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# Letters to the Editor

## The Use of Fluoxetine and Buspirone for Treatment-Refractory Depersonalization Disorder

**Sir:** Depersonalization disorder has been recognized as a disabling condition that is often resistant to treatment. Torch[1] has described that phenomenologically it shares several important features with obsessive-compulsive disorder. Subsequently, a common serotonergic basis for the two disorders has been proposed, based on similar clinical and biological findings and a common favorable therapeutic response to 5-HT reuptake blockers as reported by Hollander et al.[2,3] and Moes et al.[4]

We hereby describe the usefulness of serotonergic drugs in a patient with depersonalization disorder who was resistant to several medication trials, but whose depersonalization and derealization symptoms improved with a combination of fluoxetine and buspirone. This is, to our knowledge, one of the few reported cases of depersonalization disorder responding to fluoxetine.

***Case report.*** Ms. A, a 21-year-old medical student with a childhood history of febrile convulsions at 1 year of age, presented with an illness of 1 year's duration characterized by continuous and multiple depersonalization and derealization phenomena. There was no history of past or present substance abuse. Depersonalization symptoms included the sense that she was an observer of her own actions, an inability to feel any emotions, altered bodily sensations including the feeling that something was pushing out of her head, and feeling that her body parts were detached and that her internal world was unreal. Derealization symptoms included a disturbed perception that the environment had a foggy appearance and people and trees had changed shape and color. Ms. A had severe anxiety related to these symptoms that disrupted her social life. She felt sad and hopeless and reported having disturbed sleep and appetite, which were secondary to the intense psychic experiences and the severe anxiety.

DSM-III-R criteria for depersonalization disorder were met as Ms. A felt detached from her mental processes, her reality testing was intact, the symptoms were persistent and severe, and the depersonalization was predominant and not secondary to another disorder. She did not, however, meet DSM-III-R criteria for a primary anxiety or depressive disorder. Ms. A's prior course of treatment included successive trials of alprazolam 3 mg/day for 1 month, dothiepin 150 mg/day for 6 weeks, and a combination of imipramine 150 mg/day and nitrazepam 10 mg/day for 4 weeks. The doses of antidepressants could not be raised further because of disabling anticholinergic side effects. Her mood improved with the antidepressants, but the distorted perceptions did not change. Results of her initial physical examination and laboratory studies were unremarkable, and her electroencephalogram was normal.

Treatment at our clinic was initiated with fluoxetine 20 mg/day, which was gradually increased to a dose of 60 mg/day. Ms. A tolerated this dose without significant adverse effects. She reported about a 50% reduction in the depersonalization and derealization phenomena at 40 mg/day of fluoxetine, which was reached within 4 weeks. There was only a marginal further improvement with 60 mg/day of fluoxetine, even after 2 weeks at that dose level.

Buspirone 10 mg/day was added after 2 months in view of the anxiety, which remained unchanged, and also to augment Ms. A's response to fluoxetine. The dose of buspirone was increased to 20 mg/day in 2 weeks. After another month of combined treatment, Ms. A had a marked reduction (80%) in the depersonalization symptoms and a total resolution of anxiety. This improvement was maintained for 6 months of follow-up, and Ms. A has been able to undertake all of her daily activities since the complete resolution of the depersonalization symptoms.

This patient undoubtedly benefited from treatment with a combination of fluoxetine and buspirone, which is consistent with earlier reports.[2,3,5] In addition to the anxiolytic effects of buspirone, a 5-$HT_1$ agonist, its augmenting effect in the current case may be analogous to similar improvement seen in cases of obsessive-compulsive disorder where it has been used to augment the effects of fluoxetine.[6]

Further research with different samples of patients who have depersonalization disorder is required to cross-validate the findings of this case of therapeutic response.

### References


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## Risperidone and Tardive Dyskinesia: A Case Report

**Sir:** We report a case of tardive dyskinesia arising during the course of treatment with the new antipsychotic risperidone. To our knowledge there have been no previous published reports of tardive dyskinesia that has started during treatment with this medication, which has recently been approved for use in the United States.

***Case report.*** Ms. A, a 28-year-old single white woman with 2 years of college education, had a 6-year history of psychosis. She had worked for 1 year until the age of 22 years, when she became increasingly socially isolated and depressed. She also came to believe that she was being watched by the television. A combination of a tricyclic antidepressant and the low-potency antipsychotic thioridazine was prescribed. Her first hospitalization occurred at age 24, when she was experiencing auditory hallucinations. She was started on haloperidol 10 mg/day, chlorpromazine 300 mg/day, and flupenthixol 20 mg i.m. weekly. This combination controlled her positive symptoms. It was gradually reduced until she was taking only haloperidol 10 mg/

day. Because of Ms. A's complaints of restlessness and stiffness, her medication was changed to trifluoperazine 10 mg/day. After several months, she began to experience delusions that led to her second admission.

During her second admission, she entered a 1-year double-blind study comparing haloperidol and risperidone. On study entry, she had normal results from a general physical examination and marked psychotic symptoms evidenced by Clinical Global Impressions (CGI) scale scores.[1] Neurologic examination revealed mild subjective and objective parkinsonian symptoms, but no dystonia or dyskinesia as measured by the Extrapyramidal Symptom Rating Scale (ESRS).[2] She had an average I.Q. with no verbal performance discrepancy. After 20 days, she was discharged in a state of remission.

