PUCRS

ESCOLA DE CIÊNCIAS DA SAÚDE
PROGRAMA DE PÓS-GRADUAÇÃO EM PSICOLOGIA
MESTRADO EM PSICOLOGIA

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REVISITANDO MODELOS TEÓRICOS E MÉTODOS DE AVALIAÇÃO DAS FUNÇÕES EXECUTIVAS A PARTIR DE ANÁLISE DE VARIÁVEIS LATENTES

Porto Alegre

2018

PÓS-GRADUAÇÃO - *STRICTO SENSU*

AD VERVM DVCIT

Pontifícia Universidade Católica do Rio Grande do Sul

Ficha Catalográfica

B816r Branco, Laura Damiani

Revisitando modelos teóricos e métodos de avaliação das funções executivas a partir de análise de variáveis latentes / Laura Damiani Branco . – 2018.
81 f.
Dissertação (Mestrado) – Programa de Pós-Graduação em Psicologia, PUCRS.

Orientadora: Profa. Dra. Rochele Paz Fonseca.

1. cognição. 2. função executiva. 3. neuropsicologia. 4. análise fatorial. I. Fonseca, Rochele Paz. II. Título.

Elaborada pelo Sistema de Geração Automática de Ficha Catalográfica da PUCRS
com os dados fornecidos pelo(a) autor(a).
Bibliotecária responsável: Salete Maria Sartori CRB-10/1363

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DISSERTAÇÃO DE MESTRADO

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Dissertação apresentada ao Programa de Pós-Graduação em Psicologia da Pontifícia Universidade Católica do Rio Grande do Sul como requisito parcial para a obtenção do grau de Mestre em Psicologia.

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AGRADECIMENTOS

Agradeço, primeiramente, ao Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) pelo subsídio fornecido para a realização deste trabalho.

A Profa. Rochele Paz Fonseca, por todas as orientações fornecidas.

A André Ponsoni pelo esforço e dedicação ao projeto.

Aos membros de minha banca de qualificação por todas suas contribuições.

Aos meus pais, Ivânio e Dânia, que sempre incentivaram meu progresso acadêmico, e ao meu irmão Tomás. 谢谢 您!

A Poe, Yuma e Cocoa, minha banca avaliativa extraoficial e companheiros de escrita.

E, por fim, a Charles Cotrena. Por tudo.

SUMÁRIO

RESUMO

A presente dissertação soma-se aos esforços de pesquisadores na literatura neuropsicológica para compreender a natureza das funções executivas (FE) com base em uma combinação de dados teóricos e empíricos. Os achados aqui produzidos tem clara aplicabilidade clínica e teórica à áreas que abrangem desde a neuropsicologia até a psiquiatria. O projeto é composto por dois estudos empíricos, intitulados *"Factor analysis of cognitive tasks in healthy adults and patients with mood disorders: the challenges of finding a universal model of executive functions"* e "*Cognitive abilities underlying performance on the Modified Card Sorting Test: novel and traditional scores*", respectivamente. Os estudos seguiram delineamento retrospectivo, envolvendo amostra de aproximadamente 100 adultos sem transtornos de humor, 80 portadores de transtorno depressivo maior (TDM), 45 portadores de transtorno bipolar tipo II (TBII) e 40 portadores de transtorno bipolar tipo I (TBI). O objetivo geral do projeto e de cada um dos estudos propostos é revisitar modelos teóricos existentes de FE através de exploração estatística de tarefas e baterias de avaliação, dentro de um contexto clínico. Os objetivos do primeiro estudo incluem a identificação de fatores e agrupamentos de escores por subdomínios executivos em uma bateria flexível de avaliação neuropsicológica; a comparação da estrutura fatorial da bateria estudada a modelos existentes de FE; a verificação da estabilidade da estrutura fatorial da bateria em populações homogêneas (i.e. adultos saudáveis apenas, portadores de um transtorno psiquiátrico apenas) e heterogêneas; e a comparação da interpretação clínica de diferentes escores de FE aos resultados da análise fatorial. As análises revelaram uma estrutura subjacente que abrange de três a seis fatores dependendo da população estudada. Fatores robustos de memória de trabalho e velocidade de processamento visuoverbal foram identificados, com demais tarefas agrupando-se sozinhas em diferentes fatores, ou combinando-se com outro instrumentos de maneira inconsistente. Os achados apontam a importância do estudo de variáveis subjacentes a tarefas neuropsicológicas em diferentes populações, tanto saudáveis quanto psiquiátricas. Há necessidade, ainda, de refinar os métodos mais amplamente utilizados na clinica neuropsicológica de modo a avaliar as FE de maneira mais específica. Neste contexto, o objetivo do segundo estudo foi identificar as funções cognitivas subjacentes a escores tradicionais e alternativos para o *Modified Card Sorting Test.* Observou-se associação significativa entre o desempenho na tarefa e funções como a memória de trabalho e o controle inibitório. Escores alternativos podem complementar a avaliação por meio desta tarefa, permitindo a avaliação de diferentes funções cognitivas, e maior especificação dos resultados obtidos. Em conclusão, o presente projeto de dissertação ilustra a importante contribuição de uma abordagem estatístico-clínica para a avaliação e pesquisa neuropsicológica, utilizando uma abordagem híbrida para investigação e validação de modelos teóricos e escores avaliativos.

Palavras-chave: cognição; função executiva; neuropsicologia; análise fatorial.

Área conforme classificação CNPq: 7.07.00.00-1 (Psicologia)

Sub-área conforme classificação CNPq: 7.07.06.00-1 (Psicologia Cognitiva). 7.07.02.00-4 (Psicologia Experimental).

ABSTRACT

The goal of this dissertation was to contribute to the current literature on the underlying structure of the executive functions (EF) through a combination of theoretical and empirical approaches. The findings produced by these studies have ample clinical applicability to áreas raning from neuropsychology to psychiatry. The project contains two empirical studies, titled *"Factor analysis of cognitive tasks in healthy adults and patients with mood disorders: the challenges of finding a universal model of executive functions"* and "*Cognitive abilities underlying performance on the Modified Card Sorting Test: novel and traditional scores*", respectively. The studies followed a retrospective design, and involved a sample of approximately 100 adults with no mood disorders, 80 patients with major depressive disorder (MDD), 45 individuals with bipolar disorder type II (BDII) and 40 participants with bipolar disorder type I (BDI). The overall aim of this project and of each individual study was to revisit existing theoretical models of EF through the statistical analysis of assessment tasks and batteries within a clinical context. The goals of the first study included the identification of underlying factors in a neuropsychological assessment battery; the comparison of the fator structure across homogeneous (i.e. healthy adults, patients with a single mood disorder) and heterogeneous populations (i.e. mixed sample of adults with and without mood disorders); and the comparison between the results of these analysis and the current interpretation of EF scores in widely used assessment tasks. The analyses revealed an underlying structure with three to six factors depending on the population studied. Robust working memory and visuoverbal processing speed factors were identified across all populations, while the majority of other assessment measures loaded on to a single factor, or were inconsistently associated with different variables in each analysis. These findings highlight the importance of studying the underlying variables of EF tasks in different populations, including healthy individuals and patients with mental illnesses. There is also a need to refine the most widely used measures in neuropsychological assessment so as to provide a more specific evaluation of the EF. In light of these findings, the aim of the second study was to identify the cognitive functions underlying traditional and novel scores on the *Modified Card Sorting Test.* A significant association was observed beteween performance on this test and measure sof working memory and inhibition. Novel scores may complement assessments using this instrument, allowing for the evaluation of diferente cognitive functions and providing more detailed results. In conclusion, this dissertation project illustrates the important contributions of a hybrid empirical and clinical approach to neuropsychological assessment and research, in order to investigate and validate theoretical models and assessment tasks.

Keywords: cognition; executive function; neuropsychology; factor analysis.

APRESENTAÇÃO

O presente documento tem como objetivo a apresentação de uma dissertação de mestrado, intitulada "Revisitando modelos teóricos e métodos de avaliação das funções executivas a partir de análise de variáveis latentes". A dissertação é composta por dois estudos empíricos, intitulados *"Factor analysis of cognitive tasks in healthy adults and patients with mood disorders: the challenges of finding a universal model of executive functions"* e "*Cognitive abilities underlying performance on the Modified Card Sorting Test: novel and traditional scores*", respectivamente. O objetivo geral da dissertação e de cada um dos estudos propostos foi revisitar modelos teóricos de funções executivas (FE), através de exploração estatística de tarefas e baterias de avaliação, dentro de um contexto clínico.

A neuropsicologia é uma disciplina híbrida, que busca o rigor científico e a precisão, debruçando-se sobre objetos de estudo complexos e variáveis. No entanto, pode ser difícil avaliar de forma precisa um construto que se apresenta de maneira difusa, ou fornecer uma interpretação simples e replicável para um fenômeno multifatorial. Desta forma, muitas abordagens na neuropsicologia optam pela precisão experimental ou pelo enfoque clínico, sendo um desafio buscar um equilíbrio entre as duas abordagens. Esta abordagem resulta, por um lado, em resultados robustos e precisos porém demasiado inflexíveis para o contexto clínico, e, por outro, em hipóteses clínicas específicas e complexas, porém não generalizáveis.

O desenvolvimento da neuropsicologia depende da junção destas abordagens, buscando o desenvolvimento de teorias estatisticamente robustas e empiricamente aplicáveis, que sirvam como base para a interpretação, avaliação e reabilitação de funções cognitivas. Estas teorias devem levar em conta a variabilidade individual e as características específicas da clínica neuropsicológica – como a influência da psicopatologia nas funções mentais – assim como a necessidade de aderir a métodos de estudo replicáveis em diferentes contextos e populações.

A presente dissertação insere-se neste contexto, buscando a aproximação entre abordagens clínicas (derivada de observação empírica) e estatísticas (testagem experimental) a serviço da compreensão e modelagem de construtos neuropsicológicos. No primeiro estudo, foram discutidos modelos teóricos para as funções executivas. Esforços atuais nesta área têm produzido modelos estatisticamente robustos em amostras específicas através de tarefas experimentais. No entanto, estes modelos carecem de replicação empírica em populações clínicas: uma vez que a grande maioria foi desenvolvida em populações de adultos saudáveis, a aplicabilidade de modelos existentes a contextos clínicos não tem sido suficientemente investigada. Desta forma, o estudo realizou uma análise exploratória de uma bateria de funções executivas contendo tarefas neuropsicológicas amplamente utilizadas. A população envolvida incluiu, além de adultos saudáveis, portadores de transtorno depressivo maior e transtorno bipolar. Ambos quadros são caracterizados por prejuízo significativo nas funções executivas, e sua inclusão no estudo contribui para a representatividade da amostra com relação a populações em que há demanda de avaliações neuropsicológicas. Foram encontradas estruturas latentes distintas para a bateria de avaliação em cada uma destas subpopulações. Poucos fatores incluíram variáveis provindas de múltiplos testes, com alguns fatores agrupando apenas as variáveis referentes a uma única tarefa. Foram realizadas reflexões sobre a necessidade e a importância de uma discussão mais ampla acerca da aproximação entre tarefas e métodos clínicos e experimentais.

O segundo estudo foi realizado com o intuito de explorar algumas das variáveis que distribuíram-se em um único fator, embora sejam frequentemente utilizadas para avaliar funções distintas. O *Modified Card Sorting Test* tem sido amplamente utilizado na literatura como forma de avaliação das funções executivas. No entanto, o instrumento tem sido criticado por sua baixa especificidade e ambiguidade da interpretação interpretabilidade. No primeiro estudo desta dissertação, as variáveis provindas deste teste distribuíram-se sempre em um mesmo fator, sugerindo que possivelmente não são específicas o suficiente para avaliar funções executivas distintas. Desta forma, o segundo estudo buscou investigar as funções cognitivas subjacentes a cada um destes escores, e explorar escores adicionais que poderão aprimorar a especificidade desta tarefa.

Todos os estudos propostos inserem-se em projeto guarda-chuva intitulado "*Interface entre neuropsicologia e psicopatologia: em busca de perfis clínicos de processamento de funções executivas na depressão e no transtorno bipolar"* avaliado e aprovado pela Comissão Científica da Faculdade de Psicologia sob a responsabilidade da Profa. Dra. Rochele Paz Fonseca e do doutorando Charles Cotrena (Ofício número 014/2013), também aprovado pelo CEP da PUCRS (CAEE n° 23995513.5.0000.5336; parecer n° 482.688 de 06/12/2013).

Para fins de melhor ilustrar e descrever as investigações propostas, a presente dissertação será dividida em três grandes partes: (1) Introdução, (2) Estudos, (3) Considerações Finais. Na primeira parte, foi realizada uma breve introdução dos pressupostos teóricos subjacentes ao projeto. Na segunda seção, são apresentados os estudos propriamente ditos, no formato de artigos empíricos. Por fim, na última seção, serão discutidas algumas repercussões dos resultados obtidos, e reflexões acerca do tema da dissertação.

1 INTRODUÇÃO

1.1 FUNÇÕES EXECUTIVAS: DEFINIÇÃO E RELEVÂNCIA TEÓRICO-CLÍNICA

As funções executivas (FE) são habilidades de controle cognitivo recrutadas durante a realização de tarefas nas quais processos automáticos ou instintuais mostrariam-se inadequados ou insuficientes (Diamond, 2014). Estas habilidades incluem processos como a inibição de respostas automáticas ou dominantes, a resistência à distração ou à interferência de informações irrelevantes no ambiente ou na memória, a alternância entre tarefas, aspectos da memória de trabalho (como a manutenção, manipulação e atualização de informações), o planejamento e a fluência verbal (Friedman & Miyake, 2017).

As FE são essenciais para a funcionalidade, mostrando-se relacionadas a atividades como o desempenho acadêmico e ocupacional, a resolução de problemas interpessoais, o uso de substâncias, além da saúde física e mental (Snyder, Miyake, & Hankin, 2015). Componentes executivos ainda tem se mostrado associados a uma série de outros processos cognitivos, como a aprendizagem (Mourão Junior & Melo, 2011) e a teoria da mente (Yeh, Tsai, Tsai, Lo, & Wang, 2016). Desta forma, prejuízos executivos acarretam impacto significativo em diversos âmbitos da funcionalidade, qualidade de vida, e cognição geral (Cotrena, Branco, Shansis, & Fonseca, 2016; Wongupparaj, Kumari, & Morris, 2015).

A presença de prejuízos nas FE é frequentemente descrita como disfunção executiva ou síndrome disexecutiva (Baddeley & Wilson, 1988; Miotto, 1994). Este quadro tem sido extensamente estudado em pacientes com quadros neurológicos degenerativos como a doença de Parkinson (Roussel et al., 2016) e lesões adquiridas como o acidente vascular cerebral (Hayes, Donnellan, & Stokes, 2016) e o traumatismo crânioencefálico (Ghawami, Sadeghi, Raghibi, & Rahimi-Movaghar, 2016). No entanto, estudos recentes também apontam a presença de disfunções executivas em quadros psiquiátricos, como o transtorno obsessivo compulsivo (Snyder, Kaiser, Warren, & Heller, 2015), o transtorno de estresse pós-traumático (Woon, Farrer, Braman, Mabey, & Hedges, 2017), o transtorno depressivo maior (Cotrena et al., 2016), a esquizofrenia (Orellana & Slachevsky, 2013) e o transtorno bipolar (Bora et al., 2016). A presença de disfunções executivas não se limita a fases ativas de quadros como a esquizofrenia, ou a presença de episódios de humor no TB e TDM, persistindo mesmo em períodos de eutimia ou estabilidade (Xu et al., 2012). Em pacientes com TBI, a prevalência de disfunção executiva durante a eutimia pode chegar a até 53% (Cheung et al., 2013). Estes achados tem levado alguns autores a identificarem a presença de disfunções executivas como *trait-markers* de quadros como o transtorno bipolar (Xu et al., 2012).

