FABRICIA QUINTÃO LOSCHIAVO-ALVARES

EFICÁCIA DA REABILITAÇÃO NEUROPSICOLÓGICA NO TRANSTORNO AFETIVO BIPOLAR: UM ESTUDO CONTROLADO

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Tese apresentada ao Programa de Pós-graduação em Neurociências do Instituto de Ciências Biológicas da Universidade Federal de Minas Gerais como requisito parcial para a obtenção do título de Doutor em Neurociências.

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"Those who are enamored of practice without science are like a pilot who goes into a ship without rudder or compass and never has any certainty where he is going. Practice should always be based on a sound knowledge of theory".

Leonardo da Vinci (1452-1519, Notebooks)

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RESUMO

Introdução: Déficits cognitivos são comumente encontrados em pacientes com o transtorno afetivo bipolar (TAB), não somente nas fases de mania e depressão, mas inclusive durante a remissão dos sintomas, na eutimia. Dentre os domínios cognitivos acometidos, ressaltam-se a memória, atenção e funções executivas que estão intrinsecamente relacionadas à funcionalidade. Recentes investigações tem corroborado o fato de que para o melhor manejo terapêutico do TAB, o tratamento deve englobar intervenções focadas na cognição, neste caso a reabilitação neuropsicológica (RN). Esta consiste na proposição de esforços para melhorar a funcionalidade e a qualidade de vida de pessoas com comprometimentos cognitivos, por meio de estratégias que visam reduzir o impacto do comprometimento cognitivo nas ocupações do indivíduo, através do emprego de técnicas específicas de treinamento e compensação, que poderiam contribuir para um melhor prognóstico funcional. **Objetivo:** O presente estudo teve como objetivo geral avaliar a eficácia de um protocolo de RN, direcionado ao tratamento da memória, atenção e funções executivas em pacientes com TAB. A fim de alcançar o objetivo acima exposto, foram delineados objetivos específicos, quais sejam: adaptar culturalmente e investigar as propriedades psicométricas da escala DEX-R, uma avaliação funcional de funções executivas, memória e atenção, que foi empregada como uma das medidas de eficácia para avaliação do protocolo de RN; verificar o impacto do protocolo de RN proposto nas variáveis funções executivas, memória e atenção, qualidade de vida e coping, no pós-intervenção e no follow-up (seis meses após a suspensão do protocolo) e investigar o número de episódios de alteração do humor, hipomania, mania e/ou depressão nos seis meses após a integralização do protocolo de RN. **Métodos:** Para a realização dos estudos relativos à DEX-R, o grupo controle, formado por indivíduos saudáveis (n=300), foi recrutado a partir de uma amostra de conveniência, e o grupo TAB foi formado por pacientes com diagnóstico do transtorno, atendidos no Ambulatório Borges da Costa – Núcleos de Transtornos Afetivos do Complexo do Hospital das Clínicas. Foi realizada uma análise fatorial exploratória, seguida por uma comparação intergrupos, e investigação das propriedades psicométricas usando a análise de Rasch. Quanto à investigação relativa à análise da eficácia da RN, os pacientes com o TAB, do ambulatório acima citado, elegíveis para a pesquisa, foram alocados pseudo-aleatoriamente em dois grupos: Grupo Controle (GC), n=30, composto por pacientes tratados apenas pela farmacoterapia e Grupo Reabilitação (GRN), n=20, composto por pacientes que receberam a farmacoterapia e o protocolo de RN. O protocolo, estabelecido após a realização de um estudo piloto, foi composto de 14 sessões

semanais individuais, divididas em três módulos: psicoeducação e estratégias de monitoramento do humor, Reabilitação das Funções Executivas, Reabilitação da Memória e Atenção. Todas as sessões foram estruturadas com técnicas padronizadas para abordagem de cada domínio cognitivo. Como medidas de eficácia, foram utilizadas a Escala de Modos de Enfrentamento de Problems – EMEP (coping), Questionário Disexecutivo Revisado – DEX-R (funções executivas, memória e atenção) e WHOQOL-BREF (qualidade de vida). Foi utilizada a ANOVA para medidas repetidas delineamento misto a fim de comparar o efeito do tratamento nos escores dos grupos (pré, pós e follow-up). Todas as análises foram realizadas no pacote estatístico SPSS 20.0 – Windows e/ou RUMM 2030. Para todas as analises, o nível de significância adotado foi de $p<0.05$. **Resultados:** quanto à DEX-R, esta se mostrou ser sensível para a avaliação das funções executivas, memória e atenção no contexto brasileiro, e, portanto, foi adotada como uma das medidas de eficácia para avaliação do protocolo de RN. Os itens se agruparam em três fatores: regulação social e auto-regulação (funções relacionadas ao circuito orbito-frontal), motivação e atenção (funções relacionadas ao circuito cíngulo anteior) e flexibilidade, fluência e memória operacional (funções relacionadas ao circuito dorsolateral). Referente à eficacia da RN, para todas as comparações intergrupos (pré, pós e follow-up) foi encontrada uma diferença significativa entre os escores nas medidas de eficácia ($p<0.05$) no GRN. Não foram evidenciadas diferenças estatísticas no GC. As magnitudes de efeito das diferenças entre o pré- e o pós-teste foram maiores para o grupo sob tratamento ($d > 0.8$) para todas as medidas de eficácia. **Conclusão:** o questionário DEX-R, após sua adaptação e validação, para os pacientes do GRN exibiram uma melhora significativa em todos os domínios avaliados, logo apresentaram um importante incremento nas habilidades funcionais, com ganhos em qualidade de vida, maior emprego de habilidades de coping focadas no problema e melhora nas funções executivas, atenção e memória. Os resultados corroboram achados prévios que apontam que pacientes com TAB podem se beneficiar da RN, como uma importante ferramenta terapêutica promotora de uma melhor performance funcional. Os achados decorrentes deste trabalho de doutorado foram discutidos com base em aspectos psicométricos e neuropsicológicos, organizados em artigos específicos. Para finalizar, foram apresentadas hipóteses sobre limitações metodológicas dos estudos e propostas para aprimoramento em investigações futuras.

Palavras-chave: Transtorno afetivo bipolar, reabilitação neuropsicológica, cognição.

ABSTRACT

Background: Cognitive deficits are commonly found in patients with bipolar disorder (BD), not only in mania and depression phases, but even during the remission of symptoms, called euthymia. Among the affected cognitive domains, it is highlighted memory, attention and executive functions which are intrinsically related to functionality. Recent investigations have corroborated the fact that for the best therapeutic management of BD, the treatment should include interventions focused on cognition, more precisely, the neuropsychological rehabilitation (NR). This consists in proposing efforts to improve the functionality and quality of life of people with cognitive impairments, through strategies aimed to reducing the impact of cognitive impairment in the occupations of the individual through the use of specific technical training and compensation, which could contribute to a better functional outcome. **Objective:** This study aimed to evaluate the overall effectiveness of a NR protocol, directed to the treatment of memory, attention and executive functions in patients with BD. In order to achieve this, specific objectives were outlined, namely: cultural adaptation and investigation of psychometric properties of the DEX -R , a functional assessment of executive function , memory and attention , which was used as am efficacy measure; verify the impact of the proposed NR protocol in executive functions , memory and attention , quality of life and coping, both ate the post-intervention and at follow -up (six months after the suspension of the protocol) and investigate the number of episodes of mood swings , hypomania , mania and / or depression on the six months following the conclusion of NR protocol. **Methods**: concerning DEX –R studies, these comprised a sample of healthy subjects – control group (n = 300) (recruited from a convenience sample), as well as a group of patients diagnosed with BD. An exploratory factor analysis followed by an intergroup comparison to investigate the psychometric properties using Rasch analysis was performed. For research on the analysis of the effectiveness of NR , patients with BD eligible for the study were allocated pseudo - randomly into two groups : control group (CG) n = 30 , consisting of patients treated only by pharmacotherapy and Rehabilitation group (NRG) , n = 20 , comprising patients who received pharmacotherapy and NR protocol . The protocol established after conducting a pilot study consisted of 14 weekly individual sessions, divided into three modules: Psychoeducation and Humor Monitoring Strategies, Rehabilitation of Executive Functions, Rehabilitation and Memory Care. All sessions were structured with standardized techniques for each cognitive domain approach. EMEP (coping) , Disexecutive Questionnaire Revised - DEX -R (executive functions, memory and attention) and WHOQOL -BREF (quality of life) were used as effectiveness measures. Mixed design ANOVA for repeated measures was

conducted to compare the treatment effect in the groups scores (pre , post andfollow -up) . All analyzes were performed using SPSS 20.0 - Windows and / or RUMM 2030. For all analyzes, the level of significance was set at $p < 0.05$. **Results:** DEX -R was sensitive for the assessment of executive functions, memory and attention in the Brazilian context, and therefore was adopted as a measure of efficacy for evaluation of protocol NR . The items were grouped into three factors: social regulation and self -regulation (related to orbito -frontal circuit functions) , motivation and attention (related to its previous cingulate circuit functions) and flexibility , fluency and working memory (dorsolateral circuit -related functions) . Regarding the effectiveness of NR, for all intergroup comparisons (pre , post and follow -up) a significant difference was found on NRG scores ($p < 0.05$). No statistical differences were observed in the GC. The effect size of the differences between pre - and post-test were higher for the group under treatment ($d > 0.8$) for all efficacy measures. **Conclusion:** patients from NRG exhibited significant improvement in all domains assessed, as well as a significant increase in functional abilities, i.e., gains in quality of life, coping skills focused on problem and improvements in executive function , attention and memory. The results corroborate previous findings that indicate that patients with BD may benefit from the NR as an important therapeutic tool to promote a better functional performance. The findings arising from this PhD work were discussed based on psychometric and neuropsychological aspects, organized into specific articles. Finally, hypotheses about methodological limitations of the studies and proposals for improvement in future research were presented.

Keywords: Bipolar Disorders, Neuropsychological Rehabilitation, Cognition.

SUMÁRIO

LISTA DE ILUSTRAÇÕES

LISTA DE ABREVIATURAS E SIGLAS

AFE – Análise Fatorial Exploratória

APA – American Psychiatric Association

BDI – Inventário de Depressão de Beck

BIS – Barratt Impulsiveness Scale

CCPT – Conner's Continuous Performance Test

COEP – Comitê de Ética em Pesquisa

CPF – Córtex pré-frontal

CPT – Continuous Performance Test

DEX-R – Dysexecutive Questionnaire Revised

DSM-IV – Diagnostic and Statistical Manual of Mental Disorders - 4th edition

EMEP – Escala de Modos de Enfrentamento de Problemas

GC – Grupo Controle

GMT – Goal Management Training

GRN – Grupo Reabilitação Neuropsicológica

IGT – Iowa Gambling Task

KMO – Kaiser-Meyer-Olkin

NTA – Núcleo de Transtornos Afetivos

NTA-HC / UFMG – Núcleo de Transtornos Afetivos do Hospital das Clínicas da Universidade Federal de Minas Gerais

QV – Qualidade de Vida

RN – Reabilitação Neuropsicológica

SPSS – Statistical Package for the Social Sciences

TAB – Transtorno Afetivo Bipolar

UFMG – Universidade Federal de Minas Gerais

1 INTRODUÇÃO

O Transtorno Afetivo Bipolar (TAB) é caracterizado pela ocorrência de episódios de exacerbação do humor chamados de mania/hipomania e períodos de depressão. Nos primeiros, os pacientes apresentam euforia, hiperatividade, pensamento acelerado, loquacidade exagerada, diminuição da necessidade de sono, exacerbação da sexualidade, dificuldades em controlar os impulsos e comprometimento da crítica. Nos períodos de depressão, os pacientes com TAB frequentemente apresentam sintomas cardinais de sentimentos de culpa, tristeza profunda, desesperança e comportamento suicida (APA, 1994). Ressaltam-se os subtipos do transtorno I e II. O primeiro, de acordo com o DSM-IV, é definido por episódios maníacos ou mistos que duram pelo menos sete dias ou por sintomas maníacos que são tão graves que a pessoa necessita internação hospitalar imediata. Geralmente, a pessoa também tem episódios depressivos, tipicamente durando pelo menos duas semanas. Os sintomas de mania ou depressão devem ser uma grande mudança do comportamento normal da pessoa. Já o segundo subtipo é definido por um padrão de episódios depressivos alternando com episódios hipomaníacos, mas nunca um episódio pleno de mania ou misto.

De acordo com dados da Organização Mundial da Saúde (WHO, 2005), o TAB está entre as dez doenças que mais levam a incapacidade no exercício das tarefas laborativas. Déficits cognitivos são achados comuns nos transtornos psiquiátricos estando relacionados ao comprometimento no desempenho de habilidades produtivas, sociais e cotidianas (Corrigan et al., 2007). Por sua vez, o funcionamento cognitivo preservado é um importante preditor de um bom prognóstico na intervenção psiquiátrica nesses pacientes (Corrigan et al., 2007). Em estudos com pacientes com TAB foram encontrados déficits cognitivos persistentes, não somente nas fases de mania e depressão, mas inclusive após a remissão dos sintomas, quando os pacientes encontram-se em estado de eutimia (Martinez-Aran et al., 2004).

Uma metanálise conduzida por Robinson et al. (2006) em pacientes bipolares na fase eutímica indicou a presença de déficits residuais nas habilidades de memória episódica verbal imediata e tardia, nas funções executivas, atencionais e psicomotoras. Em relação aos diferentes perfis cognitivos nos subtipos do TAB, Hsiao et al. (2009) apontaram que o tipo I é caracterizado por um pior desempenho em habilidades de memória para conteúdo verbal, memória

operacional, funções psicomotoras e executivas, enquanto no tipo II os déficits foram evidenciados nas funções psicomotoras e memória operacional. Na medida em que as dificuldades cognitivas em pacientes bipolares são consistentes e preditoras de uma pior qualidade de vida (Brissos et al., 2008) torna-se importante a proposição de intervenções que tem o objetivo de evitar e/ou minimizar a deterioração cognitiva nesse grupo clínico bem como propiciar a estes pacientes a recuperação e/ou otimização de suas habilidades funcionais.

Segundo a Organização Mundial de Saúde (OMS), os processos de reabilitação têm como objetivo possibilitar que os pacientes atinjam o maior nível possível de adaptação física, psicológica e social, abarcando, portanto, todas as medidas que pretendam reduzir o impacto da inabilidade e condições de desvantagem, permitindo que as pessoas com alguma deficiência/incapacidade atinjam um nível adequado de integração social. Nesta perspectiva, a reabilitação neuropsicológica (RN) é um processo ativo que visa capacitar pessoas com déficits cognitivos causados por lesões adquiridas ou transtornos do desenvolvimento, no caso os neuropsiquiátricos, para que estas adquiram um satisfatório de funcionamento social, físico e psíquico (Wilson, 2005). Segundo Wilson (2004), a RN consiste na proposição de esforços para melhorar a funcionalidade e a qualidade de vida de portadores de doenças neurológicas e psiquiátricas. Para tanto, são empregadas de técnicas psicológicas, cognitivas e comportamentais, a fim de recuperar ou minimizar os efeitos de déficits cognitivos, de forma que os pacientes encontrem meios adequados e alternativos para alcançar metas funcionais específicas (Ben-Yishay, 2008).

Conforme Prigatano (1999) e Wilson (2002), a intervenção em RN deve ser compreendida de uma maneira mais ampla, a partir de referencias à pessoa no seu contexto e suas relações. Para o estabelecimento de uma intervenção em RN a avaliação do perfil de processos neuropsicológicos comprometidos e preservados é uma condição necessária, devendo estar sempre aliada à mensuração do impacto das deficiências cognitivas no cotidiano do individuo (Royall et al., 2007). Dentro desta perspectiva torna-se viável o emprego de avaliações que mensurem de maneira objetiva a funcionalidade / desempenho do indivíduo nas suas tarefas cotidianas, uma vez que uma intervenção pode apenas ser implementada baseada no nível de função individual, da extensão do desempenho nas atividades (Arthanat, 2004).

Assim mais que um procedimento diagnóstico, a avaliação da funcionalidade é a primeira etapa da intervenção. Esta deve ser designada para a identificação e quantificação de possíveis problemas e determinação de potencialidades, visando tanto o delineamento adequado de um plano terapêutico, como a delimitação de ferramentas para a avaliação da eficácia da intervenção (Farina *et al.*, 2010). Nesta perspectiva, uma das tarefas mais relevantes em qualquer programa de reabilitação/intervenção é a identificação de problemas cotidianos, portanto funcionais (Loschiavo-Alvares et al., 2011). Desde 1990, tem se observado uma maior ênfase no desenvolvimento e emprego de medidas funcionais em programas de intervenção como medidas de eficácia (McMillan & Sparkes 1999). Conforme explicitado acima, o emprego de testes cognitivos padronizados é de extrema relevância. Entretanto, cabe ao profissional da área compreender que eles respondem a perguntas específicas relacionadas ao funcionamento global do sujeito em comparação aos seus pares etários, inteligência geral, se os déficits podem ser explicados por alterações de natureza sensorial, quadros psiquiátricos e, por fim, qual é o perfil cognitivo de forças e fraquezas apresentados pelo paciente (Wilson, 2011). Nesse sentido, informações oriundas destes testes, contribuem para a construção de um perfil de fraquezas bem como de potencialidades que necessitam ser analisadas e complementadas à luz de avaliações funcionais, que explicitam como estes problemas impactam o cotidiano do indivíduo (Wilson 2002).

Assim, a partir da avaliação da funcionalidade, o profissional encontrará respostas às questões relativas a manifestação das dificuldades cognitivas na rotina do paciente, além do impacto do comprometimento funcional. A RN abarca ainda, como o paciente enfrenta e gerencia os problemas cotidianos, quais são as estratégias que melhor se adequariam às demandas funcionais, além da análise da atividade, através da qual o profissional apreenderá as demandas cognitivas necessárias ao desempenho funcional do paciente. Enfim, o emprego de avaliações funcionais tem papel relevante na delimitação de um acurado perfil de funcionamento individual, incluindo os aspectos cognitivos, emocionais, sociais e interpessoais (Solhberg; Mateer, 2001). Estas considerações são particularmente relevantes para a proposição de estudos que pretendam investigar a eficácia de intervenções, no caso, da RN. Justificando, desta forma o emprego de esforços para a adaptação de avaliações funcionais para este fim. Dentro deste pressuposto, a adaptação e validação do Questionário de Dimensões Disexecutivas (DEX-R) (Simblett & Bateman, 2011) foi uma das contribuições do presente trabalho.

Além do acima exposto, diante das possibilidades da intervenção em RN para lidar com o comprometimento cognitivo apresentado por pacientes com o TAB, é que se embasa a plausibilidade da proposição de um programa de RN para aplicação nessa população. Em particular, é importante avaliar se e como a reabilitação neuropsicológica acrescenta aos tratamentos farmacológicos convencionais ganhos na esfera cognitiva e na funcionalidade de pacientes bipolares.

Desta forma, o conteúdo do presente estudo foi construído em seis capítulos, que são seguidos por uma lista de referências bibliográficas e os anexos, além dos elementos pré-textuais. Os capítulos primeiro e segundo abarcam a introdução e o referencial teórico que fundamentaram o estudo no que diz respeito a uma breve revisão da literatura sobre a cognição e a RN no TAB. No capítulo terceiro são apresentados os objetivos e as hipóteses do estudo. O capítulo quarto abrange a metodologia de investigação utilizada para alcançar os objetivos propostos. Já o capítulo 5, destina-se à apresentação dos resultados desta pesquisa sob o formato de artigos e discussões teóricas referentes a cada um deles. A primeira publicação desta pesquisa de doutorado foi uma revisão integrativa da literatura intitulada Tools for efficacy's assessment of neuropsychological rehabilitation programs: a systematic review, já publicada na Clinical Neuropsychiatry em 2011 (Loschiavo-Alvares et al., 2011). O objetivo desta foi realizar um levantamento sobre os instrumentos de avaliação de eficácia de programas de RN.

O segundo produto desta pesquisa foi um estudo de delineamento experimental de caso único, desenvolvido como estudo piloto para investigação da viabilidade clínica do protocolo de RN delineado para o estudo de investigação da eficácia da reabilitação neuropsicológica em pacientes com o TAB. O artigo, Neuropsychological rehabilitation for bipolar disorder – a single case design, foi publicado no Translational Neuroscience em 2013 (Loschiavo-Alvares et al., 2013a).

Retomando a linha de investigação sobre os instrumentos de avaliação de eficácia para a mensuração do impacto da RN, foi elaborado o terceiro produto, o artigo Clinical Application of DEX-R for patients with Bipolar Disorder type I and II, que se tratou do estudo de tradução e adaptação DEX-R para o contexto brasileiro que forneceu a versão adaptada do instrumento que foi utilizada neste trabalho. O estudo foi publicado na Clinical Neuropsychiatry em 2013 (Loschiavo-Alvares et al., 2013b). Ainda buscando a investigação das propriedades

psicométricas do instrumento supracitado, via análise de Rasch, foi elaborado o quarto estudo, Psychometric properties of brazilian portuguese version of dysexecutive questionnaire revised (dex-r) in bipolar disorder patients using rasch analysis. Este trabalho já foi submetido ao Journal of Clinical Psychology e aguarda parecer (Loschiavo-Alvares et al., submetido a). E, finalmente, a quinta produção trouxe os resultados da análise da eficácia do protocolo de RN, intitulado Efficacy of neuropsychological rehabiliation applied for patients with bipolar disorder: a controlled study (Loschiavo-Alvares et al., submetido b). Este artigo também foi submetido no Bipolar Disorders e aguarda parecer.

O último capítulo aborda a síntese dos resultados e as considerações finais acerca das evidências teóricas e empíricas verificadas. Ademais, são apresentadas as contribuições e as limitações do presente estudo como também propostas para aprimoramento em investigações futuras.

2 REVISÃO DE LITERATURA

2.1 Aspectos cognitivos do Transtorno Afetivo Bipolar

Pesquisas que se propusessem a investigar a cognição nos transtornos neuropsiquiátricos, até recentemente, tinham como foco primário o estudo da esquizofrenia e da depressão unipolar (Quraishi; Frangou, 2002). Uma das possíveis explanações para tal fato ressalta-se um postulado de Kraepelin, em 1913, que propôs que um declínio cognitivo substancial estaria associado à esquizofrenia e não ao TAB. Para Kraepelin, na ausência do estado agudo da "Psicose Maníaco Depressiva" os déficits cognitivos estariam em remissão. Entretanto, atualmente, é estimado que 30-50% dos pacientes com TAB, na fase de remissão falham em alcançar níveis de funcionamento psicossocial pré-mórbidos, sendo grande parte desta incapacidade associada ao comprometimento cognitivo. Desta forma, embora o TAB seja caracterizado pela perda do homeostase emocional, os sintomas cognitivos representam parte deste transtorno (Strakowski et al., 2005), sendo que os déficits cognitivos, ao invés de estado, tem sido considerados traço (Chowdhury; Ferrier; Thompson, 2003). Tal fato pode ser corroborado pela persistência do comprometimento cognitivo na ausência de sintomas do humor (eutimia), o que sugere ser este comprometimento o reflexo de uma neurofisiologia disfuncional no transtorno, independente de sua fase aguda (Strakowski et al., 2005).

A concomitância entre déficits relacionados ao humor e à cognição não é surpreendente, dada a sobreposição entre circuitos corticais que modulam e humor e as funções cognitivas. Dentre os circuitos, destacam-se os relacionados ao córtex pré-frontal (Mayberg et al., 1999). De acordo com Brandshaw (2001) o córtex pré-frontal apresenta um nível de especialização funcional, onde cada sistema neural está relacionado a aspectos cognitivos e comportamentais específicos, estando interconectado com outras áreas corticais e subcorticais e participa de todos os aspectos de adaptação do organismo ao ambiente. São descritos cinco circuitos frontais subcorticais paralelos relacionados a funções distintas: motor, óculo-motor, dorsolateral, orbitofrontal e cíngulo anterior. Destes, três circuitos pré-frontais (dorsolateral, orbitofrontal e cíngulo anterior) estão particularmente envolvidos com a cognição e humor. O primeiro, dorsolateral, é particularmente importante para as funções executivas frias, relacionadas à abstração, controle atencional, memória operacional, planejamento e solução

de problemas. O circuito orbitofrontal é relacionado às funções executivas quentes, que envolvem funções como a cognição social, tomada de decisão afetiva e postergação da gratificação. Sua parte mais posterior e medial é considerada uma das principais regiões corticais para mediação autonômica e forma uma rede com outras áreas límbicas, como a ínsula, a amídala, o córtex polar temporal, o hipotálamo e o tronco cerebral. Este circuito modula estímulos emocionais internos, como por exemplo, a tristeza em resposta a eventos pessoais (Strakowski et al., 2012). Esta circuitaria já e extensamente reconhecida como o substrato neuroanatômico funcional no trantorno bipolar (Strakowski et al., 2012). As conseqüências de comprometimentos no circuito orbitofrontal lateral estão geralmente associadas a comportamentos de risco e à alteração da personalidade, caracterizada por redução da sensibilidade às normas sociais, infantilização, dependência de reforço evidente e baixa tolerância à frustração. O paciente passa a apresentar dificuldades nos processos de tomada de decisões pela não antecipação de futuras conseqüências de suas atitudes. A impulsividade relacionada a falhas de planejamento está associada a este circuito pré-frontal (Bechara; Van Der Linden, 2005). E o último, o circuito do cíngulo é importante para a motivação, a monitoração de comportamentos, o controle executivo da atenção, a seleção e o controle de respostas. Estas circuitarias já são extensamente reconhecidas como o substrato neuroanatômico funcional no trantorno bipolar (Strakowski et al., 2012).

Em concordância com recentes metanálises (Robinson et al., 2006; Torres et al., 2007) os déficits mais notáveis em pacientes adultos eutímicos permeiam os domínios da atenção e velocidade de processamento, memória e aprendizagem verbal e funções executivas, incluindo flexibilidade cognitiva, controle inibitório, memória operacional e fluência verbal. Sendo apontados ainda perfis neuropsicológicos distintos, conforme apontado anteriormente. Considerando-se os tipos de TAB. Conforme Simonsen et al. (2008), para o tipo I espera-se um comprometimento mais pronunciado e severo quando comparado ao tipo II, relacionado aos domínios de memória verbal, operacional, velocidade psicomotora e funções executivas. Sendo queixas comuns em pacientes com TAB, pensamentos mais lentificados, dificuldades em focar em e iniciar atividades, em organizar tarefas complexas e manejar múltiplos processos, bem como lembrar-se e impulsividade (Deckersbach et al., 2010). Diante do exposto, a presença de déficits cognitivos persistentes em pessoas com TAB corrobora várias implicações clínicas, relativas a prognóstico bem como terapêuticas (Balanzá-Martínez et al., 2010).

As alterações cognitivas em pacientes bipolares também parecem variar de acordo com o histórico de tentativas de suicídio. Jollant et al. (2011) sugere que as dificuldades relacionadas às funções executivas em pacientes psiquiátricos que tentam suicídio tendem a ser expressivas. Malloy-Diniz et al (2009 a e b), encontraram, assim como já apontado no estudo de Schneider et al. (2008), prejuízos neuropsicológicos no grupo de pacientes com TAB, a despeito do atual quadro de humor. Comparando o desempenho dos sujeitos do grupo de bipolares de acordo com a história de tentativas de suicídio, foram evidenciados prejuízos proeminentes no processo de tomada de decisões medidos pela versão brasileira do Iowa Gambling Test (Malloy-Diniz et al., 2008b). Do mesmo modo, as tarefas de tomada de decisão estão relacionadas a um tipo específico de impulsividade associado ao planejamento de ações levando em consideração a análise de custo/benefício das conseqüências positivas e negativas em curto, médio e longo prazos (Malloy-Diniz, Neves, Corrêa, 2009a). A associação entre a impulsividade relacionada ao processo de tomada de decisões e as tentativas de suicídio em pacientes com TAB também foi previamente corroborada no estudo de Jollant et al. (2005). Em pacientes bipolares, as tentativas de suicídio parecem estar relacionadas à dificuldades de controle de impulsos (Swan et al., 2008) e uma pior tomada de decisão. Malloy-Diniz et al., (2009a; 2011) verificaram que pacientes bipolares com histórico de tentativas de suicídio tendem a apresentar um padrão mais imediatista e disfuncional em provas de tomada de decisão em comparação a bipolares sem histórico de tentativas de suicídio. Moraes et al., (2013) verificaram associação entre o histórico de tentativas de suicídio, transtorno de pesonalidade borderline e déficits em provas que avaliam tomada de decisão.

De acordo com Goodwin & Jaminson (2007), pacientes com TAB demonstram pobres prognóstico e desfecho terapêutico, uma vez que as incapacidades cognitivas estão associadas a um reservado resultado funcional em adultos com TAB (Martínez-Aran et al., 2007). Três investigações longitudinais (Jaeger et al., 2007; Martino et al., 2009; Tabarés-Seisdedos et al., 2008) indicaram, consistentemente, que o comprometimento cognitivo é preditor de uma pobre adaptação psicossocial à longo prazo, destacando-se os déficits na atenção e velocidade psicomotora (Jaeger et al., 2007), memória verbal e funções executivas (Martino et al., 2009). Brissos et al. (2008) apontam que os sintomas cognitivos interepisódios representam barreiras para que os pacientes com TAB recobrem um adequado funcionamento social e ocupacional, o que, por sua vez, impactam negativamente na qualidade de vida. De acordo com Balanzá-Martínez et al. (2010), o comprometimento cognitivo é refratário a intervenções tradicionais,

incluindo a farmacológica, sendo que esta última pode resultar em agravamento do funcionamento cognitivo. Nesta perspectiva, os referidos autores apontam que para o manejo à longo prazo do TAB deve-se visar não somente a remissão dos sintomas de humor, mas inclusive intervenções com foco na cognição que podem ser importantes preditoras de um desfecho funcional, por resultarem na diminuição do impacto do comprometimento cognitivo nas ocupações dos pacientes com TAB, representando, portanto, em ganhos importantes na qualidade de vida. Martínez-Aran et al.(2004) destacam a RN, como intervenção não-farmacológica com potenciais aplicações para esta finalidade.

2.2 Reabilitação Neuropsicológica e Transtorno Afetivo Bipolar

Historicamente, a RN esteve intrinsecamente relacionada ao campo das lesões adquiridas. Seus principais avanços foram, inicialmente, determinados pela sobrevivência dos soldados com lesões cerebrais decorrentes da I e II Guerras Mundiais (Abrisqueta-Gomez, 2006), e de maneira mais recente, inúmeros estudos tem sido desenvolvidos no campo dos transtornos neuropsiquiátricos (Bio & Gattaz, 2010; Balanzá-Martínez et al., 2010; Loschiavo-Alvares et al., 2011). Segundo a Organização Mundial de Saúde (OMS), os processos de reabilitação têm como objetivo possibilitar que os pacientes atinjam o maior nível possível de adaptação física, psicológica e social, abarcando, portanto, todas as medidas que pretendam reduzir o impacto da inabilidade e condições de desvantagem, permitindo que as pessoas com alguma deficiência / incapacidade atinjam uma integração social ótima. Nesta perspectiva, a reabilitação neuropsicológica (RN) é um processo ativo que visa capacitar pessoas com déficits cognitivos causados por lesões adquiridas ou transtornos do desenvolvimento, no caso os neuropsiquiátricos, para que estas adquiram um bom nível de funcionamento social, físico e psíquico (Wilson, 2005). Segundo Wilson (2004), a RN consiste na proposição de esforços para melhorar a funcionalidade e a qualidade de vida de portadores de doenças neurológicas e psiquiátricas por meio do emprego de técnicas psicológicas, cognitivas e comportamentais, a fim de recuperar ou minimizar os efeitos de déficits cognitivos, de forma que os pacientes encontrem meios adequados e alternativos para alcançar metas funcionais específicas (Ben-Yishay, 2008).

Especificamente sobre a RN no TAB, são, em seguida, apresentados alguns estudos selecionados a fim de apresentar o estado da arte na área da aplicabilidade clínica desta intervenção para o referido transtorno. O primeiro trabalho, de Martínez-Arán et al. (2004), apresentou como objetivo tanto o estudo do funcionamento neuropsicológico nos distintos estados do TAB, como determinar as relações entre características clínicas, desempenho neuropsicológico, e funcionamento psicossocial. Para tanto, os domínios cognitivos foram avaliados em uma amostra dividida em quatro grupos, depressão bipolar (n=30), mania ou hipomania (n=34), eutimia (n=44) e controle (n=30). Os resultados mostraram um rebaixamento no desempenho cognitivo dos três grupos clínicos, principalmente na memória verbal e funções executivas. E, ainda, que o comprometimento neuropsicológico estava associado com pior desfecho funcional. Na conclusão, os autores apontaram, a lacuna ainda existente, de estudos que tenham como objetivo testar a aplicabilidade de reabilitação neuropsicológica para pacientes com este transtorno.

