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Electrophysiological alterations during action semantic processing in Parkinson's disease

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ABSTRACT

Assessments of action semantics consistently reveal markers of Parkinson's disease (PD). However, neurophysiological signatures of the domain remain under-examined in this population, especially under conditions that allow patients to process stimuli without stringent time constraints. Here we assessed event-related potentials and time-frequency modulations in healthy individuals (HPs) and PD patients during a delayed-response semantic judgment task involving related and unrelated action-picture pairs. Both groups had shorter response times for related than for unrelated trials, but they exhibited discrepant electrophysiological patterns. HPs presented significantly greater N400 amplitudes as well as theta enhancement and mu desynchronization for unrelated relative to related trials. Conversely, N400 and theta modulations were abolished in the patients, who further exhibited a contralateralized cluster in the mu range. None of these patterns were associated with the participants' cognitive status. Our results suggest that PD involves multidimensional neurophysiological disruptions during action-concept processing, even under task conditions that elicit canonical behavioral effects. New constraints thus emerge for translational neurocognitive models of the disease.

1. Introduction

Neurocognitive research on Parkinson's disease (PD) points to action concept processing as a key target for patient identification and characterization. This domain hinges on electrophysiological mechanisms typically compromised in the disorder. Yet, very few studies have examined such mechanisms in PD, and none has done so integrating event-related potentials (ERPs) and time-frequency (TF) measures. Also, most paradigms require fast motor responses, proving blind to how patients process such concepts in the absence of stringent time constraints. To bridge these gaps, we assessed ERPs and TF modulations as healthy persons (HPs) and PD patients performed a delayed-response semantic judgment task targeting action concepts.

Processing of action concepts (semantic units denoting bodily movements) is vital for normal functionality, as they mediate everyday life interactions with objects and people (Amoruso et al., 2013; van Elk et al., 2009). Evidence from HPs indicates that action concepts hinge on both neural and peripheral motor systems. Specifically, their processing distinctly engages motor brain regions (García et al., 2019; Pulvermüller, 2013) and networks (Moguilner et al., 2021a; 2021b), is differentially affected by M1 neurostimulation (Birba et al., 2020b; Tomasino et al., 2008; Vukovic et al., 2017), and it can modulate the planning and execution of bodily actions (García and Ibáñez, 2016a, 2016b; 2021b; Mirabella et al., 2012). Since motor system disruptions are the core signature of PD (Bloem et al., 2021), action concepts have been proposed as a strategic target to capture early markers of the

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disorder –a core claim of recent translation models, such as the disrupted motor grounded hypothesis (Birba et al., 2017).

Indeed, PD patients are impaired in comprehending (Bocanegra et al., 2017; Fernandino et al., 2013; García et al., 2018), associating (Bocanegra et al., 2015), and verbally expressing (Cotelli et al., 2007; Piatt et al., 1999; Rodríguez-Ferreiro et al., 2009; Signorini and Volpato, 2006) action concepts –although some studies have reported preserved behavioral performance in specific tasks (Aiello et al., 2022; Møller et al., 2023). Importantly, these deficits hold irrespective of patients' executive and domain-general dysfunctions, speaking to their systematicity beyond cognitive impairment (Bocanegra et al., 2015; García et al., 2017, 2018a). Moreover, they discriminate among disease subtypes (Bocanegra et al., 2017; García et al., 2018, 2022a), capture disease-specific neural disruptions (Abrevaya et al., 2017a, 2017b; Birba et al., 2022; Gallese and Cuccio, 2018), and do not emerge in disorders sparing motor circuitry (Birba et al., 2022; Moguilner et al., 2021a; 2021b). Briefly, together with exaggerated congruency effects, known as hyperpriming (Filoteo et al., 2003; Marí-Beffa et al., 2005; Spicer et al., 1994), action-concept anomalies constitute one of the best-established semantic particularities of PD.

However, most action concept research on PD only employs behavioral measures, failing to reveal relevant brain disruptions and precluding the integration of findings with neurobiological models of the disease. In particular, very few studies have used electroencephalography (EEG), a portable, low-cost technique that has revealed robust signatures of action concept processing in HPs (Amoruso et al., 2013; Cuellar and Del Toro, 2017). Relevant insights could be obtained by two EEG metrics: ERPs and TF modulations.

First, ERPs are time-locked voltage changes relative to a given event (e.g., stimulus presentation) (Sur and Sinha, 2009). In particular, the N400 component (a negative deflection peaking between 250 to 600 ms after stimulus presentation) (Kutas and Federmeier, 2011) is a key marker of the integration of action concepts evoked by images, videos, and verbs (Amoruso et al., 2013; Cervetto et al., 2021). In HPs, indeed, early (~250–300 ms) fronto-central N400 effects index the processing of action images (Amoruso et al., 2013) and efficient detection of incongruency between them (Amoruso et al., 2013; Bach et al., 2009; Mudrik et al., 2010; Proverbio and Riva, 2009; Proverbio et al., 2010), whereas later (~350–500 ms) effects are observed for action verbs (Cervetto et al., 2021; Dalla Volta et al., 2018; Zhou et al., 2022).

