PONTIFÍCIA UNIVERSIDADE CATÓLICA DO RIO GRANDE DO SUL
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PROGRAMA DE PÓS-GRADUAÇÃO EM PSICOLOGIA
MESTRADO EM PSICOLOGIA

# FUNCIONAMENTO EXECUTIVO NO TRAUMATISMO CRANIOENCEFÁLICO: ESTUDOS NEUROPSICOLÓGICOS DE DESEMPENHO E DE NEUROIMAGEM ESTRUTURAL

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Dissertação de Mestrado realizada no Programa de Pós-Graduação em Psicologia da Pontifícia Universidade Católica do Rio Grande do Sul, como parte dos requisitos para a obtenção do título de Mestre em Psicologia. Área de Concentração em Cognição Humana

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Porto Alegre, janeiro de 2013

# RESUMO GERAL

Os indivíduos que sofrem TCE podem ter grande incapacidade funcional. A maior parte dessas disfunções tem relação com manifestações clínicas de prejuízos cognitivos, o que cria diversas perdas em diferentes áreas, tais como, trabalho, autonomia e como conseqüência uma qualidade de vida não apenas o indivíduo, mas também todos aqueles que estão envolvidos com ele. Neste contexto, os estudos têm discutido a heterogeneidade das manifestações clínicas do TCE, ainda um grande desafio em ensaios clínicos e estudos de caracterização como um todo. A maior lacuna na área de neuropsicologia clínica e cognitiva é a compreensão das funções executivas (FE) pós-TCE e de seus correlatos neurais. É de grande interesse integrar a avaliação neuropsicológica, os métodos clássicos clínicos da neuropsicologia, e técnicas avançadas de neuroimagem. A presente dissertação visou ainvestigar FE no contexto clínico do TCE. Dois estudos foram realizados nesta dissertação. O primeiro estudo avaliou o perfil de funcionamento executivo de uma amostra de TCE. Este panorama executivo foi baseado em uma extensa avaliação neuropsicológica com foco principal em FE. Os resultados apontaram três perfis diferentes de FE: o Cluster 1 foi caracterizado por dificuldades em velocidade de processamento, fluência verbal fonêmica e inibição; o Cluster 2 foi formado por múltiplos déficits em FE, tais como, de velocidade de processamento, memória de trabalho, planejamento, flexibilidade cognitiva e fluência verbal; finalmente o Cluster 3 não apresentou dificuldades executivas objetivamente examinadas. O segundo estudo investigou o desempenho em tarefas de FE e índices de volumetria e de espessura cortical em regiões de interesse por seu correlato com FE em dois casos de adultos com TCE leve com diferentes escolaridades. O paciente com alta escolaridade superou o paciente de baixa escolaridade em quatro variáveis das FE e em diferentes estruturas de volume cerebral e espessura cortical. Os resultados sugerem que a educação parece ser uma característica de reserva cognitiva no TCE leve. Juntos, esses estudos contribuem com respostas a uma pergunta importante sobre possíveis soluções para a heterogeneidade neuropsicológica do TCE. Nossos achados reforçam a relevância de intervenções em grupo constituído de acordo com variáveis socioculturais e perfis cognitivos. Para a formação de subgrupos clínicos de TCE, seu funcionamento executivo parece ser sido a principal variável, na medida em que não houve diferenças quanto a fatores socioculturais,m individuais nem clínicos. No entanto, quando se considera análise de casos,

variáveis socioculturais parecem importantes para o desempenho cognitivo e para a reorganização cerebral no TCE leve.

**Palavras-chave:** traumatismo cranioencefálico, funções executivas, clusters, estudos de caso, testes neuropsicológicosheterogeneidade, recomendações de ensaios clínicos.