O trabalho de Rocca & Laffer (2006), teve como objetivo a condução de uma revisão sistemática de estudos controlados, publicados nos últimos 15 anos, sobre alterações neuropsicológicas no transtorno bipolar. Ao final das análises o *n* resultante foram 53 artigos. Após a compilação dos achados, foi corroborado o fato de que pacientes com o referido transtorno apresentavam dificuldades em vários domínios cognitivos, sendo que estas permaneciam mesmo após a remissão dos sintomas de humor, e que os déficits cognitivos estavam em grande parte, circunscritos ao domínio das funções executivas. Além destes achados, o estudo apontou uma correlação positiva entre o comprometimento cognitivo e o número de episódios ou internações, e, ainda, um possível impacto negativo das medicações utilizadas para estabilização do humor, na cognição. Embora não tenha sido feita nenhuma referencia a um estudo de intervenção em reabilitação neuropsicológica para esta população, como ocorreu no artigo citado interiormente, este trabalho ressalta a necessidade de investigações futuras para a avaliação da eficácia de programas de reabilitação, que visam a minimização do impacto dos déficits cognitivos na vida diária dos pacientes.

Já na publicação de Brissos & Kapczinski (2006), cujo objetivo foi avaliar o papel do desempenho cognitivo em medidas de auto-avaliação de qualidade de vida, os resultados apontaram que pacientes bipolares apresentaram escores rebaixados de qualidade de vida, quando comparados aos controles, e que os domínios avaliados do constructo qualidade de vida, foram significativamente, preditos pelas variáveis cognitivas. E, assim como apontado

nos artigos acima explicitados, os resultados do presente trabalho, colocam a reabilitação neuropsicológica como uma intervenção importante na otimização da qualidade de vida destes pacientes.

Os dois trabalhos mais recentes, de Deckerbach et al. (2010) e Torrent et al., (2013), foram os únicos dos compilados nesta revisão que investigaram a eficácia de um protocolo de reabilitação. O objetivo do primeiro artigo foi explorar se um novo protocolo de remediação cognitiva delineado tanto para o tratamento de sintomas residuais de depressão, como para o tratamento do comprometimento cognitivo, estaria associado à otimização do funcionamento psicossocial de pacientes com TAB. Para tanto, o trabalho contou com 18 sujeitos, todos no grupo intervenção, que receberam 14 sessões individuais de intervenção. As sessões de 1-12 foram realizadas semanalmente e as sessões 13 e 14, quinzenalmente. O protocolo foi dividido em três módulos, sendo o primeiro para o monitoramento do humor e tratamento de sintomas depressivos residuais, o segundo para organização, planejamento e manejo temporal, e o terceiro para atenção e memória. No primeiro módulo foram abordadas técnicas para manejo de atividades (aumento de atividades prazerosas, e técnicas de ritmo social) e psicoeducativas. Nos dois outros módulos foram implementadas técnicas adaptadas de Sohlberg & Mateer (2001). Mais especificamente, para o segundo módulo foram empregadas técnicas de uso de dispositivos externos (quadro de notas, listas de verificação), de priorização de atividades, segmentação de tarefas complexas em subcomponentes simples e executáveis, e técnicas para estimação realista do tempo a ser destinado em atividades / projetos. Em adição, os pacientes foram treinados a permanecerem mais atentos a pensamentos que poderiam interferir na execução dos seus trabalhos (como p.ex. pensamentos de postergação), e aprenderam a se monitorar para reduzir o impacto destes pensamentos. Para a atenção e memória os pacientes aprenderam técnicas de estruturação de tarefas, tendo em vista suas capacidades atencionais, de lidar com estímulos distratores, e de usar pistas internas e externas bem como estratégias de codificação para otimização da memória. Os resultados indicaram que tanto ao final da intervenção, como após os três meses de follow-up os pacientes demonstraram baixos sintomas residuais de depressão, e melhora do funcionamento ocupacional e psicossocial. Entretanto, o estudo não teve GC e o "n" foi pequeno, o que limita a generalização dos resultados.

Já o estudo de Torrent et al. (2013) teve como objetivo avaliar a eficácia de programa de intervenção em remediação funcional em uma amostra de pacientes bipolares eutímicos. Este foi um estudo multicêntrico randomizado que envolveu 239 pacientes, divididos no grupo remediação funcional (n=77), grupo psicoeducação (n=82) e tratamento usual – farmacoterapia (n=80). O protocolo de intervenção foi realizado em 21 semanas. Importante ressaltar, que durante este período o tratamento farmacológico foi mantido estável entre os pacientes participantes. Como medidas de eficácia foi adotada uma medida global de funcionamento psicossocial (Functional Assesment Short Test) e comparadas os escores médios pré e pós intervenção. O protocolo de intervenção foi mais extenso que o de estudo anterior, mas, em linhas gerais, abarcou as mesmas áreas, quais sejam: uma breve psicoeducação sobre o TAB e cognição, estratégias para melhora da atenção, memória e funções executivas, todas focadas em tarefas ecológicas visando a otimização da performance funcional. Os resultados evidenciaram que o grupo remediação funcional diferiu de forma significante do grupo de tratamento usual, mas não houve significância estatística quando o primeiro grupo foi comparado com o grupo psicoeducação. Entretantom, nas analises de magnitude de efeito, o grupo sob remediação funcional, apresentou maiores coeficientes (d > 0.5) quando comparados aos do grupo psicoeducação. Enquanto limitações, este estudo apresentou a não inserção de um período de follow-up o que implica na não possibilidade de extrapolação de seus resultados para a avaliação da eficácia desta intervenção em longo prazo.

Diante do exposto, na escassez de estudos sobre a reabilitação neuropsicológica na clínica do TAB, e na existência de vários os trabalhos que de forma substancial apontam o comprometimento cognitivo como preditor de uma maior funcionalidade e qualidade de vida, fazem-se particularmente necessárias abordagens de tratamento que tenham como fim o incremento de habilidades cognitivas visando ganhos consequentes no desempenho funcional. Neste contexto, enquadra-se a reabilitação neuropsicológica, que tem por objetivos a maximização das funções cognitivas, através do bem-estar psicossocial e aprimoramento de habilidades necessárias para o desempenho funcional de atividades básicas e instrumentais de vida diária e do relacionamento social (Loschiavo-Alvares et al., 2013a).

2.3 Qualidade de Vida, Coping e Funções Executivas: Variáveis Dependentes

Tendo por base o importante comprometimento funcional resultante do TAB, além da necessidade do emprego de parâmetros contextualizados às necessidades dos indivíduos para a mensuração do impacto de um programa de RN, foram, neste trabalho, consideradas três variáveis dependentes, qualidade de vida, coping e funções executivas. Considerando que a última foi abordada nas sessões prévias, serão nesta sessão apresentadas a qualidade de vida e o coping.

De acordo com a Organização Mundial de Saúde, qualidade de vida (QV) refere-se às percepções do indivíduo a respeito de sua posição na vida e nos contextos nos quais ele está inserido, bem como abrange seus objetivos, expectativas, padrões e preocupações (Whoqol Group, 1995). Apesar de menos de 4% da população sofrer do transtorno bipolar (Victor, Johnson & Gotlib, 2011; Kessler et al., 2005), estima-se que o transtorno corresponda à nona causa de deficiência global (3). Mesmo quando na fase assintomática, eutimia, pessoas com o TAB, aprensentam índices de QV abaixo dos níveis normativos (Sierra, Livianos & Roo, 2005). De acordo com Michalak, Yatham e Lam (2005), a percepção subjetiva de QV no TAB é menor que a encontrada em transtornos depressivos, transtornos de ansiedade, esquizofrenia e trantorno de abuso de substancias. Alguns estudos tem focado na investigação dos sintomas e tratamento como preditores de QV. Bonnín et al. (2012) investigaram a influencia da cognição na QV de pacientes com o TAB e encontraram um impacto moderado da primeira variável na QV. Desta forma, uma vez que as disfunções cognitivas seriam abordadas no protocolo de RN, optou-se por investigar consequentemente a QV pré e pós-intervenção.

Coping tem sido definido como o emprego de esforços cognitivos e comportamentais para administrar demandas internas e externas específicas que são avaliadas como cargas ou estressores para o indivíduo (Lazarus, Folkman, 1984). O termo coping é usado, independentemente se o processo apresenta conseqüências adaptativas ou mal adaptativas. De acordo com Folkman & Lazarus (1980), o conceito de coping compreende quatro essenciais definições, a saber: o coping é um processo ou interação entre o indivíduo e o meio-ambiente; seus mecanismos gerenciam uma situação estressante, ao invés de controlá-la ou superá-la; o processo de coping compreende a noção de avaliação (como o indivíduo percebe, interpreta e

representa mentalmente um fenômeno) e o envolve esforços para gerenciar, reduzir ou suportar demandas externas e internas que são avaliadas como "cargas" para as pessoas (Antoniazzi et al., 1998).

Considerando-se o TAB , mais precisamente as bases bioquímicas neuroprogressão, Post (2007) sugeriu que alguns dos resultados negativos neste transtorno, podem ser devido a uma falha de mecanismos compensatórios endógenos que, normalmente, atuariam para minimizar o impacto do agente estressor nas funções do sistema nervoso central. Este modelo foi posteriormente expandido com o conceito de carga alostática, proposto por Kapczinski et al. (2008). Este é descrito como um processo pelo qual os efeitos combinados da carga genética, estressores ambientais e fatores agravantes, como p.ex. abuso de substâncias, combinam-se para levar a um processo cumulativo de "desgaste" (Berk et al. , 2011). Nesta perspectiva, o conceito de coping pode ser considerado um produto e um modulador da carga alostática (Grassi - Oliveira et al. , 2010). Embora o conceito de coping pode ser aplicado a numerosas condições físicas , psicológicas e psicossociais, de acordo com o Post e Leverich (2006), há uma grande evidência de que o estresse psicossocial pode desempenhar um papel importante no curso do TAB . Estressores psicossociais podem precipitar a depressão (Ellicot et al , 1990; . Rudolp , 2000) e, presumivelmente, também a mania (Kessing et al, 2004) . Desta forma, o coping tem sido considerado como um outro relevante alvo de intervenção na clínica do TAB (Kapczinski et al., 2008 ; Grassi-Oliveira et al., 2010), e dentre as intervenções propostas para a sua abordagem, ressalta-se a RN. Diante do exposto, o coping foi considerada como outra variável dependente deste trabalho.

3 OBJETIVOS E HIPÓTESES

3.1 Objetivo Geral

O objetivo deste estudo é avaliar a eficácia de um protocolo de reabilitação neuropsicológica adaptado para pacientes portadores do TAB em uma amostra de conveniência.

3.2. Objetivos Específicos

1- Adaptar culturalmente e investigar as propriedades psicométricas da escala DEX-R para avaliação de funções executivas no contexto brasileiro (Artigos 3 e 4).

2- Verificar o impacto do protocolo de RN proposto nas variáveis funções executivas, qualidade de vida e coping, no pós-intervenção e no follow-up (6 meses após a suspensão do protocolo). (Artigos 2 e 5)

3- Investigar o número de episódios de alteração do humor, hipomania, mania e/ou depressão nos seis meses após a integralização do protocolo de RN. (Artigo 5).

3.3 Hipóteses

As principais hipóteses a serem testadas são

1- Os indivíduos do grupo reabilitação (intervenção + farmacoterapia) apresentarão maiores ganhos funcionais, com maior qualidade de vida, melhor funcionamento executivo e emprego de estratégias de coping mais eficazes em comparação aos indivíduos do grupo controle (farmacoterapia).

2- Os indivíduos do grupo reabilitação apresentarão melhores indicadores clínicos nos seis meses que irão suceder o programa de reabilitação, ou seja, menor frequência de episódios de alteração do humor –hipomania / mania e depressão em comparação ao grupo controle.

4 MÉTODO

Nesta seção foram descritos os métodos referentes ao estudo de investigação da eficácia do protocolo de RN para os pacientes com TAB, que atendem aos objetivos específicos 2 e 3. Os procedimentos metodológicos das investigações relativos à adaptação e investigações psicompetricas da DEX-R, que atendem ao objetivo específico 1, foram descritos na metodologia dos respectivos trabalhos disponíveis neste volume, no capítulo 5.

4.1- Amostra

A amostra deste estudo foi composta por indivíduos com diagnóstico de TAB, qualquer subtipo, segundo critérios do DSM-IV, do NTA- HC / UFMG. Noventa e cinco pacientes eram elegíveis para a participação neste estudo. Todos os participantes foram informados dos objetivos da pesquisa e assinaram o Termo de consentimento Livre e Esclarecido (TCLE). Para participarem do estudo, todos os participantes deveriam ser maiores de 18 anos, apresentarem inteligência dentro dos limites da normalidade, apresentarem-se eutímicos no início e durante o tratamento e há pelo menos dois meses em uso da mesma medicação. Como critérios de exclusão foram adotados pacientes com sintomas psicóticos atuais ou histórico de dependência química ou abuso de substâncias.

Os pacientes foram selecionados para a participação na pesquisa através de encaminhamentos da equipe médica do NTA- HC / UFMG. Os participantes foram submetidos a um extenso protocolo de avaliação contendo escalas de sintomas psicopatológicos, entrevista neuropsiquiátrica, avaliação neuropsicológica, e funcional. Posteriormente foram alocados pseudo-aleatoriamente em dois possíveis grupos: o grupo de tratamento farmacológico mais a Reabilitação Neuropsicológica (GRN) o grupo controle positivo, composto por pacientes que recebem apenas do tratamento convencional farmacológico, denominado grupo controle (GC), já ofertado no ambulatório. Como mencionado acima, a alocação foi feita de forma alternada, sendo um paciente para o grupo de reabilitação e o segundo paciente para o grupo controle, sucessivamente.

A fim de verificar a eficácia do protocolo proposto o desempenho dos indivíduos foi avaliado pré e pós-intervenção, bem como após seis meses (período follow-up) de suspensão da RN.

4.2 Instrumentos de Avaliação

Todos os pacientes foram submetidos no início do estudo a uma detalhada anamnese por meio de entrevista semi-estruturada com a qual foram coletadas as seguintes informações: dados pessoais, idade de início do transtorno, predominância dos episódios de humor ocorridos, histórico de ciclagem rápida, número de hospitalizações e de tentativas de suicídio, idade da primeira hospitalização, presença de sintomas psicóticos, uso de álcool, tabaco e outras drogas.

A avaliação neuropsicológica, procedimento já adotado no serviço do NTA-HC / UFMG, foi composta por uma entrevista diagnóstica psiquiátrica, escalas de auto-preenchimento e instrumentos de investigação neuropsicológica, sendo: Mini-Plus (versão brasileira 5.0; Amorim, 2000); Inventário de Temperamento e Caráter de Cloninger (versão em português, Fuentes *et al.*, 2000); Escala Barratt de Impulsividade – BIS 11 (Malloy-Diniz et al, 2010); Inventário Beck de Depressão (Gorenstein; Andrade, 1998); Escala de Avaliação de sintomas de Mania de Young (Vilela *et* al,. 2005); Avaliação da inteligência geral pelo "Teste das Matrizes Progressivas de Raven" (Escala Geral; Raven, 2000); Teste de Performance Contínua – CPT-II (Conners, 2003); Iowa Gambling Task (Malloy-Diniz, *et al.,* 2008); Teste de Seleção de Cartas de Winsconsin - Reduzido (WCST - 64). (Malloy-Diniz, *et al,*2008); Teste de Aprendizagem Auditivo-Verbal de Rey (RAVLT) (Malloy-Diniz, *et al.*, 2009c); Figura Complexa de Rey (Jamus; Mader, 2005). Os resultados desta avaliação foram utilizados como indicadores dos déficits cognitivos.

Foram estabelecidas como medidas para avaliação funcional (incapacidades cognitivas) e de eficácia do protocolo de RN, a qualidade de vida (QV), estratégias de coping e funções executivas, atenção e memória. Para a avaliação da QV foi utilizado o WHOQOL-BREF, versão portuguesa (ANEXO C). Este é um instrumento delineado para ser aplicado a indivíduos com diferentes circunstâncias, condições e cultura (Fleck et al., 1999) e abrange quatro domínios: físico, psicológico, relações sociais e meio-ambiente. O primeiro domínio engloba questões relacionadas a atividades diárias, aderência ao tratamento, doer e desconforto, sono, energia e fadiga. O segundo avalia os domínios de sentimentos positivos e negativos, autoestima, imagem corporal, crenças pessoais, atenção e concentração. O domínio de relações sociais está relacionado às relações pessoais, suporte social e atividade sexual. E, por fim, o domínio ambiental abarca as questões relativas à segurança, recursos financeiros,

disponibilidade de cuidados à saúde e social, oportunidade para aquisição de informações / conhecimentos, participação e oportunidades de lazer e acesso aos meios de transporte.

Para a avaliação do coping, foi empregada a versão brasileira de Escala de Modos de Enfrentamento de Problemas (EMEP) (Seidl et al., 2001) (ANEXO B), que é dividida em quatro fatores; estratégias de enfrentamento focalizadas no problema, estratégias de enfrentamento focalizadas na emoção, busca de práticas religiosas / pensamento fantasioso e busca de suporte social.

Para a avaliação das funções executivas, utilizou-se a DEX-R (Wilson, 1996; Simblett & Bateman, 2011; Loschiavo-Alvares et al., 2013b) que consiste em um questionário com itens que abordam comprometimentos cotidianos relativos à disfunção executiva, incluindo dificuldades com memória, atenção, processamento de informação, controle comportamental, regulação emocional e auto-regulação. Este instrumento não foi disponibilizado nos enexos, ao contrário dos demais, devido aos direitos autorais da editora Pearson.

As funções executivas referem-se a um termo "guarda-chuva" e incorporam todos os processos cognitivos complexos necessários para gerenciar o comportamento humano (Hughes; Graham, 2002). Fuster (2000) refere-se às funções executivas como aquelas responsáveis por iniciar e desenvolver uma atividade que tenha um objetivo final determinado. Fazem parte de seu sistema funcional vários processos cognitivos, como: planejamento, controle inibitório, tomada de decisões, flexibilidade cognitiva, memória operacional, atenção, categorização e fluência (Piek, et al, 2004; Arnsten & Bao-Ming, 2005; Papazian; Alfonso; Luzondo, 2006; Malloy-Diniz et al., 2008). Tais processos favorecerão a possibilidade de soluções para novos problemas propostos, pois atuam no planejamento e regulação do comportamento adaptativo, para atingir um objetivo específico (Cypel, 2007). Sobre a avaliação destas funções, existem uma série de tarefas neuropsicológicas bem estabelecidas, entretanto a avaliação da incapacidade funcional resultante dos déficits executivos, ainda permanece como uma lacuna clínica (Gilbert et al., 2010).

Diante do exposto em seções prévias, acerca do comprometimento cognitivo no TAB, o impacto e seus prejuízos nas diversas situações do cotidiano, resultantes do comprometimento das funções executivas, justificam o investimento no desenvolvimento de medidas de avaliação. Logo, tendo em vista a importância da mensuração das funções executivas no

presente estudo, e a falta de validade ecológica de alguns instrumentos neuropsicológicos que medem essas funções e de possíveis efeitos de aprendizagem em aplicações sucessivas, optamos por trabalhar com a escala DEX-R. A DEX-R é uma escala desenvolvida para avaliar dificuldades cotidianas, relacionadas à disfunção executiva, abrangendo uma série de problemas específicos de atenção, memória, processamento de informação, regulação comportamental e emocional e auto-regulação (Simblett; Bateman, 2011). Os itens são avaliados em concordância com uma escala likert de cinco pontos (0-4), sendo que cada um representa um nível de severidade do problema, variando de nunca a muito freqüente. A DEX-R é disponível em dois formatos diferentes, o primeiro de auto-preenchimento, que foi pesquisado neste estudo (Loschiavo-Alvares et al., 2013b) e o outro direcionado ao familiar e/ou cuidador do paciente.

4.3 Protocolo de intervenção RN

Tendo em vista que o comprometimento cognitivo de individuos portadores do TAB é centrado nas funções executivas, atencionais e mnemônicas, as atividades / tarefas propostas no protocolo foram focadas na reabilitação das referidas funções cognitivas. O protocolo proposto no presente trabalho foi adaptado do estudo de Deckersbach *et al.* (2010). Neste o tratamento foi conduzido em tres módulos, de 14 sessões ao total, sendo o primeiro focado no desenvolvimento de estrategias de monitoramento do humor e tratamento de sintomas depressivos residuais, o segundo na memória e atenção, e o terceiro, na reabilitação das funções executivas.

No primeiro módulo, foi realizada a psicoeducação padronizada considerando o que é o TAB, quais os sintomas, os subtipos, o que é mania, hipomania, depressão e eutimia, e a importância de implementar hábitos saudáveis, enfocados na Terapia do Ritmo Social (Bouwkamp et al., 2013). Fizeram ainda parte da psicoeducação a relevancia da adesão à farmacoterapia, além da cognição no TAB e o estabelecimento do gráfico do humor personalizado, para que os pacientes efetuassem o registro semanal deste.

As técnicas empregadas nos segundo e terceiro módulos foram embasadas nas proposições de Solhberg e Mateer (2001) e Wilson (2011). Concernente à reabilitação da atenção no segundo

módulo, foram utilizadas estratégias de controle ambiental (Sohlberg & Mateer, 2001). Estas consistem no autocontrole das tarefas (listas de verificação mental, uso de dispositivos externos, como agendas, calendários, diário de idéias) e modificações no ambiente para auxiliar os pacientes a compensarem os problemas atencionais. No tocante à memória, foram empregados auxílios externos como agendas, blocos de anotação, quadro de avisos, sendo a escolha destes, personalizada. Referente às técnicas, foram utilizados o pareamento de estímulos, aprendizagem sem erro e recuperação espaçada. A primeira técnica é embasada no pressuposto de que quanto mais estímulos de diferentes fontes (p.ex. visual, auditiva, tátil) associamos à uma informação alvo para a memorização, maior facilidade teremos em evocá-la (Wilson, 2011). Assim, para a consolidação de novas informações, os pacientes foram estimulados a associá-las com imagens (mnemônicas visuais). O aprendizado sem erro, conforme Wilson (2011), é uma técnica de ensino, através da qual, na medida do possível, se evita que as pessoas cometam erros na fase de aquisição de uma nova habilidade ou informação. Para tanto, esta técnica pode ser conduzida de diversas formas, como o fornecimento de instruções e pistas verbais ou escritas, e até mesmo orientação ao longo da tarefa. Já a recuperação espaçada é uma estratégia de intervenção que usa ensaio expandido. Neste, o inidivíduo pratica a recuperação bem-sucedida da informação através de intervalos temporais gradativamente mais longos (Sohlberg & Mateer, 2001). Este é um procedimento de modelação que é muito dependente da memória não-declarativa (Schacter, 1992). Durante o treinamento, a informação alvo é fornecida ao indivíduo e, imediatamente, este deve recuperar a informação. Nas tentantivas subsequentes é solicitado ao paciente que recupere a informação em intervalos de tempo que são dobrados, a medida que o tratamento progride. Importante ressaltar que os intervalos temporais são preenchidos com as demais atividades da reabilitação (Wilson, 2011).

O terceiro módulo foi composto por estratégias auto-instrucionais. Estas foram desenvolvidas, inicialmente, a partir da capacitação do paciente para a aplicação prática de estratégias metacognitivas, tais como: O que er estiu fazendo?; "Selecionar uma estratégia"; "Tentar a estratégia"; "Checar a estratégia". Numa etapa seguinte, o alvo terapeutico foi o autocontrole, através do feedback externo dos erros e sucessos, com os pacientes registrando os erros e comparando o desempenho através das tentativas. Em um terceiro momento, focalizou-se na mediação verbal, na qual os pacientes verbalizavam as subtarefas da atividade alvo, a fim de desenvolver, mentalmente, uma lista de verificação do que deveria ser feito. Por fim, para o processo de complementação da tarefa, foi empregado o treinamento para controlar o objetivo

(Levine et al., 2000) – GMT (goal management training), que é composto por cinco estágios: Pare; defina a tarefa principal; liste as etapas; aprenda as etapas; execute a tarefa e verifique.o protocolo do GMT, conforme Solhlberg & Mateer (2001), objetiva os parâmetros relevantes para a seleção de metas e definição de tarefas-alvo, fracionando estas em subobjetivos, mantendo as etapas conforme a tarefa estiver sendo completada e monitorando o resultado desta.

O protocolo elaborado para esta pesquisa (Figura 1) foi composto por 14 sessões, sendo a primeira destinada à apresentação do protocolo e esclarecimento de possíveis dúvidas e a última focada no emprego continuado das técnicas aprendidas e manutenção das competencias adquiridas. As demais foram divididas conforme os módulos, sendo quatro para cada. As sessões, todas individuais, foram realizadas semanalmente. Foi realizado um estudo piloto prévio a fim de investigar a viabilidade clínica do já referido protocolo (Loschiavo-Alvares et al., 2013a). Foi portanto empregado o delineamento experimental de caso único (Covre, 2012) e as comparações foram feitas considerando-se os escores da paciente caso (n=1) na linha de base, no pós-intervenção e no follow-up. Estes foram comparados aos do grupo controle sem quaisquer comprometimentos neuropsiquiátricos (n=6). Tanto no período pós-intervenção, como no follow-up, a paciente exibiu melhora sinificativa nos escores, apresentando desempenho similiar aos seus pares saudáveis. Logo, após esta investigação preliminar, que ofereceu respaldo clínico para a aplicação clínica do protocolo proposto, o mesmo foi então empregado como a intervenção experiemental no GRN.

Figura 1: Protocolo de Reabilitação Neuropsicológica

Módulos	Sessões	Conteúdo das Sessões
-	1	Apresentação do protocolo e estabelecimento de metas funcionais.
Módulo 1: Psicoeducação	2	O que é o TAB? Consciência do transtorno e hábitos saudáveis, técnicas de ritmo social (sono, atividade física e alimentação)
	3	Farmacoterapia e TAB
	4	Cognição e TAB
	5	Meus sintomas – Gráfico do Humor

	6	O que é atenção e como otimizá-la? Estratégias de controle ambiental, diário de ideias.
	7	Aplicação contextualizada das estratégias de reabilitação da atenção
Módulo 2: Reabilitação da Atenção e Memória	8	O que é memória e como otimizá-la? Uso da agenda, dispositivos mnemônicos, técnicas de aprendizado de domínios específicos do conhecimento (pareamento de estímulos, aprendizagem sem erro e recuperação espaçada).
	9	Aplicação contextualizada das estratégias de reabilitação da memória
	10	O que são funções executivas e como otimizá-las?
	11	Terapia auto-instrucional, técnicas de auto-monitoramento e Treinamento de Gestão de Metas (Goal Management Training – GMT)
Module 3: Reabilitação das Funções Executivas	12	Como programa e organizar tarefas? • Estabelecimento de prioridades • Segmentação de Tarefas • Manejo e organização temporal • Desenvolvimento de listas de verificação Estratégias de Solução de problemas
	13	Aplicação contextualizada das estratégias de reabilitação das funções executivas
-	14	Emprego continuado de estratégias e competencias adquiridas

4.4 Procedimentos

4.4.1 Procedimentos de Coleta de dados

Podem-se distinguir duas fases na coleta de dados conforme os objetivos do estudo. Para atender ao objetivo específico (1), foi realizada a aplicação da versão brasileira DEX-R (já previamente traduzida) juntamente com o questionário sociodemográfico e de saúde em uma amostra de conveniência, de indivíduos sem quaisquer transtornos neurológicos e/ou psiquiátricos. Os participantes foram informados quanto aos objetivos e ao caráter voluntário da pesquisa, e todos os procedimentos empregados nesta pesquisa foram aprovados junto ao Comitê de Ética em Pesquisa da UFMG (COEP/UFMG – ETIC 0625.0.203.000-11 - Anexo A). No primeiro momento da testagem, após a assinatura do Termo de Consentimento Livre e Esclarecido (TCLE), iniciou-se a aplicação do questionário de autorrelato de forma individual. Em um segundo momento, o mesmo questionário foi aplicado em pacientes com diagnóstico de TAB.

Para atender ao objetivo geral desta pesquisa, bem como aos objetivos específicos 2 e 3, a coleta de dados foi realizada no Núcleo de Transtornos Afetivos do Hospital das Clínicas da UFMG. Os participantes do grupo clínico foram recrutados através de encaminhamentos da equipe médica. Todos os participantes foram convidados a participar do estudo e, após a assinatura do TCLE, foi iniciada a avaliação neuropsicológica e funcional com duração total média de 3 horas. Em um segundo momento, os pacientes participantes do GRN foram encaminhados para a intervenção. Os profissionais que fizeram a avaliação, bem como as reavaliações receberam treinamento prévio e não conduziram o protocolo de intervenção e foram cegos quanto aos grupos. Após a avaliação neuropsicológica e funcional, os sujeitos do grupo experimental foram conduzidos ao tratamento com o protocolo de RN, que foi empregado por um unico profissional treinado e com formação específica na área.

4.4.2 Procedimentos de Análise de dados

A primeira etapa para a análise dos dados foi a limpeza do banco de dados e a verificação dos pressupostos de normalidade, linearidade, casos omissos e casos extremos nas variáveis das

medidas psicológicas, de saúde e sociodemográficas. Inicialmente, a amostra foi descrita por suas características demográficas e de saúde. As análises estatísticas foram realizadas no programa estatístico Statistical Package for the Social Sciences (SPSS) - versão 20.0, adotando-se o nível de significância de 5%.

No estudo das propriedades psicométricas da DEX-R (objetivo 1), investigou-se a dimensionalidade da versão adaptada para o contexto brasileiro. Inicialmente, com o objetivo de checar se a distribuição dos fatores da DEX-R coincidia com a estrutura original apresentada no estudo de validação do instrumento (Simblett & Bateman, 2011), optou-se pelo uso da técnica da análise fatorial exploratória (AFE) em uma amostra composta por 120 sujeitos com diagnóstico de TAB e 300 sujeitos sem nenhum transtorno neuológico e/ou psiquiátrico, pareados quanto ao sexo, idade e escolaridade. O teste de esfericidade de Bartlett e a medida de Kaiser-Meyer-Olkin (KMO) foram obtidos no intuito de analisar a viabilidade das respostas aos itens e a adequação da amostra para implementar a AFE. Em seguida, foi realizada a AFE com rotação oblíqua (Promax). A rotação oblíqua é adequada para a investigação das variáveis latentes para os quais se espera a obtenção de dimensões correlacionáveis (Mingoti, 2007). De acordo com Costello e Osborne (2005), as dimensões psicológicas, em sua grande maioria, apresentam algum nível de covariância. A decisão sobre o número de fatores foi feita com base nos seguintes critérios (Mingoti, 2007; Hair, Anderson, Tatham & Black, 2005): (a) análise da proporção da variância total relacionada ao autovalor de cada fator obtido, sendo que permaneceram aqueles com maiores proporções da variância total, (b) identificação do número de fatores com autovalores iguais ou maiores que 1, (c) análise do gráfico Scree Plot, no qual a identificação do momento anterior ao ponto de salto é um indicativo do número de fatores adequados para explicar a variância total e (d) interpretação teórica dos fatores obtidos. Os resultados destas análises, além da comparação entre os grupos controle e clínico (TAB) já foram publicados (Loschiavo-Alvares et al., 2013b).

Em um segundo momento, ainda trabalhando com o objetivo 1, a fim de investigar a hierarquia dos itens na escala, testar a viabilidade das subscalas propostas pele AFE, foi realizada a Análise de Rasch (Bond & Fox , 2007). Esta especifica que cada resposta a um item é tomada como um resultado da interação probabilística linear da capacidade de uma pessoa e dificuldade de uma questão. O modelo de Rasch constrói uma linha de medição com os itens alocados de maneira hierárquica e fornece estatísticas de ajuste para indicar o quão

bem diferentes estes itens descrevem o grupo de indivíduos e como sujeitos se encaixam no grupo. A análise de Rasch fornece indicadores de quão bem cada item se encaixa dentro da construção subjacente. Diante do exposto, o objetivo desta análise foi ir além dos resultados de análise fatorial e, nesse sentido, o objetivo primário era realizar a validação da versão em Português do DEX -R usando a abordagem de análise de Rasch. As análises foram rodadas no software RUMM 2030.

Para atingir o objetivo 2, as estatísticas descritas a seguir foram utilizadas. Primeiramente, foram calculadas estatísticas descritivas (média, desvio-padrão, amplitude e frequências) para caracterizar demograficamente a amostra do estudo. Em seguida, foram conduzidas ANOVA's de medidas repetidas de delineamento misto 3×2 no intuito de investigar o efeito do curso (pré-tratamento vs pós-tratamento vs acompanhamento) e do tipo de tratamento (controle vs experimental) sobre os escores nas escalas de autorrelato. Todas as análises foram realizadas no SPSS 20.0. Em todos os casos em que o teste de esferecidade de Mauchly's W indicou que a hipótese de esfericidade foi violada, as estatísticas foram reportadas com a correção de Greenhouse-Geisser. Além disso, para explorar o efeito do tratamento sobre os escores, foram calculadas as magnitudes de efeito (d de Cohen) das médias do pré- e pós-tratamento. Finalmente, a fim de comparar as variáveis clínicas de interesse no período de follouw-up, foi utilizado o teste t para a comparação da frequencia de episódios de alteração do humor. As estatísticas descritivas de ambos os grupos no pré e pós-ntervenção, bem como referentes ao follow-up estão explicitadas no Apêndice A.

