Review Article

Neuroimaging and neuropsychological performance in Parkinson's disease patients with mild cognitive impairment: a systematic review

ABSTRACT

Introduction: One of the most common non motor symptoms of Parkinson's disease (PD) is cognitive decline. Scientific evidence has demonstrated that patients with PD experience rapid cognitive decline in multiple cognitive domains, specifically executive functions, attention, visuospatial, language and memory. However, the extent of cognitive decline with its correlation to brain regions on neuroimaging have not been reviewed extensively in the literature.

Objective: The objective of this review is to summarize the existing literature that explores cognitive performance in patients with PD with mild cognitive impairment (MCI) using different neuroimaging techniques.

Methods: A comprehensive search was conducted on PubMed and Web of Science databases. This review is focused on articles that explored neuroimaging and neuropsychological performance in patients with Parkinson's disease. We screened articles and excluded those that did not fit the criteria of this study.

Results: Overall, PD-MCI patients experienced more cognitive decline than PD patients without MCI. Global cognitive ability was associated with frontal lobe, basal ganglia, para-hippocampal gyrus, occipital lobe, and the cerebellum. In addition, some specific cognitive domains were associated with specific brain regions. Attention and executive functions were associated with insula network and the parietal and frontal regions. Learning and memory were associated with

grey matter atrophy and right cingulate gyrus and the limbic lobe. Language was associated with frontal cortex, precuneus, and anterior cingulate gyrus. Visuospatial ability was associated with Salience network (SN) and White Matter Hyperintensity (WMH).

Conclusion: This review of the literature showed that PD-MCI patients display different cognitive impairment as well as different neuroanatomical changes when compared to PD-Normal Cognition (NC). These findings may suggest that cognitive impairment in PD-MCI patients require different clinical treatment and care. This review also can have diagnostic and treatment implications for this group of patients.

Keyword: Parkinson's disease, Neuroimaging, Cognition, Executive function, attention, memory.

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disease, which is characterized as a movement disorder. The global of neurological diseases reported that the incidence and prevalence of PD has increased worldwide (Chou, et al., 2011; Bloem, 2021). It has been characterized as the fastest growing neurological condition worldwide (Chou, et al., 2011; de Paula Brandão, et al., 2019). One of the most common symptoms of PD is cognitive decline (Aarsland, et al., 2017; Christine, et al., 2020; Pedro Renato de Paula Brandão, et al., 2019; Stuart, et a., 2019). Scientific evidence has demonstrated that patients with PD experience rapid cognitive decline in multiple cognitive domains, specifically executive functions, attention, visuospatial, language and memory (Aarsland, et al., 2017; de Paula Brandão, et al., 2019; Segura, et al., 2014). Moreover, Mild Cognitive Impairment (MCI) is identified in 40% of newly diagnosed PD patients (Christine, et al., 2020; Pedro Renato de Paula Brandão, et al., 2019).

Some studies have investigated cognitive performance in PD using different neuroimaging techniques. A magnetic resonance imaging (MRI) study investigating cognitive decline in PD concluded that patient with PD and mild cognitive impairment (PD-MCI), have cortical thinning in the parietotemporal regions, global atrophy, and cognitive decline in memory, executive, visuospatial and visouperceptual domains (Segura, et al., 2014). Whereas a study using positron emission tomography (PET) scan to investigate cognitive decline in patient with PD has identified impairments in cognitive domains related to memory (in the hippocampus) and attention (in the prefrontal cortex) (Firbank, et al., 2017). Another MRI study found cognitive impairment in domains of memory and executive functions (located in the hippocampus and the frontal lobe) (Foo, et al., 2017).