**Área conforme classificação CNPq**: 7.07.00.00-1 - Psicologia

**Sub-área conforme classificação CNPq**: 70.6000

# GENERAL ABSTRACT

TBI individuals may present great functional disability. Most of these dysfunctions is related to clinical manifestations of cognitive impairment, which creates several losses in different areas, such as work, autonomy and, as a consequence, on the quality of life of individuals and their relatives. In this context, studies have discussed the heterogeneity of clinical manifestations in TBI, which challenges research of clinical trials and characterization studies as a whole. One of the main issues in the field of clinical and cognitive neuropsychology is the understanding of executive functions (EF) post-TBI and their neural correlates. For this reason, it is of great interest to integrate neuropsychological evaluation, classical methods of clinical neuropsychology and neuroimaging. This dissertation aimed to investigate EF in TBI individuals by means of two studies. The first study investigated the profile of executive functioning in a sample of TBI individuals. This study included an extensive neuropsychological evaluation with a primary focus in FE. Results showed three different profiles of FE: Cluster 1 was characterized by difficulties in processing speed, phonemic verbal fluency and inhibition; Cluster 2 was formed by multiple deficits in FE, such as processing speed, working memory, planning, cognitive flexibility and verbal fluency; finally Cluster 3 had no or very mild difficulties on the EF examined. The second study investigated the two cases of adults with mild TBI with different education levels on EF performance and brain structures volumetry and cortical thickness. The patient with high education surpassed the patient with low education in four variables of FE and different structures of brain volume and cortical thickness. The results suggest that education seems to be a feature of cognitive reserve in mild TBI. Together, these studies contribute for answers to an important question about heterogeneity of TBI and clinical studies. Our findings reinforce the importance of group interventions constituted according to sociocultural variables and cognitive profiles, rather than sociocultural, individual and clinical variables. However, when considering case analysis, sociocultural variables seem to be important for cognitive performance and brain reorganization in mild TBI.



**Keywords:** traumatic brain injury, executive functions, cluster analysis, case studies, heterogeneity, clinical trials recommendations

**Área conforme classificação CNPq**: 7.07.00.00-1 - Psicologia

**Sub-área conforme classificação CNPq**: 70.6000

SUMÁRIO

# 1. INTRODUÇÃO

O tema central abordado pela presente dissertação de mestrado compreende a avaliação neuropsicológica das funções executivas (FE) em pacientes adultos com traumatismo cranioencefálico (TCE) e seus correlatos estruturais cerebrais. Os estudos aqui apresentados fazem parte de dois projetos guarda-chuvas ("Avaliação e reabilitação neuropsicológica de pacientes com Acidente Vascular Encefálico ou Traumatismo Cranioencefálico" e "Reorganização cerebral no envelhecimento, na escolarização, no AVC: evidências de avaliação e reabilitação neuropsicológicas com técnicas avançadas de neuroimagem") coordenados pela orientadora da dissertação e aprovados pela Comissão Científica da Faculdade de Psicologia e pelo Comitê de Ética em Pesquisa da Pontifícia Universidade Católica do Rio Grande do Sul, respectivamente, sob nºs 10/05134 (Anexo A) e 10/05148 (Anexo B).

Para essa finalidade, dois estudos empíricos foram desenvolvidos com o objetivo de investigar as FE em pacientes adultos com TCE a partir de métodos de avaliação comportamental (Estudo 1) e de neuroimagem estrutural associada à avaliação comportamental de desempenho e de funcionalidade (Estudo 2). Mais especificamente, o primeiro estudo buscou caracterizar os perfis de FE em uma amostra de pacientes com TCE e verificar se há influência de variáveis individuais, clínicas e socioculturais na formação desses perfis. O segundo estudo investigou dois casos de pacientes com TCE leve crônico, pareados quanto à gravidade e idade e com diferentes níveis de escolaridade no desempenho das FE e seus correlatos neuroanatômicos. Ambos os estudos estão inseridos dentro de dois temas de crescente interesse na neuropsicologia: (1) a compreensão dos componentes das FE em populações neurológicas (TCE) - evidências de associações e dissociações contribuem para a compreensão da dinâmica de funcionamento e consequentemente para a construção teórica e empírica das FE; (2) o papel de variáveis individuais, clínicas e socioculturais na cognição e suas implicações em casos de adultos com lesão cerebral – cada vez mais a compreensão sobre reserva cognitiva e cerebral se torna necessária, porém essa temática ainda carece de investigação em populações com lesão cerebral adquirida, na medida em que está mais desenvolvida no estudo de quadros neurodegenerativos. A seguir, serão exploradas as temáticas de interesse que embasam a realização dos dois estudos.