Second, TF modulations are ongoing changes in the synchronization of EEG signals over specific frequency bands (Morales and Bowers, 2022). In HPs, frontocentral theta (4–8 Hz) enhancement underlies semantic retrieval and incongruency detection (Maguire et al., 2015; Reid et al., 2009), driven by contextual expectations and conflict monitoring (Urgen et al., 2013). Also, theta modulations often precede the desynchronization of mu rhythms (8–14 Hz) (Urgen et al., 2013), commonly observed during action observation and execution (Coll et al., 2017; Pineda et al., 2000; Quandt et al., 2012, 2013) –a hallmark signature of covert action simulation, traceable to the mirror neuron system (Debnath et al., 2019; Pineda, 2005). Similar effects emerge in the face of action images during verbal (Cuellar and Del Toro, 2017) and non-verbal (Pfurtscheller et al., 2006) tasks, including semantic judgment (Moreno et al., 2015).

Yet, to our knowledge, no previous study has jointly examined ERP and TF correlates of action semantic processing in PD. A recent study on the disease found abolished N400 modulations when action concepts occur in incongruent events, pointing to abnormal semantic integration (Wyrobnik et al., 2022). Also, though theta and mu oscillations remain unexplored in action-concept research on PD, they are attenuated over mid-frontal electrodes when patients face conflict resolution and error adjustment demands (Cavanagh et al., 2018; Singh et al., 2018) –as those involved in action relatedness tasks. Though incipient, then, action-concept EEG research on PD has potential to uncover fine-grained markers of the disorder.

Here, HPs and PD patients performed an action relatedness judgment task featuring related and unrelated picture pairs and requiring delayed responses (a strategic approach to circumvent speed-related errors in PD). In each group, we first tested for action relatedness effects, namely, the response time (RT) difference between unrelated and related trials. We then established task-specific N400 and theta/mu modulations in HPs, replicated the analysis on PD patients, and examined whether detected effects were associated with participants' cognitive outcomes.

We raised three sets of hypotheses. First, we predicted that, relative to related trials, unrelated trials in HPs would yield slower responses, increased early N400 modulations, higher theta enhancement, and reduced power decreases in mu rhythms. Second, we anticipated that PD patients would also exhibit a behavioral relatedness effect (since the task gives ample time to respond), but that early electrophysiological effects observed in HPs would be abolished or altered. Finally, in light of previous works, we hypothesized that semantic EEG indexes would not correlate with patients' cognitive outcomes. By testing these conjectures, we aim to illuminate the neurocognitive bases of action semantic processing in PD.

2. Methods

2.1. Participants

The experiment was part of a larger study reported elsewhere (Bocanegra et al., 2017; García et al., 2018, 2021, 2022b). It involved 43 individuals (25 HPs, 18 PD patients). A power analysis, on MorePower 6.0.4 (Campbell and Thompson, 2012), indicated that 18 participants were required to detect an effect size of Cohen's $d = 0.7$ with 80% power (alpha =.05). This effect size was set based on previous studies reporting medium-to-large semantic relatedness effects (Luka and Van Petten, 2014; Kraemer, Wulff and Gluth, 2021). Participants were native Spanish speakers, with normal or corrected-to-normal vision, and all but one were right-handed (Oldfield, 1971). HPs presented a normal cognitive profile, were functionally autonomous, and had no history of substance abuse or psychiatric disorders. Patients were diagnosed by an expert neurologist (LM) according to the UK PD Society Brain Bank criteria (Hughes et al., 1992). All of them were on antiparkinsonian treatment and completed the study during the "on" medication phase. No patient had a history of substance abuse or major psychiatric disorders, and none had undergone deep brain stimulation. The patients' medication was converted to Levodopa equivalent daily dose (LEDD) following a reported formula (Tomlinson et al., 2010). Motor symptoms were evaluated with the Hoehn & Yahr scale (Hoehn and Yahr, 1967) and part III of the Unified Parkinson's Disease Rating Scale (UPDRS-III) (Fahn, 1987). Functional skills were assessed using the Lawton & Brody (Lawton and Brody, 1969) and Barthel (Mahoney, 1965) indexes. Executive functions were evaluated with the INECO Frontal Screening (IFS) battery (Torralva et al., 2010) and overall cognitive status was examined via the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), proven to be sensitive for PD (Gill et al., 2008; Kandiah et al., 2014; Solcà et al., 2018). Matching between both groups (in terms of sex, handedness, age, and education) was achieved via the MatchIt R package (Ho et al., 2007) and confirmed through statistical tests (Table 1).

Each participant signed a written informed consent. All procedures were approved by the institutional ethics' committee and performed according to the Declaration of Helsinki guidelines and regulations.

2.2. Stimuli

Stimuli comprised 100 pairs of black-and-white line drawings depicting motor actions. In half of these pairs, the two pictures were *related*, as they presented shared sensorimotor attributes (e.g., the effectors involved: RUN-WALK) or contextual affinities (e.g., two actions related to musical performance: PLAY-SING). In the remaining half, both pictures were *unrelated*, since they had no apparent similarity in their

Table 1
Participants' demographic and clinical data.

