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**Treatment with Ziprasidone for Schizophrenia Patients with OCD**

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Abstract

Comorbidity of obsessive-compulsive disorder (OCD) has been observed in about 15% of schizophrenic patients and has been associated with poor prognosis. Therefore, there is a need for specific treatment options for these patients (schizo-obsessive, ScOCD).

This is an open, prospective study, aiming to test the efficacy of Ziprasidone (80 to 200 mg/d) in ScOCD patients and comparing the response to the treatment between stable schizophrenic (N=16) and stable ScOCD (N=29) patients.

Treatment effect with Ziprasidone was different in schizophrenic patients when stratified based on OCD comorbidity. Overall, the effect on OCD symptoms (as measured by the Yale Brown Obsessive Compulsive Scale, YBOCS) was found to be bimodal—either no response or exacerbation (for 45% of the patients, n=13) or significant improvement of symptoms (55%, n=16). Those who improved in OCD symptoms, improved also in negative and general schizophrenia symptoms, whereas ScOCD-unimproved group worsened in all symptoms. Whereas schizophrenic patients without OCD responded in a modest Gaussian distribution, they improved in schizophrenia negative symptoms and in general anxiety.

This data suggests that schizo-obsessive disorder is a distinct and complex condition with more than one underlying pathogenesis. Definition of these ScOCD subgroups defined by their response to Ziprasidone might contribute to personalized medicine within the OCD-schizophrenia spectrum. Moreover, this finding suggests that ScOCD might be considered as a special schizophrenic subtype and their inclusion in
schizophrenia treatment studies need to be further explored due to their divergent response.

Keywords: schizophrenia, OCD, Ziprasidone, personalized medicine.
Introduction

Schizophrenia and obsessive-compulsive disorder (OCD) are distinct diagnostic entities with a high co-occurrence. Reports from epidemiological studies suggest considerably higher-than-expected co-morbidity rates. The prevalence of clinically-significant obsessive compulsive symptoms (OCS) in patients with schizophrenia ranging between 10% and 59% (Fabisch et al., 2001; Bland, Newman, & Orn, 1987; Berman, Kalinowski, Berman, Lengua, & Green, 1995; Lysaker et al., 2000; Porto et al., 1997) and between 7.8% and 29% of the schizophrenia population who meet the DSM-IV criteria for OCD (Porto et al., 1997; Eisen et al., 1997; Bermanzohn et al., 2000; Tibbo et al., 2000; Poyurovsky et al., 2001). This high prevalence rate does not appear to be the consequence result of neither chronic disease or treatment, as a similar prevalence of OCD (14%) was found amongst untreated schizophrenic patients during their first psychotic episode (Poyurovsky, Fuchs, & Weizman, 1999). Moreover, OCD comorbidity also appears to be a predictor for a poor prognosis (Berman et al., 1995; Lysaker et al., 2000; Fenton & McGlashan, 1986; Hwang, Morgan, & Losconzcy, 2000; Ohta, Kokai, & Morita, 2003) and significant neuropsychological impairments (Lysaker et al., 2000; Hwang, Morgan, & Losconzcy, 2000; Berman et al., 1998; Lysaker et al., 2002; Whitney et al., 2004; Patel et al., 2010).

Currently there are only few studies that address pharmacological options for the treatment of patients with schizophrenia and OCD (schizo-obsessive, ScOCD) (Poyurovsky et al., 2012). The commonly-accepted treatment approach is to use a combination of neuroleptics with anti-obsessive medications (Zohar, Kaplan, & Benjamin, 1993; Reznik & Sirota, 2000; Berman, Sapers, & Chang et al., 1995;
Poyurovsky et al., 1999). However, the outcome is rather disappointing (Poyurovsky & Koran, 2005). Indeed, a therapeutic lacuna for this subset of patients is consensually acknowledged (Zohar, 1997). To the best of our knowledge, this is the first study to compare the effects of a given medication (Ziprasidone in this case) between schizophrenic patients with and without OCD.

