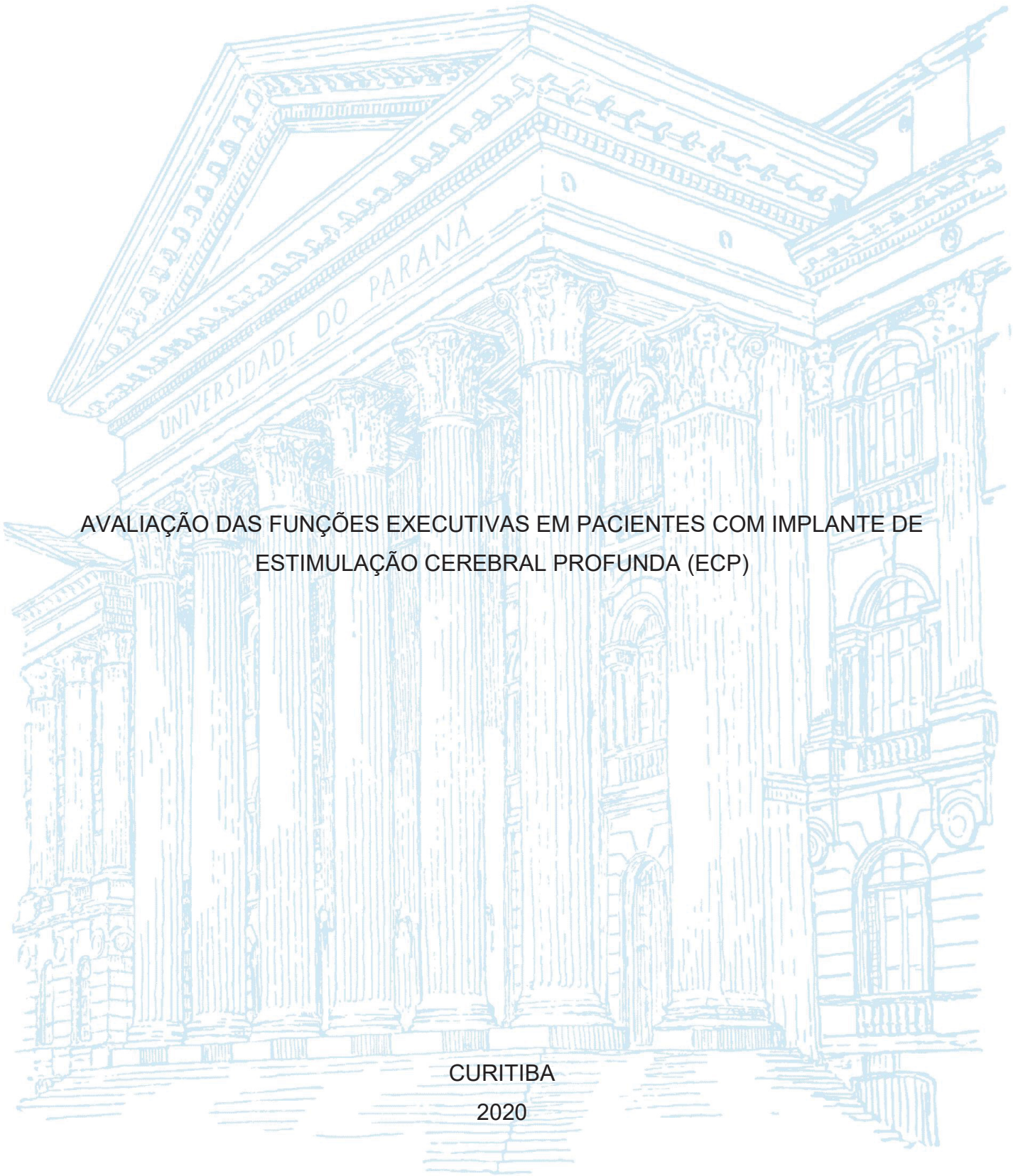
UNIVERSIDADE FEDERAL DO PARANÁ

THAYNÁ LAÍS DE SOUZA ARTEN GODOY



AVALIAÇÃO DAS FUNÇÕES EXECUTIVAS EM PACIENTES COM IMPLANTE DE ESTIMULAÇÃO CEREBRAL PROFUNDA (ECP)

CURITIBA

2020

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AVALIAÇÃO DAS FUNÇÕES EXECUTIVAS EM PACIENTES COM IMPLANTE DE ESTIMULAÇÃO CEREBRAL PROFUNDA (ECP)

Dissertação apresentada ao curso de Pós-Graduação em Psicologia, Setor de Ciências Humanas, Universidade Federal do Paraná, como requisito final à obtenção do título de Mestre em Psicologia.

Orientador: Prof. Dr. Amer Cavalheiro Hamdan

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TERMO DE APROVAÇÃO

Os membros da Banca Examinadora designada pelo Colegiado do Programa de Pós-Graduação em PSICOLOGIA da Universidade Federal do Paraná foram convocados para realizar a arguição da dissertação de Mestrado de **THAYNÁ LAÍS DE SOUZA ARTEN GODOY** intitulada: **Avaliação das funções executivas em pacientes com o implante de Estimulação Cerebral Profunda (ECP)**, sob orientação do Prof. Dr. AMER CAVALHEIRO HAMDAN, que após terem inquirido a aluna e realizada a avaliação do trabalho, são de parecer pela sua APROVAÇÃO no rito de defesa.

A outorga do título de mestre está sujeita à homologação pelo colegiado, ao atendimento de todas as indicações e correções solicitadas pela banca e ao pleno atendimento das demandas regimentais do Programa de Pós-Graduação.

CURITIBA, 30 de Julho de 2020.

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Dedico este trabalho a Jesus, o Cristo, autor e consumador da minha fé. À minha amada família e aos meus professores e mestres.

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A todos vocês, MUITO OBRIGADA!

"Eu sou a videira, vós as varas; quem está em mim, e eu nele,
esse dá muito fruto; porque sem mim nada podeis fazer."
João 15:5

"Porque nEle vivemos, nos movemos e existimos"
Atos 17:28

RESUMO

A Doença de Parkinson (DP) é um dos distúrbios do movimento mais encontrados na população idosa, e, em se tratando de uma enfermidade neurodegenerativa, está muito relacionada às Funções Executivas. Assim, o objetivo desta pesquisa foi avaliar as Funções Executivas (FE) de pacientes com o implante de Estimulação Cerebral Profunda/*Deep Brain Stimulation* (ECP/DBS) e comparar os resultados com o grupo de pacientes diagnosticados com Parkinson que fazem o tratamento apenas com medicamentos, e também com o grupo de idosos saudáveis. Como forma de mapear o conhecimento já existente sobre o assunto, foi realizada uma Revisão Sistemática, baseada nos critérios PRISMA, sendo em seguida realizada a avaliação das Funções Executivas e Memória dos pacientes por meio de uma bateria de testes neuropsicológicos. Os instrumentos utilizados foram o *Montreal Cognitive Assessment* (MoCa), o Teste Auditivo Verbal de Rey (RAVLT), o Teste de Trilhas partes A e B, o Subteste de Dígitos do WAIS III (ordem direta e inversa), o Teste de Fluência Verbal Semântica (animais e frutas) e o de Fluência Verbal Fonológica (F, A e S), além do Teste de *Stroop*. A amostra total foi de 76 participantes, sendo 30 no grupo controle, 30 sem DBS e 16 com DBS. Os principais resultados não indicaram diferenças significativas entre os grupos com Doença de Parkinson (com e sem DBS), apenas entre o grupo controle e o grupo com o diagnóstico. Estas diferenças apareceram em todas as funções avaliadas, o que era esperado, tendo em vista a diferença entre as amostras em termos cognitivos.

Palavras-chave: Doença de Parkinson. Estimulação Cerebral Profunda. Funções Executivas.

ABSTRACT

Parkinson's Disease (PD) is one of the movement disorders most found in the elderly population, and as it is a neurodegenerative disease, it is closely related to Executive Functions. Thus, the objective of this research was to evaluate the Executive Functions (EF) of patients with the Deep Brain Stimulation (ECP / DBS) implant and compare the results with the group of patients diagnosed with Parkinson's who are treated with only medications and also with the healthy elderly group. As a way of mapping the existing knowledge on the subject, a Systematic Review was carried out based on the PRISMA criteria, and then the neuropsychological assessment of patients was carried out. The evaluation was made through a battery of neuropsychological tests, and the instruments used were the Montreal Cognitive Assessment (MoCa), Rey Verbal Hearing Test (RAVLT), Trail Test Parts A and B, WAIS-III Digit Subtest (direct and inverse order), Semantic Verbal Fluency Test (animals and fruits) and Phonological Verbal Fluency (F, A, and S), and the Stroop Test. The total sample was 76 participants, 30 in the control group, 30 without DBS, and sick groups. These differences appeared in all evaluated functions, which was expected considering the difference between the samples in cognitive terms.and 16 with DBS. The main results did not indicate significant differences between the groups with Parkinson's disease (with and without DBS), only between the control.

Keywords: Parkinson Disease. Deep Brain Stimulation. Executive Functions.

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INTRODUÇÃO

A Doença de Parkinson (DP) foi descrita inicialmente por James Parkinson como “Paralisia Agitante”, em 1817 (ROMANN, 2012). Naquele primeiro momento, a doença foi descrita pela presença de movimentos tremulantes involuntários, fraqueza muscular, tendência de inclinar o tronco para frente, e alteração da marcha, tendo os sentidos e as funções cognitivas não afetadas (XIE *et al*., 2011).

Por muitos anos, a DP foi descrita como sendo apenas uma desordem motora, negligenciando-se as mudanças cognitivas associadas a ela (KAMEI *et al*., 2010). No entanto, tais alterações são importante causa de incapacidade funcional nos pacientes, podendo chegar a 93% (CAMPOS-SOUSA *et al*., 2010). Além disso, dentre os prejuízos cognitivos que mais aparecem na DP, as alterações das Funções Executivas são as mais comuns (MACUGLIA, 2012).

Atualmente, a DP é entendida pela deleção do neurotransmissor Dopamina, que resulta da degeneração de neurônios dopaminérgicos da substância negra, e as consequências para o paciente incluem alterações nos movimentos voluntários, no sistema de motivação e recompensa, no sono, no humor, na atenção e, consequentemente, na aprendizagem (CAMILLO, 2017). O tratamento mais comum para a doença é a reposição da Dopamina, mas também são utilizados outros métodos, como a implantação do aparelho de Estimulação Cerebral Profunda (ECP), que é recomendada apenas quando o uso de medicamentos não faz mais o efeito desejado. Além disso, para passar pela implantação do ECP, o paciente precisa ter o diagnóstico de DP há mais de 5 anos, além de não apresentar sinais de depressão e suspeita de demência, nem ter realizado cirurgia ablativa prévia, dentre outros critérios (CAMILLO, 2017).

Deste modo, visando a contribuir com o conhecimento a respeito dos possíveis efeitos do ECP nas funções executivas do paciente com Doença de Parkinson, este trabalho foi dividido em dois capítulos, ambos escritos em inglês e formatados de acordo com as normas das revistas científicas às quais os artigos foram submetidos. O primeiro deles (Estudo I) configura-se como artigo de revisão sistemática acerca da temática da Doença de Parkinson, uso do Aparelho de Estimulação Cerebral Profunda (ECP) e relação com as funções executivas, já publicado pela Revista *Dementia & Neuropsychologia*. O segundo (Estudo II) consiste no artigo empírico, resultado da avaliação das Funções Executivas da amostra (pacientes com Doença de Parkinson

com e sem DBS), formatado de acordo com as normas da Revista *Neurology, Psychiatry & Brain Research*, já submetido à apreciação da equipe editorial.

