

Cognitive decline in Parkinson's disease: contributions of Neuropsychology*

Declínio cognitivo na Doença de Parkinson: contribuições da neuropsicologia

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ABSTRACT

Introduction: To evaluate the prevalence of cognitive decline in Parkinson's disease (PD) and the contributions of Neuropsychology to its diagnosis and treatment. **Objectives:** to emphasize the importance of a neuropsychological assessment as a strategy for research and early diagnosis of cognitive and behavioral disorders associated with PD in addition to the role of cognitive rehabilitation in the treatment of these patients. **Methodology:** a bibliographic survey of articles in Pubmed, Medline, Lilacs, and Scielo published over the past 10 years. **Conclusions:** the cognitive alterations observed in PD are related to memory, language, visual-spatial capacity, and executive functions; however, there is a lack of information regarding the cognitive rehabilitation of these patients.

Key words: Parkinson Disease; Cognition; Neurobehavioral Manifestations; Symptom Assessment.

RESUMO

Introdução: avaliar a prevalência de declínio cognitivo na doença de Parkinson (DP) e as contribuições da Neuropsicologia para o seu diagnóstico e tratamento. **Objetivos:** enfatizar a importância da avaliação neuropsicológica como estratégia de investigação e diagnóstico precoce das desordens cognitivas e transtornos comportamentais associados à DP, além do papel da reabilitação cognitiva no tratamento desses pacientes. **Metodologia:** levantamento bibliográfico de artigos no Pubmed, Medline, Lilacs e Scielo publicados nos últimos 10 anos. **Conclusões:** são constatadas as alterações cognitivas na DP referentes a memória, linguagem, capacidade visuoespacial e funções executivas, no entanto, há carência de informações quanto à reabilitação cognitiva desses pacientes.

Palavras-chave: Doença de Parkinson; Cognição; Manifestações Neurocomportamentais; Avaliação de Sintomas..

INTRODUCTION

The incidence of Parkinson's disease (PD) among neurological diseases imposes itself as the second chronic neurodegenerative disorder detected in elderly after Alzheimer's disease, with prevalence estimated at 3.3% in patients older than 65 years old in Brazil. The prevalence is higher in the age group between 50 and 70 years old.¹

In 2025, about two billion people will be over 60 years old worldwide; Brazil is considered the sixth country with the largest number of elderly, around 32 million.² The social impact that the demographic transition announces requires the evaluation of the Brazilian population for an early approach to PD related abnormalities.

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There is great scientific difficulty in the identification of the etiology of PD, which is so far, obscure. However, several factors may be triggering such as: action of environmental neurotoxins, atherosclerosis, excessive accumulation of free oxygen radicals, viral infections, head injuries, use of antipsychotic medications, and, in 30% of cases, genetic factors.

PD, although traditionally recognized as a movement disorder, evolves with non-motor symptoms of relevant disability in all its stages. Cognitive dysfunctions, psychiatric changes, sleep disturbances, autonomic dysfunction, and pain are common. In this revision the cognitive losses during PD are highlighted.^{3,4}

MATERIAL AND METHODS

A bibliographical survey was conducted over the PD theme and cognitive functions using the Lilacs, Pubmed, Scielo, and Medline databases in search of articles, preferably dated from 2000. The reading of the articles allowed the identification of the most committed cognitive domains in PD bearers, with or without dementia, like the following: executive functions, visual-spatial skills, memory, attention, and language.

ANATOMOPATHOLOGICAL CHARACTERISTICS OF PD

In the anatomopathological point of view, PD is characterized by multiple monoaminergic dysfunctions including disability in the dopaminergic, cholinergic, serotonergic, and noradrenergic systems.⁵