The mixed dopaminergic-serotoninergic antipsychotics – known as second generation, or atypical, antipsychotics (SGA) – are theoretically ideally suited to ScOCD patients because of their affinity to both the dopaminergic and the serotoninergic systems. (Hwank et al., 2009). However, several studies have reported opposite results, namely, an exacerbation of OCS following treatment with Clozapine (Baker et al., 1992; Reznik et al., 2004), Olanzapine (de Haan et al., 2002; Lykouras et al., 2000), and Risperidone (Alevizos et al., 2002), while others report contradictory findings (Poyurovsky et al., 2000; Veznedaroglu et al., 2003; Baker et al., 1996). Similarly, there are paradoxical results for Quetiapine as well (Tranulis et al., 2005).

The antipsychotic medication Ziprasidone is a potent antagonist at 5-HT2A and D2 receptors with a high 5-HT2A/D2 affinity ratio. It is also a 5HTT reuptake inhibitor that exhibits potent interaction with 5-HT1A, 5-HT1D, and 5-HT2C receptor subtypes (Stahl et al., 2003). Clinical trials suggest that this drug is effective in treating both positive and negative symptoms of schizophrenia and schizoaffective disorders, and also proving efficacious in the treatment of affective symptoms in schizoaffective patients (Weiden et al., 2003; Gunasekara et al., 2002; Simpson et al., 2004). Given Ziprasidone’s unique pharmacological properties in comparison with other SGAs with respect to 5HT1D and the latter’s potential role in the treatment of obsessive compulsive symptoms (Zohar et al., 2004), Ziprasidone appears to constitute a
promising treatment option for ScOCD patients. We therefor initiated a study of Ziprasidone in this population subset.

The aim of the current study was to test the effect of Ziprasidone on ScOCD patients, employing the Yale-Brown Obsessive Compulsive Scale (YBOCS) and Positive and Negative Syndrome Scale (PANSS). In order to evaluate this effect, we also compared treatment response between ScOCD and schizophrenic patients without OC symptoms.
Methods

Participants

The study population consisted of 45 in- and out-patients receiving treatment at the Psychiatry Department at Chaim Sheba Medical Center who met the DSM-IV criteria for schizophrenia. Only adults (ages 18-65) who had been diagnosed at least 6 months previously and who have been stable on their antipsychotic medication for at least two months, scoring a minimum of 60 on the PANSS, were admitted to the study. Patients already receiving Ziprasidone, those diagnosed as suffering from a schizophreniform disorder, organic brain syndrome, mental retardation and/or pervasive developmental disorder, who exhibited a recent history of substance abuse or dependence, or suffered from any significant cardiovascular illness were excluded from the study. Of those admitted, 29 had concurrent OCD with a minimal score of 14 on the YBOCS (referred to herein as the “ScOCD group”) and 16 non-OCD schizophrenia (referred to herein as the “Sc group”). Of the ScOCD group, 18 patients (62%) had OCD before schizophrenia, and 11 (38%) had schizophrenia before OCD (see Table 1). The study was approved by the Institutional Review Board of Sheba Medical Center. All the subjects gave their written informed consent after being given a full explanation of the study’s protocol.

Table 1 presents the demographic and clinical characteristics of the participants during their baseline assessment.

Table 1
Study design

This study was open, prospective with a parallel group design, comparing response to treatment with Ziprasidone in patients with schizophrenia (Sc) (N=16) to patients with schizophrenia and OCD (ScOCD) (N=29). The participants underwent an initial screening evaluation based upon a medical and psychiatric assessment and completion of a demographic data questionnaire. The Structured Clinical Interview for DSM IV (SCID) was used for the diagnosis of schizophrenia and OCD during the initial baseline evaluation visit. Ratings included the Positive and Negative Syndrome Scale (PANSS), the Yale-Brown Obsessive Compulsive Scale (YBOCS), the Clinical Global Impressions—Severity of Illness (CGI-S) and Clinical Global Impressions—Improvement (CGI-I) scales, and the Global Assessment of Functioning (GAF) scale. Patients with YBOCS rates $\geq 14$ at the baseline visit were classified as ScOCD.