O estudo das FE no âmbito dos transtornos mentais tem ocasionado grandes repercussões na compreensão e manejo destes quadros. Associações entre as FE e fatores como a resposta ao tratamento farmacológico e de treino cognitivo já tem sido apontadas em amostras com transtorno depressivo maior (Gyurak et al., 2016; Morimoto et al., 2016; Pimontel et al., 2016). De forma similar, as FE tem sido identificadas como preditoras de resposta ao tratamento em transtornos somatoformes (Inamura et al., 2016) e no transtorno obsessivo compulsivo (McNamara et al., 2014). Na esquizofrenia, pacientes com resistência ao tratamento com antipsicóticos também apresentam perfis cognitivos caracterizados por maior disfunção executiva (Frydecka, Beszłej, Gościmski, Kiejna, & Misiak, 2015). Dada a associação entre as FE e o desfecho terapêutico observado em diferentes quadros clínicos, estudos tem proposto intervenções cognitivas abordando estas funções de maneira direta como possível tratamento para quadros com o transtorno de déficit de atenção/hiperatividade (Hannesdottir, Ingvarsdottir, & Bjornsson, 2017) e no transtorno de estresse pós-traumático (Saunders et al., 2015).

Embora quadros de disfunção executiva tenham sido amplamente documentados, ainda há controvérsia em torno da natureza das FE e uma falta de consenso acerca dos componentes que integram esta função mental (Elliott, 2003). Estas questões têm sido abordadas por diversos autores através da elaboração de modelos teóricos para as FE. Estes modelos, assim como suas respectivas forças, fraquezas e limitações, serão discutidos a seguir.

1.2 MODELOS TEÓRICOS PARA AS FUNÇÕES EXECUTIVAS: UMA BREVE REVISÃO HISTÓRICA

Dada a complexidade e multicomponencialidade das FE, a definição deste construto tem sofrido mudanças significativas ao longo do tempo. O mesmo pode ser dito dos modelos teóricos desenvolvidos para explicar estas funções.

Os primeiros modelos explicativos para as FE embasavam-se no estudo de pacientes com lesões cerebrais na região pré-frontal (Stuss & Benson, 1986). Destes indivíduos, surgiram observações acerca da dissociação entre aspectos fluídos e cristalizados da inteligência, uma vez que muitos apresentavam desempenho satisfatório em medidas como as Escalas Wechsler de Inteligência para Adultos, e prejuízos em instrumentos como as Matrizes Progressivas de Raven (Duncan, Burgess, & Emslie, 1995). Resultados similares foram encontrados por diversos outros autores na comparação entre avaliações neuropsicológicas tradicionais ou testes de QI e outras tarefas complexas, incluindo o teste Wisconsin de Classificação de Cartas, e as Torres de Londres ou Hanoi (Damasio, Tranel, & Damasio, 1991; Shallice & Burgess, 1991). O padrão de prejuízos cognitivos demonstrado por pacientes com lesões frontais passou, então, a fundamentar a definição de FE adotada por grande parte dos autores na literatura neuropsicológica. Apesar de alguma variabilidade na terminologia empregada, grande parte das teorias existentes convergiam no que tange às principais habilidades compreendidas sob o termo 'FE.' De acordo com revisão realizada por Pennington e Ozonoff no ano de 1996, os processos cognitivos mais frequentemente citados como FE incluem alternância e manutenção de regras, controle de interferências, inibição, integração de espaço e tempo, planejamento e memória de trabalho. Observa-se que grande parte destes termos ainda é utilizada, e integra modelos mais recentes de FE, discutidos nos parágrafos a seguir.

Uma vez alcançado o consenso acerca da definição geral das FE, surgem algumas divergências entre autores no que tange a relação entre estas funções. Autores como Duncan et al. (Duncan, Emslie, Williams, Johnson, & Freer, 1996) sugeriam a existência de uma única *função executiva* subjacente a todas as demais funções descritas na literatura. Ao mesmo tempo, outros estudos produziam evidências para a hipótese contrária, apontando para múltiplas *funções executivas* distintas (Baddeley, 1996; Godefroy, Cabaret, Petit-Chenal, Pruvo, & Rousseaux, 1999; Logan, 1985). A resolução do debate entre modelos de unidade e diversidade (*unity and diversity)* motivou a criação de alguns dos mais influentes modelos de FE na literatura.

Uma das primeiras teorias a fornecer uma alternativa aos modelos distintos de unidade e diversidade foi desenvolvida por Alan Baddeley, ao dissertar sobre o componente executivo central da memória de trabalho (Baddeley, 1996, 2012). Baddeley foi um dos primeiros autores a descrever as FE como um conjunto de processos distintos, mas relacionados entre si, identificando as seguintes habilidades como parte deste agrupamento: a coordenação do desempenho em duas tarefas simultâneas, a capacidade de alternar entre estratégias de evocação de informação e o gerenciamento da atenção seletiva juntamente com a inibição de informações irrelevantes. Baddeley incluiu, ainda, a capacidade de manter e manipular informações na memória de curto-prazo como um subcomponente do executivo central.

Enquanto o modelo de Baddeley baseava-se em evidências predominantemente neuropsicológicas para sua construção, outros autores buscaram fornecer alternativas à dicotomia *unity-diversity* através de estudos psicométricos. Um dos principais estudos a utilizar esta abordagem foi redigido por Miyake et al. (2000). Nesta investigação, tarefas como o WCST, a Torre de Hanoi e a Geração Aleatória de Números foram analisadas através de análise fatorial confirmatória e modelagem estrutural. Esta abordagem forneceu respostas importantes à muitas das questões teórico-empíricas levantadas na época acerca dos modelos existentes de FE. No estudo de Miyake et al. (2000), modelos estatísticos considerando apenas um fator subjacente às tarefas anteriormente citadas não se ajustaram aos dados de maneira satisfatória. De maneira similar, variações deste modelo em que múltiplas funções são combinadas em uma única variável latente mostraram-se inadequadas aos dados. Os autores, então, identificaram um modelo de três *core components* executivos como sendo o mais próximo à estrutura latente das tarefas de FE. Estes componentes corresponderam a alguns dos construtos mais citados na literatura acerca das FE, e foram descritos por Miyake et al. (2000) como *shifting*, controle inibitório e atualização ou *updating*. Embora estas funções tenham sido identificadas como distintas entre si, elas não são totalmente independentes. Através de modelagem estrutural, foram identificadas correlações significativas entre estes componentes, apontando que compartilham algumas fontes comuns de variabilidade. Modelos como este realizaram importante contribuição para a literatura ao conciliar abrangência e parcimônia na explicação do complexo construto de FE, além de oferecer múltiplas hipóteses testáveis sobre a relação entre as diferentes funções incluídas nesta categoria. Este modelo foi revisado e confirmado pelos próprios autores através de diversas investigações posteriores, fornecendo evidências empíricas para suas considerações acerca da unidade e diversidade das FE (Friedman et al., 2008; Friedman, Miyake, Robinson, & Hewitt, 2011).

O modelo de Miyake e colaboradores tem sido também replicado por diversas investigações empíricas (p. ex. Lehto, Juujärvi, Kooistra, & Pulkkinen, 2003) e teóricas, como a recente revisão de Diamond (2013), que teve como objetivo a atualização e complementação deste modelo teórico. Diamond (2013) define os *core components* executivos como sendo a memória de trabalho, controle inibitório e flexibilidade cognitiva. A memória de trabalho, subdividida em verbal e não verbal/visuoespacial, envolve a capacidade de manipular informações na mente, atualizando-as com dados do passado e informações atuais do ambiente. O controle inibitório, por sua vez, refere-se à habilidade de inibir estímulos internos ou externos, visando agir da forma mais adequada conforme o contexto. A memória de trabalho e controle inibitório estão correlacionados: é preciso manter o objetivo em mente para saber o que é relevante e apropriado e o que deve ser inibido, assim como a inibição de distratores é necessária para manter o foco em objetivos específicos. Já a flexibilidade cognitiva envolve a capacidade de mudança de perspectiva espacial ou interpessoal, a mudança de opiniões, e o ajustamento a novas demandas ou prioridades. A flexibilidade cognitiva, por conseguinte, necessita do controle inibitório para inibir a perspectiva anterior e da memória de trabalho para relacionar a nova visão – a flexibilidade cognitiva é fundamentada pelo controle inibitório e memória de trabalho e desenvolve-se muito depois de ambos. Estas três funções, por sua vez, servem como base para as chamadas *higher-level executive functions*, que incluem o raciocínio lógico, a resolução de problemas e o planejamento.

Em conclusão, observa-se que a natureza e estrutura das FE tem sido alvo de diversas investigações recentes, adotando abordagens psicométricas, neuropsicológicas, empíricas e/ou teóricas. Embora os resultados destas investigações tenham ocasionado importantes avanços na compreensão das FE, algumas limitações dos modelos existentes ainda impedem a compreensão integral destes construtos. Estas limitações e algumas possíveis soluções serão discutidas na seção seguinte.

1.3 CONTRIBUIÇÕES DO ESTUDO DE POPULAÇÕES PSIQUIÁTRICAS PARA A COMPREENSÃO DAS FUNÇÕES EXECUTIVAS

O estudo de populações clínicas, especialmente sujeitos com quadros neurológicos adquiridos, desempenhou papel fundamental na consolidação da neuropsicologia como área de estudo. Desde os estudos de Carl Wernicke (Wernicke, 1874) e Paul Broca (Broca, 1861), passando pelo famoso caso de Phineas Gage (J.M. Harlow, 1868; John M. Harlow, 1993) e as contribuições de Alexander Luria (A. Luria, 1972; A. R. Luria, 1963), a avaliação das funções cognitivas após dano neurológico foi responsável por grandes descobertas na história da neuropsicologia.

Dentre os construtos estudados pela neuropsicologia, as FE apresentam talvez a maior ligação com a investigação de populações clínicas. Afinal, o conceito em si é derivado de relatos de ‘síndrome frontal’ derivados de pacientes com lesões nas regiões frontal e pré-frontal do cérebro, como Phineas Gage. A partir de observações clínicas e formulações teóricas, o papel dos lobos frontais como o substrato principal das FE foi consolidado (S. Goldstein, Naglieri, Princiotta, & Otero, 2014). Estudos recentes tem levado a uma certa flexibilização neste posicionamento, uma vez que prejuízos em habilidades ditas ‘executivas’ são muitas vezes identificados após lesão ou disfunção de outras regiões neurais (Cardoso et al., 2014; Marie, 2009). No entanto, a ideia das FE como estando predominantemente associadas ao funcionamento dos lobos frontais e suas conexões com demais regiões cerebrais permanece entre as mais aceitas nesta área de estudo (Jurado & Rosselli, 2007).

Nas últimas décadas, para além do estudo do dano neurológico ocasionado por traumatismo cranioencefálico ou acidente vascular cerebral, a neuropsicologia vem se debruçando sobre as alterações cognitivas ocasionadas por disfunções cerebrais. O estudo de populações com alterações cognitivas claras na ausência de dano neurológico identificável, como é o caso dos transtornos mentais, deu luz ao campo da neuropsiquiatria (G. Goldstein, 1987). Desde o estabelecimento desta disciplina, o estudo da neuropsicologia em quadros psicopatológicos contribuiu para a identificação do substrato neural de diferentes funções cognitivas (Schmahmann, Weilburg, & Sherman, 2007; Tadayonnejad, Yang, Kumar, & Ajilore, 2014; Townsend et al., 2013) e compreensão da relação entre sintomas psiquiátricos e habilidades cognitivas. Neste âmbito destacam-se novamente as FE, que vem se mostrando associadas a manifestações sintomáticas de quadros como o autismo (Lopez, Lincoln, Ozonoff, & Lai, 2005), o transtorno depressivo maior (Clark, Chamberlain, & Sahakian, 2009; Disner, Beevers, Haigh, & Beck, 2011), transtornos externalizantes (Skogan et al., 2014; Sulik & Obradović, 2017) e a esquizofrenia (Guillem, Rinaldi, Parnpoulova, & Stip, 2008).

Apesar das contribuições históricas do estudo de populações clínicas para o avanço da neuropsicologia, estudos recentes vem demonstrando uma atuação paralela entre a neuropsicologia cognitiva e a psicologia clínica, com poucas contribuições diretas entre uma e outra área (Snyder, Miyake, et al., 2015). A baixa interseccionalidade entre estas disciplinas traz diversas dificuldades para a pesquisa e clínica neuropsicológica. Observa-se, por exemplo, a aplicação de modelos teóricos provindos da neuropsicologia cognitiva a populações clínicas sem que estas estivessem envolvidas na conceitualização e validação destes modelos. As tarefas utilizadas na avaliação neuropsicológica de populações com esquizofrenia, transtorno bipolar e transtorno depressivo maior, por exemplo, são semelhantes às utilizadas em populações com danos neurológicos adquiridos ou quadros demenciais. Estas abordagens pressupõe um modelo universal de funcionamento cognitivo, que garante a manutenção da validade e fidedignidade de instrumentos e métodos neuropsicológicos mesmo em populações distintas. Embora esta hipótese possa vir a ser confirmada, são necessários estudos adicionais destas populações, e sua inclusão em estudos empíricos que busquem investigar a estrutura subjacente de funções cognitivas. Esta abordagem permitirá a confirmação de hipóteses atuais sobre o funcionamento cognitivo, e contribuirá para o avanço da neuropsicologia, da mesma forma que o estudo de quadros neurológicos adquiridos contribuiu para o crescimento da área no passado.

1.4 LIMITAÇÕES DE MODELOS EXISTENTES PARA AS FUNÇÕES EXECUTIVAS

As FE estão entre as mais estudadas e menos compreendidas dentre as habilidades cognitivas. O desenvolvimento de modelos teóricos para as FE tem sido foco de interesse na literatura desde a década de 1970 (e.g. Teuber, 1972). No entanto, sua organização funcional ainda é alvo de diversos questionamentos, e não há consenso acerca do modelo teórico a ser utilizado para explica-las. Uma das teorias mais promissoras neste campo tem sido a de Naomi Friedman e Akira Miyake (Friedman et al., 2008, 2011; Akira Miyake et al., 2000). Desenvolvida através da modelagem estrutural de tarefas de FE, a teoria tem sido refinada desde sua publicação inicial no ano 2000, e hoje é uma das mais discutidas na literatura. Embora tenha sido replicada em diferentes amostras, grande parte das evidências para esta teoria provém de amostras norte-americanas de indivíduos saudáveis, sem patologias clínicas ou psiquiátricas. A constatação de que o modelo de unidade/diversidade pode ser utilizado como teoria universal das FE, no entanto, requer que seus pressupostos também sejam observados em outros contextos clínicos e culturais .