## 1.1. Epidemiology, clinical aspects, and neuropathology of traumatic brain injury

Traumatic brain injury (TBI) is one of the leading causes of disability among young individuals (Selassie et al., 2008). Consequences of disability may vary in a large spectrum that includes unemployment (McCrimmon & Oddy, 2006), psychiatric disorders (Ciurli, Formisano, Bivona, Cantagallo, & Angelelli, 2010), marital problems (Arango-Lasprilla et al., 2008), and inability to manage finances (Bottari, Gosselin, Guillemette, Lamoureux, & Ptito, 2011), for example. In this way, quality of life post-TBI may be lowered. In the United States of America, annually around 1.1 million people are treated and released for TBI, and 50.000 die. In consequence, it has been estimated approximately 43% of these individuals develop TBI long term disability (Corrigan, Selassie & Orman, 2010). Developing countries epidemiological studies are still scarce; however data stratified by regions and countries have been published. In Latin America and Caribbean region a study affirmed rates of causes by road traffic accident and violence are higher than the global average (Puvanachandra & Hyder, 2008). In 2010, Brazilian TBI morbidity rate for individuals with age-range 20-29 years-old was 20.218 (Data SUS, 2012). As far as we known, no studies about disabilities have been published yet with this population in Brazil, in spite of published regional data about the profile of TBI incidence. A study from São Paulo (Brazil) in 1993 reported a rate of incidence of 360 per 100.000, higher than the average reported by developed countries of 200 per 100.000 (Maset, Andrade, Martucci, & Frederico, 1993). Around 75% of patients admitted in a public hospital of Porto Alegre survived from TBI (Quevedo, 2009). In adult population in Brazil as a hole, male groups of 20 to 29 and 40 to 49 years old seems to be the most involved (Martins et al., 2009; Melo, Silva, & Moreira, 2004; Quevedo, 2009) and the main cause has been car accidents (Martins et al., 2009; Martins, Silva, & Coutinho, 2003; Melo et al., 2004). Also in Brazil, one of the major factors associated with TBI caused by car accidents is alcoholemy, with around 39.3% of occurrence (Faria et al.,2008). Among other causes of TBI, there are falls, sports practice, violence, suicide, falling objects or overpressure of the skull (Granacher, 2009; Majdan et al., 2011; Martins et al., 2009).

TBI can be defined as damage to brain tissue caused by an external force that results in clinically identifiable either loss of consciousness, post-traumatic amnesia, or

objective neurological damage identified by neuroimage techniques. Moreover, TBI can be divided into penetrating and non-penetrating disorder; penetrating TBI refers to damage in intraparenchymal space through objects such as gunshot that penetrate the skull, while non-penetrating TBI occurs when the head is exposed to acceleration and deceleration forces where the head is thrown forwards while the brain goes backwards and hits the skull. TBI is characterized as heterogeneous when it comes to its lesions and clinical features. While brain damage is not always evident at the moment of TBI, clinical investigation is necessary to identify symptoms of concussion (such as dizziness, forgetfulness, headache, nausea, fatigue, sleep disturbance, poor concentration, light and noise sensitiveness, blurred vision, depressive or frustrated feelings and low speed processing) that could be related to a causative factor (Maas, Stocchetti, & Bullock, 2008).

Neurophysiological research relates those symptoms to axonal injury that occurs at different levels depending on injury severity. Axonal injury can occur at any brain site in the division between white and grey matter; different tissue density and acceleration-deceleration movement can torn or lacerate axonal fibers that are connected to neuronal cell bodies. Axonal injury occurs in TBI of all severity levels, although it is not always identifiable by computer tomography (CT) or magnetic resonance image (MRI). In general diffuse axonal injury can be identified in these exams by means of small focal lesions all over the intersection between white and grey matter (Granacher, 2009). Currently, more specific neuroimaging techniques are sensitive to identify even very mild white matter damage, such as Diffusion Tensor Imaging (DTI) (Johnson, Stewart, & Smith, 2012, in press). In addition to diffuse axonal injury, hemorrhages, contusions, ischemia, edema and herniation are also common lesions after a TBI that can manifest hours or days after an accident. In some cases, neurosurgery is necessary to remove edemas or intracranial pressure. Those damages frequently lead to brain tissue reduced volume and enlargement of ventricles (Maas, et al.,, 2008).