After a full evaluation, the patients were down-titrated from their current antipsychotic medication (Risperidone [N=18], Olanzapine [N=14], Quetiapine [N=4], Zuclopenthixol [N=3], Perphenazine [N=2], Clozapine [N=2], Ridazine [N=1], Penfluridol [N=1]), and Ziprasidone was increased gradually until reaching the dose of 80-200 mg/day according to clinical considerations. Other concomitant medications, like SRI (fluoxetine, citalopram, and paroxetine), benzodiazepines (haloperidol), and non-benzodiazepines anxiolytics (risperidal), were continued. Each patient was monitored using the above ratings at baseline and at the end of weeks 2, 5, and 8.

Statistical analysis

Baseline characteristics were analyzed using chi-square test for categorical variables and Multivariate analysis of variance (MANOVA) for continuous variables. In the
first analysis, we measured the effect of Ziprasidone on ScOCD using one-way repeated-measures ANOVA, week of treatment serving as a within-subject variable. This analysis was carried out separately on the PANSS, YBOCS, CGI, and GAF scores. Due to bimodality in their YBOCS scores, the ScOCD participants were divided into two subgroups—ScOCD-improved (change of 25% and above) and ScOCD-unimproved. The YBOCS divergence between these subgroups was tested using two-way repeated-measures ANOVA, week of treatment serving as a within-subject variable and the ScOCD sub-group as a between-subjects variable.

The second analysis included comparison of the PANSS, YBOCS, CGI, and GAF scores between the ScOCD and Sc groups, using two-way repeated measures ANOVA with week of treatment as a within-subject variable and ScOCD sub-group as a between-subjects variable. All PANSS analyses were carried out using multivariate repeated measures ANOVA for including PANSS subscales.
Results

1. Ziprasidone effect on ScOCD

A significant effect of Ziprasidone was found on the YBOCS scores ($F_{(3,84)} = 4.42$, $p < .01$). However, no effect was found on any PANSS subscales ($F_{(9,252)} = .74$, $p > .05$), CGI-S ($F_{(3,84)} = .78$, $p > .05$), CGI-I ($F_{(2,56)} = 1.09$, $p > .05$), or GAF ($F_{(3,84)} = .64$, $p > .05$). Close examination of the data revealed that the percentage of improvement from week 0 to week 8 in YBOCS was characterized by a bimodal distribution (Skewness = 0.05, Kurtosis = -0.57) (Figure 1), whilst the other scales demonstrating Gaussian distributions. Based on this analysis, ScOCD participants were subdivided into two subgroups: ScOCD patients with 25% or more YBOCS improvement (referred to herein as “ScOCD-improved”) and ScOCD patients with no response or symptom exacerbation (referred to herein as “ScOCD-unimproved”). Table 1 presents the demographic and clinical characteristics for these sub-groups during their baseline assessment. At baseline, the ScOCD-improved had higher PANSS positive and total scores and rated more severe on the CGI-severity.

Figure 1

Table 2 presents the results for the effect of week of treatment, ScOCD subgroups, and week of treatment X ScOCD subgroups interaction for the study measures. While the results indicate a significant effect for week of treatment and ScOCD subgroups with respect to CGI-I, significant week of treatment X ScOCD subgroup was found for all the measures (Table 2 and Figures 2-5).