Ao final dos artigos, encontram-se a conclusão dos estudos, as referências gerais e os anexos. Nesta última sessão, encontram-se também os materiais utilizados na avaliação (protocolos e testes neuropsicológicos), o Termo de Aprovação no Comitê de Ética em Pesquisa e o Termo de Consentimento Livre e Esclarecido, para eventuais consultas.

ESTUDO I

Executive Function in Parkinson's Disease with and without Deep Brain Stimulation (DBS): a systematic review

ABSTRACT

Introduction: Observing the aging of the world population, it is essential to investigate which methods are most effective for treating the diseases that appear with age. This study addresses Parkinson's disease (PD). In PD has been increasing the use of the Deep Brain Stimulation (DBS) to treat the disease. Objective: To investigate the Executive Function (EF) in patients with and without the DBS. Method: We designed a systematic review of the literature according to the Preferred Reporting Items for Systematic Review and Meta-Analyzes (PRISMA) criteria. We selected scientific papers published from the Scopus, Web of Science and PsycInfo databases. Results: 13 articles were selected. Were noticed that there is no standardization in the instruments used to evaluate EF and in most studies the lack of group control may have affected the results. Conclusion: The decline in EF was observed in verbal fluency and processing speed in patients with DBS.

Keywords: Parkinson's Disease, Deep Brain Stimulation, Executive Functions, Neuropsychological Assessment.

RESUMO

Introdução: Observando o envelhecimento da população mundial, é essencial investigar quais métodos são mais eficazes no tratamento das doenças que aparecem com a idade. Este estudo aborda a Doença de Parkinson (DP). Na DP tem aumentado o uso da Estimulação Cerebral Profunda (DBS) para o tratamento da doença. Objetivo: Investigar a Função Executiva (FE) em pacientes com e sem DBS. Método: Foi realizada uma revisão sistemática da literatura de acordo com os critérios de Principais Itens para relatar Revisão Sistemática e Meta-Análises (PRISMA). Selecionamos artigos científicos publicados nas bases de dados Scopus, Web of Science e PsycInfo. Resultados: 13 artigos foram selecionados. Observou-se que não há padronização nos instrumentos utilizados para avaliar a FE e, na maioria dos estudos, a falta de controle de grupo pode ter afetado os resultados. Conclusão: Observou-se declínio na FE na fluência verbal e velocidade de processamento em pacientes com DBS.

P**alavras-Chave**: Doença de Parkinson, Estimulação Cerebral Profunda, Funções Executivas, Avaliação Neuropsicológica.

INTRODUCTION

According to data from World Population Prospects: the 2019 Revision, by 2050, one in six people in the world will be over age 65 (16%), up from one in 11 in 2019 (9%). In 2018, for the first time in history, persons aged 65 or above outnumbered children under five years of age globally. The number of persons aged 80 years or over is projected to triple, from 143 million in 2019 to 426 million in 2050 [1]. With this growth, Parkinson's Disease (PD) and other neurodegenerative problems will grow together, and PD is one of the most commonly found movement disorders in the elderly and as a neurodegenerative disease, being very related to the Executive Functions[2].

Study the possible effects of DBS implantation on Executive Functions in Parkinson's patients becomes important because Executive Dysfunctions (ED) that are the basis for manifestations of cognitive impairment in these patients (due to disruption of striatal dopamine flow). In addition, EF can also be affected by changes affected as depression, which is the most frequent mood disorder in PD[2].

Parkinson's Disease (PD) was initially described by James Parkinson as “Agitating Paralysis” in 1817[3] and several drug therapies have been applied since 1867 in the treatment of PD, been the dopamine replacement is the most common[3]. However, due to the therapeutic limitations found in the available treatments, many studies are being conducted to find other alternatives for the treatment of PD. One of these alternatives is the surgical intervention of Deep Brain Stimulation (DBS) implantation and how it is brain surgery, it is necessary to understand if there are and what the possible changes are caused by the intervention in the patient's cognition and its possible consequences in their daily lives. It should be noted that the protocol for DBS implantation is only recommended when the patient is refractory to medications[4].

Neurons are known to be structures susceptible to variations in the electrical potential of their cell membrane when exposed to a variable electric field. The DBS device activates brain structures through implanted electrodes and is used to treat neurological and psychological disorders, often reducing useless medication administration[5]. It is common to implant the DBS in Parkinson's Disease in the Subthalamic Nucleus (STN), and for psychological problems in Internal Globo Palidus (GPi). The surgical procedure is performed using stereotactic neurosurgical techniques, with local anesthesia and with an awake patient. After electrode implantation, the pulse generator (similar to a cardiac pacemaker) is placed on the patient, but under general anesthesia, and usually in the subclavicular region or chest, but can also be placed directly on the skull[5].

Looking at the growing use of surgical interventions as a treatment for PD, we sought to understand how these interventions affect the patient's cognition and their possible consequences in their daily lives, analyzing the results of other studies already conducted with these patients into the global literature. The aim of this systematic review was to analyze the empirical studies, considering that the results on the subject are controversial in the world and the fact that there is almost no research comparing ways to treat Parkinson's disease with its effects on executive functions (nothing found in the databases searched).

METHODS

We designed a systematic review of the literature according to the Preferred Reporting Items for Systematic Review and Meta-Analyzes (PRISMA)[6] criteria. The following terms were used: “Deep Brain Stimulation”, “Parkinson Disease” and “Executive Functions” with the Boolean operator “AND”. We selected scientific papers published in all languages without delimiting a period, involving comparative clinical trials in humans, from the Scopus, Web of Science and PsycInfo databases. The inclusion criteria were a neuropsychological assessment of Parkinson's patients with and without DBS, comparison between Parkinson's and control

groups, use of classic neuropsychological tests. The exclusion criteria were studies of systematic reviews, case studies, book chapters, absence of a neuropsychological assessment and inclusion and exclusion criteria and focus on other aspects that not the Executive Functions.

Study selection

Initially, this method retrieved 202 studies (Figure 1). In PsycInfo database were found 22 articles, but 2 of them were excluded because we had no access to them. In Web of Science database were found 5 articles, 1 we had no access. In Scopus database were found 175 articles, to refine the research was added a filter in "Field of Research: Psychology" because the focus of this study is to understand by neuropsychology if there is some difference between the interventions for PD, 21 articles were found, among which 17 were published in journals, and only 14 we had access.

From the material retrieved, we examined titles and abstracts for studies involving only human clinical trials and applying a neuropsychological assessment, excluding the duplicates, studies of review, case studies, meta-analysis, related only to the medicine field totalizing 27 studies to be analyzed. Reading these articles, excluding articles with problems in the methodology, we stayed with 13 studies to compare. The researchers selected the articles independently: considering suitable studies that (a) evaluated PD patient cognition with STN-DBS, (b) reported the instruments and domains evaluated, and (c) has the focus on neuropsychological assessment.

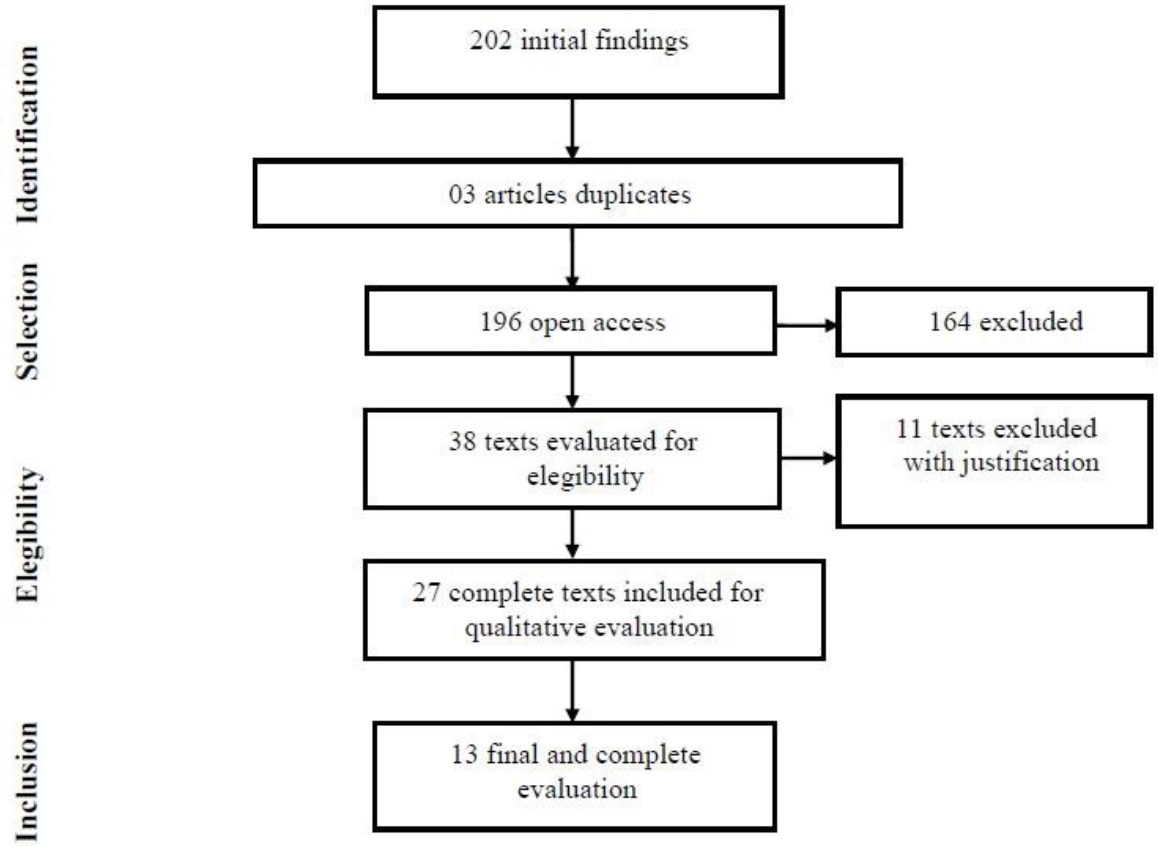

Figure 1. Literature Research Flow Diagram

RESULTS

The final list of articles included based on the search criteria in order of year, with the results are in Table 1. The list of instruments with quantity, separated by domains and behavior measured are in Table 2, and the principal conclusions come below. A total of 40 (forty) instruments were used to evaluate different aspects of patients, including batteries, subtests, scales and tasks (Table 2). These can be ordered from the most evaluated to least used, as follows: executive functions, memory, global cognitive functioning, language, and mood, visuoconstructive skills, and attention.

Of the 13 studies, only 1 had a healthy control group[15], 4 compared the only PD *versus* DBS PD patients [12, 13, 16, 18], 7 were tested before and after DBS implantation or ON/OFF condition [8, 9, 10, 11, 14, 16, 17, 19], and 1 compared DBS patients versus GPi patients[7]. It shows us the evident limitation of comparing the results with a control group in most studies and an absence of a specific assessment protocol for PD with and without STN-DBS (pointed for the variability

of instruments used in the different studies, 40 to be exact). Besides that, there was a lack of an initial screening of the patient's overall functioning, only applied in 5 of 13 studies. Thus, the construction and validation of a battery for use with this population would be interesting for future studies.

Comparing the results in Executive Functions (EF) among the healthy group and PD patients, we note that the disease stage had a linear effect on verbal fluency that worsened with the progression of the disease. In addition, the presence of depression was associated with the worsening of verbal fluency score, as depression would negatively influence tasks that require word generation, contributing to this low score. Furthermore, the authors pointed out that patients that PD started on the right side of the brain had significantly worse verbal fluency than those with left-sided onset[15].

Comparing the EF between PD patients with and without DBS we observe a statistically significant decline in the DBS group on verbal fluency and literal semantic tests, where a higher proportion of patients with DBS (50%) than controls (11%) exhibited an individual level decline in one or structures as fluency measures[12]. We need to observe here the fact that decline in Verbal Fluency should not be considered as part of disease progression, even if patients with DBS are the most severe PD patients according to the Unified Parkinson's Disease Rating Scale section III (UPDRS, section III), but that, according to the authors, could be a side effect induced by surgery[13].

