The Risk-Benefit Ratio of the Proposed DSM-5 Attenuated Psychosis Syndrome

To the Editor: We commend Dr. Weiser's editorial on early intervention in patients at risk for schizophrenia in the August 2011 issue of the *Journal* (1) and in particular his conclusion that current evidence does not support the practice of routinely offering such patients clinical treatment with antipsychotic medication. However, we must take issue with the hypothetical clinical case patient who displays the attenuated positive symptoms used to identify risk. Because the attenuated positive symptoms cause the patient no distress and his sole reason for seeking treatment is unrelated to the specific symptoms, his risk is presumably low.

As Dr. Weiser notes, such a patient might meet research criteria for ultra high risk (2) or a psychosis risk syndrome (3) if the nondistressing attenuated positive symptoms were rated as sufficiently severe to pass threshold, but this hypothetical case would *not* meet the proposed DSM-5 criteria for attenuated psychosis syndrome. The criteria currently being tested in field trials do not permit such presumably low-risk patients to receive the diagnosis because criterion D requires that the attenuated positive symptoms themselves must be "sufficiently distressing and disabling to the patient and/or parent/guardian to lead them to seek help" (4, 5). The field trials should help determine whether these criteria can be applied with reliability in the clinical setting.

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Response to Woods and McGlashan Letter

To the Editor: I thank Drs. Woods and McGlashan for reading and commenting on the editorial. Their letter examines the hypothetical case of a young man with attenuated psychotic symptoms who has "an emotional crisis when his girlfriend leaves him." Their understanding is that the symptoms "cause the patient no distress" and hence would not meet the proposed DSM-5 criteria for attenuated psychosis syndrome.

In the editorial, our hypothetical patient "might be upset, have difficulty sleeping at night, have difficulties concentrating, have decreased functioning at school or at work, and have more attenuated psychotic symptoms. If this person goes to a psychiatrist presenting with this clinical picture, he might very well meet criteria for the prodromal phase."

This is clearly a description of a distressed person who seeks the help of a psychiatrist. Since criterion D of the proposed DSM-5 criteria for attenuated psychotic syndrome requires that the attenuated positive symptoms themselves must be "sufficiently distressing and disabling to the patient and/or parent/guardian to lead them to seek help," our patient would meet the criteria.

I join Drs. Woods and McGlashan in their hope that the DSM-5 field trials will help determine whether these criteria can be applied with reliability in the clinical setting.

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Neurocognitive Response to Deep Brain Stimulation for Obsessive-Compulsive Disorder

To the Editor: When obsessive-compulsive disorder (OCD) symptoms are severe and refractory to both cognitive-behavioral therapy (CBT) and medication, deep brain stimulation (DBS) may be of value (1). Although OCD research has examined the effects of DBS on cognition (2), few studies have used translational computerized paradigms capable of fractionating dissociable aspects of cognition and their neural substrates. Neurocognitive assessments have the potential to help elucidate the underlying mechanisms of action of DBS in OCD and the optimal brain target.

Case Report

"Mr. T" is a 30-year-old man with a 5-year history of OCD with primary contamination obsessions and washing compulsions. He had stopped socializing, had dropped out of school, and was unemployed because of his OCD. Past adequate trials of all serotonin reuptake inhibitors, both as monotherapy and with multiple augmentation strategies, and 20 weeks of CBT using exposure response prevention provided only limited benefits.

After ethical review board approval, Mr. T underwent bilateral implantation of electrodes targeting the nucleus accumbens. At the time of surgery, his Yale-Brown Obsessive Compulsive Scale score was 32 while taking the following medications: clomipramine, 250 mg/day; ziprasidone, 120 mg/day; and clonazepam, 1 mg t.i.d. His medication dosages were unchanged before and after the cognitive testing.

