

The Role of DRD2 in Adolescent Reward Processing

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The dopaminergic system, known for its role in reward processing, matures over adolescence. The C allele in the SNP C957T of the dopamine D2 receptor (DRD2), has been associated with alcohol and tobacco misuse and is associated with less DRD2 expression in the striatum and greater expression in the cortex. Imaging studies found the C allele predicted greater activation in the striatum during reward learning and structural connectivity between the striatum and frontal cortex, brain regions known to play a role in addiction.

This risk allele was examined in context of the Adolescent Development Study, a longitudinal neuroimaging study of substance and alcohol use in adolescents (aged 11-14.5 years old). The N per genotype was: 11 T/T, 17 T/C, and 24 C/C with comparisons combining T/T and T/C versus CC. The Wheel of Fortune fMRI task, a measure of risky decision-making, assessed responses to variable reward/loss probabilities and magnitude of reward/loss feedback.

Comparison between BOLD activation of Wins>Losses revealed a result in the left inferior frontal gyrus, left inferior parietal lobule, and right occipital lobe, with CC's exhibiting lower activation. PPI examination of connectivity showed greater connectivity for CC's between the right nucleus accumbens and the right cuneus/posterior cingulate gyri, as well as between the left caudate and the bilateral cuneus/calcarine sulci.

Given the inferior frontal gyrus' association with reappraisal and inhibition of emotional responses, reduced activity in CC's may represent reduced inhibitory control of emotional stimulus processing. Greater connectivity between areas associated with reward processing (e.g., nucleus accumbens and caudate) and those involved in self-reflection (e.g., posterior cingulate gyrus and cuneus), could signify CC's focus on rewards more than the T's. Together, these results suggest CC allele in adolescence is associated with lower neural response to and greater connectivity to rewards, possibly increasing risk of future substance use problems.