5. APRESENTAÇÃO E DISCUSSÃO DOS RESULTADOS

Os resultados dessa tese são apresentados a seguir sob o formato de artigos e suas respectivas discussões com base na literatura. Por fim, uma breve síntese dos principais resultados é realizada tendo em vista os objetivos específicos do presente estudo.

5. 1 ARTIGOS

ARTIGO 1:

TOOLS FOR EFFICACY'S ASSESSMENT OF NEUROPSYCHOLOGICAL REHABILITATION PROGRAMS: A SYSTEMATIC REVIEW

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TOOLS FOR EFFICACY'S ASSESSMENT OF NEUROPSYCHOLOGICAL REHABILITATION PROGRAMS: A SYSTEMATIC REVIEW

Abstract

Background: There is a consensus in the field of neuropsychological rehabilitation (NR) that to measure effectiveness of a particular treatment program, one should look at the results of neuropsychological tests before and after the rehabilitation program, as well as the result of neuroimaging techniques and questionnaires of daily living and/or other behavioral and functional measures. The focus of NR is the reduction of disability, the impact of cognitive disabilities to the level of activities performed by patients and are therefore of fundamental importance the use of tools of efficacy assessment focusing on aspects of functional and environmental performance.**Objective:** This study aims to address the question of which tools are most commonly used to measure neuropsychological rehabilitation efficacy. **Method:** A systematic literature review was designed using the MEDLINE database and the following keywords in association: "neuropsychological rehabilitation", "cognitive rehabilitation", "efficacy" and "evidence-based". The publication date was used as search limit. All articles were classified according to a degree methodological efficacy (Class I, II and III). Besides that, the articles were classified according to their congruence between the rehabilitation goal and the assessment method used to insure the outcome (successes or the failure in the goal) of the rehabilitation program (A, B and C, being categories A the most congruent with the general proposal of NR and C the less one). **Results:** A total of 32 articles were selected and allocated in three different classes, being that Class I articles were comprised of randomized controlled trials (n = 12), Class II clinical series with well-designed controls that permitted subject comparisons of treatment and conditions " quasi-randomized "studies (n = 14) and Class III studies that results from one or more single cases appropriate with the use of single-subject methods (n = 6). In reference to the goal congruence analysis, 66% were classified in Category A, 12% in Category B and 22% in Category C. **Discussion:** These results show that until now there is a misleading use of assessments tools, causing misconceptions of the discussion and the interpretation at the time the results. The use of formal neuropsychological tests to evaluate treatment outcomes such as patient quality of life, independence and autonomy, remain in practice e in the art of clinical cognitive rehabilitation, however the real predictive power of this practice still needs to be evaluated more systematically. Moreover the isolated application of these tests proves to be inconsistent with the objectives

neuropsychological rehabilitation program, since the rehabilitation objectives are grounded in functional goals, which generally aim to reduce the impact of cognitive deficits in individuals daily life and not to increase the performance in specific tests.

Background

Neuropsychological Rehabilitation (NR) is the proposition of efforts to improve the functionality and quality of life of patients with neurological and psychiatric disorders through the use of psychological, cognitive and behavioral techniques (Wilson 2004). Therefore, the rehabilitation aims to maximize the cognitive functions through the psychological well-being, enhancing skills necessaries for activities of daily living (ADLs) and social relationship. According to Ben-Yishay (2008), the objective is to recover or minimize the effects of cognitive impairment, so that patients find alternative and appropriate means to achieve specific functional goals, as well as the improvement in performance and behavioral skills aiding to understanding and monitoring of emotional reactions. Therefore, the major objective of NR is to reintegrate patients to their environments of schooling, social and professional.

In according to Cicerone (2000), the best measure to evaluate treatment efficacy are randomized controlled trials, such as the Brain Injury–Interdisciplinary Special Interest Group, that divide treatment efficacy studies as highly constrained studies that typically evaluated time-limited interventions of selected, homogenous samples, primarily for research purposes. This seems to be a statement in this area, that for specific populations, one must use specific techniques, (Slomine and Locascio 2009, Tsaousides and Gordon 2009), it means that there is no support in the literature for global stimulation programs that has an useful gain for all types of patients. For example, the use of spaced retrieval training for patients with Alzheimer's disease (Lee et al. 2009) and behavioral training in leftward visual scanning, eye-patching, encouraging movement of the left limbs, an interventions designed to increase general alertness for patients with unilateral neglect (Manly 2002). However few studies addresses the efficacy of neuropsychological assessment's in rehabilitation programs in general, being this the main objective in present study.

However, one of the most important tasks in any rehabilitation program is the identification of everyday life problems. Since 1990 it is possible to observe an increasing emphasis on the development and use of outcome measures in cognitive rehabilitation as tools for estimating effectiveness (McMillan and Sparkes 1999), giving birth a philosophy change (i.e. stop using neuropsychological test to insure real life outcomes) that still today it is not fully understood and implemented. Information from standardized tests and questionnaires that contribute to

build up a profile of strengths and weaknesses need to be complemented by information from functional or behavioral assessments to build up a picture of how these problems affects everyday life (Wilson 2002). According with Solhberg and Mateer (2001), the use of goals assessment in the context of cognitive rehabilitation covers the development of an accurate profile of individual's functioning including the evaluation of cognitive, emotional and interpersonal factors. Furthermore the most important suggestion is dedicated to the comprehension of strategies that facilitate learning and cognitive dynamic functioning.

Thus, in an attempt to obtain an ecological neuropsychological evaluation and functionality assessment in its wide spectrum, the World Health Organization's International Classification of Impairments, Disabilities and Handicaps (ICIDH) distinguishes three levels of functional deficit: impairment, disability and handicap (Arthanat et al. 2004). Is important to note that these three levels do not relate to different aspects, but rather different categories of impact of a same specific health problem, in case of the subject referred to NR, deficits in cognitive functions. "Impairment" occurs at a physical, structural, organ, or system level and involves a missing or malfunctioning body part or system (for example, a person with lesion of the hippocampus and as a consequence, a memory impairment). "Disability" occurs at the activity level, as a result of impairments. It involves disturbed function in performance of usual age appropriate activities, such as Impairments in activities of daily living (ADL) and instrumental activities of daily living (IADL), for example: difficulty remembering to take medication, pay bills or finish their chores. "Handicap" occurs at the social level (job loss, family's dependency or loss of the ability to take care for himself). It involves disturbed function in the performance of social roles, such as employment. In this perspective, the overall focus of neuropsychological rehabilitation programs is to reduce the disability and handicaps. Within this perspective becomes viable the employment of different assessments that measure objectively the functionality / performance of the individual in their daily tasks, since an intervention can only be implemented based on the level of individual function, the extension of activity performance (Arthanat et al. 2004). To take an advance in the effort to systematize the knowledge about the three stages functional deficits of patients who are in the neuropsychological rehabilitation processes it is important to have tools that provide an estimation of the degree of the impact of the injury and what kind of difficulties in daily life and social losses this patient should exhibit. In this way, the goal of this study is to perform a systematic review of the current literature, which investigating which instruments were used to assess efficacy in rehabilitation programs evaluating the congruence between these

instruments and the goal of the neuropsychological rehabilitation programs they aim to evaluate.

Method

A research was conducted through MEDLINE using the follow keywords in association: "neuropsychological rehabilitation", "cognitive rehabilitation", "efficacy" and "evidence-based".

In the first selection, 157 articles were assigned to the study sample. They underwent to a second step for the selection of relevant papers that the content fulfills the designed criteria, i.e. papers that aims at neuropsychological rehabilitation programs and it effectiveness, and should have been published from January 2000 through March 2011. After this, two experts in neuropsychological rehabilitation identified and analyzed the abstracts or complete articles according to the following exclusion criteria: (1) review papers; (2) non-English language paper; (3) theoretical articles; (4) pharmacologic interventions; (5) medical rehabilitation without an specification concerning neuropsychological rehabilitation program used; (6) book chapters; (7) non-human population (8) articles with only measures of assessment based on neuroimaging studies.

Through this process, the specialists selected 32 articles and classified these in three classes based on Cicerone (2000). In accordance with this classification, the Class I covered studies that were defined as randomized controlled trials, Class II clinical trials with well-designed controls that permitted between subject comparisons of treatment conditions and "quasi-randomized" studies. Finally class III studies were defined by results from one or more single cases that used appropriate single-subject methods, such as multiple baselines cross-interventions with adequate quantification and analysis of results.

For the purpose to verify the congruence of the selected articles in the neuropsychological intervention and the clinical assessment, they were categorized in three categories with respect to the congruence between the objective of the intervention and the assessment tool employed to measure the intervention´s outcome. About the objectives of the intervention, the articles were evaluated for the proposition of goals focused on reducing disability and handicap, and focus on reducing only impairments. The category A, included interventions that had the aim to reduce the disability and / or handicap and used environmental assessments, like functional scales, performance in activity daily living, social functioning, coping and self-efficacy scales (supposedly the most congruent), category B, articles aimed

to reduce disability and / or handicaps but did not use environmental assessments, only psychometric tests, and category C, whose goals were focused only on the reduction of impairments and used psychometric tests (supposedly less congruent).

Results

The total population studied was 157 articles of which we found 32 who fulfilled the inclusion criteria. Table 1 shows the article selection and exclusion number for each search proceeded in MEDLINE.

Table 1: Selected and Excluded Articles.

Keywords	Population	Number of articles excluded	Selected
"neuropsychological rehabilitation" AND "efficacy"	39	27	12
"neuropsychological rehabilitation" AND "evidence-based"	7	6	1
"cognitive rehabilitation" AND "efficacy"	83	65	18
"cognitive rehabilitation" AND "evidence-based"	28	27	1

Following the proposal of this review, 32 studies were found, and they were classified according to the criterion of methodological efficacy, with the following description: 12 Class I studies, 14 Class II and 6 Class III, as detailed in tables 2, 3 and 4. The description of these studies is presented on table 2, 3 and 4. For each table detailed descriptions of the selected articles are provided; the total sample, the methods employed for efficacy assessment, and the classification about the NR goal/assessment congruence using the categories described above (A, B, C).

Table 2: Description of Class I Studies.

CLASS I STUDIES			
Studies	**Sample**	**Methods used for efficacy's assessment**	**Classification about the goal congruence and assessments used**
Geusgens et al. (2006)	N = 113 (stroke)	Four standardized tasks, namely: 1 (washing face and upper extremity), 2 (dressing shirt) 3 (preparing and eating a sandwich) 4 (preparing a hot chocolate).Scores were assigned according to independence, initiative, execution and control. ADL Observations, Barthel ADL Index, Apraxia Test, Action Research Arm Test (ARA), SAN Test.	A
Svendsen and Teasdale (2006)	N = 50 (stroke and traumatic brain injury)	European Brain Injury Questionnaire (EBIQ); Patient Competency Rating Scale (PCRS); Generalized Self-efficacy scale (GSEC); Locus of Control (LoC); Hospital anxiety and depression scale (HADS); WHO-Qol Bref	A
Wolwer et al. (2005)	N = 77 (schizophrenia)	PFA test: pictures of facial affect. D2, Trail Making Test A and B, AVLT, Digit span, Wais, Fluency non-verbal Test, range of positive and negative symptoms.	B
Bier et al. (2008)	N = 30 (Alzheimer's disease)	Face-name association - Performance Parameters adapted for the own task used in the rehabilitation program. Digit span and letter-number sequencing tests – WAIS III; Visuo-spatial block tapping test – WMS-III; French version of the Selective and Cued Reminding Test (SCRT) Recognition Memory Test; Verbal fluency – French version; Association match task from the Birmingham Object Recognition	A

		Battery (BORB); Benton's Face Discrimination Test; The Stroop Test; The Trail Making Test A and B, The Process Dissociation Procedure (PDP).	
Derwinger et al. (2005)	N = 81 (elderly without cognitive impairments)	Remember numbers with and without learning strategies - Performance parameters adapted for the own task used in the rehabilitation program	A
Troyer et al. (2008)	N = 54 (mild cognitive impairment)	Performance Parameters in own Task Used in Rehabilitation, The Impact Rating Scale, Strategy subscale of the Multifactorial Metamemory Questionnaire, Elaborated Memory tests to be administered (by projecting stimuli onto a screen and requiring written responses), Hopkins Verbal Learning Test (HVLT), Wechsler Memory Scale–Revised Verbal Paired Associates, Brief Visuospatial Memory Test (BVMT) and Rey-Osterreith Complex Figure Recall.	A
Winocur et al. (2007)	N = 49 (elderly without cognitive impairments)	Geriatric Depression Scale (GDS), Locus of Control Scale (LOC), Quality of Life (QOL), Self-Efficacy Scale (SE), Memorial University of Newfoundland Scale of Happiness (MUNSH), Life Orientation Test (LOT), Everyday Activity Questionnaire (EA), Ways of Coping Questionnaire (WOC), DEX.	A
Cicerone et al. (2008)	N = 68 (traumatic brain injury)	Community Integration Questionnarie (CIQ), Cognitive Energy Scale, Perceived Quality of Life Scale (PQOL) Community Integration Questionnaire (CIQ), TMT-A; California Verbal Memory Learning Test -II,Rey Figure Oral Word Association Test e Booklet Category Test. Community-based employment - Scale.	A

Buiza et al. (2008)	N = 238 (elderly without cognitive impairments)	Hachinski Scale Hachinski, Barthel ADL Index , Instrumental activities of daily living Lawton Temporal, spatial and personal orientation Information and orientation of WMS-R, Attention Direct and inverse digits of WMS-R, Working memory, Immediate execution memory Logic memory of WMS-R, Logic memory Recent word list memory Auditory Verbal Learning Test (AVLT), Short term memory Learning potential, -Designation language -Boston vocabulary test Repetition language Boston Diagnostic Aphasia Examination (BDAE), Audit compression, Written compression, Written language, Reading language, Visuo-constructive ability WAIS-III, Planning Clock drawing (order and copy) , Bimanual coordination Motor sequences of Luria, Pre-motor function, Visomanual coordination speed Trail Making Test, part A, Army Individual Test Battery, Visomanual coordination execution, Phonetic fluency FAS Benton and Hamsher, Semantic fluency, Abstraction Proverbs, Categorization Similarities of WAIS-III, ICPR Motor Sequences of Luria.	C
Fals-Stewart and Lam (2010)	N = 160 (Substances Abuse Use Disorder)	Working Alliance Inventory–Short Form (WAI-S); Staff Rating Scale (SRS); Client Assessment Summary (CAS); Client Satisfaction Questionnaire (CSQ-8); Timeline Followback Interview (TLFB); Addiction Severity Index (ASI); SureStep urine drug screen card; Neuropsychological Assessment Battery-Screening Module (NAB-SM).	A

Man et al. (2006)	N = 103 (traumatic brain injury)	Specific tests developed for performance evaluation. Category Test for Adults (Subtest I-VII); Lawton Instrumental Activities of Daily Living Scale (LIADL); Test of Non-verbal Intelligence – Version 3 (TONI-3);Letter cancellation; Test of The Rivermead Perceptual Assessment Battery (RPAB)	A
Flavia et al. (2009)	N = 150 (multiple sclerosis)	Paced auditory serial addition test (PASAT); Winsconsin Card Sort Test (WCST); controlled oral word association test with phonemic and semantic cues (COWA/P, COWA/S) for cognitive flexibility and word fluency; divided attention of Test of Everyday Attention (TEA) — median for auditory stimulus (am), for visual stimulus (vm), total omitted stimuli (to) and total errors (te) and two questionnaires: the Montgomery–Asberg Depression Rating Scale (MADRS) and the self-reported Multiple Sclerosis Quality of Life (MSQoL).	B

Table 3: Description of Class II Studies.

CLASS II STUDIES			
Studies	**Sample**	**Methods used for efficacy's assessment**	**Classification about the goal congruence and assessments used**
Brennan et al. (2009)	N = 44 (dementia)	Naturalistic Action Test (NAT)	A
Culley and Evans (2010)	N =11 (acquired brain injury)	SMS text messaging - Performance Parameters in own Task Used in Rehabilitation	A
Savorani et al. (2004)	N = 34 (mild cognitive impairment)	Mini mental state examination (MMSE), memory impairment screen (MIS), Alzheimer's disease assessment scale (ADAS), ADAS-Cog 10-word, semantic verbal fluency, digit span forward and backward and geriatric depression scale (GDS)	B
Farinamd et al. (2006)	N = 32 (Alzheimer's disease)	Mini Mental State Examination (MMSE), Rivermead Behavioural Memory Test (RBMY), Attentional Matrices, Verbal fluency for Letters and Categories, Rey figure copy and recall, Functional Living Skills Assessment (FLSA), Activities of daily living (ADL), Nurses' Observation Scale for Geriatric Patients (NOSGER), Neuropsychiatric Inventory (NPI), Revised Memory and Behaviour Problems Checklist (RMBPC), Geriatric Depression Scale (GDS), Clinical Insight Rating scale (CIR), Caregiver Burden Inventory (CBI) and Beck Depression Scale (BDI).	A
Powell et al. (2008)	N = 32 (acquired brain Injury)	Raven's Coloured Progressive Matrices, Labelling of Facial Expression, Position Discrimination Test from the Visual Object and Space Perception Battery, Unusual Views , Letter Cancellation, Similarities sub-test from the Wechsler Adult Intelligence Scale–Revised,	B

		Oldfield Naming Test, Controlled Oral Word Association Test (COWAT), Story Recall (immediate), Digit Span – total forwards and backwards, Recognition Memory Test – Words, Picture Recognition, Cognitive Estimates, Famous Faces Test ,Test of Facial Recognition, Face Matching Test, Warrington Recognition Memory Test – Faces, Face Recognition test from the Rivermead Behavioural, Memory Test and Face Learning Test.	
Kinsella et al. (2007)	N = 32(Alzheimer's disease)	Text-Reading Task, Hopkins Verbal Learning Test – Revised (HVLT-R), recognition discrimination index (HVLT-R DI), The Trail Making Test part A and B and Wechsler Digit Span.	A
Talassi et al. (2007)	N = 66 (Mild cognitive impairment and mild dementia)	Mini Mental State Examination (MMSE), forward and backward digit span, phonemic and semantic verbal fluency, sub-test for episodic memory of Rivermead behavioral memory test, visual search, digit symbol test, rey complex figure copy and recall, clock drawing test, geriatric depression scale (GDS), state-trait anxiety inventory, neuropsychiatric inventory (NPI), physical performace test (PPT), basic ADL (BADL), instrumental (IADL) and caregiver burden inventory (CBI)	A
Galante et al. (2007)	N = 11 (Alzheimer's Disease and mild cognitive decline)	Mini Mental State Examination (MMSE), Milan Overall Dementia Assessment (MODA), Bisyllabic Word Repetition Test, Prose memory, Corsi's block tapping test, Digit cancellation test, Raven's Coloured Progressive Matrices, Semantic and phonemic verbal fluency, Denomination, Constructional apraxia and Ideomotor apraxia for superior limbs, Neuropsychiatric Inventory, Geriatric Depression Scale, Basic Activities of Daily Living and Instrumental Activities of Daily	C

		Living.	
Shevil and Finlayson (2009)	N = 41 (multiple sclerosis)	Program evaluation questionnaire and qualitative analysis	A
Kesler et al. (2011)	N = 25 (cancer)	Wechsler Intelligence Scale for Children 4th Edition (WISC-IV) or Wechsler Adult Intelligence Scale 3rd Edition (WAIS-III); Wide Range Assessment of Learning and Memory 2nd Edition (WRAML2) List Memory and Picture Memory NEPSY II Animal Sort or Delis Kaplin Executive System (DKEFS); Sorting Test; Woodcock-Johnson 3rd Edition (WJ-III); Cancellation Test Motor Free Test of Visual Perception 3rd Edition (MVPT-3) and Functional MRI (fMRI)	C
McDonald et al. (2009)	N = 22 (traumatic brain injury)	Wechsler Test of Adult Reading (WTAR) Face Recognition Test; Digit Symbol Coding, Symbol Search; Matrix Reasoning and Digit Span Subtests of the Wechsler Adult Intelligence Scale (WAIS-III); Controlled Oral Word Association Test (COWAT); phonemic naming: F, A, S; category naming: animals; Trail Making Test parts A and B; Haylings test of inhibition from the Hayling-Brixton tests; LogicalMemory I and II from theWechslerMemory Scal (WMS-III); facial expression naming stimuli from the Ekman and Friesen series.	C

Boman et al. (2004)	N = 10 (acquired brain injury)	Attention Process Training test; Digit Span Test from the WAIS; Claeson-Dahl test, CD-test Rivermead Behavioural Memory test (RBMT), Assessment of Motor and Process Skills; European Brain Injury Questionnaire (EBIQ); Quality of life (QoL).	A
Cicerone et al. (2004)	N =56 (Traumatic Brain Injury)	Community Integration Questionnaire (CIQ); and Quality of Community Integration Questionnaire (QCIQ); Trail-Making Test parts A and B; California Verbal Learning Test (CVLT);Rey Complex Figure; Controlled Oral Word Association Test30 (COWAT) and Category Test.	A
O'Connell et al. (2006)	N= 15 (attention-deficit hyperactivity disorder)	Modified version of the Sustained Attention to Response Test (SART)	C

Table 4: Description of Class III Studies.

| CLASS III STUDIES			
Studies	**Sample**	**Methods used for efficacy's assessment**	**Classification about the goal congruence and assessments used**
Fillingham et al. (2006)	N = 11 (language impairments)	Picture naming tests were used to measure the degree of anomia: Boston Naming Test without standard systematic cueing, Graded Naming Test and Picture Naming PALPA 53. Single-word reading and repetition were used to assess the integrity of phonological representations (reading words, PALPA 31; and non-words, PALPA 8; repeating words (PALPA 9) and non-words (PALPA 8). Word and picture versions of the Pyramids and Palm Trees, a 100-item spoken word–picture matching test in both spoken (SWPM) and written formats (WWPM). Psychometrically-graded tests of comprehension, again run twice for auditory and written	B

		presentations, British Picture Vocabulary Scale (BPVS), Concrete and Abstract Synonyms. Assessments of episodic memory for verbal and nonverbal materials including recognition for faces, pictures, words and landscapes, Rey Complex Figure Test; Camden Memory Test) working memory (Digit Span); PALPA Auditory , Digit Matching Span, nonverbal problem-solving and reasoning (Wisconsin Card Sorting Test.	
Schweizer et al. (2008)	N = 1 (acquired brain injury)	Sustained Attention to Response Task; Delis Kaplan Executive Function System Tower Test (D-KEFS); Revised-Strategy Application Test (R-SAT); Hotel Task; Dysexecutive Questionnaire (DEX); Cognitive Failures Questionnaire (CFQ).	A
Tam et al. (2003)	N = 3 (Traumatic brain injury)	Software packages for on-line cognitive skills training and Rivermead Behavioural Memory Test (RBMT)	A
Davalos et al. (2002)	N = 5 (schizophrenia)	Action Programs Test and the Modified six elements of the Behavioural Assessment of Dysexecutive Syndrome Scale (BADS); Trail Making part B; Dysfunction of the Executive Syndrome Scale (DEX).	C
Parish and Oddy (2007)	N = 4 (traumatic brain injury)	Evaluated the percentage of independence in performing the task target.	A
Levaux et al. (2009)	N = 1 (schizophrenia)	Digit span (forward and backward), letter number frequency, logical memory, face recognition, of Manuel de l'Echelle Clinique de Mémoire (MEM III); Alpha span; Brown-Peterson; working memory, divided attention, vigilance, go/no-go, flexibility of Test of Attentional Performace (TAP); Selective Reminding Test; Mirror Tracing; Verbal fluency: Phonological/Semantic; Continuous Performance Test (CPT); Trail Making Test part A and B; Rule Shift Cards; Six Elements Test; Action Programme (BADS); Symbol Copy (WAIS-III); Memory Self-Assessment (QAM); Attention Self-Assessment (QAA); Working Memory Self-Assessment (QAMT); Subjective Scale to	A

		Investigate Cognition in Schizophrenia (SSTICS) and Self-esteem Inventory (SEI)	

In terms of clinical populations that were exposed to rehabilitation procedures, 38% had a stroke or traumatic brain injury, 23% had a diagnosis of Alzheimer's disease or mild cognitive impairment (MCI), 15% had multiple sclerosis, 13% had substance use disorder, 2% cancer related brain injury, 1%, attention deficit of hyperactive disorder (ADHD) and 1% language impairments. In the graphic below it is possible to see the frequency distribution of three levels of congruence of the studies, concerning the clinical relation between the measurement of the impairment or disability and the neuropsychological rehabilitation goals outcome. From the analysis of the results on the congruence of the studies it was observed that most (66%) had focus on the reduction of NR disability / handicap with the use of functional assessments, consistent with the proposed objectives and more consistent with the proposal of the NR. Were used parameters the actual task of rehabilitation as target for pre and post intervention, assessments of performance in activities of daily living (ADL), measures of greater ecological validity for measuring the difficulties related to memory and executive function in daily activities, self-efficacy scales and quality of life, coping, social functioning. However, 12% had goals in the intervention focused on reducing disability and / or handicaps but did not use functional assessments to measure the level of impact on activities and social level, they just used psychometric tests, showing therefore an incongruence in the evaluation of the efficacy of intervention plan. The other studies, 22%, had only focused intervention aimed at reducing the impairment and used psychometric tests, this finding is inconsistent with the proposal of NR, which considers impairment but should be focused on its impact on the individual level of activity (disability) and as in their level of social participation (handicap).

Graphic 1: Distribution of studies according to the categories of level of impairment or disabilities with respect to the congruence between the objective of the intervention and the assessment tool employed to measure the intervention´s outcome.
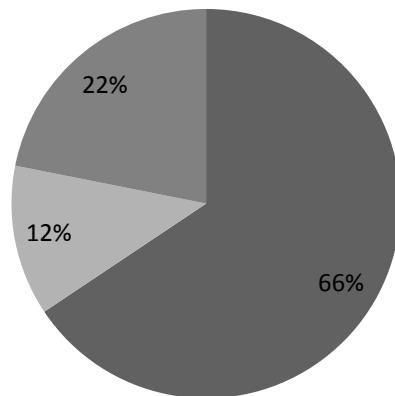
Discussion

In the articles compiled in this review was possible to see common features in the evaluation procedures for the proposed rehabilitation programs, even with different populations, different functional impairment and different intervention strategies. Most of the articles (61%) are related to neuropsychological rehabilitation with stroke, traumatic brain injury and dementia. Also it was possible to found, in a lower frequency, programs of neuropsychological rehabilitation in neurodevelopmental psychiatric disorders (2%), in this case schizophrenia and ADHD. It is important to note that there are few articles concerning the rehabilitation of neuropsychiatry and developmental disorders and a lot of researches showing that cognitive deficits are common findings in this population related to impairment in the performance of productive skills, social and daily living (Corrigan et al. 2007, Malloy-Diniz et al. 2007, Moreira et al. 2010, Bowie et al. 2010, Pigache 2010, Rocca et al. 2010, Binz and Brüne 2010). In this way, future studies are needed to assess the efficacy of clinical neuropsychological rehabilitation in this field.

Neuropsychological assessment was used in different designs and in most studies, followed by scales and questionnaires. In some ways, this finding is convergent with Wilson (2002), which emphasizes the application of standardized tests for establishment of the cognitive weaknesses and strengths of individuals. However, as pointed out by Solhberg and Mateer (2001), psychometric assessment generally addresses the level of impairment which is relevant, but it is not enough to enable professionals to completely understand the full impact of an impairment at a subject´s activity of daily living, making it difficult to formulate an appropriate and executable intervention plan.

From this perspective, it was observed eleven studies, including those with higher methodological rigor (Classes I and II), that has established as a parameter for evaluating the effectiveness of rehabilitation intervention the measurement of the performance in the task itself the target of treatment in situations ecological, according to the demands of patient rehabilitation (Cicerone et al. 2004, Derwinger et al. 2005, Farinamd et al. 2006, Geusgens et al. 2006, Man et al. 2006, Kinsella et al. 2007, Bier et al. 2008, Powell et al. 2008, Brennam et al. 2009, Culley and Evans 2010).The parameters used were numbers or percentage of correct answers in self-care tasks, questionnaries and instruments to measure activities of daily living (established as the rehabilitation program) and contextualized, effective employment of mnemonic strategies in tasks of face recognition. On the ecological situation was evident the use of rehabilitation strategies developed for remembering names, phone numbers and passwords, using available technologies to patients, as features of cellular phone

and internet (Culley and Evans 2010). Importantly, these parameters and ADL's Scales were used in studies with elderly and people that have had an acquired brain injury (Geusgens et al. 2006, Man et al. 2006, Talassi et al. 2007, Buiza et al. 2008). One possible explanation for this result would be based on the historical perspective of neuropsychological rehabilitation, since most of the initial studies were directed to the investigation of brain injury populations (Prigatano 1999), and in the elderly population, have had been increasingly need for proposals of non-pharmacological treatments. From the distribution analysis of these articles according to its category of level of impairment and disabilities, the data show that there is still an incongruence usage of techniques and assessments, certainly causing misconceptions during the discussion and interpretation of results. The use of formal neuropsychological tests to evaluate treatment success, quality of life, independence and autonomy, remains a practice still used in clinics and departments abroad, and need to be evaluated more systematically in order to fully understand the true extent of its predictive power for therapeutic success. For instance, the study of Galante et al. (2007), which used psychometric tests to measure the effectiveness of cognitive training software, showed a quite unspecific pattern, which prevents any type of generalization to the performance of functional skills, ecological activities and quality of life.

As pointed out by Wilson (2009) when planning a cognitive rehabilitation programs there are many questions that need to be answered. And many of these cannot be answered by psychometrics tests, some examples are: How are the memory difficulties manifested in everyday life? Which memory problem cause most concern to the family and the patient? What do we know about the cultural background and level of support available? What coping strategies are used? Are the problems exacerbated by depression or anxiety? Is this person likely to be able to return to work (or school)? Can this person live independently? What kind of compensatory aids did this person use premorbidly? What kind of memory compensation strategies are being used now? What is the best way for this person to learn new information? These questions and concerns are the real important ones, when the major focus of the treatment is the impairment impacts in everyday life (handicap).The main objective in the NR is the development of a set of more adaptative and functional behaviors, life quality, independence and autonomy, and it is difficult to visualize how we can perceive such developments using formal neuropsychological tests. The evaluation of the neuropsychological profile of impaired and preserved processes is a necessary condition but should always be combined with a measuring of the impact of cognitive impairments and handicaps in daily individual life (Royal et al. 2007). Some authors, such as Prigatano (1999)

and Wilson (2002), propose that NR interventions must be understood in a broader way, considering the persons in their context and their relationships.

In a way to cope with this question, a different approach is required, using diverse forms of behavioral, functional, observational and self-report measures, such as ecological tests, for example Rivermead Behavioural Memory Test – RBMT (Wilson et al. 1985), every day cognitive problems questionnaires (Crawford et al. 2006) and other scales, (also involving family members and caregivers) and interviews (Wilson 2009). Thus it is possible to elect constructs intervention, an individualized and effective practice that helps to set parameters for evaluating the effectiveness of an intervention impact after an acquired brain injury: self in relation to self; self in the world; emotions; motivation; uncertainly; basic skills; social relating; copying; outlook; activity; all important concepts that are important to capture the pre and post identity of a patient (Psaila et al. 2006).

Conclusion

Assessment is the first step in establishing a neuropsychological rehabilitation plan, as well as the basis for determining its effectiveness. In this sense it is a dangerous pitfall the use of neuropsychological tests as outcome measure, since the aim of neuropsychological rehabilitation is not the isolated improvement of cognitive functions, but rather the use of different techniques to enable people with disabilities to function the most adequately as possible in their appropriate environment. It seems rational that changes on scores of standardized tests will not give us the information we require. Therefore, still nowadays the responsibility falls to the rehabilitation professionals to give attention to the relevance and greater need to establish efficacy parameters grounded in functional performance referred by cognitive life constructs, and related to ecological tasks.

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ARTIGO 2:

NEUROPSYCHOLOGICAL REHABILITATION FOR BIPOLAR DISORDER – A SINGLE CASE DESIGN

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NEUROPSYCHOLOGICAL REHABILITATION FOR BIPOLAR DISORDER – A SINGLE CASE DESIGN

Brief Running title: NEUROPSYCHOLOGICAL REHABILITATION FOR BIPOLAR DISORDER

Background: Cognitive functions most impaired by impact of mood disorder are memory, attention and executive functions which are intrinsically related to functional performance. Cognitive impairment predicts lower quality of life and also has a negative impact on functional skills. For these reasons it is relevant to propose interventions in neuropsychological rehabilitation (NR). **Aim**: To investigate the efficacy of NR techniques for attention, memory and executive functions impairments in a person with bipolar disorder (BD) type 1. **Methods**: NR protocol consisted of fourteen weekly individual sessions, divided into three modules. The first was directed toward mood monitoring, the following focused on executive functions, and the third addressed attention and memory rehabilitation. Comparisons were made among the patient's scores in pre-intervention, post intervention and follow-up phase. Statistical analyses were conducted using *Singlims_ES.exe* program. Significant level was set at p<.05. **Results**: The patient's scores for all functional demands were significantly higher than those of the controls, at the baseline (p<.05 for all comparisons). At the post intervention phase the effect sizes were lower than the baseline, and the patient demonstrated the level of performance similar to the control sample in two of five functional demands (p>.05). At the follow-up phase the patient exhibited similar performance to the controls (p>.05 for all comparisons). **Conclusion**: This is a preliminary study in NR applied to BD, and the 14 weeks of NR program appeared to be successful in

helping to improving the patient`s functional ability toward the level of performance shown by six matched controls.