	Healthy persons (n = 25)	PDpatients (n = 18)	Pairwise comparisons		
			Estimate	*Df*	*p*-value
Sociodemographic profiles					
Sex (F:M)	8:17	4:14	.73	-	0.73[a]
Handedness (L:R)	0:25	1:17	.41	-	0.41[a]
Years of age	62.08 (7.96)	64.72 (8.45)	-1.6	35.41	0.30[b]
Years of education	13.32 (5.36)	13.22 (4.96)	.06	38.40	0.61[b]
Clinical profiles					
IFS	23.48 (2.81)	19.61 (4.13)	3.43	28.04	< .01[b]
MoCA	26.4 (1.70)	23.78 (3.6)	2.86	22.36	< .01[b]
LEDD	-	691.39 (361.01)	-	-	-
UPDRS-III	-	32.22 (12.92)	-	-	-
Hoehn & Yahr	-	2.17 (.38)	-	-	-

Data presented as mean (SD), with the exception of sex and handedness. (a) p-values calculated via Fisher's exact test; (b) p-values calculated via two-tailed independent samples t-test. PD: Parkinson's disease. IFS: INECO Frontal Screening; MoCA: Montreal Cognitive Assessment; LEDD: Levodopa equivalent daily dose; UPDRS-III: part III of the Unified Parkinson's Disease Rating Scale.

sensorimotor attributes or contextual affinities (e.g., SING-CRAWL). All action stimuli were matched for visual complexity, picture-name agreement, and lexical properties of their associated words (Table 2). Stimuli and their quantitative properties were extracted from the Center for Research in Language International Picture-Naming Project corpus (Bates et al., 2003).

2.3. Procedure

Participants sat in a dimly illuminated sound-proof EEG room, facing a computer, and performed a delayed-response semantic judgement task (Figure 1). They were instructed to view two consecutive action pictures, read a question (inserted to promote delayed responses), and decide whether the pictures were semantically related. The instruction read as follows: "Press the green button if both pictures are related. Press the red button if both pictures are not related". Each trial started with a black fixation cross for 500 ms, followed by a 200-ms white screen. An initial picture was shown for 1000 ms, followed by a 200-ms blank screen that led to a second picture, shown for 1000 ms. The intermediate question ("Are both pictures related?") was shown immediately afterwards and remained on screen for 4500 ms or until response onset. This element was strategic to prevent forcing fast responses that could prove unduly challenging for PD patients (Moustafa et al., 2016; Wu et al., 2015). Participants were instructed to press a green button if the pair was related or a red button if they were not. The inter-trial interval varied randomly between 0 and 200 ms after a response was made or after the question disappeared. The session was composed of two pseudo-randomly presented blocks, each including 25 related action trials, 25 unrelated action trials, and 50 non-action filler items to reduce attentional bias toward action processing alone. These 50 pairs comprised 25 related and 25 unrelated combinations of symbols, shapes, and non-manipulable objects. There was a 3-minute break between blocks. Six practice trials were presented at the beginning for task familiarization purposes. The full session lasted roughly 25 min per participant.

2.4. EEG recording and preprocessing

Electrophysiological data were acquired during the task from 58 electrodes mounted on an elastic Electro-Cap, arranged per the 10–10 international system, and amplified via Neuroscan (Scan 4.5, SynAmps2). An additional right auricular lobule electrode was used as reference together with a ground electrode placed between the Cz and Fz channels. Vertical and horizontal electro-oculograms were recorded to monitor eye blinks and movement through two bipolar channels placed at the outer canthus and two electrodes above and below of each eye. The signal was digitized at 1000 Hz and online filtered (pass band filter: 0.05–200 Hz; notch filter: 60 Hz). Subsequently, the signal was resampled offline to 500 Hz (pass band filter: 0.5–40 Hz) and re-referenced to the average of all electrodes. Data were preprocessed on EEGLAB v2021.1 (Delorme and Makeig, 2004) and transformed to Fieldtrip format for further data analysis (Oostenveld et al., 2011). Bad channels were interpolated using statistically weighted spherical interpolation (based on all channels).

The continuous data were segmented into epochs of 5000 ms for the stimulus-locked analyses (2500 ms before and after the onset of the second picture). Then, independent component analysis was applied to remove eye movements and blink. Also, segments containing voltage fluctuations higher than ± 200 μV were discarded. Finally, any remaining epochs with artefacts (movements, muscle activity) were rejected through visual inspection (Birba et al., 2020a; Cervetto et al., 2021; Díaz-Rivera et al., 2022; Dottori et al., 2020). All epochs were baseline-corrected from − 200 to 0 ms locked to the second picture in each trial (Verleger et al., 2013).

2.5. Data analysis

2.5.1. Behavioral data analysis

A linear mixed effects model, with individual subjects and trials as random effects, was employed to examine accuracy and RT differences between related and unrelated trials in each group separately. Trials were removed from analysis if they were incorrect or if their RTs fell below 200 ms or exceeded 3 *SD*s from each participant's mean per condition. To fulfill normality assumptions in RT analysis, data was first normalized via the Ordered Quantile transformation, identified as the

Table 2
Stimulus data.

