Behavioural Brain Research 404 (2021) 113153

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Disruptions of cortico-kinematic interactions in Parkinson's disease

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ARTICLE INFO

Keywords:
Parkinson's disease (PD)
Cortico-kinematic interactions
Complexity
Electroencephalography (EEG)
ß Oscillations

ABSTRACT

The cortical role of the motor symptoms reflected by kinematic characteristics in Parkinson's disease (PD) is poorly understood. In this study, we aim to explore how PD affects cortico-kinematic interactions. Electroencephalographic (EEG) and kinematic data were recorded from seven healthy participants and eight participants diagnosed with PD during a set of self-paced finger tapping tasks. Event-related desynchronization (ERD) was compared between groups in the α (8−14 Hz), low-ß (14−20 Hz), and high-ß (20−35 Hz) frequency bands to investigate between-group differences in the cortical activities associated with movement. Average kinematic peak amplitudes and latencies were extracted alongside Sample Entropy (SaEn), a measure of signal complexity, as variables for comparison between groups. These variables were further correlated with average EEG power in each frequency band to establish within-group interactions between cortical motor functions and kinematic motor output. High ß-band power correlated with mean kinematic peak latency and signal complexity in the healthy group, while no correlation was found in the PD group. Also, the healthy group demonstrated stronger ERD in the broad ß-band than the PD participants. Our results suggest that cortical ß-band power in healthy populations is graded to finger tapping latency and complexity of movement, but this relationship is impaired in PD. These insights could help further enhance our understanding of the role of cortical ß-band oscillations in healthy movement and the possible disruption of that relationship in PD. These outcomes can provide further directions for treatment and therapeutic applications and potentially establish cortical biomarkers of Parkinson's disease.

1. Introduction

Parkinson's disease (PD) is a neurodegenerative disease that manifests in motor and non-motor symptoms. The cardinal motor features of PD include bradykinesia, tremor, and rigidity [1]. Impairments of motor performance in PD are thought to reflect disruptions in the motor circuit, a network of cortical and subcortical neural structures in the brain. More specifically, impaired dopaminergic transmission in the basal ganglia causes disruptions in the motor circuit that affect movement generation [2]. The effects of these disruptions can be seen in multiple brain structures [3,4], in motor outcomes at rest [5], and during kinematic tasks [6–8].

Electroencephalography (EEG) has been widely used as a noninvasive modality to explore the relationships between PD pathological cortical signatures and their associated symptomatic outcomes [9,10]. Several studies have found significant differences between both medicated and unmedicated PD patients and healthy controls with respect to β-band power in the motor and premotor cortex during kinematic tasks [11–14]. Abnormal interactions between cortical β-band power and kinematic outcomes are suggested to be associated with PD, although no clear pattern has been determined. For example, Stegmöller et al. (2016) found that both medicated and unmedicated PD patients demonstrated greater desynchronization in the β-band than the healthy control population after normalizing five second epochs centered around a single finger movement taken from a paced finger-tap task with a previously recorded rest period [11]. The same group found greater desynchronization in medicated and unmedicated patients over the premotor cortex using a similar task and baseline normalization scheme [12]. However, Cheng et al. (2018) found that several interventions resulted in greater event-related desynchronization (ERD) magnitude that correlated with improved postural and gait outcomes [13]. Additionally, Brown and Mardsen (1999) found that attenuation of the β-band over the sensorimotor, premotor, and prefrontal channels was reduced in the off-medication state when compared to the on-medication state during a kinematic tracking task [14]. In this study, the authors reported β-band changes as a reflection of the maintenance of the current motor state.

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https://doi.org/10.1016/j.bbr.2021.113153
Received 24 September 2020; Received in revised form 8 January 2021; Accepted 27 January 2021
Available online 8 February 2021

Engel and Fries (2010) posit that abnormally strong β-band synchrony in the resting state may contribute to several motor symptoms common to PD by making it more difficult for individuals to change their current motor state [15]. There is also accumulating evidence that β-band may, in fact, consist of two functionally discrete sub-bands of low and high β [16,17]. This has also been shown in our previous studies in which, we demonstrated that pallidal DBS in PD differentially modulates local and network activities in the context of low-β and high-β respectively [16].

Upper limb kinematic outcomes have been recorded using multiple paradigms and assessment modalities to explore pathological patterns in PD. Tapping latency, intra-individual variability [18], tapping force [19], and frequency [20,21] have been extracted during paced and unpaced finger-tapping tasks to determine potential markers for disease and to assess the effectiveness of treatments and therapies. Kinematic complexity has been shown to have promising clinical potential in assessing PD patients [22,23]. For example, in a study conducted by Gil et al. (2010), the authors introduced the use of Approximate Entropy (ApEn) in upper limb kinematic analyses to classify accelerometer data collected from individuals with PD and healthy controls. The authors claim that ApEn measures were able to discriminate between the two groups, while more standard frequency features were unable to do so [24], suggesting the family of related algorithms that have emerged since the inception of ApEn could provide discriminatory information in similar time-series kinematic data. Richman and Moorman (2000) proposed the Sample Entropy (SaEn) algorithm, an alternative measure of complexity in real-world data, to address several concerns surrounding ApEn, including reduced sensitivity to parameter settings while addressing the bias towards regularity present in ApEn [25].

