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Quantitative EEG Spectral Power Ratio As Cognitive Biomarker For Patients With Parkinson Disease

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Abstract:

Background: Cognitive decline in patients with Parkinson disease (PD) is a major and progressing health problem that needs reliable and objective assessment tools. **Aim:** To explore the value of EEG spectral ratio as cognitive biomarker in patients with PD. **Methods:** This cross-sectional case control study enrolled 35 patients with PD and 20 matched healthy controls. All participants were evaluated by quantitative electroencephalography (EEG) spectral power ratio (slow/fast) over different head regions, in addition to clinical and neuropsychological assessment of the patients using Unified Parkinson's Disease Rating Scale (UPDRS) and Montreal Cognitive Assessment (MoCA). **Results:** The UPDRS score of the patients was (mean 46.8 ± SD 26.6) and total MoCA score was (mean 20.3 ± SD 5.7). Twenty four of PD patients had cognitive impairment (MoCA <26) and showed significant higher spectral power ratio over the occipital region compared to PD patients with normal cognition (P=0.028). No significant differences of spectral power ratio between PD patients and controls. No significant correlation was found between power spectral ratio, UPDRS and MoCA scores. **Conclusions:** The occipital EEG

spectral power ratio could be used as a complementary tool to neuropsychological assessment in evaluation and follow up of cognitive decline in patients with PD.

Keywords: Quantitative EEG; Spectral power ratio; Parkinson disease, Cognitive decline, Mild cognitive impairment**.**

1. Introduction:

Cognitive decline in patients with Parkinson disease (PD) is a major and progressing health problem. Mild cognitive impairment (PD-MCI) was reported to occur in about 15-20% of PD patients at time of diagnosis.[1] PD-MCI is defined according to movement disorder society (MDS) as impairment of one or more of the cognitive domains without significant functional decline of the activities of daily living (ADL).[2] PD-MCI is an intermediate stage that usually progresses to dementia (PDD) especially with long disease duration (more than 10 years), old age and more severe motor symptoms.[1] The cognitive impairment profile of PD includes specifically visuospatial and executive dysfunction.[1]

The most used and agreed upon method for cognitive evaluation is neuropsychological assessment to delineate the different cognitive domains impairment, however these scales are liable to misinterpretation due to several confounding factors like intelligence, education years, personality differences and fatigue.[3] Several other biomarkers were evaluated for tracing the cognitive decline such as structural and functional neuroimaging, CSF analysis in addition to electroencephalography (EEG).[1]

EEG has the advantages of being easily recorded, widely available, inexpensive, and non-invasively measures brain activity directly with high temporal resolution.[3,4] Specifically, quantitative assessment of EEG was widely used in cognitive assessment and evaluation of various neuropsychiatric disorders including Parkinson's disease. Previous literature demonstrated a leftward shift of the background rhythm frequency with a higher slower frequency power especially in the posterior region, [3,4] however there is still a large controversy regarding the most specific and accurate spectral measures that could be of more clinical values.

Our aim was to explore the value of EEG spectral ratio as cognitive biomarker in patients with PD.

2. Material and Methods:

Participants:

This cross-sectional case control study was conducted on 55 individuals divided into two groups (patients and control) in (blinded for peer review) University hospitals during the period from April 2019 till September 2020. The study protocol was approved from the local ethical committee of faculty of Medicine, (blinded for peer review) University and an informed written consent was obtained from all participants before enrollment in the study.

The patient group included 35 patients fulfilling the criteria for diagnosis of Parkinson's disease based on British Brain Bank criteria.[5] They were recruited from the neurology clinic of (blinded for peer review) University hospitals and they should be able to read, write and do simple calculations.

We excluded patients with Parkinson Plus syndromes, secondary parkinsonism, cerebrovascular stroke, major language disturbance, severe physical, auditory or visual impairment, thyroid disease, in addition to patients with MRI brain findings of multiple or extensive infarcts, severe white matter hyperintensity burden, intracerebral or subdural hemorrhage, tumors or hydrocephalus.

The control group included 20 healthy volunteers age and sex matched with the selected patients.

Methods:

Patients were subjected to the following:

-Clinical assessment through full history taking, complete general and neurological examination.

- Evaluation and staging of Parkinson's disease using Unified Parkinson's Disease Rating Scale (UPDRS).[6]

- Neuropsychological assessment and cognitive evaluation using the Montreal Cognitive Assessment (MoCA) Arabic version with cutoff value <26. It evaluates seven cognitive domains: visuospatial/executive functions, naming, memory, attention, language, abstraction, and orientation. [7,8]

-Magnetic Resonance imaging (MRI) of the brain was performed for all patients to exclude any structural lesion.

