The *OPRM1* A118G Polymorphism and Alcohol-Related Phenotypes: Converging Evidence Against Associations with Alcohol Sensitivity and Consumption

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The endogenous opioid system may be involved in the development and maintenance of alcohol use disorder (AUD) and is a target for existing AUD pharmacotherapies. A functional polymorphism of the mu-opioid receptor gene (*OPRM1* A118G, rs1799971) may alter the risk of developing AUD. Human laboratory studies have demonstrated that minor allele carriers self-administer more alcohol, show greater sensitivity to alcohol's effects, and exhibit increased alcohol-induced dopamine release. On the other hand, large genome-wide association studies and meta-analyses of candidate gene studies have not found an association between this genotype and alcohol dependence diagnosis. Given this discrepancy, the present study sought to verify whether *OPRM1* A118G was associated with alcohol self-administration, subjective response to alcohol, and craving in a sample of 106 social drinkers of European ancestry who completed an intravenous alcohol self-administration session. We found no relationship between *OPRM1* rs1799971 genotype and subjective response to alcohol or craving. *OPRM1* genotype was not associated with total alcohol exposure or likelihood of attaining a binge-level exposure (80mg%) during the intravenous alcohol self-administration session. Analysis of 90-day Timeline Followback interview data in a larger sample of 965 participants of European ancestry found no relationship between *OPRM1* genotype and alcohol consumption in either alcohol dependent or non-dependent participants. These findings suggest that there may not be an association between *OPRM1* rs1799971 genotype and alcohol consumption or sensitivity in individuals of European ancestry.