A presença de prejuízos executivos na maior parte dos transtornos mentais já tem sido documentada na literatura (Snyder, Miyake, et al., 2015). Embora modelos de análise estrutural como o de Miyake et al. (2000) já tenham sido utilizados para investigar a presença de prejuízos executivos em quadros com o transtorno obsessivo compulsivo (Snyder, Kaiser, et al., 2015) e o transtorno depressivo maior (Snyder, 2012), a aplicabilidade do modelo em si a estas populações não foi investigada. Ou seja, as similaridades ou distinções entre a estrutura funcional das FE em populações saudáveis e portadoras de psicopatologia não tem sido suficientemente estudada. Estas evidências são fundamentais para a compreensão da natureza das FE, pois poderão sinalizar a necessidade de modelos teóricos distintos para o funcionamento executivo em cada patologia, ou, por outro lado, apoiar a existência de um único modelo teórico que se mostre universalmente aplicável.

1.5 LIMITAÇÕES DE ESCORES EXISTENTES PARA TAREFAS DE FUNÇÕES EXECUTIVAS

Uma das principais limitações associadas à avaliação neuropsicológica das FE é a complexidade das tarefas utilizadas. A maior parte das tarefas avaliativas envolvem múltiplos processos cognitivos para além daquele que possuem como foco principal, constituindo uma fonte importante de erro de medida. Este conceito, descrito por Paul Burgess (1997) como o problema de *task impurity* (“impuridade de tarefa”*)*, pode ser claramente observado em tarefas como o Teste Wisconsin de Classificação de Cartas (A Miyake, Emerson, & Friedman, 2000; Pennington & Ozonoff, 1996) e o *Trail Making Test*.

O Teste Wisconsin de Classificação de Cartas (WCST) é tido como um dos exemplos clássicos de impuridade de tarefa, sendo apontado como tal desde a publicação de Pennington e Ozonoff em 1996. Estudos apontam que o desempenho neste teste depende das três FE chave, inibição, flexibilidade e memória de trabalho (Gamboz, Borella, & Brandimonte, 2009). No entanto, o desempenho nesta tarefa pode também ser influenciado por fatores como o auto-monitoramento e a sobrecarga de memória de trabalho (Lange et al., 2016a; L. J. Robinson, Gray, Ferrier, & Gallagher, 2016a). Desta forma, o WCST também tem sido alvo de investigações acerca de sua estrutura subjacente a partir de análise fatorial. No entanto, não há um consenso na literatura a este respeito: enquanto alguns autores identificam apenas um fator como responsável pela estrutura de escores no WCST (Greve, Stickle, Love, Bianchini, & Stanford, 2005), outros encontram até três (Bell, Greig, Kaplan, & Bryson, 1997). De forma interessante, tais discrepâncias são encontradas mesmo em versões reduzidas do WCST, como o M*odified Card Sorting Test* (Nelson, 1976). As dificuldades associadas aos escores desta ferramenta tem levado também a sugestão de novos sistemas de pontuação para a mesma, a fim de aumentar a qualidade dos dados coletados com a mesma (Cianchetti, Corona, Foscoliano, Contu, & Sannio-Fancello, 2007; Cianchetti, Corona, Foscoliano, Scalas, & Sannio-Fancello, 2005).

O *Trail Making Test* (TMT) também é uma das tarefas mais utilizadas na avaliação das FE, tendo sido adaptada para uso em diversos países e quadros clínicos. No entanto, esta tarefa também tem sido apontada como sendo pouco específica na avaliação das FE (Snyder, Miyake, et al., 2015). Desta forma, diferentes abordagens têm sido adotadas para aumentar a especificidade dos dados coletados a partir deste instrumento, sendo as principais a análise de erros e o uso de escores derivados.

A análise de erros no TMT é um desenvolvimento relativamente recente na literatura, uma vez que alguns dos manuais mais tradicionais de avaliação recomendam apenas a avaliação do tempo necessário para cada parte da tarefa (Heaton, Miller, Taylor, & Grant, 2004). Esta colocação foi reforçada em artigo específico sobre o TMT no periódico *Nature Reviews,* que enfatiza a "utilidade clínica limitada" do número de erros nesta medida (Bowie & Harvey, 2006). Muitos estudos atuais utilizando o TMT fazem uso desta abordagem, comparando o desempenho de grupos clínicos nesta tarefa, por exemplo, apenas em termos do tempo necessário para completar as partes A e/ou B do teste. No entanto, já há algum tempo, existem evidências de que tanto o tempo quanto a acurácia no TMT oferecem dados relevantes acerca do funcionamento cognitivo, e que as contribuições de cada um destes escores são dissociáveis, devendo ser analisadas separadamente (Ashendorf et al., 2008). Desta forma, alguns estudos buscam, inclusive, categorizar os tipos de erros apresentados por pacientes no

TMT como forma de aumentar a especificidade da avaliação realizada por esta ferramenta (Mahurin et al., 2006; Ruffolo, Guilmette, & Willis, 2000). Embora esta abordagem tenha produzido resultados promissores, ela não tem sido amplamente adotada na literatura.

O uso de escores derivados tem sido utilizado de maneira mais frequente na literatura neuropsicológica. Estes escores são calculados apenas com base nos dados originalmente coletados na aplicação do TMT, não sendo necessária a reavaliação de protocolos ou classificação de erros. Exemplos destas pontuações incluem a diferença e razão entre os tempos de cada parte do teste (tempo parte B-tempo parte A; tempo B/tempo A) (Arbuthnott & Frank, 2000). Embora estas variações sejam utilizadas a algum tempo na interpretação do TMT, a investigação psicométrica da validade destes escores foi realizada apenas no ano de 2009. Este estudo revelou que, dentre os escores derivados, apenas a diferença entre o tempo das partes B e A refletiria a flexibilidade cognitiva (Sánchez-Cubillo et al., 2009). De forma interessante, o mesmo estudo revelou que o tempo necessário para completar o TMT B, muitas vezes utilizado como medida de flexibilidade cognitiva (e.g. Bergemann et al., 2015) ou inibição (Mur, Portella, Martinez-Aran, Pifarre, & Vieta, 2009), está mais claramente correlacionada a medidas de memória de trabalho.

A avaliação de escores nestas tarefas por meio de análises de variáveis latentes, incluindo também medidas de FE consideradas mais ‘puras’, contribuirá para a compreensão dos construtos verdadeiramente mensurados por tarefas complexas, ditas ‘impuras.’ Esta abordagem irá conferir maior possibilidade de especificação dos processos executivos complexos empregados para sua realização.

2. ESTUDOS

2.1 ESTUDO 1: "FACTOR ANALYSIS OF COGNITIVE TASKS IN HEALTHY ADULTS AND PATIENTS WITH MOOD DISORDERS: THE CHALLENGES OF FINDING A UNIVERSAL MODEL OF EXECUTIVE FUNCTIONS"

Abstract

In recent years, a number of theoretical models have been developed for the executive functions (EF). Though the findings of these studies have served as the basis for several initiatives including the neuropsychological assessment and rehabilitation of psychiatric populations, the models themselves have not been replicated in patients with mental illnesses. As such, the aim of the present study was to analyze the latent variables underlying a neuropsychological assessment battery comprised of widely used, paper-and-pencil tests, in healthy adults and individuals with mood disorders. Participants included 119 control subjects, 84 patients with major depressive disorder (MDD) and 100 individuals with bipolar disorder (BD). Subjects completed the Trail Making Test (TMT), the Hayling Sentence Completion Test (HSCT), Modified Card Sorting Test (MCST) Digit Span Forwards and Backwards, the Sentence Word Span Test, the Stroop Color Word Test (SCWT) and Phonemic, Semantic and Unconstrained Verbal Fluency Tests. Exploratory factor analyses were conducted in the sample as a whole, as well as among patients with MDD and BD separately. Though working memory and visuoverbal processing speed factors were consistently identified, tasks such as the TMT, HSCT, SCWT and MCST often loaded onto a different factor each. These findings highlight the importance of the empirical confirmation of EF models in different populations, since the structure of assessment tasks may vary depending on context. There is also a need to investigate 'complex' EF tasks in greater detail, in order to determine their underlying cognitive abilities.

Introduction

The executive functions (EF) have received growing attention in neuropsychology due to the strength of their association with developmental outcomes, psychopathology, and daily functioning. EF are involved in nearly all major aspects of life, including academic achievement (Chung, Liu, McBride, Wong, & Lo, 2017), life outcomes (de Neubourg, Borghans, Coppens, & Jansen, 2017) and overall well-being (Pe, Koval, & Kuppens, 2013), and have been the focus of several cognitive training programs developed over recent years (Cantor et al., 2014; Wass, 2015). At the same time, the EF are famously ill-defined, and there is currently no universally accepted conceptual or theoretical model to capture their functional structure. This poses a significant challenge for the operationalization of EF in the form of assessment tasks. Though this has been attempted in several different ways over the years, the majority of assessment paradigms has been criticized for aspects including their sensitivity (MacAllister et al., 2017), ecological validity (Wallisch, Little, Dean, & Dunn, 2018) and construct validity (Whiteside et al., 2016).

The development of conceptual models for EF is, as such, a work in progress, with recent studies resorting to methods such neuroimaging to identify and describe its underlying components (Ardila, Bernal, & Rosselli, 2017). Another approach which has also been widely used to conceptualize the EF involves the statistical analysis of neuropsychological tests involved in the assessment of these cognitive factors. A major theoretical model to arise from this approach is the unity and diversity theory, originally developed by Miyake (Akira Miyake et al., 2000), and built upon by additional studies over the years (Friedman & Miyake, 2017; Friedman et al., 2011; Snyder, Miyake, et al., 2015). The unity-diversity model describes the EF as containing three core components – flexibility, inhibition and updating – which contribute individually to task performance, but also share a substantial amount of variance. A similar model is discussed by Diamond (Diamond, 2014), with a slight difference in terminology, whereby ‘updating’ is referred to as ‘working memory.’ This is a theoretical model based on a review of the current literature rather than experimental analysis. Nevertheless, in both models, the three core EF are thought to provide a basis for more complex abilities such as reasoning, planning and problem solving.

Though the three factor model has been replicated in some investigations, several studies involving factor analytical, structural modeling and neuroimaging methods have arrived at different conclusions regarding the underlying structure of the EF. A few studies, for instance, identify three core EF, but find that at least one of these differs from the functions described by Miyake et al. (2000) (Mcgrath et al., 2015; H. Robinson, Calamia, Gläscher, Bruss, & Tranel, 2014). Others identify a different number of factors entirely, especially in samples of children, where studies may find that only one or two latent factors can successfully account for most of the variance in executive performance (Brydges, Fox, Reid, & Anderson, 2014; Van der Ven, Kroesbergen, Boom, & Leseman, 2013; Wiebe, Espy, & Charak, 2007).

There may be several reasons for the differences between the conclusions of different studies regarding the underlying structure of EF. One such reason pertains to the population evaluated. Participant characteristics, including the presence of psychopathology or neurological illness, can influence the results of statistical modeling studies. One example is the case of EF in children with acquired head injuries. While the latent structure of these cognitive functions in most samples of children usually involves only one or two factors, a study of children with a history of brain injury found that models of EF in these individuals included four to five factors (Brookshire, Levin, Song, & Zhang, 2004). While it could be the case that the very structure of EF differs depending on the population, it could also be the case that a universal structure exists, but has not yet been captured by current theoretical models. Nevertheless, before either of these conclusions can be reached, existing models must be replicated in different populations in order to accrue evidence of their stability or lack thereof. This line of research is especially important given the ubiquitous nature of executive dysfunction in psychiatric disorders (Snyder, Miyake, et al., 2015) and other medical illnesses (Krivitzky, Walsh, Fisher, & Berl, 2016).

Another possible reason for differences in findings between studies is the type of task used. Even small changes in a neuropsychological battery may result in significant alterations of the findings produced by statistical modeling. In a study by Hull et al. (2008), for instance, the procedures performed by Miyake et al. (2000) were largely replicated, save for the inclusion of some verbal or non-verbal tasks, to ensure that each executive component was evaluated by both types of instrument. The resulting analyses revealed a different structural equation model from that identified by Miyake et al. (2000) whereby only shifting and updating factors were identified.

The use of computerized *versus* standard paper-and-pencil tasks may also represent a potential confounder in studies of EF modeling. The majority of tasks used by Miyake et al. (2000) were computerized, which may confer several advantages over paper-and-pencil tasks regarding the stability of the testing context and stimulus presentation. Nevertheless, computerized assessment tasks often tap into different constructs than paper-and-pencil instruments, even when they are ostensibly similar. Comparative studies of instruments such as the Wisconsin Card Sorting Test and the Trail Making Test, which are available in both manual and computerized form, have corroborated this hypothesis, suggesting that the different versions of each instrument are not psychometrically equivalent (Drapeau, Bastien-Toniazzo, Rous, & Carlier, 2007; Feldstein et al., 1999; Steinmetz, Brunner, Loarer, & Houssemand, 2010). As such, given that Miyake et al. (2000) used computerized versions of the Tower of Hanoi and Wisconsin Card Sorting Tests, for instance, it is possible that attempts to replicate their findings using manual versions of these tasks would reach different results.

In summary, there may be several reasons why EF models such as that produced by Miyake et al. (2000) have not been consistently replicated. Either there is no universal underlying structure for the EF, or existing attempts have not been successful at elucidating it. Nevertheless, given the relevance of the EF, it is important that studies continue to investigate its underlying structure and characteristics. As this research continues, it is important to be mindful of all previously mentioned sources of variability, such as the population studied, and the nature of the tests used in the assessment battery. The more closely a study can be replicated, the more likely other authors may be to either confirm or disprove the findings, facilitating the identification of promising models of EF. This includes using widely available assessment instruments which have been adapted and standardized for use in different locations, in order to verify whether a similar underlying structure of EF is identified using the same set of instruments across different contexts.

There is also a need to analyze the applicability of EF models different populations, especially those with medical and psychiatric disorders. Mental illnesses such as major depression (MDD) and bipolar disorder (BD) are among the most disabling conditions in the world, resulting in a significant worldwide burden in terms of disability adjusted life-years (Murray et al., 2015). Cognitive impairment is a common feature of these conditions, and the EF are often associated with outcome variables pertaining to functional capacity and quality of life in these populations (Cotrena et al., 2016). Though the need to address the impact of mental illnesses on the EF has been acknowledged, and addressed through cognitive and functional remediation programs (Bonnin et al., 2016; Zyto, Jabben, Schulte, Regeer, & Kupka, 2016), these approaches are largely borne out of clinical experience. The cognitive functions addressed by these programs come from general theoretical models such as those of Miyake et al. (2000) and Diamond et al. (2014), neither of which has been empirically replicated in these populations. Studies designed in a way which allows for their replication across populations and regions may also shed light on the possible universal invariance – or regional variability – of EF. This will allow for the development of more effective and targeted interventions which bring more benefits to these populations.

In light of these observations, the aim of the present study was to analyze the latent variables underlying a neuropsychological assessment battery comprised of widely used, paper-and-pencil tests. The analysis will involve a population of healthy adults, as well as individuals with BD and MDD, in order to investigate whether the underlying structure of the battery differs in each of these populations.

Method

Participants

The sample included a total of 303 participants, including 119 adults with no mood disorders, 84 patients with MDD and 100 individuals with BD. Patients were recruited from the mood disorders clinic of a large regional psychiatric hospital, a university teaching clinic, and private practice. Control participants were selected by convenience from work and university settings, as well as the community at large.

