EEG Responses to Exercise Intensity in Parkinson's Disease

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1. Abstract

1.1. Background

Exercise is increasingly recognized as a beneficial intervention for Parkinson's disease (PD), yet the optimal type and intensity of exercise remain unclear. This study investigated the relationship between exercise intensity and neural responses in PD patients, using electroencephalography (EEG) to explore potential neural markers for optimal exercise intensity.

1.2. Method

EEG data were collected from 14 PD patients (5 females) and 8 healthy controls (HC) performing stationary pedaling exercises at 60 RPM with resistance adjusted to target heart rates of 30%, 40%, 50%, 60%, and 70% of maximum heart rate. Subjects pedaled for 3 minutes at each intensity level in a counterbalanced order. Canonical Time-series Characteristics (Catch-22) features and Multi-set Canonical Correlation Analysis (MCCA) were utilized to identify common profiles of EEG features at increasing exercise intensity across subjects.

1.3. Results

We identified a statistically significant MCCA component demonstrating a monotonic relationship with pedaling intensity. The dominant feature in this component was Periodicity Wang (PW), reflecting the autocorrelation of neural dynamics. Analysis revealed a consistent trend across features: six features increased with intensity, indicating heightened rhythmic engagement and sustained neural activation, while three features decreased, suggesting reduced variability and enhanced predictability in neural responses. Notably, PD patients exhibited more rigid, consistent response patterns compared to healthy controls (HC), who showed greater flexibility and variability in their neural adaptation across intensities.

1.4. Conclusion

This study highlights the feasibility of using EEG-derived features to track exercise intensity in PD patients, identifying specific neural markers correlating with varying intensity levels. PD subjects demonstrate less inter-subject variability in motor responses to increasing intensity. Our results suggest that EEG biomarkers can be used to assess differing brain involvement with the same exercise of increasing intensity, potentially useful for guiding targeted therapeutic strategies and maximizing the neurological benefits of exercise in PD.

2. Introduction

PD is a neurodegenerative disease associated with the accumulation of alpha-synuclein and loss of dopamine-producing neurons, particularly in the substantia nigra (Calabresi et al., 2023). Symptoms of this dopaminergic neuron loss include inability of voluntary movements, cognitive decline, tremors, muscle rigidity, and bradykinesia (Licen et al., 2022). Current treatments such as medication and deep brain stimulation (DBS) can alleviate its symptoms but do not fundamentally alter the course of the disease and vary in effectiveness depending on the individual (Ridgel et al., 2015). Consequently, it is crucial to explore new therapeutic approaches which can have rehabilitation potential without side effects.

Numerous studies have investigated the potential of exercise in improving various neurological and psychiatric diseases such as anxiety (Pontifex et al., 2021), Alzheimer's (Valenzuela et al., 2020), and Obsessive Compulsive Disorder (OCD) (Abrantes et al., 2019). In a meta-analysis, (Ensari et al., 2015) showed that exercise provides immediate relief from state anxiety, and (Pontifex et al., 2021) demonstrated its ability to alleviate cognitive impairments associated with anxiety. In addition, (Valenzuela et al., 2020) shed light on the advantageous role of exercise in mitigating Alzheimer's disease hallmarks. Exercise has also been shown to have a positive impact on balance in patients with stroke, PD, and multiple sclerosis, according to a systematic review (Salari et al., 2022). Subsequently, these studies emphasize the positive influence of exercise on various diseases and highlight the need for more research on the impact of exercise on patients with neurodegenerative diseases.

Cycling appears to be a particularly useful form of exercise for PD. (Alberts et al., n.d.) found that a PD subject experienced an improvement in her symptoms within two days after a tandem cycling expedition. Afterward, researchers conducted extensive investigations into the effects of pedaling on PD patients (Ridgel et al., 2009, 2012) (Ridgel et al., 2015). For instance, (Ridgel et al., 2012) documented a 38% reduction in tremors and a 28% improvement in bradykinesia following eight weeks of forced exercise using a tandem bicycle. In another study, participants in the dynamic high-cadence cycling group experienced significant improvements in their motor symptoms (Ridgel et al., 2015). As a result, investigations have continued to explore the rehabilitative effects of pedaling and to determine the optimal parameters, including speed and bicycle type (Ridgel et al., 2009). Furthermore, research has revealed that cycling ability remains in PD patients (Snijders et al., 2012), even those with severe freezing of gait (FOG) (Licen et al., 2022). Additionally, cycling poses a less demanding challenge than other forms of exercise due to its repetitive nature and overall reduction in beta band activity (Licen et al., 2022). As a result, pedaling is a viable option for PD patients, even in the presence of FOG.

