The WAGER Vol. 11(1) – "Parkinson's Drug Sparks Gambling Fever!" Evaluating the scientific evidence that Mirapex causes Pathological Gambling

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In July, 2005, newspapers all over the world reported that Mirapex, a drug used to treat Parkinson's disease, caused some patients to become addicted to gambling. A recent issue of Time Magazine identified the finding as one of the most important medical breakthroughs of 2005 ("The Year in Medicine," Song, Park et al., 2005). In their eagerness to report these interesting results, however, the media failed to emphasize that the research is in its very preliminary stages and much more research is necessary before scientists can establish that a direct causal link exists. In this issue of the WAGER, we evaluate the evidence for the claim that gambling addiction is a specific side effect of Mirapex (i.e., Pramipexole dihydrochloride, in the class of dopamine agonists, or DAs).

Research by clinicians at a Parkinson's disease clinic (Dodd, Klos et al. 2005) stimulated the media reports about the Mirapex-gambling problem link. In this research, clinicians described 11 cases of Parkinson's patients who reported during routine visits that they had developed a Pathological Gambling disorder (PG) after taking high doses of either Mirapex or another DA. Like most clinicians, the clinic's staff do not routinely ask patients about gambling or other unusual behaviors; these patients freely volunteered the information. All 11 patients reported that they had not been frequent gamblers before DA treatment and that the problems ceased after withdrawing from, or lowering the dose of, the DA. Below we discuss two major limitations of this study (Dodd, Klos et al. 2005) and evaluate the validity of the authors'conclusions in the context of other relevant research.

"A mountain or a molehill?"

Scientists and interested observers must consider the size of causal effects.

Understanding effect sizes can help scientists and science journalists from overstating the conclusions that can be drawn from rare events or small differences between groups. In the Dodd et al. study, only eleven cases of self-reported PG were identified in two full years of treating Parkinson's patients. The authors did not report how many patients were seen during that time, or how many patients received DA treatment. Presumably, for a clinic that specializes in Parkinson's disease, 11 patients reflects a very low prevalence rate. For example, a previous study with 250 Parkinson's patients on DA drugs (Molina, Sainz-Artiga et al. 2000) found that only 1.5% of these patients had been diagnosed with PG. This prevalence rate falls within the rate normally observed among the general population. In addition, as the authors did not routinely ask patients about PG, we do not know the prevalence of PG among Parkinson's patients who were not taking a DA. Therefore, the rate of PG prevalence among these patients might not differ from the rate in the general adult population. Although anecdotal or case-based evidence can suggest

important research questions, only studies with certain characteristics (e.g., random assignment of subjects to groups, standard treatment within groups, a comparison group without treatment, and sufficient numbers of subjects) can identify the source of an observed phenomenon and rule out other factors, including chance, as an explanation.

"Do not seek and ye shall not find."

Researchers can report only the data they chose to obtain. In their study, Dodd and colleagues (1995) focused on patients who reported gambling problems, and they did not ask these patients about other related behaviors or disorders. Interestingly, three of the six patients whose cases were described in more detail reported experiencing compulsive behaviors in addition to PG (e.g., compulsive shopping and hypersexuality), but this

overlap was not discussed in the report. (See Table below for characteristics of these six patients.) Through these omissions, the authors implied that PG is a unique "side effect" of DAs. However, other research suggests that DAs might facilitate or trigger a larger problem of which PG is only one part. To illustrate, in two studies, DA patients developed a variety of excessive behavior patterns, including compulsive eating, PG, increased alcohol use, hypersexuality, addiction to the DA itself, and increased cigarette cravings. These studies' authors

suggested that the variety of compulsive behaviors might reflect a “global sensitization of appetitive behaviors in susceptible patients” ((Nirenberg and Waters 2005), p.4) or an “addictionlike” syndrome referred to as “Hedonistic homeostatic dysregulation” (Giovannoni, O’Sullivan et al. 2000). Alternatively, the gambling problems exhibited by the patients in Dodd and colleagues’ study might have been the result of a manic or hypomanic episode. These episodes, usually seen in the context of bipolar disorder, can manifest in excessive behaviors like compulsive gambling and hypersexuality.

If PG is not a specific “side effect” of DAs, but rather just one aspect of an addiction-like syndrome or of a manic episode that emerges secondary to DA use, perhaps high doses of DAs trigger these behaviors in patients with personal histories of, or genetic or psychosocial predispositions to, addiction or bipolar disorder. If this were the case, the DA would be said to play a faciliatative role or serve as a partial cause in developing these behaviors.

Table 1: Characteristics of “representative” patients in Dodd et al. (2005)

The current evidence for a direct causal link between DA drugs and PG is quite weak. Although the case studies are suggestive enough to warrant future research on the possible link between DA drugs and PG and/or other excessive or compulsive behaviors, at this point several factors limit the research. Among these factors are the small number of subjects and the absence of sufficient and relevant information. Further, the Dodd et al. article overstates its conclusion – that “DA drugs appear to be uniquely implicated as a cause of pathological gambling” (Dodd et al., 2005, p. 1381). In addition, Dodd et al. fail to take into account previous findings suggesting that PG is just one of a variety of addictive behaviors possibly linked to DA drugs.

What do you think? Comments on this article can be addressed to Cheryl Browne.

References

Dodd, M. L., K. J. Klos, et al. (2005). "Pathological gambling caused by drugs used to treat Parkinson Disease." Archives of Neurology 62: 1-5.

Giovannoni, G., J. D. O’Sullivan, et al. (2000). "Hedonistic homeostatic dysregulation in patients with Parkinson’s disease on dopamine replacement therapies." Journal of Neurology, Neurosurgery, & Psychiatry 68(4): 423-428.

Molina, J. A., M. J. Sainz-Artiga, et al. (2000). "Pathologic gambling in Parkinson's Disease: A behavioral manifestation of pharmacologic treatment?" Movement Disorders 15(5): 869-872.

Nirenberg, M. J. and C. Waters (2005). "Compulsive eating and weight gain related to dopamine agonist use." Movement Disorders. In Press; Published online 31 Oct 2005.

Song, S., A. Park, et al. (2005). The Year in Medicine. Time. December 5: 63-87.