

M18. AN EXPLORATORY STUDY OF THE GENETIC RELATIONSHIPS BETWEEN PLASMA-BASED MEASURES OF INFLAMMATION AND BRAIN ANATOMY

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Background Inflammation markers measured from blood and measures of brain anatomy are frequently studied as biomarkers for psychiatric diseases. Inflammation markers in particular have garnered considerable interest in recent years due to their potential to elucidate novel treatment targets. Although alterations in these two sets of measures are frequently reported in clinical samples, little is known about their relationships to one another. Such relationships, if observed, could contribute to our understanding of the biological underpinnings of psychiatric diseases, or be useful for future endophenotype-based gene-finding efforts.

Methods Data were analyzed from randomly ascertained extended pedigrees (average family size = 27.67, range = 2-128). Levels of six adipokines (insulin, leptin, hepatocyte growth factor [HGF], nerve growth factor [NGF], monocyte chemotactic protein-1 [MCP-1], tumor necrosis factor alpha [TMF α]) were measured from plasma using a Milliplex MAP multiplex assay (HADK2MAG-61K). T1-weighted structural magnetic resonance images were collected at the same time point, and measures of cortical volume, surface area, and thickness were derived via FreeSurfer. All measures were residualized for age, age squared, sex, and their interactions prior to analysis, and genetic correlations between the inflammation and brain measures were estimated using SOLAR. Each comparison was based on data from 891-1394 individuals.

Results Initially, we estimated genetic correlations between the six inflammation measures and two global measures of brain anatomy, total cortical volume and mean cortical thickness. There was a significant negative genetic correlation between insulin level and cortical volume (n=1009, $rg = -0.43$, $p = 0.0004$), which survived false-discovery rate (FDR) correction. The genetic correlation between HGF level and cortical thickness was nominally significant (n=1007, $rg = -0.34$, $p = 0.02$). Next, we estimated genetic correlations between insulin level and cortical surface areas from 34 anatomical regions of interest, eleven of which were significant at the FDR-corrected level ($-0.43 \leq rg \leq -0.30$), mostly comprising frontal and parietal regions. We also estimated genetic correlations between HGF level and region-specific cortical thicknesses, one of which was significant at the FDR-corrected level (lateral occipital thickness, $rg = -0.49$, $p = 0.0008$).

Discussion These findings suggest some shared genetic etiology between insulin level measured in plasma and cortical volume/surface area. The relationship was negative, indicating that genes responsible for higher levels of insulin are associated with smaller cortices, and appeared to be driven by overall brain size rather than any specific region. There was also a hint of a relationship between HGF level and cortical thickness, which was not driven by overall brain size.

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