Neuroimaging and neuropsychological assessment have helped associate specific brain regions with cognitive decline. However, due to the different methods of selection of participants and the variety of criteria inclusions and exclusions, results of prior studies showed discrepancy. To our knowledge, there are only three review articles up to date that explored neuroimaging correlation to cognitive decline in patients with PD. The first is a meta-analysis that was focused exclusively on functional imaging and executive functions in PD, which concluded that there is a lack of evidence in the literature to associate specific neural pathways with executive dysfunction in patients with PD (Ibarretxe-Bilbao, et al., 2011). The second literature review explored the brain correlations relating to cognitive dysfunction in patients with PD; however, it focused only on one type of neuroimaging, which is structural MRI technique (Akhtar et al., 2017). The aforementioned study concluded that there is evidence of structural changes detected by MRI associated with cognitive decline in patients with PD (Akhtar et al., 2017). The third literature review focused only on the correlation between the hippocampal and episodic memory (Pourziinal et al., 2021). All review articles did not take into consideration the stages of PD, the cognitive status of the participants, and the presence of neuropsychiatric symptoms. The exclusion of neuropsychiatric symptoms is crucial as previous studies found evidence supporting the role of neuropsychiatric symptoms to the cognitive decline experienced by patients with PD (Costa, et al., 2006; Drijgers, et al., 2010; Dujardin, et al., 2009; Fernandez, et al., 2009; Isella, et al., 2002; Morgante, et al., 2012; Oguru, et al., 2010; Santangelo, Vitale, Trojano, Longo, et al., 2009).

The objective of this study is to summarize the existing literature that explores cognitive performance in patients with PD using different neuroimaging techniques, aiming specifically to

identify if there are common specific brain regions associated with cognitive performance in early stages of PD with MCI without neuropsychiatric symptoms.

Methods:

A comprehensive search was conducted on PubMed and Web of Science databases. The search was aimed at finding articles that explored neuroimaging and neuropsychological performance in patients with Parkinson's disease. The key terms used in this search were: Parkinson's disease, Memory, Cognition, Executive function, Abstract reasoning, Cognitive performance, Learning and attention, Visual-construction, Language, Neuroimaging, Voxel-Based Morphometry (VBM), Positron Emission Tomography (PET), Single-Photon Emission Computed Tomography (SPECT), Magnetic Resonance Imaging (MRI) and functional MRI. The search includes articles until September, 2021. No time span was specified during the search. The initial search identified 4087 titles and abstracts, 3003 of them were duplicates, and 905 were excluded according to the inclusion and exclusion criteria. The full text of the remaining articles, 179 were retrieved. Based on the inclusion and exclusion criteria, 13 articles remained. Exclusion criteria was as follows: (1) review articles, (2) no neuropsychological assessment, (3) neuropsychiatric symptoms, (4) non English language studies, (5) reports published only in abstract format (6) participants with other neurological conditions, (7) case reports (8) moderate and severe Parkinson's patients (9) non-MCI (see Fig. 1). A total of 13 articles have met our inclusion criteria which included a sample of participants with Early Parkinson's Disease, used neuropsychological assessment and linked it with the used neuroimaging techniques and focused on cognition.

Results:

Thirteen studies were eligible after applying the review criteria, published between 2014 and 2021. All of them included patients with mild Parkinson's disease and mild cognitive impairment and were without neuropsychiatric symptoms. Nine studies used MRI, two study used fMRI and two studies used PET scan. Studies used various neuropsychological assessment tools, and almost all measured global cognitive ability except for one. Other cognitive domains were measured such as, attention, executive function, learning and memory, language and visuospatial abilities. Below is a summary of the results based on cognitive domains.

Global Cognitive Ability:

Global cognitive ability was measured in most of the articles reviewed except for one. Overall, patients with PD and MCI demonstrated a decrease in their global cognitions compared to patients with PD without MCI (Aracil-Bolaños, et al., 2019; Firbank, et al., 2017; Foo, et al., 2017; Gao, et al., 2017; Peraza, et al., 2017; Schneider, et al., 2017; Wang, Qingguang, et al., 2021). Research (Aracil-Bolaños, et al., 2019) found that changes in the Salience network (SN) hub correlated with impairment in global cognitive function. Whereas, another study (Gao et al., 2017), found that PD-MCI group displayed lower grey matter regions that correlated with Montreal Cognitive Assessment (MoCA) score (mainly non-memory related) including the frontal lobe, basal ganglia, parahippocampal gyrus, occipital lobe, and the cerebellum.

