DEPRESSION IS INFLUENCED BY MANY COMMON GENETIC VARIANTS WITH SMALL EFFECT, PARTLY SHARED WITH ANXIETY

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Background Genome-wide significant findings are rare in genome-wide associations studies (GWAS) in psychiatry. Is this because studies were underpowered or is the hypothesis of common genes with small effects incorrect? This study examines the genetic architecture of depression and the overlap in genetic risk factors with anxiety.

Methods From the GAIN-MDD-GWAS results (Sullivan et al, Mol Psych, 2009), sets of SNPs were selected based on p-values between <0.00001 and 1. These sets were used to calculate genetic risk scores for each individual in two independent Dutch samples: the Rotterdam study with 178 MDD and 212 anxiety cases and the Erasmus Rucphen Family (ERF) study in which symptoms of anxiety and depression were assessed in 1 886 participants. For each p-value threshold, a genetic score was calculated by multiplying the number of risk alleles per SNP with the log odds ratio in the MDD-GWAS, summed over all SNPs. (Logistic) regression analyses were performed to test the predictive value of the score (see Purcell et al, Nature, 2009).

Results Genetic scores significantly explained up to 0.6% of the variance for depression and 2.1% in anxiety (figure)

Conclusions Depression is influenced by many genes, each with a very small effect. This polygenic component is shared with anxiety. Increasing sample sizes for GWAS on anxiety and depression seems a reasonable strategy to find these genes.

Figure % variance explained by genetic risk scores based on SNP sets with rising p-values for different measures of anxiety and depression