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LETTER TO THE EDITORS

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Beneficial effects of the antiglutamatergic agent riluzole in a patient diagnosed with obsessive-compulsive disorder and major depressive disorder

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Altered glutamatergic neurotransmission has been implicated in the pathophysiology of mood and anxiety disorders (Berman et al. 2000; Rosenberg et al. 2000). Preclinical and clinical studies suggest that drugs that reduce glutamatergic activity might play a role in the treatment of both mood and obsessive-compulsive disorders (Krystal et al. 1999, 2002; Rosenberg et al. 2000). One candidate agent is the antiglutamatergic drug, riluzole (Rilutek). This drug, initially approved as a neuroprotective agent for patients with amyotrophic lateral sclerosis, has several actions in the brain that appear to contribute to its antiglutamatergic activity: an inhibitory effect on glutamate release, inactivation of voltage dependent sodium channels in cortical neurons, and blockade of GABA reuptake (Stefani et al. 1997; Jehle et al. 2000; Urbani et al. 2000). The following case describes the beneficial effects of riluzole in a patient with obsessive-compulsive disorder (OCD) and major depressive disorder. We postulated that the addition of a drug that reduces both glutamate release and its postsynaptic consequences would attenuate regional brain hyperactivity implicated in the pathophysiology of these disorders. This case is selected from an ongoing open-label study evaluating the safety and preliminary efficacy of riluzole in the treatment of obsessive-compulsive disorder.

Mr. A was a 47-year-old man whose obsessions/compulsions dated to adolescence and preceded his depressive symptoms. His obsessions and depressive symptoms worsened in the past 2 years despite appropriate primary pharmacotherapeutic and augmentation strategies. Within the last 2 years, he had been hospitalized on two occasions for suicidal ideations. Past pharmacotherapy included adequate trials of serotonin reuptake inhibitors (clomipramine, fluvoxamine, sertraline, citalopram, venlafaxine) alone or in combination with antipsychotics (risperidone, olanzapine, quetiapine). At the time of study enrollment he was taking fluvoxamine (150 mg PO bid) and clonazepam (1 mg every 4 h). He had been recently taken off risperidone (2–4mg every 4 h) by his outpatient psychiatrist. After obtaining written informed consent, Mr A. participated in a study approved by the Yale University Human Investigations Committee, New Haven, Conn..

At the time of entry into the study, Mr. A reported recurrent, ego-dystonic, intrusive thoughts and severe depression. His obsessions were so severe that they interfered with his ability to concentrate and perform sustained tasks. He also reported symptoms of decreased concentration, insomnia, feelings of hopelessness, anhedonia, decreased appetite, low energy, lack of sex drive, and suicidal ideations. He described his mood as "severely depressed." He demonstrated flat affect, psychomotor retardation, poor eye contact, and inattention to grooming. Additionally, he was unable to work for several months prior to his hospitalization. Mr. A had several family members diagnosed with OCD (sister, paternal grandfather) and his sister also was diagnosed with anorexia nervosa. Clinical diagnosis was confirmed with the Structured Clinical Interview for DSM-IV Disorders (SCID-I/P version 2.0) as OCD and major depressive disorder.

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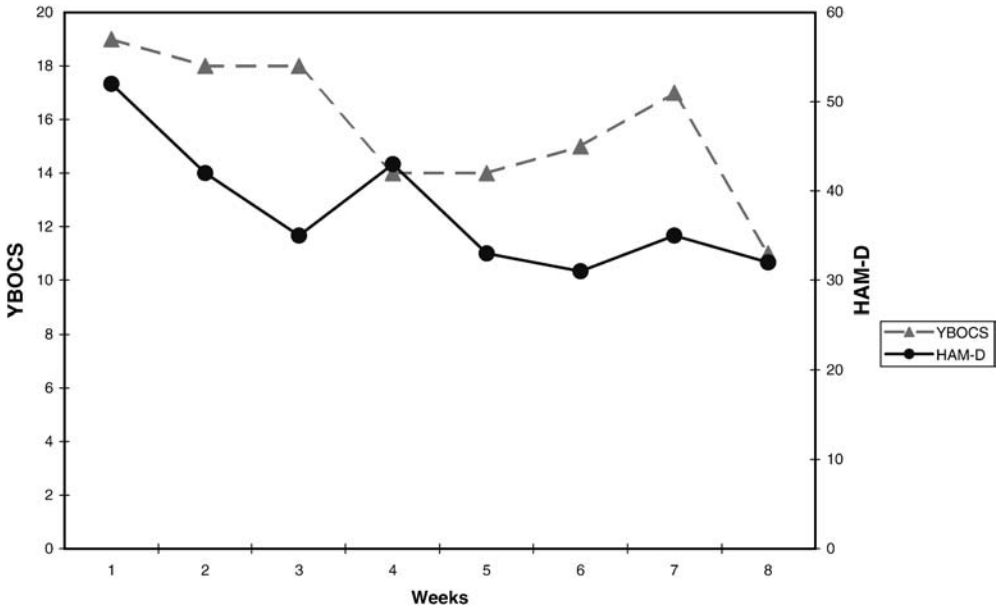

Fig. 1 YBOCS and Hamilton Depression Scale scores in a patient diagnosed with OCD and depression treated with riluzole

As part of this trial, Mr. A was hospitalized on an inpatient research unit, and riluzole 50 mg bid was added to his current psychotropic medications (which had been at stable doses for at least the preceding 4 weeks). During the 6 weeks of the riluzole augmentation, there was a clinically significant improvement in his mood and OCD symptoms. There was a noticeable reduction in the intensity and frequency of his obsessions and compulsions. More prominently, his mood improved. His suicidal ideation abated and he showed significant improvement in psychomotor activity, mood reactivity, and concentration. At the time of discharge, Mr. A was making plans to return to work. These clinical observations and self-reports were consistent with scores on the Yale Brown Obsessive Compulsive Scale (Y-BOCS) and the 25-item Hamilton Depression Scale (Fig. 1). Y-BOCS total score improved most dramatically by week 8. Upon completion of the study, Mr. A was continued on riluzole 50 mg bid and, at his request, was cross tapered from fluvoxamine 150 mg bid to venlafaxine XR 225 mg qd.

The improvement in mood symptoms would be consistent with a suggestion based on basic research that modulating glutamatergic outflow may possess antidepressant properties (Berman et al. 2000; Marek et al. 2000). While the lessons from single cases are limited in their generalizability, the efficacy of riluzole in this very treatment-refractory patient is consistent with mechanistic hypotheses related to obsessive-compulsive disorder and mood disorders. Thus, further examination of the role of antiglutamatergic agents in the treatment of these disorders appears warranted.

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