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Cortical and subcortical grey matter micro-structure is associated with polygenic risk for schizophrenia

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ABSTRACT:

The current evidence linking structural brain MRI markers to polygenic risk for schizophrenia is inconsistent. We analysed multimodal MRI and genotype data on N~30,000 UK Biobank participants to perform a phenome-wide association study using polygenic risk scores for schizophrenia (PRS) and nine cortical and five subcortical MRI phenotypes. We measured PRS for schizophrenia based on the largest genome-wide association (GWAS) dataset in a large sample from the UK Biobank who had multiple micro- and macro-structural MRI metrics measured at 180 cortical areas and seven subcortical structures. We report significant associations between PRS and regional neurite density index, fractional anisotropy, orientation dispersion index, local gyrification index, volume, surface area and intrinsic curvature. Micro-structural phenotypes derived from diffusion tensor imaging data were more robustly associated with schizophrenia PRS than macro-structural phenotypes. PRS was significantly associated with reduced neurite density index (NDI), a measure of the density of myelinated axons and dendrites, at global brain scale, at 149 cortical regions, and five subcortical structures. Genetic effects on multiple MRI phenotypes were co-located in temporal, cingulate and prefrontal cortical areas, insula, and hippocampus. These findings are in line with reported reductions in NDI in schizophrenia patients, post-mortem studies showing abnormalities in neurite structure and GWAS results pointing towards risk genes implicated in functional processes, such as synaptic organisation and transmission. Taken together, these results suggest that the genetic risk for schizophrenia is associated with cortical and subcortical brain structure.

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