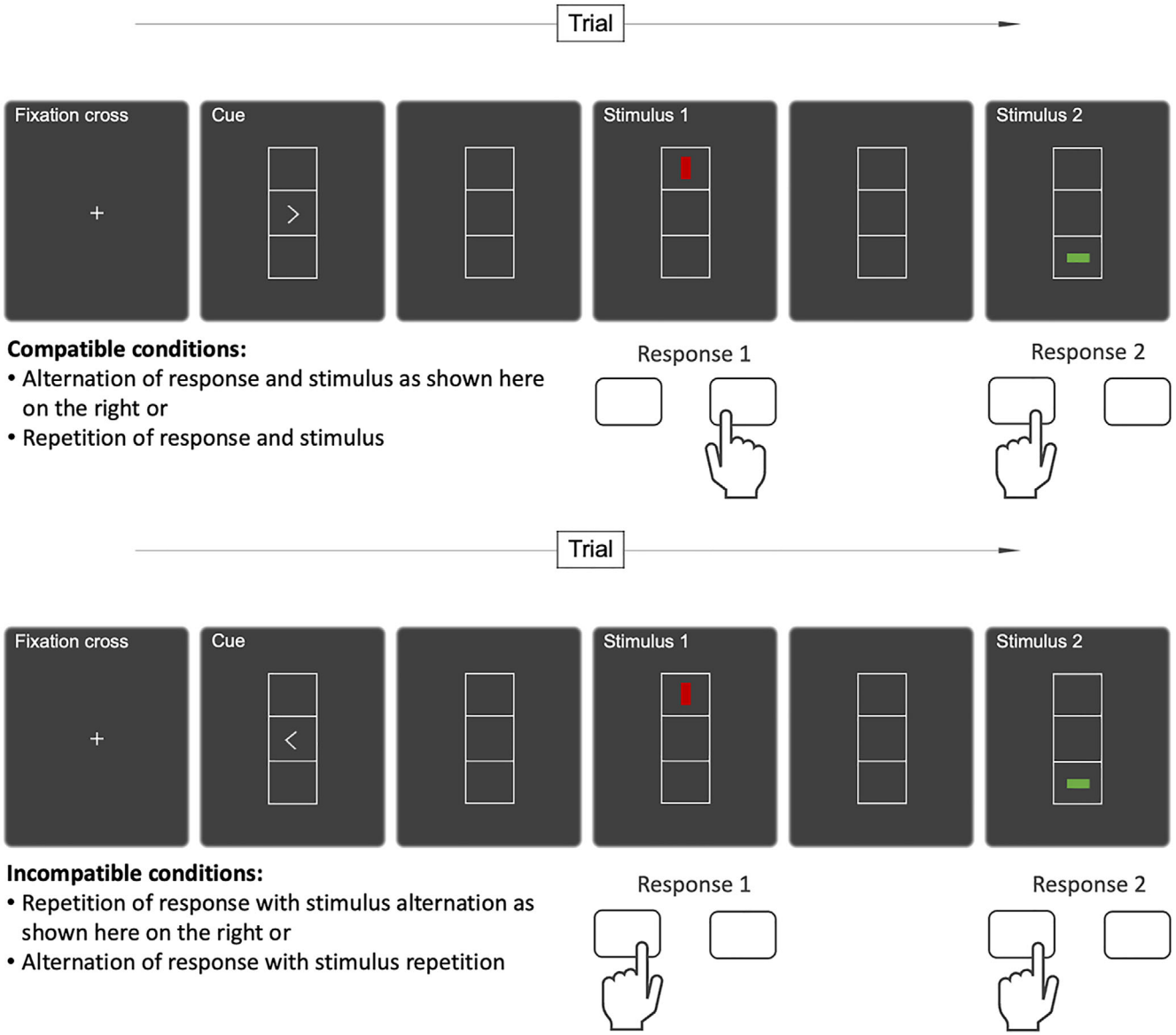

FIG. 1. Schematic illustration of the stimulus–response paradigm (for details see the "Patients and Methods" section). [Color figure can be viewed at wileyonlinelibrary.com]

experiment that comprised 192 trials (48 per condition in the 2 × 2 design, randomly presented, ie, stimulus [alternation/response] × response [alternation/response]), which were divided into 6 blocks of 32 trials each. The intertrial interval was set randomly between 1500 and 2000 ms during which a fixation cross appeared in the middle of the screen.

