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Genetic association of Nucleus Accumbens 5-HIAA level and alcohol preference drinking in Quasi-Congenic RQI Mouse Models

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ABSTRACT:

Quasi-congenic Recombinant QTL Introgression strains were initially used to identify the first gene (*Grm7*, Glutamate Metabotropic Receptor 7) as accounting for alcohol consumption in a mammalian model. Quasi-congenic mice of the alcohol avoiding C5A3 and the alcohol preferring I5B25A strains were subjected to *in vivo* microdialysis in the Nucleus Accumbens (NAc) to test the hypothesis that genetic predisposition to high alcohol drinking behavior is associated with hypoactive serotonergic function in the NAc. Neurotransmitter and metabolite contents were analyzed by HPLC in dialysate samples collected in three phases: Baseline, Control (after saline injection, i.p.), and Alcohol (after alcohol injection, 1.5 g/kg i.p.). Samples were collected every 20 min before and after each injection. 5-HIAA levels in the alcohol preferring I5B25A strain were consistently lower in dialysate samples in the course of all three phases. GLM RM ANOVA and Tests of Between-Subjects Effects showed a significant strain difference. Microsatellite DNA marker genotyping of the biallelic strains allowed the identification of differential chromosome regions associated with low 5-HIAA levels and high alcohol drinking. Testing 19 autosomal chromosomes of the C5A3 and I5B25A strains we found 16 differential markers distributed on 5 chromosomes. The results are consistent with accumulated evidence for the involvement of serotonin in reward processing, and support earlier reports of similar association in rats and primates, including *Homo sapiens*. The data suggest that further genetic selection and construction of congenic lines can lead to the identification of pleiotropic candidate gene(s) affecting both the serotonergic system and alcohol preference drinking behavior.

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