Among other important clinical features of TBI, its severity has been classically evaluated through the Glasgow Coma Scale (Teasdale & Jennett, 1974), a brief tool to assess level of consciousness in acute care patients. This scale assesses verbal, motor and ocular responses and it is applied at hospital admission; it is scored from one to 15, such that 15 represents a full conscious state and one represents death. Assessment of severity is of great importance in TBI routine since it predicts level of outcome (Dikmen et al., 2009). Other indicators of severity of trauma have been proposed, such as time of post-traumatic amnesia

and loss of consciousness or coma (Granacher, 2009; Sherer, Struchen, Yablon, Wang, & Nick, 2008). Post-traumatic amnesia (PTA) is characterized as an inability to retain short term information and also symptoms of disorientation (Forrester, Encel, & Geffen, 1994). Although memory impairments have been highlighted as the main neuropsychological disorders in TBI even after PTA, cognitive squeals are multidimensional and complex and go beyond then the frontiers of mnemonic systems (Dikmen et al., 2009).

## 1.2. Executive functions impairments in traumatic brain injury

Executive functions are considered integrated cognitive processes that work together to accomplish directed behaviors towards aims accomplishment (Anderson & Knight, 2010; Cicerone et al., 2000; Robertson & Knight, 2008). Those processes are described as the capacity of inhibition, monitoring, speed of processing, flexibility, alternance, planning, attentional control, initiation, among other several terms used to describe similar functions (Jurado & Rosseli, 2007). The relevance of studying EF relies on the important role those functions play in complex cognition and behavior; for example, reasoning, inference processing, social relationships, problem solving, and impulse control. In addition, more recent research has divided the EF in “cold” (reasoning) and “hot” (emotional) components, since they mediate the relationship between cognition and emotion (Chan, Shum, Toupoulou, & Chen, 2008).

The neuropsychological study of the EF as we understand today it is dated on the study of Phineas Gage (Harlow, 1868). Gage had a crow-bar instrument blown through his left frontal lobe while he was working. Before the accident, he was described as calm and gentle man. After it, his behavior was described as inappropriate, impatient, and rude with other people. Consequently, investigators started to discuss the role of the frontal lobes on cognition and behavior, or, on the EF. Since then, neurosciences have discussed the EF in two main levels: neuroanatomical and neuropsychological levels. However, as described by Barkley (2012), EF are related to psychological functions and there is enough evidence they are not exclusively located on the frontal lobes. Additionally, Barkley (2012) suggested that understanding of neural basis of EF requires it to be well-defined as a psychological construct, which until date they are not. There are some models developed to explain at least some

aspects of the executive functioning and some authors opted to call EF as an "umbrella term" that include several functions described on different models (Chan et al., 2008). Some theoretical models of EF are based on statistical analysis of a selected group of instruments, paradigms or scales and on studies of brain functioning or damage, while others are theoretically described and then tested. Still, EF models can be divided into unitary or multiple constructs. Unitary models are characterized for proposing one cognitive function only explains the EF and frontal lobe functioning, while multiple constructs models explain the EF as composed by different cognitive executive subcomponents. Besides that, the models can also be divided into psychological and neuroanatomical based (Tirapu, García-Molina, Luna-Lario, Roig-Rovira, & Pelegrín-Valero, 2008). See Table 1 for detailed information about the most popular EF theories.