Response accuracy (percentage correct) and mean reaction times (ms) for correct responses were determined for each condition and participant. In addition, to account for a potential speed-accuracy tradeoff, an established measure combining accuracy and response times was computed—the balanced integration score (BIS = z[accuracy] – z[response time]), where the z-transformation refers to standardization to mean 0 and standard deviation 1, applied across all conditions of all participants.[44] Thus, higher values of the BIS correspond to better performance. As a correct response to cue/S1 was required to establish the binding specified by the experimental design, trials with cue/S1 errors (1.8% of all trials, range: 0%–12.5% per participant) were excluded from the main analysis. Participants who performed just above chance level (accuracy: 50%) were excluded from the EEG analysis.

EEG Data Recording and RIDE

EEG recording and preprocessing was performed as described before.[45-48] Details are available in the Supplementary Material. The segmented EEG data were exported at the single-trial and single-subject levels to

perform decomposition. In particular, temporal signal decomposition was performed using RIDE[31,49-51] in Matlab 2019a (The MathWorks Corp., Natick, MA, USA). RIDE initially estimates clusters using either variable or static latency information. Then, an iteration scheme self-optimizes the cluster solution until convergence. Three clusters were created: S-cluster ("stimulus cluster") based on stimulus-related processes, such as perception and attention; R-cluster ("response cluster") that reflects motor preparation and execution; and C-cluster ("central cluster") that taps into intermediate or translational processes between stimulus and response, such as decision-making or response selection.[51] Importantly, the RIDE algorithm and the delineation of the three clusters (S-cluster, R-cluster, and C-cluster) are performed for each electrode separately.[49,52] In this regard, "cluster" does not refer to a specific grouping of electrode position but to a temporal decomposition of the EEG signal. In RIDE, a cluster refers to a pattern of activity (e.g., R-cluster = motor response–related activity) that can be found across all electrode sites. The decomposition requires a priori time windows for the initial cluster estimations. The following time windows were selected: 250–750 ms after stimulus presentation for the C-cluster, the time window between 300 ms before and 300 ms after the response markers for the R-cluster, and 0–500 ms after stimulus onset for the S-cluster. The overlap between the initial search windows for RIDE clusters is a common practice, as the iterative comparison between cluster solutions was designed with the assumption of simultaneous underlying processes.[31,49-51]

Next, the waveforms and their topographies were inspected visually in the four conditions, separately for the three clusters. According to our expectations, event file binding processes should be reflected by the P3 component. We base this decision on numerous findings by our group and others showing that event file processes consistently affect neurophysiological dynamics in the P3 time window during both, response selection[36,37,53] and response inhibition.[39,54] Of note, P3 modulations were also found in other movement disorders.[25] To analyze the stimulus-locked P3, we selected the centroparietal electrodes CP1 and CP2. These electrodes well reflect the scalp topography plots showing a clear centroparietal positivity and are also comparable to the electrodes chosen in previous studies[25,36,37,53] on the P3 modulation in event file dynamics. The P3 was maximal in the time window between 500 and 600 ms in the healthy control sample. Because the healthy controls are the "reference" to estimate possible differences in FMD patients, this guided the choice in the time window also for the FMD patient group. Also, previous work using this paradigm quantified the P3 to be about 500 ms.[25,37] Thus, within this time interval, the mean amplitude was quantified and extracted at the single-subject level.

Further details on the analysis using standard low-resolution brain electromagnetic tomography (sLORETA)[55] can be found in the Supplementary Material.

Statistical Analysis

Each of the dependent variables (response accuracy, mean response time, BIS, and P3 amplitude) was analyzed using a repeated-measures analysis of variance (ANOVA) with between-subject factor Group (FMD/healthy controls) and within-subject factors Stimulus (repetition/alternation), Response (repetition/alternation), and Electrode (CP1 and CP2, for the EEG data only). In the presence of significant binding effects (Stimulus × Response interaction) or group differences therein, binding effects were assessed in depth by computing binding scores (difference between compatible and incompatible conditions) separately for response repetition and response alternation conditions.[25]

Potential associations between binding effects and clinical characteristics were assessed using correlation analyses. More details on the computation of binding scores and correlation analyses are provided in the Supplementary Materials.

