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Research report

Neurocognitive changes in depressed patients in psychodynamic psychotherapy, therapy with fluoxetine and combination therapy

Andre Goettems Bastos [a,b,*], Luciano Santos Pinto Guimarães [a,c], Clarissa Marceli Trentini [a]

[a] Federal University of Rio Grande do Sul, Brazil
[b] Contemporary Institute of Psychoanalysis and Transdisciplinarity of Porto Alegre, Brazil
[c] Epidemiology and Biostatistics Unit, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

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ABSTRACT

Background: Randomized controlled trials (RCTs) examining the efficacy of different forms of therapy for depression are relatively common. However, there are not many RCTs comparing neurocognitive effects of these treatments. Neurocognitive changes across three types of treatment for depression were compared. Long-term psychodynamic psychotherapy (LTPP) was compared with fluoxetine treatment, and their combination, in the treatment of moderate depression.
Methods: A 272 adult patients with beck depression inventory (BDI) scores 20–35 were randomized to receive LTPP, fluoxetine monotherapy or their combination for a 24 months period. The Wechsler adult intelligence scale version III (WAIS-III) was the primary neuropsychological measure.
Result: Multilevel mixed model analyses indicated that there were neurocognitive changes within and between treatments, with statistically significant differences over time ($p > .01$). LTPP and combined treatment seemed to be more efficacious in modifying specific areas of cognition than fluoxetine alone.
Limitations: Sample very homogenous, threatening external validity.
Conclusions: LTPP and its combination with fluoxetine demonstrated to be effective for specific neurocognitive increasing in patients with moderate depression. This study suggests marked differences over time in the neurocognitive effects between the three treatment forms compared. Results found here may be of clinical relevance for building bridges between pharmacotherapy and psychodynamic psychotherapy.

1. Introduction

Altered neurocognitive functioning are frequently reported in some psychiatric disorders, especially depression (Christensen et al., 2007; Lezak et al., 2012). Teng (2009) highlights the fact that the relationship between cognitive functioning and depression is “intimate and evident” (p. 11) and that the number of researches in this area is still insufficient.

Previous studies reported neurocognitive problems mainly related to data processing and organization of perceptual information, working memory, attention, executive functions and inhibitory processes, as well as cognitive processing speed (Harvey et al., 2004; Marvel and Paradiso, 2004; Porter et al., 2007). The DSM-IV (American Psychiatric Association, 2000) includes, among the symptoms presented in depression, psychomotor delay and diminished concentration, and ICD-10 (World Health Organization, 1995) mentions the reduction in the capacity of concentration and psychomotor slowness.

Basso et al. (2013) compiled the foremost cognitive domains that are usually impaired in depressed patients. These are: mental flexibility, semantic fluency, working memory, processing speed and learning capacity. The ones that are not normally associated to dysfunction are: intelligence, verbal comprehension, spatial perception and object recognition.

The extension and specificity of these problems in depressed patients tend to vary a lot. Together with sadness and lack of energy, typical symptoms of depressive disorders, neurocognitive problems lead patients to different treatments, such as psychotherapy and therapy with antidepressants. The efficacy of the treatments for depression has been described in several studies and is consolidated in medical/psychological literature (Berghout and Zevalkink, 2009; Greenberg and Goldman, 2009; Tomba and Fava, 2009).

Most studies about depression treatment, however, tend to focus only on the clinical psychiatric symptoms, disregarding other important aspects (Knekt et al., 2008). Notwithstanding, little is known about the effects of the different kinds of treatment over

* Correspondence to: Rua Alfredo Miranda Obino 240, CEP 91225-100, Porto Alegre, Rs, Brazil. Tel.: +55 5181242415.
E-mail address: andregbastos@gmail.com (A.G. Bastos).

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cognition in depressive patients. Roth and Fonagy (2005) reasoned that cognition assessment could form a different level of outcome measurement. This level could comprise the investigation of undergoing mechanisms that are not easily noticed clinically. These mechanisms probably play an important role in the basis of symptoms of a disease and in the adaptation and functional problems of an individual. Kazdin and Kendall (1998), complementary, argued that the investigation of specific mechanisms through which a given treatment could improve the patient's condition might be an innovative and productive way to assess treatment outcomes and increase the clinical significance of the treatments. Regarding this subject, there are evidences which also suggest that some mechanisms that could be related to the etiology and physiopathology of depression can be found in monitoring the neurocognitive functioning (Teng, 2009).

These aspects might partly justify cognitive assessments in depressed subjects, once these evaluations tend to be deeper than the usual psychiatric assessment used in clinical routine (Porter et al., 2007; Teng and Yano, 2009). Cognitive assessment is understood here as the neuropsychological assessment of a patient's cognitive functioning, i.e., the assessment of neurocognitive performance. This includes but is not limited to functions like memory, attention, concentration, psychomotor speed, abstract reasoning, and so forth (Arnett, 2013a).