Key-words: neuropsychological rehabilitation, bipolar disorder, functional skills, cognition.

BACKGROUND

Cognitive impairments are common findings in neuropsychiatric diseases and contribute to restrictions in work and social skills [1, 2]. Cognitive functioning has been shown to be a predictor of a positive prognosis in psychiatric intervention [1, 3].

Meta-analytic studies [4, 5] have suggested medium to large effect sizes for the neuropsychological differences between people with BD and healthy comparison subjects, particularly in the domains of episodic memory, attention ∕ concentration and executive functioning. Regarding the different types of BD, Type I is a condition characterized by periods of mania (euphoria) with elevated mood and exaggerated behavior alternating with periods of depressed mood and euthymic mood. These periods are often serious enough to cause difficulties with work and social relationships. Type II is characterized by occurrence of one or more major depressive episodes accompanied by at least one Hypomanic Episode with a phase of softer mood elevation causing a lower level of problems than during the manic frames [6]. It has been well established that cognitive deficits persist in the absence of acute mood symptoms and it is thought that cognitive deficits are not solely a result of mood symptoms in bipolar disorder [6]. Given that cognitive deficits are predictive of a worse quality of life [7] it is logical that they are a potential treatment target for neuropsychological rehabilitation (NR) in BD [8].

NR is an active process of capacity building for people with cognitive deficits caused by acquired brain injury or neuropsychiatric disorders [9]. NR aims to maximize cognitive functions through enhancing well being, activity of daily living skills and social relationships, as well as aiming to minimize the consequences of cognitive deficits [10]. NR program has been proven to improve the functionality and quality of life of patients with neurological and psychiatric disorders. The use of psychological, cognitive and behavioral techniques, in a NR intervention, has as a goal functional reintegration to academic, professional and social

environments [11]. In view of the functional impact of cognitive impairments caused by BD, the relevance of neuropsychological rehabilitation for this population must be considered [7].

The objective of this case study is to examine the efficacy of a NR program for a person with bipolar disorder where the interventions were focused on rehabilitation of attention, memory and executive functions.

METHOD

Case EMB

EMB is a 61 years old, divorced, female and retired teacher. She provided written informed consent for the study, which was approved by the hospital research ethics board. After recent diagnoses of bipolar disorder, she looked for neuropsychiatric assistance. At that time, she was using mood stabilizers, but in spite of this she presented with a depressed mood, suicidal ideation, thoughts of death, anxiety and compulsive behavior. Her clinical history showed the first depressive episode was when she was thirty nine years old, after her last daughter's birth. However at that time she did not receive treatment. Following this first mood alteration, further depressive episodes occurred. These were interspersed with manic episodes producing symptoms of euphoria, accelerated thoughts, compulsive shopping and sexually disinhibited behavior. She was also inappropriately dressed and did not behave in context, in accordance with psychiatric assessment. At the beginning of this reported treatment, the psychiatrist observed that EMB presented with executive dysfunction, impaired insight, hyperthymic and incongruent affect. Since mood stabilizers had not been effective in reducing the mood episodes, Risperidone (1mg) was prescribed with an objective of reducing manic symptoms [12]. After three months of pharmacotherapy treatment, EMB was euthymic, with

Beck Depression Inventory (BDI) score < 11 [13], Young Mania Rating Scale (YMRS) score <10 [14] and she was referred for neuropsychological rehabilitation treatment.

Cognitive Profile and Functioning

A neuropsychological evaluation was performed to characterize EMB's cognitive profile before beginning NR intervention. Specific cognitive tests were used (Table 1). To evaluate verbal memory the Rey Auditory Verbal Learning Test (RAVLT) [15] was used. The Rey Complex Figure was used for evaluation of planning and non verbal memory. The Continuous Performance Test (CPT- II) [16] was used to evaluate attention. For executive functions the Iowa Gambling Task (IGT) [17] and Wisconsin Card Sorting Test (WCST) [18] were used. Finally, to evaluate impulsivity the Barratt Impulsivity Scale (BIS-11) [19] was completed by EMB. Mood was monitored using Beck Depression and Young Manic scales [13, 14] during the entire NR intervention phase and at the follow-up. It is important to highlight that at each session both scales were applied and throughout the duration of this study, EMB scored less than the cut-off points (considering depression and hypomania respectively) established for those assessments.

Table 1. EMB's cognitive profile

Tests	Scores (X; SD) or (X; %) Percentile
Barratt Impulsivity Scale (BIS-11)	
- Attentional	22 (18,76 ; 4,30)
- Motor	30 (24,22; 6,32)
- Non-planning	25 (23,29; 4,63)
- Total	77 (66,27; 11,60)
Iowa Gambling Task (IGT)	
- Block 1	0 (65%)
- Block 2	-2 (25%)
- Block 3	-4 (5%)
- Block 4	-2 (10%)
- Net Score	-14 (10%)
Continuous Performance Test (CPT-II)	
- Omissions	5 (70,6%)
- Commissions	9 (38,5%)
- Hit RT	63,63 (92,8%)
Wisconsin Card Sorting Test (WCST)	
- WCST Categories	1(6-10%)
Rey Auditory Verbal Learning Test (RAVLT)	
- A6 (Total Immediate Recall)	13 (11,1; 1,6)
- A7 (Delayed Recall)	10 (10,6; 2,4)
- ITP (Proactive Interference)	2,3 (0,8; 0,2)
- ITR (Retroactive Interference)	1,0 (0,9;0,1)
- VE (Forgetful Speed)	0,7 (1,0; 0,2)

Functionally, EMB reported specific difficulties with repeated loss of personal objects and forgetting appointments. She was unhappy about the social consequences of these memory slips. She also reported being disorganized, having problems with overspending, being in debt and often arriving late for appointments. These activity limitations were in the clinical formulation consistent wiith cognitive impairments as described in EMB's neuropsychological assessment. Further details to help describe this case are given in Table 2 which illustrates our proposed links from cognitive constructs to strategies for intervention.

Table 2. Clinical Characterization

Cognitive Constructs	Cognitive Deficits	Functional Disabilities: Baseline Parameters	NR Goals	Strategies of Intervention
Attention and Memory	Attention: Lower resistance to distracting stimulus. Memory: difficulties in episodic memory.	1- Constant loss of objects 2- Forgetting Appointments	To improve attention and memory skills to execute the everyday tasks	Self-management strategies (orienting procedures), environmental supports (environmental modifications e.g. note pads) and external devices and external aids (written checklists and calendar systems with day planners). [21]
Executive Functions	Impulsivity, Impairments in Planning, sequencing, organizations, decision making, time management and problem solving	3- Overspending 4- Being late for Appointments – (spending a lot of time with non relevant tasks) 5- Everyday errors caused by lack of planning.	To develop monitoring strategies for financial and time management, problem solutions and planning.	Environmental Management (organization of physical space and manipulation of physiological factors), Training the Selection and Execution of Cognitive Plans (planning, errand completion tasks, time management tasks trained in prioritizing activities, breaking down complex tasks into simpler tasks and making more realistic time estimations for activities/projects), Learning Task-Specific Routines (plan, practice and promote therapeutic attitudes – task analysis checklists), Metacognitive Strategies / Self-Instructional Training (Goal Management Training – GMT: Stop, Define, List, Learn, Do it, Check). [21]

Intervention

Fourteen weekly individual sessions (fifty minutes each) were divided into three modules [20], each one with four sessions (Table 3). During all modules and respective sessions, all strategies were applied in a tailored way focusing on EMB's functional demands, in this way the whole intervention was directed to reduce the functional disabilities that were thought to be caused by deficits in memory, attention and executive functions skills.

Table 3. NR Protocol

Sessions / Modules	Structure of the Sessions
First Session	Presentation of the protocol and establishment of functional measures
Module 1: Mood Monitoring	Session 2: Psycho education about BD. Session 3: Psycho education about BD. Session 4: Strategies developing for mood monitoring. Session 5: Evaluating the implementation of mood monitoring strategies.
Module 2: Executive Functions Rehabilitation	Session 6: Environmental controls strategies. Session 7: Learning Task-Specific Routines Session 8: Training the Selection and Execution of Cognitive Plans Session 9: Metacognitive Strategies / Self-Instructional Training
Module 3: Attention and Memory Rehabilitation	Session 10: Attention training tasks. Session 11: Contextual use and Self-management strategies with external aids. Session 12: Mnemonic strategies Session 13: Contextual use and Self-management strategies with external aids.
Last Session	Continual use of learned techniques and acquired competences

Measures

A tailored recording form was designed to support capture of the percentage of occurrences of daily problems related to memory, attention and executive function in daily situations. This form was used throughout the study to assess the performance of the patient during the baseline, intervention and follow-up periods. The frequency of this assessment was every fortnight. At the first column were described functional disabilities and at the others fourteen columns, related to weeks days, both patient and controls would themselves assess theirs daily performance, having as a reference a scale from 0 to100, which would represent the impact of the cognitive problems. Scores closer to 100 represented a high level of impact, while indices near to 0 showed a less level of impact. Another measure only filled by the patient, related to her perception about her level of disability, similar to the one described above was adopted.

Design

To study the efficacy of cognitive rehabilitation, a single-case design was selected. This experimental design provides an intensive and prospective study of the individual, using a specific methodology, which includes systematic observation, manipulation of variables, repeated measurement and data analysis [22]. As such, these designs are particularly useful in their ability to individually tailor an intervention to the specific characteristics of the individual while still providing empirical evidence in support of the particular therapeutic interventions. Information gleaned in carefully described case studies can be applied to interventions designed for other individuals with similar difficulties [23].

The single-subject A1-B1-A2-B2 design was utilized. The A phase involves a series of baseline observations of the natural frequency of the target behavior (s) under treatment

while in the B phase the treatment variable is introduced, and changes in the dependent measure are noted [24]. In this study it was considered five target behaviors split of in two baseline parameters (Table 2). The display of study diagram is demonstrated in Figure 1. The protocol spans fourteen weeks and the repeated measures were collected on alternate weeks. Post intervention measures were administered following the ending of intervention and at 1 – month follow-up. EMB`s performance was compared both to age and level of education matched controls (n=6), as required in Crawford statistics method.

Figure 1. Display of Study Diagram
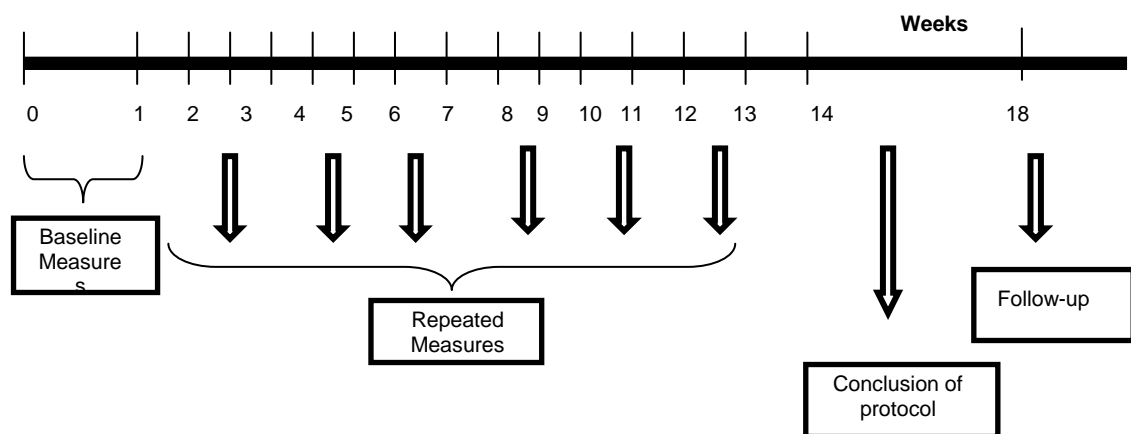
Statistical Analyses

Comparison of an individual's score against a normative sample is a fundamental feature of the assessment process in clinical neuropsychology [25]. The advances in neuropsychological theory occur at an advanced rate whereas the process of devising practical measures of new constructs is yet a complicated process [26]. In this study a case-control design was used, in which inferences concerning the performance of a single case are made

by comparing the case to a matched sample of healthy controls [25]. This method uses the modified t-test to conduct comparisons, indeed this treats the control sample as a sample, and it has been to establish the confidence interval (CIs) on the abnormality of a score [27]. These CIs quantify the uncertainty arising from using sample statistics to estimate population parameters [26] and with the effect size, provide all the pertinent information required for judgment of the single case performance on the tasks analyzed [28]. The statistical analyses were completed using the *Singlims_ES.exe* program, a tool provided by Crawford [29]. This implements classical methods for comparison of a single case score to scores obtained in a control sample and estimates the effect size for the difference between case and controls [30]. A comparison was made of EMB's performance in pre-intervention, post intervention and follow-up phases. The data (rate of occurrences of problems) of six healthy control subjects in the five functional demands pointed by EMB at the beginning of NR intervention was used. These control subjects were selected randomly by a database of normal subjects available in our research centre. The criteria used to do this selection were age, gender and educational level. For all analyses the significance level was set at p<.05.

RESULTS

Comparisons of performance in functional demands among the baseline, post intervention and follow-up

The results were expressed in the Table 4, below. The comparisons were made using the percentage of occurrences of daily problems related to memory, attention and executive function in daily situations, as explained above. The paired control group used for all comparisons was composed by females, with mean of 59,8 (SD= 3,2) years, and educational level of 13,7 (SD= 2,4) years.

Table 4. Results comparisons between the EMB's case and control sample.

	Control sample				Significance test*		Estimated percentage of the control population obtaining a lower score than the case		Estimated effect size	
Baseline Functional Disabilities	**n**	**Mean**	**SD**	**Case Score**	**t**	**p**	**Point**	**(95% CI)**	**Point**	**(95% CI)**
Loss of Objects	6	20	7.42	75	6.77	0.00	99.87	(99.34 to 100)	7.41	(2.48 to 12.44)
Forgetting Appointments	6	6.6	2.7	85	26.51	0,00	99.99	(100 to 100)	29.04	(10.08 to 48.48)
Overspending	6	3.6	3.04	85	24.44	0.00	99.99	(100 to 100)	26.77	(9.29 to 44.71)
Being late for Appointments	6	5.6	3.64	80	18.66	0.00	99.99	(100 to 100)	20.44	(7.07 to 34.14)
Everyday Errors	6	3.4	2.7	80	25,89	0.00	99.99	(100 to 100)	28.37	(9.85 to 47.38)
Post intervention Functional Disabilities	**N**	**Mean**	**SD**	**Case Score**	**t**	**p**	**Point**	**(95% CI)**	**Point**	**(95% CI)**
Loss of Objects	6	20	7.42	13	-0,86	**0,21**	21.89	(2.34 to 56.81)	- 0,94	(- 1.98 to 0.17)
Forgetting Appointments	6	6.6	2.7	13	2,16	**0.06**	95.18	(70.85 to 99.99)	2.37	(0.55 to 4.15)
Overspending	6	3.6	3.04	13	2.82	0.03	97.62	(80.39 to 99)	3.09	(0.85 to 5.31)
Being late for Appointments	6	5.6	3.64	20	3.61	0.01	98.87	(88.4 to 100)	3.95	(1.2 to 6.73)
Everyday Errors	6	3.4	2.7	15	3.92	0.00	99.13	(90.85 to 100)	4.29	(1.33 to 7.29)
Follow-up (1-month) Functional Disabilities	**n**	**Mean**	**SD**	**Case Score**	**t**	**p**	**Point**	**(95% CI)**	**Point**	**(95% CI)**
Loss of Objects	6	20	7.42	22	0.25	**0.41**	59.11	(26.08 to 87,47)	0.27	(- 0.64 to 1.15)
Forgetting Appointments	6	6.6	2.7	9	0.81	**0.23**	76.87	(41.88 to 97.21)	0.89	(- 0. 20 to 1.91)
Overspending	6	3.6	3.04	6	0.72	**0.26**	74.45	(39.47 to 96.24)	0.79	(- 0.27 to 1.78)
Being late for Appointments	6	5.6	3.64	10	1.1	**0.17**	84.42	(49.27 to 99.09)	1.20	(- 0.02 to 2.36)
Everyday Errors	6	3.4	2.7	8	1.55	**0.09**	90.26	(59.45 to 99.90)	1.70	(0.24 to 3.11)

* Legend: The results are for a one-tailed test.

As shown in Table 4, the case scores for all functional demands are significantly higher than those of the controls, at the baseline (p=0.000 for all comparisons). The effect sizes are very large, the case scores are highly abnormal and because of this, almost the whole control population is expected to exhibit scores lower than these. At the post intervention phase the effect sizes are lower than the baseline and EMB demonstrated the level of performance similar to the control sample in two of five functional demands (loss of objects p= 0.21 and forgetting appointments p= 0.06). And at the follow-up phase, for all functional demands EMB exhibited similar performance to the controls (p> 0.05 for all comparisons). In contrast with the baseline, there was no evidence for a deficit on performance in functional demands, since the case scores do not differ significantly from controls, the effect sizes are fairly modest and it is estimated that a large percentage of the control population would obtain scores such as observed in the patient.

For the visual inspection of EMB's data (her perception related to level of disability), the graphs present the level of disabilities in functional demands (Figures 2 and 3). To facilitate the analyses the data were grouped in Attention and Memory skills and Executive Functions skills, as at the clinical characterization (Table 2).

Figure 2. Results of EMB's level of disability – Attention and Memory
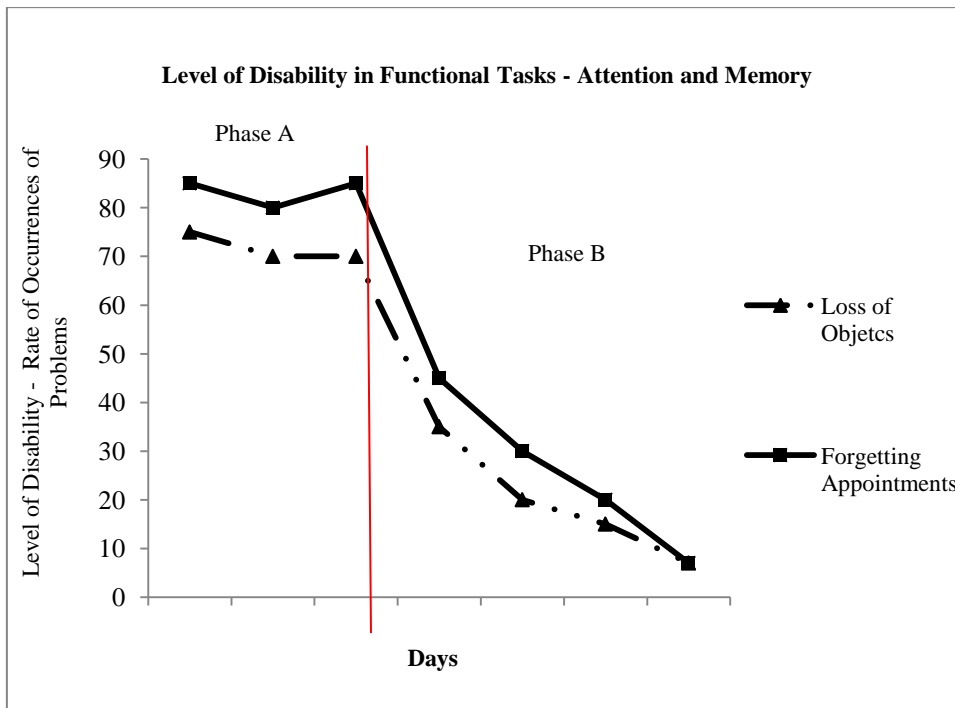
* *Legend: This figure displays the level of disability in Attention and memory skills. Phase A is correspondent to measures during the pre-intervention while phase B is related to measures during the intervention.*

Figure 3. Results of EMB's level of disability – Executive Functions

Level of Disability in Functional Tasks - Executive Functions
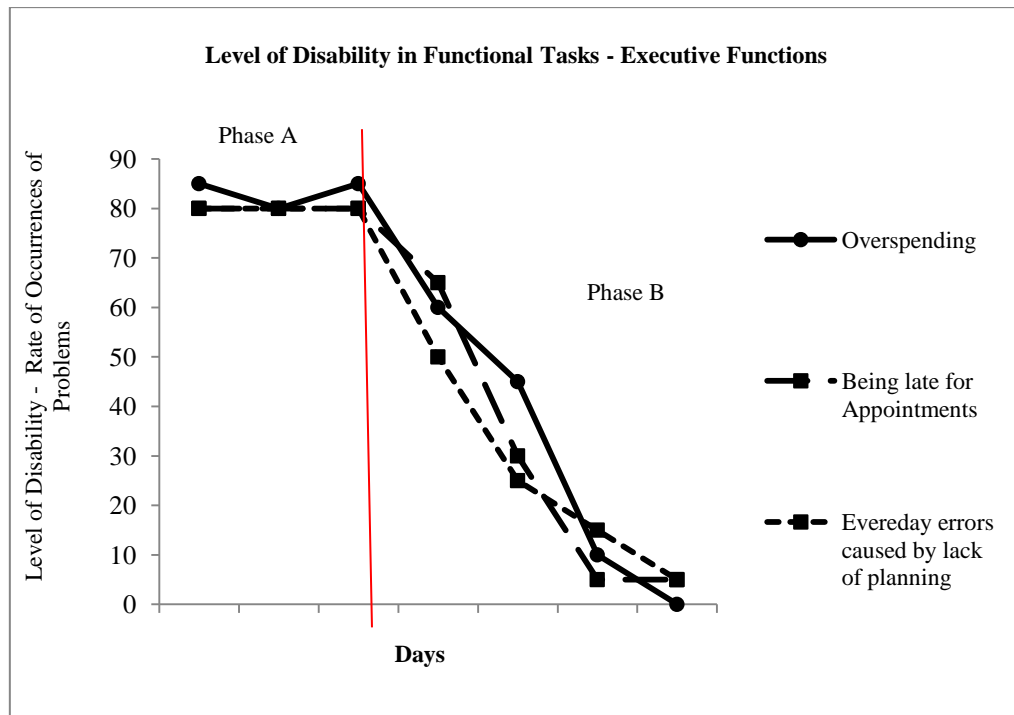
* Legend: This figure displays the level of disability in Executive Functions skills. Phase A is correspondent to measures during the pre-intervention while phase B is related to measures during the intervention.

EMB's level of disabilities decreased considerably as can be seen by the comparison between the baseline and intervention phases. In this way, through statistical analyses and visual inspection, it is possible to conclude the effectiveness of NR intervention.

DISCUSSION

In this study a structured NR protocol addressed memory, attention and executive functions in a patient with BD type I. The efficacy of that intervention was analyzed making

comparisons with a control matched sample. It was found that after fourteen sessions of NR intervention this patient demonstrated improvements in functional measures. Applying compensatory strategies to enhance memory, attention and executive functions in everyday functioning pursuits was efficient in that case.

One of the most important tasks in any rehabilitation program is the identification of everyday life problems [30]. In particular, goal assessment in the context of cognitive rehabilitation helps to develop an accurate profile of an individual's functioning and responses to therapy [21]. In the NR area there are several studies that has been investigated the efficacy of NR, being most for acquired brain injuries and few which investigated it for neuropsychiatric diseases [30]. In both the target of treatment is based on ecological situations, according to the demands of patient in rehabilitation [32,33,34].The parameters used were, e.g., numbers or rate of correct answers in self-care tasks, questionnaires and instruments to measure activities of daily living and contextualized tasks. Based on these fundaments, this research investigated the NR efficacy by using functional demands collected by a tailored questionnaire.

All results showed significant improvement in all functional aspects, demonstrating a functional increase. After both the completion of NR program and the 1 month follow-up, EMB showed an improvement in her functional skills, with significant decrease in her level of disabilities. Regarding to cognitive deficits, the International Classification of Functionality highlights the fact that cognitive impairments are conceptual constructs that are derived from behavioural observations, and that the associated disabilities are not in themselves specifically attributable to a single cognitive deficit which corroborates the necessity of a broad intervention [35]. It should consider the persons in their context and their relationships [36,37], as it was proposed in this research. Therefore, the main objective in the NR is the

development of a set of more adaptative and functional behaviors, quality of life, independence and autonomy [38]

There are currently relatively few articles concerning NR in neuropsychiatric diseases [30]. Several research having showed cognitive deficits are common findings in this population related to impairment in the performance of productive skills, social and daily living [1, 39, 40]. Three longitudinal researches [42, 43, 44] indicated that the cognitive impairment is a fundamental predictor to a weak psychosocial adaptation. In this way, future studies are needed to assess the efficacy of clinical neuropsychological rehabilitation in this field. In this perspective this study is yet a preliminary research in NR applied to BD, which used the single-subject research design. But even having been a preliminary study, the result showed above suggests that individuals with BD can benefit from NR intervention. Whereas it is well established that cognitive rehabilitation is needed and effective in other psychiatric conditions such as schizophrenia [8], there has been relatively less attention to cognitive rehabilitation among people with BD. This study represents a small step toward redressing this imbalance.

As potential limitations of this study it has been noticed the extensibility of the information coming from a single case design and the short follow-up period. However this was a pilot study designed to elaborate a standardized NR protocol and as future directions more broad studies will be developed using a case control design, having as a reference the protocol investigated at this current research, to treat cognitive impairments in people with BD.

In summary the important cognitive impairment in BD findings support the conclusion that cognitive deficits represent a target for functional rehabilitation in that disease [44], in that context the NR is highlighted as the intervention which would contribute for the positive functional outcomes [45]. It is important to highlight also, that this paper illustrates translation

of statistical sciences (eg Crawford), neuropsychology and rehabilitation science perspectives to neuropsychiatry interventions.

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ARTIGO 3

Clinical Application of DEX-R for patients with Bipolar Disorder type I and II

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Clinical Application of DEX-R for patients with Bipolar Disorder type I and II

Abstract

*Objective***:** To compare the performance of DEX Questionnaire Revised in people with bipolar disorder (type I and type II) and control population, and also examine the factor structure for this questionnaire.

*Method***:** DEX-R was administrated to 120 participants with bipolar disorder (BDG) and 300 healthy controls (CG). An exploratory factor analysis, further comparisons between Control Group (CG) and Bipolar Disorder Group (BDG) using Student *t-test,* and comparisons using Anova one way were used to explore differences among the two bipolar subgroups and CG (CG X BDG Type 1 X BDG Type II). For all analyses the significance level was set at p< .05.

Results: Three factors account for 58,10% of variance loaded in three dimensions. A significant difference between groups on DEX-R score total (t=15.63; df=418; p<00.1) was found. Considering the results from comparisons among the two clinical and controls groups, the BDG Type I exhibited higher impairments in general.

Conclusions: the factors that loaded in three main dimensions were congruent with the functions that have been attributed to orbitofrontal, dorsolateral and anterior cingulated circuits. BDG type I exhibited a higher disability in items loaded to orbitofrontal circuit. The DEX-R appears to be a useful measure to assess executive functions in bipolar patients.

Key words: executive functions, bipolar disorder, psychometric properties, DEX-R.

BACKGROUND

Bipolar disorder (BD) is characterized by oscilations in mood states (euthymic, depressed or manic/hypomanic). In the BD Type I periods of mania (euphoria) with elevated mood and exaggerated behavior serious enough to cause problems at work, social relationships are evident and also these periods alternate with periods of depressed mood and euthymic mood. BD Type II is featured by occurrence of one or more Major Depressive Episodes accompanied by at least one Hypomanic Episode (softer mood elevation causing a lower level of problems than the manic frames) (American Psychiatric Association (APA), 2004). In studies with bipolar disorder patients persistent cognitive deficits are often related, not only in the phases of mania and depression, but also during remission of symptoms (Martinez-Aran et al. 2004). In the meta-analysis conducted by Robinson et al. (2006) the presence of deficits in immediate and delayed episodic verbal memory recall, executive functions, attention and psychomotor skills were found in patients in the euthymic phase. In relation to the different cognitive subtypes in BD, Hsiao et al. (2009) showed that type I is characterized by deficits in episodic memory, working memory, psychomotor and executive functions, while in type II deficits were evident in working memory and psychomotor functions. In that way, since impairment is both cognitive and psychosocial functioning are present in asymptomatic patients, current theorizing emphasizes the important role cognitive dysfunction may play in exacerbating psychossocial and functional disability (Martinez-Aran et al 2004, 2007; Levy et al 2011). Based on the previous findings it is important to develop and validate an instrument to support investigation of cognitive impairments profile, in particular executive functions, for people with BD.

Executive functions refer to an "umbrella" term which encompasses cognitive complex processes required to manage the human behavior (Hughes and Graham 2002). Fuster (1997) refers to executive functions as a set of processes responsible for starting and developing a task which has a determined final objective. Impaired executive functioning, in accordance with Anderson (2008), is not a unitary disorder. A variety of presentations can be described, as inability to focus or maintain attention, impulsivity, disinhibition, reduced working memory, difficulties monitoring or regulating performance, inability to plan actions in advance, disorganization, poor reasoning ability, difficulties generating and/or implementing strategies, as resistance to change activities, difficulties shifting between conflicting demands and a failure to learn from mistakes (Piek et al 2004, Arnsten and Bao-Ming 2005, Papazian Alfonso and Luzondo 2006, Malloy-Diniz et al. 2008). These processes support the ability to resolve new problems and influence planning and regulation of

adaptative behavior to achieve a specific goal (Cypel 2007). In reference to assessment of these functions, there are different neuropsychological tasks well established, however methods to evaluate functional impairment resulting from executive dysfunction remain as a gap in the clinic (Gilbert et al. 2010).

Given the above, the investment in developing instruments to assess executive functions must be considered both to determine the impairment level and also to evaluate the efficacy of rehabilitation programs. In this perspective, the DEX Questionnaire Revised (DEX-R) (Simblett and Bateman, 2011) is a scale developed to evaluate the everyday difficulties related to executive dysfunction. The items encompass specific problems related to difficulties with attention, memory, processing of information, behavioral and emotional regulation and self-monitoring (Simblett and Bateman, 2011), which are mediated by executive functions. This questionnaire is widely used in acquired brain injury clinics (Benett, et al. 2005). The DEX has been shown to be a sensitive measure of executive dysfunction after brain injury (Benett et al. 2005, Yamasato et al. 2007), in Parkinson's disease (Koerts et al. 2011), and also in a sample with neuropsychiatry disorders, more precisely addictive behaviour (Perez et al. 2009, Leon et al. 2010). In these studies, the authors suggested that the DEX was a useful measure for assessing general symptoms of dysexecutive syndrome, and a valid, reliable and adequate screening test for estimating cognitive impairment. Therefore, beyond its use in assessing brain injured people, the DEX has potential for use in neuropsychiatry. In reference to its dimensionality, in accordance with Simblett and Bateman (2011), the DEX measures multiple latent variables that represent different dimensions of executive dysfunction. As reported in the DEX manual (Burgess et al. 1996), its items evaluate three dimensions, consisting of emotion, behaviour and cognition. Since it was proposed, several factor analyses studies have been performed on different samples, using original DEX version with 20 items, both with self-reported (DEX-S) and independent-rater (DEX-I) (**Table 1**).

Table 1: A summary of findings reported on the dimensional structure of the DEX.