Results

Clinical Characteristics

Patients with FMD in our study suffered from functional gait disorder (n = 15), functional tremor (n = 8), functional tics (n = 5), and functional jerks (n = 1). All patients with a functional tremor also had a functional gait disorder. The mean disorder duration was 4.43 years ± 3.94 (range: 1–12), and the mean S-FMDRS score was 9.24 ± 6.05 (range: 0–26) (see Table S1 for individual data). During participation in our study, none of the patients had another clinically relevant psychiatric or additional functional symptomatology.

Behavioral Data

ANOVA for the accuracy data revealed an interaction of the factors Response × Stimulus [$F(1, 40) = 85.21$, $P < 0.001$, $\eta_p^2 = 0.681$] (Table S2A), indicating binding processes[26]: when responses had to be repeated, accuracy increased from the stimulus alternation (incompatible: 83.9% ± 11.8%) to the stimulus repetition (compatible: 95.5% ± 4.2%) condition and vice versa; ie, when responses had to be alternated, accuracy decreased from the stimulus alternation (compatible: 95.4% ± 6.6%) to the stimulus repetition (incompatible: 82.9% ± 12.8%) condition (Fig. 2). Thus, partial repetition cost, that is, lower accuracy rates, occurred in incompatible conditions where previous binding between response R1 and stimulus S1 had to be

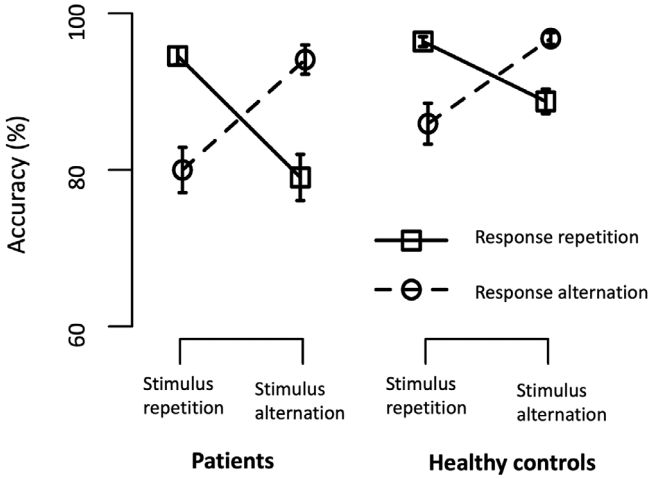

FIG. 2. Accuracy results. Higher accuracy in compatible (upper squares and circles) compared to incompatible (lower squares and circles) conditions. Binding as Stimulus × Response interaction was stronger in patients compared to controls represented by a steeper axis rise.

reconfigured. There was a main effect for the factor Group [$F(1, 40) = 5.53$, $P = 0.024$, $\eta_p^2 = 0.121$] (Table S2A), showing that overall accuracy was higher in healthy controls compared to patients (92.0% ± 5.2% vs. 86.9% ± 8.3%). Importantly, the three-way interaction Group × Response × Stimulus was significant [$F(1, 40) = 4.54$, $P = 0.039$, $\eta_p^2 = 0.102$], showing that binding effects were different between patients with FMD and healthy controls (Table S2A). In particular, there was an interaction of Stimulus × Response in FMD patients [$F(1, 40) = 47.85$, $P < 0.001$, $\eta_p{}^2 = 0.705$] and in healthy controls [$F(1, 40) = 38.71$, $P < 0.001$, $\eta_p{}^2 = 0.659$], with a higher effect size ($\eta_p{}^2$) in patients (Table S2B,C), revealing that binding effects were stronger in patients compared to controls. Figure 2 visualizes the interaction: when responses had to be repeated (solid line), the difference between the stimulus repetition (compatible) and the stimulus alternation (incompatible) condition was higher in FMD patients (15.5% ± 11.7%) compared to controls (7.6% ± 5.8%, $P = 0.018$). There was no difference between groups for the difference in the response alternation conditions (dotted line) ($P = 0.247$).

With regard to response time, there was an interaction between the factors Response × Stimulus [$F(1, 40) = 67.37$, $P < 0.001$, $\eta_p^2 = 0.627$] indicating binding, but no other effects or interactions were present (Table S3A).