A significant decline in Verbal Memory and a late retrieval of information in the DBS group compared to the treated group was also observed[13]. There was no group or individual level difference for the others tested (numbers and Boston naming test)[12], but no other study or group of counters had a higher occurrence in this task[16]. The DBS group showed a significant increase in difficulty in the Hopkins Verbal Learning Test-Revised (HVLT-R), Trail Making Test A and B, word reading and Stroop Test, and related the most severe motor dysfunction

when evaluating the condition "off"[12]. In addition, the DBS group had a decrease in Mini-Mental State Examination (MMSE), which was higher in the control group, but in both groups indicated for non-pathological performance[16]. Another interesting point in the studies was when, when offered a reward to the DBS group, patients were able to be faster and with task execution goals, suggesting that STN-DBS increased the incentive effect of promised rewards (action selection more impulsive in a low incentive context).

In general, there is a decrease in DBS groups (when compared to PD patients without DBS) in Verbal Fluency tasks, and in other cases in immediate verbal memory and in long term memory. However, DBS retains its ability to decide in many domains, does not change reaction times and response type morally, but also affects the effect of reward incentive, when offered, thus altering the processes involved in the solution of problems. Comparing cognitive functions before and after DBS surgery, we will bring the information in order of function, namely: Verbal Fluency, Memory, Processing Speed, Inhibitory Control, Global Functioning, Apathy, Depression, Anxiety, and Social Aspects.

In summary: 1. Verbal Fluency - Decrease in verbal fluency test scores[8, 10, 17, 19] no reduction in verbal fluency after STN stimulation[11,14]. 2. Memory - One of the studies showed no changes after STN DBS in memory and verbal learning, which remained stable after implantation[10]. On the other hand, there was an improvement in the results of a verbal memory test performed 6 months after the operation when reapplied 12 months after the DBS procedure in other studies[14,17]. 3. Processing speed - Significantly reduced after DBS, being the most important predictor of decline in verbal fluency tests[19]. 4. Inhibitory control - Stroop test worsening after stimulation and Random Number Generation Task (RNGT) counting after stimulation worsened in one study[8] These effects may be induced by stimulation of the associative territory of the STN, but there was no significant difference between groups with and without DBS[8]. In another study, there was a significant reduction in obsessive-compulsive

characteristics after STN DBS[10]. 5. Global Functioning - There is no global deterioration in neuropsychological function attributable to STN-DBS itself, confirming that mild postoperative cognitive decline is transient[9,10,14,17.] 6. Apathy - The apathy score has changed significantly, showing an increasing proportion of apathetic patients over time[9,19]. 7. Depression - The indices fluctuated without being significantly different[9] or remained the same after implantation[17]. It may appear with greater latency and be related to dopaminergic treatment decrease and loss of the antidepressant effect of levodopa. It should be considered that mood often was significantly reduced postoperatively[14,17]. 9. Social - after implantation, the motor benefit allows patients to be more autonomous in life, facilitating social situations[10].

Table 1. List of articles included in the systematic review criteria

Authors and year	Sample	Neuropsychological Instruments used	Location
Ceravolo, R. et al. 2011[14]	**6 total DBS group**	California Verbal Learning Test; Trail Making Test (TMT); Verbal Fluency (FAS); Boston naming test.	Subthalamic Nucleus DBS (bilateral) – STN
Obeso, I. et al. 2012[15]	217 (male) 83 (female) **300 total PD group** 22 (male) 28 (female) **50 total control group**	Frontal Assessment Battery (FAB); Verbal Fluency (letter F)	No DBS used
Fumagalli, M. et al. 2015[16]	5 (male) 6 (female) **11 total DBS group** 5 (male) 6 (female) **11 total PD group**	Digit Span; Corsi Block-Tapping test; Babcock Story Recall Test; Raven Colored Progressive Matrices; FAB; Phonological and Semantic Verbal Fluency; Attentional Matrices; Constructional Apraxia Test.	Subthalamic Nucleus DBS (bilateral) - STN
Tang, V. et al. 2015[17]	18 (male) 9 (female) **27 total DBS group**	MoCa; Chinese Auditory Verbal Learning Test (CAVLT); Benton Visual Retention Test (BVRT); a Chinese version of the Boston naming test (BNT); Hooper visual organization test (HVOT); digit span test (DST); Stroop test Chinese Victoria version; Verbal Fluency test.	Subthalamic Nucleus DBS (bilateral) – STN
Houvenaghel, JF. et al. 2016[18]	10 (male) 15 (female) **25 total PD group** 12 (male) 13 (female) **25 total DBS group**	Verbal Fluency (animals) and Phonemic Fluency (letter p); Nelson's simplified version of the Wisconsin Card Sorting Test (MCST); Trail Making Test; Stroop Test.	Subthalamic Nucleus DBS (bilateral) – STN
Foley, J. et al. 2017[19]	17 (male) 11 (female) **28 total DBS group**	Stroop; Hayling Sentence Completion Test; Brixton Spatial Anticipation Test; Elevator Counting and Distraction subtests from the Test of Everyday Attention (EC, EC-D); Nelson Modified Card Sorting Test (MCST), and Trail Making Test (TMT-B/A); Symbol Search (SS) and Digit Symbol Coding (DSC) of WAIS-III.	Subthalamic Nucleus DBS (bilateral) - STN

Table 1. List of articles included in the systematic review criteria (continuation)

Authors	Sample	Neuropsychological Instruments used	Location
Ardouin, C. et al. 1999[7]	49 STN DBS:24 (male), 25 (female) 13 GPi: 9 (male), 4 (female). **62 total DBS group**	Wisconsin Card Sorting Test; Verbal Fluency (fruits or furniture); Literal Fluency (letter V or R); Graphic and motor series; Stroop Test; Trail Making Test.	Subthalamic Nucleus DBS (bilateral) - STN Globus pallidus internal - GPi
Witt, K. et al. 2004[8]	17 (male) 6 (female) **23 total DBS group**	Digit Span (forward and backward); Verbal Fluency (female/male, first name, animals/plants); Literal Fluency (K/N or L/M), Stroop, Random Number Generation Task (RNGT).	Subthalamic Nucleus DBS (bilateral) - STN
Funkiewiez, A. et al. 2004[9]	43 (male) 34 (female) **77 total DBS group**	Wisconsin card sorting test (WCST); Category and Literal Fluency; Graphic and Motor Series; Grober and Buschke test.	Subthalamic Nucleus DBS (bilateral) - STN
Castelli, L. et al. 2006[10]	38 (male) 27 (female) **65 total DBS group**	Raven Color Matrices; Bi-syllabic Word Repetition Test (BWR); Corsi's Block-Tapping Test (CBT); Paired- Associate Learning (PAL), a Wechsler Memory Scale subtest; Trail Making Test Part B; Nelson Modified Card Sorting Test (MCST); Wisconsin Card Sorting Test; Phonemic and category verbal fluency tasks.	Subthalamic Nucleus DBS (bilateral) - STN
Fraraccio, M. et al. 2008[11]	9 (male) 6 (female) **15 total DBS group**	Rey Auditory Verbal Memory Test; Wechsler Memory Scale; Rey Osterreith Figure/Taylor Figure, WAIS-Digit Span (forward and backward); Tower of London; Wisconsin Card Sorting Test; Stroop; Symbol Digital Modalities Test; Hooper Visual Organizational Test; Rey Figure/Taylor Figure; Boston Naming Test; Controlled Oral Word Association Test.	Subthalamic Nucleus DBS (bilateral) - STN
Mikos, A. et al. 2009[12]	12 (male) 7 (female) **19 total PD group** 20 (male) 4 (female) **24 total DBS group** **43 total sample**	Verbal Fluency (Word and Animals); Digit Span Backward; Boston Naming Test; Hopkins Verbal Learning Test-Revised (HVLT-R), Logical Memory subtest of the WAIS; Trail Making Test; Stroop Test; Judgment of Line Orientation Test; Benton	Subthalamic Nucleus DBS (unilateral) - STN Right (3), left (8). Globus pallidus internal GPi Right (5), left (8)
Castelli, L. et al. 2010[13]	16 (male) 15 (female) **31 total PD group** 17 (male) 10 (female) **27 total DBS group** **58 total sample**	Raven Color Matrices; Bi-syllabic Words Repetition test; Corsi's Block Tapping; Paired Associate Learning; Trail Making B, Nelson Modified Card Sorting test, Phonemic and Category Verbal Fluency.	Subthalamic Nucleus DBS (bilateral) – STN

Table 2. List and frequency of instruments used

Instruments	Used in articles
Verbal Fluency Tasks – Semantic	9
Verbal Fluency Tasks – Phonemic	10
Wisconsin Cards Sorting Test (WCST)	4
Stroop Test	7*
Trail Making Test (TMT)	7
Digit Span Forward and Backward	6
Frontal Assessment Battery (FAB)	2
Hayling Sentence Completion Test	1
Tower of London	1
Luria graphic and motor series[18]	2
Random Number Generation Task (RNGT).	1
Nelson Modified Card Sorting Test (MCST)	4
Brixton Spatial Anticipation Test	1
Grober and Buschke test	1
Boston Naming Test (BNT)*	4*
Controlled Oral Word Association Test	1
Attentive Matrices	1
Symbol Digital Modalities	1
The judgment of Line Orientation	1
Elevator Counting and Distraction subtests from the Test of Everyday Attention (EC, EC-D);	1
Rey´s Auditory Verbal Learning Test (RAVLT)	2*

Note: *Chinese version of the Task

DISCUSSION

The results found in the present study suggest that in general after the implementation of the Deep Brain Stimulator (DBS), in most studies, there was a decrease in executive functions of Verbal Fluency, Processing Speed and some modification in apathy levels. However, the studies also suggest that there was a decrease in the degree of anxiety and in a single case there was an improvement in memory scores and obsessive-compulsive symptoms (related to inhibitory control).

When comparing DBS implant surgical interventions and Pallidus Globe internal injury, we observed an improvement in motor function in both DBS and Internal Pallidus Globe (GPi) injury surgery. There is also a slight and significant improvement in mood, but no improvement in language, memory or in other cognitive functions, indicating that the few cognitive changes shown by neuropsychological tests are subtle. Verbal fluency deficits were found under STN but not GPi stimulation and were not associated with executive deficits generally found in GPi injuries[7]. These results may be related to the methodology used for patient evaluation, such as the absence of a standard evaluation protocol, and the non-standardization of these instruments often. Moreover, the lack of control groups in most evaluations may also have contributed to the inconclusive results (no comparison with healthy groups).

The implications of the results obtained in the literature may have a direct impact on the choice of whether to perform DBS implantation surgery. However, as the results are inconclusive about improvement/worsening or a possible impact on patient cognition, it is not possible to infer whether motor improvement offsets cognitive risk for implant candidates. Thus, further research in the area is required using more advanced evaluation methods such as fMRI, PET, etc. In addition to traditional neuropsychological testing techniques. Thus, it would be possible to achieve a more satisfactory result on the subject and thus contribute to the literature and objectively instrumentalize the choice of the patient who wishes to undergo surgery, even knowing the difficulty in conducting research involving the use of neuroimaging.

Therefore, this study aimed to list the main instruments used in patients diagnosed with PD and their frequency in studies, to know the material that has been used in the evaluation of these patients. In addition, we also sought to understand the possible cognitive effects and their impacts on the patient's daily life, which may be appearing after the implementation of DBS in PD. It should be noted then that even after so many years of research on Parkinson's Disease and the use of various techniques for treating the disease, there are still no conclusions about the cognitive impacts of one of them, which is of such importance to their patients.