- Quantitative Electroencephalogram (QEEG): It was performed for all participants (patients and controls)

(A) EEG Recording:

Nineteen gold disc electrodes were placed on the subject's scalp using electrode paste; according to the international 10/20 system of electrode placement at electrode locations FP1, FP2, F7, F3, FZ, F4, F8, T3, C3, CZ, C4, T4, T5, P3, PZ, P4, T6, O1 and O2 with reference and ground electrodes placed at the forehead. The impedances of the electrodes were always below 5 kohms.

Raw EEG signals were recorded using Natus, Neurowork EEG system (Nicolet EEG V32 amplifier) with a frequency band of 1-70 Hz. The data were recorded using a sampling rate of 512 Hz.

During the twenty minutes session of EEG recording, the subject was lying supine during a state of relaxed wakefulness in a silent environment. An EEG technician was following the recording to monitor the signal quality, minimize any eye and muscle artifacts and ensure the wakeful state. The recording was alternating between eye closed and eye opened conditions (five minutes in each condition).

(B) QEEG Processing:

EEG data were re-referenced using common average reference. For EEG power analyses, a total of 10 artifact-free EEG epochs, each lasting 4 seconds, selected from the eyes opened conditions. Epochs showing findings of a drowsy state or containing eye movements, blinking, or muscle activity were carefully screened out by visual inspection.

Power spectral analysis was performed using fast fourier transformation (FFT) for the individual 4-seconds epochs yielding spectrum values in different frequency bands, and frequency spectra were averaged across the ten selected epochs at each recording site to obtain the relative band power. The frequency bands were as follow: Delta (1-4 Hz), Theta (4-8 Hz), Alpha (8-13Hz) and Beta (13-30 Hz). Regional relative band powers were averaged as follow: frontal for F3 and F4, temporal for T3 and T4, and occipital for O1 and O2.

(C) QEEG Assessment:

- Spectral power ratio:

The spectral ratio was calculated by dividing the sum of averaged relative power in delta and theta bands over the sum of averaged relative power in alpha and beta bands to obtain slow/fast spectral ratio for each

electrode site, region and averaged for all regions.

Data management and statistical analysis:

Data were analyzed using SPSS (statistical package for the social science software) Version 25.0.

Quantitative variables were expressed by mean, standard deviation and 95% confidence interval or by median and interquartile range (IQR) (as appropriate) and were compared using independent t test or Mann-Whitney U test (as appropriate).

Qualitative variables were expressed by number and percent and were compared by chi-square test. Pearson correlation was used to correlate two continuous variables, otherwise Spearman correlation was used. In all tests, p-value was considered significant if less than 0.05.

3. Results:

Demographic and clinical characteristics of the patients

The patient group included 35 patients with Parkinson's disease (16 males, their mean age was 63 ± 9.3 years). The control group included 20 participants matched with the patients in age and sex distribution (P = 0.151 and 0.787 respectively). The clinical characteristics of the patients are demonstrated in (Table 1).

Neuropsychological and cognitive assessment:

Based on the cutoff value of the MoCA score, 24 (68.6%) of the patients had cognitive impairment (Table 2).

Quantitative EEG spectral ratio

There were no statistically significant differences between the spectral power ratio (slow/fast) of the two study groups either in selected head regions or the averaged global head (Table 3).

On the contrary, PD patients with cognitive impairment showed higher spectral power ratios compared to patients without cognitive impairment especially in temporal, occipital regions, and the global values, however this difference was statistically significant only over the occipital region (Table 4).

Correlation between spectral power ratio, clinical and cognitive parameters: No statistically significant correlation was found between these different assessment tools (data not presented).

Table 1: Clinical characteristics of PD patients

		Mean	SD	Median	IQR	95% CI for mean
Disease duration (years)		**3.2**	**2.6**	**3**	**2.8**	**2.3 / 4.1**
UPDRS	**Mentation**	**4.8**	**2.9**	**5**	**4**	**3.7 / 5.8**
	ADL	**19**	**8.3**	**20**	**12**	**16.1 / 22**
	Motor	**37.5**	**16.3**	**39**	**24**	**31.8 / 43.3**
	Treatment complications	**2.3**	**1.8**	**2**	**3**	**1.7 / 2.9**
	Other complications	**1.2**	**0.9**	**1**	**1**	**0.9 / 1.5**
	Total score	**64.8**	**26.6**	**67**	**36**	**55.4 / 74.3**

ADL, activities of daily living; SD, standard deviation; IQR, inter-quartile ratio, CI, confidence interval.

