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Relation between Parkinson's Disease Severity and Cognitive Function with Monstreal Cognitive Assessment Indonesia

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ABSTRACT

Introduction: Parkinson disease is a wide-spectrum disease that can be accompanied by motor and non-motor symptoms. Non-motor symtoms can occurred before the existance of motoric symptoms until the terimal stage of the disease, where cognitive disturbance is one of the non-motor symptoms that can decrease patient's quality of life and increase patient's disability. Therefore, early detection of the cognitive function is important for patients with parkinson disease. The aim of this study was to find the association between the severity of Parkinson's disease and cognitive disturbance using the Montreal Cognitive Assesment Indonesian version (MoCA-Ina)

Method: This study used cross-sectional design. The research subject was a parkinson disease patients' who went to Neurology Clinic at Haji Adam Malik General Hospital Medan and network hospital who met the inclusion and exclusion criteria of the study. The number of sample was 39 subjects. To determine the relationship between the severity of parkinson disease and cognitive function, the Gamma test was used.

Results: There was a significant correlation between the severity of Parkinson's disease and cognitive function (p = 0.001, r = -0.858). There was a very strong correlation between the severity of Parkinson's disease and cognitive function, and the negative correlation means the higher the severity of disease, the lower the cognitive function. From this study, the most correlated domains were delayed memory, naming (r = 0.962), orientation (r = -0.944), visuospatial (r = -0.929), abstraction (r = -0.874), language (r = -0.674), attention (r = -0.592). Delayed memory could not be statistically analyzed because delayed memory were all impaired in all subjects.

Conclusion: There was a correlation between the severity of Parkinson's disease and cognitive function with a very strong correlation strength. The cognitive function domains that correlate strongly with Parkinson's severity were delayed memory, naming, orientation, visuospatial and abstraction.

Keywords

Parkinson disease, Cognitive function, Moca-Ina

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INTRODUCTION

Parkinson's disease (PP) is a chronic progressive neurodegenerative disorder that affects older and elderly adults.[1] The prevalence of Parkinson's Disease is reported to be around 1% in people over 60 years of age and increases to 1%-3% in the age group over 60 years.[2] The incidence of the disease increases with age and reaches 93.1 (per 100,000 person-years) in the age group between 70 and 79 years.[3]

As many as 20-30% of Parkinson's Disease patients have cognitive deficits in the form of Mild Cognitive Impairment (MCI), which is a condition that is very important to detect because it is associated with an

increased risk of progression to dementia.[4] The full spectrum of cognitive impairment occurs in individuals with Parkinson's Disease, from subjective cognitive decline (SCD) and mild cognitive impairment (MDI) to dementia (PDD).[5]

As many as 20-30% of Parkinson's disease patients have cognitive deficits in the form of Mild Cognitive Impairment (MCI), which is a condition that is very important to detect because it is associated with an increased risk of progression to dementia.[4] The full spectrum of cognitive impairment occurs in individuals with Parkinson's Disease, from subjective cognitive decline (SCD) and mild cognitive impairment (PD-MCI) to dementia (PDD).[5] Parkinson's disease has a 2.5-6 times higher risk of developing dementia than people without Parkinson's Disease of the same age.2 Cognitive deficits are common in Parkinson's Disease even in its early stages and more than 75% of Parkinson's Disease patients develop dementia (PDD).[6] Mild Cognitive Impairment (MCI) is found in approximately 27% of non-dementia Parkinson's Disease (PD-MCI) patients, and approximately 30% of Parkinson's Disease patients have PDD.[7] The prevalence of Parkinson's Disease with dementia (PDD) was found to be 20% at 5 years after onset, and increased to 45% after 15 years and 83% after 20 years.[8]

The Tarukbua study showed the results of MoCA-Ina examination in Parkinson's patients with normal cognitive function as much as 13%, mild cognitive function impairment 39% and moderate cognitive function decline 48%. Nazem et al. showed that more than half of the subjects rated normal by MMSE had cognitive impairment on MoCA-INA scores.[9] Disease severity significantly contributed to Parkinson's Disease patients' cognitive impairment scores with $p < .001$ and r2 of 52.8%. [10] Hanum's study showed that worsening motor impairment can increase the incidence of cognitive impairment in Parkinson's disease patients. Cognitive impairment was found in 19 people (63%) with the most commonly impaired cognitive domains being memory, language and abstraction. The results of bivariate analysis obtained a value of $p = 0.014$ ($p < 0.05$) so that a significant relationship was obtained between the degree of Parkinson's disease and impaired cognitive function using MoCA-Ina.[11] Most cases of dementia are found with abnormal MoCA scores.

METHOD

This study is an observational analytical study with a cross sectional design to assess the relationship between the degree of Parkinson's disease and impaired cognitive function using the MOCA-Ina Instrument in Outpatients at RSUP HAM Medan and Network Hospital.