Table 2
Figures 2-5

A separate post hoc repeated-measures ANOVA for each group demonstrated significant improvement for the ScOCD-improved group in all the measures, with the exception of PANSS positive (YBOCS: $F_{[3,42]} = 38.31, p<.001$; PANSS positive: $F_{[3,42]} = 1.93, p>.05$; PANSS negative: $F_{[3,42]} = 6.05, p<.01$; PANSS general: $F_{[3,42]} = 7.91, p<.01$; PANSS total $F_{[3,42]} = 6.5, p<.05$; CGI-S: $F_{[3,42]} = 3.82, p<.05$; CGI-I: $F_{[2,26]} = 4.12, p<.05$; GAF: $F_{[3,42]} = 4.44, p<.05$) and significant worsening in the ScOCD-unimproved group on all the measures and a marginal decline on the PANSS positive and GAF scores (YBOCS: $F_{[3,39]} = 4.71, p<.05$; PANSS positive: $F_{[3,39]} = 4.00, p<.06$; PANSS negative: $F_{[3,39]} = 4.28, p<.05$; PANSS general: $F_{[3,39]} = 4.81, p<.05$; PANSS total: $F_{[3,39]} = 4.93, p<.05$; CGI-S: $F_{[3,39]} = 6.45, p<.05$; CGI-I: $F_{[2,28]} = 5.87, p<.01$; GAF: $F_{[3,39]} = 3.83, p<.07$).

2. Ziprasidone effect on ScOCD vs. schizophrenia patients

Table 3 presents the ScOCD and Sc scores on study measures by week of treatment. Sc patients responded to Ziprasidone significantly better than ScOCD patients, as measured by PANSS general and total scores ($F_{[1,43]} = 14.673, p<.001$ and $F_{[1,43]} = 5.329, p<.05$, respectively) and marginally better on the CGI-S scale ($F_{[1,43]} = 3.686, p<.06$). An overall decrease in the PANSS negative score occurred during the period of the study ($F_{[3,129]} = 5.453, p<.01$), with an interaction of week of treatment X group ($F_{[3,129]} = 4.528, p<.01$).

Discussion

Schizophrenic patients response to treatment with Ziprasidone was different when stratified based on comorbidity to OCD. The effect of Ziprasidone upon schizo-
obsessive patients (as measured by Y-BOCS) was bimodal—approximately half demonstrating a clinical improvement (at least 25%, Koran et al., 2002; Koran and Simpson, 2013) and the other half no response or an exacerbation of their symptoms in particular. This biomodel response is in line with previous work which suggest a complex and at times opposite response to D2 activation (respond to both D2 antagonist and dopamine release) (Koran et al., 2002). It highlight the heterogeneous response to Ziprasidone in Schizophrenic patients in general and for ScOCD patients in particular, and emphasize the need for a personalized approach.

With respect to the ScOCD-unimproved group, the results are commensurate with the lack of effect or even exacerbation of OCD in some ScOCD patients (Baker et al., 1992; de Haan et al., 2002; Lykouras et al., 2000; Alevizos et al., 2002). Indeed other studies also indicating the response to treatment—especially with “atypical” antipsychotics (D2/5HT2 antagonists)—to be bi-directional (Hwank et al., 2009; Reznik et al., 2004; Poyurovsky et al., 2000; Veznedaroglu et al., 2003; Baker et al., 1996; Tranulis et al., 2005). These results suggest that schizo-obsessive disorder is a complex condition with more than one underlying pathogenesis.

One of the limitations of this study is its small and unequal sample size—in particular the schizophrenia without OCD group. The criteria for admission including at least two months’ stability on medication and schizo-obsessive patients frequently being treatment resistant and exhibiting severe residual symptoms (Berman et al., 1995; Fenton & McGlashan, 1986; Hwang, Morgan, & Losconzcy, 2000), more of these patients were referred than schizophrenia patients without OCD.

Another limitation is the relatively short follow up period, as late onset treatment response in OCD patients is quite common (Bandelow et al., 2008). While eight weeks might not be sufficient to achieve a maximal response in the OC component,
an evident response difference was observed between the two schizo-obssessive subgroups under identical conditions (same rating scales, rater [AJ-W], and time framework).

Patients enrolling in the study having been stable on antipsychotic medication for at least two months prior to entering the study, they lay largely at their baseline. This partially explains the relatively low PANNS positive scores at the beginning of the study and the relatively minor response to the Ziprasidone treatment.

Open studies are vulnerable to obvious limitations—including potentially biased ratings and placebo effects. The bimodal and opposite response—clear responders vs. clear exacerbators—in the schizo-obssessive group appears to suggest that no set bias existed, the rated response not being unidirectional.

