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•Forum•
Antidepressant polypharmacy

# Combining antidepressants

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**Summary:** Treatment-resistant depression is a common problem encountered by psychiatrists. These patients are often difficult to treat effectively. Strategies for addressing patients with treatment-resistant depression include changing medications, adding another antidepressant (antidepressant polypharmacy), and augmenting treatment with a non-antidepressant.

**Keywords:** Treatment-resistant depression; switching antidepressants; antidepressant polypharmacy; augmentation

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Si and Wang[1] have done an excellent job in discussing the pros and cons of combining antidepressants for individuals with treatment-resistant depression. Finding an appropriate treatment for these patients is a challenge.

Data regarding treatment-resistant depression suggest that if there is no response to the first application of antidepressant pharmacotherapy, then there is a progressive reduction in response to successive applications of antidepressant pharmacotherapy. One might expect a 70% response rate to the initial treatment with an antidepressant, but after 3 or 4 treatments with different antidepressants the response rate falls to about 10-15%.[2-4] Given this rapid fall-off in responsiveness to treatment, clinicians need to think of a range of strategies after an initial treatment failure. Alternatives include the traditional approach of switching antidepressants, but should also include other options such as adding another antidepressant or augmenting the initial antidepressant with another compound.

Regarding switching antidepressants, it makes little sense to me to use an antidepressant that is in the same class of antidepressants as the antidepressant used in the first unsuccessful treatment trial. Most treatments of depressed individuals begin with a selective serotonin reuptake inhibitor (SSRI). Thus, SSRI to SSRI switches do not appeal to me as much as switching from an SSRI to an SNRI (serotonin-norepinephrine reuptake inhibitor) or to a compound with norepinephrine-dopamine effects (such as bupropion). Although clinicians have little data upon which to predict outcome, it would seem more logical to switch classes and hopefully involve a new (presumed) mechanism of action.

The first consideration regarding combining antidepressants should be the safety of the combination. As pointed out by Si and Wang,[1] combining antidepressants with a monoamine oxidase inhibitor (MAOI) can result in a serotonin syndrome. Also, combining tricyclic antidepressants (TCAs) and SSRIs can result in exacerbated tricyclic side effects due to elevated TCA blood levels; these occur because of the effects of SSRIs on the P450 2D6 liver enzyme system which can result in a blockade of the metabolism of TCAs.

The literature suggests that many antidepressant combinations are safe, but there are questions regarding whether enhanced efficacy results from such combinations. Combinations of antidepressants may be useful to enhance efficacy, but these combinations are more commonly used as a strategy to counter the side effects of antidepressant pharmacotherapy. For example, trazodone is frequently combined with SSRIs to combat the insomnia which may result from treatment with an SSRI. Adding mirtazapine to venlafaxine was shown to be safe in the STAR*D study,[2] so it would be logical to add mirtazapine to antidepressants which are only partially effective, especially if the patient is experiencing insomnia. Adding bupropion to SSRIs or SNRIs is frequently done in the United States in order to combat sexual dysfunction, which can be a consequence of treatment with an SSRI or SNRI; however, when using this combination it should be kept in mind that bupropion is a potent inhibitor of the P450 2D6 liver enzyme system. Si and Wang[1] suggest that the lower side effect profile of SSRIs and SNRIs may result in less problems when combining multiple SSRIs or SNRIs than when combining SSRIs with

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MAOIs or TCAs; but the safety of some these potential SSRI and SNRI combinations has not been formally assessed, so clinicians need to be correspondingly cautious. Combining SSRIs can also result in a serotonin syndrome.

Many compounds have been shown to be effective antidepressant agents when used in combination with an antidepressant that is ineffective when used alone. Among these potential adjunctive treatments, the addition of atypical antipsychotics has the best efficacy and the earliest onset of response. The initial studies of augmentation were done with risperidone; in the United States both quetiapine and aripiprazole are approved for augmentation treatment in depression.[5,6] These antipsychotic medications tend to result in about a 50% response rate within about 2 weeks of adding them to antidepressants. Other compounds may also be useful as adjunctive treatment for antidepressants that are only partially effective, including lithium carbonate, thyroid preparations, alpha methyl folate, and others.[7,8]

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## 抗抑郁药的合并使用

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**概述：**难治性抑郁症是精神科医生面临的一个普遍问题。这些患者往往难以有效治疗。治疗难治性抑郁症患者的策略包括换药、增加另一种抗抑郁药（抗抑郁药联合治疗）以及抗抑郁药以外的增效治疗。

**关键词**：难治性抑郁症；抗抑郁药替换；抗抑郁药联合治疗；增效

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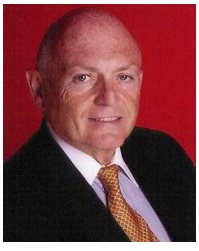

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