This research was conducted at the Outpatient Installation of H. Adam Malik Medan Central General Hospital and Network Hospital starting from September 2022 to March 2023. The subjects of the study were taken from patients who had been diagnosed with Parkinson's disease based on history, physical examination and neurological examination established based on Hughes criteria or Koller criteria or UKPD (United Kingdom Parkinson's Disease) Society Bank's Clinical Criteria for Probable Parkinson's Disease. Sample collection is carried out by consecutive sampling technique.

The inclusion criteria of this study are all Parkinson's disease patients who seek treatment at the Neurology polyclinic Haji Adam Malik Medan Hospital and Networking Hospital, patients who are willing to participate and sign informed consent in this study. Patients with secondary parkinsonism, dementia, impaired consciousness, or psychiatric disorders were excluded from the study.

MoCA testing has been reported to show high sensitivity and specificity for detecting mild cognitive impairment (MCI) in the adult population. This is a short bedside test and takes about 10 minutes. MoCA evaluates executive function, memory and attention, visuospatial function, naming, language, abstraction, and orientation. The maximum score is 30 points, and a threshold of 25 or lower indicates cognitive impairment.

The data were analyzed descriptively to see the frequency distribution of research subjects based on the characteristics of the research sample. Before bivariate analysis was carried out to assess the relationship between the degree of Parkinson's disease and impaired cognitive function using the MOCA-Ina Instrument in outpatients of Haji Adam Malik Medan Hospital Medan, and Network Hospital, normality tests were carried out first with the Kolmogorov Smirnov test. Bivariate analysis using the Gamma correlation test.

RESULT

Characteristics of the Research Subject

The average age of subjects who participated in this study was 64.3 years, with an age range of 30-40 years as many as 1 person (2.57%), 51-60 years as many as 13 people (33.3%), 61-70 years as many as 15 people (38.46%), 61-70 years as many as 15 people (38.46%), 71-80 people as many as (17.95%), and 81-90 years as many as 3 people (7.69%). The study subjects were mostly with male gender, namely as many as 29 people (74.36%), and men as many as 10 people (25.64%). The highest level of education is 26 people (66.7%), 8 people from high school (20.5%), and 5 people from junior high school (12.8%).

Table 1. Demographic Characteristic of Research Subject

Demographic Characteristic	Mean ± SD	Total (%)
Age (year)*	64,3 ± 10,7	
30-40 years old		1 (2,5)
41-50 years old		0 (0,0)
51-60 years old		13 (33,3)
61-70 years old		15 (38,4)
71-80 years old		7 (17,9)
81-90 years old		3 (7,6)
Sex		
Male		29 (74,3)
Female		10 (25,6)
Edicaton		
Junior High School		5 (12,8)
Senior High School		8 (20,5)
University		26 (66,7)
Stadium		
Stadium I		5 (12,8)
Stadium II		15 (38,5)
Stadium III		15 (38,5)
Stadium IV		4 (10,2)

* Normal distribution

The characteristics of the Moca-Ina score in the study subjects obtained data were not normally distributed where the data were presented with average data. The average MoCA-Ina score in this study was 21 with a minimum score of 9 and a maximum score of 29

Table 2. Characteristic of MoCA-Ina Score of Research Subject

	Parkinson patients (n=39)
MoCA-Ina Score* Median (Min-Max)	21 (9-29)

* Abnormal Distribution

Characteristics of Parkinson's Patients' Medical Conditions

The highest duration of treatment was under 5 years, which was 23 people (59%), while the duration of treatment over 5 years was 16 people (41%). The most common type of treatment is a combination of levodopa therapy, anticholinergics, and dopamine agonists, which is as many as 20 people (51.3%). Then followed by the use of levodopa with dopamine agonists, which was 9 people (23.1%), then the use of anticholinergics with dopamine agonists as many as 4 people (10.3%). The number of patients who only took levodopa with levodopa along with anticholinergics was the same, which was 3 people (7.7%). Assessment of the severity stage based on Hoehn and Yahr (H & Y) showed that the most stages were stage 2 and 3, amounting to 15 people (38.5%), followed by stage 1 with 5 people (12.8%), and stage 4 with 4 people (10.2%).

Table 3. Medical Condition Characteristic of Research Subject

Medical Condition Characteristic	n (%)
Disease duration	
Below 5 years	23 (59)
Above 5 years	16 (41)
Therapy	
Dopamin	3 (7,7)
Dopamin, Anticholinergic	3 (7,7)
Dopamin, Aminothiazole dopamin-agonist (nonergot)	9 (23,1)
Dopamin, Antimuscarinic, anticholinergic	20 (51,3)
Antimuscarinic, Anticholinergic	4 (10,3)

Cognitive Domain Characteristics of Research Subjects

Based on the characteristics of cognitive function in the research subjects, research subjects were found with disturbances in the visuospatial domain and executive function as many as 24 people (61.5%), naming (naming) as many as 6 people (15.4%), immediate memory as many as 3 people (7.7%), attention as many as 30 people (76.9%), language or verbal as many as 21 people (53.8%), abstraction as many as 8 people (20.5%), delayed memory as many as 39 people (100%), and orientation as many as 9 people (23.1%).