Although many studies have attempted to characterize pathological patterns in both the cortex and motor outcomes, few have attempted to directly relate these two. Among the available literature investigating brain-body interactions in PD, many assess postural and gait outcomes [26,27], and compare them to cortical signatures recorded using EEG. However, fewer studies have addressed upper limb symptoms in movement tasks [28,29]. In a recent study, Polar et al. found that β-band power in a PD rat model lacked a significant correlation with gait speed that was present during baseline recordings, in which no symptoms were present [30]. Stegmöller et al. (2017) have also suggested that the graded β-band response in the premotor cortex to increased tapping speed present in the healthy group was absent in the PD group [12], although no quantitative analysis was performed to further explore this observation.

To date, the role of cortical ß-band activity in movement generation in PD, as reflected by kinematic characteristics, is not yet well understood. Despite showing promise as a possible marker of PD, only a few studies have explored upper limb cortico-kinematic interactions between oscillatory cortical band power and kinematic outcomes in PD when compared with healthy controls. In this study, we aim to explore the relationships between EEG α and low/high-β band powers and kinematic outcomes during an unpaced finger-tapping task and compare these measures between a group of participants with PD and a group of healthy controls. Extending existing literature, we hypothesized that the relationships between cortical β-band oscillatory activities and kinematic outcomes are impaired in participants with PD. To test our hypothesis, we correlated α and low/high-β band powers recorded during the finger-tap task with mean peak latency, amplitude, and Sample Entropy values extracted from the kinematic signal recorded via a wearable smart glove. Understanding cortico-kinematic relationships could in turn help to elucidate the neural mechanisms that drive the motor symptoms characteristic of Parkinson's disease, provide further direction for treatments and therapies including neurofeedback [31,32], and deep brain stimulation (DBS) [33], and potentially establish cortical biomarkers of Parkinson's disease.

2. Methods

2.1. Participants

Eight individuals diagnosed with PD (age 72.4 ± 8.9, five female), and seven healthy controls (age 65.4 ± 9.1, five female) were recruited to participate in this study. Reported symptoms in the PD group include hypokinesia, dystonia, bradykinesia, tremor, and abnormal gait. All participants in the PD group were in the ON-medication state during data

recording, and no patients exhibited visible tremor or dyskinesia during the recording. Participants in the PD group all completed the Montreal Cognitive Assessment (MOCA); each member of the PD group aside from one was found to have mild cognitive impairment (MOCA score < 26) [34]. Control participants reported no known history of neurological disorder. Demographic information about the studied PD is presented in Table 1. The study protocol was approved by the Institutional Review Board (IRB) of the University of Rhode Island (URI), and all participants provided informed consent for the study.

2.2. Experimental protocol

Each participant completed all data recording within a single session lasting about 60 min. EEG and kinematic signals were recorded simultaneously from a single experimental run consisting of five trials. Each trial consisted of 10 s of rest, followed by 10 s of self-paced finger tapping. Participants were seated and instructed to repeatedly oppose their right index finger to their thumb in a wide motion at a pace comfortable to them. A cue presented on a monitor in front of the participants prompted each task (i.e., rest or finger tap) during the experiment. A visual representation of the experimental paradigm is included in Fig. 1A.

2.3. Data acquisition

EEG signals were recorded using a g.USBamp (g.tec Medical Tech.) and digitized at 256 Hz. Data were recorded from a 13 channel EEG montage over regions surrounding and including the motor cortex: Fc3, Fc4, C1, C2, C3, C4, Cp1, Cp2, Cp3, Cp4, P3, and P4. Subsequent analyses were performed on channel C3 due to its position over the motor cortex contralateral to the hand used to perform the task.

Kinematic signals were recorded using a smart glove (WearUP glove), which was previously designed and validated by our group [35]. The WearUP glove consists of two flexible sensors sewn into fabric, providing a single data channel that represents a unidirectional relative approximation of the flexion of the finger. The WearUP glove was connected directly to the g.USBamp amplifier and the data were digitized using the same EEG g.USBamp amplifier at 256 Hz (Fig. 1B).

Table 1
PD Participant's demographic information.

Participant	Age	Sex	Years Since Diagnosis	MOCA Score	Motor Symptoms
PD1	78	F	1	25	Bradykinesia
PD2	76	F	3	26	Gait imbalance, Bradykinesia
PD3	73	F	1	19	Tremor
PD4	80	M	10	17	Impaired speech and gait
PD5	56	M	3	23	Tremor, Dystonia, Freezing gait
PD6	76	F	15	21	Tremor
PD7	79	F	10	19	Tremor
PD8	61	M	5	20	Bradykinesia, Rigidity
Mean ± SD	72.4 ± 8.9	–	6.0 ± 5.1	21.2 ± 3.1	–

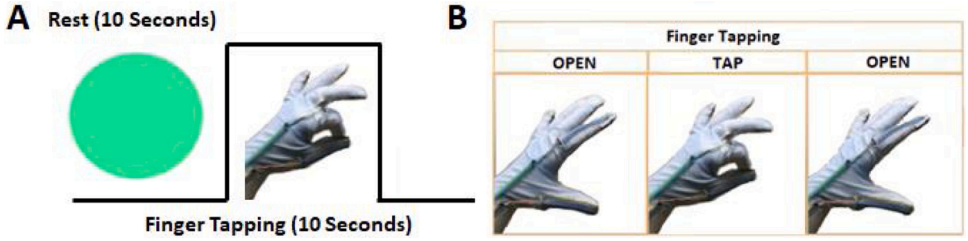

Fig. 1. **A**: Visual representation of task protocol: 10 s of rest precede 10 s of finger tapping. **B**: WearUP glove used for kinematic data collection.

Participants wore the glove on their right hands, and EEG and kinematic signals were recorded and monitored using the BCI2000 software package [36].