These findings are corroborated by control analyses. First, the three-way interaction Group × Stimulus × Response was also present for the BIS, giving equal weights to response time and accuracy rate as behavioral parameters [$F(1, 40) = 5.58$, $P = 0.023$, $\eta_p^2 = 0.123$] (Table S3B). Second, 5 participants (3 FMD patients, 2 healthy controls) performed just above chance level (50% accuracy) in some experimental conditions. To ensure that the reported group differences are not merely due to poor understanding of the task, or particularly poor performance in general, we repeated all statistical analyses, including only participants with accuracy of 60% or above in each of the four conditions. This analysis confirmed the results by showing an interaction of Group × Stimulus × Response for accuracy [$F(1, 35) = 5.75$, $P = 0.022$, $\eta_p^2 = 0.141$] and for BIS [$F(1, 35) = 10.04$, $P = 0.003$, $\eta_p^2 = 0.223$], reflecting in each case more pronounced binding in FMD compared to healthy controls (Table S4A–C). Third, when subgrouping patients based on symptom localization, that is, upper extremities affected or not, results (accuracy, response time, BIS, or binding scores) did not differ between groups, suggesting that behavioral finding is not related to symptom localization but an underlying problem of neural processing.

Neurophysiological Data

Statistical analyses were performed separately for the mean amplitude data in the R-cluster and the C-cluster. Because no P3-like waveform occurred in the S-cluster, the S-cluster data were not analyzed.

In the R-cluster time window between 500 and 600 ms (Fig. 3), ANOVA showed a main effect for the factor Response [$F(1, 35) = 9.65$, $P = 0.004$, $\eta_p{}^2 = 0.216$], with the R-cluster being smaller for alternation than for repetition trials (3.12 μV/m^2 ± 1.17 vs. 4.73 μV/m^2 ± 1.04). There was a Group × Response × Stimulus interaction [$F(1, 35) = 7.91$, $P = 0.008$, $\eta_p{}^2 = 0.184$], paralleling the behavioral results. No other main or interaction effects were significant (all $F < 3.04$, $P > 0.09$). In FMD patients, the mean amplitude of the R-cluster P3 decreased from the stimulus alternation with response alternation (compatible) condition to the stimulus repetition with response alternation (incompatible) condition (2.61 μV/m^2 ± 1.82 vs. −1.71 μV/m^2 ± 1.88, $P = 0.07$) (Fig. 3). The source localization analysis indicated that these effects were associated with activation differences between FMD and healthy participants in Brodmann area BA44 (MNI coordinates $X = 55$, $Y = 5$, and $Z = 15$, inferior frontal gyrus) (Fig. S1). No significant amplitude changes were detected in the R-cluster in healthy controls and between the response repetition conditions in the FMD group ($P > 0.107$) (Fig. 3).

Regarding the C-cluster (Fig. 4), ANOVA revealed no significant main effects for any of the three factors of Group, Stimulus, or Response. However, there were significant interactions between the factors Stimulus × Response [$F(1, 35) = 4.79$, $P = 0.035$, $\eta_p{}^2 = 0.120$], Stimulus × Response × Group [$F(1, 35) = 13.6$, $P < 0.001$, $\eta_p{}^2 = 0.280$], Stimulus × Electrode × Group [$F(1, 35) = 4.72$, $P = 0.037$, $\eta_p{}^2 = 0.119$], and Stimulus × Response

