Psychopharmacology of Comorbid Obsessive-Compulsive Disorder and Depression

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A high degree of comorbidity appears to exist between obsessive-compulsive disorder (OCD) and depression, both with respect to symptomatology and at the syndromal level. It has been argued that nonspecific effects on dysphoric mood, anxiety, and depressive symptoms account for the therapeutic efficacy of antidepressants in OCD. However, several controlled studies have shown that neither the presence nor initial severity of depression has any impact on therapeutic improvement in OCD. In particular, studies with the serotonin selective reuptake inhibitors (SSRIs) fluvoxamine and fluoxetine have revealed beneficial effects in OCD, irrespective of the presence of depressive symptoms. The efficacy of the other SSRIs in OCD requires further study. In conclusion, the improvement in OC symptoms seen with fluvoxamine and fluoxetine does not depend on concomitant affective disorder.
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COMORBIDITY OF OBSESSIVE-COMPULSIVE DISORDER AND DEPRESSION

Evidence from a number of studies suggests the presence of a significant overlap with respect to symptomatology between obsessive-compulsive disorder (OCD) and depression. For example, in a retrospective study of 398 depressed patients conducted by Gittleson,[1] 152 (38%) were also found to show obsessional symptoms. Similarly, in a prospective study in 92 depressed patients, 20 (22%) also suffered from obsessive-compulsive symptoms.[2]

A high degree of comorbidity at a syndromal level has also been reported. In a study conducted in 44 patients with OCD, Rasmussen and Tsuang[3] found that 80% also reported dysphoric mood while 75% either were currently suffering from or had a history of depression.

In general, patients seem somewhat more likely to develop symptoms of depression during the course of OCD rather than developing OCD secondary to depression. In a study of 62 OCD patients conducted by Demal et al.,[4] only 13 (21%) did not have symptoms of depression; 18 (29%) had primary depression followed by development of OCD; and 23 (37%) had secondary depression subsequent to OCD, while the relationship between OCD and depression was ill-defined in 8 (13%).

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EFFECT OF COMORBIDITY ON THERAPEUTIC OUTCOME

Some studies have shown that OCD and depressive symptomatology improve in parallel when treated with antidepressants such as clomipramine, and it has been argued that the nonspecific effects on dysphoric mood, anxiety, and depressive symptoms determine the therapeutic success of this class of compounds in patients with OCD. In a study reported by Marks in 1983,[5] OCD patients who were also suffering from depression at baseline improved to a significantly ($p \leq .05$) greater extent when treated with clomipramine than those who did not have depression. This statistically significant difference was seen in scores for depression ($p = .005$), OCD ($p = .005$), and obsessional symptoms ($p = .02$) measured using the Comprehensive Psychopathological Rating Scale (CPRS).

Several well-controlled studies, however, have shown that neither the presence nor the severity of initial depression has an impact on the degree of therapeutic improvement in OCD.

SEROTONIN SELECTIVE REUPTAKE INHIBITORS

The antiobsessional effects of serotonin selective reuptake inhibitor (SSRI) antidepressants, such as fluvoxamine and fluoxetine, do not appear to require a concomitant affective disorder.

Fluvoxamine

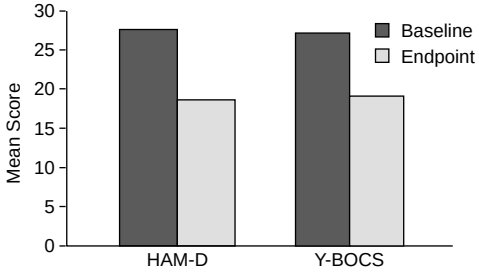
A number of double-blind, placebo-controlled studies have shown that fluvoxamine is superior to placebo in the treatment of OCD.[6–12] In particular, two recent 10-week studies involving a large number of patients (160 in each) have provided convincing evidence for the efficacy of fluvoxamine (100–300 mg/day).[10,11] Both reported that

Table 1. Correlation Between Change in Obsessive-Compulsive Symptoms and Baseline Depression After Treatment With Fluvoxamine (N = 16)*

Scale	Baseline HAM-D Score r	p	Baseline Beck Depression Score r	p
SCL-90 obsessive-compulsive score change	–.0935	.73	–.4466	.08
General Rating Scale score change				
Obsessions	.211	.47	–.0737	.80
Compulsions	.001	1.0	–.1303	.63
Maudsley Obsessive-Compulsive Inventory score change				
Obsessive-Compulsive Checklist score change	.2317	.39	–.0167	.95

*From reference 7, with permission.
Abbreviations: HAM-D = Hamilton Rating Scale for Depression, SCL-90 = Symptom Checklist-90.

Figure 1. Correlation Between Changes in Mean HAM-D and Y-BOCS From Baseline to Endpoint Following Treatment With Fluvoxamine (N = 40)*



*Data from reference 9. Abbreviation: Y-BOCS = Yale-Brown Obsessive-Compulsive Scale.

fluvoxamine was significantly ($p \leq .05$) more effective than placebo as assessed by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), the National Institute of Mental Health Obsessive-Compulsive (NIMH-OC) scale, and the Global Improvement item of the Clinical Global Impression (CGI) scale. The percentage of patients classed as responders was also significantly ($p \leq .05$) higher with fluvoxamine than with placebo. In addition, findings from a double-blind, comparative study conducted in 66 patients suggest that the efficacy of fluvoxamine is equivalent to that of clomipramine (33% and 31% reduction in mean Y-BOCS score, respectively).[13]