While the unequal number of ScOCD (N=29) vs. schizophrenia (N=16) patients may have created a statistical imbalance, the study participants were in fact divided into three (Sc, ScOCD-improved, and ScOCD-unimproved) rather than two groups (Sc and ScOCD), each having roughly equal numbers. Thus, despite the small number, the statistically-significant therapeutic differences between the groups indicate the findings’ clinical significance.

The inequality in terms of gender between the ScOCD (15 females and 14 males) and schizophrenia (15 females and 1 male) groups might hamper the interpretation of those results (Table 1). When the analysis was repeated with females only, the same results emerged. In future studies, close attention should be given to gender.

This study—in which one patient was helped by the drug and another was not—further demonstrates the need for stratified medicine in psychiatry. While characterizing subgroups and hence enhancing prediction of treatment response to Ziprasidone in the schizo-obssessive population would be of great clinical importance,
This study demonstrated no significant differences between these two subgroups with respect to age, marital status, gender, age of onset, duration of OCD or schizophrenia, family history, or type of symptom. Nevertheless, recognizing the differential response to the same intervention (Ziprasidone in this study) might be a step towards delineation of specific subgroups within the OCD-schizophrenia axis. If other endophenotypic markers for these subgroups will be found, it might pave the way to the hypothesis about specific subgroups within the ScOCD range (Hwank et al., 2009; Baker et al., 1992; Reznik et al., 2004; de Haan et al., 2002; Lykouras et al., 2000; Alevizos et al., 2002; Poyurovsky et al., 2000; Veznedaroglu et al., 2003; Baker et al., 1996; Tranulis et al., 2005).

Recent clinical and biological findings have provided better insight into the schizo-obsessive phenomenon (Patel et al., 2010, Pallanti et al., 2009, Hwang et al., 2000). As schizo-obsessive patients continue to challenge clinicians, the currently-available evidence calls for comprehensive clinical and neuropsychological assessment—as well as personalized pharmacological interventions. The administration of Ziprasidone was particularly helpful and leading to an improvement in all the clinical measures amongst approximately half of the schizo-obsessive patients in our study. Hence this study suggests that Ziprasidone is a therapeutic option to be considered in those patients.

While schizophrenia and obsessive-compulsive disorder are separate nosological entities with discrete underlying brain mechanisms, clinical presentations, and treatments, they appear to co-exist in a greater proportion of patients than might be expected (Fabisch et al., 2001; Bland, Newman, & Orn, 1987; Berman, Kalinowski, Berman, Lengua, & Green, 1995; Lysaker et al., 2000; Porto et al., 1997 Eisen et al., 1997; Bermanzohn et al., 2000; Tibbo et al., 2000; Poyurovsky et al., 2001;
Poyurovsky, Fuchs, & Weizman, 1999). Schizo-obsessive patients exhibit distinct clinical features and a different pattern of co-morbidity than schizophrenia patients (Berman et al., 1995; Lysaker et al., 2000; Fenton & McGlashan, 1986; Hwang, Morgan, & Losconzcy, 2000; Ohta, Kokai, & Morita, 2003; Berman et al., 1998; Lysaker et al., 2002; Whitney et al., 2004; Patel et al., 2010; Patel et al., 2010). Preliminary reports are also suggesting a distinct neuro-anatomical profile (Aoyama et al., 2000). Several studies have found that schizo-obsessive patients exhibit more soft neurological signs and neurocognitive deficits (Patel et al., 2010; Pallanti et al., 2009), indicating that obsessive-compulsive symptoms represent a clinically meaningful dimension of psychopathology in schizophrenia, with distinct clinical and neurobiological characteristics. Growing evidence thus points towards the existence of a schizo-obsessive subtype of schizophrenia (Poyurovsky et al., 2012).

