

Dopamine Transporter (*Dat1*) Gene Variation And Intravenous Alcohol Self-Administration In Non-Dependent Drinkers: Influence Of Sex Differences

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Genetic variation in the dopamine transporter (DAT1/SLC6A3) has been associated with alcohol dependence. The 10A repeat allele of the variable number of tandem repeats (VNTR) polymorphism has been associated with greater DAT1 expression, and greater increases in alcohol-induced stimulation and mood. The objective of this study was to characterize the effect of DAT1 variation and the role of sex differences on intravenous alcohol self-administration (IV-ASA) in non-dependent drinkers.

Healthy non-dependent drinkers (N=70) completed a progressive-ratio IV-ASA session using the Computer-Assisted Infusion System. The session consisted of a 25-min priming phase, followed by a 125-min phase during which they were required to push the button an increasing number of times for additional individually standardized alcohol infusions. Subjective response was measured serially using the Drug Effects Questionnaire (DEQ). Additional measures included the UPPS-P Impulsivity scale and the Sensitivity to Punishment and Reward Questionnaire (SPSRQ).

Results showed strong DAT1 by sex interaction effects on IV-ASA measures. Male 10A homozygotes pressed for greater number of rewards and higher peak breath alcohol concentration compared to 10A females, while 9A males pressed for less alcohol than 9A females. Subjective response showed a similar pattern, with 10A males reporting greater subjective responses for "intoxication" and "wanting alcohol" following the priming interval compared to 10A females, while 9A females reporting higher subjective responses compared to 9A males. Additionally, 10A homozygotes showed higher sensitivity to reward on the SPSRQ, and a trend for higher sensation-seeking on the UPPS-P scale compared to 9A carriers.

These results demonstrate that the DAT1 VNTR polymorphism has a significant effect on motivation and consumption of IV alcohol. Sex was a significant moderator of this effect with 10A homozygous males showing greater responses compared to females. These findings underscore the critical role of dopamine neurotransmission in the motivation and consumption of alcohol in non-dependent drinkers.