Letters to the Editor

Low-Dose D-Cycloserine for Depression?

To the Editor: Ketamine’s ability to bring about rapid and dramatic improvement in patients with refractory depression has biotech companies and clinicians scrambling for ketamine alternatives. D-cycloserine (DCS) showed efficacy in depression as early as 1959 but lay dormant until recently.

As published in the June 2015 issue of the Journal, Kantrowitz and colleagues used ketamine priming followed by a high dose of DCS (1,000 mg/d) with impressive results (also refer to the study by Heresco-Levy et al3).

We4 and a group led by Wilhelm in Boston5 independently used a low-dose DCS (Table 1) strategy to facilitate cognitive-behavioral therapy–related memory consolidation. In a dose-finding study for negative symptoms in schizophrenia, Goff and coworkers6 reported an optimal DCS dose of 50 mg/d. This glycine (associated with N-methyl-D-aspartate [NMDA] receptor) agonism concept of DCS, akin to rapastinel (formerly GLYX-13; under clinical trial), deserves a closer look.

Although the primary goal of these studies4,5 was to enhance extinction learning in exposure treatment for OCD cases, both studies documented improvement in depressive symptoms (see Table 1). Although depressive symptoms were mild in both studies, lack of posttreatment group differences in OCD symptoms preclude a possibility that improved OCD symptoms contributed to the reduction in depression.

This report is not to claim an efficacy of DCS in depression but rather to suggest further studies on intermittent application of this old agent that works through NMDA mechanisms and would possibly help clinicians manage some of their depression cases.

REFERENCES


Suck Won Kim, MD
kimxx003@umn.edu
Matt G. Kushner, PhD
Gihyun Yoon, MD
Justin Anker, PhD
Jon E. Grant, MD

Department of Psychiatry, University of Minnesota, Minneapolis
Yale University School of Medicine, VA Connecticut Healthcare System, West Haven, Connecticut
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Table 1. Mean ± SD Beck Depression Inventory Scores at Baseline and Posttreatment in 2 Studies of Low-Dose D-Cycloserine Augmentation of Exposure Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Placebo</th>
<th>D-Cycloserine</th>
<th>Statistics</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Posttreatment</td>
<td>Baseline</td>
</tr>
<tr>
<td>Minnesota data (placebo, n=17; D-cycloserine 250 mg/wk, n=15)</td>
<td>10.6 (10.3)</td>
<td>9.5 (10.9)</td>
<td>13.4 (11.4)</td>
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<tr>
<td>Boston data (placebo, n=13; D-cycloserine 200 mg/wk, n=10)</td>
<td>10.9 (8.3)</td>
<td>8.7 (9.1)</td>
<td>15.5 (12.7)</td>
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</tbody>
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aData from Kushner et al4.

bData from Wilhelm et al5.
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