Considering the small number of articles on the focus theme (Executive Functions and Parkinson's Disease), it is necessary to take these data with caution, since the numbers in the samples were small and in 12 of the 13 cases, there was no healthy control group, that difficult a more appropriate comparison. In addition, the lack of a standardized battery for evaluating these patients also made the comparison more difficult: different instruments/ different modes of analysis.

Thus, further research with larger samples and healthy control groups is suggested, as well as the standardization of instruments to enable later comparison. Moreover, longitudinal follow-up of these patients could also add to the results more reliably.

CONCLUSIONS

In summary, we sought to systematize the results obtained studies conducted with patients diagnosed with Parkinson's disease and it was observed that in theory, there are equal levels between benefits and risks in the implementation of the DBS. Results observed as improvement could be attributed to memory and social life and also decrease anxiety. The worsening after the intervention could be observed mainly in verbal fluency, processing speed, and apathy. The other aspects (inhibitory control, global development, and depression) did not show significant differences in the studies, remaining stable over time. These results highlight the need for further studies on the techniques used to treat Parkinson's disease because there is

a noticeable decline in the cognition of these patients that may or may not be attributed to their treatment. It is necessary to clarify what is causing these declines, possible rehabilitation techniques, and a standard assessment protocol. This protocol could start with an evaluation of the patient's general condition, if he/she has the diagnosis of depression and/or other comorbidities, the time of diagnosis in PD and surgery, main causes for the implantation. Then a screening instrument such as the Montreal Cognitive Assessment (MoCa) and classic neuropsychological tests could be applied for the evaluation of executive functions such as: Rey's Auditory-Verbal Learning Test (RAVLT) for auditory memory assessment. short and long term, Trail Making Test A and B for cognitive flexibility, Semantic and Phonological Verbal Fluency Test, Stroop Test for Inhibitory Control, WAIS-III Digit Subtest for auditory and working memory.

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ESTUDO II

EXECUTIVE FUNCTIONS AND MEMORY ASSESSMENT OF PARKINSON'S DISEASE PATIENTS WITH DEEP BRAIN STIMULATION

ABSTRACT

Background: It is known that Parkinson's disease (PD) in addition to affecting movements, also has an impact on the patient's cognition. One of the forms of treatment for PD is the implantation of Deep Brain Stimulation and in this study, we seek to assess the possible impacts of this implant on the patient's cognition. *Objective:* Evaluate the Executive Functions (EF) and Memory of patients with Deep Brain Stimulation (DBS) and to compare with the group of patients with Parkinson's Disease (PD) who did not receive treatment with DBS and with a group control. *Methods:* Instruments of characterization and a battery of neuropsychological tests: MoCA, RAVLT, Trail Making Test A and B parts, Subtest of Digits (WAIS-III), and Stroop Test. The sample was composed of 76 participants subdivided into the three groups, 30 healthy people, 30 diagnosed with PD treated only with drugs, and 16 with PD treated with DBS. *Results:* The groups diagnosed with PD had lower scores when compared to the control group. However, there was no significant difference between these groups. A statistically significant difference occurred between the control group and the PD and DBS groups. *Conclusion:* Due to the tests' results, it can observe that there was no significant cognitive impairment due to surgery or Deep Brain Stimulation in the patients evaluated.

Keywords: Parkinson’s disease, Deep Brain Stimulation, Executive Functions.

1. Introduction

Parkinson's Disease (PD) is the second most frequent neurodegenerative disorder (Noyce et al., 2016) and affects more than 6 million people around the world (Ray Dorsey et al., 2018). Generally, patients between 55 and 65 affect 1% to 2% of the population over 60 but can reach 3.5% of the population in people aged 85-89 (De Lau & Breteler, 2006). The diagnosis of PD is performed using clinical criteria and on the identification of clinical manifestations of motor symptoms. Meantime, known that PD presents a variety of non-motor symptoms involving neuropsychiatric symptoms (Löhle et al., 2009), changes in sleep, behavior, and cognition (Barbosa & Fichman, 2019) and which may lead to dementia (Lenka et al., 2017). In this way, because there are many impairments between cognitive functions as Memory, Executive Functions (EF), visuospatial skills, and language and PD, many studies have been drawn in the current literature (Lenka et al., 2017).

PD treatment most common use of pharmacological interventions with Levodopa replacement. However, due to the degenerative process's progression on the substantia *nigra*, there may be an increase in symptoms and, consequently, an increase in levodopa doses (Park et al., 2017). When drug treatment is no longer sufficient, other alternatives to treat PD are surgical interventions, as Deep Brain Stimulation implantation in the Sub-Thalamic Nucleus (STN) or the Internal Pale Globe (GPi).

Since 1993 with the development of STN in DBS for PD, numerous studies have demonstrated the many motor benefits of stimulation, like in lessening motor fluctuations, reducing dyskinesias, and others that result in improvement in the patients' quality of life. However, over the years, cognitive declines also began to be observed (Pham & Bronstein, 2017). The etiology of cognitive declines is multifactorial, and that can increase with PD's natural progression. However, patients with DBS regardless of the target (STN or GPi) have shown a more cognitive decline than patients undergoing treatment with the best medical therapy compared with processing speed, working memory, and other neuropsychological testing (Rothlind et al., 2015).

It is essential to clarify the electrode's path before generating the stimulation pulse and its location in the brain. The surgery's standard trajectory passes through the dorsolateral prefrontal cortex, subcortical white matter, thalamus, anterior limb of the internal capsule, and the basal nuclei (Tesio et al., 2019). Recently, the caudate nucleus has been implicated in cognitive decline after DBS, as it connects the anterior

part of the prefrontal areas to the motor and pre-motor cortices (Leh et al., 2007), which are part of the corticostriatal circuit, being, as a consequence, closely related to cognition (Kurtis et al., 2017), in particular, to the EF (Tesio et al., 2019).

The possible effects of DBS on patient's cognition are quite studied. The main conclusions point to changes in Verbal Fluency (VF) (Aono et al., 2014; De Gaspari et al., 2006; Lefaucheur et al., 2012; Sáez-Zea et al., 2012). However, these results need consideration with caution because few studies comparing the effect of the stimulation between the on/off stimulation condition. It is also essential to note that some authors defend the idea that VF's decline is due to microlesions resulting from implantation surgery. Therefore, it would be temporary declines (Romann et al., 2017), but this is not a consensus as well. Also, to the limited material relating to EF, PD, and DBS in the world, the implant has been used in several other treatments, including major depression and Obsessive-Compulsive Disorder (OCD), for example, that there are also no further studies on the consequence of use on patient cognition (Blomstedt et al., 2013).

We decided to conduct this research due to the lack of materials available in the researched literature regarding the possible cognitive consequences of DBS's implantation in EF and memory. In this way, this study aimed to evaluate these aspects (EF and memory) in two groups of patients with PD, one treated only with drugs and others treated with DBS, comparing them with the healthy group.

2. Methods

2.1 Participants

The initial sample was composed of 76 people divided into three groups. The first group was composed of 16 patients diagnosed with PD and treated with Deep Brain Stimulation (DBS). The second was composed of 30 patients diagnosed with PD without the implant (treated only with drugs), and the third, a control group of 30 healthy participants without PD and the implant. The last group comprised relatives of patients in the institution and others who made part of a Program to older aging at university. The sample consisted of both sexes, and all groups comprised people over 60 years old and with at least complete high school (12 years of schooling). In groups with PD, there was a male prevalence. The control group had a majority of women who generally accompanied family members to consultations. The time of diagnosis of PD

in the sample was higher than ten years in both groups, 10.1 (4.95; min 3 - max 20) in the PD group and 15.3 (3.73; min 10 - max 23) in the DBS group, which the average time of surgery was 4.1 (2.18; min 1 – max 8) years. Thus, although they are almost the same age, the group with DBS has been diagnosed for much longer than the group without DBS, thus suggesting a more severe form of the disease. The vast majority (14 of the 16 participants) performed the surgery bilaterally in the STN, which may have impacted cognition through the surgery and the possible effects of the stimulation itself (Table 1).

2.2 Instruments

The instruments used to characterize the sample were an Identification Protocol to obtain general patient data as age, clinical history, time since diagnosis, medications used, and sociodemographic information. The Geriatric Depression Scale (Matias et al., 2016) to verify possible levels of depression, The Activities of Daily Living (Lawton & Brody, 1969) to assess the subject's level of independence and The Montreal Cognitive Assessment (MoCA) (Carson et al., 2018) a screening test that aims to evaluate eight cognitive functions (memory, language, capacity for abstraction, visuospatial capacity, and concentration).

For neuropsychological assessment, the instruments used were The Trail Making Test Part A and B (Hamdan & Hamdan, 2009) evaluate the cognitive flexibility, The Verbal Fluency Test (Opasso et al., 2016), "Animals," and "Fruits” in semantic category and F, A and S in phonological fluency. The Stroop Test (Scarpina & Tagini, 2017) lecture of Color and Word and the interference part Color x Word to assess inhibitory control and selective attempting. Rey Auditory-Verbal Learning Test – RAVLT (Cotta et al., 2012) A1 to A5 trials with a List A, B1 with the List B, A6 and A7 trials of later memory. WAIS-III Digit Subtest (Wechsler, 2004) that measures attention, immediate and working memory.

2.3 Procedures

After Ethics Committee Approbation (approval number 3.430.248), we started the data collection conducted in a Parkinson's disease Specialized Association in Curitiba, Brazil, and was held during the waiting period for medical consultation and other specialties at the service. The data collection started explaining the research objectives and collecting the necessary signatures to agree to participate (Informed

Consent Form). After signature, we characterized the sample by identification protocols and applying MoCA Test. Then, depending on the result of this instrument, we proceeded with the testing by applying in sequence: RAVLT, Trail Making Test Part A, and B, Digits Subtest, direct and reverse order, Stroop Test, and finally the part of late memory recovery (RAVLT A7 and recognition).

2.4 Data Analysis

Measures of central tendency (mean) and variability (standard deviation, minimum and maximum value) were used for numerical variables and absolute values for qualitative variables. The research hypothesis was that there would be a significant difference in the test results in the DBS group with the group without PD when considering the evaluation battery of EF and memory. The two-tailed statistical tests used to analyze the results were ANOVA and Dunnett's Pos-hoc Test for all variables, and the groups were paired by age and education to reduce the possible bias in the data. After pairing, the DBS group was composed of 16 people, the PD group by 21, and the control group of 26 participants, totaling a sample of 63 individuals.

3. Results

The demographic characteristics of the sample are shown in Table 1. The results of the EF and memory assessment are disposed in the Table 2.

Table 1. Demographic characterization of the sample

Characteristics	Control (n=26) M (SD)	PD (n=21) M (SD)	DBS (n=16) M (SD)	P-Value
Age	66.7 (6.12)	67.4 (7.42)	61.8 (8.90)	N.S.
Scholarly	14.5 (2.94)	13.3 (3.29)	12.3 (3.42)	N.S.
MoCA	27.4 (1.81)	24.2 (4.37)	23.9 (2.01)	N.S.

M= Mean
SD= Standard Deviation
N.S.= Not significant
Control group men 7, PD group men 14, DBS men 12.

In Table 2, it is possible to observe that, in general, the results of the evaluation showed the best averages for the Control Group (CG), followed by the PD group (without DBS). In the RAVLT instrument, although the best average was healthy and

the PD groups were statistically tied, there was a statistical difference between the control groups when compared to the PD and DBS groups, which were similar. The ANOVA test indicated these differences in the gross ANOVA scores [F (2, 60) = 17.95, p < 0.001], B1 [F (2, 60) = 6.78, p = 0.002], A6 [F (2, 60) = 11.52, p <0.001], and A7 [F (2, 60) = 13.19, p <0.001]. For the Word Recognition test in RAVLT, which also found a difference between the control group to the PD and DBS groups, the Welch test was used [F (2, 31.7) = 15.90, p < 0.001].