Table 1.
*Description of main EF theories*

| Authors and theory name | Validation tool/method of development/tools to assess | EF components |
|---|---|---|
| Luria (1966) and Luria(1976) "Third unit" | Simple finger opposition, First-Edge-Palm test, Reciprocal Motor Programme Test | Programming, regulating, and verifying |
| Norman and Shallice (1986) "Supervisory attentional system" | Six Elements Test (Shallice & Burgess, 1991), Hayling Sentence Completion Test (Burgess & Shallice, 1996), Brixton-Spatial Anticipation Test (Burgess & Shallice, 1996), Sustained Attention to Response Task (Robertson, Manly, Andrade, Baddeley, & Yiend, 1997) | Contention scheduling – responsible for routine behavior<br>Supervisory attentional – regulates novel tasks |
| Stuss et al. (1986) "Tripartite model" | Stroop test, Wisconsin Card Sorting Test, Trail Making Test, verbal fluency, Rotman-Baycrest Battery to Investigate Attention | Planning, stimuli and response selection, and monitoring |
| Duncan and colleagues (Duncan, 1986, 1995; Duncan & Owen, 2000; Duncan et al., 2000) "Goal-neglect theory" | Goal Management Training (Robertson, 1996) | Formulation, storage, and checking of goals |
| Goldman-Rakic's (1992) "Working memory | Delayed-matching task<br>Cambridge Neuropsychological Test Automated Battery (CANTAB) | Inhibition and excitation |

| | | |
|---|---|---|
| model” | Letter-Number Span Test (Chan et al., 2008)<br>N-back Test (Callicott et al., 1998) | |
| Miyake et al.(2000) | Plus–minus task (Jersild, 1927; Spector & Biederman, 1976); Number–letter task (Rogers & Monsell, 1995); Local–global task (Navon, 1977); Keep track task (Yntema, 1963); Tone monitoring task (Larson, Merritt, & Williams, 1988); Letter memory task (Morris & Jones, 1990); Antisaccade task (Roberts, Hager, & Heron, 1994); Stop-signal task (Logan, 1994); Stroop task (Stroop, 1935); Wisconsin Card Sorting Test (Kimberg, D’Esposito, & Farah, 1997); Tower of Hanoi (Humes, Welsh, Retzlaff, & Cookson, 1997); Random Number Generation | Shifting, monitoring and updating, and inhibition |

Neuropsychological science still has little agreement about what composes the EF and how components relate among themselves. This problem impacts on how scientists and clinicians develop science and practice in neuropsychology. For example, lack of consensus about which component a task assess generates several papers reporting different results with regards to function with the same method; while other report the same function but with very different paradigms that may not reflect the same ability. At this point, different lines of theoretical and empirical research are necessary to accomplish this topic. Among them, researches that aim to understand how EF components might work in different clinical populations help to form body knowledge about its dynamics (Barkeley, 2012).

Specifically in TBI, EF impairments have been demonstrated in components such as inhibition (Demery, Larson, Dixit, Bauer, Perlstein, 2010; Skandsen, Finnanger, Andersson, Lydersen, Brunner, & Vik, 2010), verbal fluency (Skandsen et al., 2010), information processing speed (Fong, Chan, Ng, & Ng, 2009; Johansson, Berglund, & Rönnbäck, 2009), and cognitive flexibility (Wood & Liossi, 2006). EF components impaired in TBI were investigated by Busch, McBride, Curtiss, and Vanderploeg (2005), that found three factors: (1) self-generative behavior and cognitive flexibility; (2) mental control; (3) failure of inhibition memory errors. With regards to general neuropsychological impairments found in TBI, they can be considered as heterogeneous and typical of a diffuse acquired brain damage. Traditionally, neuropsychology investigates clinical populations through lesion paradigm;

however, a lesion-based description of TBI may be too oversimplified with regards to the complexity and heterogeneity of this neurological disorder (Vakil, 2005). Beyond diffuse axonal injury or dysfunction that can be endure for years after onset (Farbota et al., 2012), clinical variables such as neurosurgical factors, age and severity of TBI have been pointed as important factors that contribute to cognitive outcome (Kim, 2010). Particular characteristics of TBI population are also a target of bias in studies; psychiatric disorders (Whelan-Goodinson, Ponsford, & Schönberger, 2008) and a risk-taking profile, i.e. drug/alcohol abuse (Jacobs et al., 2010; Olson-Madden, Brenner, Corrigan, Emrick, & Britton, 2012), are common and frequently compose patients psychological profile.