Regardless of the already verified impact of exercise on brain activity, there is still a gap in understanding the effects of exercise as a function of duration, type, and intensity. A common approach to investigating changes in brain activity caused by exercise has been to compare immediate pre- and post-exercise states (Moraes et al., 2007) (Devilbiss et al., 2019) (Gutmann et al., 2015). However, examining EEG *during* exercise would enable the evaluation of several factors, such as exercise type, duration, and intensity (Enders et al., 2016) (Bailey et al., n.d.)..

In recent years, there has been growing interest in evaluating the advantages of dynamical features in brain recordings (such as EEG) to assess neurodegenerative brain diseases. Dynamical features can aid in providing crucial insights into the temporal fluctuations of brain connections, relations between neurodegenerative disease and clinical symptoms, and mechanisms underlying cognitive-motor impairment in neurodegenerative diseases. One approach to feature selection is to determine which features tend to be useful across many different types of data. (Lubba et al., 2019) examined the feasibility

and advantages of 4791 features of the Highly Comparative Time Series Analysis package over 93 classification tasks. They demonstrated the novelty and uniqueness of 22 Canonical Time-series Characteristics features ("Catch-22") resulting in high classification accuracy across various time-series scenarios while ensuring minimal redundancy. The Catch-22 features covered broad aspects of the temporal dynamics of different types of data, including distribution, extreme temporal events, linear and nonlinear autocorrelation, symbolic representations, incremental differences, simple forecasting, self-affine scaling, and other categories.

Here we use Catch-22 dynamical features of the EEG to monitor the impact of intensity pedaling on the brain activity of subjects with PD and healthy controls. Subjects pedaled at five different intensities while their EEG data were recorded. Using Multi-set Canonical Correlation Analysis (MCCA) (Fu et al., 2019) and we found the linear combination of EEG channels that demonstrated consistent trends across subjects as pedaling intensity was increased.

3. Methods

Experimental Protocol

In this study, 14 PD and 8 healthy control (HC) subjects were recruited from the Movement Disorders Clinic at the Pacific Parkinson's Research Centre, Vancouver, Canada. All subjects provided written, informed consent, and all research was reviewed and approved by the appropriate Ethics Boards. To optimize exercise tolerance, subjects took their usual anti-parkinsonian medication. People with stroke, severe cardiovascular disease, and other significant neurological or psychiatric disorders were excluded from the study. More information about PD subjects is in Table 1.

Table 1. Demographic information about the subjects included in this study.

Variables	Values
Age	60.66+_7.81
Male/Female	9/5
Honen-Yahr	1-3
Regular exercise	>100 minutes per week over 3 mo
Montreal Cognitive Assessment Sco	>24
Beck's Depression Score	<13
Beck's Anxiety Score	<9
Medication	Beta-blocker "Off" Anti-Parkinson "On"
Handedness (Right/Left)	11/4

Participants were seated on a stationary bicycle. A comfortable saddle position was set up so that participants could pedal comfortably. Each exercise session preceded a 5-minute warm-up to ensure the subjects' safety. Following the warm-up, subjects will be asked to pedal at different intensity levels defined as 30%, 40%, 50%, 60%, and 70% of their maximal heart rate (defined as: 0.85* (220-age)). Subjects were instructed to pedal constantly at 60 revolutions per minute (RPM), with resistance adjusted to modify the intensity level. Each intensity interval lasted 3 minutes, followed by a 3-minute recovery period. The intervals were assigned pseudo-randomly throughout the intervention, except for the 70% interval, which was never set as the first intensity interval. This intervention lasted 30 minutes since five intensity levels were used. The subjects were given a 5-minute cool-down period at the end of the pedaling period.

Nine electrodes located on F3, Fz, F4, C3, Cz, C4, P3, Pz, and P4 concerning frontal, central, and parietal regions to record EEG. These regions are crucial in capturing the brain's activity during the exercise. A stretchable head cap with Ag-AgCL electrodes (ANT Wave Guard cap, Advanced Neuro Technology B.V.) was used in this experiment. The reference electrode was positioned close to the vertex between the Cz and CPz electrodes. Over the frontal area of the scalp, between Fz and FPz electrodes, the ground electrode was positioned. Electrode impedances were kept below 10 kΩ.