We performed cognitive assessments at baseline (prestimulation) and again 8 months after DBS began. Tasks from the Cambridge Neuropsychological Test Automated Battery included the stop-signal test (assessing ability to suppress prepotent motor responses), the intradimensional/extradimensional set shift task (examining rule

TABLE 1. Cambridge Neuropsychological Test Automated Battery (CANTAB) Test Performance After Deep Brain Stimulation (DBS) Compared With Normative Data[a]

	Mean		z	
Individual Tests	Before DBS	After DBS	Before DBS	After DBS
Stop-signal test reaction time (msec)	211.58	204.70	−1.0	−0.8
Stop-signal test median go reaction time (msec)	449.00	379.00	0.1	0.5
Intradimensional/extradimensional set shift task, pre-extradimensional errors	6.00	7.00	0.2	−0.1
Intradimensional/extradimensional set shift task, extradimensional errors	1.00	2.00	0.8	0.6
Cambridge Gamble Task, overall proportion bet	0.60	0.57	0.6	0.4
Cambridge Gamble Task, quality of decision making	1.00	1.00	0.5	0.5

[a] Normative data are taken from the Cambridge Cognition CANTAB database except for the stop-signal test, where data were unavailable and therefore were taken instead from Chamberlain et al. (3).

learning and behavioral flexibility), and the Cambridge Gamble Task (assessing decision making). The results of these assessments are summarized in Table 1.

Before the DBS, Mr. T generally exhibited cognitive performance akin to healthy comparison subjects except for evidence of stop-signal reaction time impairment (z=1.0). His stop-signal reaction time performance changed little after DBS (posttreatment z=0.8); however, the DBS resulted in significant improvement in Mr. T's OCD symptoms, and his Yale-Brown Obsessive Compulsive Scale score decreased to 10. Mr. T returned to college and now has a social life and works part-time.

Discussion

This case indicates that DBS, targeting the nucleus accumbens, was associated with significant therapeutic benefits in treatment-refractory OCD in the absence of effects on response inhibition, set shifting, or decision making. The lack of effect of accumbens DBS on the stop-signal deficit accords with translational research indicating that accumbens damage (unlike cortical damage) has no effect on response inhibition on an equivalent animal task (4). While impaired response inhibition appears to be a trait marker for OCD, and was evident in Mr. T at baseline, DBS to the accumbens does not appear to ameliorate this problem. This case illustrates the value of DBS in patients with refractory OCD and the importance of including cognitive tests in such studies to identify meaningful predictors for successful DBS in OCD on an individual level.

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New-Onset Psychosis in a Patient With Spinocerebellar Ataxia Type 10

TO THE EDITOR: A 37-year-old man suffering from spinocerebellar ataxia type 10 manifested new-onset psychosis with violence. He and his brother inherited this ataxia from their father, who had also developed poorly controlled anger and aggression. Spinocerebellar ataxia type 10 is a culturally segregated and rare autosomal-dominant disease that is characterized by a slowly progressive cerebellar gait and appendicular ataxia associated with epilepsy in the majority of patients (1). This disease belongs to the rapidly enlarging family of polynucleotide expansion disorders (e.g., Huntington's disease and Friedreich's ataxia). Specifically, spinocerebellar ataxia type 10 results from an intronic pentanucleotide expansion within the ataxin-10 gene (*ATXN10*; 22q13), observed almost exclusively in patients of Mexican and Brazilian descent. In contrast to the more familiar manifestations of Huntington's disease, severe psychiatric symptoms have not been commonly described for spinocerebellar ataxia type 10 or many of the other inherited ataxias.

Until 3 months before admission, our patient was free of psychiatric symptoms, and his medical history was significant only for stable ataxia and a seizure disorder, which was well controlled on a combination of carbamazepine and zonisamide. That his affected brother developed identical neurological symptoms, but in reverse order, nicely illustrates the fact that a single mutation can produce widely varying clinical phenotypes, even among siblings with very similar genetic backgrounds.

The onset of psychiatric symptoms began with delusions of being in the presence of his deceased grandfather, but they remitted soon after treatment with risperidone (1 mg/day). Three months later, despite medication adherence, the patient abruptly developed visual illusions and hallucinations, soon followed by profound irritability and impulsive violence.