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Research article

Correlation between alpha activity and neuropsychometric tests in Parkinson's disease

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ABSTRACT

Parkinson's disease (PD) is a neurodegenerative disease that leads to memory impairment and executive and visuospatial dysfunction as the disease progresses. Alpha activity on EEG has been related to cognition in previous studies. We aimed to investigate the correlation between alpha activity and neuropsychometric tests (NPTs) in PD patients. Fifty-five idiopathic PD patients and 20 healthy controls were included. The Standardized Mini-Mental Test (SMMT), Verbal Learning Memory Test (VLMT), Wechsler Memory Scale (WMS), Stroop Color–Word Test, Categorical Verbal Fluency Test (CVFT), Benton's Face Recognition Test (BFR), and Benton Line Judgment Orientation Test (BLOT) were administered to all participants. Patients were separated into four groups according to NPT results: healthy controls (HC); PD patients with normal cognition (PDNC); PD patients with MCI (PDMCI); and PD patients with dementia (PDD). Analysis of the EEG data showed that HC had the highest alpha activity, and PDD had the lowest. High SMMT scores were correlated with high alpha activity at posterior electrode locations in all PD groups. VLMT and WMS test scores were associated with alpha activity at the parietal sites in PDMCI. VLMT, WMS, and CVFT test scores were correlated with alpha activity at parietooccipital sites in PDD. Verbal and visuospatial memory dysfunction related to low alpha activity was evident in both PDMCI and PDD, whereas executive dysfunction was more strongly associated with low alpha activity in PDD. Analysis of alpha activity could help clinicians predict the progression of cognitive dysfunction in PD patients.

1. Introduction

Parkinson's disease (PD) is a neurodegenerative disease characterised by both motor findings (bradykinesia, rigidity, rest tremor) and non-motor findings. Cognitive impairment is one of the non-motor manifestations, with half of patients complaining about forgetfulness and a lack of attention when they are questioned thoroughly [1]. Approximately 30 % of PD patients have dementia [2], and 30 % of the nondemented group have mild cognitive impairment (MCI) [3]. Memory impairment and executive and visuospatial dysfunction are the most common cognitive disorders in PD [4].

The spontaneous alpha rhythm observed on electroencephalography (EEG) is known to be related to cognition, and alpha activity is correlated with working memory and probably with long-term memory [5]. A functional network analysis of EEG revealed different characteristics among healthy aging, MCI, and Alzheimer's groups [6,7]. In studies with PD patients, slowing on EEG is more common with cognitive dysfunction [8,9], and slowing in global average EEG frequency is positively correlated with attention, executive function, fluency, and episodic long-term memory tests [10]. However, the literature provides little information about the correlation of alpha activity on EEG with detailed neuropsychiatric tests (NPTs).

This study aimed to compare spontaneous alpha activity recorded at rest in patients with PD and without cognitive deficit, PD with MCI, and PD with dementia to that of healthy controls (HC) and investigate the correlation of such activity with NPTs.

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2. Material and methods

2.1. Patient selection and clinical assessment

Fifty-five idiopathic PD patients and 20 HC were included in the study. The participants were examined by a neurologist specialising in movement disorders (N.H.Y.). The diagnosis of PD was determined according to the criteria of the United Kingdom PD Society Brain Bank [11]. The Hoehn–Yahr scale was used to detect the disease stage. Patients who had a history of head trauma, stroke, or epilepsy and those with vertical gaze paralysis and pyramidal or cerebellar neurological findings were excluded from the study. All PD patients and HC underwent behavioural and neuropsychometric tests.

The control group included healthy participants matched for age, gender, and education level. All had normal neurologic findings and were free of cognitive impairment. Approval of the ethics committee was obtained, and all participants signed an informed consent.

