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Oxycodone behaviors in *Cacna1h* knockout mice

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The genetic basis of Opioid use disorder (OUD) is largely unknown. Quantitative trait locus mapping in rodent models offers advantages to human GWAS (controlled sample sizes, controlled environment, within-species gene validation) and can elucidate genetic causes of addiction-relevant model phenotypes. To identify of the genetic basis of OUD-relevant behaviors in mice, we surveyed 29 mouse inbred strains for differences in behaviors following semi-synthetic opioid oxycodone (OXY) administration. Using an OXY conditioned place preference (CPP) experimental design, we found robust strain differences in OXY-induced locomotion, place preference, and state-dependent learning, indicating a heritable basis for these phenotypes. Subsequent haplotype association mapping identified a region on chromosome 17 associated with OXY-induced locomotion containing the candidate gene *Cacna1h*, which encodes for a voltage-gated calcium channel subunit. To assess differential responses to OXY conditioned reward, tolerance and withdrawal between genotypes, we tested *Cacna1h* knockout (KO) mice on a mixed 129/C57BL/6N background for OXY CPP and hot plate analgesia, elevated plus maze, and light-dark conflict. There were no significant genotypic differences in distance traveled in response to OXY. Additionally, we observed no genotypic differences in OXY CPP or OXY-induced state-dependent CPP, nor were there any significant differences OXY antinociceptive tolerance or spontaneous withdrawal in the elevated plus maze or the light/dark box. Our negative findings fail to support a role for *Cacna1h* in opioid addiction model behaviors, with one notable limitation that we have only tested a null mutation on a single genetic background.