As an outpatient, she continued in the double-blind study, which required ESRS ratings of tardive dyskinesia and extrapyramidal symptoms at weekly intervals for 6 weeks and thereafter at monthly intervals. Four months later, her ESRS ratings showed moderate symptoms of tardive dyskinesia, predominantly affecting the jaw and tongue. Her parents were certain that there had been no prior tardive dyskinesia symptoms and were more distressed than the patient. The double-blind code was broken, and Ms. A was found to be taking risperidone 10 mg/day. Her risperidone was reduced to 6 mg/day for a month, without remission of tardive dyskinesia, but with a return of psychotic symptoms.

She was started on clozapine therapy after risperidone was withdrawn, and her psychotic symptoms remitted, but moderate tardive dyskinesia rated on the ESRS continued 6 months later.

This is, to our knowledge, the first report of the onset of tardive dyskinesia in a patient taking risperidone. The dose of risperidone used in this case was 10 mg/day, which is just above the optimal dose for efficacy and low side effects established in dose-finding studies with risperidone.[3] The prevalence of extrapyramidal symptoms with risperidone increases as the dose is increased above the optimal dose of 6 mg/day. For this particular patient, however, 10 mg/day resulted in good symptom control without extrapyramidal symptoms.

Risk factors already present in the patient include female sex[4] and 6 years of continuous prior neuroleptic treatment, both of which may be risk factors in the development of tardive dyskinesia.[5] This prior neuroleptic treatment may have significantly contributed to the development of tardive dyskinesia in this case. As a result, the causality of the tardive dyskinesia cannot be firmly attributed to risperidone.

This case arose during the course of a clinical trial of risperidone that was sponsored by Janssen Pharmaceutica. Janssen has reviewed the manuscript as is their right under the study agreement. The authors, however, bear full responsibility for the contents of the letter.

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## Antipsychotic Effect of Cannabidiol

**Sir:** Cannabidiol, one of the major components of *Cannabis sativa*, attenuates psychotomimetic and anxiogenic effects induced by high doses of $\Delta^9$-tetrahydrocannabinol[1] and has an atypical antipsychotic profile in animal tests.[2] Since cannabidiol does not seem to induce significant adverse effects in humans,[3] we decided to test this drug in a schizophrenic patient who had significant hormonal side effects during treatment with usual neuroleptics. The study protocol was approved by the local Ethical Committee, and informed consent was obtained from close relatives of the patient.

***Case report.*** Ms. A, a 19-year-old black woman, was referred to the inpatient unit of the Clinical Hospital of Ribeirão Preto because of aggressiveness, self-injury, incoherent thoughts, and auditory hallucinations. During her first hospitalization, at the age of 17 years, she had been successfully treated with haloperidol (5 mg/day) but showed amenorrhea, galactorrhea, and weight gain after chronic treatment with the drug (2.5 to 7.5 mg/day) for 18 months. The medication was tentatively stopped twice, but the symptoms returned. The second withdrawal trial led to the present hospitalization. At this time, she was assessed by two psychiatrists who used the Structured Clinical Interview for DSM-III-R, and both agreed with the diagnosis of schizophrenia.

During the first 4 days of hospitalization, Ms. A received placebo plus usual environmental support measures. From Days 4 to 30, she received cannabidiol dissolved in corn oil and packed inside gelatin capsules. The dose was progressively increased up to 1500 mg/day in two divided doses. Cannabidiol intake was then replaced by placebo for 4 days. After that, haloperidol (5 mg/day) administration was started, and the dose was increased to 12.5 mg/day. Dose adjustments were determined by the clinical evaluation of the patient. During periods of great agitation and/or anxiety, diazepam 10 mg p.o. was administered. After 1 week of cannabidiol treatment, the mean daily dose of diazepam was reduced from 16.3 to 5.7 mg/day.

During the study, Ms. A was evaluated by two psychiatrists, who used the Brief Psychiatric Rating Scale (BPRS)[4] and the UKU Side Effect Rating Scale[5] for psychoactive drugs. Interviews were videotaped, and at the end of the study, the tapes were presented, blindly and in a random sequence, to another psychiatrist who completed the BPRS. The patient was also evaluated independently by two nurse auxiliaries who used the Interactive Observation Scale for Psychiatric Inpatients (IOSPI)[6] after daily observation periods of 6 hours.

The decrease in scores from the three measures after 4 weeks of cannabidiol therapy was as follows: open BPRS, 69%; blind BPRS, 60%; IOSPI, 69%. After cannabidiol withdrawal, there was a trend for a worsening of the symptoms. The improvement obtained with cannabidiol was not increased by haloperidol treatment (decrease from baseline after 4 weeks of haloperidol therapy: open BPRS, 62%; blind BPRS, 54%; IOSPI, 56%). The improvement with cannabidiol treatment was observed in all items of the BPRS, including those more closely related to psychotic symptoms, such as "thought disturbance" and "hostility-suspiciousness," making it improbable that nonspecific anx-