2.2. Behavioural and neuropsychometric evaluation

The Standardized Mini-Mental Test (SMMT) [12], Verbal Learning Memory Test (VLMT)-teaching and long term [13], visual subtest of the Wechsler Memory Scale (WMS)-momentary and long-term recall [14], Stroop Color–Word Test [15], Categorical Verbal Fluency Test (CVFT) (fruit, human, animal counting) [16], and Turkish versions of the Benton Face Recognition Test (BFR) and Benton Line Judgment Orientation Test (BLOT) [15] were administered to all participants.

PDMCI was diagnosed according to the criteria proposed by Litvan et al. [17]; for PD dementia, the criteria determined by Emre et al. [18] were used. The staging of dementia was conducted using the Clinical Dementia Rating Scale (CDR) [19]. The HC group was composed of participants with clinically normal cognition; all SMMT scores of the HC group were $\geq$ 24.

The patients were separated into four groups according to the NPT results: healthy controls (HC), PD patients with normal cognition (PDNC), PD patients with MCI (PDMCI), and PD patients with dementia (PDD).

2.3. Procedure

2.3.1. EEG recording

EEG was recorded for all participants in an electrically isolated and dimly lit room at the Istanbul Medipol University Hospital, REMER, Clinical Electrophysiology, Neuroimaging, and Neuromodulation Laboratory. The recordings were done with patients in the 'on' stage (60–90 min after the morning dose of levodopa).

EEG was recorded from 32 Ag/AgCl electrodes attached to an elastic cap (Easy Cap) according to the International 10–20 system. The EEG was amplified with a Brain Amp 32-channel DC system with band limits of 0.01–250 Hz and digitised online at a 500 Hz sampling rate.

Two linked earlobe electrodes (A1, A2) served as references. All electrode impedances were kept below 10 K ohm. EOG was registered from the horizontal and vertical orbital rims of the right eye.

2.3.2. EEG analysis

Spontaneous EEG eyes-open and -closed power spectrum analysis was performed in all participants. EEG data were pre-treated, and EEG analysis was performed using Brain Vision Analyzer 2 Software to analyse data from the F3, F4, C3, C4, T7, T8, TP7, TP8, P3, P4, O1, and O2 electrodes.

Before analysis, EEG artifacts were manually removed offline, and EEG and EOG recordings were studied visually.

The EEG data were segmented into eyes-open and eyes-closed data. Each section of the EEG data was divided into 1000-ms segments. The epochs containing trials with muscle artifacts, eye movements or blinking, and blink artifacts were rejected. A notch filter of 50 Hz (i.e., for city network noise) was applied to the EEG data. Power spectral analysis was performed by fast Fourier transform (FFT) in 1-s epochs. The power values were averaged across the epochs of an individual trial. After the application of FFT, EEG was digitally filtered in 8–13 Hz band limits for analysis of alpha activity. The maximum alpha frequency value for each electrode was used as the maximum individual alpha frequency value for statistical analysis (i.e., the numerical values for eyes closed and open were included separately). The absolute alpha power was calculated.

3. Statistics

3.1. ANOVA analysis using SPSS software

Statistical analyses were performed using IBM SPSS Statistics 22 and Statistica Software. Eyes-closed and eyes-open alpha power comparisons between groups were conducted using repeated-measures ANOVA. Two conditions (eyes open and closed) $\times$ seven electrode locations (frontal, central, temporal, tempo–parietal, parietal 1 [P3–P4], parietal 2 [P7–P8], and occipital) $\times$ two hemispheres (right, left) were included as within-subjects factors; four groups (HC, PDNC, PDMCI, and PDD) served as the between-subjects factor. Greenhouse–Geisser-corrected p-values are reported. Post hoc comparisons were performed with the Bonferroni test.

3.2. Correlation analysis using SPSS software

Statistical analyses were performed with IBM SPSS Statistics 22 Software. Kendall's test was used in the correlation analysis with SPSS software. Correlations between eyes-closed alpha power and NPTs were analysed in all groups (HC, PDNC, PDMCI, and PDD). The correlation analysis for each group was also performed separately.