Study author(s)	Year published	Sample population	Sample size	Version	Type of analysis conducted	Optimal dimensional structure	
						Number of subscales	Subscale labels
Burgess, Alderman, Wilson, Evans & Emslie	1996	Adults diagnosed with a neurological condition (including TBI, encephalitis, dementia, stroke, hypoxia and Korsakoff's syndrome)	78	DEX-S	Exploratory factor analysis	3	i) Emotion ii) Behaviour iii) Cognition
Burgess, Alderman, Evans, Emslie & Wilson	1998	Caregivers of adults diagnosed with a neurological condition	92	DEX-I	Exploratory factor analysis	5	i) Inhibition ii) Intentionality iii) Executive memory iv) Positive affect v) Negative affect
Chan	2001	Non-clinical sample	93	DEX-S	Exploratory factor analysis	5	i) Inhibition ii) Intentionality iii) Knowing-doing dissociation iv) In-resistence v) Social regulation
Amieva, Phillips & Della Sala	2003	Non-clinical sample of normal elderly adults	20	DEX-S	Exploratory factor analysis	5	i) Intentionality ii) Interference management iii) Inhibition iv) Planning v) Social regulation
Ho, Robbins & Barker	2006	Adults diagnosed with Huntington's disease and their carers	75 and 67 carers	DEX-S and DEX-I	Exploratory factor analysis	3	i) Cognition ii) Self-regulation iii) Insight
Mooney, Walmsley & McFarland	2006	University students (first-year psychology course)	293	DEX-S	Exploratory factor analysis	4	i) Inhibition ii) Intention iii) Social regulation iv) Abstract problem solving
Chaytor,	2008	Adults	46	DEX-S	Exploratory	5	i) Behavioural

Schmitter-Edgecombe, and Burr		diagnosed with a neurological condition (including TBI, epilepsy, tumour, stroke and multiple sclerosis)			factor analysis		inhibition ii) Goal directed behaviour iii) Executive memory/cognition iv) Lack of awareness v) Agitation/ hyperactivity
Gerstorf, Siedlecki, Tucker-Drob & Salthouse	2008	Community dwelling adults	1137	DEX-S	Confirmatory factor analysis	1	i) Executive problems
Perez, Leon, Mota, Luque, Arroyo, saiz & Garcia	2009	Sample of 131 non-clinical and 127 clinical individuals meeting the DSM-IV-TR substance abuse or dependence	127	DEX-S	Exploratory and confirmatory factor analysis	5	i) Planning ii) Problems solution iii) Making Decision iv) Apathy v) Activation
Simblett & Bateman	2011	Adults with acquired brain injury	363	DEX-S	Exploratory Rasch factor analysis	3	i) Executive cognitive functions ii) Behavioural-emotional self-regulatory functions iii) Metacognitive functions
Simblett, Badham, Greening, Ring, Adlam & Bateman	2012	Carers of adults with acquired brain injury	271	DEX-I	Confirmatory Rasch analysis	3	i) Executive cognitive functions ii) Behavioural-emotional self-regulatory functions iii) Metacognitive functions

For this reason this paper aimed to evaluate dimensionality of DEX-R self scale in its 37 items, and also to investigate its applicability to a sample with neuropsychiatry diseases (BD), and control healthy. We hypothesized that performance from people with BD would be associated with higher scores in the DEX-R, which means higher level of impairment in executive functions.

METHODS

Participants and Procedures

People recruited to take part in this study were aged between 18 and 60 years old, had achieved at least eight years of formal education, reported no history of traumatic brain injury and stroke, and scored equal or less than 10, the cut-off points, in both Beck Depression and Young Manic scales (Beck Steer and Carbin 1988, Young et al. 2000). Controls were recruited by posters displayed in the university and other community settings (Control Group – CG n=300). The patients were recruited at the specific ambulatory at the university hospital, Hospital das Clinicas, for people with mood disorders, when they attended their outpatient appointment. People with both type I and II of BD were recruited until a balanced number of participants were achieved (BD Group n=120 – BDG type I and BDG Type II). It was done based on a prospectively scanning note. To determine the sample size, one pilot study was previously conducted to investigate the mean and standard deviation parameters to calculate the most appropriated sample size. Considering the BDG, inclusion criteria also included: diagnoses of BD confirmed by psychiatry team of Nucleo de Transtornos Afetivos – Universidade Federal de Minas Gerais (NTA – UFMG). It was done by using a semi structured interview, the Mini International Neuropsychiatric Interview (M.I.N.I.), that was a short structured diagnostic interview for DSM-IV an ICD-10 psychiatric disorders and it was designed to meet the need for a short but accurate structured psychiatric interview as a tool to facilitate accurate data collection and processing of symptoms elicited by trained personnel (Sheehan et al. 1998, Amorim 2000). Furthermore, the subjects must not have been submitted electroconvulsive therapy or have been hospitalized in the six months prior to evaluation. The CG was composed by subjects without any neurological or psychiatric condition. This group was matched with BDG, considering age, educational and social level, to control for other factors which might influence the DEX-R answers. The studies from these data have been drawn have all received ethical approval from the local research ethics committee, and all participants provided written informed consent before taking part.

Instrument

The DEX-R questionnaire consists of a checklist of symptoms on a 5-point Likert scale, ranging from (0) "never" to (4) "very often". This questionnaire is available in two different versions, being self reported, used in this study, and an independent-rating one. Initially, this questionnaire was proposed as a supplement for the primary tests of Behavioural Assessment of the Dysexecutive Syndrome – BADS, which are rule shift cards, key search, temporal judgement, zoo map, adapted modified six elements (Wilson et al. 1996, Canali et al. 2011). In that context, the DEX was designed to screen for changes in observable everyday manifestations of executive dysfunction following acquired brain injury. The DEX encompassed 20 items that aimed to evaluate abstraction, impulsivity, confabulation, planning skills, mood regulation, decision making, and it covers a wide range of specific problems such as difficulties with attention, memory, information processing, behavioural control, emotion regulation and awareness (Simblett and Bateman, 2011). As pointed by Simblett and Bateman (2011), even though the DEX was originally designed for use as qualitative assessment for focusing rehabilitation on an individual`s personal difficulties, this tool is currently used as a quantitative test instrument for diagnoses purposes (Benett et al. 2005, Magar et al. 2008, Perez et al. 2009).

Based on the Rasch analyses reported by Simbett and Bateman (2011), a revised version of the questionnaire (DEX-R) has been proposed, to address some specific wording problems within existing questions and to strengthen the dimensions represented within the tool, in line with current thinking about the proposed domains of executive functioning as described by Stuss (2007). For the revised DEX, 14 new items were added which were theorised to contribute to the four psychological constructs included in Stuss' (2007, 2011) model of pre-frontal function (see **Table 2** for a list of all items and the theoretical domains that each was predicted to belong to) (Simblett, unpublished PhD Thesis in preparation).

Table 2: Items included in the DEX-R (Simblett, unpublished PhD Thesis in preparation)

Item No. in DEX-R	Item No. in DEX	Item name in DEX-R	Item name in DEX	Predicted theoretical domain
1	2	Impulsivity	Impulsivity	Metacognitive/social cognitive
2	-	Prospective memory problems	-	Executive cognitive[†]
3	8	Apathy	Apathy	Behavioural-emotional self regulatory or Activation[†]
4	-	Initiation problems	-	Activation[†]
5	4b	Planning problems	Planning problems (part b)	Executive cognitive
6	9	Social disinhibition	Disinhibition	Metacognitive/social cognitive
7	19b	Goal-neglect	Poor decision-making ability (part b)	Behavioural-emotional self regulatory
8	-	Verbal aggression	-	Activation[†]
9	-	Poor verbal fluency	-	Executive cognitive[†]
10	12*	Anger	Aggression	Metacognitive/social cognitive
11	14	Perseveration	Perseveration	Behavioural-emotional self regulatory
12	-	Poor performance monitoring	-	Activation[†]
13	4a	Abstract thinking problems	Planning problems (part a)	Executive cognitive
14	-	Meta-worry	-	Metacognitive/social cognitive[†]
15	13	Lack of concern	Lack of concern	Behavioural-emotional self regulatory or Activation[†]
16	11	Blunted affect	Shallowing of affective responses	Activation[†]
17	-	Working memory problems	-	Executive cognitive[†]
18	5*	Over-exaggeration	Euphoria	Metacognitive/social cognitive
19	7	Lack of insight and social awareness	Lack of insight and social awareness	Behavioural-emotional self regulatory
20	15	Restlessness-hyperkinesis	Restlessness-hyperkinesis	Behavioural-emotional self regulatory
21	6	Temporal sequencing problems	Temporal sequencing deficits	Executive cognitive
22	-	Cognitive control	-	Metacognitive/social cognitive[†]
23	10	Variable motivation	Variable motivation	Behavioural-emotional self regulatory or Activation[†]

24	-	Physical aggression	-	Activation[†]
25	-	Poor organisational ability	-	Executive cognitive[†]
26	16	Inability to inhibit responses	Inability to inhibit responses	Metacognitive/social cognitive
27	3*	Confabulation	Confabulation	Behavioural-emotional self regulatory
28	-	Emotional lability	-	Activation[†]
29	18	Distractibility	Distractibility	Executive cognitive
30	-	Inertia	-	Activation[†]
31	-	Poor cognitive confidence	-	Metacognitive/social cognitive[†]
32	17	Knowing-doing dissociation	Knowing-doing dissociation	Behavioural-emotional self regulatory
33	11*	Blunted affect (alternative)	Shallowing of affective response (alternative)	Activation[†]
34	1	Information processing problems	Abstract thinking problems	Executive cognitive
35	20	No concern for social rules	No concern for social rules	Metacognitive/social cognitive
36	-	Complex attention problems	-	Executive cognitive[†]
37	19a	Poor decision-making ability	Poor decision-making ability (part a)	Behavioural-emotional self regulatory

*This Table displays the names and numbers of items included in the DEX-R and their corresponding names and numbers in the original DEX (from Burgess, Alderman, Evans, Emslie & Wilson, 1998), as well as the predicted theoretical domain that each items measures, according to Stuss' (2007, 2011) model of pre-frontal function. Items from the DEX that contained double-barrelled statements were split in half and are labelled 'part a' and 'part b', accordingly; * denotes items that required other types of modification (replacement or removal of a single word to improve clarity of meaning); [†] denotes items where the predicted theoretical domain was guided by evidence-based theory rather than the prior statistical analysis reported in Simblett and Bateman (2011); and – denotes the new items that were not present in the DEX.*

The DEX-R was translated into Portuguese including cultural adaptation to current Brazilian Portuguese language specificities. Authorization from the publishers of the original was granted for the translation and adaptation of the DEX-R. The scale was independently translated from English into Brazilian Portuguese by two professional teachers proficient in English. A third teacher compared the two translations and a preliminary version was obtained. Then the scale was independently back-translated by another English teacher. This last version was evaluated and approved by some of the authors of the original instrument.

Data Analyses

The analysis followed three steps. First of all the normality assumption was checked by Kolmogorov-Smirnov test. Secondly, an exploratory factor analysis was performed with Varimax factor rotation and Kaiser Normalization (procedures as per Suhr, 2006). This analysis explored the possible underlying factor structure of a set of observed variables without imposing a preconceived structure on the outcome (Child 1990). The decision about the number of factors to retain was indicated by Eigenvalues upper than 1. Moreover, f**actorial load** equal or higher **than 0.30 was used to indicate what factor** the item belong. Further comparisons between CG and BDG were made using Student t-test. The standardized mean-difference effect size (*d*) was designed for contrasting two groups performance (Cohen 1977). Finally, comparisons using Anova one way were used to explore differences among two bipolar subgroups and CG (CG X BDG Type I X BDG Type II). For all analyses the significance level was set at $p < .05$. Analyses on data were performed using SPSS 17.

Results

The sample characteristics are presented in the **Table 3.** As the assumptions of normality were reached ($p > .05$) for all the variables it was performed parametric tests.

Table 3: Sample characteristics

Groups (n)	Mean Age (SD) years	Gender (%)		Level of Education (X/SD) years
		Male	Female	
CG (n= 300)	29.8 (11.40)	37	63	12.7 / 3.4
BDG Type I (n=63)	40.41 (12.49)	33.3	66.6	9.0 / 1.8
BDG Type II (n=57)	39.74 (11.63)	21.1	78.9	9.1/ 2.2

There was no correlation between the age and DEX-R scores. Coefficients ranged from (-0.07) to (0.08), $p > 0.01$ The Kaiser-Meyer-Olkin Measure of Sampling Adequacy and Bartlet'ts test of sphericity indicated sampling adequacy to exploratory factor analysis (KMO=0.95, statistic Bartletts test of sphericity=8212.08; df=666; p<0.001). It was found 6 factors different from the predicted theoretical domain. Total variance explained was 58.10%. Some items loaded similarly on multiple components and none of them loaded exclusively on

one factor. The authors used content analysis and criterion factorial load equal or higher than 0.30 to decide what factor the item belong to. The factors loadings are presented in Table 4.

Table 4: DEX-R items organization based on exploratory factor analysis

DEX-R	FACTORS						ITEMS DESCRIPTIONS	
	1	2	3	4	5	6		
Item 1*	**0.68**	0.23	0.12	0.01	0.16	0.10	*Impulsivity**	Social and Self-Regulation: functions related to Orbitofrontal Circuit
Item 6*	**0.48**	0.44	0.20	0.06	0.10	0.04	*Social disinhibition**	
Item 10*	**0.69**	0.09	0.24	0.010	0.09	0.31	*Anger**	
Item 12*	**0.51**	0.23	0.20	0.13	0.20	-0.11	*Poor performance monitoring**	
Item 14*	**0.46**	0.32	0.31	0.12	-0.12	0.32	Meta-worry	
Item 18*	**0.45**	0.19	0.35	-0.15	0.26	0.24	*Euphoria**	
Item 20*	**0.58**	0.17	0.26	-0.01	0.10	0.09	*Restlessness-hyperkinesis**	
Item 21*	**0.55**	0.27	0.28	0.02	0.16	-0.02	*Temporal sequencing problems**	
Item 22*	**0.51**	0.37	0.32	0.13	-0.08	0.19	Cognitive control	
Item 23*	**0.54**	0.49	0.27	0.03	0.00	-0.05	*Variable motivation**	
Item 24*	**0.58**	0.10	0.25	0.15	0.01	0.23	*Physical aggression**	
Item 26*	**0.61**	0.23	0.36	-0.02	-0.03	0.15	Inability to inhibit responses	
Item 27*	**0.70**	0.10	0.14	0.18	0.09	-0.10	*Confabulation**	
Item 28*	**0.71**	0.28	0.14	-0.05	0.07	0.08	*Emotional lability**	
Item 32*	**0.58**	0.44	0.14	0.14	0.07	-0.20	Knowing-doing dissociation	
Item 2*	0.34	**0.49**	0.32	-0.13	0.21	-0.07	Prospective memory problems	Motivation and Attention: functions related to Anterior Cingulate Circuit
Item 3*	0.22	**0.69**	0.29	0.11	-0.01	-0.04	Apathy	
Item 4*	0.19	**0.68**	0.30	0.15	0.04	0.15	Initiation problems	
Item 5*	0.16	**0.78**	0.13	0.13	0.24	0.15	Planning problems	
Item 7*	0.24	**0.71**	0.24	0.16	-0.06	0.14	Goal-neglect	
Item 13*	0.22	**0.65**	0.12	0.12	0.23	-0.04	Abstract thinking problems	
Item 19*	0.43	**0.39**	0.27	0.14	0.35	0.06	*Lack of insight* and social awareness*	
Item37*	0.27	**0.56**	0.43	0.17	0.02	0.05	*Poor decision-making ability**	
Item 9*	0.21	0.22	**0.52**	0.10	0.20	-0.02	Poor verbal fluency	Flexibility, Fluency, Working memory: functions related to Dorsolateral Circuit
Item 11*	0.27	0.06	**0.50**	0.17	0.20	0.35	*Perseveration**	
Item 17*	0.26	0.34	**0.62**	0.00	0.26	0.07	Working memory problems	
Item 25*	0.25	0.31	**0.66**	0.13	0.00	0.09	Poor organisational ability	
Item 29*	0.40	0.45	**0.49**	-0.10	-0.02	0.03	Distractibility	
Item 30*	0.31	0.42	**0.47**	0.12	-0.15	-0.24	Inertia	
Item 31*	0.41	0.42	**0.54**	-0.07	0.06	-0.16	Poor cognitive confidence	
Item 34*	0.40	0.16	**0.54**	0.23	0.06	-0.12	Information processing problems	
Item 36*	0.25	0.31	**0.69**	0.10	0.14	-0.02	Complex attention	

							problems	
Item 16*	0.02	0.13	0.09	**0.88**	0.05	-0.05	Blunted affect	
Item 33*	0.13	0.26	0.15	**0.83**	0.06	-0.04	Blunted affect (alternative)	
Item 15*	0.11	0.08	0.11	0.05	**0.80**	0.01	*Lack of concern**	
Item 35*	0.34	0.14	0.20	0.12	**0.36**	0.14	*No concern for social rules**	
Item 8	0.13	0.06	-0.06	-0.11	0.04	**0.75**	Verbal aggression	
Eignvalue	14.52	2.13	1.43	1.18	1.15	1.06		
% variance	39.25	5.76	3.87	3.16	3.11	2.85		

Note: The highest loading for each scale is in bold. Items with * denotes difference between BD Type I and BD Type II

The first factor was composed by items that respectively evaluate: impulsivity, social disinhibition, anger, poor performance monitoring, meta-worry, over-exaggeration/euphoria, restlessness / hyperkinesis, temporal sequencing problems, cognitive control, variable motivation, physical aggression, inability to inhibit responses, confabulation, emotional lability and knowing-doing dissociation. The second factor encompassed prospective memory problems, apathy, initiation and planning problems, goal-neglect, abstract thinking problems, lack of insight and social awareness and poor decision making ability. The items related to poor verbal fluency, perseveration, working memory problems, poor organizational ability, distractibility, inertia, poor cognitive confidence, information processing problems, and complex attention problems were loaded at the third factor. The fourth one was composed by blunted affect, the fifth by lack of concern and no concern for social rules, and in the last one, only one item was loaded, it was item 8, related to verbal aggression. These results analyzed conjoint with the results from Anova one-way means that it really represents a different construct in our sample.

A significant difference between groups on DEX-R score total (t=15.63; df=418; p<00.1) were found. The results from comparison between CG and BD are shown in Table 5.

Table 5: Comparisons between CG x BD

DEX-R Items	bipolar (n=120)		control (n=299)		t	d
	Mean	Std. Deviation	Mean	Std. Deviation		
Item 1	2.11	1.26	1.21	0.83	7.22**	0.86
Item 2	2.18	1.32	1.15	0.90	7.78***	0.92
Item 3	2.02	1.22	1.05	0.89	7.87***	0.92
Item 4	2.35	1.31	1.22	0.93	8.60***	1.01

Item 5	2.33	1.32	1.11	1.02	9.10***	1.05
Item 6	1.94	1.27	1.12	0.88	6.48***	0.76
Item 7	2.48	1.26	1.27	0.99	9.43***	1.08
Item 8	2.34	1.33	2.14	1.08	1.45	0.16
Item 9	1.95	1.30	1.24	0.85	5.56***	0.66
Item 10	2.07	1.33	0.91	0.87	8.79***	1.05
Item 11	2.19	1.25	1.27	0.94	7.25***	0.84
Item 12	1.73	1.04	0.94	0.76	7.51***	0.87
Item 13	1.95	1.22	0.94	0.97	8.09***	0.92
Item 14	3.32	1.00	1.71	1.15	14.19***	1.49
Item 15	1.61	1.40	1.18	1.01	3.01***	0.35
Item 16	1.57	1.25	1.27	1.01	2.28*	0.26
Item 17	2.83	1.19	1.31	1.03	12.29***	1.37
Item 18	2.38	1.33	1.26	0.91	8.45***	1.00
Item 19	1.96	1.25	0.69	0.85	10.16***	1.20
Item 20	2.15	1.29	0.96	0.98	9.10***	1.05
Item 21	2.04	1.50	0.78	0.97	8.54***	1.02
Item 22	2.55	1.33	0.94	0.96	12.07***	1.41
Item 23	2.22	1.35	0.72	0.88	11.21***	1.34
Item 24	1.34	1.35	0.41	0.78	7.11***	0.88
Item 25	2.65	1.16	1.38	1.06	10.36***	1.14
Item 26	2.18	1.35	0.87	0.87	9.79***	1.17
Item 27	1.29	1.36	0.39	0.77	6.82***	0.85
Item 28	1.90	1.43	0.60	0.87	9.28***	1.13
Item 29	2.52	1.22	1.19	1.01	10.54***	1.19
Item 30	1.62	1.29	0.65	0.84	7.56***	0.90
Item 31	2.53	1.28	1.02	0.97	11.68***	1.35
Item 32	1.73	1.22	0.86	0.83	7.17***	0.85
Item 33	1.64	1.27	1.19	1.03	3.46***	0.39
Item 34	2.05	1.34	0.93	0.89	8.44***	1.01
Item 35	1.82	1.39	1.05	0.96	5.56***	0.66
Item 36	2.67	1.18	1.26	1.00	11.56***	1.30
Item 37	2.67	1.17	1.22	0.96	12.02***	1.36
Total Score	78.84	25.66	39.29	16.56	15.63	1.87

All of the items' scores also differed between groups (t values ranged from 2.28 to 15.63; df=417; p<0.001), except for the item 8 (t=1.59; df=417; p=0.11). Effect sizes for groups comparisons were computed and the most values were upper than 0.80. These values could be interpreted as a large effect according to Cohen's effect size conventions (Cohen, 1977). The exceptions were items 8 (d=16, very small effect), 16 (d=0.26; medium effect) and 33 (d=0.33; medium effect). Results from comparisons among CG X BDI X BD2, are shown in **Table 6.**

Table 6: Comparisons among CG x BDI x BDII

Dex Items	F	Tukey post hoc tests	Dex Items	F	Tukey post hoc tests
Item 1	41.342**	**BDI>BD2>CG**	Item 19	85.715**	**BDI>BD2>CG**
Item 2	42.076**	BDI=BD2>CG	Item 20	58.782**	**BDI>BD2>CG**
Item 3	40.530**	BDI=BD2>CG	Item 21	58.742**	**BDI>BD2>CG**
Item 4	50.325**	BDI=BD2>CG	Item 22	98.061**	BDI=BD2>CG
Item 5	53.070**	BDI=BD2>CG	Item 23	93.515**	**BDI>BD2>CG**
Item 6	35.434**	**BDI>BD2>CG**	Item 24	55.815**	**BDI>BD2>CG**
Item 7	55.749**	BDI=BD2>CG	Item 25	60.514**	BDI=BD2>CG
Item 8	1.866	BDI=BD2=CG	Item 26	73.993**	**BDI>BD2>CG**
Item 9	23.225**	BDI=BD2>CG	Item 27	45.801**	**BDI>BD2>CG**
Item 10	63.563**	**BDI>BD2>CG**	Item 28	80.899**	**BDI>BD2>CG**
Item 11	43.401**	**BDI>BD2>CG**	Item 29	66.601**	BDI=BD2>CG
Item 12	42.709**	**BDI>BD2>CG**	Item 30	40.740**	BDI=BD2>CG
Item 13	39.938**	BDI=BD2>CG	Item 31	86.826**	BDI=BD2>CG
Item 14	92.126**	BDI=BD2>CG	Item 32	37.839**	BDI=BD2>CG
Item 15	9.813**	**BDI>BD2>CG**	Item 33	7.622**	BDI=BD2>CG
Item 16	3.230*	BDI=BD2=CG	Item 34	50.261**	BDI=BD2>CG
Item 17	86.465**	BDI=BD2>CG	Item 35	24.017**	**BDI>BD2>CG**
Item 18	58.743**	**BDI>BD2>CG**	Item 36	78.046**	BDI=BD2>CG
			Item 37	90.342**	**BDI>BD2>CG**

*Note: * p<0.05; **p<0.001*

In reference to results from comparisons among the two clinical and controls groups, the BD I exhibited higher impairments in general. Concerning the three main factors dimensions, BD Type I patients showed more impairment than BD Type II in the items that loaded on the first dimension (functions that have been hypothesised to be related to the Orbitofrontal Circuits), being Impulsivity, Social disinhibition, Anger, Poor performance monitoring, Euphoria, Restlessness-hyperkinesis, Temporal sequencing problems, Variable motivation, Physical aggression, Confabulation and Emotional lability. In reference to the second dimension, hypothetically linked with Anterior Cingulate functions, the differences

were founded in reported lack of insight, social awareness and poor decision-making ability. Finally for functions putatively related to dorsolateral area, located at the third dimension the difference was evident in an item relating to perseveration. Another differences were displayed in items 15 (lack of concern) and 35 (no concern for social rules), which were part of small factors.

Discussion

The current study aimed to compare the performance of people with both types of BD and a control population using the DEX-R questionnaire addressing executive functions related difficulties in everyday life (self-administered version), and also to propose a factor structure for this questionnaire. As expected, scores from BDG indicated greater frequency of symptoms than in the CG. This was observed for all comparisons except for items 8, 16 and 33. These were originally described by the English authors as "verbal aggression" and "shallowing of affective responses" respectively. However, we think that in our sample, these items may in fact be interpreted differently.

Considering the intergroup differences, our results were in line with previous research findings (Robinson et al. 2006, Green 2006, Torres et al. 2007, Deep et al 2012). These authors have suggested medium to large effect sizes for the neuropsychological differences between people with BD and healthy comparison subjects, particularly in the executive functions. Simonsen et al. (2008) also have shown that a more pronounced and severe impairment for type I patients is expected when compared to type II, as replicated in this study. It is important to highlight that several items there were more than one significant factor load (>0.30) on each components (Items 2, 6, 17, 19, 22, 23, 25, 26, 29, 30, 31, 32, 34, 35 and 36). In a recent investigation Schroeter et al. (2012) aimed to examine the neural correlates of executive functions by correlating respective test scores with reductions in glucose utilization in early dementia and its prodromal stages. In accordance with theirs results, although the analysis revealed task-specific frontoparietal networks, it consistently showed that hypometabolism in one region in the left lateral prefrontal cortex—the inferior frontal junction area—was related to performance in the various neuropsychological tests, suggesting in that an overlapping. This brain region has recently been related to the three component processes of cognitive control—working memory, task switching and inhibitory control. These results underpinning our findings considering the items pointed above. In accordance with the items description, they are related to these three components. Furthermore, considering executive functions as an "umbrella" concept it should be expected as well.

The association between mood and cognition, considering the neuroanatomical aspects, is not surprising, due to reciprocal connexions among cortical pathways which work in mood modulation and cognitive functions. Executive processes are associated with numerous, complex, and interrelated frontal neural systems, which is not surprising given that

the prefrontal cortex is dependent on efferent and afferent connections with virtually all other brain regions including the brain stem, occipital, temporal, and parietal lobes, as well as limbic and subcortical regions (Fuster 1993). Rather, while the prefrontal cortex clearly plays a critical role in executive function, it appears to be increasingly accepted that this region does not act in isolation, but is part of a broader functional system, which involves other brain regions (Anderson and Lambs 2008). Furthermore for Bradshaw (2001), the prefrontal cortex presents a level of functional organization, in which each neural system is related to specific aspects of cognition and behaviour, which are interconnected with others cortical and subcortical areas (Fuster 2000, 2002). Five frontal – subcorticals parallel circuits have been proposed that relate to different functions: motor, oculo-motor, dorsolateral, orbitofrontal and anterior cingulate. Three of these circuits (orbitofrontal, anterior cingulate and dorsolateral) are particularly engaged with cognition and mood, and tend to yield three different syndromes or clusters of symptoms, which were described as prefrontal functions by Fuster (2008), and for this reason this model was adopted as a reference to discuss our results, given the consistency with our observed performance in DEX-R.

According to Fuster (2008) in a substantial number of patients with lesions in the orbitofrontal circuits, the prevalent affect is euphoria, often accompanied by irritability, disinhibition and moral judgment may be impaired. The orbitofrontal syndrome is oftentimes undistinguishable from mania. Moreover, the orbitofrontal circuit has been associated with adaptative behaviour in the face of changing contingencies and unexpected outcomes, reward-guided behaviour and it has been implicated in a number of psychiatry disorders (Rudebeck Bannerman and Rushworth, 2008). The consequences of the impairment in this circuit are associated with risk behaviour (characterized by the reduction of sensitivity to social rules), dependence of reinforcement, low tolerance frustration, difficulties in making decision process due to non anticipation of future consequences, and impulsivity related to lack of planning (Bechara and Van Der Linden 2005). Several fMRI studies of bipolar subjects during the manic state, have demonstrated either attenuation of orbitofrontal cortex function and/or heightened amygdala activation compared to controls (Elliot et al. 2004, Altschuler et al. 2005). The presence of an attenuated orbitofrontal cortex response and a heightened amygdala response in mania suggests an alteration in a prefrontal-amygdala circuit. The orbitofrontal cortex has been purported to play a role in the integration of emotional information and the regulation of intensity of emotional response (Cabeza and Nyberg 2000, Fuster 2001). Of interest, dysfunction in this area could provide a mechanism for understanding a failure to appropriately modulate other brain regions and perhaps result in a

range of intensity of mood shifts in people with BD (Altschuler et al. 2008). Collectively these observations from the literature are consistent with the items described in our first factor. The results presented above were highly congruent with these assumptions and also with the psychiatric symptoms well described in patients with BD Type I, as manic episodes, for example. Then, more than differences between healthy subjects and BD, the differences between BD Type I and Type II were found mainly in this first factor.

The anterior cingulate circuit is fundamental for motivation, behaviour monitoring, executive control of attention, selection skills and responses control. Lesions of the anterior cingulate are also frequently accompanied by defective self-monitoring of behaviour and of the ability to correct errors. Apathy is the most prevalent disorder of affect from medial frontal damage, and people with a large medial lesion appear characteristically unaware of their own condition (Fuster 2008). The items that were grouped in our second factor seem to be associated with these functions while differences between BD Type I and Type II were also corroborated with the current literature, being well described impairments in decision making and insight abilities in BD Type I (Hsiao et al. 2009).

Finally, lesions in dorsolateral circuits cause disturbances in the capacity to suppress thoughts that can interfere with what is currently on focus, a possible explanation for observed increased distractibility. Patients with this syndrome are generally, disinterested in themselves and the world around them. The absence of a driving interest makes the patient vulnerable to interference, and this leads, among other things, to perseveration, which is another frequent lateral symptom (Fuster 2008). It is important to note that impairment in attention permeates all other frontal cognitive functions, especially those that support executive functioning. The classic dysexecutive syndrome, with attention, working-memory, flexibility, organization disorders at the core, is basically described in the dorsolateral syndrome. The items located in our third factor were compatible with the clusters of symptoms related to impairment in this area.

Several clinical implications arise from this study. In accordance with Balanzá-Martínez et al. (2010), the cognitive impairment is refractory to the standard interventions. In that perspective, these authors highlighted that the correct management of BD should target not only the remission of mood symptoms, but also, it has to include interventions focused on cognition, e.g. neuropsychological rehabilitation. This factor is based on to the assumption that these interventions encompass specific strategies which aims to decrease the impact of cognitive impairments in the subject's occupations, and so it might represents improvement in their quality of life Martínez-Aran et al. (2004). In that way, the clinical implications of this

study extend beyond of presentation of psychometric properties of DEX-R, but also aim to available an important tool to clinic of neuropsychiatry, which also can be used to evaluate the efficacy of cognitive interventions in this population. The most relevant task in any rehabilitation program is the correct identification of everyday problems (Loschiavo-Alvares et al. 2011). In this regard, our results of DEX-R showed it as a valuable instrument to perform this.

Finally, the limitations of this study must be acknowledged. Firstly the sample size of control and bipolar groups does not support the investigation of DEX-R internal structure organization from each one. Therefore we decided to conduct the exploratory factor analysis considering the whole sample. However it is important to highlight that further analysis will be conducted with a larger n in separated groups, both clinical and control sample. Another important limitation of this study is that the analyses presented are the first steps in a series of further planned tests of the properties of this measure. It is well established that factor analyses, due to their sample dependency and use of ordinal-level data, provide dimensionality information that is only partially replicable across other samples of interest. Exploratory factor analysis` widespread use in psychometrics has been subjected to relatively little critical appraisal in the neuropsychiatry literature. We are aware of modern psychometric approaches (e.g. Hobart and Cano 2009) that will form the basis of further papers about these data. The last issue refers to medication. We have been recorded these information since as well-know, some psychiatric drugs has important effects in cognition. However, Ancin et al. (2010) suggested that cognitive alterations in bipolar patients cannot be explained by medication because the alterations remained after controlling for medication variables in the statistical analyses of several studies (Fleck et al. 2001), as well as in drug-free euthymic bipolar patients (Goswami et al. 2009). Nonetheless the key message of this paper, namely that EF is impaired in BD, and can be detected using a simple questionnaire approach remains valid.

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ARTIGO 4

Psychometric Properties of Brazilian Portuguese Version of Dysexecutive Questionnaire

Revised (DEX-R) in Bipolar Disorder Patients using Rasch Analysis

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Psychometric Properties of Brazilian Portuguese Version of Dysexecutive Questionnaire Revised (DEX-R) in Bipolar Disorder Patients using Rasch Analysis

Short Title: Properties of DEX-R in Bipolar Patients

Abstract

Objective: To validate the Brazilian Portuguese version of Dysexecutive Questionnaire-Revised (DEX-R) using Rasch Analysis approach. **Methods:** 120 patients with bipolar disorder (63 Type I and 57 Type II) completed the DEX-R, an instrument to assess executive functions in an ecological context. The internal consistency reliability and construct validity, including the dimensional structure of the scale was examined.

Results: All proposed subscales were found to deviate significantly from the response pattern expected by the Rasch model, and therefore, did not display valid and reliable interval-level measurement. Others three subscales were proposed; (Subscale1-Social/Self-Regulation:X^2=36.3,Reliability=0.87; Subscale2-Motivation-Attention: X^2=26.5,Reliability=0.80; Subscale3-Flexibility-Fluency-Working Memory: X^2=29.4,Reliability= 0.79).

Conclusions: DEX-R should be interpreted in terms of subscales, and Rasch analysis conducted displayed that the items were well targeted to our sample. This corroborates that clinicians can be confident to use DEX-R, as a sensitive tool to measure executive dysfunction, among individuals with similar characteristics to those within our sample.

Key-words: Bipolar Disorder; Dysexecutive Questionnaire; DEX; Psychometric Properties; Rasch Analysis.