On the other hand, other research group (Akhtar et al., 2017) have found no significant difference between patients with PD-MCI and PD-NC on measures of global cognitions. However, they found that PD-MCI have higher Aβ amyloids in the anterior cingulate than PD

patients with normal cognition. They concluded that global measures are insensitive to Aβ amyloids in patients with PD.

Another study (Schneider et al., 2017) reported that PD-MCI group performed significantly worse on measures of global cognitive ability. Moreover, study (Firbank et al., 2017) also found that PD-MCI group performed worse on measures of global cognition than the patients with PD and without MCI.

Furthermore, a study (Firbank et al., 2017) reported that PD-MCI group had greater motor severity and fewer years of education than patient with PD-without MCI. Whereas Huang et al. noted that PD patients with MCI were noticeably older than PD with normal cognition (Huang et al., 2020).

Overall, changes in the Salience network hub (Aracil-Bolaños et al., 2019), lower grey matter in the frontal lobe, basal ganglia, parahippocampal gyrus, occipital lobe, and cerebellum correlated with decline in global cognitive abilities (Akhtar et al., 2017; Firbank et al., 2017; Gao et al., 2017).

Executive function and attention:

Previous articles (Foo et al., 2017; Nagano-Saito et al., 2014; Segura et al., 2014; Wang, Qingguang, et al., 2021) have found significant cognitive impairment in executive functions in the PD-MCI group in comparison to PD without MCI. On the other hand, a research paper (Nagano-Saito et al., 2014) demonstrated lower performance in PD-MCI patients than in PD-NC on tasks of planning. It is reported that (Park et al., 2019) that PD-MCI converters showed severe cognitive deficits in the attention domain. A study done by Schneider et al. (Schneider et al., 2017) found that PD-MCI group performed significantly worse on assessments of executive

functions and attention. A study by Firbank et al. also found that PD-MCI group performed worse on measures of attention and executive function than the patient with PD and without MCI (Firbank et al., 2017).

Moreover, Peraza and his group (Peraza et al., 2017) investigated intra and inter-connectivity in in early PD and PD-MCI using fMRI and found differences in the insula network in comparison to PD-NC. The insula network is especially important for orienting attention. One study (Garcia-Diaz et al., 2018) reported an interesting pattern. They found that the stroop colors test significantly correlates with left superior parietal and frontal regions in PD-NC patients; however, a clear pattern of such was not observed in PD-MCI patients. Instead, they observed a widespread pattern in the anterior and posterior regions that correlates with Trail Making Test Part A (TMT-A) and Stroop Color Test.

Additionally, a paper by Huang et al. investigated periventricular White Matter Hyperintensity (WMH) in early PD patients in association to cognitive decline. The study found that WMH burden was significantly associated with PD-MCI, which is also associated with worse executive function and visuospatial function (Huang et al., 2020). Aracil-Bolaños et al. found that changes in the Salience network (SN) hub correlated with impairment in executive function tasks (Aracil-Bolaños et al., 2019).

Learning and memory:

The study by Nagano-Saito et al. found that PD-MCI patients performed worse on measures of learning than PD non-MCI patients (Nagano-Saito et al., 2014). They also found that hippocampal activity is correlated with memory scores. Several studies have reported a lower

performance in PD-MCI patients. Specifically, Schneider et al. found that PD-MCI group had lower performance in relation to memory related assessments (Schneider et al., 2017). As well as, Firbank et al. found that PD-MCI group performed worse on measures of memory than the patient with PD and without MCI (Firbank et al., 2017).

Foo et al. and Segura et al. reported significant cognitive impairment in memory among the PD-MCI group in comparison to PD without MCI (Foo et al., 2017; Segura et al., 2014). Moreover, Gao et al. found that grey matter atrophy was correlated with lower score on the Mini Mental State Examination (MMSE) especially in memory related questions, including the right cingulate gyrus and the limbic lobe (Gao et al., 2017). It is reported that, higher brain connectivity was linked to a better episodic memory (Wang, Qingguang, et al., 2021).