	Related action pictures				Unrelated action pictures			
	Initial picture	Second picture	Estimate	*p*-value	Initial picture	Second picture	Estimate	*p*-value
Picture data								
Visual complexity	21569.91 (6140.57)	22102.17 (6530.55)	$t = -0.41 df = 92.85$	.68	22106.46 (6681.51)	22556.10 (6858.96)	$t = -0.33$ $df = 95.00$	.74
Name agreement	70.31 (22.46)	74.31(21.50)	$t = -0.88 df = 92.60$	.37	70.27(21.96)	73.10(23.06)	$t = -0.62 df = 94.92$	.53
Picture name data								
Age of acquisition	2.06(1.00)	2.12(1.00)	$t = -0.30 df = 92.93$	.77	2.33(0.95)	2.10(1.00)	$t = 1.16 df = 94.90$	.25
Phonemes	6.38(1.10)	6.37(1.20)	$t = 0.0$ $df = 92.58$	.97	6.41(1.17)	6.41(1.17)	$t = 0.04$, $df = 95.00$	.97
Syllables	2.38(0.49)	2.41(0.58)	$t = -0.30 df = 91.24$	.76	2.41(0.54)	2.39(0.57)	$t = 0.26 df = 94.87$	.80
Frequency	2.39(1.64)	2.51(1.64)	$t = -0.34 df = 92.95$	.73	2.39(1.68)	2.48(1.56)	$t = -0.28$ $df = 94.20$	.78

Data presented as mean (SD). All comparisons were made via two-tailed independent samples t-tests.

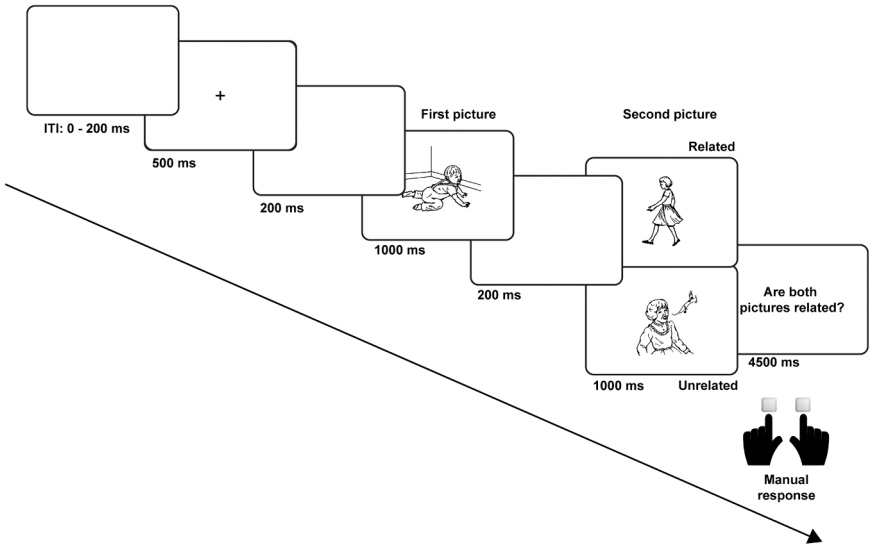

Fig. 1. Temporal structure of the experimental task. Participants first viewed a fixation cross followed by an initial action picture which was followed by another action picture which could be related or unrelated to the first one. Participants were instructed to judge whether both pictures were related or not during the presentation of a long-lasting question, introduced to promote delayed responses and circumvent speed-related errors in patients.

best fitting method by the Best Normalize R package (Peterson, 2021). Comparisons between conditions were estimated using least square means (lsmeans). Alpha levels were set at $p < 0.05$. Effect sizes were calculated through Cohen's *d* for pair-wise contrasts. All behavioral analyses were performed on R (version 3.5.2).

2.5.2. ERP analyses

ERP analyses were implemented on Fieldtrip (version 20211121) (Oostenveld et al., 2011). All analyses were performed only on correct trials. To compute the ERP waveforms, the artefact-free, correct-trial EEG data was averaged separately for each participant and conditions. The resulting data structures were analyzed using cluster-based permutation tests (Maris and Oostenveld, 2007), a data-driven procedure successfully implemented in previous action-language reports (de Vega et al., 2016; Liu et al., 2020a; Liu et al., 2020b). Using dependent-samples *t*-tests with an alpha level of 0.05, we identified the largest cluster of adjacent channels (minimum of three neighbors) and time-points displaying a comparable difference between conditions. A permutation framework was used in conjunction with spatiotemporal clustering to create a distribution of test statistics based on clusters, assuming the null hypothesis that the data is exchangeable among conditions. To determine significance, the permutation *p*-value was computed using the Monte Carlo method with 1000 random permutations. A Monte Carlo cluster *p*-value below 5% (with two-tailed testing) was considered statistically significant. All electrodes and time points were blindly scanned during the 0–800 time-window. This approach is intended for multiple pairwise comparisons of amplitude changes across spatiotemporal dimensions (here, within-group contrasts between related and unrelated conditions), while effectively controlling for type-I error rate (Beltrán et al., 2019; Díaz-Rivera et al., 2022; Wang et al., 2011).

