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Patterns of brain asymmetry associated with polygenic risks for autism and schizophrenia implicate language and executive functions but not brain masculinization

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ABSTRACT:

Autism spectrum disorder (ASD) and schizophrenia have been conceived as partly opposing disorders in terms of systemizing versus empathizing cognitive styles, with resemblances to male versus female average sex differences. Left-right asymmetry of the brain is an important aspect of its organization that shows average differences between the sexes, and can be altered in both ASD and schizophrenia. Here we mapped multivariate associations of polygenic risk scores (PRS) for ASD and schizophrenia with asymmetries of regional cerebral cortical surface area, thickness and subcortical volume measures in 32,256 participants from the UK Biobank. PRS for the two disorders were positively correlated ($r=0.08$, $p=7.13\times 10^{-50}$), and both were higher in females compared to males, consistent with biased participation against higher-risk males. Each PRS was associated with multivariate brain asymmetry after adjusting for sex, ASD PRS $r=0.03$, $p=2.17\times 10^{-9}$, schizophrenia PRS $r=0.04$, $p=2.61\times 10^{-11}$, but the multivariate patterns were mostly distinct for the two PRS, and neither resembled average sex differences. Annotation based on meta-analyzed functional imaging data showed that both PRS were associated with asymmetries of regions important for language and executive functions, consistent with behavioural associations that arose in phenome-wide association analysis. Overall, the results indicate that distinct patterns of subtly altered brain asymmetry may be functionally relevant manifestations of polygenic risk for ASD and schizophrenia, but do not support brain masculinization or feminization in their etiologies.

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