wards generated as the result of nicotine's interaction with the brain's neurochemical systems.[1] Nicotine's memory-enhancing reward is believed to result from its effects on specific nicotinic acetylcholine receptors.[2] Nicotine's attentional, antidepressant, and antianxiety rewards are thought to be due to pathways between nicotinic acetylcholine receptors and noncholinergic neuronal subtypes that selectively traffic dopamine, norepinephrine, 5-hydroxytryptamine, and gamma-aminobutyric acid.[3]

Varenicline is a new treatment for nicotine dependence and a member of the selective alpha4beta2 nicotinic acetylcholine receptor partial agonist class.[4] Central nicotinic acetylcholine receptors have been implicated in attention deficit hyperactivity disorder (ADHD),[5] and an alpha4beta2 antagonist counteracted nicotine-induced improvement in an animal model of ADHD.[6]

The first case of adult ADHD that responded to the addition of varenicline is reported here.

Case Report

Ms. A, a 26-year-old white woman, was self-referred in 2007 for difficulties staying focused, staying on task, and with reading comprehension. She fulfilled DSM-IV-TR criteria for ADHD, but was against the initial recommendation to begin taking a prescription stimulant. The administration of the antidepressants bupropion (150 mg) and venlafaxine (up to 150 mg), each alone or in combination with valproic acid, was met with either side effects or undesirable results. The medicine selected was based on office sample availability at Ms. A's request because of financial problems. A wealthier patient had previously donated a barely used varenicline prescription that she had abandoned due to nausea. Ms. A agreed to undergo a trial of varenicline taking 0.5 mg in the morning, after eating a low-acid breakfast, with an 8-oz glass of water. Her reading comprehension and ability to focus improved substantially after reaching 1 mg b.i.d. Her mild hyperactivity improved marginally. She complained of no side effects as she completed 6 weeks, including weekends, of the clinic's subsidized varenicline treatment trial. Her problematic ADHD symptoms fully resurfaced about 2 days after she ran out of varenicline. Ms. A agreed to continue medicine trials using affordable antidepressant, dopamine agonist, or nicotine replacement generics.

Comment

Although this report does not rule out the placebo effect, and a therapeutic connection between varenicline and ADHD cannot be established with certainty, this case does suggest that the new selective alpha4beta2 nicotinic acetylcholine receptor partial agonist class of medicines is useful in the management of adult ADHD. In particular, the varenicline-ADHD interface warrants further investigation using larger groups of subjects, more sophisticated study designs, and a variety of memory deficits such as depression and mild cognitive impairment.

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Withdrawal Symptoms of Trifluoperazine

To the Editor: Trifluoperazine, a typical antipsychotic, has been frequently used in major psychotic disorders for many years. Sudden discontinuation of trifluoperazine is known to cause relapse of psychotic symptoms in patients suffering from major psychosis.[1,2] Trifluoperazine is not known to cause any distinct withdrawal symptoms like craving, dysphoria, irritability, rest-

lessness, or insomnia. An extensive literature search revealed a prior report of trifluoperazine withdrawal symptoms like craving, irritability, dysphoria, and inability to work.[3] Below, we describe the development of nonpsychotic withdrawal symptoms in a patient after use of trifluoperazine for several years.

Case Report

A 78-year-old Indian man presented to us with a moderate depressive episode for 1 month. He had two previous episodes of depression which occurred 45 and 20 years ago, respectively. Both the episodes fully resolved with treatment, and the patient had no residual depressive symptoms in between the episodes. He also had severe nicotine dependence (smokeless tobacco) for about 56 years, from which he was abstinent for the previous year.

The patient was treated with antidepressants for his second episode of depression along with trifluoperazine, 2 mg/day. After 1 month, his depressive symptoms resolved completely, and he stopped taking the antidepressants. However, he continued taking trifluoperazine in the same dose for the next 20 years. He said that if he ever tried to stop this medicine he felt very weak, restless, dysphoric, and had difficulty getting to sleep. But there was never any depressive cognition, guilty feeling, or other characteristic depressive symptoms. On days when he could not take this medicine, he experienced a craving for it. He and his family members felt that this was not normal and he tried to reduce the dose to 1 mg/day. Such attempts failed when he developed the above-mentioned symptoms the next day, which forced him to restart trifluoperazine, 2 mg/day. Symptoms resolved immediately every time thereafter. At times he started taking 3 mg/day, but generally he maintained a dosage of 2 mg/day.

We treated the patient with escitalopram, 20 mg/day, for his depression and clonazepam, 1 mg/day, for associated sleep problems which developed during this depressive episode. With this he showed marked improvement in depressive symptoms. He was, however, still continuing trifluoperazine and was not motivated to stop it. When we asked him to try abstinence from trifluoperazine, he said he was unable to do away with it.

Discussion

Our patient fulfilled ICD-10 criteria of a possible trifluoperazine withdrawal syndrome. This is interesting because unlike all other dependence-producing substances, trifluoperazine is a dopamine blocking agent and is not expected to stimulate the mesolimbic/mesocortical dopaminergic reward circuit. So it might be due to a sensitive reward circuit in our patient, as evidenced by his severe nicotine dependence. Further research is needed to examine the possibility of a unique trifluoperazine withdrawal syndrome. As trifluoperazine is very commonly used in developing countries like India because of its low cost, such a finding may have important therapeutic implications.

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Pathological Hypersexuality Induced by Dopamine Replacement Therapy in a Patient with Progressive Supranuclear Palsy

To the Editor: The pathogenesis of pathological hypersexuality is still in controversy. To our knowledge, this is the first report of pathological hypersexuality induced by two different dopamine receptor agonists in a single patient with progressive supranuclear palsy. In this case, dopamine D2 receptor agonism, perhaps specifically D3 receptor subclass agonism, might have played a key role in the development of pathological hypersexuality induced by dopamine replacement therapy.

Case Report

An 83-year-old man with progressive supranuclear palsy was being treated with Sinemet (carbidopa/L-dopa 25 mg/100 mg, 125 mg t.i.d.) for 8 months. Due to nausea, Sinemet was replaced by low dose madopar (L-dopa/benserazid 100 mg/25 mg, 62.5 mg t.i.d.) and bromocriptine (2.5 mg t.i.d.). For the following 2 months, pathological hypersexuality (sexually suggestive remarks, touching, kissing, disrobing, exposing genitalia, facial flushing, penile erection, public masturbation) slowly developed. At this point, his serum testosterone level