Introduction

Bipolar disorder is well-recognized as a chronic illness with substantial psychosocial and occupational morbidity (Bearden et al., 2001). Over the past decade, a number of studies have identified neurocognitive deficits in bipolar disorder as an important determinant of this disability (Bowie et al., 2010). Recent studies have suggested medium to large effect sizes for the neuropsychological differences between people with bipolar disorder and healthy comparison subjects, especially in the domains of episodic memory, attention ⁄ concentration, and executive functioning (Torres et al., 2007; Arts et al., 2008). Notably, these deficits persist in the absence of acute symptoms, and thus cognitive deficits are not solely a result of mood symptoms in bipolar disorder (Bearden et al., 2001). Instead of being considered as a state, the cognitive impairment has been considered as trait (Chowdhury et al., 2003). This fact can be corroborated by the persistence of cognitive impairment in the absence of mood symptoms (euthymic phase), which suggests that this impairment is due to a dysfunctional neurophysiology of this disease, and furthermore appears to be independent of mood symptoms (Strakowski et al., 2005).

Several studies have shown that, after a manic episode, the majority of patients with bipolar disorder continue to exhibit significant impairment in role functioning, despite symptomatic recovery (Tohen et al., 2000a; Tohen et al., 2000b; Altshuler et al., 2007). Syndromal recovery from acute episodes of mania or bipolar major depression is achieved in as many as 90% of patients given modern treatments, however, full symptomatic and functional recovery is achieved slowly, and residual symptoms of fluctuating severity and functional impact are the main rule (Huxley and Baldessarini et al., 2007). In accordance with their results, 57–65% of patients with bipolar disorder were unemployed (as compared to 6% of the general

population), and up to 80% were considered to have at least partial vocational disability following syndromal recovery from a first-lifetime manic or mixed episode. Even in euthymic patients poorer cognitive function was associated with worse functional outcome, even after controlling for residual mood symptoms, age, and other clinical variables (Wingo et al., 2009).

Considering the information above, it makes sense that factors other than mood symptoms may contribute to poor occupational and functional performance (Wingo et al., 2010). One such factor appears to be impairment in specific cognitive domains, i.e., executive function, verbal memory, attention, and processing speed (Martinez-Aran et al., 2004; Hsiao et al., 2009; Levy et al., 2011), which are also consistently associated with poorer functional outcome in schizophrenia (Green et al., 2000) and in bipolar disorder patients (Altshuler et al., 2008).

Regarding to suicidal behaviour, Jollant et al. (2011) proposed a revision about neurocognitive model, and showed the involvement of ventrolateral orbital, dorsomedial and dorsolateral prefrontal cortices as well as the anterior cingulate gyrus in this behavior. These authors proposed some trait-like characteristics, which may stimulate the development of a suicidal crisis during stressful circumstances, e.g., an altered modulation of value attribution, an inadequate regulation of emotional and cognitive responses, and a facilitation of acts in an emotional context. In this way, Malloy-Diniz et al. (2009) showed the presence of neuropsychological deficits in memory, executive functions, attention and decision-making in bipolar disorder patients, and they report that patients that have had suicide attempts scored worse than patients without suicidal attempt on measures of decision-making. These results illustrate the relevance to study executive functions in BD.

Executive functions refer to an "umbrella" term which encompasses all the cognitive complex processes required to manage the human behavior (Hughes and Graham, 2002), which incorporate a wide range of skills and functions that are important to enable a person to engage successfully in purposeful, self-serving behaviours (Lezak, 1995; Renison et al., 2012). It is also related to the e ability to sustain an appropriate problem-solving set for attainment of a future goal, comprising the capacity to inhibit or postponing a response, to strategically plan future actions, and to maintain a mental representation of the desired goal stated and the information presented (Welsh and Pennington, 1988). Executive functions have been described as the "conductor" which controls, organizes, and directs cognitive activity, emotional responses and behaviour (Gioia et al., 2000). Given the important role of executive functions and also its relationship with functional and occupational skills, it is important, considering the clinical and research contexts, the investment in developing instruments to assess to executive functions.

Considering executive functions assessment measures, the Dysexecutive Questionnaire Revised (DEX-R) (Simblett and Bateman, 2011) is a scale developed to evaluate the everyday difficulties related to executive dysfunction. The items encompass specific problems with attention, memory, processing of information, behavioral and emotional regulation and self-monitoring (Simblett and Bateman, 2011). The DEX has been shown to be a sensitive measure of executive dysfunction after brain injury (Bennett et al., 2005; Yamasato et al., 2007), in a sample with neuropsychiatry disorders, more precisely addictive behaviour (Perez et al., 2009; Leon et al., 2010), and in a sample of bipolar disorder patients (Loschiavo-Alvares et al., 2013). This last study after an exploratory factor analysis was found three main domains, being grouped as functions related to orbitofrontal cortex, anterior cingulated cortex

and dorsolateral cortex, based on assumptions from Fuster` Model of executive functions (Fuster, 2008).

However, traditional psychometric methods, based on classical test theory (CTT), such as factor analysis, have been criticized, as soon as, the major problem is that factor analysis does not require the construction of linear, interval-level measures or factor scores from the outset, and hence the factor sizes and factor loadings rarely are reproduced when new sets of relevant data are reanalyzed with the same procedure. Rather it identifies correlations with the underlying variable, but not locations on it, and also, it does not provide a defensible framework for understanding the magnitude of and relations among possible subscales (Edelen and Reeve, 2007).

In reference to CTT, the approach most frequently employed when seeking to shorten instruments seems to be statistical, and includes factor analysis, correlations between long and short-forms, correlations between item and composite scores, Cronbach's Alpha per scale, or stepwise regression (Prieto et al., 2003; DeVellis, 2006). These procedures all are based on the same underlying scaling model. The model, which could be called additive, assigns a measure, on a scale, as the sum of the responses to each item on the scale. The additive model does not consider item hierarchy, and the criteria for the final selection are supplied by internal consistency checks (Bond and Fox, 2007). By the contrast, Rasch analysis specifies that each item response is taken as an outcome of the linear probabilistic interation of a person's ability and a question's difficulty. The Rasch model constructs a line of measurement with the items place hierarquically and provides fit statistics to indicate just how well different items describe the group of subjects and how well individual subjects fit the group. Rasch analysis provides indicators of how well each item fits within the underlying construct. Fit is as a 'quality – control mecanism'. Fit statistics indicate whether the

researcher has completed a task of sufficient quality to allow that the output can be interpreted as interval level measures (Smith et al., 2008). Given the above, the purpose of this current investigation is to go beyond the results from factor analysis, and in that way, the objective is to realize the validation of Portuguese version of DEX-R using a Rasch Analysis approach.

Materials and Methods

Participants and Procedures

People recruited to take part in this study were aged between 18 and 60 years old, had achieved at least eight years of formal education, reported no history of traumatic brain injury and stroke, confirmed diagnoses of BD by psychiatry team of NTA – UFMG, in accordance with semi structured interview using the Mini International Neuropsychiatric Interview (M.I.N.I.), based on DSM-IV an ICD-10 (Amorim, 2000), not to be submitted electroconvulsive therapy or have been hospitalized in the six months prior to evaluation, and scored equal or less than 10 in both Beck Depression Inventory and Young Manic scales (Young et al., 1978; Beck et al., 1988). The patients were recruited at the specific ambulatory of Clinical Hospital for people with mood disorders, when they attended their outpatient appointment. The studies from these data have been drawn have all received ethical approval from the local research ethics committee, and all participants provided written informed consent before taking part. There were two groups of patients, being BD type I (n=63) and BD type II (n=57).

Instrument

The DEX-R questionnaire consists of a checklist of symptoms on a 5-point Likert scale, ranging from (0) never to (4) very often. This questionnaire is available in two different versions, being self reported, used in this study, and an independent-rating one. Initially, this questionnaire was proposed as a supplement for the primary tests of BADS (Wilson et al., 1996), and it was designed to screen for changes in observable everyday manifestations of executive dysfunction following acquired brain injury. The DEX encompassed 20 items that aimed to evaluate abstraction, impulsivity, confabulation, planning skills, mood regulation,

decision making, and it covers a wide range of specific problems such as difficulties with attention, memory, information processing, behavioural control, emotion regulation and awareness (Simblett and Bateman, 2011). Based on the Rasch analyses, a revised version of the questionnaire (DEX-R) has been proposed (Simblett and Bateman, 2011), to address some specific wording problems within existing questions and to strengthen the dimensions represented within the tool, in line with current thinking about the proposed domains of executive functioning as described by Stuss's model (2011). At the DEX-R, 14 new items were added which were theorised to contribute to the four psychological constructs included in Stuss' (2007; 2011) model of pre-frontal function. A previous study investigated dimensionality of DEX-R self scale in its 37 items, and also to investigate its applicability to a sample with neuropsychiatry diseases (BD), and control healthy (Loschiavo-Alvares et al., 2013). In accordance with its results it was found three main factors, being the first one composed by items that respectively evaluate: impulsivity, social disinhibition, anger, poor performance monitoring, meta-worry, over-exaggeration/euphoria, restlessness / hyperkinesis, temporal sequencing problems, cognitive control, variable motivation, physical aggression, inability to inhibit responses, confabulation, emotional lability and knowing-doing dissociation. The second factor encompassed prospective memory problems, apathy, initiation and planning problems, goal-neglect, abstract thinking problems, lack of insight and social awareness and poor decision making ability. The items related to poor verbal fluency, perseveration, working memory problems, poor organizational ability, distractibility, inertia, poor cognitive confidence, information processing problems, and complex attention problems were loaded at the third factor. The fourth one was composed by blunted affect, the fifth by lack of concern and no concern for social rules, and in the last one, only one item was loaded, it was item 8, related to verbal aggression. These results were considered as a starting point to delineate the present investigation (Loschiavo-Alvares et al., 2013).

Data Analysis

Rasch analysis was conducted using the software package Rumm 2030, and following the guidelines for reporting Rasch analysis (Smith et al., 2003). A likelihhod ratio analysis was conducted to establish the type of Rasch measurement model would be chose to test the data. A significant Chi-square result indicates that the Masters partial credit model has to be used. This model incorporates the possibility of having differing numbers of responded opportunities for different items in the same test (Bond and Fox, 2007).

To evaluate the internal consistency reliability, it was used the Person Separation Index (PSI). The interpretation of results from PSI is similar that was used in Cronbach`s Alpha Statistic. A value higher than 0.7 indicating suitability for group-level use and a value greater than 0.85 indicating suitability for individual-level use (Simblett and Bateman, 2011). The first measure of fit, the difference between the observed and expected score, was made by an Item-Trait Interaction Chi-Square statistic. A significant result indicates a hierarquical ordering across the trait, which means that the items do not pertain to the same psychological construct. This statistic aims to investigate whether or not there is more than one variance component explaining the structure of the respondent data (Wright, 1996), and if the data are unidimensional, then components in the residuals will be at the noise level, and there will not be a significant result. The purpose of the fit statistics is to aid in measurement quality control, to identify those parts of the data which meet Rasch model specifications and those parts which do not these one do not are automatically rejected, but they are examined to identify in what way, and why they fall short, and whether, on balance they contribute to or corrupt the measurement. Fit statistics are reports in standardized form (e.g. t) in which their expected value is 0 (Bond and Fox, 2007). Using the commonly accepted interpretation of t values, fit residuals values greater than +2.5 or less than -2.5 (Pallant and Tennant, 2007)

generally are interpreted as having less compatibility with the model than expected (p<.05). Specifically about the interpretation, negative values means less variation than modelled, so the response string is closer to the Guttman-style response, which means that all easy items are endorsed then all difficult items are not endorsed (Bond and Fox, 2007). The positive values indicate more variation than model's expectation, and then the response string shows a haphazard pattern.

After these process described above, it was examined to verify whether responses to the items are consistent with the metric estimate of the underlying construct is indicated by an ordered set of response thresholds for each of the items (Smith, 2002). Where disordered thresholds were detected, the items were rescored by collapsing adjacent categories. The next step was exploring local dependency between items. It was analysed by observing the correlations between the residuals for pairs of items. It was considered the range of +/- 0.3 as low correlations, being these necessary for each of the items to be considered to measure independent aspects of the latent variable, and then to fit the model expectations (Simblett and Bateman, 2011).

After these analyses, the next step was assessing local independence; it was made using a principal component analysis of the persons residuals summed across each item (Wilson, 2004). In this analysis any subset of the items in the scale would measure the same thing as any other subset of the items from the scale, meaning that any patterns of items identified in the residuals would have no effect upon person estimates. This is made via a paired *t-test* comparison of person locations that have been estimated using two subsets of items taken from the top and another from the bottom of the first residual factor. Unidimensionality was assumed if less than 5% of the sample displayed a significant difference (p<.05), and this assumption was supported if the lower confidence interval for a binomial test on the proportion of tests that failed to meet the previous criteria was below 5%.

The differential item functioning using a two way analysis of variance (ANOVA), with a Bonferroni adjustment for multiple comparisons, on the person-response residuals for each item, by gender was conducted. The presence of DIF implies that a scale is not measuring the same thing for all respondents. It is important to note that if groups of examinees do not differ in their underlying ability distributions on the additional trait measured by the items, then DIF will not occur (Wilson, 2004; Brodersen et al., 2007).

During the data analyses an iterative process was undertaken. With this, it was tested if rescoring, removal of both items and persons, based on fit statistics, influenced the overall fit to the Rasch Model.

Results

The demographic characteristics of the sample are displayed in Table 1. All the 120 respondents completed all DEX-R questionnaire, so there were not any missing data. Initially, the likelihood ratio test (LHT) was undertaken to help establish which type of Rasch Model to test the data against. As the chi square was significant (X^2= 234, 24, p<.001) a Masters partial credits model was adopted. Then, the following results reported are based on this assumption.

Table 1: Demographic characteristics

Group (n)	Mean Age (SD) years	Gender (%)		Level of Education (X/SD) years
		Male	Female	
BDG (n= 120)	40.1 (12.04)	33	87	9.3 / 2.9
Type I (n=63)	40.41 (12.49)	33.3	66.6	9.0 / 1.8
Type II (n=57)	39.74 (11.63)	21.1	78.9	9.1/ 2.2

DEX-R displayed a person separation index of 0.93, a value greater than 0.7 indicates suitability for group-level use while a value greater then 0.85 indicated suitability for individual level use (Simblett and Bateman, 2011). However, the Item-Trait Interaction was significant (X^2= 155.01, p<.001), which means that people were not responding to all items of the questionnaire as expected by the Rasch Model. The analysis of the Item-Person Interactions statistics showed a degree of misfit within some of the items on the DEX-R (fit residual mean = 0.51, SD= 1.73), as well as amongst of the respondents (fit residual mean = - 0.14, SD= 2.11). These results suggest that not all questions on the DEX-R measure the same underlying construct, i.e., executive functions, and the existence of misfiting persons in the sample indicates that not all members understood the same meaning from the questions they were being asked.

The location of each item, in order of their difficulty is displayed in Table 2. The negative

values show the items ease to endorse, while the positive values represent the difficult items

to endorse. Both items 8 and 15, verbal aggression and lack of concern respectively, showed a

fit residual > 2.5 and a significant item-trait fit statistic after a Bonferroni adjustment for

multiple comparisons (p<0.001). While items 16 (blunted affect), 18 (euphoria) and 35 (no

concern for social rules) displayed fit residuals outside of limits. In accordance with (Bond

and Fox, 2001) much larger residual indicates that an actual performance would be quite

different from the Rasch model expectation.

Table 2: Initial fit of items on the DEX-R to the Rasch Model

Item No	Item Name	Location	SE	Fit Residual	DF	ChiSq	df	p value
14	Meta-worry	-0.927	0.103	1.587	112.78	0.957	2	0.62
17	Working Memory	-0.779	0.093	-0.292	112.78	3.015	2	0.22
36	Complex Attention problems	-0.618	0.092	-0.643	112.78	2.213	2	0.33
25	Poor organizational ability	-0.553	0.093	-0.024	112.78	0.611	2	0.74
37	poor decision making ability	-0.542	0.093	0.352	112.78	0.644	2	0.72
31	poor cognitive confidence	-0.389	0.087	-0.998	112.78	2.016	2	0.36
7	Goal-neglect	-0.357	0.087	-0.276	112.78	3.414	2	0.18
29	distractibility	-0.334	0.09	0.319	112.78	4.272	2	0.12
4	initiation problems	-0.23	0.084	0.113	112.78	0.941	2	0.62
22	cognitive control	-0.225	0.083	-0.626	112.78	2.807	2	0.25
18	euphoria	-0.135	0.081	**2.777**	112.78	1.979	2	0.37
8	verbal agression	0.087	0.079	**6.754**	112.78	22.709	2	**0.00**
5	planning problems	-0.08	0.083	-0.272	112.78	0.859	2	0.65
2	prospective memory problems	-0.066	0.084	-0.681	112.78	0.785	2	0.68

23	variable motivation	-0.047	0.083	-1.583	112.78	3.039	2	0.22
26	inability to inhibit responses	-0.023	0.082	0.041	112.78	2.828	2	0.24
20	restlessness hyperkinesis	-0.022	0.084	0.903	112.78	0.265	2	0.88
1	impulsivity	-0.016	0.089	-1.804	112.78	9.719	2	0.01
10	anger	-0.003	0.083	0.532	112.78	7.807	2	0.02
11	perseveration	0.038	0.085	2.137	112.78	5.284	2	0.07
34	information process problems	0.076	0.081	1.302	112.78	3.059	2	0.22
13	abstract thinking problems	0.106	0.089	0.711	112.78	1.271	2	0.53
3	apathy	0.137	0.09	0.024	112.78	6.926	2	0.03
21	temporal sequencing problems	0.157	0.082	-0.771	111.84	1.292	2	0.52
9	poor verbal fluency	0.184	0.084	0.926	112.78	1.6	2	0.45
19	lack of insight and social awareness	0.192	0.087	-0.239	112.78	3.326	2	0.19
6	social disinhibition	0.203	0.087	-0.589	112.78	2.029	2	0.36
28	emotional lability	0.243	0.078	-1.015	112.78	3.084	2	0.21
35	no concern for social rules	0.316	0.078	**2.918**	112.78	4.839	2	0.09
15	lack of concern	0.347	0.076	**4.832**	112.78	18.929	2	**0.00**
12	poor performance monitoring	0.391	0.104	-0.146	112.78	4.056	2	0.13
32	Knowing-doing dissociation	0.396	0.091	-1.341	112.78	7.257	2	0.03
30	inertia	0.406	0.085	0.123	112.78	3.954	2	0.14
33	blunted affect (alternative)	0.441	0.085	0.769	112.78	1.209	2	0.55
16	blunted affect	0.512	0.085	**2.843**	112.78	15.317	2	0.00
24	physical agression	0.621	0.082	0.277	112.78	0.518	2	0.77
27	confabulation	0.664	0.081	-0.104	112.78	0.187	2	0.91

The misfiting items are displayed in bold . Legend: SE = standard error; df=degrees of freedom.

Only items 3 (apathy), 11 (perseveration), 13 (abstract thinking problems), 19 (lack of insight and social awareness), 21 (temporal sequencing problems), 25 (poor organizational ability), 29 (distractibility) and 32 (knowing-doing dissociation) did not show disordered thresholds, suggesting that the sample responded to the five categories in a way expected by the Rasch model in these items. Items 1 (impulsivity); 2 (prospective memory problems); 4 (initiation problems); 5 (planning problems); 6 (social disinhibition); 7 (goal-neglect); 8 (verbal aggression); 9 (poor verbal fluency); 10 (anger); 12 (poor performance monitoring); 14 (meta-worry); 15 (lack of concern); 16 (blunted affect); 17 (working memory problems); 18 (euphoria); 20 (restlessness-hyperkynesis); 22 (cognitive control); 23 (variable motivation); 24 (physical aggression); 26 (inability to inhibit responses); 27 (confabulation); 28 Category probability curves for items with disordered thresholds (emotional lability); 30 (inertia); 31 (poor cognitive confidence); 33 (blunted affect-alternative); 34 (information process problems); 35 (no concern for social rules); 36 (complex attention problems) and 37 (poor decision making ability) have shown disordered thresholds (Figure 1).

Figure 1: Item 4 (initiation problems) as an example of disordered thresholds.

Descriptor for Item 4   Locn = -0.230   Spread = 0.266   FitRes = 0.113   ChiSq[Pr] = 0.625   SampleN = 120
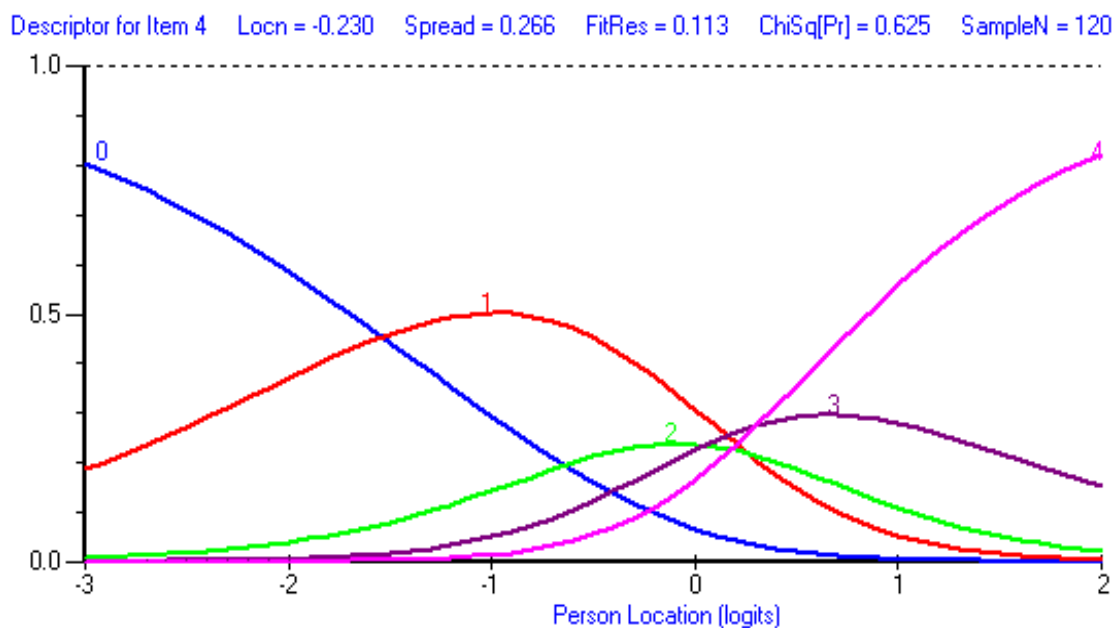
None of the items displayed significant DIF by gender or subtypes of BD with a Bonferroni adjustment for multiple comparisons. After conducting an iterative process of items (8,15,16,33 and 35) and subjects removal that misfited the Rasch model, and rescoring of items that displayed disordered thresholds, overall fit to the Rasch model improved (item fit residual mean= 0.32, SD= 1.17; X^2= 72.23, p>.05). As showed in Figure 2, the person-item distribution displayed a good match between item thresholds and ability of the sample. Concerning to local independence test, significant differences (p<.05) were found on 13.08% of the persons estimates when comparing two subtests of items. These were created by splitting items (in accordance with principal components loadings) into two equal sets, one which represented items showing the highest level of correlation with the first residual factor and another one composed by items displaying the lowest level of correlation with the factor cited above, using an independent t-test, which means that the DEX-R, as a whole, is not an interval-level measurement scale of executive functions. In other words, thus questionnaire might measure several psychological constructs as well, and then its scores may be better interpreted considering different subscales, which represent different dimensions of executive functions.

Figure 2: The person-item threshold distribution for the DEX-R.
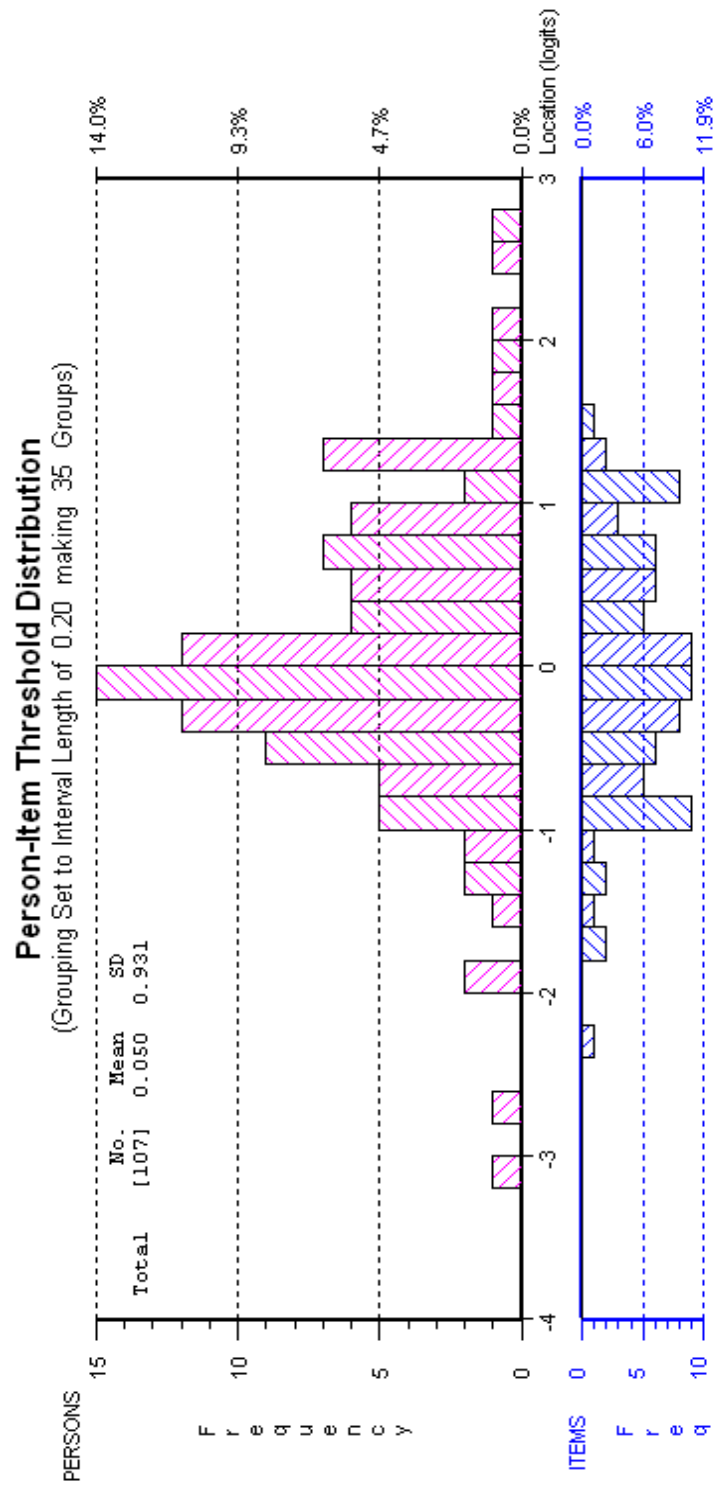
DEX Subscales

To analyse the subscales first was conducted an exploratory factorial analyses (Perez et al., 2009) which results were confirmed using Rasch Factor Analysis), see table 2. The new subscales were labelled, using as background Fuster`s model (Leon et al., 2010), as Social Self-Regulation which encompasses functions related to orbitofrontal circuit (OFC), Motivation-Attention, related to functions related to anterior cingulated circuit (AC) and the last one, Flexibility, Fluency and Working Memory which are related to dorsolateral circuit (DL). The resulting subscales were all analysed to see how well they fitted to the Rasch Measurement Model. Table 3 displays a summary of the proposed subscales and their corresponding fit criteria.

Table 3: First components loadings followed a principal component analysis of the residuals for each item on the DEX-R, and subscale groupings.

Item No.	Item Name	Loading	Subscale
10	Anger	0.63	Social Auto-Regulation – OFC Functions
27	Confabulation	0.56	Social Self-Regulation – OFC Functions
28	Emotional lability	0.42	Social Self-Regulation – OFC Functions
1	Impulsivity	0.40	Social Self-Regulation – OFC Functions
24	Physical agression	0.34	Social Self-Regulation – OFC Functions
21	Temporal sequencing problems	0.31	Social Self-Regulation – OFC Functions
26	Inability to inhibit responses	0.27	Social Self-Regulation – OFC Functions
14	Meta-worry	0.23	Social Self-Regulation – OFC Functions
20	Restlessness-hyperkinesis	0.20	Social Self-Regulation – OFC Functions
6	Social disinhibition	0.19	Social Self-Regulation – OFC Functions
18	Euphoria	0.16	Social Self-Regulation – OFC Functions
12	Poor performance monitoring	0.09	Social Self-Regulation – OFC Functions
22	cognitive control	0.01	Social Self-Regulation – OFC Functions
32	Knowing-doing dissociation	-0.04	Social Self-Regulation – OFC Functions
23	Variable motivation	-0.35	Social Self-Regulation – OFC Functions
2	Prospective memory problems	0.09	Motivation-Attention – ACC Functions
4	Initiation problems	-0.53	Motivation-Attention – ACC Functions
3	Apathy	-0.50	Motivation-Attention – ACC Functions
7	Goal-neglect	-0.49	Motivation-Attention – ACC Functions
5	Planning problems	-0.48	Motivation-Attention – ACC Functions
13	Abstract thinking problems	-0.39	Motivation-Attention – ACC Functions
37	Poor decision making ability	-0.32	Motivation-Attention – ACC Functions
19	Lack of insight and social awareness	-0.09	Motivation-Attention – ACC Functions
11	Perseveration	0.19	Flexibility, Fluency and Working Memory – DLC Functions
9	Poor verbal fluency	0.03	Flexibility, Fluency and Working Memory – DLC Functions
34	Information processes problems	-0.02	Flexibility, Fluency and Working Memory – DLC Functions
29	Distractibility	-0.03	Flexibility, Fluency and Working Memory – DLC Functions
25	Poor organisational ability	-0.14	Flexibility, Fluency and Working Memory – DLC Functions
31	Poor cognitive confidence	-0.15	Flexibility, Fluency and Working Memory – DLC Functions
17	Working memory problems	-0.17	Flexibility, Fluency and Working Memory – DLC Functions
36	Complex attention problems	-0.18	Flexibility, Fluency and Working Memory – DLC Functions
30	Inertia	-0.36	Flexibility, Fluency and Working Memory – DLC Functions

Legend: OFC = orbitofrontal cortex, ACC=anterior cingulated cortex and DLC = dorsolateral cortex.

Table 4: Rasch principal component factor analysis after rescoring or removal misfiting items and persons (n=107).

Subscale	Items	Item-Trait Interaction X^2 -	Reliability (PSI)	Percentage of t-tests <.05
1 -Social skills and Self-Regulation – Orbitofrontal Circuit Functions	1, 6, 10, 12, 14, 18, 20, 21, 22, 23, 24, 26, 27, 28 and 32	36,3	0.87	6.54
2- Motivation and Attention – Anterior Cingulate Circuit Functions	2, 3, 4, 5, 7, 13, 19 and 37	26.5	0.80	2.8
3- Flexibility, Fluency and Working Memory – Dorsolateral Circuit Functions	9, 11, 17, 25, 29, 30, 31, 34 and 36	29.4	0.79	0.93

With the results presented above, for all three subscales, the data met the expectations, suggesting that the DEX-R is composed by three subscales, each one being different interval-level measurement for distinct subset of executive functions (Table 4).

In comparisons between BD Type I and Type II it was found differences in responding on questionnaire, although the factor structure remained the same (Figure 3). The positive items represent the most difficulty items to endorse, while the negative ones showed the easiest items to endorse. As could be evidenced in the graphic below, for BD Type I patients, the easiest items to endorse were abstract thinking problems, cognitive control, social disinhibition, poor verbal fluency, while the items hardiest to endorse were problems in information processing, in complex attention, prospective memory and variable motivation. In BD Type II, the easiest items to endorse were poor organizational ability, meta-worry, distractibility and inertia, and the hardiest items were impulsivity, restlessness / hyperkinesis, knowing-doing dissociation and emotional lability.

