First author: Franke, Barbara (poster)

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Authors: Franke B. (1, 2, 5), Rijpkema M. (3, 5), Arias Vasquez A. (1, 2, 5), Veltman J. A. (1), Brunner H. G. (1), Hagoort P. (3, 5) & Fernandez G. (3, 4, 5)


Title: Genome-wide association study of regional brain volume suggests involvement of known psychiatry candidate genes, identified new candidates for psychiatric disorders and points to potential modes of their action

Text: Though most psychiatric disorders are highly heritable, it has been hard to identify genetic risk factors involved, which are most likely of small individual effect size. A possible way to aid identification of risk genes is the use of intermediate phenotypes. These are supposed to be closer to the biological substrate(s) of the disorder than psychiatric diagnoses, and therefore less genetically complex. Intermediate phenotypes can be defined e. g. at the level of brain function and of regional brain structure. Both are highly heritable, and regional brain structure is linked to brain function. Within the Brain Imaging Genetics (BIG) study at the Radboud University Nijmegen (Medical Centre) we performed a genome-wide association study (GWAS) in 1000 of the currently 1400 healthy study participants. For all BIG participants, structural MRI brain images were available. Gray and white matter volumes were determined by brain segmentation using SPM software. FSL-FIRST was used to assess volumes of specific brain structures. Genotyping was performed on Affymetrix 6.0 arrays. Results implicate known candidates from earlier GWAS and candidate gene studies in mental disorders in the regulation of regional brain structure. E. g. polymorphisms in CDH13, featuring among the top-findings of GWAS in disorders including ADHD, addiction and schizophrenia, were found associated with amygdala volume. The ADHD candidate gene SNAP25 was found associated with total brain volume. In conclusion, the use of intermediate phenotypes based on (subcortical) brain volumes may shed more light on pathways from genes to diseases, but can also be expected to facilitate gene identification in psychiatric disorders.

Theme: C - Disorders of the nervous system
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