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Augmenting SRIs for OCD: Patient preference for risperidone does not limit effectiveness of exposure and ritual prevention

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Abstract

Patients with obsessive-compulsive disorder (OCD) often only partially respond to serotonin reuptake inhibitors (SRIs), the first-line pharmacotherapy for OCD. The American Psychiatric Association's Practice Guidelines suggest augmenting SRIs with either cognitive behavioral therapy consisting of exposure and ritual prevention (EX/RP) or antipsychotic medication (e.g., risperidone) [1]. EX/RP has been shown to be more effective [2]. However, some patients prefer medications over EX/RP [3]. How should treating clinicians respond in these situations? Conventional wisdom would suggest that patients who prefer one treatment may not benefit if assigned to another. Indeed, meta-analyses of randomized controlled trials (RCTs) show that patients are less likely to improve and more likely to drop out when matched to a therapy condition they did not prefer [4]. However, this issue has never been investigated empirically for OCD treatment specifically. Therefore, we examined the effect of patient preference on outcomes in a RCT of SRI augmentation in adult OCD patients. We specifically compared the effectiveness of EX/RP in OCD patients who stated that they prefer risperidone, and vice versa.

Data came from a two-site RCT of SRI augmentation in adults with OCD conducted at two academic clinics (clinicaltrials.gov identifier: NCT00389493). Full study methods, including inclusion/exclusion criteria, are described elsewhere [2]. Institutional Review Boards at both sites approved the study protocols, and patients provided written informed consent. Patients entered the study on stable SRI doses (12 weeks) and randomized to receive EX/RP (N=40), risperidone (N=40) or pill placebo (N=20; not analyzed here). Participants met with a

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study doctor who described each treatment arm as part of the consent process. Patients then completed a self-report assessment battery that included information sheets describing EX/RP and risperidone. Participants were asked to circle a response indicating whether they preferred EX/RP or risperidone. Patients then rated their preference strength by answering, “out of 100% how much do you want to receive this treatment?” No response option for “no preference” was offered. Patients were then randomized to receive 8 weeks of either: 1) EX/RP (2 introductory sessions followed by 15 exposure sessions delivered twice-weekly by doctoral-level psychologists) or 2) risperidone (dosing began at 0.25mg/day and increased to 4.0mg/day when clinically indicated).

Independent evaluators blind to treatment condition assessed OCD symptoms using the Yale-Brown Obsessive Compulsive Scale (YBOCS) [5] at baseline, mid-treatment, and post-treatment. Treatment response was defined as ≥25% reduction in symptoms [2]. Post-treatment wellness was defined *a priori* using previously established a indicator (YBOCS ≤12) [6]. Primary analyses compared groups' post-treatment YBOCS controlling for baseline YBOCS (ANCOVA) using an intent-to-treat (ITT) approach carrying forward last available observations. Alpha was set at $p < .05$ (two-tailed). Rates of response and post-treatment wellness were calculated for both the ITT and completer samples.

Fifty-three patients (67.9%) preferred EX/RP and 25 (32.1%) preferred risperidone. Preference strength ratings were higher among EX/RP-preferring patients ($M=87.6$, $SD=15.0$) than risperidone-preferring patients ($M=74.6$, $SD=17.44$, $t=3.38$, $p=.001$). Figure 1 shows study flow based on treatment preference. Only 1 of 11 (9.1%) risperidone-preferring patients dropped from EX/RP, a rate similar to EX/RP-preferring patients (2 of 28; 7.1%). In contrast, 7 of 25 (28%) EX/RP-preferring patients failed to complete risperidone treatment, a higher rate of attrition than in risperidone-preferring patients (1 of 14; 7.1%).

For those assigned to EX/RP, ANCOVA controlling for baseline YBOCS showed that there was no difference in post-treatment YBOCS between patients who preferred risperidone ($M=11.55$, $SD=6.89$) and those who preferred EX/RP, ($M=15.18$, $SD=7.31$, $F(1,38)=2.18$, $p>.14$). In both the ITT and completer samples, risperidone-preferring patients had high rates of response (ITT: 10 of 11 [90.9%]; completer 10 of 10 [100%]) and post-treatment wellness (ITT: 7 of 11 [63.6%]; completer 7 of 10 [70%]).