Figure 3: Difference between Logits BD Type I and Logits BD Type II.
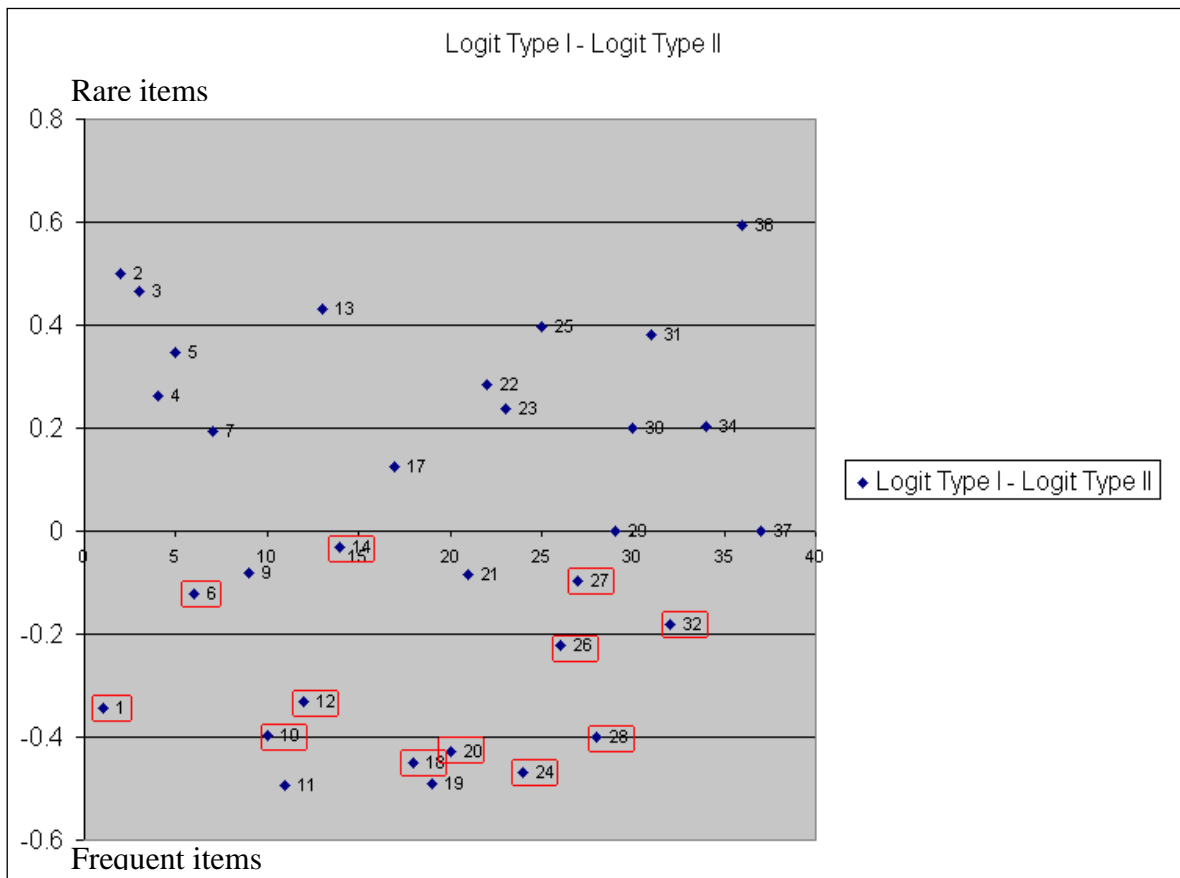
Legend: items inside the square are from Subscale 1 − Social skills and self-regulation.

Discussion

Executive function is not a unitary cognitive process, but instead is a psychological construct that is composed of multiple interrelated high-level cognitive skills, as an umbrella term that captures a collection of separable but related cognitive and behavioural functions (Wilson, 2004). As it was expected, the responses in DEX-R, analyzed using the Rasch measurement, did not work as a unidimensional and single scale of executive functions. In congruence with it was revealed in a sample with acquired brain injury (Welsh and Pennington, 1988), the DEX-R in our sample, bipolar disorder patients, it was better represented considering the subscales which measured in a separated way the several latent traits which together form the executive functions.

The problematic items (8, 15, 16, and 35) which did not fit to the model, were the same that did not load in one of the main three factors in the exploratory factor analysis (Perez et al., 2009), and joint to item 33 were excluded from the Brazilian Portuguese version of DEX-R

Concerning to the differences found between in responding on the questionnaire between two clinical groups (BD Type I and Type II), it was congruent with the distinct neuropsychological profiles expected considering the types of BD. for type I is expected a more pronounced and severe impairment when compared to the type II (Anderson and Lambs, 2008). It is important to note that the major items from the first factor, related to OFC circuit were easiest endorse in BD Type I. Dysfunction in this area, could provide a mechanism for understanding a failure to appropriately modulate other brain regions and perhaps result in a range of intensity of mood shifts in people with bipolar disorder (Altshuler et al., 2008). The results presented above were highly congruent with these assumptions and also with the

psychiatric symptoms well described in patients with BD Type II, in which were not expected hyperkinesis, impulsivity, and emotional lability for example, items related to first factor, which encompassed OFC expected functions.

The subscales previously proposed (Perez et al., 2009) met the assumption of unidimensionality, which suggest that all items were measuring the same construct. In line with previous results (Renison et al., 2012), executive function is not exclusive to cognitive processes, but is also characterized in emotional responses and behavioural actions, and in this perspective the DEX-R showed to be a good clinical tool to assess it. Different from the first assumption made by Simblett (unpublished), the newer subscales from the Brazilian version of DEX-R, did not match with the four psychological constructs included in Stuss' model of pre-frontal function (Stuss, 2007a; Stuss, 2007b). By the way, the three scales were consistent with the Fuster`s model of executive functions (Fuster, 2008), which consider the three pre frontal circuits (orbitofrontal, anterior cingulate and dorsolateral cortex) as particularly engaged with cognition and mood, being described syndromes or clusters of symptoms, related to them.

In a substantial number of patients with lesion in orbitofrontal area, the prevalent affect is euphoria, often accompanied by irritability, instincts are disinhibited and also moral judgment is impaired (Leon et al., 2010). The orbitofrontal syndrome is oftentimes undistinguishable from mania. More than this, the orbitofrontal circuit has been associated with adaptative behaviour in the face of changing contingencies and unexpected outcomes, reward-guided behaviour and it has been implicated in a number of psychiatry disorders (Bond and Fox, 2001). The consequences of the impairment is this circuit are associated with risk behaviour (characterized by the reduction of sensitivity to social rules), dependence of reinforcement,

low tolerance frustration, difficulties in making decision process due to non anticipation of future consequences, and impulsivity related to lack of planning (Simonsen et al., 2008), according items described in our first factor. Related to anterior cingulate circuit, it is fundamental for motivation, behaviour monitoring, executive control of attention, selection skills and responses control. Lesions of the anterior cingulate are also frequently accompanied by defective self-monitoring of behaviour and of the ability to correct errors. Apathy is the most prevalent disorder of affect from medial frontal damage, and subjects with a large medial lesion appear characteristically unaware of their own condition (Leon et al., 2010). The functions related to our second factor were strictly associated with these assumptions.

Lesions in dorsolateral circuit causes disturbs in the capacity to suppress from sensorium or inner experience items that can interfere with what is currently on focus, which will increase the distractibility. At its foundation seems to be a lack of drive and awareness. Patients with this syndrome are generally, disinterested in themselves and the world around them. The absence of a driving interest makes the patient vulnerable to interference, and this leads, among other things, to perseveration, which is another frequent lateral symptom (Leon et al., 2010). It is important to note that the impairment in attention permeates all other frontal cognitive functions, especially those that support executive functioning. The classic dysexecutive syndrome, with attention, working-memory, flexibility, organization disorders at the core, is basically described in the dorsolateral syndrome. As seen above, the items located in our third factor were compatible with the clusters of symptoms related to impairment in this area.

In summary, the results from the present study stated that the DEX-R should be interpreted in terms of subscales, and also, the Rasch analysis conducted displayed that the items were well targeted to our sample. It is a very important assumption, which corroborates that clinicians

can be confident to use DEX-R, as a sensitive tool to measure the level of executive dysfunction, among individuals with similar characteristics to those within our sample.

However, it is important to know that the original scoring methods (Burgess et al., 1996) did not function properly for the majority of items on the DEX-R only 8 from 37 initially proposed items did not displayed disordered thresholds.

Conclusions

This study showed that the DEX-R was an useful measure to assess executive functions in bipolar patients and also, the results from this research provide a platform for future evaluation of cognitive rehabilitation programmes, focused on executive functions, in bipolar disorder. Future studies, with large samples, considering BD Type I and Type II, must be conducted to investigate directly the relationship between patients' performance in DEX-R, and the different pre frontal circuits through fMRI measures.

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ARTIGO 5

EFFICACY OF NEUROPSYCHOLOGICAL REHABILIATION APPLIED FOR

PATIENTS WITH BIPOLAR DISORDER: A CONTROLLED STUDY.

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EFFICACY OF NEUROPSYCHOLOGICAL REHABILIATION APPLIED FOR
PATIENTS WITH BIPOLAR DISORDER: A CONTROLLED STUDY.

Abstract

Objective: to assess the efficacy of neuropsychological rehabilitation on executive functions, quality of life and coping strategies in a sample of euthymic patients with for bipolar disorder.

Method: It was a quasi experimental and longitudinal study which enrolled 50 outpatients with DSM-IV bipolar disorder. Neuropsychological rehabilitation (NR) plus Pharmacotherapy Group (NRG=20) was compared with Pharmacotherapy – Control Group (CG= 30) over 14 weeks. The NR protocol was divided into three modules. The first was directed toward mood monitoring, the following focused on executive functions, and the third addressed attention and memory rehabilitation. As outcome measures, it was used an ecological questionnaire of executive functions, DEX-R, quality of life indicators Whoqol-Bref and Ways of Coping Scale. It was also assessed clinical variables, such as frequence of manic, hypomanic and depression episodes.

Results: Mixed- design ANOVA demonstrated significant improvements in all measures applied from baseline to endpoint as well as after the conclusion of NR protocol (6 months), suggesting an interaction between treatment and time. Cohen's d for the differences between the mean scores of pre-and post-treatment for the two groups revealed very robust effect size for the NRG ($d > .80$)

Conclusions: The results show greater improvements for the NRG, highlighting the intervention's efficacy and its superiority as well, when it was compared with treatment as usual, pharmacotherapy only.

Key-words: Neuropsychological Rehabilitation, Cognition, Bipolar Disorder.

INTRODUCTION

Bipolar disorder is well-recognized as a chronic illness with substantial psychosocial and occupational morbidity [1]. Over the past decade, a number of studies have identified cognitive deficits in bipolar disorder as an important determinant of this disability [2], and these deficits persist in the absence of acute symptoms and seems to worsen with cumulative episodes [3,4]. Neuropsychological deficits have been recognised as one core feature of bipolar disorder due to their prominent nature and debilitating functional consequences [5]. Recent studies have suggested medium to large effect sizes for the neuropsychological differences between people with bipolar disorder and control subjects, especially in the domains of episodic memory, attention ∕ concentration, and executive functioning [3,4]. The main cognitive impairment has been demonstrated to affect executive functions, while moderate cognitive deficits was observed in other cognitive tests, such as verbal memory, response inhibition, sustained attention, psychomotor speed, abstraction and set-shifting [6]. Efforts to improve the prognosis and functional outcomes in bipolar disorder have prompted the interest and development of neuropsychological rehabilitation programmes, which comprises neurocognitive techniques, training psychoeducation on cognitive-related issues as well as problem-solving within an ecological framework, having as a ultimate goal the improvement of everyday functioning [7].

To the best of our knowledge, until recently, there were two studies which investigated the neuropsychological rehabilitation in bipolar disorder (BD). The former [8] explored whether a new cognitive remediation (CR) treatment designed to treat residual depressive symptoms as well as addressed to cognitive impairment would be associated with improvement in psychosocial functioning in individuals with bipolar disorder. It found that 18 individuals

with BD both at the end of treatment, as well as at the 3-months follow-up, showed lower residual depressive symptoms, and increased occupational, as well as overall psychosocial functioning. These findings have suggested that treating residual depressive symptoms and cognitive impairment may be an avenue to improving occupational and overall functioning in individuals with bipolar disorder. The second one [9] sought to assess the efficacy of functional remediation on functional improvement in a sample composed by euthymic patients with BD. This was a multicenter, randomized, rater-blind clinical trial involving 239 outpatients. The sample was divided by in three groups; functional remediation (n=77), psychoeducation (n=82) and usual treatment (n=80) over 21 weeks. The results have shown that functional remediation differed significantly from treatment as usual, but not from psychoeducation.

In the present study, we sought to assess specifically the efficacy of neuropsychological rehabilitation for bipolar patients, which comprised a set of neurocognitive techniques and strategies addressed to attention, memory and executive functions having as a final goal the optimisation of functional capacities. Based on the literature, it was hypothesised that the patients in the neuropsychological rehabilitation group would have greater improvement in the functional measures adopted when compared with the other group.

METHODS

Study Design and Sample

The research conducted was a quasi experimental and longitudinal study, which aimed to investigate the effect of a protocol of neuropsychological rehabilitation in bipolar disorder, and so it was used a pseudo random allocation between groups, which were control passive group - CG (pharmacotherapy only without any adjunctive psychosocial therapy) and intervention group - NRG (pharmacotherapy plus NR treatment). The pharmacological treatment was prescribed according to local guidelines for the best management of bipolar disorders, and this treatment was kept stable in two groups. The patients were assessed with the efficacy measures adopted at the beginning of the protocol, after its completion (14 week) and after 6 months of follow-up (withdrawn phase).

Participants

The current study included 50 patients with diagnoses of bipolar I or II disorder according to DSM-IV criteria (Figure 1), so it was used a semi structured interview - Mini International Neuropsychiatric Interview (M.I.N.I.) [10]. All of patients were tested with a comprehensive neuropsychological battery addressed to assess memory, attention and executive functions. Those patients with cognitive and functional impairments were referred to NR. The NR program was part of ongoing psychiatric outpatient treatment at Clinical Hospital, in Belo Horizonte, Brazil. It was required to be part of this study at least 3 months of clinical remission, be euthymic as well as taking the same medication for at least three months. To best define euthymia, it was used Young Mania Rating Scale score <10 [11] and Beck

Depression Inventory score < 10 [12]. Exclusion criteria adopted were any medical condition that could affect neuropsychological performance (such as neurological diseases), substance abuse or dependence, ECT, participating in any structured psychological intervention, such as psychotherapy or psychoeducation, and any co morbid psychiatric condition. This research was approved by an ethic committee and all patients provided written informed consent before take part of this study.
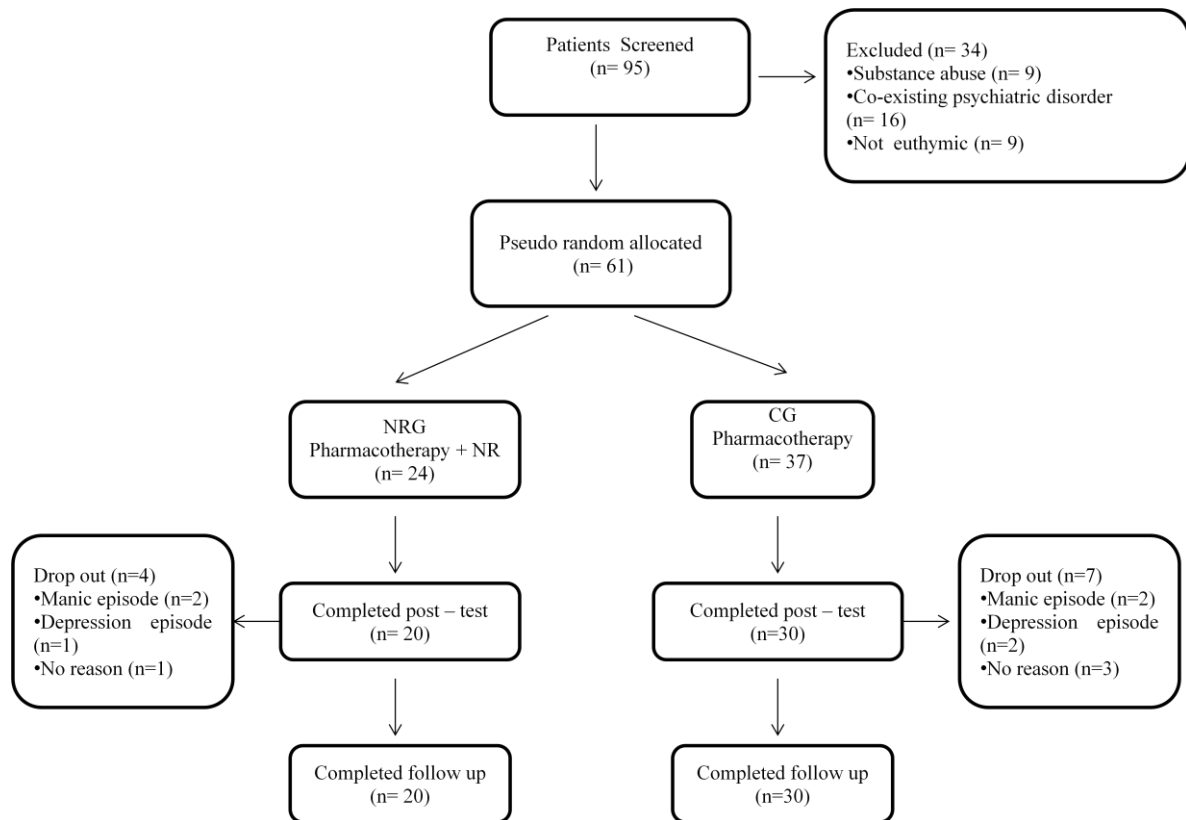

Figure 1: Flowchart of patient participation.

Neuropsychological Rehabilitation Intervention

Firstly it was developed a pilot study to best define the protocol of NR [13]. It was conducted an investigation using a single case design. The protocol proposed was based on previous research [8]. It was applied and it has shown to be successful in improving the patient' functional ability toward the level of performance shown by six matched controls. After this pilot, in whom the feasibility of the protocol was demonstrated, this was adopted in this current investigation. It is important to highlight that only one therapist worked with all patients.

The NR protocol comprises fourteen weekly individual sessions (fifty minutes each) divided into three modules each of them containing four sessions, so the role protocol lasted three and half months (Table 1). During all modules and respective sessions, all strategies were applied in a tailored way, focused on patients' functional needs considering their occupations. The content of this intervention was based on ecological tasks which were required to be performed in the clinical setting, as well as at home [9]. The techniques and strategies adopted were proposed in accordance with consolidated programs for neuropsychological rehabilitation [14, 15] and most of them were paper and pencil tasks.

Table 1: NR Protocol

Modules	Sessions	Sessions Content
-	1	Presentation of the protocol and establishment of functional measures
Module 1: Psychoeducation	2	What is bipolar disorder? Illness awareness and lifestyle regularity
	3	Pharmacotherapy and Bipolar Disorder
	4	Cognition and Bipolar Disorder
	5	My symptoms - Mood chart
Module 2: Rehabilitation of Attention and Memory	6	What is attention and strategies to improve it
	7	Daily life application of attention strategies
	8	What is memory and strategies to improve it; agenda and external devices
	9	Daily life application of memory strategies.
Module 3: Rehabilitation of Executive Functions	10	What is executive functions and strategies to improve it considering functional needs
	11	Self-instructions and self-monitoring. Goal Management Training
	12	How to program and organize tasks: priorities, tasks segmentation, time management, feedback, checklists. Problem-solving techniques.
	13	Daily life application of executive functions strategies
-	14	Continuous use of learned techniques and acquired competences

Assessments

Innitially the sociodemographic data were collected, such as: age, sex, education level, occupational status, illness duration, age at illness onset and number of hospitalizations. As efficacy measures were used DEX-R, Whoqol- Bref and Ways of Coping Scale, which were described below. A single-blind evaluation by a therapist not involved in this study was conducted in order to reduce bias.

Whoqol – BREF Portuguese Version

The WHOQOL-BREF is a self-administered, multidimensional questionnaire with 26-item containing four domains: physical health (questions related to pain, sleep and energy, treatment adherence and daily activities) psychological (questions related to positive and negative feelings, self-esteem, personal beliefs, attention and concentration and body image) social relationships (addresses to personal relationships, social support and sexual activity), and environmental (encompasses questions related to security, financial support, health and social care, access to knowledge, participation and leisure). Each domain includes three to eight items [16]. The first item (Q1) asks the overall quality of life, and the second item (Q2) asks questions on general health satisfaction. Each item is based upon a self-report using a 5-point scale, which is applied in all questions. Respondents then check one of the following degrees–'not at all', 'a little', 'moderately', 'mostly', and 'completely' [17]. This questionnaire has already used to assess quality of life in bipolar disorder patients [18].

Ways of Coping Scale

The Ways of Coping Scale [19], comprises four factors: coping strategies based on the stressor, coping strategies based on the emotion, religiosity/fantasy thinking and search for social support.

Coping can be defined as thoughts and behaviors that individuals use to manage the internal and external demands of situations that are appraised as stressful [20] .Coping strategies in those with bipolar disorder have long been investigated. Coping strategies focused on low levels of acceptance and high levels of denial have been linked with poor medication adherence in bipolar I disorder [21], while maladaptive coping strategies such as rumination about negative states are linked to increased depression [22]. Considering that this construct has a very important contribution on the relationship between stress and bipolar disorder [23]. In accordance to those data, encourage the development of a more adaptative coping strategies is one of the central components of a cognitive intervention [23, 24]. Based on this assumption the coping was used in this study as a measure of efficacy of the NR protocol.

Dex-R

The DEX-R questionnaire consists of a checklist of symptoms on a 5-point Likert scale, ranging from (0) "never" to (4) "very often". This questionnaire is available in two different versions, being self reported, used in this study, and an independent-rating one. Initially, this questionnaire was proposed as a supplement for the primary tests of BADS [25] , and it was designed to screen for changes in observable everyday manifestations of executive dysfunction following acquired brain injury. The DEX encompassed 20 items that aimed to

evaluate abstraction, impulsivity, confabulation, planning skills, mood regulation, decision making, and it covers a wide range of specific problems such as difficulties with attention, memory, information processing, behavioural control, emotion regulation and awareness [26]. Even though the DEX was originally designed for use as qualitative assessment for focusing rehabilitation on an individual`s personal difficulties, this tool is currently used as a quantitative test instrument for diagnoses purposes [26, 27, 28]. A recent investigation [29] have found three dimensions for a sample with bipolar disorder (n=120). The factors which loaded in three main dimensions were congruent with the functions that have been attributed to orbitofrontal (OFC – Social-Regulation); dorsolateral (DL - Flexibility, Fluency and Working Memory) and anterior cingulated (AC – Motivation and Attention) circuits. In that way, the former dimension was composed by functions related to social skills and Self-Regulation, the second one by motivation and attention functions and the last dimension was comprised by flexibility, fluency and working memory.

Data Analyses

All statistical analyses were conducted using the Statistical Package for Social Sciences, Version 20.0 (SPSS Inc). As a first step, descriptive analyses were conducted. Then mixed design anova 3 X 2 were used to examine the treatment effect (pre- X post-NR protocol X follow up) considering the two groups (NRG X CG). In all cases which the Mauchly W's test indicated that the sphericity assumption was violated, the statistics were reported with the Greenhouse-Geisser correction. Furthermore, to explore the effect of the intervention on scores the effect size within groups were calculated (d Cohen) considering the pre-and post-treatment means. Finally it was conducted t-test to compare the mean of hypo/manic and depression episodes as well as the mean of suicidal attempts between groups.

RESULTS

Sample demographics were compared across both groups. There were no significant differences on age, gender, education level, estimated IQ, BD Types, illness duration, age at illness onset and number of hospitalizations (all *ps* > .10). It suggests that the pseudo-randomization process was efficient. Demographic data are summarised in Table 2. During the intervention, 16.6% and 18.9% of the patients discontinued in the NRG and CG respectively. There were no significantly differences between groups.

Table 2: Sociodemographic and Clinical characteristics for all participants [a]

Demographic and Clinical Variables	NRG (n=20)	CG (n=30)
	Mean (SD) or %	Mean (SD) or %
Age (years)	41.7 (15.1)	39.8 (14.9)
Gender - % Female	72%	69%
Education Level (years)	13.5 (5.23)	14.1 (5.34)
Estimated IQ *	35.6 (12.06)	32.5 (13.7)
BD Types - % Type I	60%	58%
Age at illness onset (years)	23.4 (7.48)	26.6 (8.54)
Illness duration (years)	24.8 (13.5)	22.6 (14.7)
Number of hospitalizations	3.72 (2.7)	2.98 (2.2)
Pharmacological Treatment:		
- Mood Stabilizers (Lithium or Valproate) and Antipsychotics (Risperidone, Quetiapine)	74%	69%
-Only Mood Stabilizers (Lithium or Valproate)	25%	28%
-Only Antipsychotics (Risperidone, Quetiapine)	1%	3%

*Estimated IQ based on Raven Score.

[a] No significant differences between groups.

DEX-R

Mixed-model repeated measures analysis indicated a significant interaction between the treatment and time for all the three subscales (OFC, CA and DL), as well as for the total score, (OFC = F[2, 98] = 17,54, $p < 0,001$, $\eta_p^2 = 0,26$; CA= F [2,9] = 55,91, p < 0,001, $\eta_p^2 = 0,53$; DL= F[1,49] = 51,08, p < 0,001, $\eta_p^2 = 0,08$; TOTAL = F[2, 98] = 11,82, $p < 0,001$, $\eta_p^2 = 0,19$). These results showed that the performance in DEX-R over the three assessments differed between GC and GRN. The direction of these effects is displayed in Figure 2.

The contrast measure for groups difference regarding pre- and post-treatment were significant (OFC= F[1, 49] = 20,74, $p < 0,001$; CA = F[1,49] = 39,15, p < 0,001, $\eta_p^2 = 0,44$; CA= F[1,49] = 5,51, p = 0,02, $\eta_p^2 = 0,10$; TOTAL = F[1, 49] = 34,54, $p < 0,001$), which means that changes in scores, in other words, the important decrease of these, was greater for the group under NR intervention.

On the other hand, the contrast measure for the difference between post-treatment and follow-up scores, when compared groups, considering OFC subscale was not significant (F [1, 49] = 0.02, p = 0.89). However, an important difference were found in CA scores (F[1,49] = 29,49, p < 0,001, $\eta_p^2 = 0,37$), DL subscale (DL = F[1,49] = 13,0, p = 0,001, $\eta_p^2 = 0,21$) as well as for Total Score (F[1, 49] = 11,23, $p = 0,002$). Taking together, these results demonstrate specific effects after the NR intervention. The difference between post and follow up scores were significant, with a greater change in scores for the CG, which means deterioration in executive functions, whereas the NRG scores remained similar to post-treatment.

Figure 2: Changes in DEX-R scores in pre-, post-intervention and follow-up.
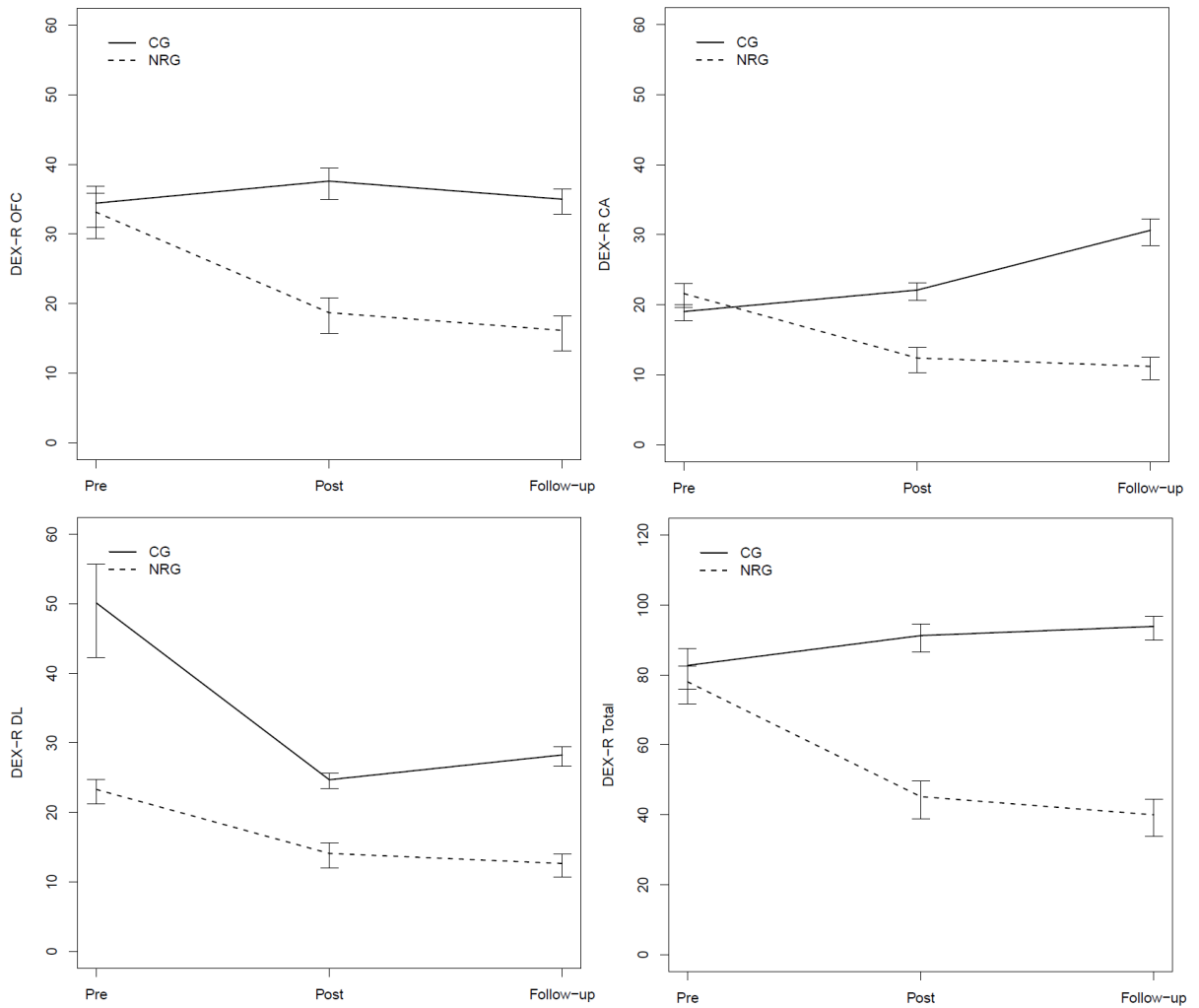
Ways of Coping

The analyses for Coping Strategies focused on Problems as well as for Coping Emotions subscale demonstrated a significant interaction between time measurements and type of treatment (F[2, 98] = 11,12, p <0,001,η_p^2 = 0.19; F[2, 98] = 5,94, p = 0,01, η_p^2 = 0,11, respectively), which indicated that the performance over three assessments differed between the CG and NRG. The contrast to the difference between pre-and post-treatment when comparing the CG and NRG was also significant for both subscales (PROBLEMS = F[1, 49] = 18,91 1, p <0,001, EMOTIONS = F[1, 49] = 5,99, p = 0,01, η^2 = 0,11). However, the contrast for post-treatment and follow-up was significant only for Coping strategies focused on problems (F[1, 49] = 4,78, p = 0,03), whereas for coping strategies focused on emotions there was no difference (F[2, 98] = 2,03, p = 0,14, η_p^2 = 0,04) (Figure 3).

The main effect of time on the Coping Religiosity/Fantasy Thinking scores was not significant (F[2, 98] = 0,40, p = 0.67, η_p^2 = 0,08) indicating that there were no differences between the three measurements in different times (pre, post and follow up). Moreover, the results indicated that also there were no significant differences between groups (F[1, 49] = 0,50, p = 0,46, η_p^2 = 0,01) as well as no interaction between these two variables (F[2, 98] = 1,03, p = 0,36, η_p^2 = 0,02).

Regarding Coping strategies based on Seeking Social Support, the main effect of time was not significant (F[2, 98] = 1,37, p = 0,26, η^2 = 0,03) which indicated that there were no significant differences between the three measurements taken at different times (pre, post and follow up). The presence of a significant main effect of treatment type F[1, 49] = 8,27, p < 0,01, η_p^2 = 0,14) indicated an important difference between the two groups investigated.

Finally, there was no significant interaction between measures and type of treatment (F[2, 98] = 1,37, p = 0,26, η_p^2 = 0,03).