In the correlation analysis, results of the CDR, VLMT teaching, VPMT long term, WMS momentary recall, WMS long-term recall, Stroop Test, CVFT, BLOT, and BFR and eyes-closed F3, Fz, F4, C3, CZ, C4, T7, T8, TP7, TP8, P3, Pz, P4, P7, P8, O1, Oz, and O2 electrode values were analysed.

4. Results

Characteristics of the HC and PD patients are summarised in Table 1.

4.1. Group comparisons of spontaneous alpha activity

Group comparisons showed that differences between groups in alpha activity were specific to the eye condition (eyes closed or open) and electrode location. Condition $\times$ location $\times$ group comparisons were significant ($F(6.794) = 2.861$, $\boldsymbol{p = 0.008}$, $\eta_p^2 = 0.108$). The post hoc tests showed that group differences were mainly found for the eyes-closed condition and the parietal and occipital electrodes. The controls had higher parietal 1 (P3 [$\boldsymbol{M \pm SD = 1.91 \pm 2.91}$], P4 [$\boldsymbol{M \pm SD = 2.52 \pm 5.23}$]), parietal 2 (P7 [$\boldsymbol{M \pm SD = 1.02 \pm 0.91}$], P8 [$\boldsymbol{M \pm SD = 2.08 \pm 5.40}$]), and occipital (O1 [$\boldsymbol{M \pm SD = 2.36 \pm 4.03}$], O2 [$\boldsymbol{M \pm SD = 1.44 \pm 1.58}$]) alpha activity than the PDNC, PDMCI, and PDD patients ($\boldsymbol{p < 0.05}$ for all comparisons). Furthermore, PDNC patients exhibited higher alpha activity than did PDMCI and PDD patients ($\boldsymbol{p < 0.05}$ for all comparisons). Fig. 1 shows the grand average power spectrum analysis for all groups over the O1 location under the eyes-closed condition. There was a gradual decrease in alpha activity with cognitive decline (Fig. 1). Controls had the highest alpha activity under the eyes-closed condition, and PDD had the lowest.

Fig. 2 shows significant comparisons among groups at the parietal 1 (P3–P4), parietal 2 (P7–P8), and occipital sites.

As shown in Figs. 1 and 2, HC had the highest alpha activity, and PDD patients had the lowest under the eyes-closed condition. Furthermore, HC had higher alpha activity during the eyes-closed than during the

Table 1
Demographic data and disease characteristics of the groups.

	HC (n = 20) M ± SD	PDNC (n = 19) M ± SD	PDMCI (n = 18) M ± SD	PDD (n = 18) M ± SD	*p*
Age	61.85 ± 7.61	60.21 ± 6.94	67.72 ± 8.41	71.33 ± 8.06	0.000[a]
Gender (F/M)	11/9	7/12	4/14	4/14	0.104[b]
Education	8.20 ± 4.45	9.57 ± 5.06	4.77 ± 3.42	5.27 ± 5.26	0.016[a]
Disease Duration (month)	–	52.68 ± 53.26	66.66 ± 51.14	102.00 ± 62.12	**0.000**[a]
Hoehn and Yahr Scale	–	1.52 ± 0.57	1.62 ± 0.80	2.52 ± 0.78	**0.001**[a]
MMSE	27.80 ± 1.57	26.38 ± 2.09	22.55 ± 5.78	18.44 ± 4.66	**0.000**[a]
CDR	–	–	0.50 ± 0.00	1.19 ± 0.34	**0.000**[a]
UPDRS III	–	14.53 ± 6.72	17.11 ± 7.21	23.78 ± 11.75	**0.000**[a]

M: mean; SD: standard deviation; HC: healthy controls; PDNC: Parkinson's disease with normal cognition; MCI: mild cognitive impairment; PDD: Parkinson's disease with dementia; M: male; F: female; HYS: Hoehn and Yahr Scale; MMSE: Mini-Mental State Examination; CDR: Clinical Dementia Rating; [a] Kruskal-Wallis-h, [b]Chi Square Test.