Of those assigned to risperidone, ANCOVA controlling for baseline YBOCS showed that patients who preferred EX/RP had significantly higher post-treatment YBOCS scores ($M=25.68$, $SD=5.98$) compared to risperidone-preferring patients ($M=19.36$, $SD=10.37$, $F(1,38)=5.37$, $p=.026$). In both the ITT and completer samples, risperidone-preferring patients who received risperidone had higher rates of response (ITT: 6 of 14[42.9%]; completer: 6 of 13[46.2%]) and wellness (ITT: 4 of 14[28.6%]; completer: 4 of 13[30.8%]) compared to EX/RP-preferring patients (response rate: ITT: 3 of 25[12%]; completer: 3 of 18[16.7%]; wellness rate: ITT: 1 of 25[4%]; completer: 1 of 18[5.6%]). Preference strength was not significantly correlated with post-treatment YBOCS in any condition (p 's>.16).

This report is the first to assess the effect of patient preference on outcomes of SRI augmentation in OCD patients. In this sample, preferring risperidone did not preclude

individuals from benefitting from EX/RP. In fact, individuals who preferred risperidone but received EX/RP had similar outcomes to those who preferred and received EX/RP, and very few risperidone-preferring patients dropped out of EX/RP. Although preference strength was stronger among EX/RP-preferring patients, most patients who preferred risperidone had a moderately strong preference and strength of preference was not associated with post-treatment severity, suggesting that it is unlikely preference strength drove our results.

Of note, the risperidone response rate among risperidone-preferring patients (42.9% in ITT sample, 46.2% in completers) was similar to that reported in some previous risperidone trials [7] (consonant with the suggestion that medication-only trials recruit medication-preferring patients) [2]. At the same time, the EX/RP treatment response rate in risperidone-preferring patients was much higher (90.9% in ITT sample, 100% in completers).

In contrast, patients who preferred EX/RP had particularly poor outcomes with risperidone. Some of these patients subsequently went on to have good outcomes with EX/RP after they completed study participation [8]. These data suggest that EX/RP should be recommended to all OCD patients needing SRI augmentation, even those who report that they would actually prefer risperidone. On a broader level, our results hint that matching patient preference may be more important for medications than exposure-based therapy. That preference did not relate to EX/RP outcomes is consistent with a recent study in PTSD, in which preference for another treatment (interpersonal therapy or relaxation training) was not associated with worse response to prolonged exposure [9]. It is possible that the effectiveness of exposure-based approaches allows patients who would prefer other treatments to benefit, so long as they are willing to try initially.

Limitations of the present report should be noted. Although our data came from a large RCT, group sizes by treatment preference and assigned treatment condition were relatively small. Our sample was also mainly non-Hispanic White, potentially limiting generalizability. In addition, all participants were already currently taking an SRI at study entry, which may have influenced medication preference. Finally, preference was assessed via self-report without a response choice for “no preference”.

Our findings suggest that more research is needed to understand the effects of patient preference on treatment outcome, not only when patients are deciding whether to augment an SRI with EX/RP or another medication, but also when patients choose between first-line treatments (i.e., EX/RP versus SRIs). As some patients may not begin EX/RP based on preference, further research is needed to explore how patients derive treatment preferences and how preferences can be modified. A recent in-depth examination using mixed-qualitative and quantitative methods found that in addition to prior treatment experiences, concerns about treatment effectiveness are prominent in determining which OCD treatments patients prefer [10]. Thus it is possible that educating patients about the effectiveness of EX/RP (even in patients who initially prefer medications) might improve EX/RP acceptability and allow more patients to enter treatment.

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Figure 1.

Note. *one participant lost to follow up before receiving any medication, one withdrew because wanted to continue outside therapy. RIS = risperidone; EXRP = Exposure and response prevention; Treatment response = 25% reduction in YBOCS symptoms; Wellness = post-treatment YBOCS 12.