Original Article

The Relationship Between Motor, Non-Motor And Cognitive Impairment In Patients With Parkinson' Disease

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Abstract

Background Non motor symptoms and cognitive dysfunction are common in Parkinson's disease. These symptoms often contribute to disability and impact negatively on quality of life even in early-stage disease. They are frequently underrecognized and undertreated. **Aim and objectives** study the relationship between motor symptoms and both cognitive and non-motor symptoms in Parkinson's disease patients**. Subjects and methods** this study was conducted in neurology department, Beni Suef University Hospital, The study included 100 subjects (50 patients of Parkinson's disease and 50 healthy control were included). Motor assessment using the Unified Parkinson's Disease Rating Scale (UPDRS), non-motor symptoms assessment using non motor symptoms scale and cognitive assessment using Montreal Cognitive Assessment (MOCA) test were done for all patients. **Result** During OFF state, UPDRS was positively correlated with perception /hallucination, sleep and GIT symptoms. There was statistically significant positive correlation between UPDRS during ON state and both sleep and gastrointestinal tract symptoms There was a statistically significant positive correlation between UPDRS during both ON and OFF states and total non motor symptoms scale. The total Montreal Cognitive Assessment (MOCA) score was negatively correlated with UPDRS during ON state. UPDRS during ON state was negatively correlated with executive functions, visuospatial functions, calculation, abstract thinking and orientation. **Conclusion** There was a statistically significant positive correlation between UPDRS during both ON and OFF states and total non motor symptoms scale. The total MOCA score was negatively correlated with UPDRS during ON state. Family history, Level of Education, Pesticide exposure, Coffee intake, living in Rural area and Smoking were not significant risk factors for Parkinson's disease

Keywords: Non-motor, Cognition, UPDRS, MOCA, Parkinson's disease.

INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disease. This condition mainly affects motor function, but also causes non motor symptoms. [1]
The onset of PD is usually after 50 years old, and a sharp increase of the incidence is seen after the age of 60 (1% of the population).[2]

Although PD's etiology remains unclear, the interaction between genetic and environmental substrates has been associated with the development of the disease .[3]

Parkinson's disease (PD) has been associated with rural living, well-water consumption, and pesticide exposure; however, the individual risk contribution of these variables has not been established

Neurodegenerative progression in Parkinson's disease (PD) involves not only dopaminergic neurons, but also non-dopaminergic neurons including serotonergic, noradrenergic, and cholinergic neurons .[4]

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized primarily by motor symptoms including bradykinesia, resting tremor, rigidity, and postural instability. Motor features of PD are just the "tip of the iceberg." It is now known that in addition to the typical motor symptoms of PD, the clinical picture includes many non-motor symptoms .[5]

Besides motor symptoms-related disability, patients with PD frequently suffer from various non-motor symptoms including constipation, sleep disturbance, pain, and cognitive decline. Non-motor symptoms in PD are known to be heterogeneous since multi-systemic neurodegeneration and related

neuropsychological changes are not constant .[6] Especially, cognitive impairment is one of the major factors that lower the quality of life in patients with PD .[7,8]

It has become increasingly apparent that PD patients, at all stages of the disease, can experience cognitive dysfunction. Although there is heterogeneity to the clinical presentation of cognitive impairment in PD in general [9] and particularly earlier in the disease process, the cognitive impairment in PD often involves executive function, attention, visuospatial function and working memory, suggesting a frontal or fronto-striatal nature to these cognitive deficits. [10,11,12,13]

Several studies have examined relationships between motor symptoms and cognitive functions in PD and in general, such studies have reported that bradykinesia and rigidity are correlated with at least some types of cognitive impairment while tremor is less likely to correlate with cognitive impairment. [14,15,16,17] The aim of this work was to study relationship between motor, non-motor and cognitive impairment in patients with Parkinson' disease.

Patients and Methods

This study is a case control study which was conducted in neurology department, Beni Suef University Hospital, the study included 100 subjects divided into 2 groups

1. **Patient group**

50 patients of Parkinson disease were included.

Inclusion Criteria

Patients fulfilling the criteria for diagnosis of Parkinson's disease based on British Brain Bank criteria .[18]

Exclusion Criteria

Patients with the following conditions were excluded from this study: Patients with secondary Parkinsonism (Drug-induced, post traumatic, or post infectious) or atypical Parkinsonism, Patients with concomitant cerebrovascular stroke, Patient with any concomitant medical or metabolic illness known to affect cognition e.g., thyroid, or parathyroid disease, hepatic or renal failure, Patients with MRI brain showing any structural lesion like multiple or extensive infarcts, severe white matter hyperintensity burden, intracerebral hemorrhage, subdural hematoma, tumors, encephalitis, or hydrocephalus.