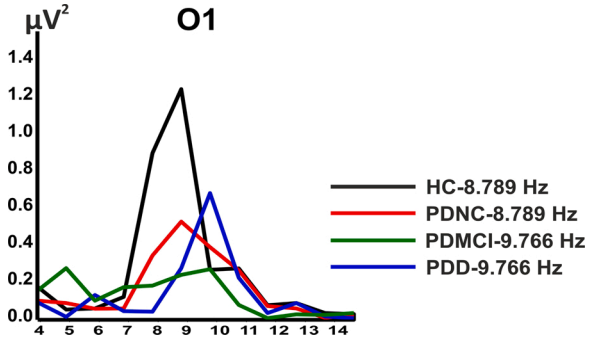

Fig. 1. Grand average of power spectrum analysis of the eyes closed EEG data over the O1 electrode. The black line represents the power spectrum of HC; the red line represents the power spectrum of the PD patients without cognitive decline. The blue line represents the power spectrum of PDMCI, and the green line represents the power spectrum of PDD. The numerical value clear for all groups represents the peak frequency.

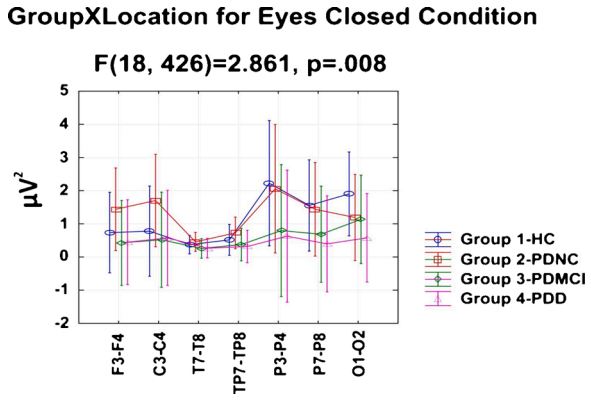

Fig. 2. Shows significant comparisons between groups (HC, PDNC, PDMCI, and PDD), locations (frontal [F3-F4], central [C3-C4], temporal [T7-T8], temporo–parietal [TP7-TP8], parietal 1 [P3–P4], parietal 2 [P7–P8], and occipital [O1-O2]) for eyes close condition.

eyes-open state. This differentiation between eyes-closed and eyes-open alpha activity was also found in PD patients, but was not found in the PDMCI and PDD groups.

The comparison between conditions (eyes open, eyes closed) was also significant. The post hoc comparison indicated that the spontaneous EEG alpha power for the eyes-closed state was significantly higher than that for the eyes-open condition ($p < 0.05$).

Alpha activity also differed significantly with location ($F(1,748) = 11.506$, $p = 0.000$, $\eta_p^2 = .139$). Post hoc comparisons showed that alpha activity at occipital locations (O1 [$M \pm SD = 1.42 \pm 2.73$], O2 [$M \pm SD = 1.01 \pm 1.47$]), was higher than that at frontal, central, and parietal 2 (P7–P8) locations ($p < 0.05$ for all comparisons). Furthermore, alpha activity over parietal 1 (P3 [$M \pm SD = 1.46 \pm 3.21$]), P4 [$M \pm SD = 1.44 \pm 3.16$]), locations was higher than that over frontal, central, and parietal 2 (P7–P8) locations ($p < 0.05$ for all comparisons) (Table 2).

