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Receptor Roulette: Pathological Gambling to the Use of Dopamine Agonists

A number of neurological and neuropsychiatric studies have linked dopamine agonists to a form of medication-induced pathological gambling.

When Dottie V., after a lifetime of responsible and modest behavior, suddenly developed a gambling addiction at age 67, her husband and children were shocked and frightened. In less than a year, the retired church secretary put over half of her life savings into the local casino’s high denomination slots before her exasperated husband finally threatened divorce if Dottie did not get help for her gambling problem.

Admitted to a behavioral health treatment center in Arizona, Dottie’s initial physical examination and psychiatric evaluation were unremarkable. Except for her recent gambling problem, the doctors noted only a family history of alcoholism and the fact that Dottie had, for the five years prior to admission, suffered from restless legs syndrome (RLS). The medical record also indicated that Dottie’s RLS had responded well to dopamine agonist therapy.

Dottie’s problem with RLS was not unusual for a woman her age. RLS is a well-known neurological disorder, more prevalent in older adults, in which the affected person suffers unpleasant sensations deep within their limbs. These are accompanied by an irresistible urge to move the legs. Chronic and progressive, RLS is typically worse at night and during periods of inactivity. Symptoms are temporarily relieved when the person moves his or her legs. It is estimated that about 10 percent of the general population suffers from some degree of RLS symptomology (Montplaisir, et al., 2007).

There are two commonly prescribed medications for RLS, pramipexole (Mirapex®) and ropinirole (Requip®). Both are dopamine agonists and work by increasing dopamine transmission in several areas of the brain. In recent years, however, a number of neurological and neuropsychiatric studies have linked dopamine agonists to a form of medication-induced pathological gambling. Hundreds, perhaps thousands of patients have developed pathological gambling and other impulse control problems after beginning dopamine agonist therapy.

Pathological gambling and dopamine agonists

With the recent proliferation of Native American casinos and increasingly easy access to Internet gaming sites, gambling problems are bringing more and more people into counselors’ offices. For most behavioral health clinicians, effective treatment of pathological gambling is well understood: help the patient appreciate and accept the level of impulsivity of their gambling and the need for an ongoing and proactive recovery effort — usually involving regular attendance of Gamblers Anonymous meetings. Typically, clinicians also work to help the gambling patient learn more adaptive ways to handle the affective, cognitive and behavioral precursors to their urges to gamble.

Although effective treatment for pathological gambling is well understood, the etiology of the disorder is not. A number of researchers believe that problematic gambling is related to the dopaminergic system — especially that part of the dopaminergic system located in the area of the limbic brain known as the nucleus accumbens (Lu, et al., 2006). A key reward center, the nucleus accumbens has also been implicated in addiction to alcohol and other drugs of abuse. Proper regulation of dopamine within this part of the brain, it seems, is critical in mediating a wide range of emotion and behavior.
The idea that dopamine figures in problematic gambling is also supported by the work of Dr. Valerie Voon, a researcher at the National Institute of Neurological Disorders and Stroke (NINDS). In a study of 297 patients receiving dopamine agonists (in this case they were Parkinson's disease patients) she found that 7.2 percent of those studied reported the development of pathological gambling or some other kind of impulse-control problem (the normal prevalence of pathological gambling is about 3.4 percent in the general population). For the patients in Dr. Voon's study, problematic gambling began only after the subject started on or had a dose escalation of dopamine agonists.

Further evidence of a relationship between dopamine agonists and pathological gambling is that, in affected patients, problematic gambling that began coincident with the initiation of a dopamine agonist, stopped soon after the medication was discontinued (Lu, et al., 2006). In fact, a majority of patients studied experienced a resolution of their gambling problems within a month of discontinuing dopamine agonist therapy. Patients who reported other impulse-control problems, like hypersexuality or impulsive spending also reported cessation of these activities within a month of stopping the use of a dopamine agonist (Barclay & Vega, 2005).

Some researchers believe that dopamine agonists can heighten behavioral impulsivity because they may disproportionately stimulate dopamine D3 receptors located in the limbic system (Dodd, et al., 2005). Pramipexole and ropinirole have a strong affinity with the D3 receptor and are the medications implicated in the development of problematic gambling or other impulse control problems (Barclay & Vega, 2005).

Why dopamine agonists awaken an impulse to gamble in only a few of the patients who take them may have something to do with the genetic version of dopamine receptors the affected patients have inherited. Researchers think that some variations of dopamine receptors may be more prone to dopamine stimulation than others. Genetic research and functional brain imaging might eventually reveal more about this (Archart-Treichel, 2005).

Dr. Voon found that study subjects who reported problematic gambling, when compared to non-affected patients, scored higher in personality testing for novelty seeking and impulsivity. Affected patients also reported a personal or family history of alcohol abuse or dependence (Voon, et al., 2007). These data seem to imply that patients being considered for dopamine agonist therapy should be screened for risk factors — such as impulsivity, novelty-seeking and a personal or family history of alcohol use disorders — that might predispose them to develop gambling problems while on these medications. It also might be a good practice to inform prospective dopamine agonist patients, and even members of their families, about the potential behavioral risks associated with the therapy, and to monitor patients for the emergence of impulse control problems throughout the course of their treatment (Lu, et al., 2006). Extra caution on the part of medical practitioners may be key here, considering that dopamine agonists are being marketed directly to the consumer through television and other mass media ads.

If patients on dopamine agonist therapy do develop impulse control difficulties, treatment providers may want to explore alternative, behaviorally-focused strategies to manage RLS symptoms. RLS has been associated with a sedentary lifestyle, and some believe that exercise is a promising non-pharmacological treatment option. In fact, a recent randomized controlled study showed that RLS patients who exercised for 30 minutes three times a week reported significant relief from RLS symptoms (Montplaisir, et al., 2007).

Dottie's case highlights the importance of a thorough multi-axial assessment of gambling patients. Her report of alcoholism in her family, at first thought to be an innocuous point of information, turned out to be a risk factor for developing gambling problems after starting on dopamine agonists. After cutting her dose of dopamine agonist by about half, Dottie reported increased symptoms of RLS, but, significantly, fewer and less severe urges to gamble. The behavioral focus of Dottie's treatment involved helping her find more adaptive ways to manage stress, learning good sleep hygiene and developing an exercise regimen to reduce the remaining symptoms of RLS.

Assessing the root causes of gambling problems or other behavioral impulsivity is best done deliberately and thoroughly. At the facility where Dottie sought treatment, clinicians adhere to a policy of making a complete assessment of Axis III conditions and current medications, screening for dopamine agonists. Personality testing also is routinely ordered for patients taking dopamine agonists who are experiencing impulse control difficulties.

References