Douglas and Porter (2009), in a literature review that aimed to determine the neuropsychological domains that are more related to the clinical status of depression, concluded that the most relevant research subject to be developed in this field is the one that focuses on the changes in neuropsychological functioning associated with response to treatment, once this would promote new ways to assess different therapeutic strategies to treat depression. Porter et al. (2007) addressed that there is growing evidence that the measurement of neuropsychological functioning is becoming an extremely powerful method to the prediction of clinical response and relapse.

Yazigi et al. (2011), for example, assessed patients with different psychiatric disorders who were receiving long-term psychoanalytic psychotherapy. Researchers used the WAIS-III (a set of well-known neuropsychological tests) to assess patients (basal, 12 months and 24 months). The depressed patients evaluated showed an increase in the attention capacity and processing speed. The authors' discussion of results came to conclude that the clinical improvement of the symptoms provided by treatment eventually enabled cognitive improvement. One point to consider, however, is that the clinical sample was quite heterogeneous and attrition rates achieved 60% in the last retest. These aspects somehow threaten the validity of the findings.

Furthermore, it is not certain that cognitive deficits are a consequence of depressive symptoms, or that depressive humor stems from problematic cognitive functioning (Teng and Yano, 2009). Austin et al. (2001) claim that cognitive problems do not always seem to be epiphenomena of depression and should not be hastily interpreted this way. Chepenik et al. (2007) raised the possibility that cognitive deficits in depressive patients may be an independent component of the disease. Nevertheless, the general scenario seem related to the idea that the relationship between cognitive deficits and the clinical situation of depressed patients is not yet clear (Douglas and Porter, 2009), although this relationship has been reported very often in researches and by clinicians who treat these patients (Arnett, 2013b).

Some evidence has suggested that neurocognitive improvement takes place before the clinical improvement of depression, not the other way around (e.g., Dunkin et al., 2000; Harmer, 2008; Roiser et al., 2012). Recent neuroimaging studies have come to conclude that some clinical symptoms and certain cognitive deficits in depression probably share the same dysfunctional neurobiological activity (Thomas and Elliott, 2009; Buchheim et al., 2012). Basso et al. (2013) raised the possibility that neurocognitive deficits precede the onset of depression and its symptoms, which could reveal a cerebral vulnerability to depression.

Therefore, monitoring cognition longitudinally along different types of treatment may help to find hidden variables which might be significant for the treatment. This study aimed to investigate and monitor the neurocognition in depressed patients along three types of treatment: long-term psychodynamic psychotherapy (LTPP), fluoxetine therapy (FLU) and their combination (COM).

2. Materials and methods

2.1. Design

The study is a randomized controlled trial comparing LTPP, fluoxetine therapy and combined treatment, investigating changes in neurocognition of depressed patients. The investigation followed the Declaration of Helsinki, and the informed consent of the participants was obtained. The study design was approved by the local Ethics Committee.

2.2. Participants

Inclusion criteria were: presence of major depressive disorder or depressive disorder not otherwise specified, according to the criteria of the DSM-IV, moderate depressive symptoms (BDI scores between 20 and 35), age between 26 and 34 (this relatively young age span was intentionally chosen in order to minimize the chances of selecting subjects with chronic depression and/or subjects with possible aging effects over cognition, since it could bias the results), and to have signed the informed consent to participate in the research.

Exclusion criteria were: DSM-IV-TR Axis I and II comorbidities, risk of suicide, use of other medications that may influence the mental functioning, severe somatic diseases, history of neurological problems, and contraindication to treatment with fluoxetine.

2.3. Procedure

Participants were selected among patients of a psychiatric clinic in the city of Porto Alegre/Brazil. They were initially interviewed by a clinical psychologist. Patients with signs of depressive disorder and absence of clear exclusion criteria were invited for a complete baseline assessment a week later.

The inclusion and exclusion criteria were then checked again with the Structured Clinical Interview for the DSM, SCID-I and SCID-II (Del-Ben et al., 1996, 1998, 2001), and the BDI in order to quantify the severity of the depressive episode. Upon diagnostic confirmation, the research and its objectives were explained. Independent researchers assessed patients with the WAIS-III for neurocognitive basal screening. After, patients were randomized to one of the treatments. The treatments started in the following week. WAIS-III and BDI assessments took place every six months after basal assessment, and were always performed by independent evaluators who were not aware of which treatment patients were receiving.

2.4. Interventions

Long-term psychodynamic psychotherapy refers to an approach based on Sigmund Freud's theories (Kaplan and Sadock, 2008). The long-term psychodynamic psychotherapy used in this study was alike to the one proposed by Gabbard (2004, 2010). Psychotherapy was carried out individually, in weekly appointments.