Table 2: Cognitive assessment of PD patients

		Mean	SD	Median	IQR	95% CI for mean
MoCA	**visuospatial/executive functions**	**2.8**	**1.6**	**3**	**3**	**2.2 / 3.4**
	naming	**2.5**	**0.5**	**2**	**1**	**2.3 / 2.7**
	memory	**2.6**	**1.4**	**2**	**2**	**2.1 / 3.1**
	attention	**4.1**	**1.8**	**5**	**3**	**3.4 / 4.7**
	language	**2.1**	**0.8**	**2**	**1**	**1.8 / 2.4**
	abstraction	**1**	**0.7**	**1**	**2**	**0.8 / 1.3**
	orientation	**5.2**	**1.4**	**6**	**1**	**4.7 / 5.7**
	Total score	**20.3**	**5.7**	**19**	**12**	**18.3 / 22.3**

MoCA, Montreal Cognitive Assessment; SD, standard deviation; IQR, inter-quartile ratio, CI, confidence interval.

Table 3: Quantitative spectral EEG power ratio of PD patients and controls

Parameter	Group	Mean	SD	Median	IQR	95% CI for mean	P value
Frontal spectral power ratio	Patients (n=35)	1.03	0.64	0.8	0.94	0.8 / 1.25	0.695
	Controls (n=20)	1.05	0.54	0.98	0.71	0.7 / 1.4	
Temporal spectral power ratio	Patients (n=35)	0.84	0.53	0.71	0.6	0.65 / 1.03	0.713
	Controls (n=20)	0.9	0.62	0.75	0.5	0.51 / 1.3	
Occipital spectral power ratio	Patients (n=35)	0.85	0.62	0.64	0.74	0.63 / 1.07	0.830
	Controls (n=20)	0.86	0.61	0.77	0.67	0.47 / 1.24	
Global spectral power ratio	Patients (n=35)	0.86	0.49	0.73	0.74	0.69 / 1.03	0.676
	Controls (n=20)	0.92	0.55	0.79	0.6	0.57 / 1.27	

*SD, standard deviation; IQR, inter-quartile ratio, CI, confidence interval. * Significant P value <0.05*

Table 4: Quantitative spectral EEG power ratio of PD patients with and without cognitive impairment

Parameter	Group	Mean	SD	Median	IQR	95% CI for mean	P value
Frontal spectral power ratio	Impaired cognition (n=24)	1.03	0.59	0.77	0.99	0.78 / 1.29	0.802
	Normal cognition (n=11)	1.01	0.76	0.85	1.3	0.46 / 1.55	
Temporal spectral power ratio	Impaired cognition (n=24)	0.94	0.56	0.76	0.73	0.7 / 1.19	0.089
	Normal cognition (n=11)	0.61	0.36	0.56	0.7	0.35 / 0.87	
Occipital spectral power ratio	Impaired cognition (n=24)	0.94	0.62	0.77	0.61	0.68 / 1.21	0.028*
	Normal cognition (n=11)	0.64	0.6	0.49	0.52	0.21 / 1.07	
Global spectral power ratio	Impaired cognition (n=24)	0.93	0.49	0.76	0.66	0.72 / 1.14	0.180
	Normal cognition (n=11)	0.69	0.46	0.65	0.87	0.37 / 1.02	

*SD, standard deviation; IQR, inter-quartile ratio, CI, confidence interval. * Significant P value <0.05*

4. Discussion:

This study was conducted to explore the value of quantitative EEG spectral power ratio as cognitive biomarker in patients with PD. The patient group included a heterogenous presentation regarding disease duration and severity of clinical and neuropsychological symptoms. The main finding of this study was a higher spectral power ratio in PD patients with significant cognitive decline compared to PD patients with normal cognition. This pathological spectral ratio indicates a left ward shift of the cortical oscillations towards the slower delta and theta rhythms. The absence of significant difference between all PD patients and healthy controls in our study supports that the cognitive decline (and not Parkinson disease) is the factor related to the EEG slowing. This pathological slowing accords with previous studies.[9-11] The power spectral ratio was used in a previous study to assess non-dopaminergic disease severity in PD patients and authors found a higher spectral ratio both globally and over all head regions in the PD patients with the more severe symptoms.[3] The high spectral ratio in our study was statistically significant only over the posterior head region which usually shows the highest alpha power in normal conditions. The EEG background slowing may indicate cortical desynchronization or disconnection of cortical areas,[3] changes in subcortical-cortical projections or more severe cortical and subcortical injury.[12] Such slowing could also be related to the disturbed cholinergic input in PD.[12] The cortical oscillatory slowing was observed in different neurodegenerative and psychiatric diseases which may indicate that such cortical disruption is not specific to PD.[3]

In conclusion, the present study showed posterior dominant higher slow rhythm spectral power ratio which could be used as a complementary tool to neuropsychological assessment in evaluation and follow up of cognitive decline in patients with PD.

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