Language:

One study showed that PD MCI patients had lower performance on measures of language than the PD non-MCI patients (Nagano-Saito et al., 2014). Akhtar et al. reported that Aβ amyloid in the frontal cortex, precuneus, and anterior cingulate gyrus correlate with language performance. Moreover, memory and naming in MCI depends on regional Aβ amyloids (Akhtar et al., 2017). A study reported that PD-MCI group performed significantly worse in all the neuropsychological assessments except for Bosting naming test (Schneider et al., 2017). Another article also reported that PD-MCI group performed worse on measures of language than the patients with PD and without MCI (Firbank et al., 2017).

Visuospatial Ability:

Segura et al. found significant cognitive impairment in visuospatial and visuoperceptual domains in the PD-MCI group in comparison to PD without MCI (Segura et al., 2014). Another study found that PD-MCI group performed significantly worse on tasks measuring visuospatial ability (Schneider et al., 2017).

Aracil-Bolaños et al. found that changes in the Salience network (SN) hub correlated with impairment in visuospatial tasks (Aracil-Bolaños et al., 2019), whereas, Huang et al. investigated periventricular White Matter Hyperintensity (WMH) in early PD patients in association to cognitive decline (Huang et al., 2020). The study found that WMH burden was significantly associated with PD-MCI, which is also associated with worse visuospatial function.

Neuroimaging outcomes (comparison between PD-MCI and PD without MCI)

A study found that older age is associated with thinner cortex in various brain regions, especially in the frontal and temporal cortex bilaterally. They concluded that overall, cortical thickness did not differ between PD-NC and PD-MCI. However, the hippocampal volume is smaller in PD-MCI (Schneider et al., 2017). On the other hand, another study showed that PD-NC patients and PD-MCI differed significantly in the progression of cortical thinning in posterior regions, where PD-MCI patients showed significantly greater cortical thinning in left lateral occipital and inferior parietal regions, and in right medial temporal regions (Garcia-Diaz et al., 2018). Moreover, Segura et al. have found that patients with MCI displayed regional cortical thinning in parietotemporal regions, increased global atrophy: global cortical thinning, gray matter reduction, and ventricular enlargement (Segura et al., 2014). A study showed that PD-MCI group demonstrated thalamus atrophy and progressive atrophy in the thalamus, caudate nucleus, hippocampal atrophy, and presubiculum atrophy (Foo et al., 2017).

Another group of researchers argued that PD-MCI group displayed significantly less gray matter in the bilateral precuneus and the posterior cingulate cortex than patients with PD-NC (Aracil-Bolaños et al., 2019). Moreover, increasement in gray matter was not observed in the PD-MCI group compared to PD-NC. Furthermore, a study found that PD-MCI patients displayed grey matter atrophy in the frontal lobe, limbic lobe, basal ganglia and cerebellum (Gao et al., 2017). When compared to the PD-NC patients, patient with PD-MCI displayed grey matter atrophy in the left side middle temporal gyrus, inferior temporal gyrus and frontal lobe.

Akhtar et al. reported that the overall Aβ amyloid value did not significantly differ between PD-NC and PD-MCI (Akhtar et al., 2017). However, there were regional difference between the groups. Hence, PD-MCI patients demonstrated Aβ amyloid in the posterior Cingulate more the PD-NC. While, Firbank et al. pointed that patient with PD-MCI, had reduced metabolism in the inferior parietal and posterior temporal regions (Firbank et al., 2017). And have not found any other difference in any region between the PD-MCI and PD-NC. Furthermore, Park et al. discussed that examining visible perivascular space (PVS) in the basal ganglia region can be a predictor of cognitive decline in PD-MCI patients, they also found lower scores of MMSE to be a predictor of cognitive decline (Park et al., 2019). Another paper reported that patients with MCI have reduced activity in the cognitive corticostriatal loop, which includes the caudate nucleus and prefrontal cortex. However, patients without MCI did not exhibit such pattern. Instead, Patients without MCI demonstrated a pattern similar to healthy participants (Nagano-Saito et al., 2014).

