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Rania Hamed

*Department of Psychiatry, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt.,  
drrania96@gmail.com*

Manal Maabady

*Department of Neurology, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt.,  
husseinabdelhamed1900@gmail.com*

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## Cognitive Impairment in Parkinson's disease

Rania A. Hamed<sup>1\*</sup> MD and Manal H. Maabady<sup>2</sup> MD

### \*Corresponding Author

Rania Ahmed Hamed  
[drrania96@gmail.com](mailto:drrania96@gmail.com)

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<sup>1</sup> Department of Psychiatry, Faculty of Medicine for Girls Al-Azhar University, Cairo, Egypt

<sup>2</sup> Department of Neurology, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt

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### INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative condition in the elderly population <sup>1</sup>. Clinicians are frequently faced with complex clinical pictures when treating patients with Parkinson's disease (PD), including cognitive and neuropsychiatric changes as well the movement disorder <sup>2</sup>.

Cognitive dysfunction is one of the most common non-motor symptoms of Parkinson's disease (PD) <sup>3</sup>. Deterioration of cognitive functions is common as Parkinson's disease (PD) progresses & it varies from mild cognitive impairment (MCI) to dementia <sup>4</sup>. 20% –33% of patients already have MCI when first diagnosed with PD <sup>5</sup>.

### ABSTRACT

#### Background

Deterioration of cognitive functions is common as Parkinson's disease (PD) progresses and it varies from mild cognitive impairment (MCI) to dementia.

#### Objective

We aimed to focus on MCI in PD patients, both newly diagnosed cases and chronic cases.

#### Patients and Methods

Our study was conducted on 50 PD male patients, 25 newly diagnosed, 25 chronic patients as well as 50 healthy persons as matched control group were selected. Participants were subjected to Complete neuropsychiatric examination, Structured Clinical Interview for DSM IV-TR Axis I Disorders (SCID I), Montreal Cognitive Assessment (MoCA), P300( auditory event-related potential).

#### Results

27 (54%) of patients score < 26 in the MoCA test compared to 12 (24%) of the control group with high statistical significance. A comparison between newly diagnosed cases & chronic cases of PD regarding the cognitive subarea of the MoCA test shows that there was a statistically significant difference regarding attention, language, and delayed recall. P300 shows that 32 (64%) of patients with PD had prolonged latency & 30 (60%) had low amplitude compared to [14 (28%), 16 (23%) respectively] of the control group with statistical significance. Comparison between newly diagnosed cases & chronic cases of PD regarding P300 shows that 20 (80%) of patients with chronic Parkinson's disease had prolonged latency and 18 (72%) had low amplitude compared to newly diagnosed cases in which 12 (48%) had prolonged latency and 12 (48%) had low amplitude with a statistically significant difference.

#### Conclusion

PD patients are frequently encountered with issues concerning cognitive deficits. Prediction and early diagnosis of these deficits are mandatory.

**Keywords:** Parkinson's disease; cognitive; MoCA; P300

Caviness et al. <sup>6</sup> first identified mild cognitive impairment (MCI) in PD as an intermediate state between normal cognition and dementia. Studies show that 60% –80% develop dementia 12 years as the disease progresses <sup>7</sup>, making necessary the establishment of appropriate markers to help doctors in diagnosing patients at greater risk of poor prognosis <sup>8</sup>.

Recent research suggests that non-motor subtypes of PD may affect neurotransmitters other than dopamine, leading to different cognitive and behavioral features <sup>9</sup>.

For patients with PD the cognitive dysfunction profile is heterogeneous <sup>4</sup>, but typically involves attention, executive functions, visual-spatial abilities, as well as episodic memory <sup>10</sup>.

Cognitive disorders can be measured by various neuropsychological assessments such as the Montreal Cognitive Assessment (MoCA) which is a screening test for mild cognitive impairment (MCI) in PD <sup>11</sup>. Its main limitation that it relies on patient's compliance, therefore, cognitive electrophysiology

plays an important role as it is not restricted by the presence of a physical disability<sup>12</sup>.

Electrophysiological studies have the advantage over MRI neuroimaging as they can record the electrical activity of neural networks in the cerebral cortex<sup>13</sup>.