3.1. Preprocessing

The first step of pre-processing involved artifact removal due to a significant amount of movement during the experiments. First, the common average reference (CAR) technique was applied, followed by high pass FIR filtering, low pass FIR filtering, and notch filtering to remove frequencies below 0.1, above 100, and 60 Hz line noise. A recursive least squares (RLS) algorithm was applied to remove eye-related (ocular) artifacts, and an adaptive filter was used in this method to remove eye blinks from the EEG signal by adjusting its coefficients in each iteration according to the difference between the EEG signal and the EOG signal. The automatic artifact rejection (AAR) plugin was used in EEGLAB in MATLAB 2018b to reject this artifact. Then, the EMG artifact was removed with the principal component analysis (PCA). In the last step, another remaining artifact source was removed with the help of the IClabel plugin of EEGLAB, and two of the nine components were removed.

3.2. Feature Extraction Using Catch-22

We utilized the Catch-22 package, which allows for extraction of 22 distinct features from each EEG channel, as listed in Table S1. The duration for feature extraction was specifically set to one second, corresponding to one complete cycle of pedaling (60 RPM). By synchronizing the feature extraction window with the pedaling cycle, we effectively isolated and minimized the impact of pedaling frequency on the EEG signals, ensuring that the extracted features more accurately reflected the underlying brain activity rather than the mechanical motion.

3.3. MCCA-Based Extraction of Intensity-Linked Neural Signatures

MCCA extends traditional CCA by analyzing relationships across multiple datasets. It identifies optimal linear combinations of variables (canonical variates) that maximize correlations between datasets. In this study, MCCA was applied to EEG data from 14 participants in a two-step process (Fig. 1).

3.3.1. First Round: Feature Selection
In the first round (upper dashed rectangle in Fig. 1), the data matrix for each subject was structured as 9 EEG channels by 110 observations (22 features across five intensity levels). This round served as a feature selection

step, aiming to identify features that consistently represented shared neural dynamics across EEG channels of all subjects. Nine canonical components were extracted (corresponding to the number of EEG channels), and features with the highest consistency across subjects were identified for further analysis.

3.3.2. Second Round: Detecting Neural Signatures

Building on the results above, the second round of MCCA focused on detecting the neural signatures of exercise intensity. Informative features selected from the first round, evaluated for their consistency across subjects within components 2–5 (as detailed in the results section), were used to refine the data matrices. These matrices, structured as 9 channels by 45 observations (9 features across 5 intensities), enabled more targeted analysis. This two-step approach ensured improved interpretability and computational efficiency by concentrating on features most relevant to exercise-induced neural dynamics.

3.4. Weighted Signal Analysis and Wavelet Transformation

To integrate the multichannel EEG data, a weighted aggregate signal was computed using channel weights derived from the MCCA analysis. To capture critical events in both the time and frequency domains, the Wavelet Transform was employed. Before transformation, EEG signals were averaged over one-second windows (corresponding to a single pedaling cycle at 60 RPM) to minimize noise and artifacts. This averaging step ensured that the signals reflected underlying neural activity rather than transient noise or mechanical motion.

Fig. 1. The pipeline displays the identification process of the most consistent features across EEG channels, highlighting those with the strongest relationship to exercise intensity.

4. Results

Artifact Identification via Principal Component Analysis

According to (De Cheveigné et al., 2019), the first component of MCCA may fail to provide a reliable reconstruction in the presence of significant artifacts. Following the findings of (Jiang et al., 2019), which suggest that PCA components with the highest variation are affected by motion artifacts, we conducted a detailed examination of the covariance matrix of our initial dataset to assess the variability of PCA outcomes. Our analysis suggested that the first component was considered an artifact, as illustrated in Fig. 2 for one subject. We therefore excluded the first component and concentrated our further investigations on components 2-4.

Figure. 2. Upper panel: Normalized variance of each component of MCCA. Lower panel: Normalized cumulative variance of components 2-9.