4.2. Correlation analysis between alpha activity and NPTs

4.2.1. Correlation analysis for HC and PDNC

The correlation analysis between alpha activity and NPTs in the HC and PDNC groups showed only one significant result during the eyes-closed condition, namely that activity under the eyes-closed condition was positively correlated with SMMT scores. Specifically, SMMT test scores were positively correlated with frontal [F3 (r_k = ***.246**, p = **0.040**), Fz (r_k = ***.237**, p = **0.049**)]; temporal [T8 (r_k = 0.260**, p = **0.030**)]; temporoparietal [TP8 (r_k = 0.268**, p = **0.026**)]; parietal [P3 (r_k = 0.271**, p = **0.024**), Pz (r_k = 0.335**, p = **0.005**), P4 (r_k = 0.372**, p = **0.002**), P7 (r_k = 0.294**, p = **0.014**), P8 (r_k = 0.314**, p = **0.009**)]; and occipital [O1 (r_k = 0.326**, p = **0.007**), Oz (r_k = 0.307**, p = **0.010**), O2 (r_k = 0.378**, p = **0.002**)] locations. Spontaneous eyes-closed alpha activity over these electrodes increased as MMSE test scores increased.

4.2.2. Correlation analysis in HC and PDMCI

The correlation analysis showed that SMMT test scores were positively correlated with alpha activity under the eyes-closed condition at the temporoparietal [TP8 (r_k = 0.259**, p = **0.027**)]; parietal [Pz (r_k = 0.250**, p = **0.033**), P4 (r_k = 0.339**, p = **0.004**), P7 (r_k = 0.279**, p = **0.017**), P8 (r_k = 0.262**, p = **0.026**)]; and occipital [O1 (r_k = 0.247**, p = **0.035**), O2 (r_k = 0.244**, p = **0.038**)] locations. The correlation analysis showed that alpha activity during the eyes-closed condition was positively correlated with VLMT scores [Pz (r_k = 0.239**, p = **0.036**), P4 (r_k = 0.231**, p = **0.043**), P7 (r_k = 0.268**, p = **0.019**)]. The VLMT long-term recall score was positively correlated with activity at the parietal location [Pz (r_k = 0.267**, p = **0.023**); P4 (r_k = 0.252**, p = **0.032**)]; P7 (r_k = 0.240**, p = **0.041**)]. The WMS visual momentary recall score was only significantly positively correlated with activity at the P4 (r_k = 0.265**, p = **0.024**) location, and the WMS visual long-term recall score was only significantly positively correlated with activity at P4 (r_k = 0.264**, p = **0.025**).

4.2.3. Correlation analysis in controls and PD patients with dementia

The correlation analysis showed a relationship between alpha activity and NPT scores in the HC and PDD groups, with significant correlations over the temporoparietal, parietal, and occipital location under only the eyes-closed condition. SMMT scores were positively correlated with activity at temporoparietal [TP7 (r_k = 0.256**, p = **0.028**), P3 (r_k = 0.264**, p = **0.023**), P4 (r_k = 0.229**, p = **0.049**), P7 (r_k = 0.334**, p = **0.004**), P8 (r_k = 0.273**, p = **0.019**)] and occipital [O1 (r_k = 0.299**, p = **0.010**), Oz (r_k = 0.242**, p = **0.037**), O2 (r_k = 0.287**, p = **0.013**)] locations. Spontaneous eyes-closed alpha activity over

Table 2
The mean values of NPT scores of the HC, PDNC, PDMCI and PDD groups NPT: Neuropsychiatric Test; HC: Healthy Control; PDNC: Parkinson's Disease patients with normal cognition PDMCI: Parkinson's Disease patients with mild cognitive impairment; PDD: Parkinson's Disease with dementia; VLMT: Verbal Learning Memory Test; WMS: Wechsler Memory Scale; BLOT: Benton Line Judgment Orientation Test; BFR: Benton's Face Recognition Test; CVFT: Categorical Verbal Fluency Test; a: Kruskal–Wallis-h.