Although some of these studies have specifically excluded patients with concurrent depression,[6,8,13] the majority indicate that the improvement in obsessive-compulsive symptoms is not correlated with baseline Hamilton Rating Scale for Depression (HAM-D) score. For example, in a double-blind, placebo-controlled, crossover study conducted by Perse et al.,[7] 13 (81%) of 16 patients improved after 8 weeks' treatment with fluvoxamine (50–300 mg/day) compared with only 3 (19%) of 16 after the placebo phase. Although changes in obsessive-compulsive symptoms, as assessed by the Symptom Checklist-90 (SCL-90) obsessive-compulsive score, the General Rating Scale score, the Maudsley Obsessive-Compulsive Inventory score, and the Obsessive-Compulsive Checklist, were highly correlated with changes in depression, as assessed by the HAM-D score, SCL-90 depression score, and the Beck depression score, the presence of depression at the study onset was not significantly related to changes in obsessive-compulsive symptoms (Table 1). Indeed, it is interesting to note that the patient with the lowest baseline HAM-D score showed the greatest improvement on the Maudsley Obsessive-Compulsive Inventory.

Similar findings were reported in a double-blind comparison between fluvoxamine and desipramine carried out in 40 patients with a principal diagnosis of OCD.[9] Patients with concurrent depression (HAM-D ≥ 20 and DSM-III-R criteria) were included providing the depression was secondary to OCD and had occurred after the onset of OCD. Fluvoxamine (50–300 mg/day) was significantly more effective than desipramine in reducing obsessive-compulsive symptoms, as assessed by the Y-BOCS and the global response rate. In addition, fluvoxamine, but not desipramine, reduced the severity of secondary depression, as assessed by the HAM-D. However, although changes in the Y-BOCS correlated significantly with changes in the HAM-D (Figure 1), they were not correlated with the severity of the baseline depressive symptoms. Moreover, as reported by Perse et al.,[7] there was a trend toward a less favorable response to fluvoxamine in patients with more severe depression. For example, the baseline HAM-D tended to be somewhat lower in patients whose obsessive-compulsive symptoms responded to fluvoxamine compared with nonresponders ($p = .07$). Likewise, among the five patients who had HAM-D scores of more than 40 at baseline, only one was classed as a responder to fluvoxamine in terms of improvement in obsessive-compulsive symptoms while four of the five patients with the lowest HAM-D baseline scores were responders.

In an earlier placebo-controlled study that utilized the same inclusion criteria and was conducted in 42 patients with OCD, about 50% of whom also had concurrent depression, the beneficial effects of fluvoxamine on obsessive-compulsive symptoms were again not correlated with the severity of baseline depression.[11] As previously reported, the changes in the Y-BOCS correlated with changes in HAM-D, although antidepressant effects were not related to responses in obsessive-compulsive symptoms. There was no evidence of any significant reduction in the Hamilton Rating Scale for Anxiety in either group.

While patients with concurrent depression (HAM-D ≥ 20) were excluded from the studies reported by Goodman et al.[10] and Greist et al,[12] possible correlations between the presence of secondary depression (HAM-D > 12 but < 20) and the therapeutic response to fluvoxamine were investigated. Neither study suggested that the efficacy of fluvoxamine in OCD was biased by the presence of second-

ary depression, with similarly good therapeutic responses being observed in both subgroups of patients.

Fluoxetine

Positive results in the treatment of OCD have also been reported with another SSRI, fluoxetine.[14–17] In a recent double-blind study in 355 patients with OCD,[14] patients with comorbid nonbipolar depression were included providing depression was judged to be secondary to OCD and began after the onset of OCD. After 13 weeks of treatment, all doses of fluoxetine (20, 40, and 60 mg/day) were significantly superior to placebo on the Y-BOCS (obsession and compulsion subscores) and the HAM-D-17 total score, as well as the CGI severity and improvement scores, the Patient Global Impression Scale, and the CPRS. However, the beneficial effects on OCD were shown to be independent of the antidepressant response. In another large study conducted in 214 patients,[15] treatment with fluoxetine (40 or 60 mg/day) for 8 weeks was significantly more effective than placebo in reducing the total Y-BOCS score. Although patients with secondary depression were included in this study, any correlation between antidepressant effects and improvements in obsessions and compulsions was not analyzed. Similarly, this correlation was not assessed in a double-blind study reported by Pigott et al.[16] in which fluoxetine (up to 80 mg/day) and clomipramine (up to 250 mg/day) were both shown to significantly reduce Y-BOCS and HAM-D scores.

Other SSRIs

Experience with other SSRIs, including sertraline, paroxetine, and citalopram, in the treatment of OCD is currently limited. However, preliminary evidence suggests that both sertraline and paroxetine may have some beneficial effects in OCD, irrespective of the presence of depressive symptoms, although these findings are only speculative at present. Most of the data on paroxetine are unpublished, although it was shown to have similar efficacy to clomipramine in reducing obsessive-compulsive symptoms in a recent double-blind study conducted in 437 patients.[18] These findings, however, require confirmation in other double-blind studies. It is interesting to note, however, that a double-blind, placebo-controlled study conducted with sertraline[19] failed to confirm the efficacy demonstrated in an earlier open study.[20] None of these studies with other SSRIs have attempted to conduct a separate analysis of depression scores.

DISCUSSION

In summary, there is good evidence that the SSRIs fluvoxamine and fluoxetine are effective treatments for OCD, although the efficacy of sertraline, paroxetine, and citalopram requires further study. Most studies indicate that the improvement in obsessive-compulsive symptoms resulting from fluvoxamine or fluoxetine treatment appears to be unrelated to the presence or severity of initial depression. This suggests that the antiobsessional activity of these SSRIs is independent of any antidepressant effect.

Drug names: clomipramine (Anafranil), desipramine (Norpramin and others), fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft).

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