All patients were at least 18 years old, and had at least one year of formal education. The following exclusion criteria were applied to the sample: uncorrected sensory impairments which would interfere with task performance, neurological conditions, and pregnancy or lactation. Patients with psychotic symptoms at the time of testing or who reported substance abuse within the previous month were also excluded from participation. The control group was selected using the same criteria, and was screened for mood disorders according to DSM-5 criteria, cognitive impairment and intellectual disability.

Instruments and Procedures

This study was approved by the Research Ethics Board of the institution where it was conducted (protocol number FAPSI/PUCRS: 014/2013; CAEE nº 23995513.5.0000.5336; report nº 482.688 de 06/12/2013), and all subjects provided written consent for participation. Participants were evaluated in individual testing sessions, and the presence of mood disorders was examined using DSM-5 criteria (American Psychiatric Association, 2013). All diagnoses were made using the Mini International Neuropsychiatric Interview (MINI) (Amorim, 2000), and confirmed by consensus with a clinical psychologist with expertise in mood disorders. All subjects took part in at least two assessment sessions lasting approximately one and a half hours each.

Inclusion and exclusion criteria were first investigated using a sociocultural and health questionnaire and semi-structured interview. Participants were then administered the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975), adapted by (Chaves & Izquierdo, 1992) for the local population. Subjects also completed the Block Design and Vocabulary Subtests from the Wechsler Adult Intelligence Scales (WAIS-III) (Nascimento, 2004), whose scores were converted to estimated IQ using the tables provided by Jeyakumar, Warriner, Raval, and Ahmad, (2004). These instruments were used to screen for cognitive impairment and intellectual disability, respectively. Symptoms of depression and mania were investigated using the Hamilton Depression Rating Scale (HDRS) (Gorenstein, Andrade, & Zuardi, 2000; Hamilton, 1960) and the Young Mania Rating Scale (YMRS) (Vilela & Loureiro, 2000; Young, Biggs, Ziegler, & Meyer, 1978).

All participants completed an identical assessment battery, containing the following instruments: i) Hayling Sentence Completion Test (Burgess & Shallice, 1997; Fonseca et al., 2010), which yields the following variables: time to completion (part A, part B), number of errors (part B) and difference score (part B time-part A time); ii) Trail Making Test (Reitan & Wolfson, 1995) which yields the following variables: time to completion (part A, part B), number of errors (part B), difference score (part B time-part A time), and ratio score (part B/part A); iii) Modified Card Sorting Test (Nelson, 1976), which yields the following variables: number of categories completed, perseverative errors, nonperseverative errors and failure to maintain set; iv) Sentence Word Span (Fonseca, Salles, & Parente, 2009), which provides a total score and a score for the longest sequence of correctly recalled items; v) Digit Span Forwards and Backwards (Wechsler, 2002), which yields a total score and a score for the longest sequence of correctly recalled items for each portion of the test (forwards and backwards); vi) Stroop Color-Word Test (Stroop, 1935), which yields scores for the total number of correct and incorrect responses for each of the three parts of the test (Words, Colors and Color-Words), in addition to an interference score; vii) Verbal fluency tests (Fonseca, Parente, Cote, Ska, & Joanette, 2008; Joanette, Ska, & Cote, 2004), which inform the total number of words recalled using each production criteria (phonemic, semantic and unconstrained).

Data analysis

The data was analyzed using the Statistical Package for Social Sciences (SPSS), version 23.0. The Kaiser-Meyer-Olkin (KMO) Measure of Sampling Adequacy was used to determine the suitability of the data for factor analysis. Demographic and clinical characteristics were analyzed using descriptive methods. Performance on EF tasks was converted into Z-scores based on normative data stratified by age and education. EF scores were then submitted to exploratory data analysis, with Oblimin rotation. The number of factors was selected based on the Kaiser method (eigenvalues>1) and the Scree plot (Cattell, 1966; Field, 2009). Factor loadings were interpreted using a conservative approach, whereby only loadings with a magnitude of at least 0.35 were considered (Field, 2009).

Results

Participant characteristics are shown in Table 1.

Table 1. *Participant demographic and clinical characteristics.*

	BD (n=100)	MDD (n=84)	C (n=119)
Age*	42.83(13.31)	37.96(14.53)	29.08(11.52)
Education*[1]	13.21(3.53)	14.64(4.48)	15.33(3.82)
SES*	28.56(9.33)	30.57(8.30)	30.54(7.23)

HDRS*	13.19(9.45)	9.69(7.48)	2.14(3.01)
YMRS*	3.16(3.75)	1.42(1.83)	0.76(1.45)
IQ*	107.02(12.64)	114.55(12.32)	119.78(10.72)
MMSE*	27.83(2.25)	27.28(2.43)	29.16(1.41)
Gender (F/M)[2]	81/20	61/23	57/63

Note: BD = Bipolar disorder; MDD = Major depressive disorder; C = control participants; SES = Socioeconomic status; HDRS = Hamilton Depression Rating Scale; YMRS = Young Mania Rating Scale; IQ = Estimated intelligence quotient; MMSE = Mini Mental State Examination.

The analysis yielded a model in which nine factors had an Eigenvalue of at least one. However, upon analysis of the Scree plot, six factors were retained in the model. The factor loadings in this model are shown in Table 3.

Table 3. Factor loadings in exploratory factor analysis of EF battery in healthy adults and patients with mood disorders.

Variables	Factor loadings					
	1	2	3	4	5	6
DigSpan Fwd	.775					
DigSpan Fwd - LSeq	.734					
DigSpan Bwd	.707					
DigSpan Bwd - LSeq	.637					
Hayling A Time				-.366		
Hayling B Time			.978			
Hayling B Err			.460			
Hayling B-A Time			.865			
TMT A Time				-.451		
TMT B Time		.769				
TMT B Err		.685				
TMT B-A Time		.878				
TMT B/A Time		.776				
SWS Total	.576					
SWS – Lseq	.597					
MCST NCat						.644
MCST PersErr						.600
MCST NPersErr						.503
MCST FMS						
Stroop - Word				-.611		
Stroop – Word Err						
Stroop - Color				-.561		
Stroop – Color Err						
Stroop - Color-Word					.680	
Stroop – Color-Word Err					.450	
Stroop - Interference					.887	
SVF				-.439		
UVF				-.603		

PVF	-.551

DigSpan Fwd = Digit Span Forward, Total score; DigSpan Fwd - LSeq = Digit Span Forward, Longest correct sequence; DigSpan Bwd = Digit Span Backward, Total score; DigSpan Bwd - LSeq = Digit Span Backward, Longest correct sequence; Hayling A Time = Time taken to complete part A of the Hayling Test; Hayling B Time = Time taken to complete part B of the Hayling Test; Hayling B Err = Number of errors in Part B of the Hayling Test; Hayling B-A Time = difference between time taken to complete parts A and B of the Hayling Sentence Completion Test; TMT A Time = Time taken to complete part A of the Trail Making Test; TMT B Time = Time taken to complete part B of the Trail Making Test; TMT B Err = Number of errors in part B of the Trail Making Test; TMT B-A Time = difference between time taken to complete parts A and B of the Trail Making Test; TMT B/A Time = ratio score of the time taken to complete parts B and A of the Trail Making Test; SWS Total = Sentence Word Span Task, Total score; SWS LSeq = Sentence Word Span Task, Longest correct sequence; MSCT NCat = number of categories completed in the Modified Card Sorting Test; MCST PersErr = Number of perseverative errors in the Modified Card Sorting Test; MCST NPersErr = Number of nonperseverative errors in the Modified Card Sorting Test; MCST FMS = Number of failures to maintain set on the Modified Card Soritng Test; Stroop - Word = Number of correct responses in the Word portion of the Stroop Color Word Test; Stroop – Word Err = Number of errors in the Word portion of the Stroop Color Word Test; Stroop - Color = Number of correct responses in the Color portion of the Stroop Color Word Test; Stroop – Color Err = Number of errors in the Color portion of the Stroop Color Word Test; Stroop - Color-Word = Number of correct responses in the Color-Word portion of the Stroop Color Word Test; Stroop - Color-Word Err = Number of errors in the Color-Word portion of the Stroop Color Word Test; Stroop - Interference = Interference score for the Stroop Color Word Test; SVF = Semantic Verbal Fluency; UVF = Unconstrained verbal fluency; PVF = Phonemic verbal fluency.

As can be seen in Table 2, working memory tasks loaded exclusively on to Factor 1. Variables obtained from the Trail Making Test loaded onto factor 2, while those drawn from the Hayling Sentence Completion Test loaded onto factor 3. Factor 4 included measures of processing speed derived from part A of the Trail Making Test and Hayling Sentence Completion Test, in addition to the number of words read in the first two portions of the Stroop Color-Word Test, and the number of words elicited in measures of verbal fluency. The fifth factor included the number of correct and incorrect responses to the interference portion of the Stroop Color-Word Test, as well as its derived interference score. Lastly, Factor 6 included three of the four variables pertaining to the Modified Card Sorting Test. It is important to note that Factor 1 accounted for a significant portion of variability in participant scores (17.51%). For contrast, the second factor accounted for only 8.67% of the variance.

The applicability of the six-factor model to a subsample of participants, consisting only of patients with MDD, was then examined. The analysis of the Scree plot suggested that a five-factor model would be more appropriate for the data, and as such, the model was adjusted. The factor loadings for EF tasks in patients with MDD, according to a five-factor model, are shown in Table 3.

Table 3. Factor loadings in exploratory factor analysis of EF battery in patients with major depressive disorder.

Variables	Factor loadings				
	1	2	3	4	5
DigSpan Fwd	.443				
DigSpan Fwd - LSeq	.512				
DigSpan Bwd	.419		.356		
DigSpan Bwd - LSeq	.467				
Hayling A Time					
Hayling B Time				.821	
Hayling B Err	.575			.355	
Hayling B-A Time				.781	
TMT A Time	.358				
TMT B Time		-.830			
TMT B Err		-.861			
TMT B-A Time		-.928			
TMT B/A Time		-.865			
SWS Total				-.459	
SWS – Lseq				-.433	-.398
MCST NCat	.836				
MCST PersErr	.618				
MCST NPersErr	.594				
MCST FMS	.748				
Stroop - Word			.380		
Stroop – Word Err					
Stroop - Color					-.507
Stroop – Color Err					
Stroop - Color-Word					-.986
Stroop – Color-Word Err					-.494
Stroop - Interference					-.935
SVF			.594		
UVF			.882		
PVF			.661		

DigSpan Fwd = Digit Span Forward, Total score; DigSpan Fwd - LSeq = Digit Span Forward, Longest correct sequence; DigSpan Bwd = Digit Span Backward, Total score; DigSpan Bwd - LSeq = Digit Span Backward, Longest correct sequence; Hayling A Time = Time taken to complete part A of the Hayling Test; Hayling B Time = Time taken to complete part B of the Hayling Test; Hayling B Err = Number of errors in Part B of the Hayling Test; Hayling B-A Time = difference between time taken to complete parts A and B of the Hayling Sentence Completion Test; TMT A Time = Time taken to complete part A of the Trail Making Test; TMT B Time = Time taken to complete part B of the Trail Making Test; TMT B Err = Number of errors in part B of the Trail Making Test; TMT B-A Time = difference between time taken to complete parts A and B of the Trail Making Test; TMT B/A Time = ratio score of the time taken to complete parts B and A of the Trail Making Test; SWS Total = Sentence Word Span Task, Total score; SWS LSeq = Sentence Word Span Task, Longest correct sequence; MSCT NCat = number of categories completed in the Modified Card Sorting Test; MCST PersErr = Number of perseverative errors in the Modified Card Sorting Test; MCST NPersErr = Number of nonperseverative errors in the Modified Card Sorting Test; MCST FMS = Number of failures to maintain set on the Modified Card Soritng Test; Stroop - Word = Number of correct responses in the Word portion of the Stroop Color Word Test; Stroop – Word Err = Number of errors in the Word portion of the Stroop Color Word Test; Stroop - Color = Number of correct responses in the Color portion of the Stroop Color Word Test; Stroop – Color Err = Number of errors in the Color portion of the Stroop Color Word Test; Stroop - Color-Word = Number of correct responses in the Color-Word portion of the Stroop Color Word Test; Stroop - Color-Word Err = Number of errors in the Color-Word portion of the Stroop Color Word Test; Stroop - Interference = Interference score for the Stroop Color Word Test; SVF = Semantic Verbal Fluency; UVF = Unconstrained verbal fluency; PVF = Phonemic verbal fluency.

The distribution of factor loadings for the EF battery in patients with MDD was somewhat different from that observed in the sample as a whole. The first factor included the Forward and Backward Digit Span Tasks, as well as the number of errors in part B of the Hayling Sentence

Completion Test, the time taken to complete part A of the Trail Making Test, and all variables in the Modified Card Sorting Test. Though many of these tasks evaluate cognitive flexibility (e.g. the Modified Card Sorting Test and part B of the Hayling Sentence Completion Test), some also evaluate focused attention and processing speed (Forward Digit Span and Trail Making Test part A). The second factor included all scores from part B of the Trail Making Test, as well as ratio and difference scores for this instrument. This factor may be interpreted as a measure of visuospatial inhibitory control and cognitive flexibility. Factor three appeared to reflect verbal fluency, while factor four included both the Hayling Sentence Completion Test and the Sentence Word Span task. Both tasks involve language processing at a sentence level. Lastly, factor six included scores for the Color and Interference sections of the Stroop Color Word Test, which may represent verbal inhibition.

Lastly, the analysis was repeated for the subsample of patients with bipolar disorder. However, in this case, the analysis of the Scree plot suggested that a three-factor model may be more suited to the data. The factor loadings in the three-factor model are therefore shown in Table 4.

Table 4. Factor loadings in exploratory factor analysis of EF battery in patients with bipolar disorder.

Variables	Factor loadings		
	1	2	3
DigSpan Fwd			.791
DigSpan Fwd - LSeq			.706
DigSpan Bwd			.632
DigSpan Bwd - LSeq			.582
Hayling A Time	.610		
Hayling B Time	.498		
Hayling B Err			
Hayling B-A Time			
TMT A Time	.774		
TMT B Time		.878	
TMT B Err		.776	
TMT B-A Time		.847	
TMT B/A Time	-.396	.714	
SWS Total			.528
SWS – Lseq			.537

MCST NCat			
MCST PersErr			
MCST NPersErr			
MCST FMS			
Stroop - Word	.731		
Stroop – Word Err			
Stroop - Color	.640		
Stroop – Color Err			
Stroop - Color-Word			.454
Stroop – Color-Word Err			
Stroop - Interference			.371
SVF	.376		
UVF	.626		
PVF	.595		

DigSpan Fwd = Digit Span Forward, Total score; DigSpan Fwd - LSeq = Digit Span Forward, Longest correct sequence; DigSpan Bwd = Digit Span Backward, Total score; DigSpan Bwd - LSeq = Digit Span Backward, Longest correct sequence; Hayling A Time = Time taken to complete part A of the Hayling Test; Hayling B Time = Time taken to complete part B of the Hayling Test; Hayling B Err = Number of errors in Part B of the Hayling Test; Hayling B-A Time = difference between time taken to complete parts A and B of the Hayling Sentence Completion Test; TMT A Time = Time taken to complete part A of the Trail Making Test; TMT B Time = Time taken to complete part B of the Trail Making Test; TMT B Err = Number of errors in part B of the Trail Making Test; TMT B-A Time = difference between time taken to complete parts A and B of the Trail Making Test; TMT B/A Time = ratio score of the time taken to complete parts B and A of the Trail Making Test; SWS Total = Sentence Word Span Task, Total score; SWS LSeq = Sentence Word Span Task, Longest correct sequence; MSCT NCat = number of categories completed in the Modified Card Sorting Test; MCST PersErr = Number of perseverative errors in the Modified Card Sorting Test; MCST NPersErr = Number of nonperseverative errors in the Modified Card Sorting Test; MCST FMS = Number of failures to maintain set on the Modified Card Soritng Test; Stroop - Word = Number of correct responses in the Word portion of the Stroop Color Word Test; Stroop – Word Err = Number of errors in the Word portion of the Stroop Color Word Test; Stroop - Color = Number of correct responses in the Color portion of the Stroop Color Word Test; Stroop – Color Err = Number of errors in the Color portion of the Stroop Color Word Test; Stroop - Color-Word = Number of correct responses in the Color-Word portion of the Stroop Color Word Test; Stroop - Color-Word Err = Number of errors in the Color-Word portion of the Stroop Color Word Test; Stroop - Interference = Interference score for the Stroop Color Word Test; SVF = Semantic Verbal Fluency; UVF = Unconstrained verbal fluency; PVF = Phonemic verbal fluency.