EF impairments can be identified also in communicative difficulties. Pragmatic deficits are commonly associated to adverse social-function outcomes, as diminished social interaction and difficulties in obtaining and maintaining jobs (Isaki & Turkstra, 2000). This field of investigation – in which communication is studied as a function – has also raised questions to whether communicative impairments are manifested alone or secondary to deficits on the EF (Coelho, Liles, & Duffy, 1995; Struchen et al., 2008). For example, Channon and Watts (2003) investigated closed head injury patients in pragmatic tasks (social vignettes) and non-social EF tests. Results reported that Hayling Test scores, associated with inhibitory abilities, were associated with pragmatic performance. In conclusion, EF impairments are frequently reported in TBI literature due to its importance in social life and recovery. In addition, neuropsychological rehabilitation approaches are still a matter of challenge among researches in this area, which is explained by the heterogeneity of TBI samples (Institute of Medicine, 2011).

In this context, trying to solve the lack of homogeneity in clinical neuropsychology of EF and of TBI, different designs and data analyses can contribute. Two main paradigms can accomplish strategies towards solutions: group studies with cluster analysis and multiple case studies.

## 1.3. Utility of cluster analysis in neuropsychology

Cluster analysis is a quasi-statistical method to analyze descriptive multivariate data. It enables researches to verify which individuals within a group have similar characteristics. The final aim of cluster analysis is to benefit health studies that investigate methods of treatment or

intervention. Particularly in psychology, this analysis helps to identify subjects that might best benefit from interventions. This information is used for researches to create specific guidelines for subgroups, then helping to become interventions more efficient and specific. Validation of clusters must be relevant to the field of study. For this reason, many studies investigate whether clusters are associated to independent variables not considered in analysis in a first place (Clatworthy, Buick, Hankins, Weinman, & Horne, 2005).

Specifically in neuropsychology, cluster analysis is performed with psychometric tests scores while neuropsychological diagnosis or at least screening assessments are made by means of these tools. The applicability of cluster analysis for comprehension of different neurocognitive clinical profiles has been demonstrated in learning disabilities (Morris et al., 1998), normal and pathological aging (Ylikoski et al., 1999), schizophrenia (Seaton et al., 1999), and TBI (Crosson, Green, Roth, Farr, & Adams, 1990), always classifying subgroups according to their performance in specific tasks/tests. Since there is no established classification system of neuropsychological disorders, cluster analysis can be very helpful to build theoretical and empirical knowledge in this field (Morris et al., 1981).

From Morris et al. (1981) to Clatworthy et al., (2005), there is an agreement in the lack of standard method to define the clusters. Besides, since cluster analysis is not built upon a statistical theory, this method is, without exception, heuristic. The steps to conduct a cluster analysis study in neuropsychology proposed by Morris et al. (1981) are the following: (1) definition of target population; (2) selection of variables – always giving preference to the ones that will maximize subgroups differences; (3) similarity measure choice – decision will depend on the expected subject's profiles whether they will be similar or not; (4) cluster method (hierarchical or two step, for example); (5) number of clusters methods. In conclusion, cluster analysis is a promising method of study in neuropsychology, since it allows observation of associations and dissociations in samples, which is classical for neuropsychological rationale.

## 1.4. Neuroimaging on the study of TBI

Neuroimaging investigation has great importance on neuropsychology for identifying neural correlates of cognitive impairments or dysfunctions associated to different clinical conditions. The study of neural basis of TBI related to cognitive impairment has

progressively advanced with neuroimaging techniques. More initially, research interest was focused on classical lesion paradigm studies, in which TBI individuals with different brain damaged were compared to one another. As an example, Anderson, Bigler, and Blatter (1995) compared frontal and non-frontal TBI patients in EF tasks. The authors found no differences between groups, concluding that the tasks generally used to assess EF are not exclusively impaired when frontal lobe is affected in TBI. A study investigated neural structures of TBI as dependent variables by volumetric measurement of brain areas. Results indicated TBI patients with axonal injuries had decreased volume in brain structures as hippocampus, amygdala, thalamus, postcentral gyrus, precuneus, paracentral lobule, frontal and parietal cortices, and corpus callosum, when compared to healthy controls. Those results indicated atrophy in these cases is not diffuse, some regions are perhaps more susceptible. In addition, atrophy in pars orbitalis, supramarginal gyrus, pericalcarine cortex, and inferior parietal cortex predicted long-term outcome (Warner et al., 2010a). Another study also from Warner et al. (2010b), found correlations between superior frontal and parietal, thalamus, and precuneus cortices and measures of EF. Investigations regarding brain structures size and volume, for example, contributed for the understanding of TBI injury beyond the lesion site.

