Cognitive functioning in depressed people treated with SSRI or TCA

Key words: cognitive functioning, selective serotonine reuptake inhibitors (SSRI), tricyclic antidepressants (TCA), major depressive disorder (MDD).

1. General part of the paper

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- Global disability and functioning in depression
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- Pharmacological treatment in depression

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1.3. Selective serotonin reuptake inhibitors (SSRI)

1.4. Efficacy and safety evaluation in antidepressive medication

1.5. Antidepressants effect on cognitive functioning

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- Discussions related to secondary objective in the study

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- Conclusions on therapeutically remission
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**Background**

Patients with acute MDD usually present alterations in various cognitive functions (Rogers and al. 2004). Neuropsychological deficit in depressed patients may be detected in attention (Porter et al., 2003; Weiland-Fielder et al., 2004), mental processing speed and motor performance (Sobin and Sackeim, 1997; Gualtieri et al., 2006), memory (Airaksinen et al., 2004; Austin et al., 2001; MacQueen et al., 2002), working memory (Harvey et al., 2004), and executive functions (Rogers et al., 2004; Gualtieri et al., 2006), including allocation of attentional resources, inhibitory control, fluency, planning, and self-monitoring (Rogers et al., 2004, 1998). Taken together, these studies suggest that at least some cognitive deficits in depression could be a trait characteristic of the illness, rather than state-dependent deficits, although there are also works suggesting that several neuropsychological deficits in MDD are related to acute symptomatic state of the illness and are not present in remission (Merens et al., 2008) or during long-term recovery (Westheide et al., 2007). However, the majority of these works usually did not account for the possible impact of medication on cognitive function in patients with MDD. Several works showed that antidepressant treatment could ameliorate cognitive dysfunction in MDD. Depressive disorders have a large impact on both social as well as physical domains of functioning (Coryell et al., 1993; Judd et al., 1996; Rapaport et al., 2005; Wells et al., 1992) similar to or even exceeding the impact noted in common medical illnesses (Buist-Bouwman et
al., 2004, 2006; Merikangas et al., 2007; Ormel et al., 1994; Schonfeld et al., 1997; Wells et al., 1989, 1992). The level of functional impairment is positively associated with the severity of depressive disorders (Judd and Akiskal, 2000; Kruijshaar et al., 2003; Ormel et al., 1994, 2004; Rapaport et al., 2005; Spijker et al., 2004a). Depression is a common illness, with a lifetime prevalence of 15% (Bijl et al., 1997) and a burden greater than that of various common chronic medical conditions, such as arthritis (Wells et al., 1989), hypertension (Hays et al., 1995) and diabetes (Hays et al., 1995; Wells et al., 1989). The World Health Organization predicts that by the year 2020, major depression will be the second most disabling condition worldwide, measured in disability-adjusted life years (Murray and Lopez, 1997). Additionally, chronicity of the depressive disorder might affect the level of functioning of persons with depressive disorders (Rytsala et al., 2006). After remission of the depressive symptoms, social and physical functioning returns to levels found among healthy subjects, although some functional impairment may persist after recovery (Buist-Bouwman et al., 2004; Coryell et al., 1993; Hirschfeld et al., 2002; Judd et al., 2000; Ormel et al., 2004). This postmorbid impaired functioning may be a trait, state or scar effect (Ormel et al., 2004), or a consequence of so-called “trajectory of recovery”, in which recovery of functioning parallels, but lags considerably behind the curve of depressive symptoms recovery (Bijl and Ravelli, 2000a; Mintz et al., 1992). Since persistence of a lower level of functioning predicts recurrence of a depressive episode, even after the symptoms of depression are alleviated (Faravelli et al., 1986; Judd et al., 2000; Judd and Akiskal, 2000; Solomon et al., 2004; Spijker et al., 2004b), insight into the course of social and physical functioning of persons with depressive disorders, and into the determinants of an impaired recovery of functioning may facilitate recurrence prevention and limit the burden of disease. Moreover, much less work have been done in studying the possible correlations between antidepressant medication and the level of functioning in remitted depressed patients. The purpose of our study is to compare the level of functioning in remitted depressed patients treated with SSRI or TCA.