Discussion

Most of the articles in this review reported difference in cognitive domains in PD-MCI patients in comparison to PD-NC patients. A pattern of lower education and older age was observed in PD-MCI patients. Overall, global cognitive ability was associated with frontal lobe, basal ganglia, parahippocampal gyrus, occipital lobe and the cerebellum. In addition, some specific brain regions were associated with specific cognitive domains. Attention and executive functions were associated with insula network and the parietal and frontal regions. Learning and memory were associated with grey matter atrophy and right cingulate gyrus and the limbic lobe. Language was associated with frontal cortex, precuneus and anterior cingulate gyrus. Visuospatial ability was associated with SN and WMH.

This review attempted to establish a rigorous criterion to exclude any confounding variables that may influence cognitive decline. The purpose of this excluding criteria to investigate the cognitive domains pattern in PD-MCI in comparison to PD-NC.

The strengths of this study include rigorous criterion to exclude confounding variables such psychiatric illnesses which was not taken into consideration in previous literature reviews (Giehl, et a., 2019; Ibarretxe-Bilbao, et al., 2011). We also defined “early stage” and only included articles that examined PD in early stages in comparison to cognitive functions. Furthermore, we included all neuroimaging techniques to have broad picture about the brain areas that may contribute to cognitive performance in this group of patients.

We acknowledge some limitations to our study. It has the drawbacks of conducting systematic reviews and its dependence on the quality of the studies reviewed. We have not looked for on or off state of dopaminergic medications.

In conclusion, our findings indicate that PD-MCI patients display different cognitive impairment, as well as, different neuroanatomical changes when compared to PD-NC. These findings suggest that cognitive impairment in PD-MCI patients requires different clinical treatment and care. This review also can have diagnostic and treatment implications for this group of patients. Providing an understanding of the extent of cognitive decline in early stages of PD as well as an earlier picture of the nature of this disease.

ETHICAL STANDAEDS

This project was approved by the Institutional Review Board of the Research Center, King Fahad Medical City, Riyadh, Saudi Arabia.

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Tables and figures:

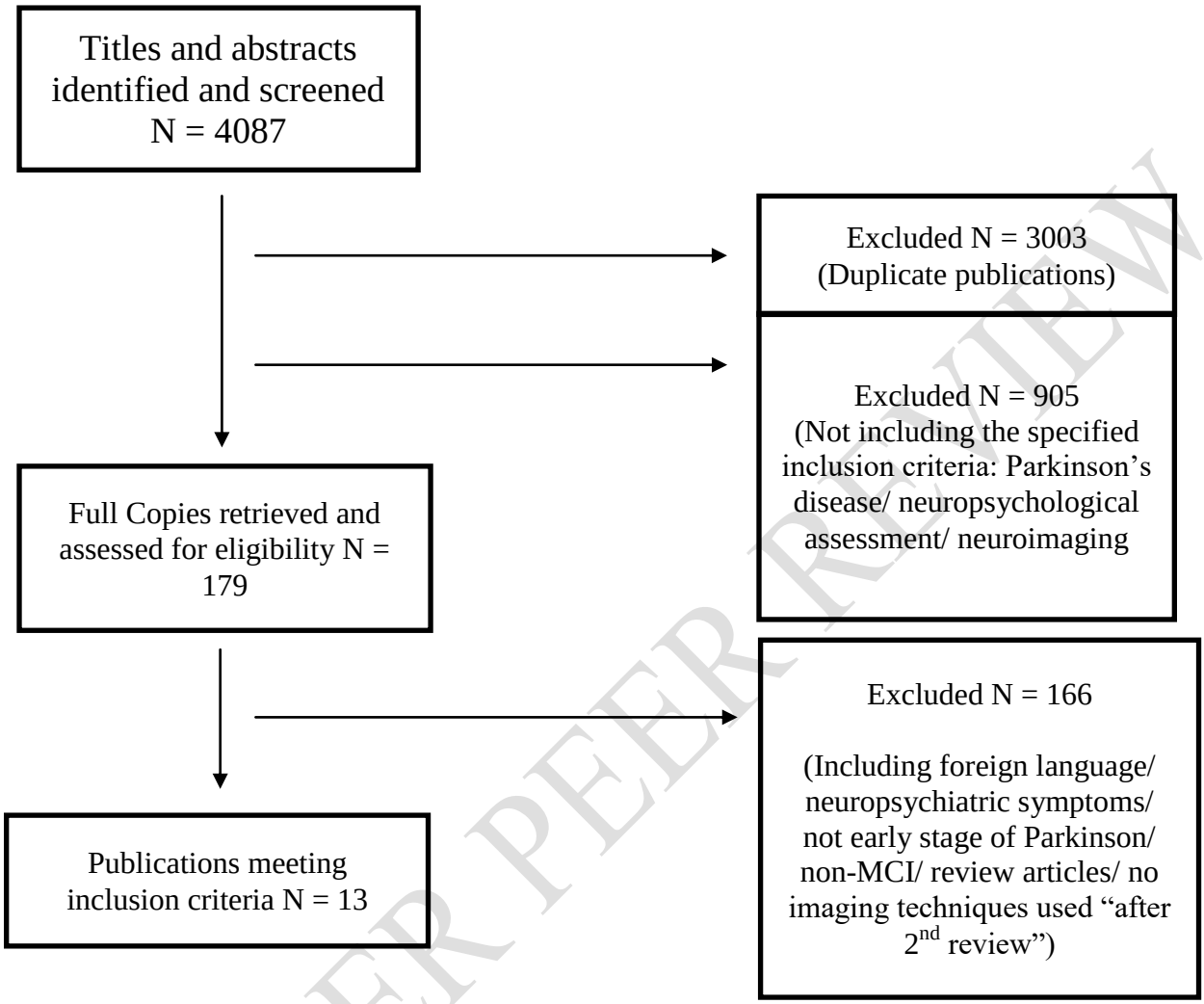

Fig. 1. Flow chart of the study selection process

Table 1. Summary of reviewed articles

Study	# Participants		Age [years]	Cognitive Domains Studied	Neuropsychological Tests	Imaging Technique	Results
Nagano-Saito, Atsuko, et al., 2014	33	PD patients without MCI = 19 PD patients with MCI = 14	SD, 61.0 5.3 years	Global cognitive ability, executive function and attention, learning and memory, language, and visuospatial ability.	MoCA, DST, TMT/B, SCWT, TOL, BSAT, VFL: orthographic criteria subtest of the protocole MEC, Logical memory subtest of WMS-III, RAVLT, BNT, VFL: semantic criteria subtest of the MEC, Vocabulary subtest of WASI-II, HVOT, Clock-drawing subtest of MoCA, and ROCF/ copy.	fMRI	It was found that the higher the participants (non-MCI) scored on Brixton, the more activity was found in the caudate head and body. As well as, higher scores on (non-MCI) RAVLT correlated with an activity increase in the hippocampus. And, the higher the errors made on WCST (MCI), the less individual activation in the caudate.
Segura, Bàrbara, et al., 2014	122	PD non MCI = 43 PD MCI = 47 HC = 32	60.77 ± 10.51 67.72 ± 9.71 64.69 ± 8.63	Global cognitive ability, executive function and attention, learning and memory, language, and visuospatial ability.	MMSE, TMT, SDMT, DST, SCWT, BNT, SFT, RAVLT, JLO, and VFD.	MRI	PD patients with MCI scored significantly worse than the other two groups on all test except on Digit Span which measures attention and executive functions. They also exhibited a posterior pattern of atrophy shown through a cortical thinning in the bilateral superior parietal and supramarginal regions and in the inferior temporal area, parahippocampal gyrus, fusiform gyrus, and precuneus.
Akhtar, Rizwan S., et al., 2017	61	PD-NC = 42	age at scan time was 67.0 (64.9 to 69.0) years	Global cognitive ability, executive function and attention, learning and memory, language, and visuospatial ability.	DRS-2, BNT, TMT, SDGMT, HVLT-R, IDFR, LNST, VFL, F-A-S, and SFT.	PET	Significant differences between patients with PD-MCI and PD-NC were found on measures of global cognitions. They concluded that global measures are insensitive to AB amyloids in patients with PD. And that AB amyloid in the frontal cortex, precuneus, and