Table 4. Domain Cognitive Characteristic

Domain Cognitive	Parkinson Patient	
	Decline (%)	Normal (%)
Visuospatial	24 (61,5)	15 (38,5)
N*aming*	6 (15,4)	33 (84,6)
Recnt memorry	3 (7,7)	36 (92,3)
Attention	30 (76,9)	9 (23,1)
Language	21 (53,8)	18 (46,2)
Abstraction	8 (20,5)	31 (79,5)
Delayed Memorry	39 (100)	0 (0)
Orientation	9 (23,1)	3 (76,9)

The Relationship of Parkinson's Severity with Cognitive Function

From the results of cognitive function examination with MoCA-Ina, 2 (5.1%) of 5 research subjects in stage 1 who experienced impaired cognitive function, then as many as 5 (12.8%) of 15 research subjects in stage 2 who experienced impaired cognitive function. In stage 3 there were as many as 15 (38.5%) and in stage 4 as many as 4 people (10.3%) who experienced impairment in cognitive function. Based on the *Gamma* statistical test in this study, a significant relationship was obtained between the severity of Parkinson's and cognitive function with a significance value of p = 0.001, which can be interpreted that there is a significant correlation between the degree of severity and cognitive function in Parkinson's patients. Then obtained an r value of -0.858 with a negative correlation direction which means that the value of 0.858 indicates a very strong correlation strength and the higher the degree of disease stage, the smaller the value of cognitive function.

Table 5. The Relationship of Parkinson's Severity with Cognitive Function

Cognitive Function			*p*	*r*
Stadium	Decline	Normal		
Stadium 1	2 (5,1)	3 (7,7)	0,001*	-0,858
Stadium 2	5 (12,8)	10 (25,6)		
Stadium 3	15 (38,5)	0 (0)		
Stadium 4	4(10,3)	0 (0)		

*Gamma

Association of Demographic Characteristics with Medical Conditions With Cognitive Function in Parkinson's Patients

Of the 19 male patients, 19 (48.7%) had impaired cognitive function. Meanwhile, out of 10 female subjects, there were 7 people (17.9%) with impaired cognitive function. The results of the analysis showed no relationship between sex (p = 0.06), age (p = 0.36), ethnicity (0.5), education level (0.8), duration of therapy (0.053), and cognitive function.

In this study, from the group of subjects aged 30-40 years, there was 1 person (2.6%) who experienced impaired cognitive function, in the age group of 50-60 years there were 6 people (15.4%) who experienced impaired cognitive function, while at the age of 60-70 years as many as 10 people (25.6%) who experienced impaired cognitive function, and at the age of 70-80 years and 80-90 years as many as 6 (15.4%) and 3 people (7.7%) who experienced a decline in cognitive function sequentially. In this study, patients with junior high school education level experienced cognitive function impairment as many as 9 people (23.1%). While the study subjects with a higher education level experienced the most cognitive decline function, which was as many as 19 people (43.6%).

Relationship of Parkinson's Severity with Cognitive Function by Moca-Ina Score Domain Visuospatial dan excecutive function

Of the 39 subjects with Parkinson's disease, there was 1 person (2.6%) at stage 1 who had visuospatial disorders. Meanwhile, in stage 2, there were as many as 4 people (10.3%) research subjects who experienced visuospatial disorders. In stage 3, the most visuospatial disorders accounted for, which was 15 people (38.5%). In stage 4, all patients experienced impaired cognitive function, where there were 4 (10.3%) study subjects with visuospatial disorders. The results of the analysis using the *Gamma* test show that there is a significant relationship between degrees Parkinson's severity with visuospatial disturbances and executive function (p = 0.001). Then obtained an r value of -0.929 with a negative correlation direction which means that the value of 0.929 indicates a very strong correlation strength and the strength of the correlation is negative whose sickle the heavier the degree of disease stage, the smaller the visuospatial domain value on cognitive function examination.