Table 2. Memory and Executive Functions assessment results

Assessments	Control (n=26) M (SD)	PD (n=21) M (SD)	DBS (n=16) M (SD)	*P-Value*
Memory				
Gross score	38.6 (8.67)	27 (9.63)	24.6 (5.35)	<0.001
Recognition	12.4 (1.96)	8.6 (4.36)	8.6 (2.66)	<0.001
Trial B1	4.6 (1.6)	3.1 (1.8)	3.2 (1.3)	0.002
Trial A6	7.3 (2.4)	4.4 (2.9)	4.1 (1.9)	< 0.001
Trial A7	7.2 (2.9)	4.3 (3.0)	3.1 (1.6)	<0.001
Executive Functions				
Trial-A	42 (13.89)	62,4 (20.6)	68,8 (20.46)	<0,001
Trial-B	101 (31.3)	143.5 (63.1)	150.1 (47)	0.002
FV Fruits	14.9 (2.94)	12 (3.39)	11.5 (2.63)	0.001
FAS	39.9 (7.47)	29.5 (12.95)	26.3 (10.80)	<0.001
Stroop 3	31.3 (6.89)	40.3 (12.18)	41 (13.25)	0.004

M= Mean
SD= Standard Deviation

On the Trail Making Test in both part A and part B, the times were close between the PD and DBS groups, and the best time was in the control group. The statistical analysis also found a significant difference between the PD and DBS groups (similar) with the control group. In part A of the ANOVA test [F (2, 60) = 13.12, p < 0.001] and in part B [F (2, 60) = 6.97, p = 0.002].

In the Verbal Fluency Tests, the best scores were in the control group, followed by the PD and DBS group. The statistical analysis also pointed out differences between the control group about the PD and DBS groups that were similar. In the Fruit Verbal

Fluency test, the result was ANOVA [F (2, 60) = 8.33, p < 0.001], whereas in FAS [F (2, 60) = 10.26, p < 0.001].

In the Stroop Test, the *color x word* interference part (Stroop 3) took less time for patients with DBS than for the PD group when looking at the averages alone. The control group remained with the highest scores throughout the test. Regarding corrections, it was possible to observe that these occurred more abundantly in the DBS group. The statistical analysis revealed a difference only between the control and PD and DBS, not between those that were similar once again. The result was ANOVA [F (2, 60) = 5.96, p = 0.004].

4. Discussion

The study's objectives were to evaluate the EF and memory of patients with DBS and compare with the group of patients with PD who did not receive treatment with DBS and with a group control. We could observe that the test results' significant differences occurred only in the control group about the groups with PD, and not between the groups with and without DBS as was expected. To VF in our research, the worst score was in the DBS group. Approaching VF in isolation is complicated because it involves other fundamental mechanisms such as language development, for example, and because other cognitive abilities and dysfunctions can easily affect performance, such as lexical search, memory recovery, selection of stimuli, and the executive functioning itself (Højlund et al., 2017). In addition, some studies suggest that DBS implanted in STN and GPi may be involved in VF through the basal-ganglia-thalamocortical network (Jahanshahi, Obeso, Rothwell, et al., 2015; Temel et al., 2005), and other areas such as the dorsolateral prefrontal cortex and the inferior frontal gyrus (Schroeder et al., 2003). We can point out factors that may contribute to the lower performance in this regard in the DBS group, such the natural progression of the disease that involves the motor part of speech, the reduction of dopaminergic medications, which in some studies have shown to be effective in stimulating of this function (Sáez-Zea et al., 2012), the position of the electrodes and the inconclusion about the effects of the surgery itself to the consequences of stimulation (Højlund et al., 2017).

Also, some studies have observed this function when comparing the stimulation frequencies and concluded that when submitted to high frequencies (130 Hz or more) there was a worsening in VF, while patients who submitted to low-frequency

stimulation (less than 130 Hz) showed improvement in the same function (Wojtecki et al., 2006). These authors suggested that the low frequency could activate the frontal regions, while the high frequency could deactivate them. However, we cannot corroborate this idea only because the stimulation frequency was not data raised at the evaluation time.

In the assessment of working memory and also long-term, no significant difference observed between the groups with DBS and PD, but again the worst results were found in the DBS group. Some studies suggest that this result may be related to flow penetration, which could induce a risk of global impairment in cognition (Witt et al., 2013). However, other studies revealed that this relationship could only establish in the six months after surgery, and that, therefore, it could not be conclusive for the cognitive worsening in working memory (Tesio et al., 2019).

The dysfunction of the frontal-basal ganglia circuits caused by PD affects, among other functions, the ability to inhibit impulsive action trends (van Wouwe et al., 2017) that occurs in approximately 17% of PD patients receiving dopamine replacement therapy (Weintraub et al., 2010). Thus, we seek to evaluate this function using the Stroop test classic. As expected, groups with PD had the worst scores on the test compared to the control group. However, the means PD and DBS were very close.

Subsequent research has investigated the potential of the STN in inhibitory control, suggesting that STN failures can result in impulsive acts (Jahanshahi, Obeso, Baunez, et al., 2015). Thus, the implementation of DBS in both STN and GPi can increase the speed of response initiative resulting in the inhibitory control dysfunction observed in patients (Pan et al., 2018), which in our case, it was also the participants who most corrected their incorrect answers in the interference part of the task.

The last function evaluated in our study was cognitive flexibility, which defined as the ability to alternate perspectives, thoughts, thinking styles, and strategies (Diamond, 2013). In this way, cognitive flexibility facilitates the performance of adaptive behavior that is essential for achieving goals, including the ability to control thoughts, emotions, impulses, and behaviors (Gailliot et al., 2007). In PD with the lack of dopamine in the dorsal striatum and the dysfunction in the frontostriatal loops, patients' cognitive deficits could sustain in instruments that assess Cognitive Flexibility could be related to repetitive, excessive and compulsive behaviors that interfere in the daily life

of the patient (Schreiber et al., 2011). The worst results were of the DBS group, corroborate what is reported in the literature so far in this function.

4.1 Limitations

The study's limitations consist mainly of the lack of a pre-test in patients with DBS as a baseline for further comparison and the evaluation of DBS patients under ON/OFF conditions. In addition, the lack of a standardized battery for evaluation prevents them from being compared with data from the literature in general, which presents similar methods. Future researches, it would be exciting monitor patients and after implantation for some years to assess whether there is any difference in cognition that can identify after the healing of the surgery, which also cannot do in this research, in addition to the use of other sources of data such as imaging exams.

5. Conclusion

This study's main objective was to evaluate EF and memory in patients with PD treated with medications to patients treated with DBS. Due to the results obtained in the assessment, it can conclude that there was no significant cognitive impairment due to surgery or Deep Brain Stimulation in the patients evaluated.

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CONCLUSÃO

O Estudo I teve como objetivo analisar os artigos empíricos, considerando seus principais resultados em relação às possíveis consequências do uso do Estimulador Cerebral Profundo (ECP) nos pacientes com Doença de Parkinson. Ao analisar os trabalhos, pudemos concluir que, em geral, os resultados sugerem diminuição da capacidade cognitiva, principalmente na Fluência Verbal, na Velocidade de Processamento e nas características de apatia. As demais funções, como controle inibitório, desenvolvimento global outros aspectos, como características depressivas não apresentaram diferenças significativas nos estudos, permanecendo estáveis ao longo do tempo.

O Estudo II, por sua vez, objetivou avaliar as Funções Executivas e Memória em dois grupos de pacientes com Doença de Parkinson (um grupo tratado apenas com medicamentos e o outro tratado com o ECP), comparando-os entre si e com o grupo saudável. O resultado das avaliações apresentou diferença significativa nas funções de Fluência Verbal, Flexibilidade Cognitiva, Controle Inibitório, Memória Verbal e de Trabalho. Aplicando a análise *Post Hoc,* observou-se que esta diferença ocorreu apenas entre o grupo controle quando comparado aos grupos com DP, mas, nestes, não ocorreu entre o grupo com ECP em relação ao grupo tratado apenas com medicamento. As demais características, como humor e desenvolvimento global, não foram avaliadas.

Deste modo, podemos concluir que a maioria dos estudos analisados na revisão sistemática comparava apenas o grupo ECP em relação ao grupo controle saudável. Apenas 4 estudos compararam pessoas com DP com e sem o ECP – uma comparação mais justa, tendo em vista que a progressão natural da doença por si só já afeta a cognição do paciente. Em nosso estudo, no entanto, buscamos comparar o grupo saudável em relação aos dois grupos com DP (com e sem ECP), tendo em vista essa limitação encontrada nos estudos anteriores. Como limitações do nosso estudo, podemos citar a amostra reduzida no grupo ECP, a falta de uma linha de base destes pacientes e um protocolo que abarque toda a cognição do paciente.

Este trabalho evidenciou a necessidade de mais pesquisas a respeito do tema, sugerindo que novas pesquisas sejam realizadas considerando um acompanhamento maior dos pacientes do grupo ECP, para que os dados obtidos sejam mais robustos e possam ser comparados ao longo do tempo. Além disso, os resultados obtidos

podem contribuir com os profissionais de saúde porque, entre outros fatos, auxiliam no desenho de tratamentos, tendo em vista um prognóstico mais adequado da doença. Ademais, levando em consideração os nossos resultados, é possível propor intervenções melhor direcionadas à estimulação das funções mais afetadas, além de possibilitar maior adesão ao tratamento por parte dos pacientes.

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ANEXOS

ANEXO 1. PARECER CONSUBSTANCIADO DO CEP

UFPR - SETOR DE CIÊNCIAS DA SAÚDE DA UNIVERSIDADE FEDERAL DO PARANÁ -

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Avaliação das funções executivas em pacientes com o implante de Estimulação Cerebral Profunda (ECP)

Pesquisador: Amer Cavalheiro Hamdan

Área Temática:

Versão: 2

CAAE: 15033719.1.0000.0102

Instituição Proponente: Programa de pós-graduação em psicologia

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 3.430.248

Apresentação do Projeto:

Trata-se de projeto de pesquisa intitulado "Avaliação das funções executivas em pacientes com o implante de Estimulação Cerebral Profunda (ECP)" sob a coordenação e orientação do Prof. Dr. Amer Cavalheiro Hamdan, do Programa de Pós-Graduação em Psicologia da Universidade Federal do Paraná, com a participação da mestranda Thayná Laís de Souza Arten Godoy.

Objetivo da Pesquisa:

O presente projeto de pesquisa tem como objetivo geral "avaliar as funções executivas de pacientes com o implante de Estimulação Cerebral Profunda/Deep Brain Stimulation (ECP/DBS)."

Objetivos Específicos

"I. Avaliar os aspectos de fluência verbal, controle inibitório, atenção, memória operacional e flexibilidade cognitiva em pacientes com o implante de ECP;"

"II. Comparar o desempenho de pacientes com o implante de ECP em relação a pacientes sem o implante nos diversos instrumentos aplicados;"

"III. Verificar se existem diferenças significativas entre as amostras."

Avaliação dos Riscos e Benefícios:

Quanto aos riscos, os pesquisadores informam "possível desconforto inicial ao ver-se diante de um ambiente de testagem e análise."

