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PDYN RS2281285 VARIANT IS ASSOCIATED WITH ALCOHOL DEPENDENCE IN MALE BUT NOT FEMALE SUBJECTS

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Introduction: Recent findings support sex-specific effects of *PDYN* polymorphisms on association with opioid addiction (Clarke et al. 2012). We have demonstrated that *PDYN* haplotypes, which include rs2281285, are associated with alcohol dependence and propensity to drink in negative emotional situations (negative craving) (Karpyak et al 2012). The rs2281285 variant may contribute to regulation of alternative PDYN mRNA transcription specific to brain area or physiological condition.
Objectives: To investigate sex-specific effects of the *PDYN* rs2281285 variant on risk for alcohol dependence.
Aims: To examine the association of the *PDYN* rs2281285 variant with alcohol dependence in male and female subjects.
Methods: rs2281285 was genotyped in the investigation cohort of 816 (554 males) alcohol dependent subjects (DSM-IV-TR) and 1248 (603 males) non-alcoholic controls and in the replication cohort of 467 (347 males) alcohol dependent subjects and 431 (224 males) non-alcoholic controls. Logistic regression models were used to test for sex-specific associations after controlling for age.
Results: As previously reported, significant association of the *PDYN* rs2281285 variant with alcohol dependence was found in the investigation (p=0.008, odds ratio=1.299), but not the replication cohort (0.223, OR=0.118). However, sex-specific analyses revealed stronger association in males (p=0.002, OR=1.493) but not females (p=0.684, OR=1.066) in the investigation cohort, and a trend for association in males (p=0.086, OR=1.352) but not females (p=0.808, OR=0.947) in the replication cohort.
Conclusions: Our findings support association of *PDYN* rs2281285 variant with alcohol dependence in male but not female subjects. Future studies should investigate functional mechanisms of this effect.

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