The objective of our study is to compare whether the patients with therapeutic response from the 2 groups (SSRI or TCA) differ regarding cognitive functioning both in acute phase and during remission.
Materials and methods

Participants

The present study evaluates the subjects successfully treated with SSRI or TCA for an MDD episode; the evaluation was performed for a period of 2 years during 6 visits. Patients analyzed were treated in our hospital for MMD between January 2004- December 2007. We take in consideration for this paper only the subjects who finished the study period of 2 years and showed clinical response at 3 months. The study is designed to assess the possible different effects of SSRI and TCA treatments on cognitive functions in our patients with MDD, therefore we chosen to analyze only the data for successfully treated patients in order to eliminate the putative effects of acute depression on cognitive functioning.

Inclusion and exclusion criteria

Patients participating in our study had to meet the following inclusion criteria: diagnosis of Major Depressive Disorder according to DSM-IV criteria made by a senior psychiatrist, score of 24 points or higher in the Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979), score of 24 points or higher in the MMSE (Folstein et al., 1975) scale , age between 18 and 55 years old, antidepressant drug-free for minimum 6 months before the study and drug-free of other psychopharmacological compounds, never treated with the antidepressant used during the study, obtaining remission with the same antidepressant medication during the study.

Statistical analyses.

We used independent T-sample test to compare the 2 groups, using as dependent variable MADRS score, MMSE score and Rey score. The analyses were carried out with SPSS 13.

Instruments

The subjects were assessed by means of the MADRS scale, the MMSE scale and Rey scale (Rey, 1961).

Depression severity: MADRS scale. The main measure was the total score.

Overall cognitive functioning: MMSE scale. The main measure was the total score also.

Verbal learning and memory: Rey Test). The main measure is the sum of number of words recalled in the fifth trial.

Shehan Disability Scale (SDS). The main measure is the sum of three domains.

Procedure

Initially and during the study, the subjects were tested with the clinical and neuropsychological tests described above. Patients from the 2 groups which present therapeutic response were treated with standard doses of SSRI or TCA used in clinical practice. All the subjects were tested with the same clinical and neuropsychological tests. We evaluate in this paper only the patients who finished the 2 year study period.
Results

No differences exist among the two groups regarding age, gender, and years of formal education. The table 1 below presents demographical and socio-economic status of the patients.

<table>
<thead>
<tr>
<th></th>
<th>SSRI (%)</th>
<th>TCA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%females, %males)</td>
<td>49 (16 males-32.7%, 33 females-67.3%)</td>
<td>25 (10 males-40%, 15 females-60%)</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>42.08(+/-8.09)</td>
<td>42.56(+/-7.65)</td>
</tr>
<tr>
<td>Education</td>
<td>No education 3 (6.1%)</td>
<td>No education 1 (4%)</td>
</tr>
<tr>
<td></td>
<td>4 years 5 (10.2%)</td>
<td>4 years 4 (16%)</td>
</tr>
<tr>
<td></td>
<td>8 years 10 (20.4%)</td>
<td>8 years 3 (12%)</td>
</tr>
<tr>
<td></td>
<td>High school 21 (42.9%)</td>
<td>High school 12 (48%)</td>
</tr>
<tr>
<td></td>
<td>University 10 (20.4%)</td>
<td>University 5 (20%)</td>
</tr>
<tr>
<td>Marital status</td>
<td>Unmarried 4 (8.2%)</td>
<td>Unmarried 2 (8%)</td>
</tr>
<tr>
<td></td>
<td>Married 18 (36.7%)</td>
<td>Married 6 (24%)</td>
</tr>
<tr>
<td></td>
<td>Divorced 18 (36.7%)</td>
<td>Divorced 9 (36%)</td>
</tr>
<tr>
<td></td>
<td>Widow 2 (4.1%)</td>
<td>Widow 1 (4%)</td>
</tr>
<tr>
<td></td>
<td>Concubine 7 (14.3%)</td>
<td>Concubine 7 (28%)</td>
</tr>
<tr>
<td>Professional status</td>
<td>Farmer 10 (20.4%)</td>
<td>Farmer 5 (20%)</td>
</tr>
<tr>
<td></td>
<td>Unqualified worker 8 (16.3%)</td>
<td>Unqualified worker 3 (12%)</td>
</tr>
<tr>
<td></td>
<td>Qualified worker 3 (6.1%)</td>
<td>Qualified worker 4 (16%)</td>
</tr>
<tr>
<td></td>
<td>Medium qualified 15 (30.6%)</td>
<td>Medium qualified 7 (28%)</td>
</tr>
<tr>
<td></td>
<td>Professionals 8 (16.3%)</td>
<td>Professionals 3 (12%)</td>
</tr>
<tr>
<td></td>
<td>Management 2 (4.1%)</td>
<td>Management 2 (8%)</td>
</tr>
<tr>
<td></td>
<td>Employer 2 (4.1%)</td>
<td>Employer 1 (4%)</td>
</tr>
<tr>
<td></td>
<td>Retired 1 (2%)</td>
<td>Retired 1 (2%)</td>
</tr>
</tbody>
</table>
There were not found statistical differences between the groups regarding therapeutic remission during the study and at the end point in this population of patients which is obvious since we selected only patients with remission. Both groups presented therapeutical remission at 3 months as showed in graph 1.

