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Timothy J. Walter, M.D.
Uma Marar, M.D.

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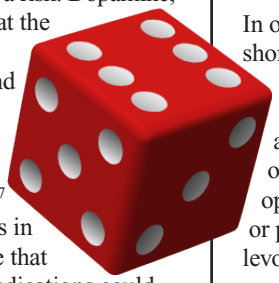
Restless Legs and Gambling

Restless legs syndrome (RLS) is a neurological disorder characterized by the urge to move the legs, that is partially but temporarily relieved by movement. Patients may have a worsening of symptoms at rest and in the evening. RLS is a common disorder that may affect 10% of the population. Evidence-based and clinical guidelines identify dopamine agonists as a first-line treatment for daily restless legs symptoms.[1] There has been recent buzz in the media regarding the possibility of dopaminergic agonist medications such as pramipexole (Mirapex) causing pathologic gambling in some patients.[2] [3] What is the real science regarding the risk for dopaminergic agonist medications causing pathologic gambling?

Any pharmaceutical treatment may have adverse events or side effects. Dopaminergic agonist medications have been implicated in causing compulsive behaviors not only in patients with restless legs syndrome, but also in patients with Parkinson's disease (PD). In addition to gambling, these medications can result in compulsive behaviors including card and video game playing, fishing, gardening, intense interest in established hobbies, hypersexuality, compulsive eating, compulsive shopping, locking and unlocking doors, and even repetitive dressing and undressing.[4] Pathological hypersexuality has been reported in a study of 13 patients with PD and two patients ultimately diagnosed clinically with multiple system atrophy. The hypersexuality began within 8 months after starting dopaminegic agonist therapy in 14 of 15 of the cases, including four on dopamine agonist monotherapy. It resolved in the four cases where the agonist was stopped, despite continued therapy with levodopa. Additional compulsive or addictive behaviors including pathologic gambling occurred in 60% of this patient group.[5] Another case report exists where 7 patients developed compulsive eating in the context of pramipexole use. All of these patients had significant, undesired weight gain and 4 had other comorbid compulsive behaviors. In 5 of these patients the dose of pramipexole was subsequently lowered or discontinued, which then resulted in a remission of the overeating behavior.[6]

How could it be that medications can lead to pathologic gambling and other compulsive behaviors? On a simplistic level, gambling can be though of as a form of instant gratification, or instant reward in exchange for taking a risk. Dopamine, especially at the level of the ventral tegmental area and the nucleus accumbens, has a role in the neural representations of what we experience as reward,[7] such as that which occurs in gambling. It makes sense that dopaminergic agonist medications could have an affect on this, since mice with chronically elevated extracellular dopamine levels due to a dopamine transporter knockdown mutation may have a much higher intake for a sweet food rewards.[8]



Which patients are at risk for this tendency to gamble on dopaminergic agonist medication? Clearly some people love to gamble while others shy away from such risk. Are there trait markers to help identify patients who may be at a greater risk for developing pathologic gambling while taking dopaminergic agonist medications? A study of 42 patients with idiopathic PD without compulsive behaviors demonstrated that those having a younger age of disease onset, higher novelty seeking traits, and a personal or family history of alcohol use disorders may have a greater risk of developing pathological gambling with dopamine agonist medications.[9] Another similar study confirmed increased risk with younger age of disease onset, but also revealed increased risk for male gender and longer duration of treatment with dopaminergic agonist medication.[10]

Some authors have suggested that patients with PD treated with a dopamine agonist should be made aware of the risk of developing an impulse control disorders and monitored clinically. Further, because dopamine agonists are increasingly being used for other indications, future research should assess the dopamine agonist-associated risk for impulse control disorders in other populations,[11] which could include patients with restless legs syndrome.

In one patient whose gambling behavior occurred shortly after reaching the final dose of a combined levodopa and pramipexole therapy, the gambling behavior resolved completely after stopping pramipexole.[12] In several previously mentioned studies, patients who developed pathologic gambling on either pergolide or pramipexole did not exhibit such behavior on levodopa.[5, 7]

Gambling aside, clearly these medications do an enormous amount of good. Dopaminergic agonist medications are very effective in the treatment of both PD and RLS. Pramipexole has practically been singled out as the agent most likely to lead to pathologic gambling, but this is a relatively uncommon side effect and pramipexole is also clearly efficacious in the treatment of RLS.[13]

Be sure to warn patients and watch out for the rare instances of pathologic gambling and other compulsive behaviors that may be brought about by the use of dopaminergic agonist medications, but don't get too caught up in the media by preventing yourself from giving these patients the help that they need.[14]

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