The P300 can assess cognitive disorders in the early stages of PD<sup>14</sup>. It is an endogenous potential that belongs to the event-related potential, reflecting the electrical activity of the brain associated with the anticipation of the stimulus, decision making, and control of behavior<sup>15</sup>. P300 is especially important in the diagnosis of cognitive disorders in the early stages of PD when cognitive impairment is more subtle than in the later stages of the disease<sup>16</sup>. The P300 variable (amplitude and latency) has been regarded as a cognitive impairment marker, the P300 amplitude represents the degree of information processing, while the P300 latency represents the process of updating the working memory, selective attention, stimulus evaluation period and the prolongation of the P300 latency indicates poor cognitive performance<sup>17</sup>.

Our aim was to focus on the MCI in patients with PD without dementia in both newly diagnosed cases and chronic cases and a matched control group of individuals without PD.

We aimed to settle tools helping in diagnosing high-risk patients to delay progression to more severe phases of cognitive impairment.

## PATIENTS AND METHODS

A case-control study was conducted on a convenience sample of 50 male patients aged between 50-60 years old. They diagnosed with PD recruited from the Neurology outpatient clinic in Al-Zahraa Hospital, Cairo, Egypt. 25 of them were newly diagnosed cases (they didn't receive any treatment for PD), whilst 25 patients were chronic (duration of illness > 2 years). Female patients were not included in our study as they were very few in number, uncooperative & not educated.

All patients at least had primary stage education & had no history of psychiatric disease nor any other chronic medical or neurological disease that could affect cognitive function. Cognitive function & at least had primary stage education.

50 concurrent age, sex-matched control group were selected from relatives of other patients with no history of PD, psychiatric disease, chronic medical

or neurological disease, and not receiving any treatment that could affect.

Consent was taken from all subjects & the importance of study and confidentiality of data was explained. The study was done consistently with good clinical practice and the Declaration of Helsinki principles. All participants were subjected to the following:

1-Complete neuropsychiatric sheet and examination with emphasis on past or present history of medical, neurological, or psychiatric history.

2- Structured Clinical Interview for DSM IV-TR Axis I Disorders (SCID I)<sup>18</sup>- Arabic version<sup>19</sup>

SCID-I is a diagnostic interview used for making DSM-IV Axis I diagnosis. Any participant with a confirmed psychiatric diagnosis was excluded from the study.

3- The Montreal Cognitive Assessment (MoCA)<sup>20</sup>

It is a cognitive screening tool that was proved to be effective in diagnosing MCI and scoring < 26 was the used cutoff point for such diagnosis. It assesses the following cognitive subarea: Visuospatial ability, Naming, Attention, Language, Abstraction, Delayed recall, and Orientation.

4- P300 (auditory event-related potential). The P300 component is identified as positive deflection which peaks between 250 and 500 ms from the stimulus onset<sup>21</sup>. Analysis of the P300 involved identification of the waveform, latency, and amplitude.

Data were statistically analyzed by using the Statistical Package for the Social Sciences (SPSS) version 21, Armonk, NY: IBM Corp. Differences were considered as statistically significant when the P-value is less than 0.05, highly significant at P-value < 0.001.

## RESULTS

The present study included 50 patients with PD and a similar number of healthy persons as a control group.

Table 1 shows the sociodemographic characteristics of both patients group and control group, the mean age of patients group was  $54.7 \pm 2.83$  & that of the control group was  $54.64 \pm 2.75$ , both groups were also matched for marital status and education level.

	Patients group (N=50)	Control group (N=50)	P-value
<b>Age (mean <math>\pm</math> SD)</b>	54.7 $\pm$ 2.83	54.64 $\pm$ 2.75	0.9
<b>Marital status</b>			
Married	39(78%)	41(82%)	0.88
Divorced	6(12%)	5(10%)	
Widowed	5(10%)	4(8%)	
<b>Education</b>			
Primary	23(46%)	28(56%)	0.8
Preparatory	10(20%)	8(16%)	
High	12(24%)	10(20%)	
University	5(10%)	4(8%)	

**Table 1:** Sociodemographic characteristics of the sample

Table 2 shows MoCA test scoring in patients group and control group, 27(54%) of patients group score < 26 compared to 12(24%) of the control group with statistical significance (P-value 0.002).

	Patients group (N=50)	Control group (N=50)	$\chi^2$	P-value
<b>MOCA score</b>				
< 26	27(54%)	12(24%)	9.45	0.002*
≥ 26	23(46%)	38(76%)		

\*Significant < 0.05

**Table 2:** MoCA test scoring in patients group and control group

Table 3 shows a comparison between newly diagnosed cases & chronic cases of PD regarding cognitive subarea of MoCA test & there was a statistically significant difference regarding attention, language, and delayed recall (P value<0.001,<0.001,<0.01 respectively).