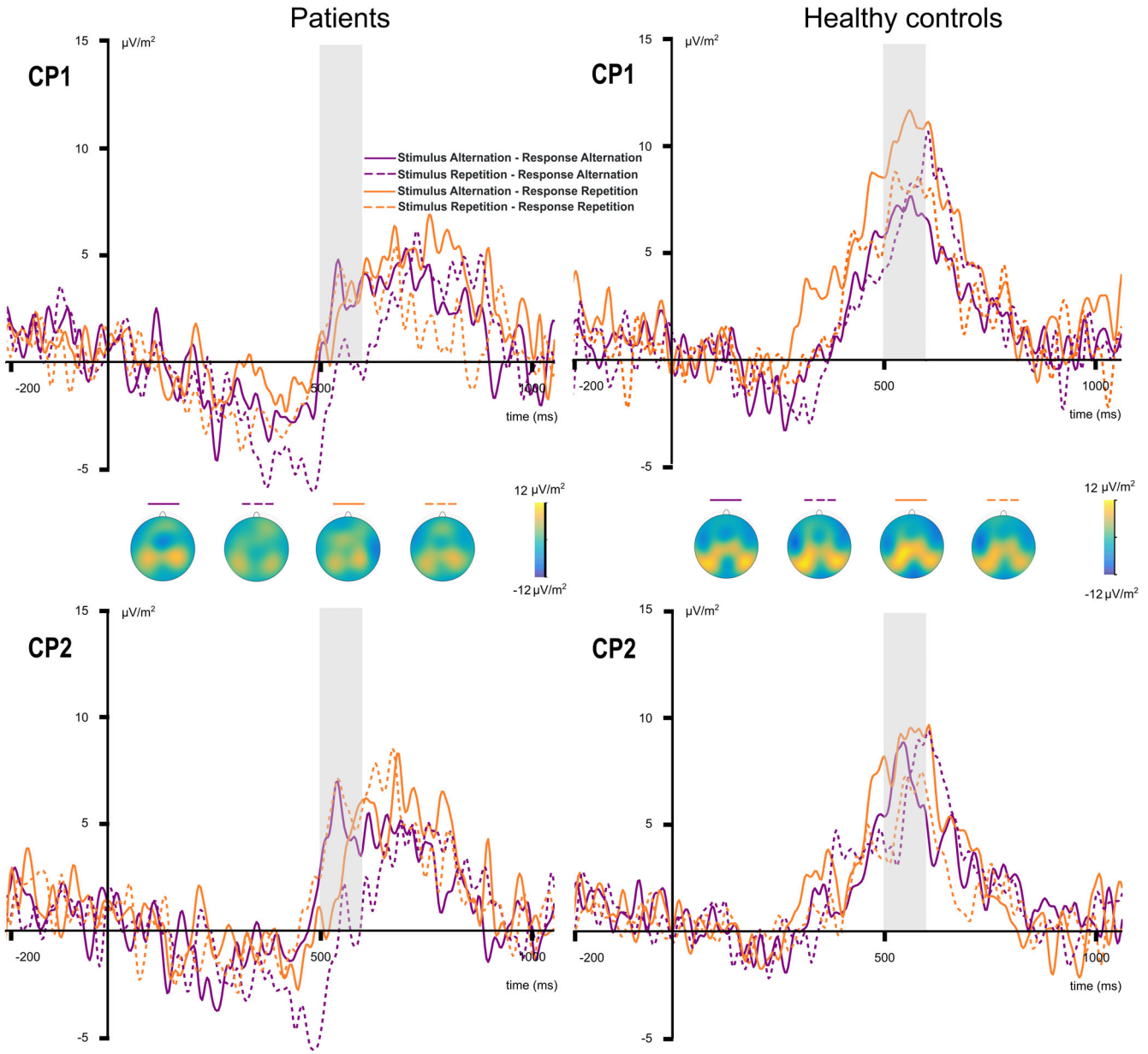

FIG. 3. P3 R-cluster waveforms on electrodes CP1 and CP2 as a function of stimulus and response type. Stimulus S2 was presented at 0 ms. Shaded area is the analyzed time window. Scalp topography plots show distribution of mean activity of the four conditions. [Color figure can be viewed at wileyonlinelibrary.com]

× Electrode × Group [$F(1, 35) = 5.33$, $P = 0.027$, $\eta_p^2 = 0.132$]. On the electrode CP2, healthy controls showed a decrease in the mean P3 amplitude from the stimulus alternation with response alternation (compatible) to the stimulus repetition with response alternation (incompatible) condition ($8.98\ \mu V/m^2 \pm 2.09$ vs. $5.47\ \mu V/m^2 \pm 1.93$, $P = 0.026$) and a decrease from the stimulus repetition with response repetition (compatible) to the stimulus alternation with response repetition (incompatible) condition ($11.87\ \mu V/m^2 \pm 2.38$ vs. $4.23\ \mu V/m^2 \pm 2.31$, $P < 0.001$) (Fig. 4). That is, the healthy controls showed binding-related amplitude modulations in the C-cluster, which is in line with previous findings.[25,37] There were no significant binding effects on electrode CP1 in the control group ($P > 0.077$) and no binding-related amplitude changes in the FMD group ($P > 0.109$). The source localization analysis using sLORETA revealed that the group differences in binding effects of the C-cluster data were associated with differential activation in the BA40 area (MNI [Montreal Neurological Institute] coordinates $X = 65$, $Y = -35$, and $Z = 35$, inferior parietal cortex) for the response alternation and BA31 area (MNI coordinates $X = -10$, $Y = -45$, and $Z = 35$, cingulate gyrus) for the response repetition conditions (Fig. S1).