Table 6. Relationship between Parkinson Severity with Visuospatial

Stadium	Visuospatial		P	r
	Decline	Normal		
Stadium 1	1 (2,6)	4 (10,3)	0,001*	0,-929
Stadium 2	4 (10,3)	11 (28,2)		
Stadium 3	15 (38,5)	0 (0)		
Stadium 4	4 (10,3)	0 (0)		

* Gamma

Naming

Of the 39 study subjects with Parkinson's disease, there were 6 people (15.4%) who experienced disorders in the visuospatial domain. Where of the 6 people there were as many as 3 people (7.7%) from each stage 3 and stage 4 who experienced naming disorders on the MoCA-Ina cognitive function examination. Based on the results of data analysis using the *Gamma test*, a p-value of 0.003 (<0.05) was obtained, which means that there is a significant relationship between the severity of Parkinson's and cognitive function. Then obtained an r value of -0.962 with a negative correlation direction which means that the value of 0.962 indicates a very strong correlation strength, the correlation strength is negative whose sickle is the higher the degree of disease stage, the smaller the naming domain value on cognitive function, or the worse the naming domain on cognitive function.

Table 7. Relationship between Parkinson Severity with Naming

Stadium	Naming		*p*	*r*
	Decline	Normal		
Stadium 1	0 (0)	5 (12,8)	0,003*	-0,962
Stadium 2	0 (0)	15 (38,5)		
Stadium 3	3 (7,7)	12 (30,8)		
Stadium 4	3 (7,7)	1 (2,6)		

* Gamma

Immidiate Recall

Of the 39 study subjects with Parkinson's disease, there were 3 people who experienced immediate domain disorders on MoCA-INA examination. Where in stages 1 and 2 there were no research subjects who experienced disorders in the immediate memory domain, while in stage 3 there were as many as 2 people (5.1%) research subjects who experienced immediate memory domain disorders, while in stage 4 1 (2.6%) people were found to experience impairments in the immediate meori assessment on the MoCA-INA examination. The results of the analysis using the Gamma test showed no significant relationship between the severity of Parkinson's and immediate memory (p = 0.075).

Table 8. Relationship between Parkinson Severity with Immidiate Recall

Stadium	Recent Memmory		*p*	*r*
	Decline	Normal		
Stadium 1	0 (0)	5 (12,8)	0,075*	-0,848
Stadium 2	0 (0)	15 (38,5)		
Stadium 3	2 (5,1)	13 (33,3)		
Stadium 4	1 (2,6)	3 (7,7)		

* Gamma

Attention

Of the 39 study subjects with Parkinson's disease, disorders in the attentional domain were found at each stage. Where the attentional domain is most impaired in Parkinson's patients with stage 3 severity, which is 14 people (35.9%), then followed by stage 2, which is 8 people (20.5%). In stages 1 and 4, the same number of research subjects was 4 people (10.3%). The results of the analysis using *Gamma* showed a relationship between the severity of Parkinson's and the attentional domain (p = 0.014). Then obtained an r value of -0.592 with a negative correlation direction which means that the value of 0.592 indicates a moderate correlation strength and a negative correlation strength which means that the higher the degree of disease stage, the smaller the attention domain on cognitive function examination.

Table 9. Relationship between Parkinson Severity with Attention

Stadium	Attention		*p*	*r*
	Decline	Normal		
Stadium 1	4 (10,3)	1 (2,6)	0,014*	-0,592
Stadium 2	8 (20,5)	7 (17,9)		
Stadium 3	14 (35,9)	1 (2,6)		
Stadium 4	4 (10,3)	0 (0)		

* Gamma

Laanguage

Of the 39 study subjects with Parkinson's disease, there were 30 (76.9%) patients who experienced language domain disorders on the MoCA-Ina examination. When viewed from table 4.12 in stage 1, out of 5 research subjects there was 1 person who experienced language domain disorders (20%), while in stage 2 of 15 research subjects there were 6 (40%) people who experienced language domain disorders. Furthermore, there were as

many as 10 (67%) of the 15 stage 3 research subjects who experienced language domain disorders. In this study, all stage 4 Parkinson's patients experienced language domain disorders on the MoCA-Ina examination, where *the Gamma test* found a relationship between the severity of Parkinson's and the attentional domain (p = 0.01). Then obtained an r value of -0.674 with a negative correlation direction which means that the value of 0.674 indicates a strong correlation strength and the correlation strength is negative which means that the higher the degree of disease stage, the smaller the value of the language domain on cognitive function examination.

Table 10. Relationship between Parkinson Severity with Language

Stadium	Language		*p*	*r*
	Decline	Normal		
Stadium 1	1 (2,6)	4 (10,3)	0,001*	-0,674
Stadium 2	6 (15,4)	9 (23,1)		
Stadium 3	10 (25,6)	5 (12,8)		
Stadium 4	4 (10,3)	0 (0)		

* Gamma

Abstraction

Of the 39 research subjects of Parkinson's patients, there were 8 people who experienced abstraction domain disorders on the Moca-Ina examination. In stage 1 and stage 2, there were no research subjects who experienced abstraction domain disorders, while in stage 3, out of 15 research subjects, there were 6 (40%) who experienced abstraction domain disorders. While in stage 4, there are 2 (50%) out of a total of 4 people who experience interference in the abstraction domain on the MoCA-Ina examination. The results of the analysis using the Gamma test showed that there was a significant relationship between the severity of Parkinson's and the abstraction domain on the examination of cognitive function (p = 0.001). Then obtained an r value of -0.874 with a negative correlation direction which means that the value of 0.874 indicates a very strong correlation strength and the correlation strength is negative which means that the higher the degree of disease stage, the smaller the abstraction domain value on cognitive function.