"A probabilidade de os riscos ocorrerem é muito baixa, mas caso ocorram será minimizado pela

Endereço: Rua Padre Camargo, 285 - 1º andar
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ANEXO 2. TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Nós, **Amer Cavalheiro Hamdan** e **Thayná Laís de Souza Arten Godoy** da Universidade Federal do Paraná, estamos convidando o (a) senhor (a), participantes de mais de 18 anos **com ou sem** o implante de **Estimulação Cerebral Profunda (ECP)** a participar da pesquisa intitulada **Avaliação das funções executivas em pacientes com o implante de Estimulação Cerebral Profunda/Deep Brain Stimulation (ECP/DBS)**. Esta pesquisa pretende estudar a relação das funções executivas e o implante de ECP. As funções executivas são habilidades que trabalham conjuntamente para direcionar nossos comportamentos e incluem a memória, o planejamento, a solução de problemas, o controle, entre outros. Esta pesquisa é importante para entender se as pessoas com Parkinson que tenham o implante aprendem de modo diferente das que fazem apenas o uso de remédios.

a) O objetivo desta pesquisa é analisar as funções executivas de pacientes com o implante de Estimulação Cerebral Profunda
b) Caso o (a) senhor (a) senhora participe da pesquisa, será necessário conseguir responder a questionários pessoais, e a 5 testes de avaliação neuropsicológica.
c) Para tanto o (a) senhor (a) deverá comparecer à Associação Paranaense de Portadores de Parkinsonismo, localizado à Avenida Silva Jardim, nº3180, no dia combinado com a pesquisadora para preencher os questionários e fazer as avaliações, que devem levar aproximadamente 40 minutos.
d) É pouco provável, mas é possível que o (a) senhor (a) experimente algum desconforto, principalmente relacionado ao cansaço.
e) Alguns riscos relacionados ao estudo podem ser constrangimento e desconforto relacionado ao ambiente da testagem.
f) Os benefícios esperados com essa pesquisa são indiretos. O (a) senhor (a) poderá contribuir para o conhecimento sobre o impacto do ECP nas funções executivas.
g) Os pesquisadores Amer Cavalheiro Hamdan e Thayná Laís de Souza Arten, responsáveis por este estudo poderão ser localizados Universidade Federal do Paraná no Departamento de Psicologia, à Praça Santos Andrade 50, no telefone (41) 33102644, no site www.psicologia.ufpr.br, no horário 8-18h e nos e-mails amerc.hamdan@gmail.com e thayarten@hotmail.com, para esclarecer eventuais dúvidas que o (a) senhor (a) possa ter e fornecer-lhe as informações que queira, antes, durante ou depois de encerrado o estudo.
h) A sua participação neste estudo é **voluntária** e se o (a) senhor (a) não quiser mais fazer parte da pesquisa, poderá desistir a qualquer momento e solicitar que lhe devolvam este Termo de Consentimento Livre e Esclarecido assinado.
i) As informações relacionadas ao estudo poderão ser conhecidas por pessoas autorizadas [pesquisadores e colaboradores]. No entanto, se qualquer informação for divulgada em relatório ou publicação, isto será feito de forma codificada, para que a **sua identidade seja preservada e mantida sua confidencialidade.**
j) O material obtido (questionários e avaliações) será utilizado unicamente para essa pesquisa e será destruído ao término do estudo, no prazo de 5 anos.
k) As despesas necessárias para a realização da pesquisa (impressões de questionários, escalas e avaliações) não são de sua responsabilidade e o (a) senhor (a) **não receberá qualquer valor em dinheiro pela sua participação**, que não terá custo nenhum.
l) O (a) senhor (a) terá a garantia de que problemas tais como desconforto ou mal-estar decorrentes do estudo serão tratados no Centro de Psicologia Aplicada da UFPR.
m) Quando os resultados forem publicados, não aparecerá o seu nome, mas sim um código.
n) Se o (a) senhor (a) tiver dúvidas sobre seus direitos como participante de pesquisa, você pode contatar também o Comitê de Ética em Pesquisa em Seres Humanos (CEP/SD) do Setor de Ciências da Saúde da Universidade Federal do Paraná, pelo telefone 3360-7259. O Comitê de Ética em Pesquisa é um órgão colegiado multi e transdisciplinar que existe nas instituições que realizam pesquisa envolvendo seres humanos no Brasil e foi criado com o objetivo de proteger os participantes de pesquisa, em sua integridade e dignidade, e assegurar que as pesquisas sejam desenvolvidas dentro de padrões éticos (Resolução nº 466/12 Conselho Nacional de Saúde).

Eu,_____li esse Termo de Consentimento e compreendi a natureza e objetivo do estudo do qual concordei em participar. A explicação que recebi menciona os riscos e benefícios. Eu entendi que sou livre para interromper minha participação a qualquer momento sem justificar minha decisão e sem qualquer prejuízo para mim. Fui informado que serei atendido sem custos para mim se eu apresentar algum dos problemas relacionados no item L.

Eu concordo voluntariamente em participar deste estudo.

Curitiba,_____de_____de 2019.

[Assinatura do Participante de Pesquisa]

_____

_____

[Assinatura do Pesquisador Responsável ou quem aplicou o TCLE]

ANEXO 3. PROTOCOLO DE IDENTIFICAÇÃO

I. Identificação

Nome:	
Sexo:	Escolaridade (em anos):
Profissão:	Aposentado: ( ) Sim ( ) Não
Situação previdenciária: ( ) Privada ( ) Pública	Desenvolve alguma outra atividade produtiva remunerada? ( ) Sim ( ) Não
Serviço de Saúde: Público ( ) Privado ( )	
Idade:	Data de Nascimento:
Naturalidade:	Estado: País:
Estado Civil: ( ) Casado ( ) Solteiro ( ) Viúvo ( ) Separado ( ) Outros	
Quantos filhos ____	Filhas _____
Informante (se for o caso):	Parentesco:
Endereço atual:	

V. História pessoal atual e pregressa

1. Tabagismo.....( ) sim ( ) não
Número de cigarros/dia: _____ Duração/anos:
Outros:_____

2. Etilismo.....( ) sim ( ) não
Tipo de bebida: _____ Dose diária: _____ Duração/anos: -

3. Sexualidade
Vida sexual ativa .....( ) sim ( ) não
Parceiro.....( ) sim ( ) não

4. Sono
Distúrbio do sono.....( ) sim ( ) não
( ) insônia ( ) hipersonia
O transtorno do sono interfere com as atividades do dia .....( ) sim ( ) não
O paciente acorda muito cedo ou muito tarde.....( ) sim ( ) não
O paciente demora a adormecer... .....( ) sim ( ) não
O paciente tem despertares noturnos .....( ) sim ( ) não
Noctúria ( ) Pesadelos ( ) Preocupação ( ) Dispnéia ( ) Dor ( )
Roncos ( ) Mioclonia das pernas ( )
Os cochilos diurnos são.....
( ) Freqüentes ( ) Pouco freqüentes mas longos ( ) Ausentes

ANEXO 4 – QUESTIONÁRIO BRASIL

P.XX Agora vou fazer algumas perguntas sobre itens do domicílio para efeito de classifica econômica. Todos os itens de eletroeletrônicos que vou citar devem estar funcionando, inclui os que estão guardados. Caso não estejam funcionando, considere apenas se tiver intenção consertar ou repor nos próximos seis meses.

INSTRUÇÃO: Todos os itens devem ser perguntados pelo entrevistador e respondidos p entrevistado.
Vamos começar? No domicílio tem_____ (LEIA CADA ITEM)

		QUANTIDADE QUE POSSUI			
ITENS DE CONFORTO	NÃO POSSUI	1	2	3	4+
Quantidade de automóveis de passeio exclusivamente para uso particular					
Quantidade de empregados mensalistas, considerando apenas os que trabalham pelo menos cinco dias por semana					
Quantidade de máquinas de lavar roupa, excluindo tanquinho					
Quantidade de banheiros					
DVD, incluindo qualquer dispositivo que leia DVD e desconsiderando DVD de automóvel					
Quantidade de geladeiras					
Quantidade de *freezers* independentes ou parte da geladeira duplex					
Quantidade de microcomputadores, considerando computadores de mesa, laptops, notebooks e netbooks e desconsiderando tablets, palms ou smartphones					
Quantidade de lavadora de louças					
Quantidade de fornos de micro-ondas					
Quantidade de motocicletas, desconsiderando as usadas exclusivamente para uso profissional					
Quantidade de máquinas secadoras de roupas, considerando lava e seca					

A água utilizada neste domicílio é proveniente de?	
1	Rede geral de distribuição
2	Poço ou nascente
3	Outro meio

Considerando o trecho da rua do seu domicílio, você diria que a rua é:	
1	Asfaltada/Pavimentada
2	Terra/Cascalho

Qual é o grau de instrução do chefe da família? Considere como chefe da família a pessoa que contribui com a maior parte da renda do domicílio.

Nomenclatura atual	Nomenclatura anterior
Analfabeto / Fundamental I incompleto	Analfabeto/Primário Incompleto
Fundamental I completo / Fundamental II incompleto	Primário Completo/Ginásio Incompleto
Fundamental completo/Médio	Ginásio Completo/Colegial

ANEXO 5 - ESCALA DE DEPRESSÃO GERIÁTRICA

ESCALA DE DEPRESSÃO GERIÁTRICA
GERIATRIC DEPRESSION SCALE (short Form)

Instruções: Eu vou ler algumas frases para avaliar como o Sr (a) se sentiu na última semana. Responda apenas sim ou não:

Nº	Questão	Resposta	Pont.
1	Você está satisfeito, de modo geral, com sua vida	SIM / **NÃO**	
2	Você abandonou muitas atividades ou interesses de que gostava?ĩ	**SIM** / NÃO	
3	Você acha que sua vida está vazia?	**SIM** / NÃO	
4	Você tem ficado aborrecido com frequência?	**SIM** / NÃO	
5	Você está de bom-humor a maior parte do tempo?	SIM / **NÃO**	
6	Você teme que algo ruim aconteça a você?	**SIM** / NÃO	.
7	Você se sente feliz a maior parte do tempo?	SIM / **NÃO**	
8	Você se sente frequentemente desamparado?	**SIM** / NÃO	
9	Você prefere ficar em casa do que sair e fazer coisas novas?	**SIM** / NÃO	.
10	Você acha que tem mais problemas de memória que a maioria?ĩ	**SIM** / NÃO	
11	Você acha que é maravilhoso estar vivo agora?	SIM / **NÃO**	
12	Você se sente inútil do jeito que está hoje em dia?	**SIM** / NÃO	
13	Você se sente cheio de energia?	SIM / **NÃO**	
14	Você sente sem esperança a situação em que você se encontra agora?ĩ	**SIM** / NÃO	
15	Você acha que a maioria das pessoas está melhor que você?	**SIM** / NÃO	
		TOTAL	

Pontuação:
Os escores inferiores a 5 são normais: entre 5 e 10 indicam depressão leve a moderada; escores maiores que 10 indicam depressão grave.

Fonte: Sheikh, J. I.& Yesavage, J. A. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. Clinical Gerontology. 1986, 5(1/2): 165-173.
Yesavage, J. A.Geriatric Depression Scale. Psychopharmacol Bull. 1988, 24(4):709-711.

ANEXO 6 – ATIVIDADES DA VIDA DIÁRIA

Atividades de Vida Diária Instrumentais segundo Lawton-Brody			
Atividade de vida diária	Sem ajuda	Com ajuda parcial	Incapaz
Você é capaz de preparar as suas refeições?			
Você é capaz de tomar os seus remédios?			
Você é capaz de fazer compras?			
Você é capaz de controlar o seu dinheiro?			
Você é capaz de usar o telefone?			
Você é capaz arrumar a sua casa?			
Você é capaz de lavar a sua roupa?			
Você é capaz de fazer pequenos trabalhos domésticos?			
Você é capaz de sair de casa sozinho para lugares mais distantes?			
Você é capaz de sair de condução?			