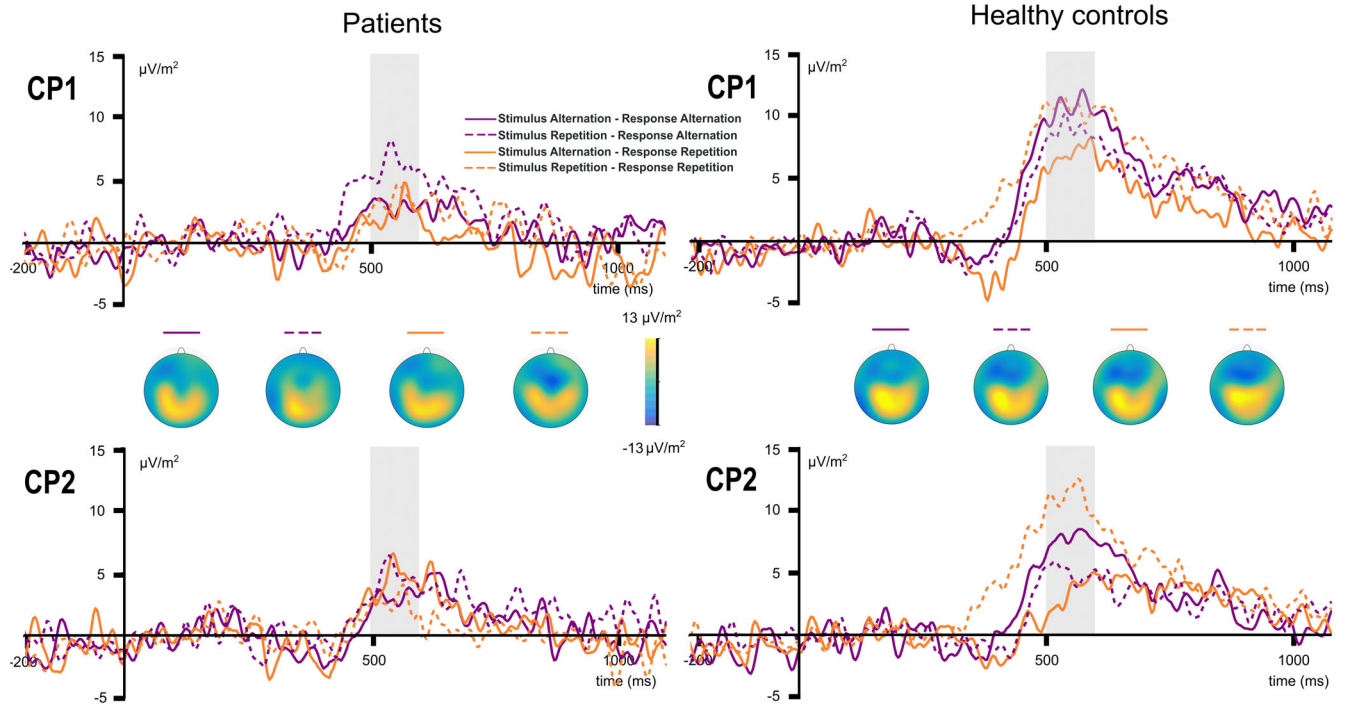

FIG. 4. P3 C-cluster waveforms on electrodes CP1 and CP2 as a function of stimulus and response type. Stimulus S2 was presented at 0 ms. Shaded area is the analyzed time window. Scalp topography plots show distribution of mean activity of the four conditions. [Color figure can be viewed at wileyonlinelibrary.com]

Correlation Analysis

We found a positive correlation between the S-FMDRS score and the behavioral binding effects of the response alternation conditions. That is, stronger binding (ie, larger accuracy differences between compatible and incompatible conditions) was associated with higher S-FMDRS scores ($r = 0.475$, $P = 0.029$) (Fig. 5A). No correlation was found between S-FMDRS scores and the behavioral binding effects of the response repetition conditions.