	HC (n = 20) M ± SD	PDNC (n = 19) M ± SD	PDMCI (n = 18) M ± SD	PDD (n = 18) M ± SD	*p*
VLMT (total learning)	118.35 ± 14.93	105.84 ± 20.37	67.61 ± 19.71	42.70 ± 13.82	**0.000[a]**
VLMT (delayed recall)	13.30 ± 1.65	12.21 ± 1.98	6.55 ± 3.16	1.76 ± 2.04	**0.000[a]**
WMS (immediate recall)	9.65 ± 3.68	9.68 ± 3.05	4.44 ± 2.50	1.00 ± 1.53	**0.000[a]**
WMS (delayed recall)	10.90 ± 2.61	10.36 ± 3.09	6.00 ± 2.89	1.72 ± 2.49	**0.000[a]**
Stroop Test	50.85 ± 17.18	55.73 ± 22.13	71.28 ± 31.86	94.46 ± 85.27	**0.039[a]**
BLOT	21.80 ± 4.59	20.47 ± 4.31	14.28 ± 5.49	6.66 ± 8.14	**0.000[a]**
BFR	42.95 ± 4.17	43.78 ± 4.17	37.72 ± 4.22	29.66 ± 11.27	**0.000[a]**
CVFT (Fruit-human)	7.90 ± 2.31	8.53 ± 2.56	6.06 ± 1.55	2.94 ± 2.10	**0.000[a]**
CVFT (Animal counting)	21.05 ± 6.35	21.58 ± 6.74	14.44 ± 4.11	8.89 ± 3.17	**0.000[a]**

these electrodes increased as the SMMT score increased. The correlation analysis showed that VLMT teaching scores were positively correlated with alpha power during the eyes-closed condition at parietal [P3 (r_k = 0.267**, $p = 0.021$), P4 (r_k = 0.243**, $p = 0.036$), P7 (r_k = 0.361**, $p = 0.002$)] and occipital [O1 (r_k = 0.313**, $p = 0.007$), Oz (r_k = 0.248**, $p = 0.033$), O2 (r_k = 297*, $p = 0.010$)] sites. Spontaneous eyes-closed alpha activity over electrodes P3, P4, P7, O1, Oz, and O2 decreased as VLMT test scores increased. The VLMT long-term recall score was positively correlated with activity at the P7 (r_k = 0.324**, $p = 0.007$), O1 (r_k = 269*, $p = 0.025$), and O2 (r_k = 0.241**, $p = 0.045$) electrode. Spontaneous eyes-closed alpha activity over the P7, O1, and O2 electrodes decreased as VLMT long-term test scores increased. WMS visual long-term recall scores were positively correlated with activity over the P4 (r_k = 0.250**, $p = 0.034$), O1 (r_k = 0.250**, $p = 0.034$), and O2 (r_k = 0.292**, $p = 0.013$) electrodes. CVFT (fruit–human) scores were positively correlated with alpha activity at the P3 (r_k = 0.231**, $p = 0.048$), P7 (r_k = 0.291**, $p = 0.013$), O1 (r_k = 0.276**, $p = 0.018$), and O2 (r_k = 0.246**, $p = 0.035$) locations, and CVFT (animal counting) scores were positively correlated with alpha activity at the P3 (r_k = 0.233**, $p = 0.043$), P7 (r_k = 0.267**, $p = 0.020$), O1 (r_k = 0.262**, $p = 0.023$), and O2 (r_k = 0.230**, $p = 0.045$) electrode locations.

Stroop test, BLOT, and BFR test scores were not correlated with alpha activity in any group (Table 3).

Table 3
p values for the correlation of alpha activity of all electrodes and Stroop, BFR and BLOT tests.

All electrodes	Stroop	BFR	BLOT
F3	0.745	0.471	0.255
FZ	0.905	0.451	0.298
F4	0.598	0.249	0.096
C3	0.801	0.401	0.222
CZ	0.700	0.948	0.648
C4	0.700	0.259	0.367
T7	0.414	0.979	0.498
T8	0.663	0.788	0.426
TP7	0.381	0.932	0.744
TP8	0.427	0.533	0.163
P3	0.883	0.316	0.277
PZ	0.938	0.352	0.568
P4	0.486	0.778	0.151
P7	0.488	0.922	0.747
P8	0.748	0.582	0.313
O1	0.982	0.181	0.359
OZ	0.894	0.373	0.389
O2	0.909	0.704	0.599

BFR: Benton's Face Recognition Test; BLOT: Benton Line Judgment Orientation Test.