The traditional methods employed by studies do not emphasize individual variations in responses to treatment. This study suggests the need for stratified medicine in psychiatry—specifically, the paying of particular attention to schizo-obsessive patients in order to ensure better treatment targeting. In the light of “individualized medicine” and in order to prevent any “blurring” of results, the exclusion of this subset of schizophrenia patients (ScOCD) from studies on the effect of “antipsychotic” drugs in schizophrenia should be reevaluated.

Conclusion

From the therapeutic perspective and in line with the promotion of personalized medicine, this open prospective pilot study suggests that ScOCD patients respond differently to Ziprasidone. As approximately half of them finding the intervention
particularly beneficial, it indicates that Ziprasidone trial constitutes a reasonable therapeutic option for such patients.

Theoretically, the biphasic distribution of response to Ziprasidone—clear responders versus exacerbators—together with earlier reports of exacerbation or de novo surfacing of OC symptoms following the administration of Clozapine and/or other D2/5HT2 antagonists suggests a divergent underlying pathology. Following up this lead may uncover a hidden endophenotype door.

From a methodological point of view, the different response of ScOC (as compared to Sc without OCD) suggests that including ScOC patients in treatment studies has a potential to blur the signal as those patients respond differently to D2/5HT2 antagonist as compared to schizophrenic patients without OCD.

The conceptual framework of this study was to focus on symptoms (OCD) rather than syndrome (schizophrenia) accordingly, tested the response along the domains of compulsivity, negative symptoms etc. this approach is in line with the Research Domain Criteria (RDoC), which suggest examining domain across different diagnosis ("horizontal" vs. "vertical" approach). Indeed, the main finding of this study is that compulsivity as a domain should be taken into account both in the clinical level and the drug design study as it affected the outcome of drug intervention.
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<table>
<thead>
<tr>
<th></th>
<th>Schizophrenia (without OCD) (N=16)</th>
<th>ScOCD (N=29)</th>
<th>ScOCD-improved</th>
<th>ScOCD-unimproved</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>39.25 (15.17) (11.77)</td>
<td>38.59</td>
<td>34.6 (11.6)</td>
<td>35.6 (14.3)</td>
</tr>
<tr>
<td><strong>Sex (m/f)</strong></td>
<td>1/15</td>
<td>14/15</td>
<td>8/7</td>
<td>6/8</td>
</tr>
<tr>
<td><strong>χ² (1) = 8.195</strong></td>
<td><strong>F (1,45) = .027</strong></td>
<td><strong>χ² (1) = .037</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean age at onset of schizophrenia</strong></td>
<td>28.93 (12.0) (5.33)</td>
<td>23.21</td>
<td>21.6 (5.4)</td>
<td>23.6 (6.1)</td>
</tr>
<tr>
<td><strong>Mean age at onset of OCD</strong></td>
<td>—</td>
<td>18.32 (10.68)</td>
<td>15.6 (2.7)</td>
<td>24.6 (13.5)</td>
</tr>
<tr>
<td><strong>Mean duration of schizophrenia (years)</strong></td>
<td>9.29 (9.79) (10.35)</td>
<td>15.38</td>
<td>13 (11.9)</td>
<td>12 (10.1)</td>
</tr>
<tr>
<td><strong>Mean duration of OCD (years)</strong></td>
<td>—</td>
<td>15.23 (10.47)</td>
<td>18.8 (9.0)</td>
<td>10.6 (9.6)</td>
</tr>
<tr>
<td><strong>Baseline PANSS positive</strong></td>
<td>14.38 (5.4) (6.0)</td>
<td>13.97</td>
<td>16.1 (6.7)</td>
<td>11.7 (4.4)</td>
</tr>
<tr>
<td><strong>Baseline PANSS negative</strong></td>
<td>26.88 (6.38) (5.73)</td>
<td>26.31</td>
<td>27.4 (5.7)</td>
<td>25.1 (5.7)</td>
</tr>
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</table>
Table 1: Mean (SD) and group differences of background and baseline variables for Schizophrenia patients with and without OCD