With regard to the neurophysiological data and given the significant Group × Stimulus × Response × Electrode interaction in the C-cluster, binding scores were calculated separately for the electrodes CP1 and CP2. In the R-cluster, there was no interaction with the factor Electrode; thus, the signal of the two electrodes was averaged. The correlation was significant in the C-cluster between the S-FMDRS score and the response repetition binding on CP1 ($r = -0.481$, $P = 0.043$) and CP2 ($r = -0.626$, $P = 0.005$), respectively (Fig. 5B). Higher binding scores, that is, positive values, represented higher P3 amplitudes in the compatible response repetition condition compared to the incompatible response repetition condition, as seen in healthy controls. Thus, in patients, higher symptom severity was associated with lower or even negative binding scores in the C-cluster (Fig. 5B). The correlations were not significant for the response alternation binding in the C-cluster ($P > 0.928$) or between either type of behavioral binding scores and the R-cluster-based binding measure ($P > 0.072$).

Discussion

This study aims for a better characterization of perception–action integration to conceptually advance the understanding of FMD. Using a well-established stimulus–response EEG paradigm, we show that on a behavioral level perception–action binding in patients with FMD is increased as evidenced by difficulties in reconfiguring previously bound perception–action connections. On a neurophysiological level, such hyperbinding was paralleled by a decrease in the P3 amplitude during response alternation from compatible to incompatible conditions in the R-cluster. Importantly, binding effects in healthy controls were not reflected by neurophysiological processes in the R-cluster but, in keeping with previous findings, in the C-cluster.[36,37,39,40] Thus, in addition to quantitative differences between patients with FMD and healthy controls as regards binding with patients showing hyperbinding, there were qualitative group differences. Patients with FMD showed altered (increased) motor processing reflected by R-cluster modulations, leading to abnormal perception–action integration. Thus, in contrast to healthy controls, in whom stimulus–response translation processes reflected by C-cluster modulations mediate binding on a behavioral

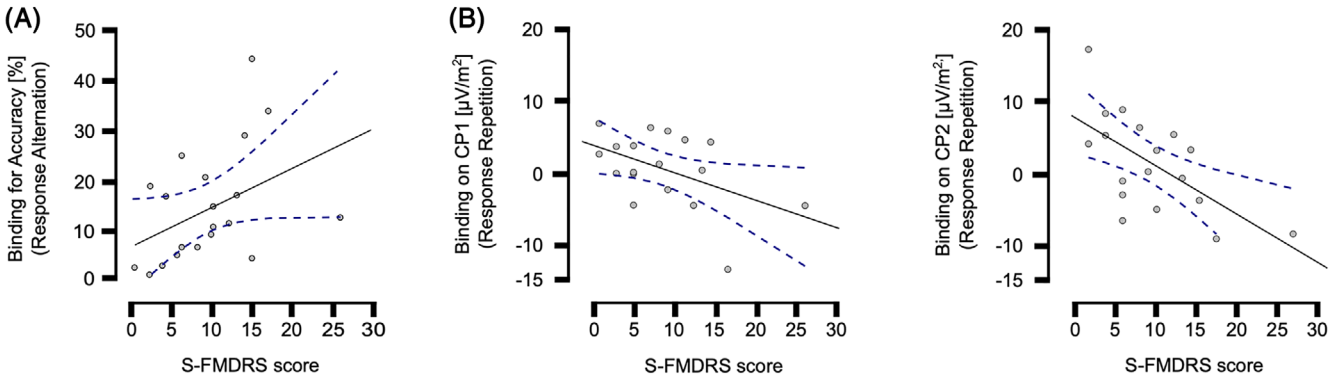

FIG. 5. Scatterplots depicting correlations between (**A**) behavioral or (**B**) neurophysiological binding scores (CP1 and CP2 electrodes) and clinical scores of the Simplified Functional Movement Disorders Rating Scale (S-FMDRS). Dashed lines indicate confidence intervals (95%). [Color figure can be viewed at wileyonlinelibrary.com]

level,[38,56] the motor component of perception–action integration processing is accentuated in FMD. The latter finding does not contradict the conceptualization of altered perception–action integration in FMD because both sensory and motor processes (R-cluster)[57,58] constitute processes occurring in an event file.[23] R-cluster effects were associated with activation differences in the inferior frontal gyrus, that is, BA44, a hub region of inhibitory control processes to implement executive control,[59,60] which have been shown to be altered in FMD.[61]