		PD-MCI = 19					anterior cingulate gyrus correlate with language performance, and that memory and naming in MCI depend on regional AB amyloids.
Firbank, Michael J., et al., 2017	99	Control = 20	71.9 (9.7)	Global cognitive ability, executive function and attention, learning and memory, language, and visuospatial ability.	MMSE, MoCA, PRM, SRM, and PAL from CANTAB.	PET	Significant correlation was found in the FDG angular gyrus/cerebellum uptake ratio which predicted both of MMSE and MoCA at 18 months in the PD-MCI group. Significant correlation was also found in the lateral parietotemporal–occipital region.
		PD-NC = 38	72.3 (6.4)				
		PD-MCI = 41	74.2 (4.8)				
Foo, H., et al., 2017	65	PD-NCI = 54	63.39 ± 6.86	Global cognitive ability, executive function and attention, learning and memory, language, and visuospatial ability.	MMSE, MoCA, word-list delayed and recognition recall, CDT, DST, Maze test and constructional praxis and animal fluency.	MRI	Memory performance was significantly correlated with the left thalamus in the PD-MCI group.
		PD-MCI = 11	69.45 ± 10.19				
Gao, Yuyuan, et al., 2017	67	Control = 21	63.76 ± 5.42	Global cognitive ability, executive function and attention, learning and memory, language, and visuospatial ability.	MMSE, MoCA.	MRI/ VBM	MMSE scores were linked to brain structural changes in PD-MCI. This group also suffered from grey matter atrophy in the frontal lobe, limbic lobe, basal ganglia and cerebellum.
		PD-NC = 23	62.35 ± 7.73				
		PD-MCI = 23	65.09 ± 8.71				
Peraza, Luis R., et al., 2017	129	HC = 30	64.05 (7.92)	Global cognitive ability.	MMSE, MoCA, Power of Attention, DVT, PRM, SRM, TOL, ANT, Language total score and PAL.	MRI	SRM variable and cluster FPN-20 had a significant relation, which demonstrated a disconnection between the frontal pole network and the right middle frontal gyrus. There was also a significant positive relation between this inter-network connectivity and PAL.
		PD-NC = 62	62.77 (10.83)				
		PD-MCI = 37	70.40 (9.13)				
Schneider, Christine B., et al., 2017	68	PD = 31	67.7 (7.5)	Executive function and attention, learning and memory, language, and visuospatial ability.	CERAD, Word list learning, Word list recall, Word list recognition, MCST, Categories, Nonperseverative errors, Perseverative errors, VFL, Animal, Words with S, TMT, SCWT, Words, Colors,	MRI	This study suggests accelerated aging-related decline in hippocampal volume for patients with PD-MCI.
		PD-MCI = 32	68.3 (6.8)				

					Interference, LPS subtest 7, LPS subtest 9, CERAD constructional praxis, and BNT.		
Garcia-Diaz, Anna I., et al., 2018	64	HC = 20 PD-NC = 28 PD-MCI = 16	65.50 ± 8.00 59.50 ± 9.58 64.63 ± 9.67	Global cognitive ability and visuospatial ability.	PCT, JLOT, VFDT, FRT, and SDMT.	MRI	They found that the stroop colors test significantly correlates with left superior parietal and frontal regions in PD-NC patients; however, a clear pattern of such was not observed in PD-MCI patients. Instead, in the PD-MCI group they observed a widespread pattern in the anterior and posterior regions that correlates with TMT-A and stroop colors test.
Aracil-Bolaños, Ignacio, et al., 2019	53	PD-NC = 34 PD-MCI = 19	65.8 ± 6.7 73 ± 4.5	Global cognitive ability, executive function and attention, learning and memory, language, and visuospatial ability.	TMT/B, ROCFT, VOSP; number location, BNT and Token Test, and FCSRTR.	MRI	They found that changes in the Salience network (SN) hub correlated with impairment in global cognitive ability, executive function, and visuospatial tasks. (in which group?)
Park, Yae Won, et al., 2019	271	PD-IC (intact cognition) = 106 PD-MCI = 165		Global cognitive ability, executive function and attention, learning and memory, language, and visuospatial ability.	MMSE and SNSB.	MRI	Results showed that PD-MCI converters showed severe cognitive deficits in the attention domain.