2.4. EEG data processing

All data preprocessing/processing was performed using MATLAB (R2016b). EEG data preprocessing was accomplished using the EEGLab toolbox [37]. Further processing of the EEG data was completed using custom scripts in MATLAB. EEG signals were first band-pass filtered 0.5−40 Hz using a 1691-point FIR Hamming windowed-sinc filter. Data were then subjected to Independent Components Analysis (ICA, runica algorithm). Components containing artifacts, including those related to eye blinks and instrumentation noise were marked and rejected from further analysis (5.9 ± 1.6 components rejected). Segments of EEG data were epoched from -10 s to 10 s relative to the cue indicating movement onset. Each epoch, therefore, consisted of 10 s of rest followed by 10 s of movement. Trials were also visually inspected, and artifactual trials were discarded.

EEG data were subjected to two distinct analyses. A time-frequency decomposition was performed via complex morlet wavelet decomposition. 20 complex morlet wavelets ranging from 2 to 40 Hz in 2 Hz steps were generated using a variable number of cycles (4–8 cycles). These wavelets were convolved with the 20-second epochs and squared power was extracted from the result. A percentage change baseline correction was applied to the mean time-frequency map for each participant using a baseline window of −4 to −2 s relative to movement onset as below:

$$TF_{corrected}(t,f,channel) = \frac{TF(t,f,channel) - \overline{TF}_{baseline}(f,channel)}{\overline{TF}_{baseline}(f,channel)} \quad (1)$$

where t is time, f is frequency, $TF_{corrected}$ is the baseline-corrected time-frequency map, TF is the uncorrected time-frequency map, and $\overline{TF}_{baseline}$ is the time average over the baseline window of the uncorrected time-frequency map. Coefficients were then summed over the frequency ranges of the α (8−14 Hz), low-β (14−20 Hz), and high-β (20−35 Hz) bands, and averaged over the time window from movement onset to 7 s after movement onset to determine an average ERD value for each participant.

The power spectral density (PSD) of each trial was also estimated using Welch's spectral estimate in order to correlate the aforementioned EEG band powers with kinematic features explained in the following sections. This was accomplished using 2-second windows with a 50 % overlap over the same sub-epoch of 0–7 s relative to movement onset.

2.5. Kinematic data processing

Kinematic data were first zero-phase filtered using a 3rd order Butterworth high-pass filter with a cutoff frequency of 0.5 Hz. Peak amplitudes and latencies were then extracted by finding all local maxima in the signal 1–8 s after movement onset. The peaks were then retained based on individual thresholds for minimum distance between peaks and peak prominence. Peak prominence is a single value determined by comparing each local maximum with the larger of the two minima in the regions extending outwards from the point of the maximum to either the point where the value of that local maximum is reached again or the end of the signal. A list of peak amplitudes was generated by taking the value of the signal at the detected peaks, while latencies were determined by subtracting the time indices of subsequent peaks. Average peak amplitude and latency were calculated for each trial within that window.

Sample Entropy (SaEn), an estimate of signal complexity, was also determined for each trial to quantify the irregularity of the kinematic data for each study group using a premade script [38]. Sample entropy is parameterized by two input parameters, along with the length of the data vector N: the embedding dimension m and the tolerance distance r. The value of m determines the length of the vectors to be compared, and r acts as a filtering threshold. Following similar previous works, we set the value of m to 2 [39] and the value of r to 0.2 times the standard deviation of the input data of each participant [40] Sample entropy is defined as below:

$$SaEn(m,r,N) = -\ln\left(\frac{\Phi^{'m+1}(r)}{\Phi^{'m}(r)}\right) \quad (2)$$

$$\Phi^{'m}(r) = [N-m]^{-1}\sum_{i=1}^{N-m}\frac{B_i}{N-(m+1)}$$

B_i = number of j, where $|X_i - X_j| < r,\ i \neq j$

$$X_i = (x_i, x_{i+1}, \ldots, x_{i+(m-1)})$$

$$X_j = (x_j, x_{j+1}, \ldots, x_{j+(m-1)})$$

where X_i and Xj are non-matching template vectors sampled starting from the i_{th} and j_{th} index of the time series data, $\Phi^{'m}$ is the average of the natural logarithm of the probability of the number of matching pairs of embedding vectors of length m within the data series with a distance less than or equal to r. The algorithm was applied to the same 7-second window used in the peak picking analysis (1–8 s relative to movement onset), resulting in an N of 1792 consistent with previous suggestions [39].

2.6. Cortico-kinematic analysis

A repeated-measures correlation (r_{rm}) analysis was applied to correlate the PSD measures of each trial with the corresponding kinematic variables, including mean peak latency, mean peak amplitude, and SaEn. Repeated-measures correlation analysis determines within-group correlations when each individual contributes multiple non-independent observations [41]. This analysis was applied to explore the linear cortico-kinematic relationships between repeated variables within each participant in each group. Each trial was treated as a measure, and trials in each group were labeled by participants to account for individuals' contributions to the overall correlation.

2.7. Statistical analysis

Univariate statistical analyses were performed on the means of the kinematic variables and the mean ERD variables for each frequency

band and participant. Due to the low sample size and lack of normality in our data, a non-parametric permutation test was used to determine if the groups differed significantly in any of the obtained variables. To do so, a null distribution of test statistics (*t*-values) was generated by randomizing the group labels of each observation and performing a two-sample *t*-test on each of 1000 iterations. The *t*-values of each iteration were stored and compared against the observed *t*-value. The ratio of null-distribution test statistics more extreme than the observed test statistic to the number of iterations was used to determine the *p*-value. A significance threshold was set to $\alpha = 0.05$. Spearman correlation between MOCA scores and cortical and kinematic with a significance threshold $\alpha = 0.05$ was also conducted to assess the univariate impact of cognitive state in PD on the physiological outcomes measured during this study.