More advanced techniques started to be utilized on the study of TBI lesions, as diffusion tensor imaging (DTI). DTI allows the investigation of axonal integrity in the brain, which is especially relevant for TBI for its mechanisms of brain injury, as the classically involved coup and contra coup movement. Kraus et al. (2007) demonstrated white matter is damaged in a continuum in TBI, even in mild cases. For mild injuries, regions with decreased fractional anisotropy were found, as the superior longitudinal fasciculus, cortico-spinal tract, and sagittal stratum; while in moderate to severe injuries additional regions presented decreased fractional anisotropy, as cingulum, external capsule, inferior frontal-occipital fasciculus, anterior and posterior corona radiate, forceps major and minor, superior longitudinal fasciculus, and corpus callosum. In agreement with those findings, Lipton et al. (2009) found a negative correlation between axonal injury in the dorsolateral prefrontal cortex and EF measures in a mild TBI sample. DTI studies contribute to the investigation of TBI beyond magnetic resonance imaging (MRI) classical techniques, since they have proved not to be the best tools to identify lesions that predict dysfunction in TBI (Zappala et al., 2012). Some of the challenges in neuroimaging studies still rely on a better understanding of functional MRI regarding correlations between different outcome measures and areas

activations (McDonald, Saykin, & McAllister, 2012), and on the little known dynamics that underlies tissue and cognitive recovery (Hunter, Wilde, Tong, & Holshouser, 2012).

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## 5. CONSIDERAÇÕES FINAIS

A dissertação de mestrado apresentada teve como objetivo geral investigar as FE no complexo quadro de TCE através de dois estudos empíricos. O primeiro estudo investigou os perfis de funcionamento executivo em uma amostra de TCE heterogênea; enquanto que o segundo estudo buscou compreender a relação entre o TCE leve e suas diferentes manifestações, o funcionamento executivo e o papel da variável escolaridade como preditora de reserva cognitiva, medida em tarefas clínicas e em neuroimagem estrutural, no TCE.

Os resultados encontrados no Estudo 1 indicaram que a partir da bateria de avaliação das FE utilizada, três perfis de funcionamento executivo foram encontrados. O primeiro cluster ou perfil caracterizou-se por déficits inibitórios, de velocidade de processamento e fluência verbal fonêmica; o Cluster 2 caracterizou-se por déficits mistos nas FE, como de velocidade de processamento, flexibilidade cognitiva, planejamento/integração de informações, habilidades de fluência verbal e memória de trabalho. Finalmente, o terceiro cluster não apresentou déficits significativos nas variáveis analisadas. A análise comparativa dos clusters quanto a variáveis individuais, clínicas, sociodemográficas e culturais demonstrou somente uma diferença. O Cluster 3 apresentou significativamente mais lesões frontais que o Cluster 2. As características do Cluster 1 foram corroboradas por outros estudos que investigaram FE em TCE com métodos semelhantes. Em geral, as análises indicaram que os perfis de FE do TCE como uma patologia independem de variáveis que são relevantes em estudos comparativos de grupos estratificados por elas. Além disso, a lesão frontal não parece ser indicadora de prejuízos mais evidentes nessas funções, na medida em que o melhor cluster foi aquele com maior frequencia deste local de lesão. Este achado que foi corroborado por outros estudos e que pode ter sido também influenciado pela baixa acurácia de exames de tomografia computadorizada e ressonância magnética nas lesões do TCE. Os achados se mostraram principalmente relevantes para o planejamento e estratégia de programas de reabilitação em serviços públicos, ou de grupos de pacientes com TCE, indicando que esses pacientes devem ser recrutados por seus perfis executivos, ao invés de suas características clínicas. Além disso, se contrapôs ao paradigma clássico da lesão em neuropsicologia e indicou a necessidade do uso padrão de exames mais acurados para a patologia do TCE.