Table 11. Relationship between Parkinson Severity with Abstraction

Stadium	Abstraction		*p*	r
	Decline	Normal		
Stadium 1	0	5 (12,8)	0,001*	-0,874
Stadium 2	0	15 (38,5)		
Stadium 3	6 (15,4)	9 (23,1)		
Stadium 4	2 (5,1)	2 (5,1)		

* Gamma

Delayed Recall

Of the 39 study subjects with Parkinson's disease, delayed recall domain disorders were obtained at each stage of Parkinson's severity. The results of the analysis using the *Gamma test* showed that there was a significant relationship between the severity of Parkinson's and delayed memory impairment (p = 0.001).

Table 12. Relationship between Parkinson Severity with Delayed Recall

Stadium	Delayed Recall		p
	Decline	Normal	
Stadium 1	5 (12,82)	0	0,001*
Stadium 2	15 (38,46)	0	
Stadium 3	15 (38,46)	0	
Stadium 4	4 (10,26)	0	

* Gamma

Orientation

Of the 39 study subjects, 6 out of 15 Parkinson's patients in stage 3 experienced disturbances in the orientation domain on the MoCA-Ina examination, while in stage 4, there were 3 out of 4 Parkinson's patients in stage 4 who experienced orientation domain disorders. There was no orientation domain disturbance in stage 1 and stage 2 research subjects. The results of the analysis using the *Gamma test* showed that there was a significant relationship between the severity of Parkinson's and orientation domain disturbances on cognitive function examination using the MoCA-Ina instrument (p = 0.001). Then obtained the value of r - 0.944 with a negative correlation direction which means that the value of 0.944 indicates a very strong correlation strength and the correlation strength is negative which means that the higher the degree of disease stage, the smaller the value of the orientation domain on cognitive function.

Table 13. Relationship between Parkinson Severity with Orientation

Stadium	Orientasi		*p*	*r*
	Decline	Normal		
Stadium 1	0 (0.0%)	5 (12,8%)	0,001*	-0,944
Stadium 2	0 (0,0%)	15 (38,5%)		
Stadium 3	6 (15,4%)	9 (23,1%)		
Stadium 4	3 (7,7%)	1 (2,61%)		

* Gamma

DISCUSSION

Examination of cognitive function in this study using the MoCA-Ina instrument which covers 8 cognitive domains, namely visuospatial and cognitive function, naming, immidiate recall, attention, language, abstraction, delayed recall, and orientation. In this study, it was found that the most disturbed cognitive domain was delayed memory; 39 subjects, attention; 30 subjects, visospatial; 24 subjects on MoCA-Ina examination. This is in accordance with research conducted by Tarukbua in 2016, where based on the prospective descriptive study, it was found that all of the research subjects studied experienced memory domain disorders (100%), then followed by disturbances in the visuospatial domain (67.7%). [9] In a 2009 study conducted by Nazem and colleagues in Pennsylvania, 131 Parkinson's disease sufferers using Moca found the most cognitive impairment was executive function and attentional function. [12] In the early stages of Parkinson's disease, the most common cognitive impairment is executive function. This cognitive impairment indicates involvement of the frontal lobes, specifically the dorsolateral prefrontal cortex due to degeneration of the nigrostriatal or mesocortical dopaminergic pathways. [13] Executive functions are specifically concerned with the prefrontal cortex and related subcortical structures that make up the "striatal-cortical-frontal" control circuit. This circuit runs along the dorsolateral, orbitofrontal, and prefrontal mesial cortex up to the striatum. This circuit then forms a network to the globus palidus and thalamus, then back again to the prefrontal cortex. Damage to the substantia grisea or substantia alba in this circuit is associated with executive function deficits. In a study conducted by Nindela and colleagues in 2021, where in 38 patients who sought treatment at Mohammad Hoesin Hospital Palembang, the most domain disorders in the MoCA-Ina examination were in the domain of executive function and delayed memory [14]. The results of this study are also relevant to research conducted by Desravima in 2019, where the most impaired domains of cognitive function are memory, visuospatial, and attention. [15] A 2010 study conducted by Watson et al found that the underlying pathological incidence of cognitive impairment in Parkinson's patients varied from patient to patient, and research on the underlying pathologic abnormalities in Parkinson's patients was limited. This is supported by several previous studies conducted by Janvin in 2006 found the predominant cognitive function domains found in Parkinson's patients are the executive and attentional domains. However, in other studies, it is not uncommon for Parkinson's patients to find memory impairment, so there are many variations in the profile of cognitive impairment, time and progression of cognitive impairment in Parkinson's patients. Watson revealed this is motivated by the many possible underlying pathological events resulting in various variations of cognitive impairment. [16]