3. Results

3.1. EEG analysis

Fig. 2 depicts the average baseline-corrected time-frequency map of each group. Overall, the healthy group showed greater desynchronization at motor-related frequencies (α and β-band frequencies) for the duration of the task when compared with the PD participants. Desynchronization was strongest in both groups at the beginning of the task and continued for the duration. The healthy group demonstrated mean desynchronization values of -34.5 ± 14.7 % in the α band, -47.9 ± 15.9 % in the low-β band, and -30.5 ± 11.4 % in the high-β band. The PD group demonstrated mean desynchronization values of -21.6 ± 27.0 % in the α band, -28.1 ± 19.5.0 % in the low-β band, and -11.0 ± 21.7 % in the high-β band. There was significantly stronger desynchronization in the healthy group than in the PD group in both the low-β ($p = 0.044$) and high-β ($p = 0.039$) bands within the 0–7 s time window relative to movement onset. However, no such significant difference was seen in the α band ($p > 0.05$). Fig. 3 shows a series of boxplots comparing EEG power statistics in each band between the two groups. As shown, the healthy group demonstrated greater desynchronization in all three frequency bands, though these differences were only significant in the low- and high-β bands. Furthermore, no significant correlation between MOCA scores and power in any of the assessed EEG bands was determined ($p > 0.05$).

3.2. Kinematic analysis

The kinematic data analysis revealed that the healthy group demonstrated a mean peak amplitude value of 1.04 ± 0.35 mV, a mean latency of 0.52 ± 0.19 s, and a mean entropy value of 0.20 ± 0.068. The PD group demonstrated a mean peak amplitude value of 0.97 ± 0.29 mV, a mean peak latency value of 0.50 ± 0.11 s, and a mean entropy value of 0.16 ± 0.08. However, no statistically significant differences between groups were found between the means of finger tap amplitude, latency, or Sample Entropy ($p > 0.05$). Fig. 4 illustrates kinematic data from two representative trials for one participant in each group, demonstrating the implemented peak-picking and Sample Entropy algorithms. As shown, the healthy participant exhibits a near-sinusoidal oscillatory pattern, though not all healthy participants showed this pattern. In the PD participant, a distinct pattern of larger amplitude peaks followed by a smaller peak is visible. Although not all participants in the PD group demonstrated this pattern, it was present in several, while no healthy participant showed this pattern. No significant correlation between MOCA scores and any of the assessed kinematic outcomes was observed ($p > 0.05$).

3.3. Cortico-kinematic analysis

Fig. 5depicts the repeated measures correlations (r_{rm}) between α, low-β, and high-β EEG band powers and kinematic peak latency measures in both groups. Power in the high-β ($r_{rm} = 0.46$, $p = 0.04$) band significantly correlated with average peak latency in the healthy group, while power in the α band ($r_{rm} = 0.15$, $p = 0.54$) and low-β band ($r_{rm} = 0.13$, $p = 0.59$) did not. In the PD group, no significant correlation was observed between α band power ($r_{rm} = 0.01$, $p = 0.97$), low-β band power ($r_{rm} = 0.08$, $p = 0.72$), and high-β band power ($r_{rm} = 0.26$, $p = 0.24$) and latency measures. This translates to a direct relationship between high-β power and tapping peak latency–as peak latency decreases (faster finger tapping), high-β power is also lowered.

However, no significant correlation was observed between kinematic peak amplitude and the aforementioned frequency bands in either group (i.e., healthy group: correlations between mean peak amplitude and α band power ($r_{rm} = -0.09$, $p = 0.71$), low-ß band power ($r_{rm} = 0.35$, $p = 0.13$), and high-ß band power ($r_{rm} = 0.34$, $p = 0.14$) and PD group: correlations between mean peak amplitude and α band power ($r_{rm} = -0.04$, $p = 0.87$), low-ß band power ($r_{rm} = 0.05$, $p = 0.82$), and high-ß band power ($r_{rm} = 0.16$, $p = 0.47$).

Fig. 6 depicts the repeated measures correlations (r_{rm}) between α, low-β, and high-β EEG band powers and kinematic sample entropy (SaEn) measures for each group. As shown, the healthy group demonstrated a significant correlation between sample entropy and high-β ($r_{rm} = -0.54$, $p = 0.01$), while the correlations between sample entropy and α band ($r_{rm} = -0.17$, $p = 0.47$) and low-β band ($r_{rm} = -0.18$, $p = 0.45$) were not significant. In other words, trials demonstrating higher kinematic signal complexity were associated with lower high-β band power. However, in the PD group, sample entropy did not significantly correlate with α ($r_{rm} = 0.11$, $p = 0.63$), low-β ($r_{rm} = 0.09$, $p = 0.68$), or high-β ($r_{rm} = -0.06$, $p = 0.81$) band power.