The pathological process begins in the dorsal motor nucleus of the vagus and anterior olfactory with caudo-rostral progression in six stages (Table 1).^{6,7} In its early stage, alterations occur mainly in the dorsal motor nucleus of the glossopharyngeal and vagus nerves in addition to the intermediate reticular and anterior olfactory bulb zone leading to constipation, sleep disorders, and hyposmia. In the second stage, additional involvement of the raphe nuclei, nucleus gigantocellular reticular nucleus, and locus ceruleus are observed, which can induce depression, anxiety, sleep disturbances, and pain of central origin. In the third stage, the degeneration of the compact part of the substantia nigra in the midbrain determines the onset of motor symptoms, abnormalities in the

sleep-wake cycle, and mild cognitive disorder such as decreasing capacity of abstraction, losses in operating memory, both in inattention amplitude and cognitive processing speed. In the fourth stage, the injuries mainly affect the temporal mesocortex and amygdala creating mnemonics and executive dysfunctions, and neuropsychiatric alterations. In the fifth stage, the involvement of the neocortex occurs, particularly in the prefrontal areas, and of sensitive associations accentuating the cognitive dysfunction. In the last stage, the diffuse involvement of the primary cortical areas is observed, and therefore, motor difficulties are aggravated with the possibility of installation of dementia.^{7,8}

Table 1 - Correlation between the neuropathological stages, the structures involved, and clinical manifestations in Parkinson's disease (according to Braak et al)⁶

Neuropathological stages	Structures involved	Clinical manifestations
1	- n. dorsal motor of the vagus - reticular formation - n. anterior olfactory	- constipation - sleep disorders (DC – REM) - hyposmia
2	- n. caudal of the raphe - reticular formation - n. coeruleus and subcoeruleus	- depression - sleep disorders - primary central pain
3	- locus niger - n. basals of the forebrain	- motor classic sympt. - cognitive alter. and sleep disord.
4	- temporal mesocortex - amygdala - n. oral of the raphe	- bradifrema - apathy - SED and depression
5	- pre-frontal areas - sensitive neocortex - insula - angle swivel	- inattention and hypomnesia - agnosia and apraxia - dementia
6	- pre-motor areas - primary motor area - areas of sensitive association	- sensorial-motor dysfunctions - severe dementia

The neurobiological mechanisms involved in dementia associated with PD are not completely understood. The involvement of dopaminergic handles from the midbrain to other subcortical nuclei is observed (frontostriatal non-motor circuit), alteration of cholinergic projections to the cerebral cortex and neuropathological elements, similar to those found in Alzheimer's disease and Lewy bodies, with cellular and synaptic loss in the cortical and limbic structures.⁵ The involvement of domains of responsibility in the frontal lobe leads to cognitive losses that are characteristics of the disease such as: operating

memory deficiency, attention alteration, and reduced performance in executive functions.⁹

COGNITIVE LOSSES IN PD – CLINICAL CHARACTERISTICS

The cognitive domains most involved in people with PD, with or without dementia, are related to executive functions, visual-spatial skills, memory, attention, and language. These cognitive difficulties are often associated with bradykinesia and rigidity, being less frequent when the tremor constitutes the predominant symptom.¹⁰

The early recognition of these alterations is important and can be useful for the introduction of new therapeutic strategies because the cognitive loss seems to associate with the development of neuropsychiatric manifestations, mainly major depression, with influence over disease evolution.¹¹ Among cognitive alterations, dementia is the most severe state of the disease, increasing the risk of death due to clinical complications linked to respiratory functioning, side effects of medications that can lead to sedation, and cardiac disorders.¹²

The prevalence of dementia in PD varies from 24 to 31% and its risk factors are: old age, severity of motor impairment, rapid progression of disease, emergence in old age; low response to levodopa with exuberant side effects; early presence of hallucinations, gravity, and akinetic rigid forms.¹³ The Mini Mental Status Exam (MMSE) with a low score and the Mini Mental Parkinson Test (MMP) appear to be significant predictors for the manifestation of dementia.^{10,14} Early postural instability can also be a risk factor for cognitive loss in these patients. There is an association between dementia and the degree of clinical impairment, with the inclusion of a higher incidence of autonomic involvement and depressive and psychotic symptoms in these cases.¹³

Dementia in PD refers to the set of cognitive and behavioral alterations that develop at least 12 months after the installation of motor alterations. And when symptoms appear in the first 12 months of disease evolution, the criterion for the diagnosis of dementia with Lewy bodies is fulfilled.¹⁵

Dementia in PD seems to consist of a subcortical dis-executive syndrome, with attention, executive functions and, secondarily, memory impairment.¹⁶ Thus, reduction or lack of initiative for spontaneous activities, inability to develop successful strategies for problem

solving, slowness in global information processing and mnemonic processes, visual-spatial perception impairment, and difficulties in conceptualization in the generation of lists of words are detected.

