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Association between dopamine D4 receptor genotype and trait impulsiveness

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Impulsiveness is a heritable personality trait playing a substantial role in the development of certain psychiatric disorders such as addiction. A link between trait impulsiveness and 48-bp variable tandem repeat (VNTR) polymorphism in exon III polymorphism of the dopamine D4 receptor gene (*DRD4*) is viewed as highly controversial. We aimed to test the association between the *DRD4* VNTR and trait impulsiveness.

In all, 192 healthy European individuals of self-reported German ancestry ($M = 39.1$ years, $SD = 12.9$ years; 90 women) were recruited. Written informed consent was obtained from all participants. A psychiatrist screened volunteers for exclusion criteria (axis I disorders, psychiatric diagnoses in first-degree relatives, neurological diseases).

Participants were asked to fill in the Barratt Impulsiveness Scale (BIS 11, Preuss *et al.*, 2008). The *DRD4* 48-bp VNTR polymorphism was amplified by PCR using fluorescent-labelled primers as described earlier (Lichter *et al.*, 1993), and the individual VNTR genotypes were assessed by DNA fragment length analysis on an Applied Biosystems 3730 DNA analyzer (Life Technologies, Carlsbad, California, USA).

In terms of the *DRD4* VNTR and in accordance with the literature, individuals were grouped as either carriers of two short alleles (both alleles \leq six 48bp repeats) or individuals carrying, at least, one long allele (\geq seven repeats). Analysis of covariance was conducted controlling for effects of age and sex.

Individuals with short alleles only (S/S: $n = 141$) of the *DRD4* VNTR showed statistically significant higher BIS total scores ($M = 62.5$, $SD = 7.0$) than individuals carrying at least one long allele [$n = 51$; L/L: $n = 6$, L/S: $n = 45$; $M = 58.5$, $SD = 7.1$, $F(1, 191) = 10.03$, $P = 0.002$; $d = 0.56$].

Our result suggests that there might be genetic contributions to impulsiveness mediated through neurotransmitter systems such as dopamine alongside serotonin in mentally healthy adults. Unlike Munafó *et al.* (2008), more recent studies suggest an association between long *DRD4* repeats and lower trait impulsiveness supporting our finding.

Interestingly, imaging studies have found further associations between dopamine *DRD4* gene variants and impulsiveness-related behaviour, as well as with its underlying brain activity. Significant differences in the blood oxygen level-dependent response in the inferior frontal gyrus, precuneus and cingulate gyrus associated with motor impulsiveness have been described as a function of the *DRD4* VNTR. Of note, behavioural measures only partly overlap with trait impulsiveness. They may have both an overlapping and distinct biological background (Schilling *et al.*, 2012).

Clinical research suggest that *DRD4* gene variants have an important role in mental health. Findings implicate the *DRD4* polymorphism in the development of alcohol use disorders. Combined genetic and fMRI data suggest that variants within *DRD4* VNTR appear to influence processes related to impulsive behaviour, which may increase the risk for alcohol abuse and dependence. In addition, moderating effects of *DRD4* VNTR on social interactions are also discussed.

Generally, these data highlight the potential utility of integrating transdisciplinary methods such as genetics, and neuroimaging techniques such as single-photon emission computed tomography, functional and structural MRI to improve the theories of impulsiveness-related disorders.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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