The first factor among patients with BD is associated with verbal and motor processing speed, as evidenced by the high loadings of variables such as the time taken to complete parts A of the Trail Making Test and Hayling Sentence Completion Test, and the number of correct responses to the Stroop Word and Color Sections. The second factor included scores from part of the Trail Making Test B, as well as the derived A/B and B-A scores, both of which are associated with visuospatial inhibition and mental flexibility. The last factor included all working memory tests, in addition to the interference condition of the Stroop test (cognitive flexibility and inhibitory control).

Discussion

The aim of this study was to analyze the latent structure of EF in a population of healthy adults and individuals with mood disorders, through the factor analysis of a neuropsychological assessment battery designed to evaluate mainly EF. The analyses revealed that the latent structure of EF differed from that described by experimental theoretical models such as those of Miyake et al. (2000) and clinical models like that of Diamond (2014). In addition to identifying more than three latent factors among the assessment tasks, many factors included all scores from a single task rather than a mix of variables from several different instruments. This was not the case, however, for the factors which included measures of working memory and processing speed. While the working memory factor included two different instruments which evaluate this cognitive function – Sentence Word Span and Digit Span Backwards – the processing speed factor included variables from the TMT, Hayling Sentence Completion Test, Stroop Color-Word Test and verbal fluency instruments. These findings have important implications for the study of EF models, and for neuropsychological assessment.

The difference between the latent structure of the assessment battery in the present study and that described by other models in the literature may reflect the susceptibility of EF models to external variables, including the way in which these constructs are operationalized for the purpose of assessment. While most existing models were developed using scores derived from ostensibly healthy populations, it is important to verify whether findings from these subjects translate to other contexts. The present investigation appears to suggest that this may not be the case. The number and configuration of factors differed greatly between this sample of patients with MDD, BD, and no mood disorders, and studies of healthy adults in the literature (Friedman et al., 2008; Akira Miyake et al., 2000). This finding underscores the importance of replicating existing models of EF across different populations rather than simply assuming their generalizability.

One possible reason why the number of factors differed so sharply among populations may be the fact that, though the tasks themselves are the same, the underlying mechanisms used to complete them may differ between individuals. Tasks such as the Wisconsin Card Sorting Test are often said to measure cognitive shifting (Strauss, Sherman, & Spreen, 2006), but they are also known to rely on working memory: a recent study has found that a decrease in working memory capacity or an increase in working memory load can lead to impairments in rule inference (Lange et al., 2016b). As a result, the variability in card sorting tasks may mirror that of working memory instruments in populations where the latter in impaired. This was observed in the present study in the MDD sample, where the MCST loaded onto the same factor as the Digit Span Forward and Backward. However, it was not the case for either BD or the sample as a whole. In the full sample, the MCST loaded on to a separate factor. Perhaps in this population, which contained control subjects who are unlikely to have impairments in working memory, performance on the MCST relied on separate inferential or logical reasoning processes. Since these processes differed from those used in the remaining tasks, the instrument loaded onto a different factor. A similar analysis of the cognitive underpinnings of each EF instrument may help shed light on the other differences identified between the latent structure of the assessment battery in each of these populations.

Another possible explanation for the difference between our findings refers to the nature of EF and of the concepts examined by the tasks which purportedly evaluate them. It has been previously hypothesized that the components of EF, as currently defined, refer to task-specific behaviors rather than cognitive functions per se (Packwood, Hodgetts, & Tremblay, 2011). This may explain why in many instances, tasks loaded on to their own individual factors. It could be the case that each of the tasks used in the present study evaluates a distinct behavior, and that there is little overlap between the instruments used. This would have important implications for the current literature, seeing as the instruments used in the present study consist of some of the most widely used measures of EF in neuropsychological assessment. There is a need to look more closely at instruments such as the Wisconsin Card Sorting Test, the Trail Making Test and the Stroop Color Word Test, and verify the similarities between the abilities evaluated by each of these tasks and those observed in other daily life activities or assessment instruments.

Despite the variability between the different latent structure models, it is important to note that some tasks showed a similar loading structure in different samples. The working memory tasks, for instance, both loaded onto the same factor in the overall sample and the subgroup of patients with BD. This may be because working memory is more easily operationalized. Despite recent changes in the way working memory is conceptualized (Ma, Husain, & Bays, 2014), the dominant perspective in the area is still Alan Baddeley's multicomponent model (Baddeley, 2012). As a result, most tasks operationalize this construct in a similar way, requiring that the respondent maintain a series of items in working memory while performing some form of manipulation upon this information. Similarly, measures such as the Trail Making Test part A and verbal fluency tasks also loaded onto the same factor across different models. This may be attributed to the contribution of processing speed to performance in both of these instruments (Elgamal, Roy, & Sharratt, 2011; Johansson, Berglund, & Ronnback, 2009; Shao, Janse, Visser, & Meyer, 2014).

The present study had some limitations, such as the lower statistical power in the subgroup analysis given the reduced sample size. We were also unable to control for variables such as medication use and number of mood episodes in the clinical groups Nevertheless, from an exploratory standpoint, we believed these analyses may have contributed to current reflections on the nature of EF in different clinical contexts. The lack of visuospatial working memory assessments may also be seen as a limitation, given that both tasks used to evaluate working memory in the present study were predominantly verbal. Future studies may wish to include, in addition to the instruments used in the present investigation, verbal and non-verbal equivalents. The inclusion of the Oral TMT (Ricker & Axelrod, 1994), for instance, may help reveal whether verbal and visuospatial components load onto similar or different factors. Though the current study appears to suggest that this is the case, the verbal and visuospatial tasks used in our assessment battery (such as the Hayling Sentence Completion Test and the Trail Making Test) have other differences in addition to the sensory modality. As such, this investigation cannot conclusively claim that verbal and visuospatial tasks evaluate fundamentally different underlying processes.

These findings underscore the importance of replicating models of EF across different populations, seeing as they may differ even when the tasks used to evaluate the constructs are the same. There is also a need to evaluate ‘complex’ EF more closely, in order to identify their cognitive underpinnings, and verify whether these are the same across different populations. If multiple subscores are available for EF tasks, different sets of scores may be used according to the profile of the populations studied. Lastly, future attempts to develop theoretical models of EF may wish to combine computerized, simple tasks with more complex instruments, in order to determine how individual EF skills may contribute to performance in more widely used tasks such as the Wisconsin Card Sorting Test and Trail Making Test. With regards to implications for neuropsychological intervention, given that the underlying cognitive abilities for a particular score may differ between populations, this must be considered when selecting pre-post intervention outcomes as well as the tasks used to stimulate each ability.

2.2 ESTUDO 2: "COGNITIVE ABILITIES UNDERLYING PERFORMANCE ON THE MODIFIED CARD SORTING TEST: NOVEL AND TRADITIONAL SCORES"

Abstract

The Wisconsin Card Sorting Test (WCST; Heaton, 1993) is among the most traditional instruments for the assessment of executive functions (EF). Although several variations of the original task are available, one of the most widely used is Nelson's 1976 Modified Card Sorting Test (MCST). Though the MCST is faster to administer, less frustrating for respondents and less ambiguous in its scoring than the WCST, it has been criticized for its low discriminability between clinical conditions and for the fact that it seems to evaluate multiple EF at once. The aim of the present study was to examine the underlying cognitive functions of the MCST and develop novel scores which may be more specific and closely related to different EF than the most traditionally used scores for this instrument (number of categories completed, perseverative errors). The sample included 94 control participants, 87 individuals with bipolar disorder (BD) and 64 patients with major depressive disorder (MDD). The correlation between novel and traditional MCST scores and several widely used measures of EF was examined. Regression analyses were used to examine predictors of MCST scores. The majority of novel and traditional scores were predicted by the Trail Making Test B and at least one measure of working memory, save for the percentage of perseverative and nonperseverative errors. Both traditional and novel scores differentiated between some clinical and control groups. These findings highlight the need to isolate working memory processes in the MCST, and identify new scoring methods which may be used to confer greater specificity and interpretability to the results of the MCST.

Introduction

The Wisconsin Card Sorting Test (WCST; Heaton, Chelune, Curtiss, Kay, & Talley, 1993) is among the most traditional instruments for the assessment of executive functions (EF). Though it is still widely used in the assessment of several executive components, its low specificity has long been a point of contention. In addition to showing similar rates of impairment in populations with both frontal and non-frontal neurological damage (Nyhus & Barcelo, 2009), the WCST is also sensitive to cognitive alterations observed in psychiatric and neurodevelopmental disorders, such as bipolar disorder (L. J. Robinson, Gray, Ferrier, & Gallagher, 2016b), schizophrenia (Singh, Aich, & Bhattarai, 2017), Tourette syndrome (Eddy & Cavanna, 2017), and autism (Westwood, Stahl, Mandy, & Tchanturia, 2016). At the same time, the test has been unable to differentiate between conditions such as autism and anorexia nervosa (Westwood et al., 2016), attention-deficit hyperactivity disorder and disruptive mood dysregulation disorder (Taskiran, Mutluer, & Necef, 2017), and bipolar disorder and major depression (Poletti et al., 2017).

One possible reason for the low specificity of the WCST is the fact that, though it is widely described as a measure of EF (Lezak, Howieson, Bigler, & Tranel, 2012), its first version was developed in the 1940s (Berg, 1948). The instrument therefore predates the introduction of concepts such as the "central executive" (Baddeley & Hitch, 1974) component of working memory, an early precursor to the modern definition of EF, by approximately 30 years. As a result, the cognitive constructs it was developed to evaluate may not fully correspond to those referred to by the term EF in more modern theories. Nevertheless, it continues to be used for this purpose, perhaps due to the similarity between the terms used in the original description of the test- such as "abstract thinking" and "shift of set" – and the terminology used to describe EF in the current literature (Berg, 1948; Diamond, 2014).

Although the general format of the WCST continues to be used in current studies, variations of the original task have been developed over the years. In order to address both practical and psychometric concerns, there have been several attempts to develop additional scoring metrics or different versions of the original WCST. The original version of the test, developed by Berg et al. (1948) contained a single pack of 60 response cards. Yet the most widely used version of the instrument today contains 128 cards, and was developed by Heaton et al. (Heaton et al., 1993). There are also computerized and reduced versions of the instrument, containing 64 (Kongs, Thompson, Iverson, & Heaton, 2000) or 48 cards (Nelson, 1976).

The 48-card version of the WCST, hereby referred to as the Modified Card Sorting Test (MCST), represents one of the first attempts to increase the specificity of the instrument. It differed from the original WCST in that every card had at most a single feature in common with another, reducing the ambiguity associated with interpreting the strategies used by participants in the original WCST. In the long version of the test, when participants combine cards which have more than one feature in common, it may be unclear to the researcher which of the features is guiding the selection. In these situations, examiners may have to rely on assumption or inference to judge whether a given response is correct. By removing ambiguous cards, Nelson created an instrument which, though potentially distinct from the standard WCST, has been able to evaluate similar cognitive functions in a number of populations (e.g. bipolar disorder: (Xu et al., 2012); schizophrenia (Sasabayashi et al., 2016); Parkinson's disease (Meyer et al., 2015)). It is also important to note that the reduction in the number of cards had an additional objective. By reducing the number of trials, the test would be shorter, and therefore expose participants who had trouble completing it to a shorter period of stress. This has led the MCST to be recommended as an alternative to the traditional WCST in elderly individuals, who may become much too stressed by the 128-card version of the instrument (Greve & Smith, 1991)

Despite these modifications, there is still room for ambiguity in the MCST. The scores proposed by Nelson – total number of categories, number and type of errors – are still quite vague. They have shown no sensitivity to a history of child adversity in major depression (Dannehl, Rief, & Euteneuer, 2017) and been unable to distinguish between patients with major depression and bipolar disorder (Cotrena et al., 2016), or patients with Asperger's syndrome, attention-deficit/hyperactivity disorder and control subjects (Gonzalez-Gadea et al., 2013). Findings such as these have prompted some researchers to develop additional scoring metrics for the MCST. The most comprehensive attempts at modifying the way in which the MCST is scored were made by Cianchetti et al. (Cianchetti et al., 2007, 2005), who derived a series of additional measures from the MCST, including the percentage of perseverative and non-perseverative errors, and categorizing efficiency.

Though many of the newly-developed scores appeared to provide an interesting complement to existing measures derived from the MSCT, they have not been widely adopted in recent studies. As can be seen in recent publications of normative data for the MCST, studies still tend to rely on original scores such as the number of categories and perseverative errors (Arango-Lasprilla et al., 2015, 2017; Wang et al., 2011; Zimmermann, Cardoso, Trentini, Grassi-Oliveira, & Fonseca, 2015). This may be because no studies similar to that of Cianchetti et al. have been conducted in adult populations. Additionally, no attempts have yet been made to identify the association between MCST scores and performance in other measures of EF in order to shed light on the cognitive processes underlying this task. Such an approach would be useful in developing novel types of score, which may reflect different cognitive abilities than those examined by traditional outcome measures on the MCST. In addition to investigating the relationship between the MCST and other measures of EF, it would be important to verify whether the use of additional scores could contribute to the discriminability of the assessment instrument.

As previously mentioned, some of the criticism aimed at card sorting tests such as the MCST pertains to its inability to differentiate between, for instance, clinical groups with varying levels of executive dysfunction. An interesting context in which to evaluate the discriminative validity of the MCST may be in the comparison between patients with major depressive disorder (MDD) and bipolar disorder (BD). Though some studies have identified differences between these populations (Xu et al., 2012), others have found them to be neuropsychologically indistinguishable (Samamé, Szmulewicz, Valerio, Martino, & Strejilevich, 2017). The ability to reveal differences between the cognitive performance of clinical groups which other assessment tasks may not have been able to differentiate would provide important evidence of the validity of scores on the MCST.

Given the advantages of the MCST over the traditional WCST, and the fact that it is still widely used in the literature, it may be useful to examine whether additional scores for the MCST may be better able to reflect EF and differentiate between clinical groups than scores such as the number of categories and perseverative errors. As such, the aim of the present study was to examine which cognitive and executive abilities underlie existing and novel scores for the MCST, and to identify their potential contributions to the literature.