2. Control group:

Included 50 healthy subjects (age and sex matched to the patient group) from the general population without neurological disease or family history of PD.

Methods

All patients were subjected to the

***Clinical assessment**

History taking

Information of demographic variables and medical history, such as sex, age, education level, age at PD onset and disease duration. Family history was considered positive until second-degree relatives. A structured questionnaire of environmental factors delivered information about risk factors (pesticide exposition, living in rural areas) and protective (smoking habits, coffee intake, physical exercises and cognitive activities) factors.

History of smoking was defined on basis of self-report as never vs. ever having smoked at least once a day for at least one year .[19] Coffee consumption was assessed on basis of self -report and consumption was defined as more than two coffee cups per day .[20] Similarly, self-reported physical exercises or cognitive actives (i.e., reading, crossword puzzles ,card games, chess, and others) was considered when carried out at least once a week.

Thorough neurological examination

Evaluation of Parkinson's disease

It was done using Unified Parkinson's Disease Rating Scale (UPDRS)[21] during both OFF and ON state. The 'practical' off medication state (Parkinson's disease OFF) for both clinical and imaging assessments was defined as ≥ 72 h off extended-release dopamine agonists, selective MAO-inhibitors, and long-acting levodopa, and ≥ 12 h off short acting dopamine agonists and levodopa. The on-medication state (Parkinson's disease ON) for both clinical and imaging assessments was defined as the patients taking their normal daily medications in the optimally medicated state, as determined by both the patient and the movement disorders neurologist .[22]

The UPDRS is a scale in common practice for Parkinson's disease. It objectively rates an individual patient's disability at a particular moment in time. Its score reflects disease burden on the individual patient and is useful in describing disease progression and treatment response with time. The UPDRS is scored from a total of 195 points; higher scores reflect worsening disability.

Non motor symptoms assessment

It was assessed by non motor symptoms scale. The Non-Motor Symptoms Scale (NMSS) has 30 items, nine domains: cardiovascular (2 items), sleep/fatigue (4 items), mood/ cognition (6 items), perceptual problems/hallucinations (3 items), attention/memory (3 items), gastrointestinal tract (3 items), urinary function (3 items), sexual function (2 items), and miscellaneous (4 items). Each item scores on a multiple of severity (from 0 to 3) and frequency scores (from 1 to 4) and the theoretical range of the NMSS total score is 0 to 360 .[23,24]

Cognitive assessment

The Montreal Cognitive Assessment

For educated patients Which is a cognitive scale designed to cover the full spectrum of cognitive deficits (total score: 30). It includes the following tests: test for assessment of excutive functions and visuospatial functions, Test for assessment of confrontation naming, test for assessment of memory, test for assessment of attention, test for assessment of language, test for assessment of delayed free recall verbal memory and test for assessment of orientation. The cutoff point is <26. As patients with MOCA score > or = 26 are considered to have normal cognition .[25]

The Montreal Cognitive Assessment-Basic

It was developed to facilitate the detection of mild cognitive impairment in illiterate and lower educated subjects. The MoCA-B assesses similar cognitive domains as the original MoCA: executive functions, language, orientation, calculations, conceptual thinking, memory, visuoperception, attention and concentration. It is scored on 30 points. Cut off score is <24. As patients with score > or = 24 are considered to have normal cognition.[26]

Statistical methods

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using Independent sample t- test. For comparing categorical data, Chi square (c2) test was performed. Exact test was used instead when the expected frequency is less than 5 (Chan, 2003b). Pearson correlation was used to test the relationship between quantitative variables. P-values less than 0.05 were considered as statistically significant.

Results

The current study is a case control study conducted on 30 patients diagnosed as Parkinson's disease and 30 normal healthy controls matched with age and sex.

Descriptive data

A. Demographic Data

1. **Age**

   The age of PD patients in this study ranged from (35 to 77) years with a mean value of 61.90 (SD=9.21) years, while the age of control subjects ranged from (37 to 81) years with a mean value of 62.62(SD=12.32) years. There was no statistically significant difference between patients and controls (P-value= 0.882) [Table 1].