Huang, X., et al., 2020	175	PD-MCI = 94	52 (55.3%)	Global cognitive ability, executive function and attention, learning and memory, language, and visuospatial ability.	ADAS, ROCF, JLO, WAIS-IV, DST, WMS- IV; symbol span, BNT, WAIS-IV similarities, Fruit Fluency and FAB.	MRI	Study found that periventricular and deep-subcortical WMH (White Matter Hyperintensity) burden was significantly associated with PD-MCI, which is also associated with worse executive function and visuospatial function. There are significant differences between patient with PD-MCI and NC-PD in total brain WMH and periventricular WMH.
		PD-NC = 81	47 (58.0%)				
Wang, Qingguang, et al., 2021	46	HC = 13	70.2±7.1	Global cognitive ability, episodic memory, visuospatial function, information processing speed and executive function.	MMSE, AVALT, ROCF, TMT A&B, VFT, DSST, and CDT.	fMRI	It was found that PD-MCI performed significantly worse on global cognition, episodic memory, visuospatial function, information processing speed, and executive function. Compared with the HCs, PD-NC and PD-MCI showed significantly decreased Functional Connectivity within bilateral precuneus (BPcu).
		PD-NC = 13	70.4±6.4				
		PD-MCI = 20	72.6±6.1				

Key: MMSE: Mini Mental Status Examination; TMT: Trail Making Test; SDMT: Symbol Digit Modalities Test; DST: Digit Span Test; SCWT: Stroop Color and Word Test; BNT: Boston Naming Test; JLO: Benton's Judgement of Line Orientation; VFD: Visual Form Discrimination Tests; DRS-2: The Dementia Rating Scale-2; SDGMT: Symbol-Digit Modalities Test; HVLT-R: Hopkins Verbal Learning Test-R; IDFR: Immediate & delayed free recall; LNST: Letter-Number Sequencing Test; VFL: Verbal Fluency; F-A-S: The F-A-S Test assesses phonemic verbal fluency by requesting an individual to orally produce words that begin with the letters F, A and S; SFT: Semantic Fluency Test; MoCA: The Montreal Cognitive Assessment; TOL: Tower of London; BSAT: Brixton Spatial Anticipation Test; VFL: Verbal fluency test orthographic criteria subtest of the protocol MEC; WMS-III: Wechsler Memory Scale; RAVLT: Rey Auditory Verbal Learning Test; BNT: Boston Naming Test; VFL: Verbal fluency: semantic criteria subtest of the MEC; WASI-II: Vocabulary subtest of the Wechsler Abbreviated Scale of Intelligence; HVOT: Hooper Visual Organization; ROCF: Rey-Osterrieth figure copy; PRM: Pattern Recognition Memory; SRM: Spatial Recognition Memory; PAL: Paired Associates Learning from (CANTAB); CANTAB: Cambridge Neuropsychological Test Automated Battery; CDT: 10-point clock drawing and frontal assessment battery; DVT: Digit Vigilance Accuracy; ANT: Animal naming; CERAD: Consortium to Establish a Registry for Alzheimer's Disease; MCST: Modified card sorting test; PCT: Pentagon Copying Test; JLOT: Judgment of Line Orientation Test; VFDT: Visual Form Discrimination Test; FRT: Facial Recognition Test; SDMT: Symbol Digit Modalities Test; VOSP: Visual Object and Space Perception Battery; FCSRTR: Free and Cued Selective Reminding Test; SNSB: Seoul Neuropsychological Screening Battery; ADAS: Alzheimer's Disease Assessment Scale; WAIS-IV: Wechsler Adult Intelligence Scale-

Fourth Edition; WMS- IV: Wechsler Memory Scale-Fourth Edition; FAB: Frontal Assessment Battery. WMH: White Matter Hyperintensity; AVLT: Auditory Verbal Learning Test; DSST: Digital Symbol Substitution Test; CDT; Clock Drawing Test.