Based on bivariate tests, it shows that demographic aspects and patient conditions in research subjects are not significantly significant with the cognitive function experienced by patients, this is inversely proportional to research conducted by Pradyaning in 2020, that in this study age is a major risk factor for Parkinson's disease. [17]

In this study, based on statistical analysis tests, it was found that around 66.7% of research subjects experienced impaired cognitive function. Based on statistical tests, a significant relationship was obtained between the severity of Parkinson's and cognitive function ($p = 0.001$). This result is in accordance with several previous studies, namely in research conducted by Desravima in 2019, that the more severe the degree of Parkinson's disease, the more severe the incidence of cognitive impairment. [15] This study is also in accordance with a cohort study conducted by Uc et al in 2009, that the incidence of cognitive impairment in Parkinson's sufferers is 2.4% in the first 2 years of diagnosis of Parkinson's disease, and as much as 5.8% in the year diagnosed. [18] Research by Silalahi in 2012 at Sanglah Despansar Hospital also showed similar results, where the higher the Parkinson's stage, the greater the occurrence of cognitive function disorders. [19] As with motor symptoms, the characteristics of cognitive impairment in Parkinson's disease vary between individuals. At first impaired cognitive function in Parkinson's disease was considered purely impaired cognitive function due to lack of dopamine in the nigrostriatal pathway, but in the course of it the entire cognitive domain can be disrupted. [20] The involvement of impaired cognitive domains in Parkinson's disease depends on the timing of disease onset and disease progressivity. The initial pattern of impaired cognitive function in Parkinson's disease is believed to be caused by pathological processes that occur. [21]

In research conducted by Zhang and colleagues, cognitive impairment in Parkinson's patients varies from mild cognitive impairment such as Mild Cognitive Impairment (MCI) to even dementia with progressive deficits that interfere with daily activities. Cognition impairment greatly affects important aspects of life such as work and even in the early phases of Parkinson's disease can be a key predictor of home treatment and death later in life. A more detailed mechanism in looking at the underlying mechanisms of cognitive impairment in Parkinson's patients is still not known with certainty. However, in some studies it is said that in Parkinson's patients there is degeneration of cholinergic nerve fibers in the basal part of the cerebrum, which provides cholinergic innervation throughout the neocortex. Then next, there will be abnormalities in the dopaminergic system in the prefrontal and other neurotransmitter systems such as noradrenergic and serotoninergic innervation. Memory impairment in this study was obtained by 100%. Research conducted by Broeders et al that in Parkinson's patients memory impairment is the most common disorder, and memory impairment is a predictor of the occurrence of further neurocognitive disorders in patients with Parkinson's after diagnosis.[22] Other studies have suggested that in Parkinson's patients, memory function is impaired after executive function is impaired. The earliest memory functions disrupted in Parkinson's patients are immidate and delayed memory, while remote memory will be disrupted when it reaches the stage of dementia. Implicit memory also begins to decline in the early stages of Parkinson's disease. [16]

In this study, the visuospatial domain was one of the domains that experienced the most disturbances in the MoCA-Ina examination, where all subjects in stages 3 and 4 experienced visuospatial disorders. Looking at the pathophysiology of impaired cognitive function in Parkinson's patients including prefrontal circuits in the early stages, this is said to be a cause that executive function is the earliest and most frequent disorder in Parkinson's patients. Impaired executive function can even be found in the pre-motor stage. After executive function is impaired, the next disorders that can be encountered in Parkinson's patients are visuospatial and attentional related to the executive frontal circuit. [21]

After visuospatial, the most impaired cognitive domain in this study was attention (76.9%). Attention is closely related to executive function, because the regulation of attention and executive function through the same circuit, namely the prefrontal dorsolateral circuit. Attention can also be divided into simple attention and complex attention. [16]

Language disorders were the least common in this study, accounting for 15.4% of all subjects. This is in accordance with previous studies where language disorders in Parkinson's sufferers can still be debated. Some studies identify language disorders as minor disorders in Parkinson's disease. [16]

