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Influence of depression in mild Parkinson's disease on longitudinal motor and cognitive function

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ABSTRACT

Background: Studies have suggested a relationship between non-motor symptoms with motor fluctuations in patients with Parkinson's disease (PD). We studied the influence of depression on longitudinal motor and cognitive function among mild PD patients.

Methods: A 1.5 years longitudinal study of 102 patients with mild idiopathic PD. Patients were assessed with a standardized clinical assessment battery including motor and non-motor scales. Patients also underwent serial neurocognitive testing that assessed global cognition, memory, attention, language, visuospatial and executive function.

Results: 81 patients with mean age of 64.9(SD = 7.9) years and mean Hoehn & Yahr of 1.9(SD = 0.4) completed baseline and follow-up visits. 22 patients had clinically significant depression at baseline with mean Geriatric Depression Scale of 6.9(SD = 2.4). These patients presented with concomitant apathy and anxiety and were more likely to be females with longer duration of PD. At baseline, patients with depression had poorer performance on global cognition and all cognitive domains although not significantly different from patients without depression. At follow-up, there was no statistically significant difference on cognitive performance between those with and without baseline depression. Patients with baseline depression demonstrated worsening of motor function after 18 months (UPDRS Motor Score Change: +5.0[7.0]vs.+0.2[7.3]; p = 0.015). On multivariate analysis Baseline Motor Score (B = −0.229,CI = −0.445to-0.013,p = 0.038), Baseline GDS (B = 0.622,CI = 0.078to1.166,p = 0.026) and PD duration (B = 0.520,CI = 0.105to0.935,p = 0.015) independently predicted increase in UPDRS Motor Score.

Conclusions: The findings suggest a relationship between early depression with motor worsening and cognition decline in PD patients. Further biomarker-supported studies investigating the role of depression on motor and cognitive function are needed.

1. Introduction

Motor symptoms have been the mainstay for the diagnosis of Parkinson's disease (PD). PD is a neurodegenerative disorder where bradykinesia, tremors, rigidity, gait and postural problems present as cardinal symptoms [1]. Non-motor symptoms (NMS) have also been found to be highly prevalent in PD, affecting about 30–40% of PD patients [2]. However, NMS is under recognized as patients may not be reporting NMS symptoms to their clinicians and clinicians not routinely enquiring about NMS due to lack of awareness among health care professionals [3–5].

Among the components of NMS, depression has been demonstrated to influence cognitive function [6]. One study reported premorbid depression to adversely affect improvement of motor symptoms after deep brain stimulation for PD [7]. Smaller volumes of amygdala and disruption to prefrontal cortex-limbic axis have also been demonstrated among PD patients with depression [8–10]. The influence of depression on longitudinal cognitive function, motor function and progression of disease is not clearly understood.

If depression is demonstrated to influence longitudinal disease progression, greater awareness among patients and clinicians on the importance of diagnosis and treatment of depression will need to be created. These facts highlight the need to study the influence

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of NMS particularly depressive symptoms on the progression of motor and cognitive symptoms in PD. In this longitudinal study, we investigated the influence of baseline depression on longitudinal cognitive and motor performance.

2. Methods

2.1. Participants

The cohort of participants was recruited between 2011 and 2012 in a tertiary neurology setting. PD was diagnosed based on the National Institute of Neurological Disorders and Stroke (NINDS) criteria. Literate participants aged between 50 and 90 years old with mild PD, defined by Hoehn & Yahr score of <3 were recruited. Patients were screened for presence of any serious medical or surgical co-morbidities, history of stroke(s) and/or other neurodegenerative diseases other than PD.

2.2. Study design

All participants underwent a full clinical interview and a neurocognitive assessment at baseline and at follow-up at 1.5 years. Informed consent from all participants and approval from the Centralized Institutional Review Board were obtained prior to the start of the study. Patients were stratified to Positive for Depression (DepPos) and Negative for Depression (DepNeg) based on presence of clinical symptoms of depression and locally validated cutoffs for the Geriatric Depression Scale (GDS) [11]. A GDS≥5 was required for the diagnosis of depression.

2.3. Clinical and neurocognitive assessments

All patients underwent a clinical interview prior to a comprehensive neurocognitive assessment. The Unified Parkinson's Disease Rating Scale (UPDRS) motor scale was performed for all patients at baseline and at 18 months [12]. Trained psychologists evaluated cognitive performance, behavioral and functional abilities of the participants based on a standardized protocol. As recommended by the Movement Disorder Society Taskforce, cognitive assessments were grouped into specific cognitive domains namely [13]: Global (Mini Mental State Examination [MMSE], Montreal Cognitive Assessment [MoCA]), Memory (Word-list Delayed Recall, Word-list Recognition), Executive Function (Color Trails 2, Sunderland 10-point Clock Drawing Test), Attention/Working Memory (Digit Span Forward & Backwards, Color Trails 1), Language (Objective Naming Test, Verbal Commands Test) and Visuospatial (Constructional Praxis Test, Maze Test [Errors]). Behavioral and functional scales included the Barthel Index [14], Geriatric Depression Scale (GDS) [15], Apathy Scale (AS) [16], Hospital Anxiety and Depression Scale – Anxiety (HADS Anxiety subscale) and Epworth Sleepiness Scale (ESS) [17,18]. All cognitive, behavioral and motor assessments were performed in the levodopa "ON" state.

