associated with AD, like the hippocampus and amygdala, as important predictors of the most significant SNPs. In summary, our results indicate that non-linear methods like random forests may offer additional insights into phenotype-genotype associations compared to traditional linear multivariate GWAS methods.

**Discussion:** While reverse genotype prediction correctly picks up these correlations between the phenotypic traits, the corresponding correlations and shared effects between SNPs are currently ignored, since reverse genotype prediction approaches tend to learn prediction models for each SNP individually. Thus, a logical extension of our approach would be to use multi-task regression, i.e., to predict multiple SNPs simultaneously. However, this raises important computational challenges, and it may be infeasible to predict SNPs simultaneously on a genome-wide scale. Further future research could investigate additional non-linear machine learning methods such as neural networks, including deep neural networks for predicting genotypes using MRI recordings of the brain directly instead of extracted features.

**Disclosure:** Nothing to disclose.

# W81.
## THE GENETIC ARCHITECTURE OF THE CORPUS CALLOSUM AND ITS SUBREGIONS

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**Background:** Regional surface area and thickness of the cerebral cortex and volume of subcortical structures are highly heritable brain morphological features with complex genetic architectures, involving many common genetic variants with small effect sizes. However, the genetic architecture of the corpus callosum (CC) and its subregions remains largely unclear. We aim to determine the heritability and genetic architecture of CC volume and each subregion and the extent to which this overlaps with that of psychiatric disorders.

**Methods:** Genetic and T1-weighted MRI data of 40,894 individuals from the UK-biobank was used to construct a multivariate GWAS. Here, we utilized a multivariate approach (Multivariate Omnibus Statistical Test, MOSTest) to assess the distributive effects of common variants across the five subregions of the CC (posterior, mid posterior, central, mid anterior and anterior) obtained by running the automatic subcortical segmentation algorithm in FreeSurfer 5.3. Gene-set enrichment analyses were performed using MAGMA. Linkage disequilibrium score regression was used to determine the SNP-based heritability of the CC and will

be used to assess the genetic correlation between each subregion and a variety of psychiatric disorders.

**Results:** Following MOSTest, 70 independent loci show pooled effects across the 5 subregions of the CC ($p < 5 \times 10^{-8}$). Using LDSC, we found evidence to suggest that CC volume is heritable (h2SNP= 0.38, SE=0.03). Significant variants showed enrichment in pathways related to regulation of the nervous system and cell development, neurogenesis, and regulation of neuron differentiation. Gene-set analysis revealed 156 significant genes ($p < 2.6 \times 10^{-6}$). Many of the significant SNPs have been previously associated with white matter hyperintensity volume as well as a range of psychiatric disorders.

**Discussion:** Here we provide the first preliminary evidence to suggest that volume of the CC is heritable. Gene set enrichment analyses identified pathways related to neuron development and neurogenesis, suggesting that CC alteration may have an independent developmental origin. Further investigation into the shared genetic architecture of CC subregions and psychiatric disorders may provide novel insight into disease manifestation.

**Disclosure:** Nothing to disclose.

# W82.
## THE GENETIC ARCHITECTURE OF CEREBELLAR LOBULES, THEIR EVOLUTIONARY HISTORY AND GENETIC OVERLAP WITH PSYCHIATRIC DISORDERS AND COGNITIVE TRAITS

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**Background:** Although classically implicated in movement coordination and balance, the cerebellum is now seen as a central node in higher-order cognition. There is also mounting evidence for the evolutionary implication of cerebellar expansion in our lineage, specifically of the posterior regions Crus I and II. Recently, studies investigating the genetics of cerebellar volume have established that it is a heritable structure, identified multiple associated genetic loci, and revealed links with mental disorders. However, these studies have mostly focused on global cerebellar volume. We remedy this by investigating the genetic underpinnings of the different cerebellar lobes, their evolutionary history and their genetic relationship to psychiatric disorders, cognitive performance, and the cortical language network.

**Methods:** We leveraged publicly available GWAS summary statistics for imaging-derived phenotypes (IDPs; based on the UK Biobank N~31,000), schizophrenia (SCZ), autism spectrum disorder (ASD) and cognitive performance. The IDPs included 32 cerebellar measures, as well as cortical volumes of regions implicated in language and reading. We first examined the genetic architecture of cerebellar subregions, by computing their heritability and the genetic correlation (rg) across the cerebellar lobules using linkage disequilibrium score regression (LDSC). Next, we used stratified LDSC