RESEARCH SYNOPSIS

Sabbatini da Silva Lobo, D., Vallada, H. P., Knight, J., Martins, S. S., Tavares, H., Gentil, V., & Kennedy, J. L. (2007). Dopamine genes and pathological gambling in discordant sib-pairs. ***Journal of Gambling Studies, 23*****(4), 421-433. doi:10.1007/s10899-007-9060-x**

RESEARCH QUESTIONS

Is the dopaminergic system, more specifically the dopamine receptor genes DRD1, DRD2, DRD4, and DRD5 related to pathological gambling (PG)?

PURPOSE

Neurobiological research has found a link between the dopaminergic system and psychiatric disorders such as pathological gambling and other addictions. There is also evidence that inherited genetic factors play a large role in the diagnosis of PG, however, this research was only conducted with male pathological gamblers. This will be the first epidemiological study of pathological gambling in Brazil, and will be the first investigation of the molecular genetics of PG using a family-based association design (discordant sib-pairs).

HYPOTHESIS

None stated.

PARTICIPANTS

Participants were recruited from the Gambling Outpatient Unit at the Institute of Psychiatry, University of Sao Paulo. A total of 140 discordant sibling pairs (one pathological gambler, one non-pathological gambler) participated in this study. The mean age of the gambler and non-gambler sibling was 40 years (*SD*=8.9 and 9.8, respectively). There were 70 male pathological gamblers (PG), of the pathological gamblers 37 male non-pathological gambler siblings (NPG) and 33 had a female non-pathological gambler sibling. In terms of ethnicity, 78% were Caucasian. Since this study was examining the molecular genetic basis of PG, the study participants had to be full siblings, with one individual of the sibling pair diagnosed with PG and the other not meeting any of the DSM-IV criteria for PG. Gamblers and non-gambler participants were excluded if they reported any lifetime history of psychosis, bipolar disorder type I, and neurological diseases.

PROCEDURE

Trained psychiatrists diagnosed patients with PG based on DSM-IV diagnostic criteria.

DRD1: Participants were genotyped for a T/C nucleotide substitution located 800 bp upstream from exon I. This polymorphism was chosen because of evidence that it alters function of the DRD1 gene, and because of findings of its association with ADHD.

DRD2: The TaqIA polymorphism located 10 kb downstream from exon VIII was genotyped. TaqIA is associated with reduced D2 recpetor density and with altered substrate-binding specificity, and substance dependence disorders.

DRD3: A serine to glycine amino acid substitution at position 9 in the receptor protein corresponding to nucleotide 25 in exon I was genotyped because it is responsible for a significant decrease in the receptor's affinity for dopamine.

DRD4: The 48 bp variable number of tandem repeats (VNTR) located at exon III was genotyped because it appears to alter the pharmacological profile of the receptor and is associated with substance dependence, PG, and ADHD.

DRD5: Participants were genotyped for dinucleotide (CA) repeat located downstream from exon II. Alleles 136-, 146-, and 148-bp were associated with ADHD. Although there was no evidence suggesting that this polymorphism is functional, a joint analysis of 14 independent samples has shown an association with the DRD5 locus, supporting a previous hypothesis that this microsatellite may be in linkage disequilibrium with 1 or more functional variants.

Dopamine Transporter Gene (SLC6A3): Participants were genotyped for the 40 bp VNTR located downstream from exon 15 in the 3' un-translated region. Genotype 9/10 is related to decrease in protein transcription and has been found to be related to ADHD and alcohol dependence.

All genotyping was conducting according to the polymerase chain reaction (PCR) protocol.

MAIN OUTCOME MEASURES

Participants were genotyped for the DRD1, DRD2, DRD3, DRD4, DRD5, and the Dopamine Transporter

Gene (SLC6A3). The DSM-IV was used to diagnosed PG.

KEY RESULTS

A significant relationship was only found between PG and one of the dopamine receptor genes (specifically allele T of DRD1). No other significant differences were found between the PG sibling and the NPG sibling on any of the other dopamine receptor genes.

LIMITATIONS

The study design was not powerful enough to detect small effect sizes because the sample size was small; thus, results need to be replicated with a larger number of participants to assess the validity of the results.

CONCLUSIONS

The results of this study show that the DRD1 allele T is significantly related to PG. These results suggest that PGs may possess genetic vulnerabilities that make them prone to developing pathological gambling.

KEYWORDS: reward system, pathological gambling, genetics, dopamine

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