5. Discussion

5.1. Analysis of the alpha activity of PD patients according to cognitive level

According to the results of our study, the alpha activity amplitude in the bilateral parietal and occipital locations was low in all patient groups compared to the controls. One striking result was the lower amplitude in the anterior parts of each hemisphere (lower in the parietal than the occipital area, and lower in the anterior portions of the parietal region). The alpha amplitude in the parietal and occipital regions was higher when the eyes were closed in HC and PDNC patients. The amplitudes did not differ between eyes open and closed in PDMCI and PDD patients.

Global cognitive status is known to affect alpha activity decreases [20]. Low alpha band amplitude was found in the PDMCI and PDD patient groups [21]. Furthermore, in a 2-year follow-up study, there was a further decrease in alpha band strength in the group that progressed to PDD from PDMCI [22]. Babiloni et al. observed a decrease in alpha activity, particularly in the parietal and occipital regions, in PDMCI patients, similar to our study [23].

5.2. Alpha activity and NPT correlations

The relationship between quantitative EEG (QEEG) findings and cognitive test scores is not clear. In a study conducted with PD patients without dementia, slowing of EEG activity was found not to be associated with executive function, verbal fluency, episodic memory, visuospatial tests, or working memory [24].

SMMT is a routine test used to screen for dementia [25], but is not sufficient to thoroughly evaluate patients' cognitive functioning, so additional NPTs are required [26]. In our study, SMMT scores were correlated with alpha activity in the parietal, temporal, and occipital locations among PDNC, PDMCI, and PDD patients. The amplitude of alpha activity decreased as SMMT scores decreased. In a study by Morita et al., widespread slowing in the frontal, central, parietal, and occipital regions was correlated with low scores on the SMMT [27]. In a study by Güner et al., although a global deceleration in alpha activity was mainly observed in patients whose SMMT scores were ≥ 25, low EEG amplitude was moderately correlated with SMMT scores [28]. Babiloni et al. showed that low posterior (temporal, parietal, and occipital) alpha activity was associated with SMMT [23].

PD comprises deficits in recall, recognition, and prospective memory, all of which deteriorate with disease progression [29]. Verbal memory deficits appear to suggest parietal and temporal dysfunction in PD patients without dementia [30]. These changes in verbal memory in PD have been thought to be associated with hippocampal atrophy [31]. In functional MRI studies, a deficit in verbal recognition was associated with activity in parts of the anterior cingulate and inferior orbitofrontal cortex [32]. In our research, verbal memory tests were correlated with spontaneous alpha activity in the parietal region in PDMCI, and in

parietooccipital areas in PDD. Alpha power increased as the test scores increased. Based on these results, we consider that verbal deficits, which reflect complex functions, develop due not only to impairment in one anatomical location but also to connection deficits between cortical and subcortical structures. The functional impairments between prefrontal, parietal, temporal, thalamic, and basal ganglia structures become evident as the disease progresses. These impairments may explain the correlation between the verbal memory deficit and low alpha activity in PD.

