served for other psychiatric disorders and for the quantitative traits of height, body mass index, and years of education. Regarding gene expression, the schizophrenia polygenic score predicted a composite measure of schizophrenia gene expression in donors with African ancestry (r=.17, p=.04) and in donors of European ancestry (r=.22, p=.01).
Discussion: Polygenic scores were significant predictors of clinical status and quantitative traits for Human Brain Collection Core donors with African ancestry and those of European ancestry. Schizophrenia polygenic scores were positively correlated with schizophrenia-associated dorsolateral prefrontal cortex (DLPFC) gene expression, suggesting that inherited risk for schizophrenia influences gene expression, even in adulthood. These and other polygenic scores are available for selecting samples, and for analyses, using postmortem tissue from the Human Brain Collection Core.

Disclosure: Nothing to disclose.

F115.

POLYGENIC RISK SCORE ANALYSES OF ANTIPSYCHOTIC-INDUCED WEIGHT GAIN IN SCHIZOPHRENIA: AN EXPLORATORY STUDY

Abstract not included.

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F116.

CHARACTERISING THE SHARED GENETIC INFLUENCES BETWEEN SCHIZOPHRENIA AND SUBCORTICAL BRAIN REGIONS

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Background: Abnormalities in brain structural volumes are well established in schizophrenia (SZ) and have been proposed as an endophenotype for the disorder. Despite increasing interest in the genetic relationship between brain structural volumes and SZ, our knowledge of the genetic overlap between the phenotypes is limited. This study aims to extend our current understanding of the shared genetic influences between SZ and subcortical brain volumes using data from the latest genome-wide association studies for the respective phenotypes (GWAS) and novel statistical approaches. Additionally, we will explore whether the association between schizophrenia and abnormal regional brain volumes is causal in nature.
Methods: Summary statistics were obtained from the largest Psychiatric Genomic Consortium (PGC)-SZ GWAS (Ncase = 69,369, Ncontrol = 236,642) and the CHARGE-ENIGMA-UKBB GWAS of volumetric measures for eight subcortical brain regions (the nucleus accumbens, amygdala, brainstem, caudate nucleus, hippocampus, globus pallidus, putamen, and thalamus), and total intracranial volume (N = 30,983 - 40,380). Single nucleotide polymorphism (SNP) effect concordance analysis (SECA) was used to assess pleiotropy and concordance. Genetic correlation was assessed using linkage disequilibrium score regression (LDSR) and the pleiotropy informed conditional FDR approach was applied to identify SNPs associated with SZ conditional on their association with subcortical brain volumes. Mendelian randomization (MR) was used to test for causal association between SZ and each brain region.
Results: There was evidence of global pleiotropy between SZ, and all examined subcortical brain regions. Inverse concordance between the genetic determinants of SZ and volumes of the nucleus accumbens, amygdala, brainstem, hippocampus, and thalamus was observed. Increased statistical power to detect SZ risk loci was shown when conditioning on subcortical brain volumes. There was no significant evidence for a causal effect of any of the examined brain regions on schizophrenia risk.
Discussion: These data confirm the shared genetic basis of SZ and specific intracranial and subcortical brain volumes and provide evidence for negative concordance between SZ and volumes of the nucleus accumbens, amygdala, brainstem, hippocampus, and thalamus. Leveraging the genetic overlap between SZ and subcortical brain volumes has the potential to provide novel insights into the biological basis of the disorder.

Disclosure: Nothing to disclose.

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F117.

THE ASSOCIATION BETWEEN POLYGENIC RISK FOR SCHIZOPHRENIA AND BRAIN AGE IN A POPULATION-BASED SAMPLE OF YOUNG ADULTS: A RECALL-BY-GENOTYPE-BASED APPROACH

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Background: Schizophrenia is a neurodevelopmental, heritable disorder with a reduced life expectancy of approximately 15 years. Research has also shown advanced structural brain ageing in patients with schizophrenia. However, whether advanced brain ageing in schizophrenia is genetically driven remains unclear. Here, we hypothesised that high polygenic risk for schizophrenia (SCZ-PRS) is associated with advanced brain ageing in young adults. We utilised a recall-by-genotype (RbG) approach, recruiting participants from the general population who have either a relatively