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CADM2 is implicated in impulsive personality and numerous other traits by genome- and phenome-wide association studies in humans and mice

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Impulsivity is a multidimensional heritable phenotype that broadly refers to the tendency to act prematurely and is associated with multiple forms of psychopathology, including substance use disorders. We performed genome-wide association studies (GWAS) of eight impulsive personality traits from the Barratt Impulsiveness Scale and the short UPPS-P Impulsive Personality Scale (N=123,509-133,517 23andMe research participants of European ancestry), and a measure of Drug Experimentation (N=130,684). Because these GWAS implicated the gene *CADM2*, we next performed single-SNP phenome-wide studies (PheWAS) of several of the implicated variants in *CADM2* in a multi-ancestral 23andMe cohort (N=3,229,317, European; N=579,623, Latin American; N=199,663, African American). Finally, we produced *Cadm2* mutant mice and used them to perform a Mouse-PheWAS ("MouseWAS") by testing them with a battery of relevant behavioral tasks. In humans, impulsive personality traits showed modest chip-heritability (~6-11%), and moderate genetic correlations (r_g=.20-.50) with other personality traits, and various psychiatric and medical traits. We replicated associations from earlier GWAS of these traits and found novel associations including *DRD2*, *CRHR1, FOXP2, TCF4, PTPRF*. PheWAS for *CADM2* variants identified associations with 378 traits in European participants, and 47 traits in Latin American participants, replicating associations with risky behaviors, cognition and BMI, and revealing novel associations including allergies, anxiety, irritable bowel syndrome, and migraine. Our MouseWAS recapitulated some of the associations found in humans, including impulsivity, cognition, and BMI. Our results further delineate the role of *CADM2* in impulsivity and numerous other psychiatric and somatic traits across ancestries and species.