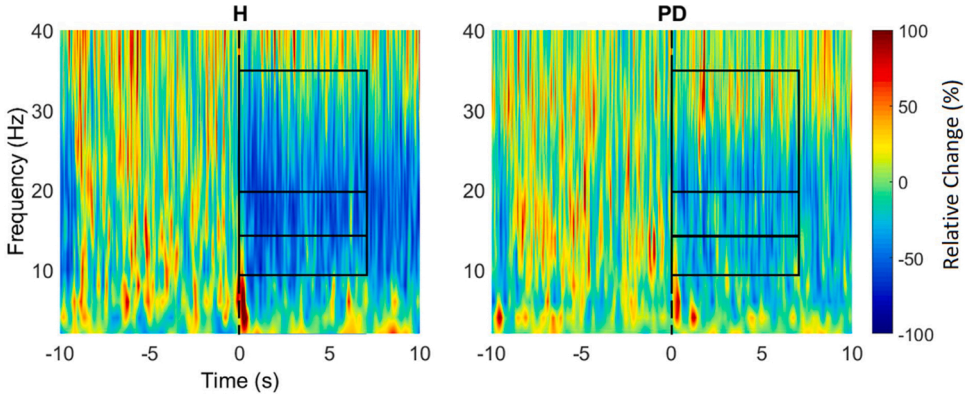

Fig. 2. Average baseline-corrected time-frequency maps for both groups of healthy (H) and Parkinson's disease (PD). Redder areas depict areas of greater synchronization, and bluer areas represent areas of greater desynchronization during the finger tapping task relative to the baseline. Black boxes denote the time/frequency ranges averaged over for each band.

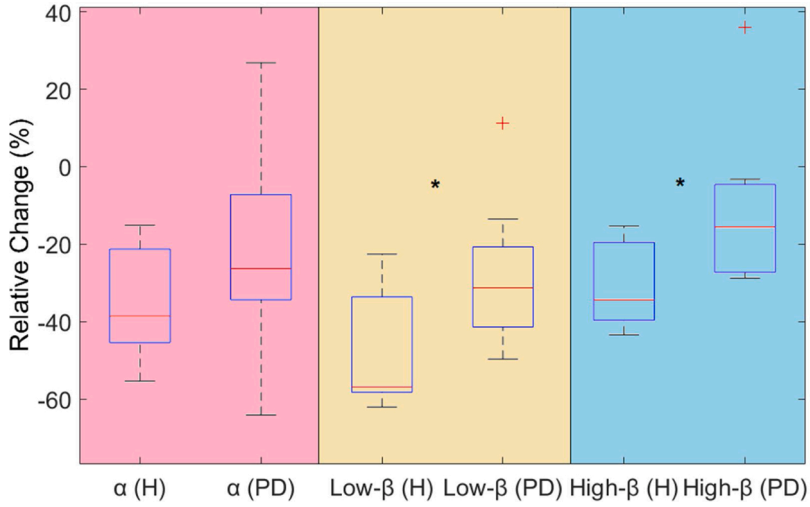

Fig. 3. Boxplots of EEG power. Significant ($p < 0.05$) differences between groups are marked with an asterisk (*). Means of each measure are denoted with a red bar. The upper bound of the box represents the 75th percentile and the lower bound represents the 25th percentile. Outliers are marked with a red cross.

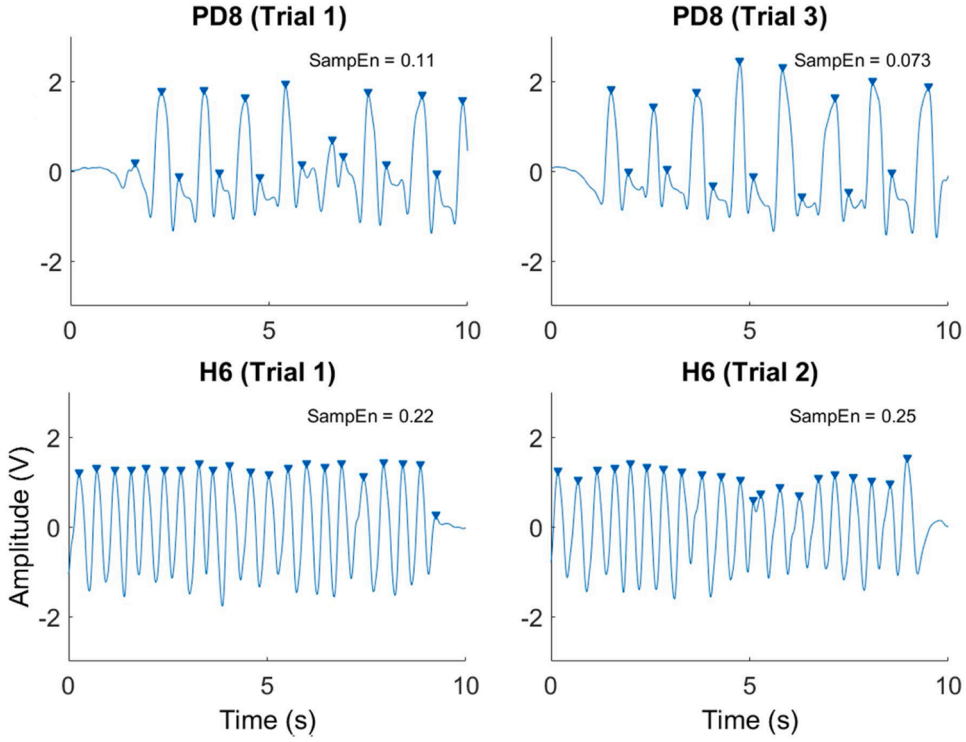

Fig. 4. Examples of kinematic data from two representative trials demonstrating the detected peaks and Sample Entropy values corresponding with individual trials taken from a participant in the PD group (top) and healthy (bottom).

4. Discussion

This study aims to assess the effects of Parkinson's disease on cortical, kinematic, and cortico-kinematic interactions during self-paced finger tapping tasks. Our main finding is that peak latency, and Sample Entropy in the kinematic data correlate with cortical high-β power in the healthy group, but this relationship is disrupted in the PD group. Additionally, the healthy group demonstrated stronger broad-β band reduction than the PD group, suggesting that one possible reason for these observed differences in relationships between variables might be partially associated with disruptions at the cortical level.

