

Genome-wide association study of delay discounting identifies *GPM6B* and demonstrates co-heritability with smoking

**Presenter:** Abraham A Palmer

**Full author list:** Sandra Sanchez Roige, Pierre Fontanillas\*, Sarah Elson\*, Josh Gray, Harriet de Wit, James MacKillop, Abraham A Palmer

\*23andMe, Inc., Mountain View, CA

**Abstract:** One of the most widely used behavioral economic measures is delay discounting, which refers to the devaluation of delayed rewards. Delay discounting is correlated with drug abuse. We performed a genome-wide association study for delay discounting in collaboration with 23andMe, Inc., a consumer genetics company. Our sample consisted of 23,217 male and female adult research participants, all of whom were of European descent. Chip heritability was estimated at about 12%, supporting a role for common genetic variation. We detected a genome-wide significant association ( $p=2.4 \times 10^{-8}$ ) that was centered on the gene *GPM6B*, which is known to regulate internalization of the serotonin transporter. Because *GPM6B* is located on the X chromosome, we examined males and females separately; although the signal was stronger in males, it was observed in both sexes (meta-analysis of males and females:  $p=2.8 \times 10^{-8}$ ). A second locus on chromosome 17 approached significance ( $p=1.4 \times 10^{-7}$ ) and harbors several intriguing regulatory polymorphisms. We used polygenic methods to examine co-heritability between delay discounting and several personality and psychiatric traits. We identified strong genetic correlations between delay discounting, smoking behavior, educational attainment, obesity and other neuropsychiatric conditions. We are currently seeking replication samples and will begin testing genetic rodent models in the coming months.