4.1. MCCA-Based Extraction of Intensity-Linked Neural Signatures

MCCA analysis at the first round showed that nine features exhibit high consistency across subjects within the meaningful components 2, 3, and 4. The feature values were normalized separately to obtain a better visual representation. Nine out of the 22 features exhibited consistent behavior across subjects. A detailed description of these nine consistent features is presented in Table 2. The results for component 3 are shown in Fig. 3 and Fig. 4, with supplementary Fig. S1 showing the control group for comparison. Six features, as mentioned in the second column of Table 2, showed an increasing trend with rising exercise intensity, while three features showed a decreasing trend.

Moreover, by focusing on the weighted vector of EEG data computing by multiplying EEG by the weights of MCCA, we observed a distinct cluster of harmonics that was concentrated around the alpha band, as depicted in the supplementary section in Fig. S4.

Table 2: Most consistent features of the Catch-22 package. Feature numbers and names are mentioned based on numbers listed in the Lubba et al. [REF].

Feature No.	Direction	Feature name	Description	Justification for Relevance to Pedaling Effects
4	Increasing	FirstMin_acf	Lag time to the first minimum of the autocorrelation function	The first moment of decreasing signals self-similarity. Important detecting changes in brain activity due to rhythmic pedaling
5	Increasing	HistogramAMI_even_25	Dependency between successive points of the time series	The extent of information sharing over intervals is useful for analyzing regular, cyclical motion impacts
7	Decreasing	Hrv_classic	The proportion of pairs of successive differing more than 4% of standard deviation, a classic measure in heart rate variability studies	Changes induced by physical exertion from pedaling
8	Increasing	BinaryStats_meanlongstretch	Length of the longest sequence above the mean, indicative of sustained higher activity levels	Prolonged periods of high brain activity, potentially induced by consistent pedaling
10	Increasing	PeriodicityWang	The regularity and periodicity in data at a fine scale	Directly relevant to detecting rhythmic patterns in EEG signals correlated with pedaling cadence
11	Increasing	Embed2_Dist_expfit_meandiff	Goodness of fit of an exponential curve to the time series, capturing the average change over embedded dimensions	Useful for understanding the adaption of brain dynamics over time during continuous pedaling
12	Increasing	AutoMutualInfoStat	The first minimum of auto mutual information, reflecting the least predictable Point in time	Moment of maximum change in brain state, triggered by variations in pedaling speed or intensity
18	Decreasing	MotifThree_quantile	Entropy in three-symbol motifs, assessing the predictability and complexity of patterns	Effective in capturing the complexity of brain signal responses to repetitive physical activities like pedaling
22	Decreasing	LocalSimple_mean3stderr	Standard error of a local simple mean with a window of three, assessing prediction error in the short-term	predictability of brain activity during physical exercise

Figure. 3. Trend across intensity for features of component 3 of PD subjects. The figure shows the aggregated (normalized) mean and standard deviation across subjects.

Figure. 4. Trend across intensity for features of component 3 of PD subjects. The figure displays (normalized) values of features for individual subjects (x-axis) for each feature.

4.2. Post-hoc Analysis: investigation of the Difference between PD and HC

To evaluate the differences in intensities and compare individuals with PD to HC subjects, we performed a repeated measures Analysis of Variance (ANOVA). We examined both the within-subject factor of pedaling intensity and the between-subject factor of group classification (PD vs. HC) to understand how features vary under different conditions. The results revealed a significant intensity interaction in the PD group ($10.25 < F < 514.5$, $0 < p < 0.004$) and a significant difference between PD and HC ($8.79 < F < 533.77$, $0 < p < 0.007$) groups, indicating that the changes in the features across varying intensity levels differed between the two groups. Also, the visual analysis showed that the HC subjects exhibited greater variability and inconsistency (in terms of the feature values) across different intensities, suggesting a less stable response to intensity changes. In contrast, the PD subjects displayed a more consistent pattern in their feature values, with relatively predictable changes across intensity levels. Details of the ANOVA test are shown in Table supplementary 5, Table S2.

5. Discussion

This study provides novel insights into the relationship between exercise intensity and brain dynamics in PD patients, revealing distinct patterns of neural activity during pedaling. The key finding is identifying consistent features that closely track pedaling intensity. These features, derived from MCCA of features extracted from EEG data, show that the neural response to varying exercise intensities is measurable and relatively robust across subjects. This offers potential biomarkers for optimizing exercise interventions in PD.

