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

was normal (2.3 ng/ml), whereas serum prolactin level was suppressed to 1.3 ng/ml.

His pathological hypersexuality completely disappeared 2 weeks after discontinuation of bromocriptine. After 4 weeks, pramipexole (0.125 mg b.i.d.), another dopamine receptor agonist, was added instead of bromocriptine since his motor performance deteriorated. After 1 week of pramipexole, all the hypersexual symptoms reemerged. At this point, his serum prolactin level was 2.2 ng/ml.

His pathological hypersexuality completely disappeared again just by discontinuing pramipexole. Then we titrated madopar up to 125 mg t.i.d. instead of adding other dopamine receptor agonist. After 3 weeks, his motor performance improved with partial reemergence of hypersexual symptoms (penile erection, facial flushing, sexually suggestive remarks, touching). However, the severity of the reemerged symptoms was much more tolerable than those induced by dopamine receptor agonist. At this point, his serum prolactin level was not suppressed (13.3 ng/ml).

Comments

This case confirmed an earlier observation[1] through rechallenging two different kinds of dopamine receptor agonists alternatively in a single patient, and illustrated several characteristics of dopamine replacement therapy-induced pathological hypersexuality.

First, dopamine receptor agonists may be more likely to induce pathological hypersexuality than L-dopa since pathological hypersexuality induced by combination therapy of either bromocriptine or pramipexole with L-dopa was much more severe than that induced by L-dopa monotherapy.

Second, dopamine replacement therapy-induced pathological hypersexuality may be mediated by D2 receptor agonism since pramipexole has no affinity for D1 receptor classes.[2]

Third, dopamine receptor agonist-induced pathological hypersexuality may perhaps be mediated by the excessive stimulation of the D3 receptor subclass since pramipexole binds preferentially to D3 receptors with high affinity.[2]

Fourth, the difference in the risk of pathological hypersexuality between dopamine receptor agonists and L-dopa may be attributed to their differential suppression of prolactin secretion since serum prolactin was abruptly suppressed when bromocriptine or pramipexole was added to L-dopa. Inhibitory effect of dopamine receptor agonists on prolactin secretion was suggested as a main pathogenic mechanism of hypersexuality.[3]

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Varenicline, Appetite, and Weight Reduction

To the Editor: Nicotine is possibly one of the most prevalent dependence-producing drugs because of the central nicotinic-cholinergic, dopaminergic, serotonergic, and gabaminergic pathways with which it has been associated.[1] Nicotine-dependent behavior may conceivably be reinforced by the drug's focus and memory enhancing properties,[2] as well as antidepressant,[3] anxiolytic,[4] and appetite-suppressing properties.[5] Nicotine is a unique paradigm in that it suppresses appetite and stabilizes mood. Nicotine withdrawal leads to the emergence of craving in dependent individuals, which can include impaired memory[6] and concentration, depressed mood, anxiety, and increased appetite.[7]

Although less clearly understood than nicotine withdrawal, food-seeking behavior also is believed to involve an array of neuropsychiatric reward pathways. Nicotinic-cholinergic,[8] dopaminergic,[9] serotonergic, and GABA-ergic[10] reward systems are among the likely candidates that motivate us to eat. Food-seeking has been associated with depression, stress, and emotional discomfort,[11] and food tasting alone can stabilize mood.[12]

Varenicline is a new treatment for nicotine dependence and a nicotinic-cholinergic receptor partial agonist that behaves like nicotine. We report a case of varenicline-associated appetite suppression and weight loss accompanied by improved mood.

Case Report

Ms. A, a 66-year-old white woman, was referred by another patient in November 2006 for alcohol, depression, anxiety, panic, and chronic