Our study also shows that translation processes between stimulus processing and responding (C-cluster) are affected in FMD. In fact, C-cluster effects were associated with different activity modulations in the inferior parietal cortex, that is, BA40, an area well known to be relevant for event file coding.[25,36,62] This included parts of the temporoparietal junction previously shown to be abnormally active in FMD.[63] Notably, patients with higher behavioral perception–action binding scores and reduced modulations in the C-cluster in the response repetition conditions as a sign of dysfunctional reconfiguration processing had higher scores in the S-FMDRS. All this suggests a direct relevance of altered perception–action integration processes for the understanding of the pathophysiology and clinical phenomenology of FMD.

The present findings can be reconciled within the predictive coding framework and the mismatch between feedforward and feedback information within the so-called "agency network" with the temporoparietal junction as an important hub leading to altered sense of agency as a core theme in patients with FMD.[16,17] Similar to the reductions in physiological sensory attenuation[13] and temporal compression in FMD,[7] hyperbinding along with reorganization of perception–action integration processes shown here, that is, deviations from physiological perception–action processing, will likely lead to changes in the perception and contextualization of movements and may contribute to the difficulties patients with FMD have to relate (functional) extra movements to other voluntarily or spontaneously generated movements.

Importantly, our findings extend current concepts of FMD particularly with a view to novel treatment approaches. FMD patients show abnormally increased and focused attention toward their motor symptoms.[41] In the present study, this might be reflected by increased binding between perceptual stimuli and motor responses along with difficulties in decoupling such bindings and reconfiguring new perception–action associations at a behavioral level. At a neurophysiological level, it was probably reflected by a shift in cognitive processing, that is, P3 amplitude modulations from the C- to the R-cluster. Treatment strategies aiming at redirecting attention more flexibly, for example, from an affected body region to an unaffected body part or even toward environmental stimuli, might help to attenuate existing perception–action bindings and to facilitate the formation of new bindings, so that cognitive resources can be used more effectively.[64] At a behavioral level, this might then be reflected by abnormal hyperbinding being reduced and/or reconfiguration of perception–action bindings becoming more efficient. At the neurophysiological level, this may be paralleled by P3 amplitude modulations in the C- rather than the R-cluster, that is, more physiological cognitive processing.

The "motive" of increased perception–action binding in a neuropsychiatric disorder is not unprecedented. It has previously been shown in Tourette syndrome, where altered sensorimotor processing is a key finding.[65-67] However, other than in patients with FMD, in whom neurophysiological processing has apparently been "shifted" or rebalanced from C-cluster to R-cluster processing, this was not the case in patients with Tourette syndrome. In these patients, hyperbinding was associated with perception–action processing in the C-cluster as in healthy controls but dysfunctional such

that behaviorally more demanding stimulus–response processes requiring reconfiguration were less efficient.[25] Collectively, these findings suggest that neurophysiological signatures of perception–action integration processes allow fine-grained delineation of possibly disorder-specific underlying mechanisms in patients with neuropsychiatric disorders within a common conceptual framework, which may also turn out to be useful to neurophysiologically characterize and cluster clinical syndromes.

Although the study provides behavioral and neurophysiological insights that perception–action binding (event files) is abnormally strong in FMD, further mechanistic studies replicating and extending the current findings are necessary, particularly because different processes can modulate the strength of binding in event files and how these are handled.[24]

In conclusion, patients with FMD show perception–action hyperbinding associated with nonphysiological modulation of R-cluster activity in the inferior frontal gyrus (BA 44) and altered activation patterns of C-cluster processes in the inferior parietal cortex (BA40), including parts of the temporoparietal junction that has previously shown to be abnormally active in FMD. Because symptom severity in patients was attributed to both abnormal behavioral performance and neurophysiological abnormalities of perception–action integration, these processes appear to be central for the understanding of FMD. ■

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Data Availability Statement

Data and analysis scripts are available upon request from the corresponding author.

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