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Virtual Histology of Cortical Thickness and Shared Neurobiology in 6 Psychiatric Disorders

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Abstract

Importance: Large-scale neuroimaging studies have revealed group differences in cortical thickness across many psychiatric disorders. The underlying neurobiology behind these differences is not well understood.

Objective: To determine neurobiologic correlates of group differences in cortical thickness between cases and controls in 6 disorders: attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), bipolar disorder (BD), major depressive disorder (MDD), obsessive-compulsive disorder (OCD), and schizophrenia.

Design, setting, and participants: Profiles of group differences in cortical thickness between cases and controls were generated using T1-weighted magnetic resonance images. Similarity between interregional profiles of cell-specific gene expression and those in the group differences in cortical thickness were investigated in each disorder. Next, principal component analysis was used to reveal a shared profile of group difference in thickness across the disorders. Analysis for gene coexpression, clustering, and enrichment for genes associated with these disorders were conducted. Data analysis was conducted between June and December 2019. The analysis included 145 cohorts across 6 psychiatric disorders drawn from the ENIGMA consortium. The numbers of cases and controls in each of the 6 disorders were as follows: ADHD: 1814 and 1602; ASD: 1748 and 1770; BD: 1547 and 3405; MDD: 2658 and 3572; OCD: 2266 and 2007; and schizophrenia: 2688 and 3244.

Main outcomes and measures: Interregional profiles of group difference in cortical thickness between cases and controls.

Results: A total of 12 721 cases and 15 600 controls, ranging from ages 2 to 89 years, were included in this study. Interregional profiles of group differences in cortical thickness for each of the 6 psychiatric disorders were associated with profiles of gene expression specific to pyramidal (CA1) cells, astrocytes (except for BD), and microglia (except for OCD); collectively, gene-expression profiles of the 3 cell types explain between 25% and 54% of variance in interregional profiles of group differences in cortical thickness. Principal component analysis revealed a shared profile of difference in cortical thickness across the 6 disorders (48% variance explained); interregional profile of this principal component 1 was associated with that of the pyramidal-cell gene expression (explaining 56% of interregional variation). Coexpression analyses of these genes revealed 2 clusters: (1) a prenatal cluster enriched with genes involved in neurodevelopmental (axon guidance) processes and (2) a postnatal cluster enriched with

genes involved in synaptic activity and plasticity-related processes. These clusters were enriched with genes associated with all 6 psychiatric disorders.

Conclusions and relevance: In this study, shared neurobiologic processes were associated with differences in cortical thickness across multiple psychiatric disorders. These processes implicate a common role of prenatal development and postnatal functioning of the cerebral cortex in these disorders.