In addition to motor alterations, motor cognitive functioning disorders with losses in language, attention amplitude, visual-spatial skills, and executive functioning is noted in PD and in patients without diagnostic criteria for dementia, even in their early stages.¹⁷

NEUROPSYCHOLOGICAL EVALUATION IN PD

The neuropsychological approach consists in strategic and interventional diagnosis useful and necessary for an early detection of risk factors for dementia, prevention of complications, and cognitive, emotional, and global social rehabilitation, both for the patient and their family members or caregivers. The identification of damage and establishment of appropriate follow-up of patients allows a more specific and individualized clinical treatment.¹⁸

The neuropsychological functions constitute a group of complex cognitive functions including attention, memory, language, reasoning, and executive and visual-spatial functions.

The main cognitive alterations in PD carriers are executive and visual-spatial functions, which are essential for performing activities of daily living. The main neuropsychological instruments to evaluate these functions are: MMSE, Mattis Dementia Rating Scale (MDRS), Scales for Outcomes in Parkinson's disease-COGnition (SCOPA-COG), Wisconsin Card Sorting Test (WCST), Frontal Evaluation Battery (FAB), WAIS III Subtests: Digits amplitude - Reverse Order (RO), Verbal Fluency Test (Animals Category), Hooper Visual Organization Test (HVOT), Judgment of Line Orientation – V Shape (JOL), and the Clock Drawing Test (Table 2).¹⁹

Table 2 - Neuropsychological instruments for the evaluation of altered cognitive functions in PD

Cognitive functions	Neuropsychological indicated instruments
Executive functions	WCST, FAB, Stroop, Trails A and B
Language	Verbal Fluency (Animal Category), Boston
Attention	Digits (WAIS-III), Sequence of Numbers and Letters (WAIS III), Stroop, WCST, Trails A and B
Memory	Verbal Fluency, MMSE, Digits (WAIS III)
Visual-spatial organization	Hooper, CDT

The MMSE is probably the most widely used instrument, with versions in several languages and countries and validated for the Brazilian population, providing information on various cognitive parameters, containing questions grouped into seven categories, each one designed to evaluate specific cognitive functions such as temporal orientation (five points), spatial orientation (five points), record of three words (three points), attention and calculation (five points), memory of three words (three points), language (eight points), and constructive visual capacity (one point). The MMSE score can vary from a minimum of zero points, which indicates the highest degree of cognitive impairment to up to a maximum of 30 points, which corresponds to the best cognitive ability.²⁰

The MDRS is composed of 36 items, distributed in five subscales: attention (eight items, total of 37 points), initiation and perseveration (11 items, total of 37 points), construction (six items, total of 6 points), conceptualization (six items, total of 39 points), and memory (5 items, total of 25 points). The sum of the five subscales provides a total that represents the degree of cognitive impairment and/or severity of dementia.²¹

The SCOPA-COG is an instrument developed specifically to evaluate dementia associated with PD, measuring the following cognitive domains: learning ability, attention, and executive, visual-spatial, and memory functions.²²

The WCST is an instrument created in 1948, extended and subsequently revised, which assesses abstract reasoning and ability of the subject to generate troubleshooting strategies in response to changing conditions of stimulation.²³ Thus, it can be considered a measure of flexibility of thought. Designed for the general population, it became increasingly employed as a tool in clinical neuropsychological assessment of executive functions involving the frontal lobes.²⁴ It is composed of four stimulus cards and 128 response cards, represented with figures of different shapes (crosses, circles, triangles, or stars), colors (red, green, yellow, or blue), and a number (one, two, three, or four). On the task, the examinee is asked to combine stimulus cards with response cards. For each combination performed the subject receives the feedback of right or wrong from the examiner. The principle of combination is previously established and is never revealed to the examinee. The idea is that the subject can use the feedback from the examiner to maintain or develop new strategies.²³

