Clinical/Scientific Notes

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CRACK COCAINE USE DUE TO DOPAMINE AGONIST THERAPY IN PARKINSON DISEASE

Impulse control disorders (ICD)[1] and the dopamine dysregulation syndrome (DDS)[2] are dopaminergic complications of Parkinson disease (PD) treatment. A large number of ICDs have been associated with dopamine agonists (DAA), such as gambling, hypersexuality, and consumerism, but none, to our knowledge, involved drugs of abuse.[1] DDS is a condition in which patients with PD abuse L-dopa, taking it excessively despite the dyskinesias or psychotic symptoms that result.[2] DDS produces L-dopa craving, whereas ICDs produce compulsions, and the 2 may coexist.[2] DDS has rarely been associated with dopamine agonists other than apomorphine.

We report 3 cases of crack cocaine use associated with dopamine. Two involved new use of the drug. The third involved recidivism. The cases are of theoretical interest because their cocaine use was a compulsion related to dopamine agonist use, hence an ICD, whereas L-dopa craving is the core problem in DDS.

Case reports. ***Case 1.*** A 70-year-old man was diagnosed with PD in 2007. He had a good motor response to pramipexole 3.375 mg and carbidopa-levodopa 175/650 mg daily but became hypersexual and mildly anxious. After pramipexole was increased to 3.75 mg/day, anxiety increased. Several months later he began provoking fistfights. Pramipexole was reduced to 3 mg/day and carbidopa-levodopa to 150/600 mg/day. Fighting stopped but hypersexuality continued, compulsive eating of sweets began, and he started smoking crack cocaine. He had never tried cocaine before. Cocaine craving and all abnormal behaviors ended when pramipexole was stopped. Cocaine did not alter motor function.

Case 2. A 44-year-old man, whose maternal grandfather was diagnosed with PD at age 80, was diagnosed with PD at age 32. His younger sister was later diagnosed at age 35. He had a good response to pramipexole but after 4 years developed social anxiety on 3 mg/day. He then began collecting nonworking lawn mowers, small engines, baseball cards, garbage, and coins. He gambled pathologically and subsequently started to use crack cocaine. He had never abused drugs or used cocaine previously. He reported that his Parkinson symptoms "disappeared" on cocaine. All compulsions and cocaine craving resolved on stopping pramipexole. He had never taken L-dopa and denied using to treat motor symptoms.

In both cases, the cocaine use was opportunistic and neither patient expressed any interest in trying cocaine once off the pramipexole. Neither had motor fluctuations.

Case 3. A 58-year-old man had used crack cocaine until 2005, and was diagnosed with PD in May 2010. He improved on ropinirole but at 6 mg/day he began to gamble, imbibe alcohol excessively, and experience depression. He then binged on cocaine for the first time in 5 years. Ropinirole was replaced by L-dopa and cocaine craving improved dramatically, with use limited to once every 6 weeks, when depressed. On L-dopa 400 mg/day he uses cocaine approximately every 2 months. He states that cocaine improves motor function, including tremor, for about 3 hours, but denies using it for this purpose.

Discussion. These cases expand the spectrum of ICDs seen with DAAs. In each case, other behavioral problems coexisted with the cocaine abuse. In each case, cocaine use was one aspect of a constellation of behavioral alterations that included ICDs.

Cocaine binds to the dopamine transporter, blocking reuptake of both catecholamines and serotonin. Cocaine may induce dystonia or chorea[3] and 2 cases of inhaled cocaine taken to treat motor "off" in PD were reported.[4] Both were taking pramipexole and at least one had ICD (personal communication, A. Di Rocco, 2013).

Cocaine is highly addictive and animal research has demonstrated that sensitization, a process in which repeated exposures produce earlier and greater effects, is a major reason for its addictive properties. In experimental animals, DAAs increase sensitization and dopamine D2 and D3 receptor antagonists reduce it.[5] Primates abstinent after IV cocaine addiction are more likely to relapse if given a dopamine agonist.[6] Similarities between ICD and drug addiction have been noted, both associated with abnormalities of striatal dopamine synapses.[7]

In our first 2 cases, the patients developed a craving for cocaine, never having used it before, as a direct consequence of DAA (possibly with the added stimulus of L-dopa), as demonstrated by the loss of craving on stopping the DAA. Pramipexole is primarily a D2, D3 stimulating drug. L-dopa, which is transformed into dopamine within the brain, stimulates these

receptors as well. Each case had DAA-induced ICDs, as well as craving, which is the central problem in DDS. Our cases raise the question of whether some patients with PD with DAA-induced ICDs might be "presensitized" to cocaine and therefore highly subject to addiction with minimal exposure.

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