**Figure 3: Changes in Coping Subscales scores in pre-, post-intervention and follow-up**
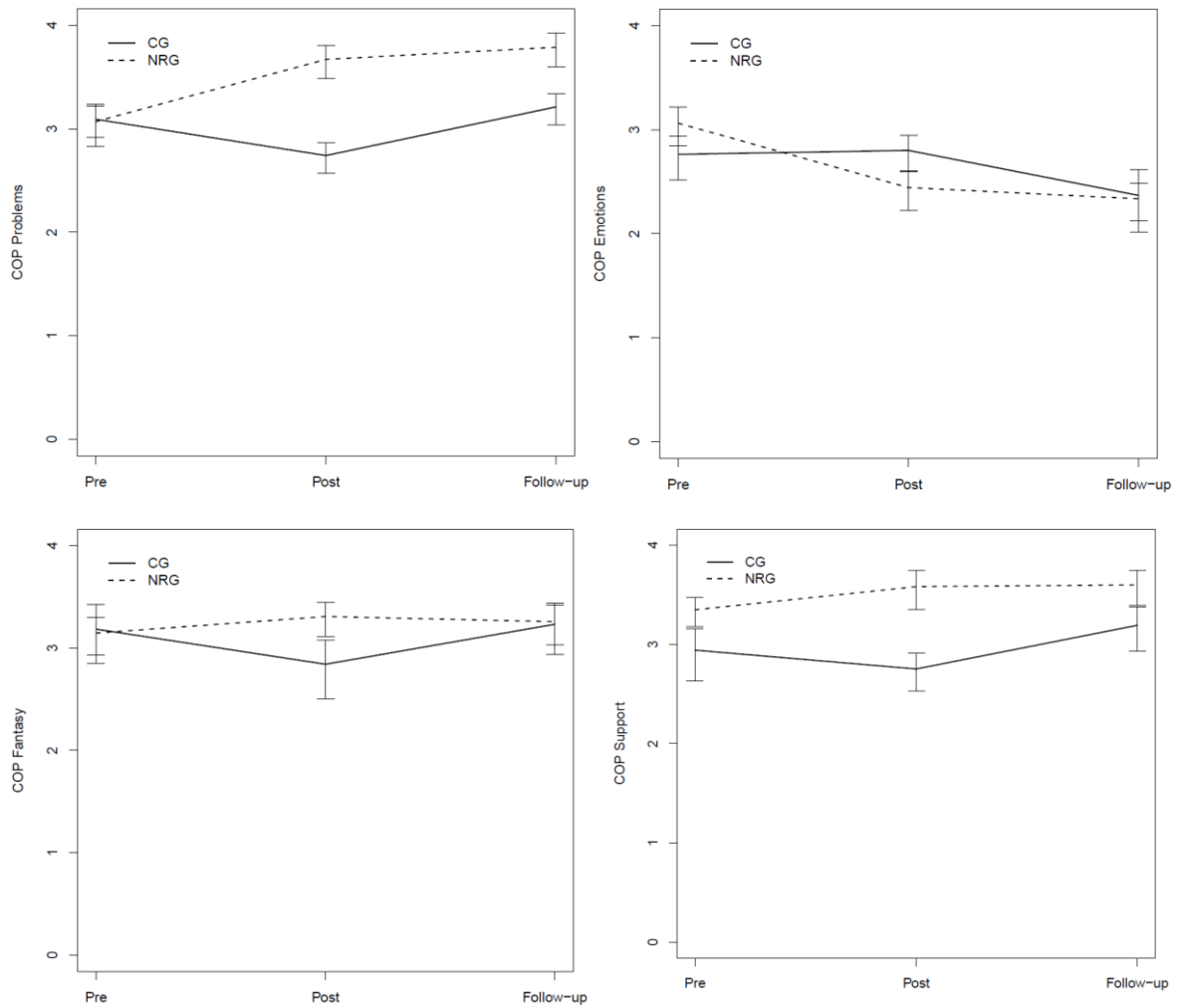
Whoqol-Bref

It was observed a significant interaction between type measures time and treatment group only for Physical health (F[2, 98] = 6,14, *p=0,004*, η_p^2 = 0,11) and for Psychological domains (F[2, 98] = 10,39, p<0,001, η_p^2 = 0,18), indicating that the performance in these domains over the three assessments differed between the CG and NRG. There were no differences for the other domains; social relationships (F[2, 96] = 1,47, *p=0,24*, η_p^2 = 0,03) and environmental (F[2, 96] = 2,94, *p=0,07*, η_p^2 = 0,06).

Both contrast measures pre- X post-treament and post-treament X follow up were statistically significant considering only the first two domains (Physical domain = F[1, 48] = 8,22, *p* = 0,006; F[1, 48] = 8,37, *p* = 0,006 and Psychological domain = F[1, 48] = 13,83, p = 0,001; F[1, 48] = 15,54, p < 0,001) respectively. Together these data show specific effects of the intervention were significant between groups (Figure 4).

Figure 4: Changes in Whoqol-Bref Subscales scores in pre-, post-intervention and follow-up
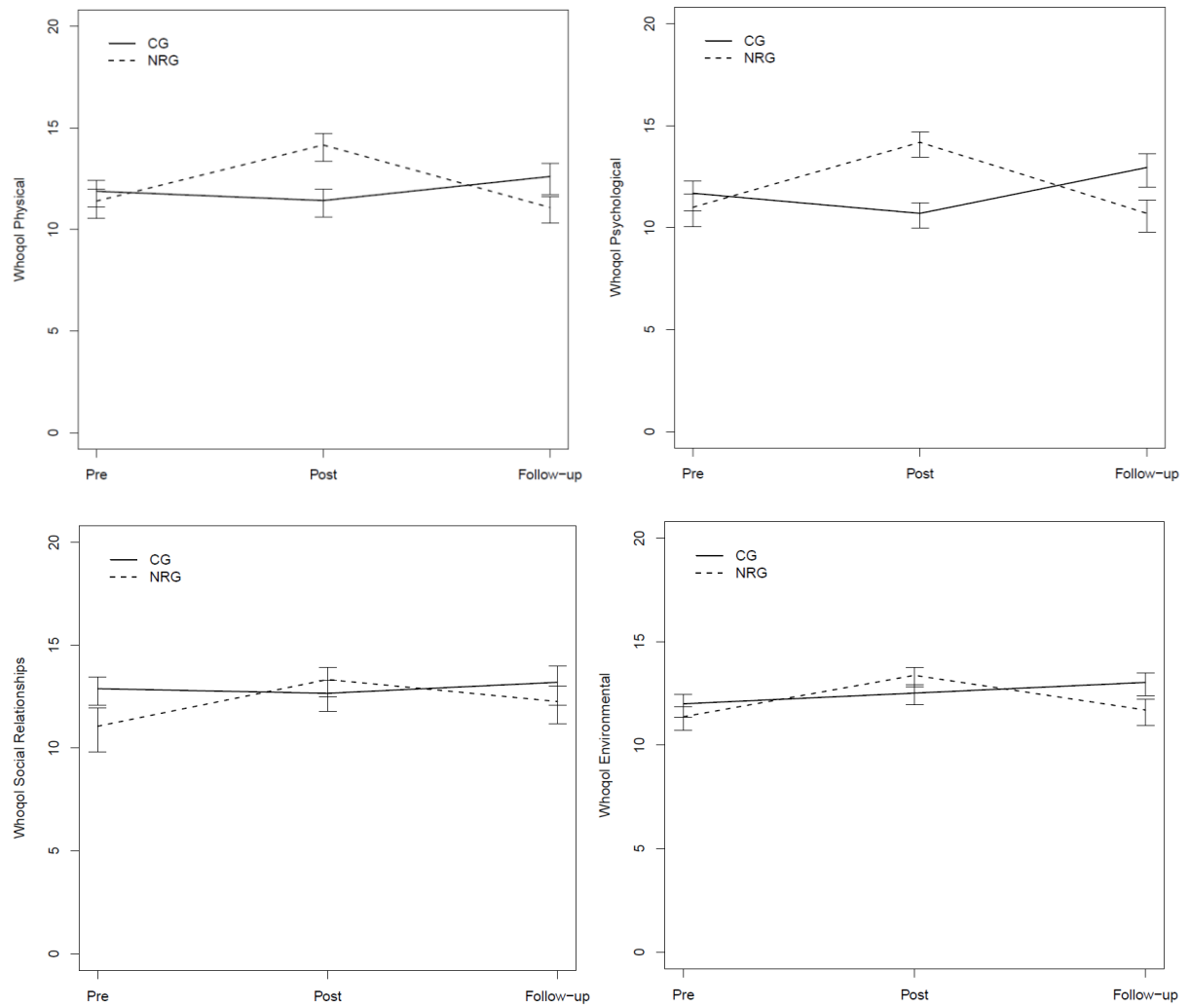
Effects Sizes in Efficacy Measures

Figure 5 displays the effects sizes (Cohen's d) calculated for the differences between the mean scores of pre-and post-treatment for the two groups of interest. In general, the effects size were very robust for the NRG (d > .80) [30].

Figure 5: Effects sizes between groups for Dex-R, Whoqol-Bref and Ways of Coping Scale.
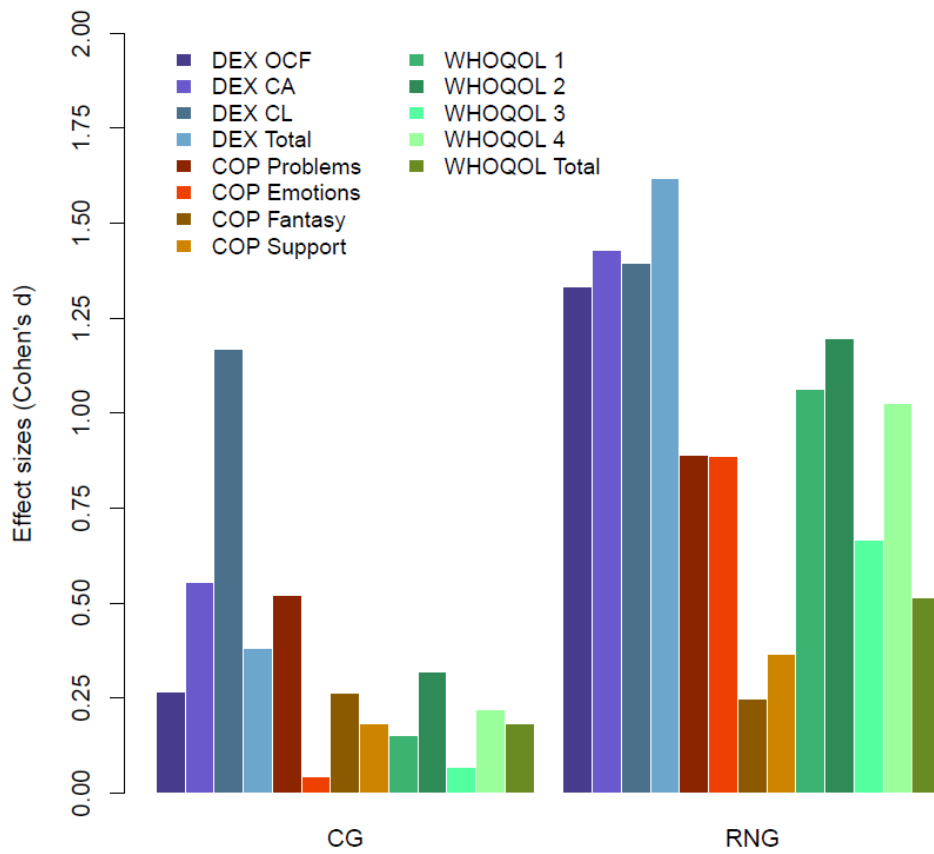
T-test

The differences between groups comparison regarding the average of mood swings epidodes
are displayed in Table 4.

Table 4: Comparisons of clinical variables

Groups	Number of mood swings episodes	
	Mean (SD)	**t –test / p**
CG	3,3 (1,7)	t= 5,823 /
NRG	1,6 (0,68)	p<.05

DISCUSSION

In this study we set out to investigate the efficacy of neuropsychological rehabilitation for bipolar patients. It was hypothesized that pharmacotherapy plus NR intervention would enhance the patient's functionality, which comprises in this study, a better performance in an ecological executive functions scale, an improvement in quality of life measures as well as the use of a more adaptive coping strategies, i.e., strategies focused on problems instead of focused on emotions. The results presented above show significantly greater improvements for the NRG, highlighting the intervention's efficacy, and its superiority as well. At the completion of the NR protocol, the NRG exhibited a greater effect size within the range of the most pharmacotherapies and psychosocial therapies. Our results support the feasibility of broad, multi-domain NR intervention, focused on functional demands, for patients with BD. Firstly we will comment the results in general and afterwards we will focus on specific measures.

To our knowledge, until currently, there were only two studies [8,9] which have investigated the efficacy of a cognitive intervention program in bipolar patients. The former indicated that at the end of treatment, as well as at the 3-months follow-up, patients showed lower residual depressive symptoms, increased occupational, as well as overall psychosocial functioning. The most recent investigation [9] has found significant functional improvement from baseline to endpoint over the 21 weeks of treatment. However, in this investigation it was not considered the long-term outcome. Considering our results, it was in line with these studies. We have found a greater improvement in all functional measures, with specific gains in quality of life indicators as well as in more advantageous coping styles, which are more focused on problems rather than on emotions. And these results were sustained even though the suspension of NR protocol for the many of the measures adopted, i.e., DL and CA DEX-R

subscales and Total DEX-R score, Coping Strategies focused on Problems as well as for the Physical and Psychological domains of Whoqol-Bref. Then more than the expected improvement at the endpoint of intervention, our investigation has demonstrated the positive long-term outcome as a consequence of NR treatment, which was a fundamental strength of it.

As pointed above repeated-measures analysis revealed significant functional improvement from baseline to endpoint for all DEX-R measures, for Coping specific subscales which were coping strategies focused in problems as well as in emotions, and also for Physical and Psychological domains from Whoqol-Bref. For the others measures (Coping Strategies focused on Religiosity/Fantasy Thinking and Seeking Social Support and Social Relationships and Environmental domains from Whoqol-Bref) in which we have not found differences, it was expected, since they represent a more broad constructs, that goes beyond the reach of NR strategies, i.e., faith and religiosity, availability of financial resources, transportation. Similar great results were also found in comparisons between post-treatment and follow-up measures, except for OFC DEX-R subscale and Coping focused on emotions. Specifically about OFC subscale, even though the average and standard deviation were different, the groups have shown the same pattern and because of that the test has not detected the difference. However, clinically, their behaviour can be considered distinct. Regarding Coping Emotions, we have not found any differences between groups at the follow-up.

Beyond the results presented above, other important contribuition of this study was the differences found in the clinical variables. Then, beyond the increment in functional skills as a result of NR protocol, we have found a decrease in frequence of mood swings episodes. These

results were in line with previous investigations that have demostrated a intrinsic conexion between cognition and mood [5, 31].

The study has also some limitations. Considering that the main objective of a neuropsychological rehabilitation intervention is a broad functional improvement, comprehended as beyond cognitive improvement, we have chosen to not consider the cognitive performance in purely neuropsychological tests. Our decision was laid on previous investigations [9] that have highlighted that even though the significant functional improvement it was not found any statistical significance on these tests. We decided to comprise cognitive functions in a more contextualized way, through the functional questionnaires applied. Then our results have a more ecological meaning. Second, we did not have a control passive group for NR intervention, which should be a group that would receive pharmacotherapy and should have a placebo weekly intervention at our centre. However, future investigations are now being delineated, which means that we are working on the inclusion of that group to expand the power of our analyses.

As such, understand the positive effect of NR treatment in BD is the first step towards ensuring that patients have more successful treatment outcomes. This was the first study to date to examine the efficacy of NR applied for BD patients, through a standardized and at the same time tailored protocol, which have considered the 6 months follow-up, and has had as a clinical aim the functional improvement.

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6 – SÍNTESE DOS RESULTADOS E CONSIDERAÇÕES FINAIS

Inicialmente será apresentada, uma síntese dos principais resultados dos artigos tendo em vista os objetivos específicos do presente trabalho no intuito de oferecer um panorama geral dos mesmos.

Como passo inicial foi conduzida uma revisão integrativa da literatura buscando verificar quais eram as avaliações mais empregadas para a mensuração da eficácia de um protocolo de intervenção em RN. A partir de nossos resultados, já publicados no Artigo 1, foi observada a escassez de estudos sistematizados na área da psiquiatria, além do emprego de instrumentos não específicos para este fim. Considerando o foco maior do presente trabalho que era a avaliação da eficácia de um protocolo de RN em pacientes com o TAB, não poderíamos proceder com nossa investigação sem contarmos com um instrumento específico para mensuração das funções executivas, além da memória e atenção, em uma abordagem ecológica. Desta feita, após uma extensa investigação, optamos por trabalhar com o Questionário Disexecutivos Revisado, a DEX-R (Simblett; Bateman, 2011).

Para atender o objetivo acima exposto, o questionário foi traduzido por três pesquisadores bilíngües especialistas na área. Após isso, foi efetivado um consenso para a escolha da melhor tradução. Em um segundo momento foi realizada a retrotradução por outro profissional bilíngue para analisar a equivalência entre a versão traduzida e a original, contendo a tradução de todos os itens do instrumento. Por fim, foi conduzida a avaliação da equivalência. Essa etapa consistiu da avaliação da concordância entre a versão original e a versão retraduzida pelos autores originais do questionário, para que a versão brasileira correspondesse ao conteúdo da versão originalmente proposta pelos mesmos. A fim de verificar a se esta nova versão seria sensível para avaliar perfil executivo de pessoas com o TAB, a DEX-R foi aplicada em uma amostra de indivíduos controles sem nenhum transtorno neuropsiquiátrico e comparado com uma amostra de sujeitos com o diagnóstico de TAB tipo I e tipo II. Na comparação intergrupos, houve diferença significativa no desempenho no questionário, com o grupo clínico, apresentando maior comprometimento executivo. Em seguida, procedemos à comparação dos subgrupos clínicos, TAB I x TAB II, e também foi evidenciado para alguns itens, um comprometimento maior no subgrupo tipo I, resultado este corroborado por investigações prévias que apontam um maior comprometimento cognitivo neste subgrupo. Em sequencia, como também demonstrado em nosso Artigo 3, foi conduzida uma AFE, e

evidenciamos que os itens se agruparam em 3 fatores, sendo o primeiro relativo às funções, dentre outras, de auto-regulação, comportamento social, controle do humor, comportamento guiado por recompensas, tolerância à frustração, tomada de decisão. Já o segundo fator abarcou funções relacionadas ao monitoramento do humor, controle executivo da atenção, seleção de habilidades e controle de respostas, e por fim, o ultimo grupo foi composto por itens específicos de flexibilidade cognitiva, fluência, memória de trabalho, organização e atenção. Considerando a neuroanatomia das funções executivas e os circuitos fronto estriatais, optamos por nomear os fatores como funções relativas ao circuito orbito-frontal (OFC), circuito do cíngulo anterior (CA) e dorsolateral (DL) respectivamente. Em um estudo posterior, já submetido (Artigo 4), verificamos a adequação das subscalas e investigamos as propriedades psicométricas de DEX-R de acordo com o Modelo Rasch. As subscalas então mostraram ser unidimensionais, ou seja, mediam o mesmo constructo latente, e tiveram um alto índice de confiabilidades (> .80).

Uma vez que já tínhamos um questionário sensível e funcional, procedemos à realização de um estudo piloto para a adequação do protocolo de intervenção em RN, e para tanto realizamos o delineamento experimental de caso único (Artigo 2). Na avaliação pós intervenção e no follow-up, verificamos que a paciente apresentava uma redução significativa do comprometimento funcional, e que, portanto, a protocolo com suas específicas abordagens e estrategias focadas na reabilitação da atenção, memória e funções executivas, atendeu às nossas expectativas iniciais.

Por fim, empregamos este protocolo de RN e conduzimos nossa principal pesquisa (Artigo 5). Comparamos o grupo experimental, que era a RN mais a farmacoterapia, o chamado GRN com o GC, composto de pacientes tratados apenas com a farmacoterapia. Encontramos tanto no pós-intervenção como no follow-up uma melhora significativa nas escalas empregadas, a DEX-R, Whoqol-Bref e a EMEP, com manutenção dos ganhos após a suspensão da RN. E ademais, considerando as variáveis clínicas adotadas, nossos grupos também se comportaram de formas diferentes, com o GRN demonstrando menor frequência de episódios de alteração do humor e de tentativas de suicídio, além de uma maior frequência de sucesso em atividades laborativas e acadêmicas.

Diante do exposto, conclui-se que os resultados apresentados nesse trabalho enfatizam a relevância do tema de investigação proposto para a população de indivíduos com TAB, tanto

no que se refere ao estudo sistemático de uma intervenção não-farmacológica, a reabilitação neuropsicológica, quanto ao desenvolvimento e emprego de medidas ecológicas de avaliação.

Uma importante contribuição deste trabalho, além de fornecer dados clínicos que endossam a relevância da RN como viável e importante propedêutica no tratamento do TAB, foi o fato de, mesmo após os 6 meses sem a RN, houve uma permanência dos ganhos, o que corrobora a atuação a longo prazo da intervenção estudada. Outra relevente contribuição desta investigação foi a constatação do positivo impacto em variáveis clínicas, no caso, a redução da frequência de episódios de alteração do humor, o que corrobora a interseção entre cognição e humor, já apontada em pesquisas prévias (Lewandowski et al., 2011).

Como limitações, ressalta-se a não existência de um grupo controle ativo, ou seja, um grupo com uma intervenção placebo para a RN. Não foi possível cumprirmos com este importante quisito metodológico porque não dispúnhamos de uma amostra suficientemente robusta que nos permitisse a criação de um terceiro grupo. Outra importante questão, foi a impossibilidade de controlarmos a medicação estabilizadora do humor. Mas, ressalta-se que houve, ao longo desta pesquisa, o rigor metodológico de garantir que todos os pacientes, enquanto estivesem sob tratamento, mantivessem com a mesma medicação em uso, para assim, diminuirmos a viés da interação entre cognição e medicação.

Finalmente, considerando as perspectivas futuras suscitadas a partir dos resultados aqui apresentados, explicita-se a continuidade desta investigação abarcando o grupo controle ativo da RN, com a proposiçãode uma intervenção não farmacológica placebo, além da inclusão de exames de imagem cerebral, a fim de comparar os possíveis efeitos da RN no funcionamento cerebral pré e pós - intervenção. Considerando a relevância das variáveis clínicas como tipo do suicídio, idade de início, e alterações cognitivas dos pacientes bipolares, para a futura condução desta linha de pesquisa, tem-se como objetivos a formação de grupos mais homogêneos. E por fim, através da ampliação da amostra do estudo, pretende-se comparar o impacto do protocolo de RN considerando os subtipos I e II do transtorno.

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APÊNDICES
APÊNDICE A: Estatísticas descritivas referentes às medidas pré e pós-intervenção e follow-up.

Medidas	Controle (GC)		Reabilitação (GRN)	
	Média	Desvio-padrão	Média	Desvio-padrão
PRE_dexofc	34,13	13,33	33,15	12,01
PRE_dexca	18,81	5,34	21,60	6,18
PRE_dexdl	50,71	30,04	23,30	6,47
PRE_dextotal	81,97	26,00	78,05	20,21
POS_dexofc	37,19	10,16	18,70	9,50
POS_dexca	22,19	5,69	12,40	6,69
POS_dexdl	24,74	4,86	14,10	6,72
POS_dextotal	90,77	17,89	45,20	20,41
FOL_dexofc	34,97	8,12	16,15	9,17
FOL_dexca	30,55	8,53	11,20	6,00
FOL_dexdl	28,35	6,21	12,65	6,20
FOL_dextotal	93,87	15,10	40,00	19,70
PRE_COPPROBLEMA	3,09	0,66	3,07	0,75
POS_COPPROBLEMA	2,74	0,66	3,67	0,59
FOL_COPPROBLEMA	3,21	0,67	3,79	0,61
PRE_COPEMOÇÔES	2,76	0,95	3,06	0,70
POS_COPEMOÇÔES	2,80	0,78	2,44	0,70
FOL_COPEOMOÇOES	2,37	1,35	2,34	0,67
PRE_COPFANTASIA	3,19	1,28	3,15	0,67
POS_COPFANTASIA	2,84	1,28	3,31	0,63
FOL_COPFANTASIA	3,23	1,13	3,26	0,71
PRE_COPSUPORTE	2,94	1,18	3,35	0,54
POS_COPSUPORTE	2,75	0,84	3,58	0,72
FOL_COPSUPORTE	3,19	1,00	3,60	0,66
who1_pre	11,89	2,95	11,40	2,68
who2_pre	11,69	3,33	11,00	2,98
who3_pre	12,89	3,14	11,07	3,99
who4_pre	12,00	2,50	11,38	2,12
whoTotal_pre	12,40	3,08	11,40	3,95
who1_pos	11,43	3,12	14,16	2,52
who2_pos	10,70	2,83	14,19	2,31
who3_pos	12,67	3,39	13,33	2,70
who4_pos	12,52	2,20	13,38	1,76
whoTotal_pos	11,80	3,50	13,40	3,84
who1_follow	12,55	3,43	11,09	2,39
who2_follow	12,81	3,74	10,70	2,91
who3_follow	13,03	4,34	12,27	3,37
who4_follow	13,05	2,50	11,70	2,37
whoTotal_follow	13,10	3,68	11,70	3,45

ANEXOS

ANEXO A: Parecer de aprovação do Comitê de Ética em Pesquisa da Universidade Federal de Minas Gerais – COEP/UFMG

UNIVERSIDADE FEDERAL DE MINAS GERAIS
COMITÊ DE ÉTICA EM PESQUISA - COEP

Projeto: CAAE – 0625.0.203.000-11

Interessado(a): Prof. Fernando Silva Neves
Departamento de Saúde Mental
Faculdade de Medicina - UFMG

DECISÃO

O Comitê de Ética em Pesquisa da UFMG – COEP aprovou, no dia 14 de dezembro de 2011, o projeto de pesquisa intitulado **"Avaliação da eficácia de um protocolo de reabilitação neuropsicológica direcionado a pacientes com transtorno bipolar "** bem como o Termo de Consentimento Livre e Esclarecido.

O relatório final ou parcial deverá ser encaminhado ao COEP um ano após o início do projeto.

Profa. Maria Teresa Marques Amaral
Coordenadora do COEP-UFMG

ANEXO B: Escala de Modo de Enfrentamento de Problemas - EMEP

Escala de Modos de Enfrentamento de Problemas - EMEP

As pessoas reagem de diferentes maneiras a situações difíceis ou estressantes. Para responder a este questionário, pense sobre como você está lidando com a bipolaridade, nesse momento do seu tratamento. Concentre-se nas coisas que você faz, pensa ou sente para enfrentar essa condição, no momento atual.

Veja um exemplo: **Eu estou buscando ajuda de um profissional para enfrentar o meu problema de saúde.**

1	2	3	4	5
Eu nunca faço isso	**Eu faço isso um pouco**	**Eu faço isso às vezes**	**Eu faço isso muito**	**Eu faço isso sempre**

Você deve assinalar a alternativa que corresponde melhor ao que você está fazendo quanto à busca de ajuda profissional para enfrentar o seu problema de saúde. Se você <u>não</u> está buscando ajuda profissional, marque com um X ou um círculo o número 1 (nunca faço isso); se você <u>está buscando sempre</u> esse tipo de ajuda, marque o número 5 (eu faço isso sempre). Se a sua busca de ajuda profissional é diferente dessas duas opções, marque 2, 3 ou 4, conforme ela está ocorrendo.

Não há respostas certas ou erradas. O que importa é como você está lidando com a situação. Pedimos que você responda a todas as questões, não deixando nenhuma em branco.

Muito obrigada pela sua participação!

Afirmativas	**Eu nunca faço isso**	**Eu faço isso um pouco**	**Eu faço isso às vezes**	**Eu faço isso muito**	**Eu faço isso sempre**
1. Eu levo em conta o lado positivo das coisas.					
2. Eu me culpo.					
3. Eu me concentro em alguma coisa boa que pode vir desta situação.					
4. Eu tento guardar meus sentimentos para mim mesmo.					

5. Procuro um culpado para a situação.					
6. Espero que um milagre aconteça.					
7. Peço conselho a um parente ou a um amigo que eu respeite.					
8. Eu rezo/ oro.					
9. Converso com alguém sobre como estou me sentindo.					
10. Eu insisto e luto pelo que eu quero.					
11. Eu me recuso a acreditar que isto esteja acontecendo.					
12. Eu brigo comigo mesmo; eu fico falando comigo mesmo o que devo fazer.					
13. Desconto em outras pessoas.					
14. Encontro diferentes soluções para o meu problema.					
15. Tento ser uma pessoa mais forte e otimista.					
16. Eu tento evitar que os meus sentimentos atrapalhem em outras coisas na minha vida.					
17. Eu me concentro nas coisas boas da minha vida.					
18. Eu desejaria mudar o modo como eu me sinto.					
19. Aceito a simpatia e a compreensão de alguém.					
20. Demonstro raiva para as pessoas que causaram o problema.					
21. Pratico mais a religião desde que tenho esse problema.					
22. Eu percebo que eu mesmo trouxe o problema para mim.					
23. Eu me sinto mal por não ter podido evitar o problema.					
24. Eu sei o que deve ser feito e estou aumentando meus esforços para ser bem sucedido.					
25. Eu acho que as pessoas foram injustas comigo.					
26. Eu sonho ou imagino um tempo					

melhor do que aquele em que estou.					
27. Tento esquecer o problema todo.					
28. Estou mudando e me tornando uma pessoa mais experiente.					
29. Eu culpo os outros.					
30. Eu fico me lembrando que as coisas poderiam ser piores.					
31. Converso com alguém que possa fazer alguma coisa para resolver o meu problema.					
32. Eu tento não agir tão precipitadamente ou seguir minha primeira idéia.					
33. Mudo alguma coisa para que as coisas acabem dando certo.					
34. Procuro me afastar das pessoas em geral.					
35. Eu imagino e tenho desejos sobre como as coisas poderiam acontecer.					
36. Encaro a situação por etapas, fazendo uma coisa de cada vez.					
37. Descubro quem mais é ou foi responsável.					
38. Penso em coisas fantásticas ou irreais (como uma vingança ou achar muito dinheiro) que me fazem sentir melhor.					
39. Eu sairei dessa experiência melhor do que entrei nela.					
40. Eu digo a mim mesmo o quanto já consegui.					
41. Eu desejaria poder mudar o que aconteceu comigo.					
42. Eu fiz um plano de ação para resolver o meu problema e o estou cumprindo.					
43. Converso com alguém para obter informações sobre a situação.					
44. Eu me apego à minha fé para superar esta situação.					
45. Eu tento não fechar portas atrás de mim. Tento deixar em aberto várias saídas para o problema.					

ANEXO C: Whoqol Bref

WHOQOL BREF

Este questionário é sobre como você se sente a respeito de sua qualidade de vida, saúde e outras áreas de sua vida. Se você não tem certeza sobre que resposta dar em uma questão, escolha entre as alternativas a que lhe parece mais apropriada. Esta, muitas vezes, poderá ser sua primeira escolha. Tenha em mente seus valores, aspirações, prazeres e preocupações. Nós estamos perguntando o que você acha de sua vida, tomando como referência . Leia cada questão, veja o que você acha e circule no número e lhe parece a melhor resposta. as duas últimas semanas. Por favor, responda a todas as questões.

Afirmativa	Muito ruim	Ruim	Nem reuim nem boa	Boa	Muito boa
1. Como avalia sua qualidade de vida?					

Afirmativa	Muito insatisfeito	Insatisfeito	Nem satisfeto nem insatisfeito	Satisfeito	Muito satisfeito
2. Quão satisfeito(a) você está com a sua saúde?					

As questões seguintes são sobre o quanto você tem sentido algumas coisas nas últimas duas semanas.					
Afirmativas	**Nada**	**Muito pouco**	**Mais ou menos**	**Bastante**	**Extremamente**
3. Em que medida você acha que sua dor (física) impede você de fazer o que você precisa?					
4. O quanto você precisa de algum tratamento médico para levar sua vida diária?					
5. O quanto você aproveita a vida?					
6. Em que medida você acha que a sua vida tem sentido?					
7. O quanto você consegue se concentrar?					
8. Quão seguro(a) você se sente em sua vida diária?					
9. Quão saudável é o seu					

ambiente físico (clima, barulho, poluição, atrativos)?					

As questões seguintes perguntam sobre quão completamente você tem sentido ou é capaz de
fazer certas coisas nestas últimas duas semanas.

Afirmativas	Nada	Muito pouco	Médio	Muito	Completamente
10. Você tem energia suficiente para seu dia-a-dia?					
11. Você é capaz de aceitar sua aparência física?					
12. Você tem dinheiro suficiente para satisfazer suas necessidades?					
13. Quão disponíveis para você estão as informações que precisa no seu dia-a-dia?					
14. Em que medida você tem oportunidades de atividade de lazer?					

As questões seguintes perguntam sobre quão bem ou satisfeito você se sentiu a respeito de
vários aspectos de sua vida nas últimas duas semanas.

Afirmativa	Muito ruim	Ruim	Nem ruim nem bom	Bom	Muito satisfeito
15. Quão bem você é capaz de se locomover?					

Afirmativas	Muito insatisfeito	Insatisfeito	Nem satisfeito nem insatisfeito	Satisfeito	Muito satisfeito
16. Quão satisfeito(a) você está com o seu sono?					
17. Quão satisfeito(a) você está com sua capacidade de desempenhar as atividades do seu dia-a-dia?					
18. Quão satisfeito(a) você está com sua capacidade para o trabalho?					
19. Quão satisfeito(a) você					

está consigo mesmo?					
20. Quão satisfeito(a) você está com suas relações pessoais (amigos, parentes, conhecidos, colegas)?					
21. Quão satisfeito(a) você está com sua vida sexual?					
22. Quão satisfeito(a) você está com o apoio que você recebe de seus amigos?					
23. Quão satisfeito(a) você está com as condições do local onde mora?					
24. Quão satisfeito(a) você está com o seu acesso aos serviços de saúde?					
25. Quão satisfeito(a) você está com o seu meio de transporte?					
A questão seguinte refere-se a com que frequência você sentiu ou experimentou certas coisas nas últimas duas semanas.					
Afirmativa	**Nunca**	**Algumas vezes**	**Frequentem ente**	**Muito frequente mente**	**Sempre**
26. Com que frequência você tem sentimentos negativos tais como mau humor, desespero, ansiedade, depressão?					