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DRD4 POLYMORPHISM PREDICTS THE EFFECT OF L-DOPA ON GAMBLING BEHAVIOUR

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A challenging question in the fields of neuroscience and addiction research is why some individuals are more vulnerable than others to addictive disorders. Pharmacogenetic studies investigating how genetic variation leads to differential drug response offer a way to unravel this mystery.

In recent years, impulse control disorders, in particular pathological gambling, have been described in Parkinson's patients; these problems are most likely associated with dopaminergic treatment. Interestingly, only a subgroup of Parkinson´s patients develops pathological gambling, raising the question whether there might be an interaction between genetic predisposition and dopaminergic drug administration. By applying a pharmacogenetic approach in 200 healthy subjects, we observed a differential effect of dopaminergic stimulation using 300 mg of L-DOPA on gambling behaviour, depending on variation in the dopamine D4 receptor gene. Carriers of the 7 repeats allele of the DRD4 exon III variable number tandem repeat polymorphism show an increased propensity to gamble after dopamine modulation. These findings may have implications for the dopaminergic treatment of Parkinson's disease patients by offering a genotype approach for determining individual susceptibilities for pathological gambling. They may also afford insights into the vulnerability mechanisms underlying addictive behaviour.

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