2.5.3. Time-frequency analyses

TF representations of power were estimated from artefact-free, correct-trial EEG segments at frequencies between 2–30 Hz. Based on action semantic research (Coll et al., 2017; Moreno et al., 2015; Pineda et al., 2000; Quandt et al., 2013; Quandt et al., 2012; Urgen et al., 2013), we restricted our analyses to the theta (4–8 Hz) and the mu (8–14 Hz) bands. We used a frequency-independent Hanning taper and a 500-ms sliding window advancing in 50-ms steps. Power was normalized to reflect the relative change from a baseline period (200 ms before the second picture). Finally, for each participant, TF representations were averaged over the related and the unrelated trials separately. Differences between conditions were assessed using cluster-based permutation tests based on dependent-samples *t*-tests implemented in Fieldtrip (version 20211121) (Maris and Oostenveld, 2007). Clusters were established following the same parameters used for ERP analyses.

2.5.4. Exploratory correlations between EEG patterns and cognitive outcomes

To test whether task-related semantic processes were related to cognitive outcomes, we performed exploratory correlations between ERP/TF indexes and scores on measures of executive functions (the IFS) and overall cognitive status the (MoCA). First, we subtracted the mean amplitude (for ERPs) and power (for TF) of the related and unrelated conditions corresponding to significant spatiotemporal clusters (in the case of non-significant clusters emerge in PD patients, their EEG indices would be estimated from masks derived from HPs' significant clusters). Then, we correlated every index with each participant's total IFS and MoCA scores via Spearman's rank coefficient, with an alpha level set at $p < 0.05$, and corrected through the false discovery rate (FDR) tests (Birba et al., 2022).

3. Results

3.1. Healthy persons

3.1.1. Behavioral results

For HPs, accuracy analyses yielded no significant differences (*t*-ratio = −5.20, $df = 41$, $p = 0.6$) between related ($M = 0.88$, $SD = 0.06$) and unrelated ($M = 0.89$, $SD = 0.10$) trials. Conversely, RT analyses revealed a significant effect of condition (*t*-ratio = −3.174, $df = 3405$, $p < 0.001$), with faster responses for related ($M = 1163.80$, $SD = 434.93$) compared to unrelated ($M = 1174.20$, $SD = 453.77$) trials (Cohen's $d = -0.05$, 95% C.I. = −0.13, 0.04).

3.1.2. EEG results

HPs exhibited consistent relatedness effects. ERP analysis yielded a significant effect [*t*(maxsum) = 1994, $p = 0.004$] on ERP analysis, with more negative amplitudes for unrelated than for related action pictures. This effect was distributed over bilateral fronto-central electrodes, and the most prominent time interval of the cluster was from 222 to 360 ms

after the presentation of the second picture (Fig. 2A1). As regards TF analyses, significant differences were observed in the theta (4–8 Hz) band [t(maxsum) = −203.20, $p < 0.01$], with reduced power for related than for unrelated trials over left fronto-temporal electrodes between 550 and 800 ms (Fig. 2A2, top). A significant effect [t(maxsum) = −156.44, $p = 0.02$] was also observed in mu rhythms (8–14 Hz), with prominent modulations over left temporo-parietal electrodes from 400 to 750 ms (Fig. 2A2, bottom).

3.2. PD patients

3.2.1. Behavioral results

For PD patients, accuracy analyses revealed no significant differences (t-ratio = 0.58, $df = 41$, $p = 0.6$) between related ($M = 0.82$, $SD = 0.08$) and unrelated ($M = 0.85$, $SD = 0.20$) trials. Yet, significant differences did emerge in RT analyses (t-ratio = −5.642, $df = 3406$, $p < 0.001$), with faster responses for related ($M = 1322.10$, $SD = 474.40$) compared to unrelated ($M = 1451.90$, $SD = 470.60$) trials (Cohen's $d = -0.40$, 95% C.I. = −0.40, −0.18).

3.2.2. EEG results

ERP effects were not replicated in PD patients. Non-significant relatedness effects were observed in both the ERP ($p > 0.05$; Fig. 2, B1) and the theta-band ($p = 0.07$; Fig. 2B2, top) analyses. Conversely, mu rhythm results revealed a significant relatedness effect [t(maxsum) = −160.82, $p < 0.01$] over fronto-centro-parietal electrodes between 550 and 800 ms, but this cluster, unlike that of HPs, was right-lateralized (Fig. 2B2, bottom). Also, in an exploratory fashion, we ran separate cluster-based permutation analyses on ERP amplitudes and theta/mu oscillations over frontal, central, centroparietal, parietal, parietooccipital, and occipital regions of interest (see Supplementary materials, Section 1). These results align with our main data-driven results.