No que concerne ao Estudo 2, foram apresentados dois casos de adultos com TCE leve: o primeiro de alta escolaridade, alta frequência de hábitos de leitura e escrita, com

complicações no TCE (mais sequelas de lesão cerebral) e menor tempo pós-lesão e, o segundo de baixa escolaridade, baixa frequência de hábitos de leitura e escrita, com TCE sem complicações e maior tempo pós lesão. Os resultados apontaram que o caso de alta escolaridade teve um melhor desempenho em todas as tarefas de funções executivas avaliadas quando comparado ao caso de baixa escolaridade. Além disso, os exames de volumetria e espessura cortical apontaram achados na mesma direção: o paciente com maior escolaridade teve estruturas com volume e espessura significativamente superiores ao paciente com baixa escolaridade. As estruturas e os prejuízos executivos pareceram ter associações. No desempenho das tarefas de funções executivas, as tarefas que diferenciaram os sujeitos foram predominantemente as não-verbais, como o MWCST e o TMT. No que se refere às áreas, a maioria foi relacionada na literatura com o processamento de informações visuais e/ou as funções executivas associadas à inibição. Dessa forma, os achados deste estudo demonstraram evidências até então pouco claras na literatura de correlatos neuroanatômicos da reserva cognitiva em pacientes com TCE associada às funções executivas. Neste estudo, a escolaridade pareceu mais importante que fatores como severidade da lesão cerebral e o tempo pós-lesão no funcionamento executivo de pacientes com TCE leve. Como estas funções apresentam fonte de grande queixa por parte dos pacientes e familiares e, por ter grande impacto na autonomia, as considerações desses achados tem relevância tanto para a clínica, quanto para a pesquisa nesse âmbito. Sugere-se então que as investigações futuras busquem replicar esses achados em amostras maiores e com dissociações semelhantes em variáveis de reserva, utilizando técnicas mais avançadas de neuroimagem.

Os achados dos dois estudos quando analisados em conjunto trazem em comum a importância de considerar em diferentes âmbitos de intervenção as variáveis individuais, sociodemográficas, culturais e clínicas dos pacientes com TCE. Os estudos internacionais de consenso são claros ao afirmar que é irrelevante desconsiderarmos as particularidades dos pacientes e do quadro clínico que são diversas e heterogêneas. Essa afirmativa é baseada nas evidências de que não é provável e, por isso, não relevante, obtermos em qualquer contexto clínico ou de pesquisa pacientes com características semelhantes. Muitos estudos ainda questionam quais características devem ser consideradas. Nossos achados indicam que quando se trata de pacientes com TCE que buscam, ou tem acesso a serviços de atendimento, as diferentes variáveis podem influenciar, ao mesmo tempo, e de diferentes maneiras o desempenho executivo. Analisando esses pacientes como um grupo, é mais relevante pensar em estratégias e planejamento de reabilitação neuropsicológica a partir dos déficits executivos

apresentados, isto porque: um sujeito pode ser devido à dependência química, e outro devido à extensão de remoção de um hematoma e, um terceiro pode ser devido à baixa estimulação cognitiva prévia. Todos esses fatores e muitos outros compõem a população de pacientes com TCE e em cenários reais acontecem e devem ser trabalhados em conjunto. Em contraponto, o segundo estudo propõe que a variável escolaridade deve ser considerada quando se analisa pacientes com TCE leve caso-a-caso com as características clínicas descritas no estudo.

Dessa forma, a dissertação apresentada responde, entre outras mais específicas, uma questão ainda muito discutida na literatura internacional sobre TCE: como lidar com a heterogeneidade dessa população? A resposta parece depender da decisão da relação custo-benefício do tratamento de grupos, sujeitos únicos ou de duplas de pacientes; o que pode variar de acordo com o cenário que o clínico ou pesquisador se encontra. Quando se busca tratar ou intervir em grupos de pacientes a heterogeneidade pode não ser tão relevante quanto o desempenho determinado pelas diversas variáveis influentes. No entanto, quando se trata de casos únicos tratados individualmente, ou em método cabine em dupla, a variável escolaridade investigada nesse estudo é relevante no que concerne ao TCE leve.