Methods

Participants

The sample was composed of 245 participants, of whom 94 were adults with no mood disorders, 40 had a diagnosis of BD type I, 47 suffered from BD type II, and 64 had been diagnosed with MDD. Patients were recruited from the mood disorders outpatient unit of a psychiatric hospital, a university teaching clinic, and private practice. Control participants were selected by convenience from work and university settings, as well as the community at large.

All patients were at least 18 years old, and had at least one year of formal education. The following exclusion criteria were applied to the sample: uncorrected sensory impairments which would interfere with task performance, neurological conditions, and pregnancy or lactation. Patients with psychotic symptoms at the time of testing were also excluded from participation. The control group was selected using the same criteria, and was screened for mood disorders according to DSM-5 criteria, cognitive impairment and intellectual disability.

Instruments

All participants provided written consent for participation, and the present study was approved by the Research Ethics Committee of the institution where it was conducted. Subjects were evaluated in individual sessions, and the presence of mood disorders was examined using DSM-5 criteria (American Psychiatric Association, 2013), and confirmed by consensus with a clinical psychologist with expertise in mood disorders. All subjects took part in at least two assessment sessions lasting approximately one and a half hours each.

Inclusion and exclusion criteria were first investigated using a sociocultural and health questionnaire. Intellectual disability was screened using the Block Design and Vocabulary Subtests from the Wechsler Adult Intelligence Scales (WAIS-III) (Nascimento, 2004), which were used to calculate estimated IQ using the tables provided by (Jeyakumar et al., 2004). Participants were then administered the Mini-Mental State Examination (MMSE; (Chaves & Izquierdo, 1992; Folstein et al., 1975), in order to screen for cognitive impairments.

Clinical assessments were performed using the Mini International Neuropsychiatric Interview (MINI) (Amorim, 2000). Symptoms of depression and mania were investigated using the Hamilton Depression Rating Scale (HDRS) (Gorenstein et al., 2000; HAMILTON, 1960) and the Young Mania Rating Scale (YMRS) (Vilela & Loureiro, 2000; Young et al., 1978), respectively.

In addition to the MCST (Nelson, 1976), participants were administered the following measures of EF: i) Hayling Sentence Completion Test (Burgess & Shallice, 1997; Fonseca et al., 2010), which yields the following variables: time to completion (part A, part B), number of errors (part B) and difference score (part B time-part A time); ii) Trail Making Test (Reitan & Wolfson, 1995) which yields the following variables: time to completion (part A, part B), number of errors (part B), difference score (part B time-part A time), and ratio score (part B/part A); iii) Sentence Word Span (Fonseca, Salles, & Parente, 2009), which provides a total score and a score for the longest sequence of correctly recalled items; iv) Digit Span Forwards and Backwards (Wechsler, 2002), which yields a total score and a score for the longest sequence of correctly recalled items for each portion of the test (forwards and backwards); v) Stroop Color-Word Test (Stroop, 1935), which yields scores for the total number of correct and incorrect responses for each of the three parts of the test (Words, Colors and Color-Words), in addition to an interference score.

Data analysis

Participant characteristics were first analyzed using descriptive statistics. Derived scores for the WCST were then calculated as described in Table 1. Neither the classical scores nor the derived scores were found to be normally distributed, as determined by Kolmogorov-Smirnov tests. As such, the correlation between the WCST and executive function tasks was examined using Spearman correlation coefficients.

A series of stepwise regression analyses was then performed, one for each classical and derived score on the WCST. Measures of EF found to be significantly correlated with each outcome variable on the WCST were entered into its regression model as predictors. In addition to these variables, all models included diagnosis, age and education as potential predictors. This was done in order to control for the potential confounding effect of these variables.

Lastly, scores were compared between participants with BD type I, BD type II, MDD and no mood disorders, using Kruskal-Wallis tests. In order to reduce the confounding effects of demographic and clinical variables on this analysis, only a subgroup of participants was selected for these comparisons. These particular subgroups did not differ with regards to age or education, and had mild to no symptoms of depression (HAMD<17; Zimmermann et al., 2013), as well as no symptoms of mania (YMRS < 7).

Table 1. Description of WCST scores.

	Description
Number of categories completed	Number of six-card sequences correctly completed throughout the test.
Number of perseverative errors	Participant persists in a category after a) completing a run of six correct trials and being informed of the rule change or b) attempting a card placement and being told the rule is incorrect.
Number of non perseverative errors	Number of errors not classified as perseverative
Failure to Maintain Set	Participant places a card incorrectly after at least three correct responses within a given category
Percent perseverative errors*	Number of perseverative errors divided by total number of errors
Percent nonperseverative errors*	Number of nonperseverative errors divided by total number of errors
Perseverative erros – nonperseverative errors*	Difference between the number of perseverative and nonperseverative errors.
Percent errors*	Number of errors divided by total number of trials completed
Percent correct responses (% conceptual level responses)*	Number of errors divided by total number of trials completed
Categorizing efficiency*	Number of trials administered divided by number of categories completed (i.e. the best possible performance, in which only 36 trials are required to complete the six categories, will receive a score of [36/6]=6; higher scores indicate a lower efficiency, in that the number of cards required to complete each category was higher than the minimum possible)

Note: *Novel scores.

Results

Participant characteristics are shown in Table 2.

Table 2. *Participant demographic and clinical characteristics.*

	BDI (n=40)	BDII (n=47)	MDD (n=64)	C (n=94)
Age*	44.15(11.99)	41.37(14.04)	39.22(15.06)	29.58(12.28)
Education*[1]	11.54(4.88)	15.26(5.34)	14.39(4.63)	15.20(3.67)
SES*	4.05(1.43)	2.84(1.29)	3.49(1.19)	3.62(3.30)
HDRS*	14.53(9.15)	12.64(10.51)	8.51(6.45)	2.10(3.01)
YMRS*	2.60(3.78)	3.57(3.91)	1.22(1.71)	0.78(1.56)
IQ*	102.95(11.00)	111.66(12.63)	113.79(12.84)	120.38(10.92)
MMSE*	26.87(2.34)	27.79(2.48)	27.87(2.30)	29.17(1.43)

Gender (F/M)[2]	34/6	36/11	50/14	46/48

*Note. BDI: Bipolar Disorder type I; BDII: Bipolar Disorder type II; MDD: major depressive disorder; C: control participants; *Data presented as mean and standard deviation; ¹ Years of formal education; ² Number of female and male participants; SES: socioeconomic status; HDRS: Hamilton Depression Rating Scale; YMRS: Young Mania Rating Scale; IQ: Estimated intelligence quotient; MMSE: Mini-Mental State examination. ³Classified according to Zimmermann et al., (2013).*

The results of Spearman correlations between scores on the MCST and all other measures of EF used in the present study are shown in Table 3. The failure to maintain set on the MCST was not included in the table, as its correlations with the remainder of the variables were weak to nonexistent. Additionally, the ratio of Trail Making Test B-A, and the number of errors made by participants on each of the three parts of the Stroop Test showed no significant correlations with any variables on the MCST. As a result, neither of these variables were included in the table.

Table 3. Spearman correlation coefficients between scores on the MCST and other measures of EF.

	Modified Card Sorting Test								
	NCat	PersErr	NPersErr	%PersErr	%NPersErr	PersErr-NPersErr	%Err	%Corr	CatEff
Hayling B Time	-.387**	.367**	.267**	.209**	-.204**	.272**	.374**	-.364**	.380**
Hayling B Err	-.445**	.439**	.305**	.278**	-.255**	.359**	.429**	-.440**	.431**
Hayling B-A Time	-.310**	.295**	.211**	.143*	-.154*	.197**	.306**	-.297**	.311**
DigSpan Fwd	.369**	-.366**	-.232**	-.223**	.232**	-.247**	-.380**	.378**	-.367**
DigSpan Fwd - LSeq	.335**	-.362**	-.212**	-.235**	.246**	-.271**	-.360**	.354**	-.345**
DigSpan Bwd	.449**	-.466**	-.364**	-.250**	.252**	-.314**	.500**	.468**	-.480**
DigSpan Bwd - LSeq	.483**	-.504**	-.373**	-.298**	.301**	-.366**	.524**	.497**	-.490**
SWS Total	.499**	-.508**	-.319**	-.351**	.334**	-.409**	-.482**	.469**	-.482**
SWS – Lseq	.445**	-.458**	-.304**	-.279**	.275**	-.331**	-.442**	.442**	-.456**
TMT A Time	-.457**	.457**	.274**	.292**	-.264**	.365**	.431**	-.438**	.444**
TMT B Time	-.477**	.485**	.258**	.373**	-.355**	.421**	.434**	-.450**	.445**
TMT B Err	-.322**	.262**	.133*	.178*	-.182*	.212**	.248**	-.266**	.267**

Stroop – Word	.390**	-.353**	-.217**	-.232**	.203**	-.292**	-.334**	.346**	-.345**
Stroop – Color	.456**	-.443**	-.324**	-.264**	.233**	-.362**	-.426**	.433**	-.452**
Stroop – Color-Word	.493**	-.536**	-.316**	-.414**	.385**	-.447**	-.490**	.508**	-.501**
Stroop Interference	.315**	-.381**	-.191**	-.325**	.305**	-.312**	-.332**	.354**	-.334**

Note: *p<0,05;**p<0,01. NCat = Number of categories completed; PersErr = Number of perseverative errors; NPersErr = Number of non-perseverative errors; %PersErr = percentage of perseverative errors; %NPersErr = percentage of nonperseverative errors; PersErr-NPersErr = perseverative errors minus nonperseverative errors; %Errors = percentage of errors out of total number of trials; %Corr = percentage of correct responses out of total number of trials; CatEff = categorizing efficiency.

As can be seen in Table 3, the MCST variables most strongly correlated with other EF scores were the number of categories, perseverative errors, the percentage of correct and incorrect answers, and the categorizing efficiency score. Interestingly, the variables which most strongly correlated with performance on the WCST were obtained from working memory tests and the Stroop Color-Word Test.

As previously described, the variables with at least a moderate correlation with MCST scores were then included as predictors in a series of regression analyses. The results of these analyses are shown in Table 4.

Table 4. Stepwise regression analysis of MCST variables.

DV	R^2 adj.	Predictors	B	Std. Error	β	t	Sig
MCST NCat	0.415	(constant)	5.989	.466		12.838	<.001
		TMT B Time	-.007	.001	-.318	-5.100	<.001
		Age	-.022	.007	-.206	-3.316	.001
		SWS Total	.053	.019	.161	2.813	.005
		Hayling B Err	-.085	.032	-.159	-2.706	.007
MCST PersErr	.480	(Constant)	3.613	2.590		1.395	.164
		TMT B time	.039	.008	.322	5.142	<.001

		Age	.114	.032	.206	3.554	<.001
		Hayling B Err	.029	.009	.170	3.294	.001
		SWS Total	-.267	.092	-.156	-2.900	.004
		Education	-.215	.093	-.128	-2.305	.022
MCST NPersErr	.120	(Constant)	2.325	1.051		2.213	.028
		Hayling B Err	.202	.087	.164	2.328	.021
		Age	.037	.016	.154	2.264	.025
		Digit Span Bwd	-.275	.123	-.153	-2.241	.026
MCST %PersErr	.201	(Constant)	73.511	13.826		5.317	<.001
		SCWT - WordColor	-.557	.227	-.204	-2.460	.015
		Education	-1.318	.474	-.197	-2.779	.006
		Age	.474	.179	.204	2.650	.009
MCST %NPersErr	.165	(Constant)	27.303	14.069		1.941	.054
		SCWT - WordColor	.536	.231	.197	2.325	.021
		Education	1.152	.483	.173	2.387	.018
		Age	-.415	.182	-.180	-2.282	.024
MCST PerErr-NPersErr	.340	(Constant)	.146	1.904		.077	.939
		TMT B Time	.032	.008	.290	4.196	<.001
		Age	.121	.031	.242	3.957	<.001
		Education	-.349	.093	-.229	-3.755	<.001
MCST %Err	.403	(Constant)	8.383	6.429		1.304	.194
		TMT B Time	.113	.020	.347	5.617	<.001
		SWS Total	-.785	.260	-.173	-3.022	.003
		Hayling B Errors	1.285	.432	.173	2.976	.003
		Age	.221	.091	.150	2.424	.016
MCST %Corr	.438	(Constant)	93.953	6.070		15.477	<.001
		TMT B Time	-.116	.019	-.368	-6.132	<.001
		SWS Total	-.1354	.407	-.188	-3.323	.001
		Hayling B Errors	.703	.246	.159	2.858	.005
		Age	-.228	.086	-.160	-2.653	.009
MCST CatEff	.279	(Constant)	8.825	3.332		2.649	.009
		TMT B Time	.049	.010	.322	4.944	<.001
		SWS Total	-.404	.134	-.188	-3.006	.003
		Age	.114	.046	.163	2.446	.015

Note: NCat = Number of categories completed; PersErr = Number of perseverative errors; NPersErr = Number of non-perseverative errors; %PersErr = percentage of perseverative errors; %NPersErr = percentage of nonperseverative errors; PersErr-NPersErr = perseverative errors minus nonperseverative errors; %Errors = percentage of errors out of total number of trials; %Corr = percentage of correct responses out of total number of trials; CatEff = categorizing efficiency.

As can be seen in Table 4, the time taken to complete part B of the Trail Making Test was an important predictor in six of the nine models tested. The Sentence Word Span test, which evaluates working memory, and the number of errors in part B of the Hayling Sentence Completion Test were also identified as relevant predictors in five of the models examined. Age was a relevant predictor in all models, which underscores the importance of accounting for this demographic variable when conducting studies using the MCST.

Lastly, each of the scores on the MCST was compared between participants with no mood disorders and individuals with BD type I, BD type II and MDD. The results of these analyses are shown in Table 5.

Table 5. Difference between healthy adults and individuals with major depression, bipolar disorder type I and bipolar disorder type II on novel and traditional MCST scores.

	Group				Sig.	η2	Post-hoc
	BDI (n=24)	BDII(n=24)	MDD(n=48)	C(n=48)			
MCST NCat	4.08(1.86)	5.08(1.56)	5.19(1.47)	5.31(1.37)	0.013	0.053	BDI<MDD,C
MCST PersErr	9.92(8.41)	6.33(8.62)	5.35(7.90)	3.69(5.62)	0.020	0.046	BDI>C
MCST NPersErr	4.83(4.53)	2.88(3.68)	2.56(3.24)	2.69(3.37)	0.142	0.016	-
MCST FMS	0.67(0.87)	0.42(1.28)	0.21(0.46)	0.25(0.70)	0.016	0.050	BDI>BDII,MDD,C
MCST %PersErr	56.48(30.24)	53.95(33.81)	53.34(33.90)	42.30(32.89)	0.219	0.010	-
MCST %NPersErr	43.36(30.29)	41.18(33.04)	48.82(32.71)	58.26(33.85)	0.173	0.013	-
MCST PerErr-NPersErr	5.08(6.65)	3.46(7.72)	2.79(6.90)	1.00(4.70)	0.060	0.030	-
MCST %Err	31.03(31.03)	23.63(26.91)	16.57(20.23)	13.68(16.53)	0.022	0.045	BDI>C
MCST %Corr	68.97(24.36)	80.42(22.25)	82.75(20.39)	86.09(16.63)	0.035	0.038	BDI>C
MCST CatEff	16.29(13.51)	10.84(9.46)	10.74(10.33)	9.81(8.42)	0.017	0.049	BDI<MDD,C

Note: NCat = Number of categories completed; PersErr = Number of perseverative errors; NPersErr = Number of non-perseverative errors; %PersErr = percentage of perseverative errors; %NPersErr = percentage of nonperseverative errors; PersErr-NPersErr = perseverative errors minus nonperseverative errors; %Errors = percentage of errors out of total number of trials; %Corr = percentage of correct responses out of total number of trials; CatEff = categorizing efficiency.