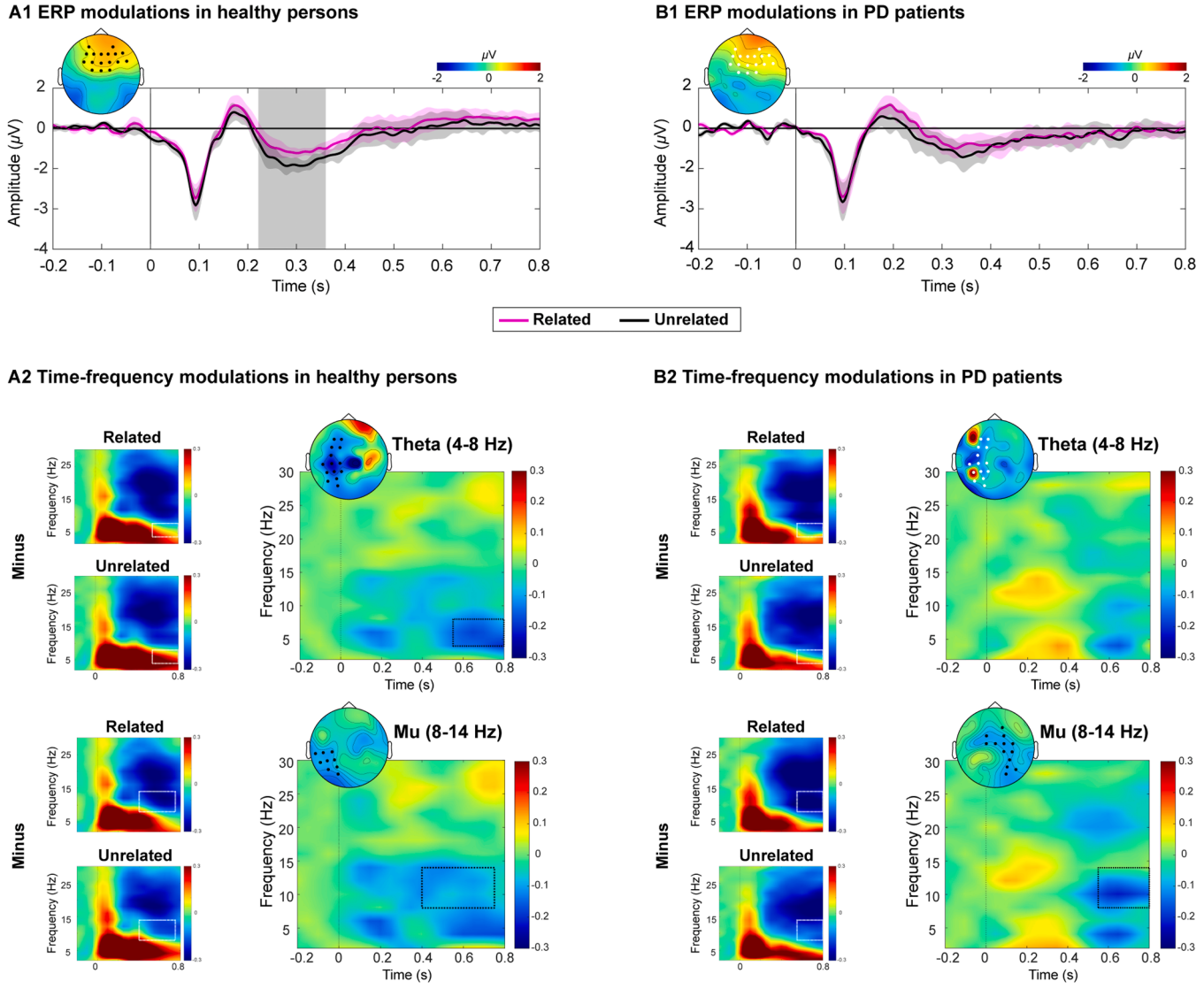

Fig. 2. Electrophysiological results. **A.** Results for healthy persons. **A1.** ERP analysis revealed significantly greater N400 amplitudes for unrelated than for related trials over a frontocentral cluster (the gray rectangle represents significant differences across time-points). **A2.** Between-condition comparison of time-frequency charts revealed significant spatiotemporal oscillatory clusters in the theta (4–8 Hz) and mu (8–14 Hz) frequency bands. Both frequency charts demonstrate modulations in both the related and unrelated conditions on the left side (white rectangle denotes significant effects), with the subtraction and respective left-lateralized cluster depicted on the right side (black rectangle denotes significant effects). **B.** Results for persons with PD. **B1.** The contrast between conditions revealed no significant ERP modulations in the patients. **B2.** Theta band modulations were also abolished in the patients, while analysis of mu rhythms revealed a contralateralized (right-hemisphere) cluster.

3.3. Correlation results

No significant associations were found between any of the EEG indices (N400, theta, mu) and either IFS or MoCA scores (Table 3).

4. Discussion

We leveraged a delayed-response task to investigate neural correlates of action-concept processing in HPs and PD patients. While both groups responded faster to related than to unrelated action pictures, they exhibited different EEG signatures. In HPs, unrelated trials involved greater N400 amplitude as well as greater theta and mu modulations. In PD patients, conversely, N400 and theta signatures were abolished while mu effects were contralateralized. Modulations of these indices were not correlated with cognitive outcomes in either group. Such findings offer new insights on the neurobiology of action concept processing in PD, as discussed below.