Table 1
Baseline profile.

	DepNeg (n = 59)	DepPos (n = 22)	Total (n = 81)	p Value
Demographics				
Age at Baseline Visit, years (mean, SD)	64.7 (7.7)	65.3 (8.4)	64.9 (7.9)	0.770[a]
PD Symptom Duration at time of diagnosis, years (mean, SD)	4.9 (4.1)	6.5 (2.5)	59.5 (9.0)	**0.013**[b]
Gender, male (N, %)	47 (79.7)	12 (54.5)	59 (72.8)	**0.047**[c]
Education, years (mean, SD)	10.9 (3.0)	10.4 (3.9)	10.8 (3.2)	0.263[b]
Clinical Information				
UPDRS Motor Score (mean, SD)	18.3 (7.6)	19.5 (9.6)	18.7 (8.2)	0.915[b]
Hoehn and Yahr (mean, SD)	1.9 (0.4)	2.0 (0.4)	1.9 (0.4)	0.149[b]
Schwab and England (mean, SD)	91.3 (6.2)	90.3 (6.6)	91.0 (6.3)	0.589[b]
Total LED (mean, SD)	578.5 (408.7)	717.1 (391.2)	616.6 (406.3)	0.098[b]
Barthel Index (mean, SD)	98.1 (2.9)	95.7 (4.4)	97.4 (3.5)	**0.017**[b]
Non-Motor Assessments				
GDS[d] (mean, SD)	1.7 (1.2)	6.9 (2.4)	3.1 (2.8)	**<0.001**[b]
Apathy Score[d] (mean, SD)	11.7 (4.9)	14.8 (4.3)	12.5 (4.9)	**0.010**[a]
Anxiety Score[d] (mean, SD)	3.9 (3.2)	7.4 (3.4)	4.9 (3.6)	**<0.001**[b]
ESS[d] (mean, SD)	7.3 (4.4)	8.3 (5.9)	7.6 (4.9)	0.686[b]
Neurocognitive Assessments				
Global Cognition				
MMSE (mean, SD)	28.2 (1.7)	27.2 (2.8)	28.0 (2.1)	0.130[b]
MoCA Adjusted (mean, SD)	26.7 (2.6)	25.7 (3.5)	26.4 (2.9)	0.079[b]
Memory				
ADAS-Cog Delayed Word Recall[d] (mean, SD)	2.4 (2.0)	2.7 (2.4)	2.5 (2.1)	0.295[b]
ADAS-Cog Recognition[d] (mean, SD)	1.6 (2.0)	1.3 (1.2)	1.5 (1.8)	0.769[b]
Executive Function				
Sunderland Clock (mean, SD)	9.1 (1.6)	8.2 (2.1)	8.8 (1.8)	0.663[b]
Color Trails 2, seconds (mean, SD)	142.5 (60.2)	154.7 (52.6)	145.7 (58.3)	0.113[b]
Attention				
Digit Span Forward (mean, SD)	10.9 (2.4)	10.5 (2.3)	10.8 (2.3)	0.755[b]
Digit Span Backwards (mean, SD)	6.3 (2.1)	5.3 (1.5)	6.0 (2.0)	0.052[a]
Color Trails 1, seconds (mean, SD)	81.7 (38.5)	100.6 (41.0)	86.7 (39.8)	0.382[b]
Language				
ADAS-Cog Naming[d] (mean, SD)	0.8 (0.7)	1.0 (0.8)	0.9 (0.7)	0.743[b]
ADAS-Cog Commands[d] (mean, SD)	0.5 (0.6)	0.5 (0.6)	0.5 (0.6)	0.965[b]
Visuospatial				
ADAS-Cog Constructional Praxis[d] (mean, SD)	0.2 (0.4)	0.4 (0.5)	0.3 (0.4)	0.118[b]
ADAS-Cog Maze Time, seconds (mean, SD)	20.3 (12.4)	23.8 (12.6)	21.3 (12.5)	0.940[b]

[a] t-test.
[b] Mann-Whitney.
[c] χ^2 test, N (%).
[d] Reverse scored, higher value suggests greater impairment.

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