Although none of our kinematic outcomes significantly differed between groups (peak amplitude, peak latency, Sample Entropy), certain qualitative differences between groups could be observed in the kinematic data, especially within specific individuals with PD. Individuals within both groups exhibited different tapping patterns; however, several PD participants demonstrated a pattern of a high amplitude peak directly followed by a lower amplitude peak. Rejection of these shorter peaks would drastically increase the inter-tap latency measures of these participants in the PD group. Similar abnormal kinematic patterns in PD have been previously reported by other groups. For example, Puyjarinet et al. (2019) observed arrhythmicity in several motor systems, including upper limb motor systems, in individuals with PD even in the on-medication state [42]. Joundi et al. (2012) also found that finger tap rhythmicity was impaired in a PD cohort, which was improved after DBS of the subthalamic nucleus (STN) [43], while Freeman et al. (1993)

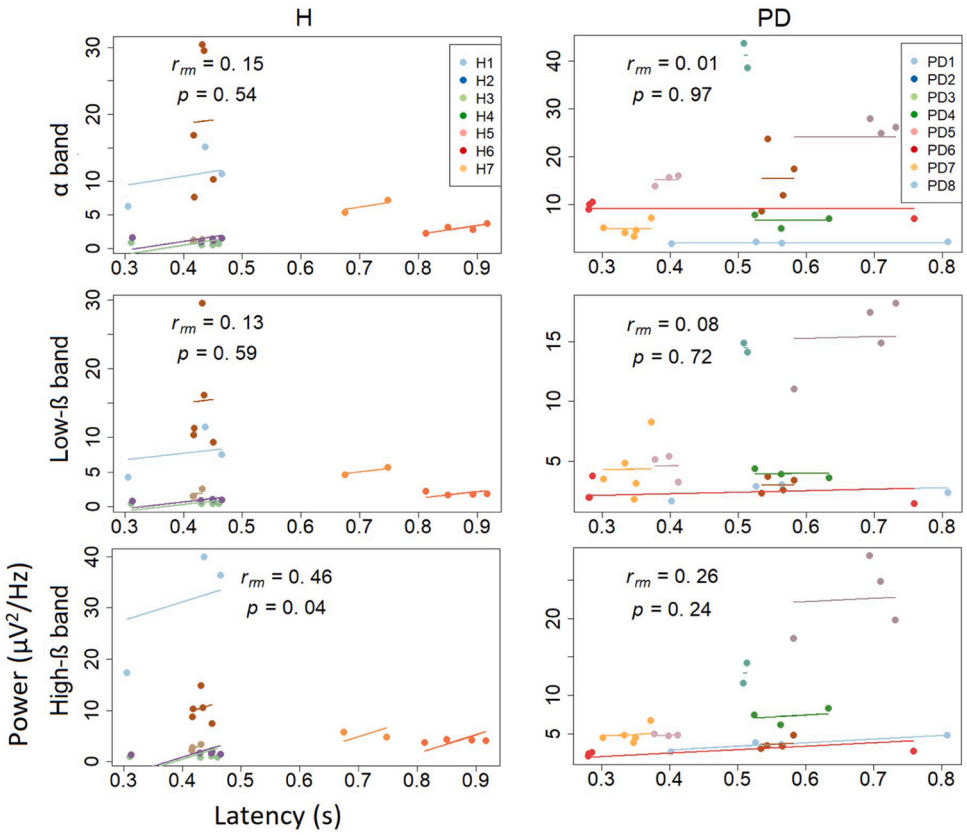

Fig. 5. Repeated measures correlations (r_{rm}) between mean kinematic latency measures and α (top), low-β (middle), and high-β powers (bottom) in the healthy (left) and PD (right) groups. Each color represents an individual within each group, and points correspond to single trial data. Note: A variable number of trials per participant were retained after trial rejection.

found that tap latency variability was increased in a medicated PD group, attributing this increased variability to disruptions in the basal ganglia that occur in PD [20]. One potential explanation for the lack of direct kinematic differences between groups could be the methods of data recording and peak detection- our analysis included the smaller kinematic peaks that may not be detected using other recording modalities (i.e. contact/pressure plates). The inclusion of more peaks decreases the mean peak latency of the PD group. These smaller peaks are also accounted for in the Sample Entropy as their associated discrete-time waveforms are included in the data segments over which the algorithm was applied.