HPs had shorter RTs to related action pictures. This replicates previous findings from movement-object congruency (Vainio et al., 2008) and action-verb access (Vigliocco et al., 2004) studies, corroborating that action concept processing benefits from priming of relevant semantic features (Spruyt et al., 2009). More interestingly, the same effect was observed in the patient group. While this might seem counterintuitive given the robustness of action concept deficits in PD, such finding was predictable given the use of a delayed-response paradigm. Indeed, preserved behavioral outcomes have been reported in this population when performing temporally unconstrained action semantic tasks (Aiello et al., 2022; Møller et al., 2023). Moreover, this RT pattern had a larger effect size in the patients. Tentatively, this might be a manifestation of hyperpriming –namely, the tendency of PD patients to over-rely on preactivated conceptual features due to reduced semantic inhibition (Toro-Hernández et al., 2024), leading to greater difficulty to identify unrelated actions (Filoteo et al., 2003; Marí-Beffa et al., 2005; Spicer et al., 1994). Though further testing is required, behavioral recognition of action relatedness in PD seems preserved if sufficient time is provided for responding. However, this result could be partly influenced by different response strategies in each group and should thus be interpreted cautiously (Benjamin, 2005).

Conversely, early neurophysiological effects in HPs were not replicated in the patients. In HPs, unrelated actions involved more negative ERP amplitudes in a ≈ 230–350 ms window, mirroring the direction and latency of previous action picture congruency studies and suggesting fast detection of semantic conflict (Amoruso et al., 2013; Bach et al., 2009; Mudrik et al., 2010; Proverbio and Riva, 2009; Proverbio et al., 2010). This was accompanied by left-lateralized theta and mu effects, similar to those observed during dynamic action observation, execution, and imagery (Coll et al., 2017; Cuellar and Del Toro, 2017; Pfurtscheller et al., 2006; Pineda et al., 2000; Quandt et al., 2012, 2013; Urgen et al., 2013). In line with previous accounts, such effects would index sustained neural reactivity to semantic incongruence (Atienza et al., 2011; Hald et al., 2006) and motor simulation under conceptual conflict (Lam et al., 2017; Wamain et al., 2023), respectively. Briefly, present and previous EEG findings suggest that, in HPs, action-relatedness judgments entail early and long-lasting modulations of motor-sensitive mechanisms.

Table 3
Correlations between semantic electrophysiological indices and cognitive outcomes.

EEG index	Cognitive Test	Healthy persons		PD patients	
		rho	*p*-value	*Rho*	*p*-value
N400	IFS	-0.12	0.98[a]	-0.26	0.98[a]
	MoCA	-0.08	0.98[a]	-0.47	0.49[a]
Theta	IFS	0.05	0.98[a]	0.01	0.98[a]
	MoCA	0.04	0.98[a]	0.16	0.98[a]
Mu	IFS	-0.16	0.98[a]	0.41	0.49[a]
	MoCA	-0.04	0.98[a]	0.20	0.98[a]

All *p*-values were calculated via Spearman's test adjusted for multiple comparisons via the false discovery rate method. EEG: electroencephalography; IFS: INECO Frontal Screening battery; MoCA: Montreal Cognitive Assessment.

These signatures were altered in PD. N400 and theta effects were abolished across patients. By the same token, previous PD research has reported null N400 modulations during action-verb processing (Wyrobnik et al., 2022) and dampened theta oscillations in tasks that tax conflict resolution and error adjustment mechanisms (Cavanagh et al., 2018; Singh et al., 2018) –a potentially selective pattern, as PD patients exhibit preserved N400 effects for non-action categories (e.g., static objects) (Angwin et al., 2017; Dissanayaka et al., 2017; León-Cabrera et al., 2021) and selective connectivity alterations during processing of action as opposed to object words (Abrevaya et al., 2017a, 2017b). Suggestively, mu rhythms did show a relatedness effect in the patients, though contralateralized to the right hemisphere. This anomaly may reflect compensatory mechanisms to support action semantic processing when putative systems are disrupted. Indeed, this pattern has been posited for PD in fMRI action concept research (Abrevaya et al., 2017a, 2017b), and it is commonly observed in focal (Amoruso et al., 2021; Quiñones et al., 2021) and neurodegenerative (Tyler et al., 2010; Verma and Howard, 2012) damage in diverse brain areas. Accordingly, we surmise, PD patients may be neurally desensitized to mismatches among sensorimotor features, potentially recruiting alternative mechanisms to support action concept construal.

Interestingly, neither ERP nor TF modulations correlated with the participants' executive skills nor with their overall cognitive status. Such patterns reinforce the view that action semantic deficits in PD might be *sui generis*, that is, not epiphenomenal to domain-general neuropsychological deficits (Bocanegra et al., 2015; García et al., 2018, 2022a). This is a particularly promising insight, given that deficits in non-action semantic categories in PD do seem to be driven by broader cognitive dysfunctions (Bocanegra et al., 2017; García et al., 2022a). EEG assessments of action semantics, then, could aid the quest for PD markers that generalize across the disease's cognitive phenotypes (García et al., 2021, 2022a).