2. **Gender**

   In the present study, 58 %(n=29) of the included PD patients were males and a number of 42.0 %(n=21 were females with a male: female ratio = 1.4:1. Regarding controls, 56.0% (n=28 were males and 44.0% (n=22 were females with a male: female ratio =1.3:1. There was no statistically significant difference between patients and controls (P-value = 0.840) [Table 1].

Table (1) Demographics of patients and controls

Variable		Patients(n=50) (%=100)	Controls (n=50) (%=100)	P-value
Age in years [mean (SD)]		61.90±9.21	62.62±12.32	0.882
Sex	Male [n (%)]	29 (58.0%)	28(56.0%)	0.840
	Female [n (%)]	21(42.0%)	22(44.0%)	

P value ≥ 0.05 (non-significant).

B. Risk and protective factors

1. Risk factors

There was 2 patients (4.0%) having positive paternal family history of Parkinson's disease while non of controls had positive family history of Parkinson's disease. 50.0 % of patients had history of regular pesticide exposure in certain period in their lives while 38.0 % of controls had history of pesticide exposure. Eighty percent of patients had lived in a rural area while seventy two percent of controls had that history with no significant difference between both groups (P- value = 0.349) **[Table 2**].

2. Protective factors

Only one patient had history of coffee intake daily. None of controls report history of regular coffee intake. Eighty percent of Parkinson's disease had history of moderate to vigorous physical activity in accordance with Centre for Disease Control and Prevention (CDC) and American College of Sports Medicine (ACSM) guidelines while eighty four percent of controls had that history with no significant difference between two groups (P-value = 0.603) **[Table 2].**

Eleven patients of Parkinson's disease reported history of cognitive exercises. Eleven controls reported history of cognitive exercises as well.

Table (2) Risk factors, protective factors and education in patients and controls

		Cases		Controls		P value
		Count	**%**	**Count**	**%**	
Family history	positive (father)	2	4.0%	0	0.0%	0.495
	negative	48	96.0%	50	100.0%	
Pesticide exposure	positive	25	50.0%	19	38.0%	0.227
	negative	25	50.0%	31	62.0%	
Coffee intake	positive	1	2.0%	0	0.0%	1
	negative	49	98.0%	50	100.0%	
Rural area	positive	40	80.0%	36	72.0%	0.349
	negative	10	20.0%	14	28.0%	
Smoking	smoker	8	16.0%	14	28.0%	0.148
	no	42	84.0%	36	72.0%	
Physical activity	positive	40	80.0%	42	84.0%	0.603
	negative	10	20.0%	8	16.0%	
Cognitive exercise	positive	11	22.0%	11	22.0%	1
	negative	39	78.0%	39	78.0%	
Education	educated	22	44.0%	19	38.0%	0.542
	Not educated	28	56.0%	31	62.0%	

C. Clinical characteristics of PD patients

1. Clinical assessment of PD patients

The total score of UPDRS for PD patients during OFF state with a range of 16 to 112 and with a mean value 61.10 (SD=25.57) while total UPDRS for those patients during ON state ranged from 11 to 95 with a mean value 42.72 (SD=20.40) . The mean value of mentation score was 3.26 (SD = 1.68) and mean value of Medication complication was 3.26 (68 is 17.55(SD=8.77). **[Table 3].**

Table 3 are showing mean value of motor assessment and activities domains of UPDRS in both ON and OFF states. For example, during OFF state the mean values of tremors, rigidity, postural instability and bradykinesia were 7.46 (SD=4.81), 8.26.50 (SD=3.67), 1.50 (SD=0.76) and 2.06 (SD=1.02) respectively. While during ON state the mean values of the same domains were 4.30 (SD=4.14), 6.50 (SD=3.03),1.18 (SD=1.08) and 1.34 (SD=1.08) respectively.[Table 3]. The mean value of total UPDRS in OFF state was 60.36(SD=25.33) and was 42.72 (SD=20.40) in ON state. **[Table 3].**

Table (3) Motor assessment of PD patients during ON and OFF state

UPDRS			PD patients (n=50)	
			During ON state	**During OFF state**
Motor score	Tremors	Rest tremors	2.64±2.95	5.14±3.63
		Action/postural tremors	1.66±1.48	2.32±1.67
		Total tremors	4.30±4.14	7.46±4.81
	Rigidity		6.50 ±3.03	8.26 ± 3.67
	Postural instability		1.18 ±1.08	1.50 ±0.76
	Bradykinesia		1.34 ±1.08	2.06 ±1.02
	Total motor score		26.10 ±13.53	37.62 ± 16.39
Mentation score			3.26 ±1.68	
Activities score			9.86 ±7.13	16.72 ± 9.23
Medication complication			3.46 ±2.53	
Total score			42.72 ± 20.40	60.3625.33

2. NON-motor symptoms:

a. Non motor scale (NMS)

The total score of non motor scale (NMS) ranged between 8 to 150 with mean value 47.18 (SD=33.57).

