Letters to the Editor

Sertraline Treatment of Hallucinogen Persisting Perception Disorder

Sir: Hallucinogen persisting perception disorder is the reexperiencing of the perceptual symptoms experienced while intoxicated with the hallucinogen. Examples of these perceptual distortions include geometric hallucinations, false perceptions of movement in the peripheral visual fields, flashes of color, positive afterimages, macropsia, and micropsia. Various pharmacologic treatments of "flashbacks," including neuroleptics and benzodiazepines, and electroconvulsive therapy have met with limited success.[1]

Case report. Mr. A, a 22-year-old male college student, presented to a college counseling center with symptoms of mild depression. Six months prior to his evaluation, he had stopped using lysergic acid diethylamide (LSD), after an 8-month history of LSD abuse during which he had used between 1000 to 1800 μg at least twice a week. Despite his abstinence, he noticed the persistence of LSD-like phenomena. These phenomena included visual illusions, trailing images, depersonalization, images in his peripheral field, and visions of colorful geometric forms when he closed his eyes. They occurred almost daily, were not distressing to the patient, and had preceded the onset of his depressive symptoms. He had no history of seizures or migraines.

Antidepressant treatment was begun with sertraline 25 mg and was titrated upward slowly owing to concern about these flashbacks. Mild exacerbations of these LSD-like phenomena were noted for 2 to 4 days after each dosage increase, primarily as flashes of color, positive afterimages, and fleeting hallucinations in his peripheral vision. Within 1 month after the target dose of 100 mg was reached, these perceptual disturbances decreased until they had almost completely remitted. The depressive symptoms also improved. These gains were maintained for 4 months, at which point Mr. A graduated and terminated treatment.

The pathophysiology of hallucinogen persisting perception disorder remains unclear, although several theories have been suggested.[2] One theory holds that LSD causes excitotoxic destruction of serotonergic inhibitory interneurons. Alternatively, these phenomena may represent visual seizures. Several measures of visual functioning indicate that patients with this disorder continue to centrally process visual imagery after the image has been removed. Despite uncertain pathophysiology, it has been observed that hallucinogen persisting perception disorder recapitulates the acute LSD experience.[3]

The preponderance of evidence suggests that the acute effects of LSD are serotonergic. LSD has been found to bind selectively in vivo to 5-HT_2 receptors and causes a drop in receptor density after one dose. Repeated administration over a 5-day period decreases binding of serotonin to the 5-HT_2 in the cortex.[4] This decrease correlates clinically with the rapidly developed tolerance to the effects of LSD. Sertraline has been shown to decrease the typical physiologic responses to serotonergic agonist on 5-HT_2 receptors when administered over a 2-week period.[5] This progressive down-regulation may account for the delayed clinical efficacy. A recent survey of LSD users who were concomitantly prescribed antidepressants found that chronic administration of serotonergic antidepressants attenuated the subjective experience of LSD.[6] Many of these patients also reported LSD-like perceptual phenomena at the initiation of treatment with serotonin selective reuptake inhibitors in the absence of LSD.

It is hypothesized that hallucinogen persisting perception disorder is serotonergically mediated. Sertraline appears to have exacerbated the perceptual disturbances initially, but attenuated them after chronic administration, adding further evidence to support the serotonergic mechanism of flashbacks. The down-regulation of 5-HT_2 that occurs with chronic administration of a serotonin reuptake inhibitor may have provided this patient with tolerance to the remote effects of LSD.

References

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Dyskinesia With Fluoxetine: Tardive or Late-Onset Persistent, Acute Norfluoxetine Dyskinesia?

Sir: N. H. Sandler, M.D. (February 1996 issue), reported a fascinating fluoxetine-related lingual dyskinesia.[1] We wish to pose some additional considerations. While these lingual movements may represent tardive dyskinesia (TD), Schooler and Kane[2] described properties of TD not reported in this case: masking of TD with dyskinetogenic drug dose increases, rebound worsening with dose reductions, and the necessity of excluding other dyskinesia etiologies.

The tardive dyskinesia properties depicted in the reported case and described in the American Psychiatric Association (APA) Task Force Report are not specific to TD. The dyskinesia case description suggests differential diagnostic considerations including fluoxetine-delayed tic provocation[3] in OCD (including dystonic tics), dystonia[4,5] (including fast dystonic movements simulating chorea), chorea, and myoclonus.[4] Gross thrusting lingual movements suggest dystonia. Alternative dystonia and chorea etiologies include striatal lesions associated with compulsions and dystonia[6] and Wilson's, Huntington's, or Sydenham's diseases. A detailed family history and laboratory investigation might prove rewarding.

The long half-life of norfluoxetine (fluoxetine's active metabolite) may delay acute dyskinesia and produce subtle onset as serum norfluoxetine levels slowly rise to steady state. It may also prolong resolution of dyskinesia without rebound worsen-