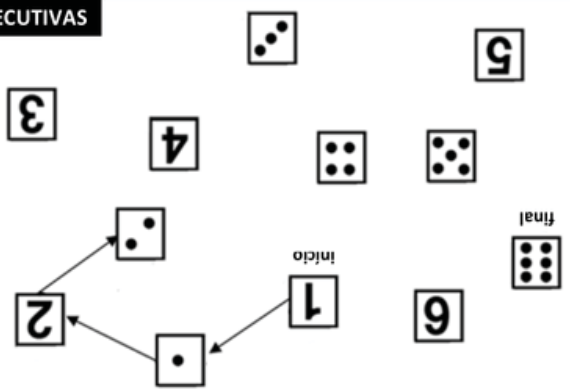
ANEXO 7 - MONTREAL COGNITIVE ASSESSMENT (MOCA)

Nome _____
Sexo _____ Idade _____
Escolaridade _____ Data _____
Administrado por _____

MONTREAL COGNITIVE ASSESSMENT - BASIC (MoCA-B)

Versão Brasileira

FUNÇÕES EXECUTIVAS — PONTUAÇÃO



HORÁRIO DE INÍCIO _____

(/1)

EVOCAÇÃO IMEDIATA — Não pontua

	VIOLÃO	SOFÁ	JOELHO	AZUL	COLHER
1ª tentativa					
2ª tentativa					

Realize 2 tentativas mesmo que a 1ª tenha sido bem sucedida

FLUÊNCIA — Diga o maior número de **FRUTAS** que conseguir em 1 minuto — Nº _____ (/2)

1 ..... 2 ..... 3 ..... 4 ..... 5 ..... 6 .....
7 ..... 8 ..... 9 ..... 10 ..... 11 ..... 12 .....
13 ..... 14 ..... 15 ..... 16 ..... 17 ..... 18 .....

2 pontos se ≥ 13
1 ponto se 8-12
0 pontos se ≤ 7

ORIENTAÇÃO — [ ] horário (± 2h) [ ] dia da semana [ ] mês [ ] ano [ ] local [ ] cidade (/6)

CÁLCULO — Diga 3 formas de pagar por um produto que custa R$ 13: usando moedas de R$ 1, notas de R$ 5 e notas de R$ 10. (/3)

[ ] 1. ..... [ ] 2. ..... [ ] 3. .....

ABSTRAÇÃO — A que categorias essas palavras pertencem ? (e.g. laranja - banana = frutas) (/3)

[ ] trem - barco [ ] norte - sul [ ] tambor - flauta

EVOCAÇÃO TARDIA — Pontos são atribuídos às evocações livres (1 ponto para cada item) (/5)

	VIOLÃO	SOFÁ	JOELHO	AZUL	COLHER
Evocação livre	[ ]	[ ]	[ ]	[ ]	[ ]
Evocação com pista	[ ] instrumento musical	[ ] peça de mobília	[ ] parte do corpo	[ ] cor	[ ] utensílio de cozinha
Reconhecimento	[ ] violão/piano/tambor	[ ] mesa/sofá/cama	[ ] perna/joelho/braço	[ ] azul/marrom/verde	[ ] garfo/faca/colher

PERCEPÇÃO VISUAL — Identifique as figuras. Máximo de 60 segundos. *(folha de estímulos)* (/3)

tesoura	camiseta	banana	abajur	vela
relógio	xícara	folha	chave	colher

3 pontos se 9-10
2 pontos se 6-8
1 ponto se 4-5
0 pontos se 0-3

NOMEAÇÃO — Identifique os animais. *(folha de estímulos)* [ ] zebra [ ] pavão [ ] tigre [ ] borboleta (/4)

ATENÇÃO — Diga os números nos **círculos**. *(folha de estímulos)* 1 5 8 3 9 2 0 3 9 4 0 2 1 6 8 7 4 6 7 5 — Nº DE ERROS _____ Não pontua se ≥ 2 erros (/1)

Diga os números nos **círculos e quadrados**: *(folha de estímulos)*
3 8 5 1 3 0 2 9 2 0 4 9 7 8 6 1 5 7 6 4
1 5 8 3 9 2 0 3 9 4 0 2 1 6 8 7 4 6 7 5

Nº DE ERROS _____
2 pontos se ≤ 2 erros
1 ponto se 3 erros
0 pontos se ≥ 4 erros

(/2)
HORÁRIO FINAL _____

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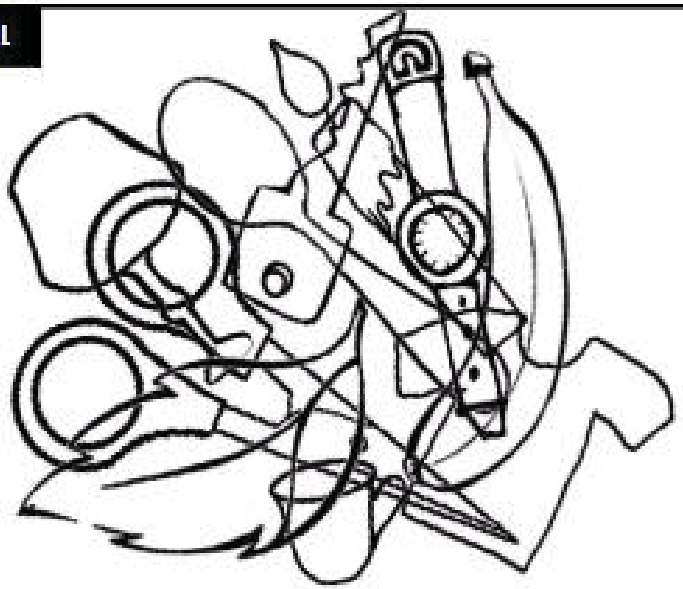
PONTUAÇÃO TOTAL (/30)
Some 1 ponto se escolaridade < 4 anos + 1 ponto se analfabeto(a)

ANEXO 7 - MONTREAL COGNITIVE ASSESSMENT (MOCA)

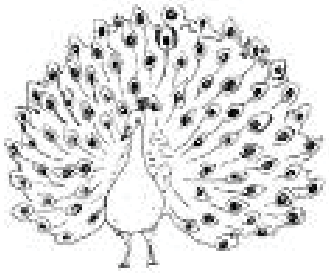
MONTREAL COGNITIVE ASSESSMENT - BASIC
(MoCA-B)

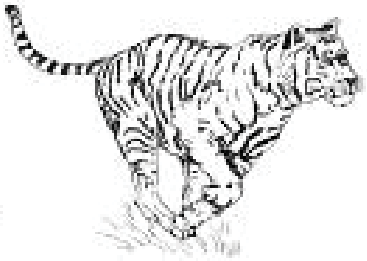
FOLHA DE ESTÍMULOS

PERCEPÇÃO VISUAL



NOMEAÇÃO





ATENÇÃO

1 5 8 3 9 2 0 3 9 4 0 2 1 6 8 7 4 6 7 5

3 8 5 1 3 0 2 9 2 0 4 9 7 8 6 1 5 7 6 4

1 5 8 3 9 2 0 3 9 4 0 2 1 6 8 7 4 6 7 5

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ANEXO 8 – TESTES NEUROPSICOLÓGICOS (RAVLT)

TESTE DE APRENDIZAGEM AUDITIVO-VERBAL DE REY – RAVLT

Nome: _____

Examinador: _____ Data _____

Escola: Nascimento: _____

LISTA A	1	2	3	4	5	LISTA B	B1	A6	A7	LISTA A
BALÃO						CARRO				BALÃO
FLOR						MEIA				FLOR
SALA						PATO				SALA
BOCA						FOGO				BOCA
CHUVA						SOFÁ				CHUVA
MÃE						DOCE				MÃE
CIRCO						PONTO				CIRCO
PEIXE						VASO				PEIXE
LUA						LIVRO				LUA
CORPO						PORTA				CORPO
CESTA						INDIO				CESTA
LÁPIS						VACA				LÁPIS
MESA						ROUPA				MESA
CHAPÉU						CAIXA				CHAPÉU
MILHO						RIO				MILHO

Total A1 a A5 – (5 x A1): _____

B1/A1: _____

A6/A5: _____

A7/A6: _____

LISTA PARA O RECONHECIMENTO:

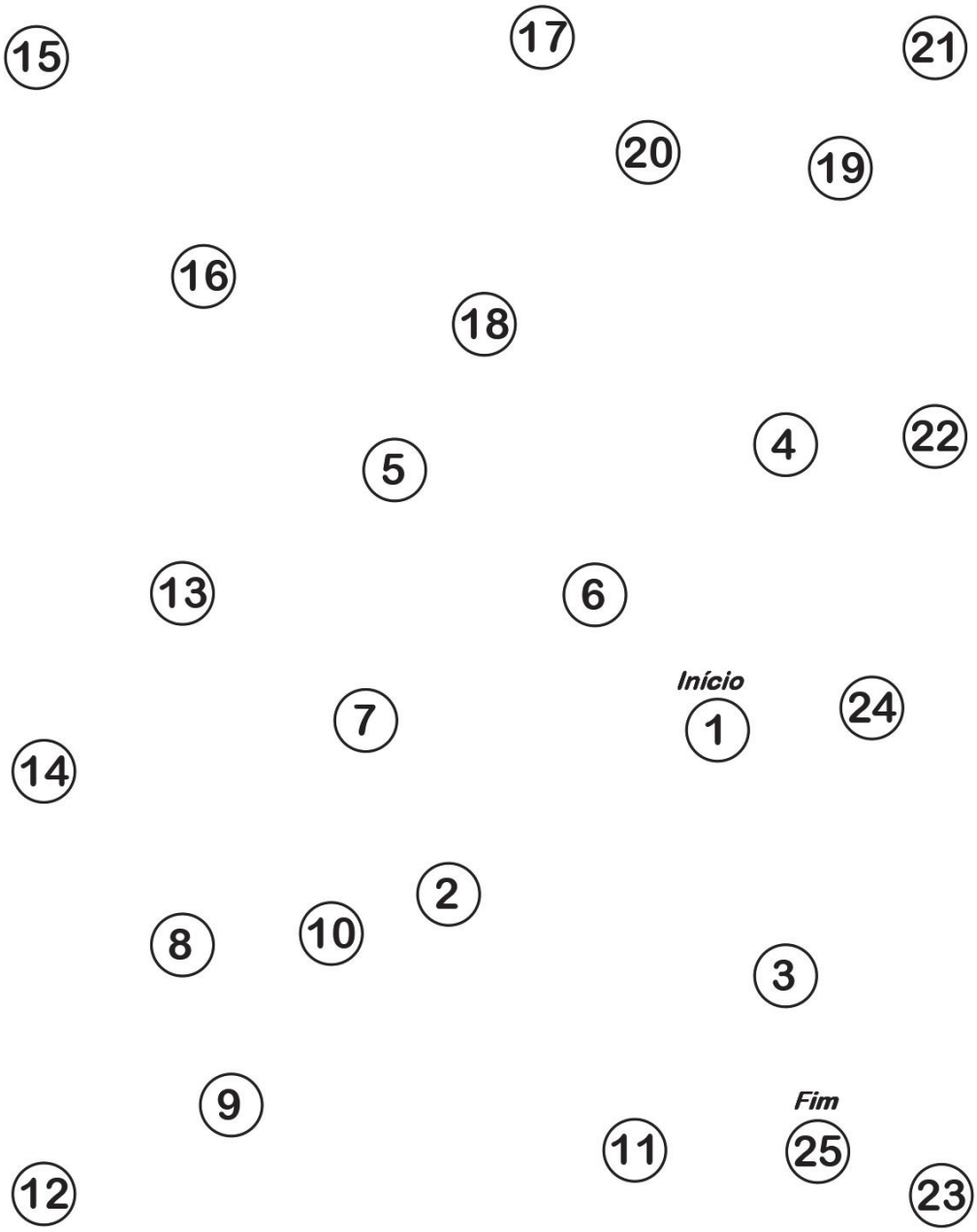
LUA (A)	COR (FA)	PONTO (B)	VACA (B)	MEIA (B)
GALO (SB)	INDIO (B)	**FLOR (A)**	**SALA (A)**	JARDIM (SA)
FOGO (B)	**BALÃO (A)**	ISCA (SA)	FILHO (SA /FA)	SOFA (B)
CHAPEU (A)	RUA (FA)	**BOCA (A)**	BOLA (SA)	FESTA (FA)
VASO (B)	PLANTA (SA/SB)	**CHUVA (A)**	AULA (SA)	DOCE (B)
MESA (A)	ROUPA (B)	CAIXA (B)	**MILHO (A)**	SOL (SA)
LAGO (SB)	**CORPo (A)**	ROSA (SA)	BOLO (SB)	**MAE (A)**
PORTA (B)	PATO (B)	**CIRCO (A)**	**PEIXE (A)**	PAPEL (FA)
DENTE (SA)	**CESTA (A)**	CARRO (B)	BOTAO (FA)	MAR (SB)
RIO (B)	LIVRO (B)	**LAPIS (A)**	LEITE (SA)	VENTO (FB)