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>F(1,45)</th>
<th>P-value</th>
<th>F(1,29)</th>
<th>P-value</th>
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<tr>
<td>PANSS general</td>
<td>39.5 (8.68)</td>
<td>48.52</td>
<td>9/719**</td>
<td>.004</td>
<td>3.004</td>
<td>.051</td>
</tr>
<tr>
<td>PANSS total</td>
<td>80.75 (15.12)</td>
<td>88.79</td>
<td>2.347</td>
<td>.129</td>
<td>4.048*</td>
<td>.048</td>
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<tr>
<td>CGI-S</td>
<td>4.44 (.89)</td>
<td>4.76</td>
<td>1.375</td>
<td>.247</td>
<td>6.950*</td>
<td>.012</td>
</tr>
<tr>
<td>GAF</td>
<td>38.75 (12.5)</td>
<td>37.48</td>
<td>.156</td>
<td>.695</td>
<td>2.250</td>
<td>.135</td>
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<tr>
<td>YBOCS</td>
<td>—</td>
<td>23.97</td>
<td>—</td>
<td>—</td>
<td>1.541</td>
<td>.219</td>
</tr>
<tr>
<td>Treated with SRIs</td>
<td>3</td>
<td>23</td>
<td>15.502***</td>
<td>.0009</td>
<td></td>
<td></td>
</tr>
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</table>

*p = .07, *p < .05, **p < .01, ***p < .001

ScOCD = Schizophrenia with OCD
<table>
<thead>
<tr>
<th></th>
<th>Week of treatment</th>
<th>ScOCD subgroups</th>
<th>Week of treatment X ScOCD subgroups</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>YBOCS</strong></td>
<td>8.49**</td>
<td>2.32</td>
<td>34.47***</td>
</tr>
<tr>
<td>PANSS positive</td>
<td>.61</td>
<td>.28</td>
<td>5.41*</td>
</tr>
<tr>
<td>PANSS negative</td>
<td>1.5</td>
<td>.11</td>
<td>8.81***</td>
</tr>
<tr>
<td>PANSS general</td>
<td>.54</td>
<td>.17</td>
<td>11.53***</td>
</tr>
<tr>
<td>PANSS total</td>
<td>.66</td>
<td>.003</td>
<td>10.56**</td>
</tr>
<tr>
<td>CGI-S</td>
<td>1.08</td>
<td>.67</td>
<td>9.13**</td>
</tr>
<tr>
<td>CGI-I</td>
<td>1.46</td>
<td>18.8***</td>
<td>8.71**</td>
</tr>
<tr>
<td>GAF</td>
<td>.89</td>
<td>.07</td>
<td>7.35**</td>
</tr>
</tbody>
</table>

*p<.05; **p<.01; ***p<.001

Table 2: Repeated measures ANOVA results (F) for the effect of week of treatment / ScOCD subgroups and week of treatment X ScOCD subgroups interaction

<table>
<thead>
<tr>
<th></th>
<th>Week 0</th>
<th>Week 2</th>
<th>Week 5</th>
<th>Week 8</th>
<th>p^a</th>
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<tbody>
<tr>
<td><strong>PANSS positive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ScOCD</td>
<td>13.97 (6.0)</td>
<td>13.07 (5.8)</td>
<td>14.38 (6.1)</td>
<td>13.83 (6.8)</td>
<td>.545</td>
</tr>
<tr>
<td>Sc</td>
<td>14.38 (5.4)</td>
<td>14.94 (5.8)</td>
<td>14.00 (5.4)</td>
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<td>48.97 (11.1)</td>
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* Effect for week of treatment

Table 3: Mean (SD) scores for all the study measures and the effect of week of treatment for ScOCD and Sc patients by week of treatment
Figure 1: Distribution of the percentage of improvement in YBOCS from week 0 to week 8 for ScOCD group
Figure 2: Mean (SE) of YBOCS score by week of treatment for ScOCD subgroups
Figure 3: Mean (SE) of PANSS subscales by week of treatment for ScOCD subgroups
Figure 4: Mean (SE) CGI severity and improvement by week of treatment for ScOCD subgroups
Figure 5: Mean (SE) GAF by week of treatment for ScOCD subgroups