Urinary manifestations had the highest score among the other NMS domains with mean value 11.58 (SD=9.81) followed by Mood and cognition affection with the mean value 8.04 (SD=8.41).

Perception and hallucination domain was the lowest affected one amon PD patients with mean value 0.76 (SD=2.70). **[Table 4]**

Table (4) Non motor scale domains distribution in PD patients

	Range	**Mean +/- SD**
CVS	0-15	2.66 +/- 3.29
Sleep/Fatigue	0-30	5.84 +/- 6.91
Mood/Cognition	0-34	8.04 +/- 8.41
Perception /Hallucination	0-12	0.76 +/- 2.70
Attention/Memory	0-32	3.54 +/- 7.88
GIT	0-27	6.44 +/- 7.83
Urinary	0-36	11.58 +/- 9.81
Sexual func	0-24	4.98 +/- 7.17
Miscellaneous	0-24	3.34 +/- 5.24
Total score	8-150	47.18+/- 33.57

b. Cognitive assessment of PD patients

The total score of MoCA for PD patients ranged from 7 to 29 with a mean value 16.70 (SD= 6.14**) [Table 5].** Based on cut off score it was found that only six patients (12%) had no cognitive impairments while forty four patients were cognitively impaired based on MoCA score**.**

In MoCA score, the highest impaired domain was the excutive functions with mean value of 10.00% (SD=30.30%), followed by visuospatial functions with mean value of 28.67%(SD=36.70%). The least impired domain was orientation with the mean value 88.33% (SD=15.52%). **[Table 5]**

Table (5) Cognitive assessment of PD patients by MoCA**.**

MoCA	PD patients (n=47)	
	Range (minimum-maximum)	**Mean (SD)**
Executive functions %	(0%-100%)	10.00% ± 30.30%
Visuospatial functions %	(0%-100%)	28.67% ± 36.70%
Language %	(0%-100%)	46.00% ± 25.99%
Attention %	(0%-100%)	42.67% ± 45.69%
Calculation %	(0%-100%)	51.33% ± 37.02%
Abstract thinking %	(0%-100%)	33.00% ±37.57%
Orientation %	(50%-100%)	88.33% ± 15.52%
Delayed recall%	(0%-100%)	51.60% ± 33.83%
Total MoCA score	(7-29)	16.70 ± 6.14

Correlation between total UPDRS and non-motor symptoms

A) Correlation between total UPDRS and non-motor symptoms scale

There was a statistically significant positive correlation between UPDRS during both ON and OFF states and total non motor symptoms scale [(r) co efficient=0.6 , P value=0.002], [(r) co efficient=0.39 , P-value=0.005] respectively.

During OFF state, UPDRS was positive correlated with perception /hallucination, sleep and GIT symptoms [(r) co efficient=0.305, P-value=0.031], [(r) co efficient=0.286 , P value=0.044], [(r) co efficient=0.413 , P-value=0.002] respectively.

There was a statically significant positive correlation between UPDRS during ON state and both sleep and GIT symptoms [(r) co efficient=0.33 , P value=0.019], [(r) co efficient=0.502 , P-value=0.000] respectively.**[Table6]**

Table (6) Correlation between total UPDRS and non-motor

Non motor symptoms scale	UPDRS ON		UPDRS OFF	
	(r) coefficient	**P-value**	**(r) coefficient**	**P-value**
Perception /Hallucination	.246	.064	.305	.031*
Attention/Memory	.046	.750	.005	.975
CVS	.227	.113	.034	.814
Sleep/Fatigue	.330	.019*	.286	.044*
Mood/Cognition	.245	.087	.355	.011
GIT	.502	.000*	.413	.003*
Urinary	.274	.054	.152	.291
Sexual	.006	.965	.029	.839
Miscellaneous	.268	.424	.422	.002*
Total.NMS	.060	.002*	.390	.005*

B) Correlation between total UPDRS and cognitive functions by MOCA test:

The total MOCA score was negatively correlated with UPDRS during ON state [(r) co efficient=-0.371 , P value=0.008].