5.1. Adaptive vs. Predictable Neural Responses: Increasing and Decreasing Trends

Six features in component 3 showed an increasing trend with rising exercise intensity. "FirstMin_acf" and "HistogramAMI_even_25" imply enhanced rhythmic coordination and dependency between neural signals. "BinaryStats_meanlongstretch" and "PeriodicityWang" indicate prolonged engagement and consistency in neural activity, which align with the requirements of high-intensity movements. "Embed2_Dist_expfit_meandiff" and "AutoMutualInfoStats" related smoother adjustments and moments of significant change, reflecting adaptive neural responses. On the other hand, three features showed a decreasing trend, signifying reduced variability and enhanced predictability. "Hrv_classic" suggests streamlined processing, "MotifThree_quantile" reflects decreased complexity, and LocalSimple_mean3stderr indicates reduced short-term fluctuations, highlighting a shift toward efficiency and stability as intensity increases.

5.2. Flexibility in Healthy Controls vs. Rigidity in Parkinson's Disease

The comparison between flexibility and rigidity in neural responses highlights significant differences between HC and people with PD. HCs exhibit more flexible and variable neural activity, with patterns that adapt and fluctuate based on the intensity level of pedaling. In contrast, PD patients display more rigid and consistent neural response patterns, potentially indicating a fixed motor response strategy. This rigidity likely reflects the challenges PD patients face in adjusting motor control. Furthermore, HCs show

more significant inter-subject variability and adaptability to changes in intensity, emphasizing their capacity for dynamic motor adjustments. In comparison, the uniform responses observed in PD patients underscore the disease's impact on their ability to modulate motor control effectively.

Our results demonstrate that features in component 3 show clear monotonic relationships with pedaling intensity, as visualized in Fig. 3, where higher intensities were associated with prolonged periodic activity in the EEG signals. This trend aligns with prior work indicating that increased exercise intensity influences neural oscillations, particularly in the alpha frequency range (Ciria et al., 2018).

5.3. Therapeutic Role of Cycling in Parkinson's Disease Through Neural Biomarkers

Our findings build on existing evidence that cycling has rehabilitative benefits in PD by identifying a neural marker—e.g., Periodicity Wang (PW)—that may help tailor exercise intensity for therapeutic outcomes. Prior research has shown that cycling reduces symptoms such as tremors and bradykinesia in PD patients. Our study extends this understanding by providing a quantitative neural correlate of exercise intensity that can be used to optimize these interventions.

5.4. Limitations and Future Works

Our analysis relied on linear methods like MCCA, which may only partially capture the complexity of neural responses during exercise. Future work should explore nonlinear approaches to refine the detection of exercise-induced neural changes. Additionally, using only nine EEG electrodes limits the spatial resolution of the brain regions involved in these processes, which could be addressed in future studies using higher-density EEG arrays or multimodal neuroimaging techniques.

Future work related to this study could focus on testing the consistency of the features (over different pedaling intensities) among a larger number of subjects to confirm its applicability. In addition, the possible feasibility of the PW feature in developing biomarkers by other modalities, such as fMRI and ECG can also be scrutinized to determine its significance in wider contexts of neural and physiological measurements. Moreover, as MCCA provides common profiles through linear canonical analysis, nonlinear techniques could also be considered to capture the complexity of neural dynamics more effectively. as they could reveal subtle patterns and interactions that are not accessible through linear methods. Although we note that the CATCH-22 features included many non-linear measures.

6. Conclusion

This study underscores the potential of leveraging EEG-derived features to monitor exercise intensity in PD patients. In particular, the Periodicity Wang (PW) feature, which captures the autocorrelation of neural dynamics, demonstrated a reliable association with changes in pedaling intensity. Using Catch-22 features and MCCA, we identified a consistent neural response across subjects at varying intensity levels. Notably, features exhibited increasing trends, reflecting heightened rhythmic engagement and sustained neural activation, while other features showed decreasing trends, indicating reduced variability and a shift toward stabilized, predictable neural patterns. Together, these findings provide valuable insights for optimizing exercise-based interventions in PD, offering potential neural biomarkers to guide future therapeutic strategies.

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8. Code/Data Availability

The GitHub repository, including the codes of this paper, can be accessed here: https://github.com/zahraalz3523.
All data produced in the present study are available upon request to the authors.

9. Conflict of Interest Statement

None of the authors have potential conflicts of interest to be disclose.

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