A = palavra da lista A.; B = Palavra da lista B; SA = Semanticamente semelhante a palavra da lista A; SB = Semanticamente semelhante a palavra da lista B; FA = fonologicamente semelhante a palavra da lista A; FB = fonologicamente semelhante a palavra da lista B;

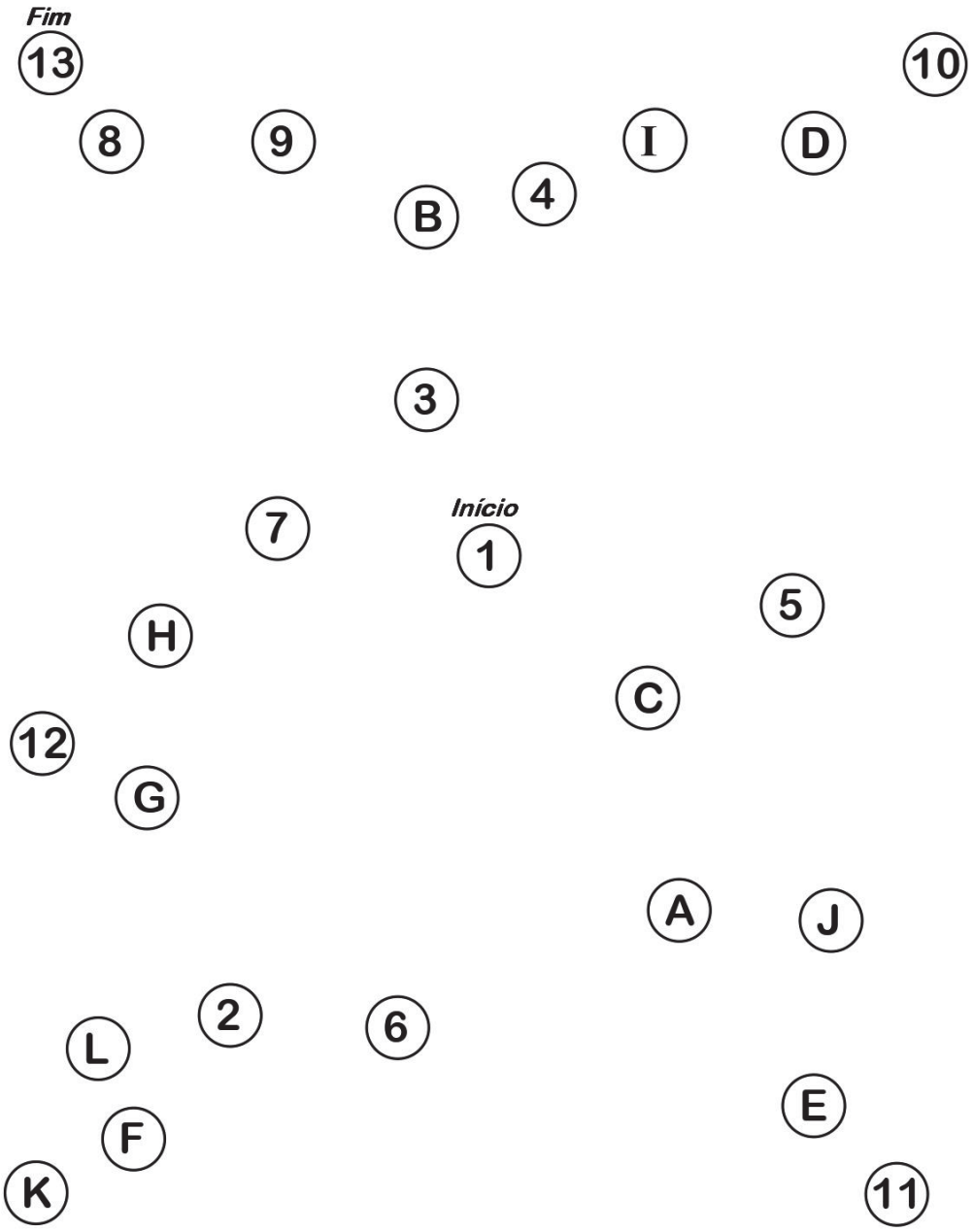
RECONHECIMENTO:

Número de palavras-alvo corretamente identificadas

ANEXO 8 – TESTES NEUROPSICOLÓGICOS (TRILHAS A)



ANEXO 8 – TESTES NEUROPSICOLÓGICOS (TRILHAS B)



ANEXO 8 – TESTES NEUROPSICOLÓGICOS (Subteste de Dígitos do WAIS III)

SUBTESTE DÍGITOS WAIS (III) – Ordem Direta

Eu vou dizer alguns números. Escute cuidadosamente e quando eu acabar, o Sr (a) deve repeti-los na mesma ordem.

Interromper caso ocorra erro nas duas tentativas de um mesmo item. Prosseguir com a Ordem Inversa.

Dígitos Ordem Direta			Pontos Tentativa (0 ou 1)	Pontos Itens (0, 1 ou 2)
1.	1	1 – 7		
	2	6 – 3		
2.	1	5 - 8 – 2		
	2	6 – 9 – 4		
3.	1	6 – 4 – 3 – 9		
	2	7 – 2 – 8 – 6		
4.	1	4 – 2 – 7 – 3 – 1		
	2	7 – 5 – 8 – 3 – 6		
5.	1	6 – 1 – 9 – 4 – 7 – 3		
	2	3 – 9 – 2 – 4 – 8 – 7		
6.	1	5 – 9 – 1 – 7 – 4 – 2 – 8		
	2	4 – 1 – 7 – 9 – 3 – 8 – 6		
7.	1	3 – 8 – 2 – 9 – 5 – 1 – 7 – 4		
	2	5 – 8 – 1 – 9 – 2 – 6 – 4 – 7		
8.	1	2 – 7 – 5 – 8 – 6 – 2 – 5 – 8 – 4		
	2	7 – 1 – 3 – 9 – 4 – 2 – 5 – 6 – 8		
		Total de Pontos Ordem Direta (Máximo = 16)		

ANEXO 8 – TESTES NEUROPSICOLÓGICOS (Subteste de Dígitos do WAIS III - continuação)

SUBTESTE DÍGITOS WAIS (III) – Ordem Inversa

Agora eu vou dizer mais alguns números, mas desta vez, quando eu parar, quero que você os repita na ordem inversa. Por exemplo, se eu dizer 7 – 1 – 9, o que você/Sr/Sra deverá dizer?

Se o examinando responder corretamente (9 – 1 – 7), dizer: **Muito bem.**

Prosseguir com a tentativa 1 do item 1.

Entretanto, se o examinando responder incorretamente, dar a resposta correta e dizer: **Não. Você/Sr/Sra deveria dizer 9 – 1 – 7. Eu disse 7 – 1 – 9, então para falar de trás para frente, você/ser/ara deveria dizer 9 – 1 – 7. Agora tente estes números. Lembre-se que você falar os números na ordem inversa: 3 – 4 – 8.**

Não oferecer nenhuma ajuda neste exemplo ou em qualquer outro item do teste. Independentemente do examinando acertar (ou seja, responder 8 – 4 – 3), passar para a tentativa 1 do item 1.

Interromper caso ocorra erro nas duas tentativas do mesmo item.

		Dígitos Ordem Inversa	Pontos Tentativa (0 ou 1)	Pontos Itens (0, 1 ou 2)
1.	1	2 – 4		
	2	5 – 7		
2.	1	4 – 1 – 5		
	2	6 – 2 – 9		
3.	1	3 – 2 – 7 – 9		
	2	4 – 9 – 6 – 8		
4.	1	1 – 5 – 2 – 8 – 6		
	2	6 – 1 – 8 – 4 – 3		
5.	1	5 – 3 – 9 – 4 – 1 – 8		
	2	7 – 2 – 4 – 8 – 5 – 6		
6.	1	8 – 1 – 2 – 9 – 3 – 6 – 5		
	2	4 – 7 – 3 – 9 – 1 – 2 – 8		
7.	1	7 – 2 – 8 – 1 – 9 – 6 – 5 – 3		
	2	9 – 4 – 3 – 7 – 6 – 2 – 5 – 8		
			Total de Pontos Ordem Inversa (Máximo = 14)	

Ordem Direta		Ordem Inversa		Máximo = 30
	+		=	

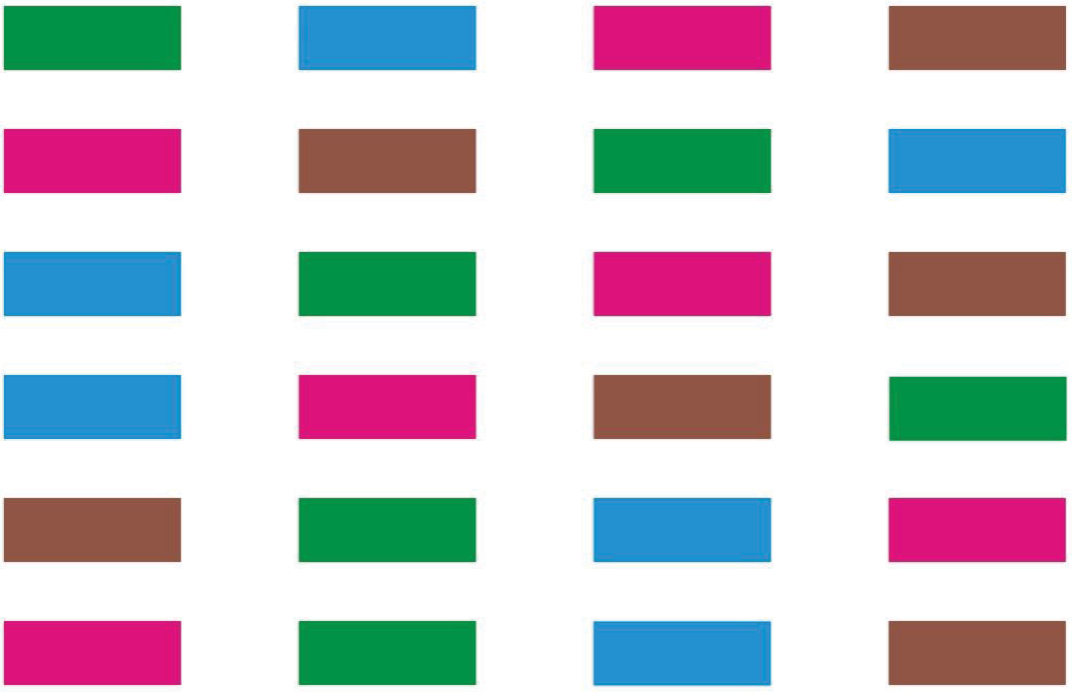
ANEXO 8 – TESTES NEUROPSICOLÓGICOS (Teste de Fluência Verbal)

FLUÊNCIA VERBAL

NOME:_____DATA_____

Animais	Frutas	F	A
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

ANEXO 8 – TESTES NEUROPSICOLÓGICOS (Teste de Stroop parte 1 e 2)



CADA NUNCA HOJE TUDO

NUNCA HOJE TUDO CADA

CADA NUNCA TUDO HOJE

NUNCA CADA TUDO HOJE

TUDO NUNCA CADA HOJE

TUDO HOJE NUNCA CADA

ANEXO 8 – TESTES NEUROPSICOLÓGICOS (Teste de Stroop parte 3)