UPDRS during ON state was negatively correlated with executive functions, visuospatial functions, calculation, abstract thinking and orientation. [(r) co efficient=-.279 , P value=.049*], [(r) co efficient=-.316 , P-value=.026], [(r) co efficient=-0.294 , P value=..038 *], [(r) co efficient=-.331 , P-value=0.019*] and [(r) co efficient=-0.392 , P value=..005 *]respectively.

During OFF state, UPDRS was negatively correlated with abstract thinking [(r) co efficient=-0.282 , P value=0.047].**(Table7)**

Table (7) Correlation between total UPDRS and MOCA

MOCA	UPDRS ON		UPDRS OFF	
	(r) coefficient	P-value	(r) coefficient	P-value
Executive functions %	-.279	.049*	.017	.906
Visuospatial functions %	-.316	.026*	-.150	.300
Language %	-.228	.111	-.052	.722
Attention %	-.170	.239	-.176	.221
Calculation %	-.294	.038 *	-.146	.310
Abstract thinking %	-.331	.019*	-.282	.047*
Orientation %	-.392	.005*	-.202	.160
Delayed recall%	-.141	.330	.014	.922
Total MoCA score	-.371	.008*	-.138	.339

Discussion

Parkinson's disease, which is the second most common neurodegenerative disorder after Alzheimer's disease, has a late onset and is diagnosed in about 1% of individuals over the age of 65. PD is an incurable and progressive disorder that gradually affect the motor control. Traditionally, PD has been considered an idiopathic or sporadic disease characterized pathologically by the degeneration and loss of the dopaminergic neurons in the nigral striatal pathway and the presence of Lewy pathology **.**[27]

Non motor symptoms are common in PD. These symptoms often contribute to disability and impact negatively on quality of life even in early-stage disease. They are frequently underrecognized and undertreated. [28]

These symptoms are diverse and may reflect dysfunction in non-dopaminergic systems, though dopaminergic transmission dysfunction may play a role.

Regarding to family history, in the present study, positive family history represented 4% of all 50 Parkinson disease patients. While ***Campelo et al. 2017*** reported positive family history in 42.9% of total 105 PD patients in Brazil**.**[29] Positive family history was also reported in 16% of total 840 PD patients in mayo clinic **.**[30] 16% of total 114 PD patients also had positive family history in Oregon in ***Payami etal, 1994***. [31] In Italy, positive first-degree family history represented 13.1% of 634 PD patients**.**[32]

In the current study, positive first-degree relative family history didn't show risk to develop PD as there was no significant differences between patients and controls. Similar to our findings, In Italy, a case control study demonstrated that positive family history wasn't considered a significant risk factor when family history was restricted to first degree members **.**[32]

In line with our finding, ***MARTTILARJ, et al (1976), DUVOlS1N et al (1969), ROYM, et al (1983)*** and ***CLEEVELS, et al (1988)*** did not show association between family history of PD and the risk for PD .[33,34,35,36]

In contrast, in Spain, a case control study demonsterated a higher frequency of family history of PD in PD patients.[37] In Oregon, ***Payami , etal*** (***1994)*** demonstrated significantly elevated risk for development of PD in first-degree relatives of patients. [31]

As shown, there are different positive family history distribution among different studies. These disparate results may be attributed to different numbers of cases included in each study, also may be due to different populations with heteogeneous genetic background and ethenic variations of each study.

Regarding to risk factors, many environmental factors were suggested to be risk factors for Parkinson's disease. In the current, pesticide exposure and living in rural areas were studied as being suspected risk factors for developing PD but there was no significant difference between Parkinson's disease patients and controls [(50% versus 38%) and (80% versus 72%) respectively].

These results are in concordance with ***Campelo et al. (2017),*** who mentioned that there was similar frequency of exposure to pesticide and living in rural areas between cases and controls, without significant association with PD risk.[29]

In the present study, there was no association between smoking, caffeine consumption, physical activity and cognitive activity -as a protective factors- and PD risk. As there was higher frequency of smoking and physical activity in controls than cases without significant difference between cases and controls. Frequency of cognitive activity was equal between cases and controls. Frequency of coffee consumption was higher in PD patients than controls without significant difference.