In a study conducted by Brandao in 2020, disruptions in several neurotransmitter systems were associated with PD- MCI and PDD. Some of these are acetylcholine (most associated with executive disorders and posterior cortex), dopamine (associated with executive disorders), noradrenaline (most associated with attentional disorders, inhibitory control, and mood disorders), and serotonin (associated with mood depression, and hallucinations). Knowledge of the performance of each neurotransmitter system that causes specific symptoms is still very difficult to determine, because many of the multiple nerve projections cross different anatomical regions. Executive disorders based on some theories have found that it is caused by functional disorders of the dorsolateral/vetrolateral parts of the prefrontal cortex and striatum, due to dysfunction of parallel associative circuits of the cortico-striatal section, which these circuits rely heavily on dopamine. Damage to the dopaminergic tube in the mesocortical plays an important role in executive dysfunction. It begins at the VTA and projects into the neocortex, insula, and gyrus singulata. This structure implies cognitive flexibility and reconciles other circuits such as the attentional network in the fronto-temporal attentional network (PFAN), where this cognitive flexibility plays a role in adaptations or attentional responses when there are changes in the environment. Impaired attentional changes between cognitive tasks occur in Parkinson's patients, where they improve after dopamine administration, and worsen again if dopamine administration is stopped. Parkinson's patients generally have difficulty inhibiting incoming information, and experience a very high sensitivity to distractions in attention. The basal ganglia, specifically the dorsal region and its connection to the prefrontal cortex, have a special role in selecting and inhibiting cognitive information. Anatomical pathology studies in PDD patients show a decrease in choline-acetyltransferase activity and density of acetylcholine receptors throughout the neurocortex layer. Then in Parkinson's patients with dementia, there was a massive and global decrease in the acetylcholine marker, 11C-MP41A PET uptake (k3) in the cortex, whereas in Parkinson's patients without cognitive impairment, the disorder occurred only in the occipital lobe. Shimada et al confirmed that cholinergic disorders of the occipital lobe (cuteus) are an initial finding in Parkinson's patients. Disruption in the number of muscarinic receptors occurs in the substantia nigra, hippocampus, and neurocortex, however, the cholinergic system not only originates in the large brain nucleus, such as BNM (Ch4 neurons), but is also present in brainstem locations, such as in the pontin pedunculus nucleus (Ch5 group), and the laterodorsal tegmentum nucleus. [16]

The dorsalis nucleus in the rapha innervates the basal ganglia and projects to the frontal cortex and limbic system. This serotonin produced in the nucleus facilitates dopaminergic transmission through several receptors, such as 5-HT1A, 5-HT1B, 5-HT2A, and 5-HT4 receptors. The serotonin system is also a modulator of GABA and glutamate activity. Based on research conducted by Halliday et al, the serotonin system originating in the raphe nucleus, many experience a decrease in PDD, along with a decrease in 5-HT and 5-HT2A receptors. This serotonin system is consistently associated with mood disorders and psychosis. Visual hallucinations are clinically most commonly found in Parkinson's patients who are at an advanced stage. The involvement of 5-HT2 receptors in hallucinations and psychosis in Parkinson's patients has been well documented, and it has been confirmed that administration of 5-HT2A/2C can improve the patient's clinical condition. [16]

Once diagnosed with Parkinson's disease, patients may present with subjective complaints, but are not seen in the objective examination. Although the patient does not experience impairment at the time of objective examination, the patient's cognitive must be monitored for 2 years to predict the cognitive deterioration of the patient. In the clinical appearance of cognitive impairment in patients newly diagnosed with Parkinson's disease, most patients experience single-domain non-amnestic cognitive decline with impaired visuospatial, attentional, and executive examinations. In addition, impairments in language function and visuospatial function have a high sensitivity to predict dementia. However, not every patient has impairment in one domain, and impairment may occur in some or all of the cognitive domains. The background of this difference,

explained by a "dual syndrome" hypothesis, states that in patients with more severe damage to the fronto-striatum tissue, which is modulated by dopamine, attentional function and working memory and executive function are impaired, while in patients with degeneration in the posterior cortex, memory, language and visuospatial functions are more impaired due to the massive decrease in cholinergic neurons. Therefore, a comprehensive cognitive evaluation of each individual is essential in predicting the underlying pathophysiology in order to provide the best management for the patient. [16]

This study has limitations such as there are other factors that can affect cognitive function such as the type of therapy where in this study no further study was examined regarding the regularity of the use of dopaminergic (levodopa) daily doses consumed by Parkinson's patients in most study subjects. Patients with advanced Parkinson's can give clinical symptoms such as loss of response to dopamine as well as provide cognitive impairment output. In addition to the use of levodopa therapy, this study did not examine further the effects of treatment consumed by patients with decreased cognitive function experienced, as well as the duration of disease onset. So that in future studies it is expected to assess the relationship between the type of therapy, disease onset and cognitive function in Parkinson's patients.

CONCLUSION

There is a relationship between the severity of Parkinson's disease and cognitive function with a very strong correlation strength. The domains of cognitive function that correlate particularly strongly with Parkinson's severity are delayed memory, naming, orientation, visuospatial and abstraction

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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REFERENCE

1. He Y, Tian Y, Han H, Cui J, Ge X, Qin Y. et al. The path linking disease severity and cognitive function with quality of life in Parkinson's disease: the mediating effect of activities of daily living and depression. Health Qual Life Outcomes. 2021; 19:92.
2. DeMaagd G, Philip A. Parkinson's Disease and Its Management. P&T. 2015; 40 (8): 504-512.