As shown in graphs 2 and 3 the patients in remitted phase performed better on cognitive functioning than patients in acute phase. As shown in graphs 2 and 3 the patients in remitted phase performed better on cognitive functioning than patients in acute phase.

According to graphs 2 and 3 initially there were no differences regarding cognitive functioning between the 2 groups: MMSE (p=0.374), Rey (p=0.415). After 3 months of treatment there weren’t significant differences between the groups: MMSE (p=0.685) and Rey (p=0.279); the same for 6 months of treatment: MMSE (p= 0.623) and Rey (p= 0.452). The differences in cognitive functioning between the 2 groups became significant (better cognitive functioning in SSRI group compared with TCA group) at 1 year of treatment: MMSE-p=0.009, Rey-p=0.01. The difference continue to be significant favoring SSRI at 18 months: MMSE-p=0.001, Rey-p=0.001, and the performances remain better for the SSRI group until the end of treatment period: MMSE-p=0.001 and Rey-p=0.001
As shown in graph 4 at the beginning of the study, there weren’t significant differences regarding global functional impairment: at V1 (p=0.208) and after 3 months-V2 (p=0.943). The difference between groups remains the same after 6 months-at V3 (p=0.363). After 1 year of treatment (V4), patients treated with SSRI estimated a global functions improvement, according to SDS (p=0.015). A decrease in SDS score is seen after 18 months of treatment, being statistical significant, only in patients treated with SSRI- V5 (p=0.001). At the final visit, (24 months) patients in the SSRI group scored better in global functions which demonstrated a significant decrease in global impairment vs TCA patients (p=0.01).
**Discussions. Conclusions.**

Data shows that MDD patients treated with SSRI perform better than patients treated with TCA on verbal memory and overall cognitive functioning after 1 year of continuous treatment, and this differences increase at the end of study (2 years with continuous medication). There weren’t significantly differences between the 2 groups on cognitive function during the first year. In the present work, our data indicate that, when MDD patients were in remission phase, those treated with SSRI continued to improve their verbal episodic memory functioning, and cognition as measured with MMSE while the memory levels of those treated with TCA and MMSE level tend to remain quite stable even though they had a small improvement. Because both groups equally improved on depression, we can assume that the differences in cognitive functioning between groups are somehow related to medication. Usually there is an improvement in cognition together with the improvement of depression, yet the cognitive deficits in depressed people most probably persist in remitted phase. We can therefore just speculate that either SSRI per se improve cognitive functioning in depressed people, either TCA exerts a deleterious effect on cognition in depressed patient. Either way, the differences became significant only after 1 year of continuous treatment. Regarding global disability, when MDD patients were in remission phase, those treated with SSRI continued to improve their global functioning, and psychosocial performances as measured with SDS while the disability levels of those treated with TCA also improved but to a lesser degree. Because both groups equally improved on depressive symptoms, we can assume that the differences in global psychosocial functioning between groups are somehow related to medication. Our data show that global disability in remitted depressed patients could be more or less affected by the pharmacological treatment, and the positive effects caused on psychosocial functioning by the SSRI over the TCA treatment are persistent on a longer period in remitted depressed patients.
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Dec 2008-may2009: Project Coordinator-Phare 018-147.03.12/2006 Project; SamuSocial Romania;  
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Publications:
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Skills and Qualifications:
• Microsoft Office, Internet
• Fluent in English and French

References: References available upon request.