As can be seen in the table, the majority of scores differentiated between control participants and at least one of the patient groups.

Discussion

The aim of the present study was to examine the executive abilities which underlie existing and novel scores for the MCST. Our findings showed that the majority of scores on this instrument were associated with measures of both inhibition and working memory. The only variables on the MCST to show a correlation of 0.5 or greater with other measures of EF were the number of perseverative errors, the percentage of errors and conceptual level responses, and categorizing efficiency. These variables correlated most strongly with digit span backwards, sentence word span, and Stroop Color-Word test scores. However, the variable most often identified in regression models as the strongest predictor of MCST performance was the time taken to complete Part B of the Trail Making Test. Our group comparisons revealed that control subjects outperformed patients with BD type I on nearly all variables of MCST. Three variables (the number of categories completed, failure to maintain set, and categorizing efficiency) also differentiated between patients with BD type I and MDD. The failure to maintain set was the only factor to distinguish between patients with BD type I and BD type II.

The first major finding of the present study concerns the strength of the association between MCST performance and WM. Previous studies have also obtained similar findings, concluding the impairments in WM capacity may lead to rule-inference errors, and as such, poorer performance on the WCST (Lange et al., 2016a). The only variables which were not at least partly predicted by working memory were the percentage – but not the raw number - of perseverative and nonperseverative errors on the MCST. At the same time, these two scores were significantly predicted by performance in the Color-Word portion of the Stroop Test. These findings suggest that the percentage of perseverative and nonperseverative errors may be a purer measure of inhibition than the raw number of errors, which may be more heavily influenced by working memory. This must be explored in further studies, involving larger samples and different populations, including individuals with both preserved and impaired working memory.

The regression analyses also showed a major contribution of the time taken to complete part B of the Trail Making Test in the prediction of 6 outcome variables in the MCST. Though the Trail Making Test is also described as a measure of mental flexibility (Strauss et al., 2006), some studies have questioned the use of its most traditional score (time taken to complete part B) as a measure of this construct. In a study by Sanchez-Cubillo et al. (2009), the time taken to complete the Trail Making Test B was found to be associated with working memory rather than inhibition or flexibility. The difference between the time taken to complete parts A and B of the Trail Making Test, as well as the number of errors in part B of the instrument, have been found to be more strongly related to inhibitory control (Kopp et al., 2015; Muir et al., 2015). As such, the association between the time taken to complete the Trail Making Test B and the MCST may corroborate its association with working memory rather than flexibility or inhibition. Nevertheless, the association between these two measures may be interpreted differently depending on what the Trail Making Test is believed to evaluate. Studies similar to the present investigation which focus on the Trail Making Test rather than the MCST may help clear up this issue.

The comparisons between control and clinical groups showed that several scores on the MCST were able to distinguish between patients with BD type I and adults with no mood disorders. These scores included the number of categories completed and perseverative errors, the two most widely used scores on the MCST. However, novel scores such as the failure to maintain set, the percentage of errors and conceptual level responses, as well as categorizing efficiency, also proved useful in differentiating between participant groups. These findings suggest that novel scores may contribute to the assessment of EF in populations with psychiatric disorders. The applicability of these scores to populations with other types of mental illness should be investigated, as they may be able to identify patterns of executive dysfunction which traditional scores may not detect.

The present study had some limitations, such as our inability to control for variables such as medication use and number of mood episodes in the clinical groups. It is possible that these variables may have confounded our analyses. Nevertheless, the MCST was still able to distinguish between some patient groups and control subjects, suggesting it may be applicable even in situations where some aspects of patients' medical histories are unaccounted for. The lack of visuospatial working memory assessments may also be seen as a limitation, given that both tasks used to evaluate working memory in the present study were predominantly verbal.

In conclusion, our findings support the use of the MCST as a measure of EF, but highlight the importance of continuing to study the test in order to define which specific functions is most likely investigates. The present findings point to a strong association between the MCST and inhibition, but also working memory, which must be investigated in further studies. The use of additional scoring methods yielded variables which showed a different pattern of relationships to other EF, and in some cases minimized the influence of working memory on the test. Novel and traditional scores were also able to distinguish between participant groups with different levels of executive dysfunction. The MCST has a long history, and for much of it, the statistical and theoretical methods which could be used to improve its interpretation and application were simply not available. Now that such methods can be employed, we encourage future studies to look into additional scoring methods and investigate the cognitive constructs which the instrument evaluates.

3 CONSIDERAÇÕES FINAIS

A presente dissertação teve como objetivo revisitar modelos teóricos de funções executivas (FE) através de exploração estatística de tarefas e baterias de avaliação, dentro de um contexto clínico. Foram avaliadas populações heterogêneas em termos de seu perfil cognitivo e características clínicas, de modo a aproximar as condições destes estudos às circunstâncias reais da clínica neuropsicológica.

O primeiro estudo permitiu diversas reflexões acerca da modelagem teórica das FE. Modelos de variáveis latentes, apesar de realizar grande contribuição para compreensão de funções cognitivas, são suscetíveis a diversos fatores externos. Estes incluem aspectos como as características e representatividade da amostra envolvida, assim como os métodos de avaliação neuropsicológica empregados. O estudo revelou estruturas latentes de três a seis fatores para amostras compostas de populações heterogêneas (adultos saudáveis e portadores de transtornos do humor) e homogêneas (portadores de transtorno bipolar e transtorno depressivo maior).

Fatores de memória de trabalho e velocidade de processamento foram claramente identificados, realçando a robustez destes construtos e sua constância entre tarefas e amostras. No entanto, observou-se maior ambiguidade referente aos demais componentes e tarefas avaliativas de FE. Não foi possível identificar uma associação clara e constante entre escores de tarefas complexas de FE, incluindo aquelas já amplamente utilizadas e tidas como padrão-ouro na literatura. Estes resultados apontam que, apesar do grande progresso realizado pela neuropsicologia ao longo dos anos, ainda é necessário maior refinamento de construtos teóricos e cuidado na operacionalização de variáveis na forma de tarefas avaliativas. Para além do desenvolvimento de tarefas e abordagens a partir de uma perspectiva puramente teórica ou experimental, faz-se necessário considerar estes dados em seu contexto clínico.

O segundo estudo representou um passo nesta direção, ao realizar uma exploração mais detalhada do *Modified Card Sorting Test,* tarefa já amplamente utilizada na avaliação das FE. O estudo permitiu uma melhor compreensão das variáveis subjacentes a esta tarefa com base na comparação com outros instrumentos e avaliação de grupos clínicos. A partir destas diferentes fontes de informação, foi possível identificar novos escores para a tarefa, que poderão complementar sua aplicação e fornecer dados mais detalhados acerca do desempenho de participantes. Foi reforçado, neste estudo, o papel da memória de trabalho em tarefas complexas de FE. No entanto, mais uma vez, foi observada a necessidade de desenvolver definições e tarefas mais específicas de FE, que possam isolar componentes específicos, ao mesmo tempo que produzem dados clinicamente significativos sobre o desempenho cognitivo.

Os estudos aqui apresentados permitiram reflexões importantes acerca dos passos a serem seguidos pela literatura na busca por modelos e tarefas mais específicas e clinicamente robustas de FE. A partir destes achados, abordagens similares poderão ser aplicadas a outros instrumentos existentes, a fim de aprimorar seu uso ou melhor compreender suas bases cognitivas. A aproximação de métodos provindos da psicologia clínica e das neurociências cognitivas constitui um importante caminho para esta busca.

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ANEXO A - Termo de Consentimento Livre e Esclarecido para participantes controle

Termo de consentimento livre e esclarecido para participantes saudáveis

PUCRS
VIVA ESSE MUNDO

PROPESTH
PROGRAMA DE PESQUISA E ENSINO EM TRANSTORNOS DE HUMOR

Autorização para participação de um projeto de pesquisa

Nome do estudo: Interface entre neuropsicologia e psicopatologia: em busca de perfis clínicos de processamento de funções executivas na depressão e no transtorno bipolar.
Instituições: Hospital Psiquiátrico São Pedro e Pontifícia Universidade Católica do Rio Grande do Sul
Pesquisadores responsáveis: Dra. Rochele Paz Fonseca, Flávio Shansis e Charles Cotrena
Telefone para contato: Dra. Rochele Paz Fonseca – 3020-3500, ramal 7742

Nome do participante: ____ Protocolo Nº: _________

Você está sendo convidado(a) a participar de um estudo sobre a neuropsicologia dos quadros de humor, ou seja, sobre funções cerebrais e sua relação com depressão e transtorno bipolar. Abaixo, você receberá informações sobre os objetivos do estudo, os procedimentos que serão realizados, e seus direitos como participante.

1. Objetivo do estudo
Esta pesquisa buscará investigar algumas funções do cérebro, ou funções cognitivas, como a capacidade de organização, gerenciamento, tomada de decisão, memória, assim como outras habilidades mentais relacionadas a comportamentos orientados a objetivos em pacientes portadores de transtornos do humor, como a depressão ou o transtorno do humor bipolar. Investigará, também, alguns traços de funcionamento de personalidade, e sua relação com os itens descritos acima. O desempenho destes pacientes será comparado ao de indivíduos sem transtornos do humor para identificar as funções cerebrais mais fortes e as menos preservadas, auxiliando na avaliação e no tratamento de pacientes com transtornos do humor.

2. Explicação dos procedimentos
O(A) senhor(a) será convidado a responder a questionários e realizar tarefas de avaliação das funções do cérebro mencionadas acima. Estas atividades envolvem utilização de lápis e papel, gravação de algumas tarefas em equipamento de áudio para transcrição com total sigilo, e uso de computador. A avaliação incluirá até dois encontros de aproximadamente 1 hora e 30 minutos de duração cada, que serão realizados no Serviço de Atendimento e Pesquisa em Psicologia (SAPP), sem qualquer custo, exceto o valor da passagem para os deslocamentos até o local de avaliação. Sua participação é completamente voluntária e o(a) senhor(a) tem o direito de desistir da avaliação caso desejar, em qualquer momento, sem sofrer qualquer prejuízo.
Alguns meses após esta avaliação, o(a) senhor(a) poderá ser convidado a participar de uma nova entrevista, na qual realizará as mesmas atividades, pelo mesmo número de sessões, e envolvendo os mesmos equipamentos.

3. Possíveis riscos e desconfortos
Os possíveis desconfortos deste estudo poderão ser o tempo de avaliação ou o deslocamento até o local de avaliação. Caso alterações sejam encontradas em algumas de suas funções cognitivas cerebrais, você e sua família serão orientados e encaminhados para atendimento quando necessário.

4. Direito de desistência
O(A) senhor(a) pode desistir a qualquer momento de participar do estudo, não havendo qualquer consequência aos tratamentos oferecidos por este hospital por causa desta decisão.

5. Sigilo
As informações que forem fornecidas nesta pesquisa poderão ser divulgadas em trabalhos com fins científicos, preservando-se o anonimato dos participantes.

6. Consentimento
Declaro que tive oportunidade de fazer perguntas adicionais esclarecendo dúvidas. Declaro que ficou clara a garantia de atendimento no caso de qualquer dificuldade observada na pesquisa, e que para qualquer informação estou ciente que devo contatar o pesquisador Dra. Rochele Paz Fonseca pelo telefone (51)30203500, ramal 7742, ou ligar para o Comitê de Ética em Pesquisa da Pontifícia Universidade Católica do Rio Grande do Sul, no telefone 33203345. Este comitê funciona na Av. Ipiranga, 6681, prédio 40, sala 505, de segundas a sextas-feiras das 8h às 12h e das 13h35 às 17h. Desta forma, aceito participar voluntariamente desse estudo.

Porto Alegre, _____ de ________________ de 201____.

____
Assinatura do participante
Nome:
RG:

Declaro que obtive de forma apropriada e voluntária o Consentimento Livre e Esclarecido deste paciente ou representante legal para a participação neste estudo.

____
Assinatura do pesquisador
Nome:
RG:
Data: ______/______/______

ANEXO B - Termo de Consentimento Livre e Esclarecido para participantes portadores de transtornos do humor

Termo de consentimento livre e esclarecido para participantes portadores de transtornos do humor

Autorização para participação de um projeto de pesquisa

Nome do estudo: Interface entre neuropsicologia e psicopatologia: em busca de perfis clínicos de processamento de funções executivas na depressão e no transtorno bipolar.
Instituições: Hospital Psiquiátrico São Pedro e Pontifícia Universidade Católica do Rio Grande do Sul
Pesquisadores responsáveis: Dra. Rochele Paz Fonseca, Flávio Shansis e Charles Cotrena
Telefone para contato: Dra. Rochele Paz Fonseca – 3020-3500, ramal 7742

Nome do participante: ____ Protocolo Nº: ________

Você está sendo convidado(a) a participar de um estudo sobre a neuropsicologia dos quadros de humor, ou seja, sobre funções cerebrais e sua relação com depressão e transtorno bipolar. Abaixo, você receberá informações sobre os objetivos do estudo, os procedimentos que serão realizados, e seus direitos como participante.

1. Objetivo do estudo

Esta pesquisa buscará investigar algumas funções do cérebro, ou funções cognitivas, como a capacidade de organização, gerenciamento, tomada de decisão, memória, assim como outras habilidades mentais relacionadas a comportamentos orientados a objetivos em pacientes portadores de transtornos do humor, como a depressão ou o transtorno do humor bipolar. Investigará, também, alguns traços de funcionamento de personalidade, e sua relação com os itens descritos acima. O desempenho destes pacientes será comparado ao de indivíduos sem transtornos do humor para identificar as funções cerebrais mais fortes e as menos preservadas, auxiliando na avaliação e no tratamento de pacientes com transtornos do humor.

2. Explicação dos procedimentos

Serão selecionados participantes que sejam portadores de transtornos do humor e que não tenham participado de programas de tratamento neuropsicológico. Serão ainda requisitadas algumas informações de familiares, se necessário, para complementação dos dados da avaliação realizada. O(A) senhor(a) será convidado a responder a questionários e realizar tarefas de avaliação das funções do cérebro mencionadas acima. Estas atividades envolvem utilização de lápis e papel, gravação de algumas tarefas em equipamento de áudio para transcrição com total sigilo, e uso de computador. A avaliação incluirá até dois encontros de aproximadamente 1 hora e 30 minutos de duração cada, que serão realizados no Hospital Psiquiátrico São Pedro ou no Serviço de Atendimento e Pesquisa em Psicologia (SAPP), sem qualquer custo, exceto o valor da passagem para os deslocamentos até o hospital. Sua participação é completamente voluntária e o(a) senhor(a) tem o direito de desistir da

avaliação caso desejar, em qualquer momento, sem nenhum prejuízo para o tratamento que vem recebendo do Hospital Psiquiátrico São Pedro.
Alguns meses após esta avaliação, o(a) senhor(a) poderá ser convidado a participar de uma nova entrevista, na qual realizará as mesmas atividades de avaliação, pelo mesmo número de sessões, e envolvendo os mesmos equipamentos.

