

O-25 - VARIATIONS IN PDYN SEQUENCE ARE ASSOCIATED WITH NEGATIVE CRAVING IN ALCOHOL DEPENDENT SUBJECTS

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Introduction: Craving in negative emotional situations (negative craving) is commonly associated with relapse and heavy alcohol use. Elevated dynorphin levels were associated with negative emotions, while variations in the OPRK1 and PDYN genes encoding OPRK1 receptor and dynorphins were associated with alcohol dependence.

Objectives: To investigate potential overlap in the genetic factors underlying, negative craving and alcohol dependence.

Aims: Examine the association of the negative craving and genetic variation in the OPRK1 and PDYN genes.

Methods: 13 PDYN and 10 OPRK1 Single Nucleotide Polymorphisms (SNPs), including those previously reported to be associated with alcohol dependence were genotyped in 196 alcohol dependent subjects. The raw scores of the negative subscale of Inventory of Drug Taking Situations (IDTS) were utilized as a quantitative measure of negative craving. Logistic regression models were used to test for associations after controlling for age and gender.

Results: Gene-level haplotype testing demonstrated significant association of negative craving with variation in PDYN ($p < 0.05$) but not OPRK1 gene. The rs2281285 - rs199794 haplotype showed significant association ($p = 0.0236$) with negative craving, while rs2235749 - rs10485703 haplotype showed marginally significant association ($p = 0.055$). This replicates previous findings of association between these haplotypes and alcohol dependence. Negative craving was also associated with PDYN rs2281285 variant ($p = 0.012$) with estimated effect size of 6.95 ($SE = 2.75$). This new association finding was not significant after correction for multiple testing ($p = 0.18$).

Conclusions: Our findings support association of PDYN sequence variation with negative craving in alcohol dependent subjects. Future studies should investigate functional mechanisms of this association.