In the healthy group, the significant positive correlation between kinematic peak latency and β-band power suggests that as the mean latency between consecutive finger taps decreases, β-band power decreases as well. Decreased β synchronization is suggested to correspond with the changing of motor states, while increased β synchronization is suggested to correspond with the maintenance of the current motor state [44]. Furthermore, studies have demonstrated that increased β synchronization is associated with slowed voluntary movement in neurotypical individuals [45] and animal models [30], a finding that is reflected in our peak latency analysis as well. Additionally, the speed of repeated kinematic tasks has been shown to correlate with β-band power in healthy groups [46]. The lack of correlation in the PD group can complement the results observed by Polar et al. (2018), who determined that a correlation present in healthy animals between cortical β-band power and gait speed was disrupted in an animal model of PD. However, when the abnormally elevated cortical β-band power of the PD model cohort was reduced via STN DBS, the amount of β reduction did not strongly correlate with motor improvement [30]. Joundi et al. (2013) also describe a similar lack of a linear STN β-band desynchronization when movement speed was varied in a PD population [47]. A possible interpretation of these observations is that impaired desynchronization during motor tasks in PD drives the disruption of the normal association between motor performance and β-band desynchronization, but does not necessarily drive motor task pathological disruption. We also found no significant differences between groups in the motor task, which supports this observation. It appears likely that the cortical between-group differences observed are reflective of disruptions of the basal ganglia that appear further along the motor circuit. Several studies have also determined that PD patients exhibit pathologically disrupted functional connectivity and coupling between deeper brain structures, including the basal ganglia [48,49] and globus pallidus internus (GPi) [16] and motor/sensorimotor cortex. For example, Tinkhauser et al. observed that pathological β-band bursts in the STN in unmedicated individuals with PD exhibited increased phasic coupling with the β-band activity over the sensorimotor cortex during rest. This group interprets the β-band burst activity as potentially limiting the amount of motor information encoded across the motor circuit. Similarly, in one of our previous studies we found that deep brain stimulation in PD participants targeting the GPi reduced coherence between the GPi and the motor cortex in the high β-band during a motor task, further suggesting that network-level disruptions in the cortical circuit may be present in PD [16]. Further work could elucidate the relationship between short-time β-burst activity in the cortex and deeper brain structures and kinematic outcomes more commonly used in the clinical setting to develop enhanced methods to diagnose and characterize PD. Furthermore, additional research should be done to explore whether cortico-kinematic characteristics can be clinically viable biomarkers for the diagnosis and assessment for PD. The discovery and standardized assessment of biomarkers of PD may prove to effectively supplement current objective clinical assessments by providing quantitative information from patients' cortical and kinematic data that is known to be

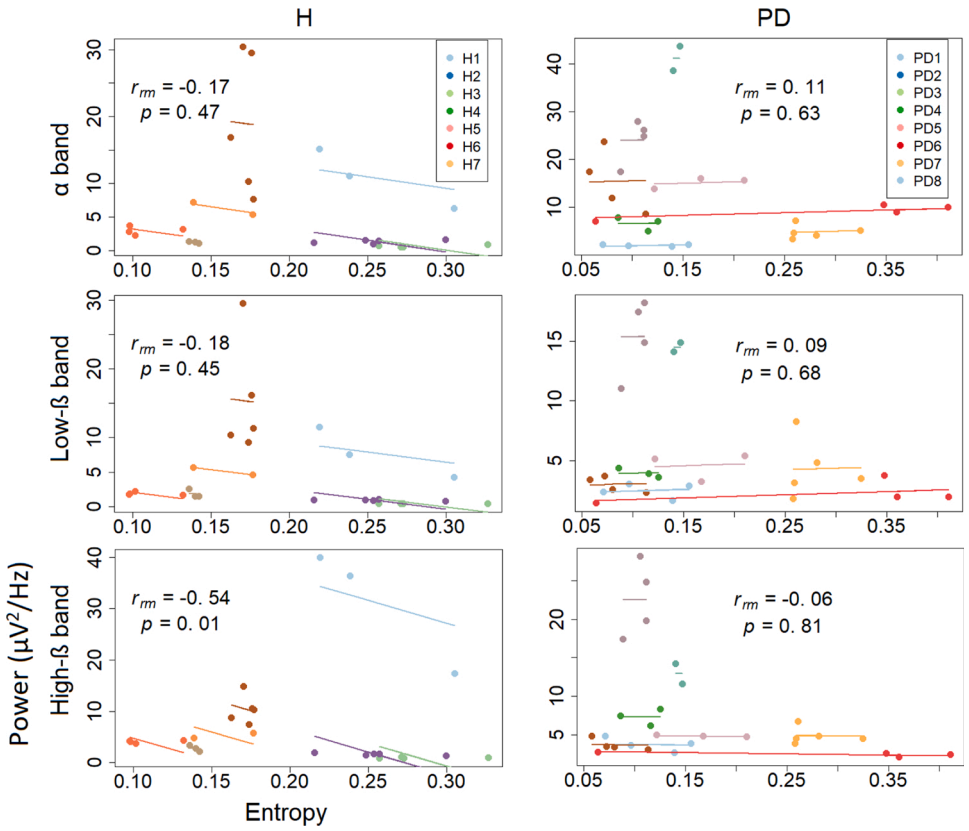

Fig. 6. Repeated measures correlations (r_{rm}) between the α (top), low-β (middle), and high-β powers (bottom) and entropy measures for the healthy (left) and PD (right) groups. Individual colors represent data from a single participant, and points correspond to single trial data. Note: A variable number of trials per participant were retained after trial rejection.

relevant to the disease state [50]."

Our results also demonstrated that Sample Entropy significantly correlates with high-β band power in the healthy group, while no such correlation was found in the PD group. Cortical ERD has been shown to intensify along with increased movement complexity [51], though it has not been correlated with a quantitative assessment of kinematic complexity such as Sample Entropy. This correlation was slightly stronger than the correlation between mean peak latency and high β-band power in our analysis, suggesting that Sample Entropy is capable of effectively capturing meaningful kinematic information from a single trial in healthy populations. It also establishes that this relationship between movement complexity and cortical high β-band ERD can be represented linearly. However, the lack of correlation in the PD group reinforces the notion that there is a level of cortico-kinematic decoupling in PD by establishing that the graded reduction of high β-band power during more complex kinematic tasks in the healthy group does not occur in PD.