Cognitive subarea	Newly diagnosed cases N=25	Chronic cases N=25	t-test	P-value
<b>Visuospatial (mean ± SD)</b>	2.68 ± 1.28	2.12 ± 1.23	1.573	0.12
<b>Naming (mean ± SD)</b>	1.72 ± 0.84	1.44 ± 0.71	1.26	0.21
<b>Attention (mean ± SD)</b>	4.56 ± 1.15	2.24 ± 0.72	8.4	<0.001* *
<b>Language (mean ± SD)</b>	2.16 ± 0.55	0.56 ± 0.58	9.94	<0.001* *
<b>Abstraction (mean ± SD)</b>	1.40 ± 0.76	1.08 ± 0.40	1.85	0.072
<b>Delayed recall (mean ± SD)</b>	3.08 ± 1.41	2.28 ± 0.54	2.64	<0.01*
<b>Orientation (mean ± SD)</b>	4.00 ± 1.15	3.52 ± 0.87	1.65	0.1

**Table 3:** Cognitive subarea of the MoCA test in newly diagnosed cases & chronic cases of PD

Table 4 shows P300 (auditory event-related potential) in patients and control groups, patients with PD had prolonged targeted and frequent stimulus latency in 32 (64%) compared to 14 (28%) of the control group with mean ± SD of (317.84 ± 16.75, 307 ± 14.36 respectively) & low amplitude in 30 (60%) compared to 13 (26%) of the control group with mean ± SD of (14.281 ± 1.45, 15.04 ± 0.98 respectively) & there was a statistically significant difference at P-value.

	Patients group (N=50)			Control group (N=50)			t-test	P-value
	mean ±SD	Normal (N,%)	Abnormal (N,%)	(mean ± SD)	Normal (N,%)	Abnormal (N,%)		
<b>P300 latency (ms)</b>	317.84 ±16.75	18(36%)	32(64%)	307 ±14.36	36(72%)	14(28%)	3.47	0.001*
<b>P300 amplitude (µV)</b>	14.281 ±1.45	20(40%)	30(60%)	15.04 ± 0.98	37(74%)	13(26%)	3.05	0.003*

\*Significant < 0.05

**Table 4:** P300 (Auditory event-related potential) in patients and control groups

Table 5 shows a comparison between newly diagnosed cases & chronic cases of PD regarding P300 (auditory event-related potential). Chronic patients with PD had prolonged targeted and frequent stimulus latency in 20 (80%) compared to 12 (48%) of the newly diagnosed cases with mean  $\pm$  SD of ( $326.28 \pm 15.27$ ,  $309.4 \pm 13.82$  respectively) & low amplitude in 18 (72%) compared to 12 (48%) of the newly diagnosed cases with mean  $\pm$  SD of ( $13.8 \pm 1.6$ ,  $14.88 \pm 1.33$  respectively) & there was a statistically significant difference at P-value.

	Newly diagnosed cases N=25			Chronic cases N=25			t-test	P-value
	mean $\pm$ SD	Normal (N,%)	Abnormal (N,%)	mean $\pm$ SD	Normal (N,%)	Abnormal (N,%)		
<b>P300 latency (ms)</b>	309.4 $\pm$ 13.82	13(52%)	12(48%)	326.28 $\pm$ 15.27	5(20%)	20(80%)	4.09	< 0.001**
<b>P300 amplitude (<math>\mu</math>V)</b>	14.88 $\pm$ 1.33	13(52%)	12(48%)	13.8 $\pm$ 1.6	7(28%)	18(72%)	2.58	0.013*

**Table 5:** P300 (auditory event-related potential) in newly diagnosed cases and chronic cases of PD

## DISCUSSION

The cognitive symptoms in patients with PD are highly important as they directly affect their quality of life, the prognosis of illness, and the stress on caregivers<sup>22</sup>.

In our study, 27(54%) of PD patients had more cognitive impairment compared to the control group as only 12(24%) score < 26 on MoCA testing.

These results were following the study of Nazem et al.<sup>23</sup> who administered the MoCA test on 131 patients with idiopathic PD and found the mean MoCA scores  $24.9 \pm 3.1$  & 52.0% had criteria for cognitive impairment by MoCA scoring (<26).