Taken together, results from both groups motivate a neurofunctional account of action concept disruptions in PD. In a healthy brain, we propose, identification of unrelated actions would be supported by fast detection of semantic conflict (indexed by the N400) followed by taxing of executive/attentional mechanisms (theta enhancement) and parallel motoric simulation (mu desynchronization). Conversely, in PD, identification of unrelated actions would lack early conflict detection (absent N400) and executive/attentional resources for response preparation (abolished theta modulations), accompanied by atypical motor simulation (contralateralized mu desynchronization). Combined, these processes would entail sustained activation of previous semantic information (i.e., the first picture), hindering efficient recognition of action incongruence (hence the increased effect size of the behavioral relatedness effect). Such disruptions, we surmise, would be sufficiently robust to hold irrespective of each patient's cognitive status (as shown by null correlations with neuropsychological outcomes).

More generally, our study supports the 'disrupted motor grounding hypothesis', which posits that, since action-semantic processes rely on brain motor mechanisms, the former become distinctly altered upon disruption of the latter (Birba et al., 2017). More particularly, current findings extend this framework in two ways. First, while its supporting neural evidence has come from MRI, fMRI, and EEG connectivity studies (Birba et al., 2022; Moguilner et al., 2021a; 2021b; Steeb et al., 2018), we showed that motor grounding disruptions may also extend to ERP and TF mechanisms. This broadens the scope of relevant empirico-theoretical dimensions for the field. Second, present results suggest that (delayed) behavioral patterns can be preserved despite (earlier) neural alterations, echoing reports of normal memory priming effects in a context of abnormal ERP signatures (Tachibana et al., 1999). Thus, for PD patients, detection of action incongruence in

delayed-response settings may entail partly dissociable neural and behavioral signatures. Both notions capture insights that seem absent from current models of action semantics in PD (Gallese and Cuccio, 2018), including the 'disrupted motor grounding hypothesis'(Birba et al., 2017).

Finally, our study underscores the relevance of EEG measures for in-depth neurocognitive characterizations of the disease. Though limited, EEG studies on PD have revealed abnormal neural oscillations and connectivity patterns underlying patients' attentional, mnesic, and executive outcomes (Hassin-Baer et al., 2022; Hünerli et al., 2019; Pezzetta et al., 2023), hinting to potential biomarkers for early detection and phenotyping. These assets become even more promising considering the non-invasiveness, portability, and affordability of EEG. In this sense, our study meets and reinforces recent calls to incorporate EEG measures in the search for candidate markers of PD (Prado et al., 2022).

5. Limitations and avenues for further research

Our study has limitations. First, though similar to that of other EEG studies on PD (Angwin et al., 2017; Cavanagh et al., 2018; Singh et al., 2018), our sample size was modest, calling for replications with more participants. Second, our study focused solely on action pictures, without a control condition. Future studies should evaluate the potential specificity of the reported patterns differ by including non-action stimuli (e.g., object pictures). Third, novel tasks could be developed to enable response-locked EEG analyses –a possibility that escapes our design due to the large RT dispersion induced by our delayed-response task. Fourth, alternative paradigms could manipulate semantic inhibition demands to illuminate the role of hyperpriming effects during action relatedness judgments. Fifth, future elaborations of our approach could investigate the potential role of visual deficits in PD, related to reduced retinal dopamine. Although visual demands were controlled across conditions, complementary insights could be gained, for instance, by assessing flash visual evoked potentials (Hünerli-Gündüz et al., 2023) and correlating them with our target EEG measures. Sixth, future works should also contemplate additional control conditions to account for potential motoric effects by circumventing manual responses. Finally, future research could benefit from magnetoencephalographic recordings to complement temporal insights with spatial precision –a critical point to better understand the contralateralization of mu rhythms observed in the patients.

6. Conclusion

This study offers new insights on the neurophysiology of action semantics in PD. We found that, in this disorder, action relatedness judgments involve early ERP and TF alterations even when task conditions allow for preserved behavioral outcomes. Together with previous EEG research on semantics and other cognitive domains, our results highlight the relevance of this technique for fine-grained neurocognitive characterization of the disease. Future works along this line could aid the quest for affordable and generalizable markers of PD.

CRediT authorship contribution statement

Díaz Rivera Mariano Nicolás: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing – original draft. **García Adolfo Martín:** Conceptualization, Funding acquisition, Investigation, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing. **Suárez Jazmín:** Data curation, Software. **Muñoz Edinson:** Writing – review & editing. **Birba Agustina:** Conceptualization, Data curation, Formal analysis, Methodology, Software, Supervision, Writing – review & editing. **Bocanegra Yamile:** Conceptualization, Methodology, Software. **Moreno Leonardo:** Resources. **Amoruso Lucía:** Formal analysis, Software, Supervision, Visualization, Writing – review & editing.

Declaration of Competing Interest

The authors report no conflict of interest.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neurobiolaging.2024.01.001.

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