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Scrutinizing the Genetic Relationship between Psychiatric Disorders

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ABSTRACT:

Previous studies have shown that psychiatric disorders (PDs) are highly comorbid and considerably genetically correlated. Including 12 major PDs, this study aimed to scrutinize their genetic overlap as well as their genetic distinctness. SNP-based heritability (h^2_{SNP}) of the 12 PDs ranged between 4.4% (anxiety) and 36.7% (obsessive-compulsive disorder; OCD). Genetic correlations (r_g) between the 12 PDs ranged from -0.13 (ADHD-OCD) to 0.83 (depression-anxiety; median $r_g=0.24$). Using LAVA to estimate local r_g , we observed 29 significant local r_g 's (range= -0.84 - 0.98, median=0.76), 23 involving schizophrenia, 2 of which were negative, and none were shared between more than 2 traits. Additionally, significant local r_g 's were observed between pairs of traits that showed non-significant global r_g 's (e.g., insomnia and schizophrenia: global r_g : 0.05; 1 significant opposing local r_g 's). Cross-trait meta-analysis on the 12 PDs yielded 222 significant genes, 102 of which overlapped with the 332 genes associated to the 12 individual PDs. Only 39 of 332 genes were associated to two PDs, and three to 3 PDs. Cross-trait meta-analysis yielded 3 biological pathways not observed for any of the 12 individual PDs. Overall, this study shows that while global r_g 's between PDs are considerable, local r_g 's are unique to certain trait pairs and top genes tend to show little overlap. While low power and low h^2_{SNP} play a role here, it may also suggest that the genetic similarity between PDs is driven by a more dispersed signal that does not accumulate in pleiotropic loci but, rather, converges on another level (e.g., biological function).

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