The observation of greater desynchronization in the broad β-band in the healthy group when compared to the PD group contributes to a number of conflicting reports. Several studies have demonstrated that stronger ERD in the β-band is observed in the on-medication state relative to the off medication state during kinematic tasks [14,29], suggesting that low ERD could be associated with the pathological motor functions that medication is used to treat. Others claim that there is no clear pathological increase in cortical β-band in PD groups [52,53], although characteristics of waveform shape in that band or interactions with other frequency bands are indicative of disease. Still others have observed increased β-band ERD in a PD population relative to a control population, including Stegmöller et al. (2015) [11], who determined that β-band ERD was stronger in the PD group relative to the healthy group in both the off and on medication states. The same study also found that cortical β-band desynchronization was stronger in both PD groups at rest relative to the control group. However, Pollok et al. (2012) reported that cortical β-band oscillations were stronger in the PD group at rest when compared to a healthy group in the early disease stage [54]. The lack of a clear difference in cortical β-band power between groups suggests that band power alone does not differentiate groups, and that further work is required to fully understand and characterize the role of β-band ERD in PD compared to healthy populations. However, in our study, we demonstrated that the relationships between cortical band power and kinematic outcomes in real movement tasks could potentially be used to differentiate PD patients from healthy controls.

The main limitation of this study is the small number of trials and sample-size. Repeating this study with a greater number of trials and larger sample size would substantially increase the generalizability of our findings as well as the signal-to-noise ratio of our observations, especially those recorded using EEG and thus would inspire greater confidence in any subsequent findings. Including a cued finger-tap examination would also provide more critical information, as it has been shown that PD groups respond differently to different cued movement rates [11,12]. Recruiting PD participants from a more homogeneous pool (same affected side, similar symptom profile, etc.) would also be appropriate to investigate more detailed cortico-kinematic interactive features. Another potential limitation of this study is the use of EEG, which is notably susceptible to movement artifacts [55] during a kinematic task. The integration of other imaging modalities, including functional near-infrared spectroscopy (fNIRS) into further analyses during a similar experimental task, could provide additional insight into cortical dynamics during movement tasks. fNIRS has been demonstrated to be somewhat resistant to the motion artifacts that are common to EEG [56] and could be more appropriate for future clinical applications involving cortical monitoring during kinematic tasks in PD patients and

other neuromotor diseases. Other studies also utilize invasive methods to image the sensorimotor cortex, such as electrocorticography (ECoG) [33,57], which has been shown to provide higher signal quality when compared with EEG at the cost of accessibility and increased risk due to the invasive nature of the technique [58]. Further clinical applications of the findings of this study also remain limited by the relatively high cost of the EEG systems and their maintenance. EEG systems also require significant training to use appropriately and interpret results in a meaningful way. Additionally, due to clinical constraint, this study did not explore the associations with clinical measures of disease severity including Unified Parkinson's disease Rating Scale (UPDRS) scores, nor did this study control for levodopa equivalent dose (LED) [59], although the lack of correlation between MOCA scores and cortical or kinematic outcomes suggests that cognitive state of the participants did not impact the patterns observed. Thus, including clinical measures of disease progression and medication dose into future studies has the potential to provide more clinically relevant understanding about the role of cortical signatures in measured kinematic outcomes.

5. Conclusion

This study investigated the interactions between cortical oscillatory changes and kinematic outcomes through simultaneously recorded EEG and kinematic signals during a self-paced finger tapping task in two groups of people with PD and healthy controls. Overall, we demonstrated that the relationship between high-ß band cortical oscillations and kinematic measures are disrupted during a self-paced finger tap task, measured as mean kinematic peak latency and SaEn in PD groups. Our results additionally suggest that motor cortical high-ß band power inversely correlates with movement complexity in healthy groups and that this inverse correlation is absent in participants with PD. We also observed stronger broad ß-band ERD in the healthy group when compared with the PD group. These results suggest that cortical ß-band oscillations and their function in the normal movement are disrupted in people with PD, plausibly due to malfunctions of deeper brain structures in these cohorts. Our findings contribute to a better understanding of mechanisms underlying impaired interactive associations between cortical motor functions and motor kinematic outputs in Parkinson's disease. These outcomes can provide further directions for treatment and therapeutic applications and potentially establish cortical biomarkers of PD. Further studies of cortico-kinematic interactions could help to elucidate the pathological mechanisms through which motor symptoms of PD manifest and the role of cortical oscillations in normal motor function, as well as address the clinical need for objective assessments of clinical outcomes in PD on both the cortical and kinematic levels.

Author statement

Dr. Shahriari is the corresponding author and had supervised all the aspects of this project, including the IRB process, subject recruitment, data recording, data analysis, the interpretation of the results, and the manuscript preparation. John McLinden is the first author and had performed all the necessary computational analyses, interpretation of the results, and primarily completed the manuscript. Roohollah Jafari Deligani primarily had assisted in the signal processing and statistical analysis. Mohammadreza Abtahi had assisted in the healthy and patient recruitment and data collection. Dr. Akbar had assisted in patient recruitment, interpretation of the results, and proofreading of the manuscript. Dr. Mankodiya had provided financial support and assisted in technical aspects of the study and proofreading of the manuscript.

Data availability statement

The data are restricted from public availability, as they contain confidential information that may conflict with the privacy of the research participants

Ethics statement

All procedures were in accordance with the study protocol approved by the Institutional Review Board (IRB) of the University of Rhode Island. All participants provided informed consent prior to the experiment.

Funding statement

This study was supported by the National Science Foundation (NSF-1652538).

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgements

This study was supported by the National Science Foundation [grant number NSF-1652538]. The authors would like to thank the participants who took part in this study, without whom this study would not have been possible. We would also like to thank Alyssa Hillary Zisk for proofreading the manuscript and Seyyed Bahram Borgheai for assisting in data collection.

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