A case-control study had found a similar frequency of exposure to protective factors (coffee consumption, smoking habits, and physical activities) between PD patients and controls without significant associations with PD risk. As coffee consumption was higher in patients than controls and smokers were higher in controls than cases. But regarding cognitive activity, they found a higher frequency of cognitive activities' practice in the control group with significant difference between patients and controls. Cognitive activity showed a strong protective effect against PD .[29]

In the current study, level of education didn't show protective effect against PD as there was no significant difference between PD patients and controls. This result is in concordance with a case control of 105 PD patients .[29]

In contrast, ***Szwedo*** **(2021)** found that there was significant difference between patients and controls regarding education in years. This may be explained by that education was not that common in our population as whole in this age category so there was no significant difference between cases and controls.[38]

In the present study the mean value of total non-motor scale (NMS) was 47.18 (SD=33.57) of 50 PD patients. The main score points were in urinary system then in mood /cognition then in GIT. There was a statistically significant positive correlation was found between total UPDRS during both ON and OFF states and total non motor symptoms scale. During OFF state, UPDRS was positive correlated with perception /hallucination, sleep and GIT symptoms. There was significantly correlation between UPDRS during ON state and both sleep and GIT symptoms.

In ***Shalash et al., (2021),*** the mean value of total NMS was 62.52 (SD=40.64) of 72 PD patients main score points were in mood then in sleep/fatigue then urinary system.[39]

In ***Ragab et al.,*** all 41 newly diagnosed PD patients included in that study suffered one or more NMSs; constipation was the most frequent followed by sexual dysfunction, depressive symptoms, and sleep disturbance, while pain, sialorrhea, and restless leg were the least reported.[40]

Tibar et al., (2018) showed that all patients of total 117 parkinsonian disease patient have presented at least one NMS. Autonomic and sleep disorders were the most frequent, and in contrast to other studies, digestive and cardiovascular disorders were rather the factors influencing negatively the QoL of patients.[41]

Depression is common in patients with any stage of PD. Its relationship with cognitive dysfunction has been widely studied, showing a significant association .[8]

Rolinski et al., 2014 reported no correlation between REM behavioral disorders and motor symptoms of PD, as they recruited more than 400 medicated and non-medicated patients.[42]

In ***Ba et al., 2017*** UPDRS-III total score and H&Y staging correlated with a higher NMS Quest score ($p=0.0001$, and $p<0.0001$, respectively). In the same study, in the PIDG type, the total PIGD score was a significant predictor of worse NMS profile ($p<0.0001$, $R^2=0.064$), while in the TD and indeterminate groups, no significant correlation was observed between NMS Quest score and UPDRS-III total score.[43]

Our study showed The total MOCA score was negatively correlated with UPDRS during ON state .

UPDRS during ON state was negatively correlated with executive functions, visuospatial functions, calculation, abstract thinking and orientation.

During OFF state, UPDRS was negatively correlated with abstract thinking

Kwon et al., 2022 found that the PD-MCI group showed higher scores of motor severity, including rigidity score, total motor score, and HY stage in compared to non-PD-MCI,[44] in line with the literature .[45,46]

Also, ***Kwon*** et al., 2022 found that memory impairment, visuospatial impairment and executive impairment was related to higher motor scores of the UPDRS-III (OR = 0.0242, 95% CI = 1.0087–1.1322, p = 0.0242) , (OR = 1.0970, 95% CI = 1.0225–1.1770, p = 0.0099) , (OR = 1.0651, 95% CI = 1.0034–1.1306, p = 0.0383) respectively. Motor symptoms were widely associated with cognitive deficits in that study population. On the other hand, non-motor symptoms showed different patterns of cognitive impairments. Especially, dysautonomia and depression were significantly related to cognitive deficits in visuospatial and frontal-executive domains.[44]

In Siciliano et al., 2017 study conducted on Forty de novo PD patients at HY stage I and 40 patients at HY stage II , they concluded, In de novo PD patients, the severity of motor impairment at the diagnosis is associated to cognitive deficits and higher risk of MCI.[46]

Yamawaki etal., 2018 's findings indicated that the cognitive impairment was observed in deterioration of the motor impairment in PD patients. Specifically, in the factor scale level, the low processing speed index and the low verbal memory quotient reduced each of the PIQ and GMQ in the lowest HY group patients. Therefore, we suggest that a careful assessment of cognitive impairments, especially processing speed and verbal memory, is important in identifying appropriate interventions for PD with severe stage.[47]

Conclusion

Our results showed that positive relation was found between UPDRS during both ON and OFF states and total non motor symptoms scale. The total MOCA score was negatively correlated with UPDRS during ON state.

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