The visuospatial function comprises visual perception, construction, and visual memory. Visuospatial impairment is seen at every stage of PD [33]. Conversion to dementia is high in PDMCI, and visuospatial deficits detected in NPTs are a predictor of the progression to dementia [33]. Visuospatial functions are also impaired in patients with PDNC with low parietal EEG activity [34]. In a previous study, although visuospatial functions were affected in PD cases that progressed to dementia, the reduction in the parietal alpha/theta ratio was more striking [35]. There was no correlation between visual memory tests and alpha activity in the PDNC group in the present study. However, there was a correlation between the visual memory tests and alpha activity in the right parietal region in the PDMCI group and in the bilateral parietooccipital area in the dementia group. The factors that lead to these results may be explained by the mechanisms that lead to visuospatial dysfunction. Visuospatial dysfunction in PD develops mainly from the basal ganglia–-thalamocortical pathway (particularly the dorsolateral prefrontal and posterior parietal cortex) [36]. In voxel-based studies, visuospatial dysfunction in PD patients was correlated with a reduction in posterior temporal and parietal grey matter density [37]. Cortical thinning was evident in the posterior cerebral regions (temporal, parietal, occipital) of PDMCI patients compared to subjects with normal cognition [38]. In our study, although changes in alpha activity were closely correlated with visual memory, the scores on other tests of visuospatial functioning (BFR and BLOT tests) were not associated with low alpha activity. However, the scores decreased significantly as cognitive impairment increased. The correlation between QEEG and NPT is more complicated than suggested.

Verbal fluency tests evaluate both executive and verbal functions [39]; furthermore, these are sensitive screening tests for assessment of executive dysfunction in PD [40]. Executive dysfunction in PD may be explained by impairment in the frontostriatal pathway [41]. In our study, although verbal fluency was impaired in PDMCI and PDD, no correlation was found between the verbal fluency tests and EEG findings in PDMCI. Additionally, our results showed a correlation between verbal fluency tests and bilateral parietooccipital alpha activity in the PDD group. This result may be related to the association of alpha activity with frontobasal ganglia–thalamus connections and posterior cerebral structures.

In our study, we showed that sites showing low alpha activity were more affected by the severity of cognitive deficit, suggesting that this condition may be associated with the location of alpha-synuclein shown in the staging of Braak et al. [42]. Cortical Lewy bodies are known to spread to the cortex in stages 5 and 6 [42]. It is generally considered that cortical involvement is initially located toward the frontoparietal region and then moves toward the temporal cortex. In our study, the amplitude reduction in parietal and occipital alpha activity in the posterior areas was associated with cognitive rather than frontal alpha activity according to the results obtained from QEEG.

It is difficult to detect the anatomical and pathophysiological locations of cognitive deficits in PD. The diversity of PD patients, methodological differences among studies, and broad range and overlapping nature of domains covered by cognitive tests contribute to this difficulty. This research is a pioneering study due to the detailed EEG correlations and subgroupings of NPT instruments addressing cognitive impairment in PD. The progression from normal cognition to dementia in PD can be monitored not only by objective tests such as the SMMT and various verbal and visual memory tests but also by the decline in parietooccipital alpha activity amplitude. Low alpha activity amplitude on EEG may be a leading finding for the development of dementia, detectable long before NPT results are informative.

Levodopa can cause a reduction in alpha activity in PD patients under dopaminergic treatment [43]. The possible effects of levodopa on alpha amplitude, the small number of patients, the lack of classification by PD subtypes, and the absence of functional imaging data to supplement QEEG are limitations of our study.

6. Conclusions

We obtained results that could shed light on the relationship between NPTs and cortical alpha activity. Although SMMT scores were correlated with alpha activity at multiple locations at every stage of the disease, verbal memory tests and visual memory tests were correlated with alpha activity in the parietal region in PDMCI and the parietooccipital area in PDD. The effect of PD on executive function was associated with alpha activity in the posterior cerebral cortex in PDD patients only.

In previous studies, QEEG was identified as a biomarker for diagnosis and follow-up of non-motor symptoms in PD [44]. As seen in the present research, analysis of alpha activity provides clinicians with another perspective regarding which cognitive domain is affected and which might be affected with increasing cognitive dysfunction, one of the non-motor symptoms of PD. Further studies are required to investigate this issue.

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CRediT authorship contribution statement

Nesrin Helvacı Yılmaz: Conceptualization; Investigation; Methodology; Validation; Writing original draft. **Pervin Çalışoğlu:** Data curation; Formal analysis; Software; Visualization. **Bahar Güntekin:** Writing-review and editing; Project administration; Resources. **Lütfü Hanoğlu:** Data Supervision.

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