

## Can Mild Behaviour Impairment be an Early Predictor of MCI and Dementia in Parkinson's Disease Similar to the Role of MBI in Alzheimer's Disease?

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### Abstract

Mild behavioral impairment (MBI) is associated with cognitive deficits and has been proposed as a risk factor and an early manifestation of dementia. Neuropsychiatric symptoms (NPS) have been frequently described in Parkinson's disease (PD), even in the earliest stages of the disease. These cognitive and behavioral symptoms are so common that it may occur even in the prodromal stages of the disease, worsen with disease progression and surpass motor symptoms as the major factors affecting patient quality of life and caregiver burden. Understanding the longitudinal course of MBI and finding markers or construct to predict cognitive decline in Parkinson's disease (PD), are our priorities. Mild behavioral impairment checklist (MBI-C) can be one such questionnaire which can solve this puzzle predicting conversion from MCI to dementia in PD.

**Keywords:** Mild Behavioral Impairment; Neuropsychiatric Symptoms; MBI-C; Cognition; Dementia; Risk Factor

### Introduction

It is firmly believed now that neuropsychiatric symptoms (NPS) in older adults are the earliest markers of progression of cognitive decline in community and clinical settings [1]. The presence of these deficits impedes activities of daily living and responsible for patient and caregiver burden [2]. NPS are common in dementia and are recognized as core to the dementia process by the National Institute on Aging-Alzheimer's Association, NPS NIA-AA core criteria for all-cause of dementia are described as "changes in personality, behavior, or symptoms that include: uncharacteristic mood fluctuations such as agitation, impaired motivation, impaired initiative, apathy, loss of drive, social withdrawal, decreased interest in previous activities, loss of empathy, compulsive or obsessive behaviors, social unacceptable behaviors [3]. In mild cognitive impairment (MCI), those NPS have been more characterized and the presence of apathy, depression, agitation, delusions, hallucinations and sleep disorders has been associated with an increased risk of progression to dementia. In dementia, NPS occur in 80 - 90% of patients during the clinical course of the disease and fluctuate over time [4-6].

Taragano and Allegri proposed the existence of a syndrome named "Mild Behavioral Impairment" (MBI). MBI defines a late life syndrome with prominent psychiatric and related behavioral symptoms in the absence of major cognitive symptoms [7] and it is associated with a greater and faster progression to dementia [8]. A first scale to measure MBI symptoms has been published in 2017, widely known as MBI-C [9]. Since then researchers believed that this scale can also be used in PD patients but very recently Yoon., *et al.* showed MBI is linked to worse cognition and brain atrophy in PD [10].

NPS are frequently encountered non motor symptoms in PD, which can be present in drug naïve or early untreated prodromal phase. These symptoms are very common in PD-mild cognitive impairment (PD-MCI) and PD dementia (PDD) [11-14]. Yoon., *et al.* found significant

group differences in global and domain-specific cognitive function. The PD-MBI group had significantly lower MoCA and z scores in all 5 domains and the global score compared to healthy controls and those with PD-no MBI. Within the PD-MCI group, the overall distribution of MCI subtypes was similar between the PD-MBI and PD-noMBI groups. Amnestic, multiple-domain impairment was the most common subtype of MCI in both groups. They also reported patients with PD-MBI had cortical thinning and reduced cortical volume and surface area compared to those with PD-noMBI and healthy controls. The right middle temporal cortex showed thinning and decreased volume in the PD-MBI group compared with the PD-no MBI group. Thinning in the left parahippocampal cortex, decreased volume and surface area in the right precuneus, and decreased volume in the right lingual cortex and lateral frontal pole was found in patients with PD-MBI when compared to healthy controls. These microstructural cortical changes were not found in PD no MBI group. The PD-noMBI group showed decreased volume and area in the right superior parietal cortex and decreased area in the left inferior parietal cortex compared to healthy controls. Both PD-MBI and PD-noMBI groups revealed reduced volume of the left inferior parietal cortex compared to healthy controls. They also reported the proportion with MCI was significantly higher in the PD-MBI group than the PD-noMBI group [10].

Executive dysfunction in patients with PD with NPS has been reported previously but not with too much details [15]. Total Neuropsychiatric Inventory Questionnaire (NPI-Q) scores correlated with executive dysfunction in patients with PD without dementia [16]. Frontostriatal dysfunction in PD is common in early disease which can be attributed to decline in executive function [17]. Multiple NPS are associated with overall cognitive impairment in multiple domains, not only executive function, and that the MBI-C is a useful instrument to evaluate the elevated global NPS in PD. Kehagia, *et al.* previously reported the posterior cortical profile of the dual syndrome hypothesis of cognitive decline in PD, which has been associated with faster cognitive decline compared with the dopamine-sensitive frontostriatal profile [19] further in line with the findings of Yoon, *et al* [10].

## Discussion

Both NPI-Q and MBI-C has been used by researchers but the major importance and development of MBI-C was to specifically capture emergent and sustained NPS and behavioral changes in individuals without dementia as a dementia risk marker [9] as compared to NPI which was used to find NPS in a demented population [19]. NPI-Q and MBI-C both measure different things and different stage of disease.

Neuropsychiatric symptoms (NPS) are frequent in dementia and MCI amounting to worse prognosis [20,21]. NPS have been frequently described in Parkinson's disease (PD) even in the early, untreated phases of the disease, being associated with a reduced quality of life and advanced disease [22,23]. Nearly 90% of patients with PD dementia had at least one NPS, with depression, apathy, anxiety, and hallucinations being the most prevalent symptoms [22].

The presence of MBI without cognitive impairment determines a higher risk of conversion to dementia than the presence of MCI without psychiatric complaints [8,24]. Baschi, *et al.* in their PACOS study reported 5 findings a) the frequency of MBI was 84.1% throughout the whole sample of PD and 36.1% in newly diagnosed patients b) Affective dysregulation and decreased motivation were in decreasing order the most frequent domains, while impulse dyscontrol was significantly more prevalent in PD-MBI with a disease duration > 1 year, compared to newly diagnosed PD-MBI c) MBI showed a tendency to increase with disease progression, particularly for social inappropriateness and abnormal perception d) when compared to PD without MBI, the presence of MBI in newly diagnosed patients was significantly associated with motor disability and antidepressant treatment, while in patients with a disease duration > 1 year PD MBI was associated with motor impairment e) no association of MCI with MBI, also after stratifying by disease duration [25].

## Conclusion

Behavioral impairment in PD is probably linked to motor progression and disability, in the absence of a significant relationship with MCI. MBI in PD patient is quite frequent. So early diagnosis and characterization is of utmost importance and implementation of

appropriate therapeutic strategy is mandatory. MBI in late phase of the disease is easy to diagnose however in early stage of the disease, more use of MBI-C rather than NPI-Q in large prospective cohorts and randomized control trials will open a new door of research and will clear the role of MBI in predicting conversion from MCI to dementia in PD.

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