Association between dopamine D4 receptor genotype and trait impulsiveness

Christina Schilling[a], Simone Kühn[b], Thomas Sander[c] and Jürgen Gallinat[a], [a]Department of Psychiatry and Psychotherapy, Charité University Medicine Campus Mitte, [b]Center for Lifespan Psychology, Max Planck Institute for Human Development, Berlin and [c]Cologne Center for Genomics (CCG), Cologne University, Cologne, Germany

Correspondence to Christina Schilling, PhD, St Hedwig Hospital, Große Hamburger Str. 5-11, 10115 Berlin, Germany
Tel: +49 30 2311 2904; fax: +49 30 2311 2750;
e-mail: christina.schilling@charite.de

Received 21 March 2013 **Revised** 1 August 2013 **Accepted** 14 May 2013

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 48 bp 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 Munafò *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.

References

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