Also, Wojtala et al.<sup>24</sup> who studied cognitive profiles among patients with PD and found approximately 40% of PD patients showing cognitive dysfunction.

A multicenter study performed by Aarsland et al.<sup>4</sup> reported discrepancies in the frequency of MCI in PD patients between the centers owing to differences in the procedures and neuropsychological tests used along with changes in patient populations being the lowest in unmedicated patients (18.9%) which reflects patients the earliest stages of the disease.

Another Egyptian study was held on 20 PD patients and 20 healthy individuals, cognitive functions were tested by MoCA and yielded that 70% of PD patients had MCI<sup>25</sup>.

It is important to note that while all participants had at least the primary stage of education to complete the MoCA test, yet, there may have been some bias because of their quality of education leading to the higher incidence of MCI in PD patients in Egypt.

In our study, chronic patients scored worse than newly diagnosed patients on 3 of MoCA cognitive subarea, namely attention, language, and delayed recall subscores.

Similarly to our results, Pauletti et al.<sup>26</sup> studied 15 patients with PD with fatigue (as a feature of chronicity), 17 patients with PD without fatigue, and 37 healthy controls, they found that PD patients with fatigue perform worse than PD patients without fatigue concerning the attention network test.

Also, Orтели et al.<sup>27</sup> deduced that in the early PD, the alertness and the executive portion of attention are retained but later the asymmetric degeneration

of the dopaminergic system would affect the attention functions.

A study conducted by Liu et al.<sup>28</sup> assessing the language abilities of 31 PD patients revealed that the PD group scored significantly lower than that of the control group on the Western Aphasia Battery (WAB) & this correlated significantly with the deterioration rate of motor function.

Altmann and Trosh<sup>29</sup> explained language impairment in chronic patients with PD by the fact that neural circuits used mainly in language are autonomously damaged in PD.

Also, The study of Whittington et al.<sup>30</sup> revealed that memory deficits in nondemented PD were found only in patients on parkinsonism medication but not in drug-naive patients.

A study by Cooper et al.<sup>31</sup> revealed that short-term memory and temporal ordering deficits in chronically medicated patients were higher than newly diagnosed cases. They indicated that much of the cognitive impairment in PD patients stemmed from attentional deficits affecting short-term and working memory.

In our study, P300 (auditory event-related potential) revealed that 80% of patients with chronic Parkinson's disease had prolonged targeted and frequent stimulus latency and 72% had low amplitude compared to newly diagnosed cases in which only 48% had prolonged latency and 48% had low amplitude and also compared to the reference value for the healthy population (28% had prolonged latency and 26% had low amplitude).

Our results coincided with that of Balaban et al.<sup>32</sup>, they performed a study on 30 patients with Parkinson's disease and revealed latency prolongation and decrease of the average amplitude in patients with greater cognitive alteration suggesting a decrease in the speed of information processing and a tendency to decrease the discrimination capacity.

Also, Sarikaya et al.<sup>33</sup> evaluated cognitive functions in PD patients without dementia with P300 and found that P300 latencies in PD patients were significantly prolonged compared to the control group & there was a decrease in P300 amplitude.

Also, Yilmaz et al.<sup>34</sup> checked P300 changes in 41 non-demented PD patients (20 patients with PD with MCI & 21 patients with PD without cognitive impairment). They found that the P300 amplitude was significantly lower in PD with the MCI group than in the PD without cognitive impairment. They deduced that P300 can be used as a parameter in the diagnosis of PD with MCI.

Also, the studies of Matsui et al.<sup>35</sup>, Solís-Vivanco et al.<sup>12</sup> revealed that PD patients had pathological P300 frequent stimulus amplitude and prolonged P300 latency.

Moreover, Prabhakar et al.<sup>36</sup> investigated changes in P300 in the early stages of PD and the effects of dopaminergic therapy. They found that the P300 latency was not significantly increased in early Parkinson's disease, meanwhile, it was increased later with dopaminergic treatment.

Huster et al.<sup>37</sup> explained deterioration of cognition, in the chronic stages of PD and pathological changes of P300 are due to destruction of efferent fibers in the cortex or subcortical pathology in addition to amyloid deposition along the course of the disease as mentioned by Hepp et al.<sup>38</sup>.

### CONCLUSION

PD patients are frequently encountered with issues concerning cognitive deficits, this markedly affects their quality of life and impose more burden on caregivers. Prediction and early diagnosis of these deficits are mandatory and early intervention is a current challenge to doctors.

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