3. Kouli A, Torsney KM, Kuan WL. Parkinson's Disease: Etiology, Neuropathology, and Pathogenesis. Parkinson's Disease: Pathogenesis and Clinical Aspects. 2018: 1-25
4. Vasquez KA, Valverde EM, Aguilar DV, Gabarain HJH. Montreal Cognitive Assessment scale in patients with Parkinson Disease with normal scores in the Mini-Mental State Examination. Dement. Nuerophyschol. 2019; 13(1).
5. Aarsland D, Batzu L, Halliday GM, Geurtsen GJ, Ballard C, Chaudhuri KR. et al. Parkinson disease-associated cognitive impairment. Nature Reviews. 2021; 7: 47.
6. Painous C, Marti MJ. Cognitive Impairment in Parkinson's Disease: What We Know so Far. Research and Reviews in Parkinsonism. 2020:10 7–17.
7. Fengler S, Kessler J, Timmermann L, Zapf A, Elben S, Wojtecki L . et al. Screening for Cognitive Impairment in Parkinson's Disease: Improving the Diagnostic Utility of the MoCA through Subtest Weighting. PLoS ONE. 2016; 11(7): e0159318.
8. Wakamori T , Agari T , Yasuhara T , Kameda M , Konso A , Shinko A. et al. Cognitive functions in Parkinson's disease: Relationship to disease severity and hallucination. Kibi International University. 2014:1-2
9. Tarukbua FR , Tumewah R, Maja J. Gambaran functional cognitive impairment of parkinsonism at the Polyclinic Saraf RSUP Prof. Dr. A.S. RD Kandou Manado. e-Clinic Journal. 2016; 4(1): 1-7
10. Brett B. Neurocognitive Functioning in Parkinson's Disease Patients: Assessing the Unique Contributions of Depression and Fatique While Controlling for Disease Severity. The University of Memphis. 2018: 1-29.
11. Hanum L. Hubungan Derajat Penyakit Parkinsond engan Gangguan Fungsi Kognitif Menggunakan Instrumen Montreal Cognitive Assessment versi Indonesia. Fakultas Kedokteran Universitas Andalas. 2019: 1-3.
12. Nazem S, Sideorwf AD, Duda JE. Montreal Cognitive Assesment Performance in Patients with Parkinson's Disease with "Normal" Global Cognition According to MMSE Score. J AM Geriatr Soc. 2009; 57: 304-8.
13. Vingerhoets G, Verleden S, Santens P. Predictors of Cognitive Impairment in Advanced Parkinson's Disease. J Neurol. 2003. Neurosurg Psychiatry; 74: 793-6
14. Nindela, Rini , Tambun, Oktavianus and Marisdina, Selly, Bahar, Erial. Cognitive Impairment in Parkinson's disease Patients: a Descriptive Study. Movement Disorders. 2021; 36 (supp. 1): 296-297.
15. Desravima MB. The relationship between the degree of Parkinson's disease and cognitive dysfunction using the Mini Mental State Examination (MMSE) instrument. Diploma thesis, Andalas University. 2019
16. Watson GS, Leverenx JB. Profile of Cognitive Impairment in Parkinson's Disease . Brain Pathol. 2010; 20(3): 640-645.
17. Pradyaning PE, Widyastuti K, Laksmidewi AA . Profile of Neurocognitive Disorders in Parkinson's Disease Patients at Referral Hospitals in Despansar City in 2018. Callosum Neurology. Denpasar. 2020.
18. Uc EY, Mc Dermot MP, Marder KS. Incidence of and Risk Factors for Cognitive Impairment in an Early Parkinson Disease Clinica Trial Cohor. Neurology. 2009; 73(18): 1469-77.
19. Silalahi PY. Korelasi Gangguan Fungsi Kognitif dengan Stadium Penyakit Parkinson. Udayana University. 2012.
20. Biundo R, Weis L, Antonini A. Cognitive Decline in Parkinson's Disease: The Complex Picture. Npj Park Dis. 2016;2(1):16018.
21. Adwani S, Yadav R, Kumar K. Neuropsychological Profile in Early Parkinson's Disease: Comparison between Patients with Right Side Onset Versus Left Side Onset of Motor Symptoms. Ann Indian Acad Neurol. 2016; 19 (1): 74-8.
22. Broeders M, Velsboer DC, de Bie R. Cognitive change in Newly-Diagnosed Patients with Parkinson's Disease: a 5-year Follow-up Study. J iNt Neuropsychol Soc. 2013; 19 (6): 695-708.