The FAB is a new neurocognitive evaluation instrument that has been shown to be useful for track-

ing problems in executive functions associated with the functioning of the frontal cortex in the human brain. The battery comprises six subtests that evaluate the formation of concepts (abstraction), verbal fluency (mental flexibility), motor programming, susceptibility to interference (tendency to distraction), and inhibitory control and autonomy. They are: similarities, verbal fluency (cognitive flexibility), motor series, conflicting instructions, inhibitory control (Go-No Go), and manual grip – autonomy.²⁵

The WAIS-III scale²⁶ is an instrument adapted and validated for Brazil, indicated for adults of age between 16 and 89 years. This is a complete test, with broad interpretation from 14 subtests, four factorial indices (verbal comprehension, perceptual organization, working memory, and processing speed), and three composite measures (verbal IQs, of execution, and total). It is of great importance for the elderly by evaluating specific cognitive functions in each subtest. The most used subtests and their respective roles in the neuropsychological evaluation of the elderly are: vocabulary (learning skills, quality, and character of thought processes), codes (concentration, visuomotor coordination, motor speed, and directionality), similarities (ability to establish generalizations), cubes (visuomotor coordination, spatial orientation, integration, and abstraction), digits (short-term memory and attention), and search for symbols (rapidity and concentrated attention).²⁷

The verbal fluency test provides information about the storage capacity of the semantic memory system, ability to retrieve information stored in memory, and processing of executive functions, especially those through the ability to organize thoughts and strategies used for searching words. The verbal fluency test involves generating the largest number of words possible in a fixed time period. There are the tests: for phonological fluency with the evocation of words that begin with a certain letter, usually F, A, or S; and for fluency by category or semantics with the generation of words in a semantic class as for example, animal category.²⁸

The HVOT aims to evaluate the ability of discrimination and visual organization. It consists of 30 stimuli presented to the subject in figures of fragmented objects and rearranged on cards. The stimuli are presented in increasing difficulty and the subject is asked to organize each figure visually and name them.²⁹

The CDT, of easy and fast application, helps in cognitive evaluation and can be employed in research of cognitive impairment of some cognitive skills such as visual-constructives and visual-spatial

functions, symbolic and graphomotor representation, auditory language, semantic memory, and executive functions. Deficiencies in these skills are possibly related to frontal temporoparietal cortex impairment.³⁰

Among the cited instruments, MMSE and CDT are used by doctors in brief tracking, whereas the others are in the domain of the neuropsychologist.

The evaluation of PD progression is conducted from staging methods such as the Hoehn and Yahr scale (HY) and Unified Parkinson's Disease Rating Scale (UPDRS), widely used in clinical routine neurological evaluations for the determination of possible treatments.

NEUROPSYCHOLOGICAL REHABILITATION IN PD

The neuropsychological rehabilitation aims to improve the quality of life of patients and their families optimizing the use of functions, totally or partly preserved, through the teaching of compensatory strategies, acquisition of new skills, and adaptation to permanent losses. The rehabilitation process provides awareness to patients regarding their remaining capacities, leading to changes in self-observation, and the possibility of accepting their new reality.³¹The neuropsychological rehabilitation encompasses, in addition to cognitive rehabilitation – whose main focus is the improvement of cognitive functions by means of cognitive-training - the psychotherapy, establishment of a therapeutic environment, work with family members and protected education with patients, and may be developed by professionals of Occupational Therapy, Speech Therapy, Physiotherapy, Psychology, Pedagogy, and others.

FINAL CONSIDERATIONS

The abnormalities in PD are motor, cognitive, and behavioral. Among the effects of motor order affecting carriers are: body and face stiffening; resting tremor; standstill amid an action; festination (opposite trend of accelerated step, speech, and writing); difficulty of balance; inability to move, slower volunteer movements with loss of agility even in simple tasks, and automatic, among others.

In PD, it is noted that patients present alterations in memory, language, visual-spatial and executive func-

tions capacity, emotional alterations, sleep, speech, and writing disturbances. The cognitive alterations in PD, in spite of the emphasis on motor alterations, have crippling effects leading to social isolation and low integration in everyday activities, with varying impact on quality of life.

The early recognition of alterations related to PD through appropriate neuropsychological instruments is essential, in particular with regard to cognitive loss and neuropsychiatric disorders, so that patients may be rehabilitated and treated preventively through pharmacology and cognitive rehabilitation that stimulate the use of these functions.

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