3. Possíveis riscos e desconfortos
Os possíveis desconfortos deste estudo poderão ser o tempo de avaliação ou o deslocamento até o local de avaliação. Caso alterações sejam encontradas em algumas de suas funções cognitivas cerebrais, você e sua família serão orientados e encaminhados para atendimento quando necessário.

4. Direito de desistência
O(A) senhor(a) pode desistir a qualquer momento de participar do estudo, não havendo qualquer consequência aos tratamentos oferecidos por este hospital por causa desta decisão.
5. Sigilo
As informações que forem fornecidas nesta pesquisa poderão ser divulgadas em trabalhos com fins científicos, preservando-se o anonimato dos participantes.
6. Consentimento
Declaro que tive oportunidade de fazer perguntas adicionais esclarecendo dúvidas. Declaro que ficou clara a garantia de atendimento no caso de qualquer dificuldade observada na pesquisa, e que para qualquer informação estou ciente que devo contatar o pesquisador Dra. Rochele Paz Fonseca pelo telefone (51)30203500, ramal 7742, ou ligar para o Comitê de Ética em Pesquisa da Pontifícia Universidade Católica do Rio Grande do Sul, no telefone 33203345. Este comitê funciona na Av. Ipiranga, 6681, prédio 40, sala 505, de segundas a sextas-feiras das 8h às 12h e das 13h35 às 17h. Desta forma, aceito participar voluntariamente desse estudo.

Porto Alegre, _____ de ________________ de 201____.

____
Assinatura do paciente
Nome:
RG:

____
Assinatura do familiar
Nome:
RG:

Declaro que obtive de forma apropriada e voluntária o Consentimento Livre e Esclarecido deste paciente ou representante legal para a participação neste estudo.

____
Assinatura do pesquisador
Nome:
RG:
Data: ______/______/_____

Anexo C – Protocolo de coleta neuropsicológica

Nome do participante:______________________________ Idade:_________ Escolaridade:____________________
Contato:____________________________ Avaliador:____________________________________

QUESTIONÁRIO DE DADOS SOCIOCULTURAIS, MÉDICOS E NEUROPSICOLÓGICOS PARA TRANSTORNOS DO HUMOR

MINIMENTAL

ORIENTAÇÃO

● Dia do mês: ______________________	(0) (1)	● Local/Rua: ______________________	(0) (1)
● Dia da semana:____________________	(0) (1)	● Andar:__________________________	(0) (1)
● Mês:____________________________	(0) (1)	● Cidade:_________________________	(0) (1)
● Ano:_____________________________	(0) (1)	● Estado:_________________________	(0) (1)
● Estação:_________________________	(0) (1)	● País:___________________________	(0) (1)

TOTAL: ____/10

REGISTRO: repetir pente, rua e azul

CÁLCULO: a partir de 100, subtraia 7 progressivamente

Errou o primeiro ou o segundo cálculo, próxima tarefa: Atenção.

☐ Pente	(0) (1)	● 93_______☐	(0) (1)
☐ Rua	(0) (1)	● 86_______☐	(0) (1)
☐ Azul	(0) (1)	● 79_______☐	(0) (1)
		● 72_______☐	(0) (1)
		● 65_______☐	(0) (1)

TOTAL: ____/3

TOTAL: ____/5

***ATENÇÃO**: repetir a sequência

EVOCAÇÃO: lembrar as três palavras anteriormente

5 8 2 6 9 4 1	☐ Pente	(0) (1)
______________________________	☐ Rua	(0) (1)
*tarefa alternativa	☐ Azul	(0) (1)

TOTAL: ____/5

TOTAL: ____/3

LINGUAGEM

● Nomear caneta ☐ e relógio ☐	(0) (1) (2)
● Repetir: *nem aqui, nem ali, nem lá*	(0) (1)
● Pegar o papel com a mão direita ☐, dobrar ☐ e pôr no chão ☐	(0) (1) (2) (3)
● Fechar os olhos	(0) (1)
● Escrever uma frase	(0) (1)
● Copiar desenho pentágono	(0) (1)

TOTAL MINIMENTAL: _____/30

SPAN VERBAL DE DÍGITOS

CUIDADO: ENTONAÇÃO INTERROMPER SE HOUVER 4 ERROS CONSECUTIVOS.

ORDEM DIRETA		ORDEM INDIRETA	
3-10	(1)(0)	7-4	(1)(0)
7-4	(1)(0)	3-10	(1)(0)
1-9-3	(1)(0)	8-2-7	(1)(0)
8-2-7	(1)(0)	1-9-3	(1)(0)
4-9-1-6	(1)(0)	10-6-2-7	(1)(0)
10-6-2-7	(1)(0)	4-9-1-6	(1)(0)
6-5-1-4-8	(1)(0)	5-7-9-8-2	(1)(0)
5-7-9-8-2	(1)(0)	6-5-1-4-8	(1)(0)
4-1-9-3-8-10	(1)(0)	9-2-6-7-3-5	(1)(0)
9-2-6-7-3-5	(1)(0)	4-1-9-3-8-10	(1)(0)
10-1-6-4-8-5-7	(1)(0)	2-6-3-8-2-10-1	(1)(0)

2-6-3-8-2-10-1	(1)(0)	10-1-6-4-8-5-7	(1)(0)
7-3-10-5-7-8-4-9	(1)(0)	6-9-3-2-1-7-10-5	(1)(0)
6-9-3-2-1-7-10-5	(1)(0)	7-3-10-5-7-8-4-9	(1)(0)
5-8-4-10-7-3-1-9-6	(1)(0)	8-2-6-1-10-3-7-4-9	(1)(0)
8-2-6-1-10-3-7-4-9	(1)(0)	5-8-4-10-7-3-1-9-6	(1)(0)
Total acertos: ___ /16 Total de erros:___/16 Maior seqüência evocada corretamente:_____		Total acertos: ___ /16 Total de erros:___/16 Maior seqüência evocada corretamente:_____	

HAYLING TEST	
PARTE A	
CRONOMETRAR PARTE A E B **TEMPO LIMITE: 60 SEGUNDOS PARTE A E B**	
FRASES	**t (s)**
EXEMPLO A – O bebê chorava no:	
EXEMPLO B – São Paulo é uma grande:	
01 - O nadador mergulhou na:	
02 - O homem enviou a carta pelo:	
03 - A professora escreveu no:	
04 - A moça gosta de se olhar no:	
05 - O menino jogou a bola na:	
06 - A chuva caia no:	
07 - O casaco estava no:	
08 - O jogador de futebol fez uma:	
09 - Ele retirou o alimento frio da:	
10 - A criança tomou banho de:	
11 - Sua demissão surpreendeu todos seus:	
12 - O ladrão fugiu da:	
13 - A louça suja ficou na:	
14 - Os gatos enxergam bem à:	
15 - O senhor bebeu café na:	
Total acertos:____/15 **Total erros:**____/15 **Total tempo:**	

PARTE B		
SE ERRAR: "VOCÊ DEVE PROCURAR FORNECER UMA PALAVRA QUE NÃO ESTEJA RELACIONADA COM O SENTIDO DA FRASE"		
FRASES	**t (s)**	**Cat.**
EXEMPLO A – A taxa de criminalidade aumentou neste:		
EXEMPLO B – Estes novos sapatos eram de má:		
01 - A criança nasceu no:		
02 - A mulher viajou para a praia de:		
03 - O repórter falou na:		
04 - A avó leva sua neta para brincar no:		
05 - A senhora pegou o copo da:		
06 - O rapaz brigava com sua:		
07 - A fumaça saia da:		
08 - O capitão afundou o:		
09 - A cozinheira colocou o bolo no:		
10 - Ela telefonou para o marido de sua:		
11 - Todos os convidados tiveram uma excelente:		
12 - Ele comprou doces na:		
13 - O médico receitou um:		
14 - O sol brilha muito durante o:		
15- A adolescente cortou carne no:		
Total acertos:____/15 **Total erros:**____/15 **Total Categoria erros:**___/45 Tempo total:		

FLUÊNCIA VERBAL SEMÂNTICA- MAC (LETRA P)			
ESCREVER, NO MÍNIMO, A PRIMEIRA E A ÚLTIMA PALAVRA DE CADA BLOCO		GRAVAR	
0-30	**30-60**	**60-90**	**90-120**

TRAIL MAKING TEST (TMT)

AVISE QUANDO O PACIENTE ERRAR E PEÇA PARA CONTINUAR DO PONTO ONDE PAROU. NÃO PARE O CRONÊMETRO!

INTERROMPER TAREFA APÓS 5 MINUTOS

PARTE A	Total acertos: ______________________ Total erros: ______________________ Tempo(s): ______________________	PARTE B	Total acertos: ______________________ Total erros: ______________________ Tempo(s): ______________________

FLUÊNCIA VERBAL ORTOGRÁFICA- MAC (ROUPAS/VESTIMENTAS)

ESCREVER, NO MÍNIMO, A PRIMEIRA E A ÚLTIMA PALAVRA DE CADA BLOCO		GRAVAR	
0-30	**30-60**	**60-90**	**90-120**

CUBOS E VOCABULÁRIO WAIS III

SUBTESTES WAIS-III		
Subteste	Bruto	Ponderado
Vocabulário		
Cubos		

SPAN AUDITIVO DE PALAVRAS EM SENTENÇAS- NEUPSILIN

A menina sentou na cama.______________(2)(1)(0)
O coelho comeu ração. ______________(2)(1)(0)

A vaca mordeu o milho. ______________(2)(1)(0)
O menino subiu no sótão. ______________(2)(1)(0)
A aula ocorreu no pátio. ______________(2)(1)(0)

A mulher pegou o vaso. ______________(2)(1)(0)
O professor leu o jornal. ______________(2)(1)(0)
A vovó passou a calça.
______________(2)(1)(0)
O pássaro bicou a planta.
______________(2)(1)(0)

O porco derrubou a cerca. ______________(2)(1)(0)
A criança cortou a perna. ______________(2)(1)(0)
A titia colocou o brinco. ______________(2)(1)(0)
O amigo comprou um carro. ______________(2)(1)(0)
A moça gostou do sítio. ______________(2)(1)(0)

Total: ____ /28
Maior bloco repetido correto (0) (2) (3) (4) (5)
Análise qualitativa:
( ) alteração na repetição das sentenças
( ) fonológica ( ) outras:_________________

WISCONSIN CARD SORTING TEST (WCST)

NÃO ESQUECER DE SALVAR E ENVIAR OS DADOS POR EMAIL!

C F N C F N

______ 01. C F N O	______ 33. C F N O
______ 02. C F N O	______ 34. C F N O
______ 03. C F N O	______ 35. C F N O
______ 04. C F N O	______ 36. C F N O
______ 05. C F N O	______ 37. C F N O
______ 06. C F N O	______ 38. C F N O
______ 07. C F N O	______ 39. C F N O
______ 08. C F N O	______ 40. C F N O
______ 09. C F N O	______ 41. C F N O
______ 10. C F N O	______ 42. C F N O
______ 11. C F N O	______ 43. C F N O
______ 12. C F N O	______ 44. C F N O
______ 13. C F N O	______ 45. C F N O
______ 14. C F N O	______ 46. C F N O
______ 15. C F N O	______ 47. C F N O
______ 16. C F N O	______ 48. C F N O
______ 17. C F N O	______ 49. C F N O
______ 18. C F N O	______ 50. C F N O
______ 19. C F N O	______ 51. C F N O
______ 20. C F N O	______ 52. C F N O
______ 21. C F N O	______ 53. C F N O
______ 22. C F N O	______ 54. C F N O
______ 23. C F N O	______ 55. C F N O
______ 24. C F N O	______ 56. C F N O
______ 25. C F N O	______ 57. C F N O
______ 26. C F N O	______ 58. C F N O
______ 27. C F N O	______ 59. C F N O
______ 28. C F N O	______ 60. C F N O
______ 29. C F N O	______ 61. C F N O
______ 30. C F N O	______ 62. C F N O
______ 31. C F N O	______ 63. C F N O
______ 32. C F N O	______ 64. C F N O

PONTUAÇÃO	
N° ensaios administrados:	N° total de rupturas:
N° de categorias completadas:	Erros perseverativos:
N° total de acertos:	Erros não-perseverativos:
N° total de erros:	

FLUÊNCIA VERBAL LIVRE - MAC

ESCREVER, NO MÍNIMO, A PRIMEIRA E A ÚLTIMA PALAVRA DE CADA BLOCO **GRAVAR**

0-30	30-60	60-90	90-120	120-150

TESTE STROOP

PÁGINA PALAVRAS

	Coluna A	Coluna B	Coluna C	Coluna D	Coluna E
1	ROSA	AZUL	VERDE	ROSA	AZUL
2	VERDE	VERDE	ROSA	AZUL	VERDE
3	AZUL	ROSA	AZUL	VERDE	ROSA
4	VERDE	AZUL	ROSA	ROSA	AZUL
5	ROSA	ROSA	VERDE	AZUL	VERDE
6	AZUL	VERDE	AZUL	VERDE	ROSA
7	ROSA	AZUL	VERDE	AZUL	VERDE
8	AZUL	VERDE	ROSA	VERDE	ROSA
9	VERDE	ROSA	AZUL	ROSA	AZUL
10	AZUL	VERDE	VERDE	AZUL	VERDE
11	VERDE	ROSA	AZUL	ROSA	ROSA

PÁGINA CORES

	Coluna A	Coluna B	Coluna C	Coluna D	Coluna E
1	AZUL	ROSA	AZUL	VERDE	ROSA
2	ROSA	AZUL	VERDE	ROSA	AZUL
3	VERDE	VERDE	ROSA	AZUL	VERDE
4	AZUL	ROSA	AZUL	VERDE	ROSA
5	VERDE	VERDE	ROSA	ROSA	AZUL
6	ROSA	AZUL	VERDE	AZUL	VERDE
7	VERDE	VERDE	ROSA	VERDE	ROSA
8	ROSA	ROSA	AZUL	ROSA	AZUL
9	AZUL	AZUL	VERDE	AZUL	VERDE
10	ROSA	ROSA	ROSA	VERDE	AZUL
11	AZUL	AZUL	VERDE	AZUL	VERDE

PÁGINA PALAVRA-COR

	Coluna A	Coluna B	Coluna C	Coluna D	Coluna E
1	AZUL	ROSA	AZUL	VERDE	ROSA
2	ROSA	AZUL	VERDE	ROSA	AZUL
3	VERDE	VERDE	ROSA	AZUL	VERDE
4	AZUL	ROSA	AZUL	VERDE	ROSA
5	VERDE	VERDE	ROSA	ROSA	AZUL
6	ROSA	AZUL	VERDE	AZUL	VERDE
7	VERDE	VERDE	ROSA	VERDE	ROSA
8	ROSA	ROSA	AZUL	ROSA	AZUL
9	AZUL	AZUL	VERDE	AZUL	VERDE
10	ROSA	ROSA	ROSA	VERDE	AZUL
11	AZUL	AZUL	VERDE	AZUL	VERDE

ESCORES TOTAIS STROOP

PALAVRAS

Total acertos: ______________ Total erros: ______________

CORES

Total acertos: ______________ Total erros: ______________

PALAVRA-COR

Total acertos: ______________ Total erros: ______________

Escore Esperado

$CP = \frac{P \times C}{P + C}$ = ______

Escore de interferência

Escore Página Palavra-Cor – Escore Esperado =