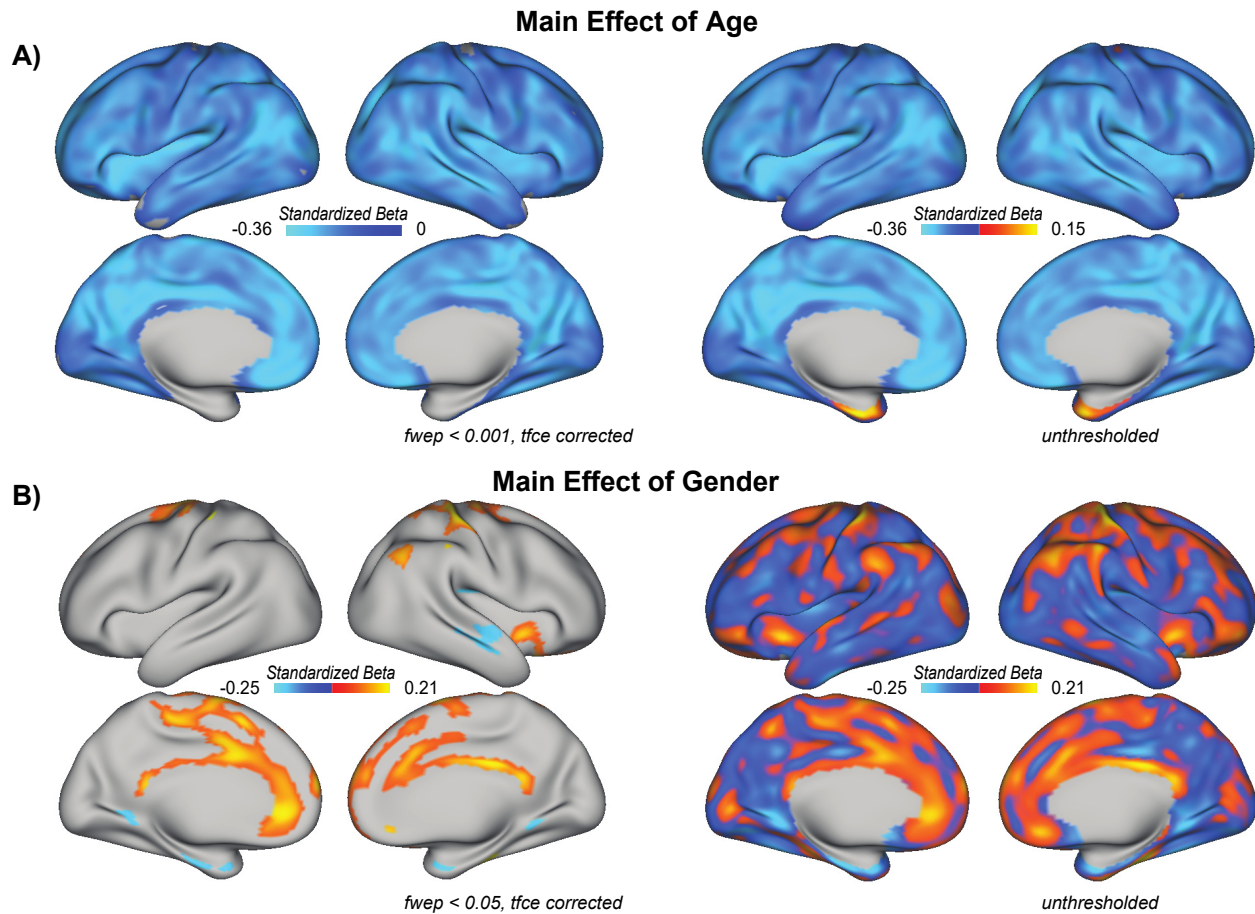


Life Event Stress and Reduced Cortical Thickness in Youths at Clinical High-Risk for Psychosis and Healthy Youths

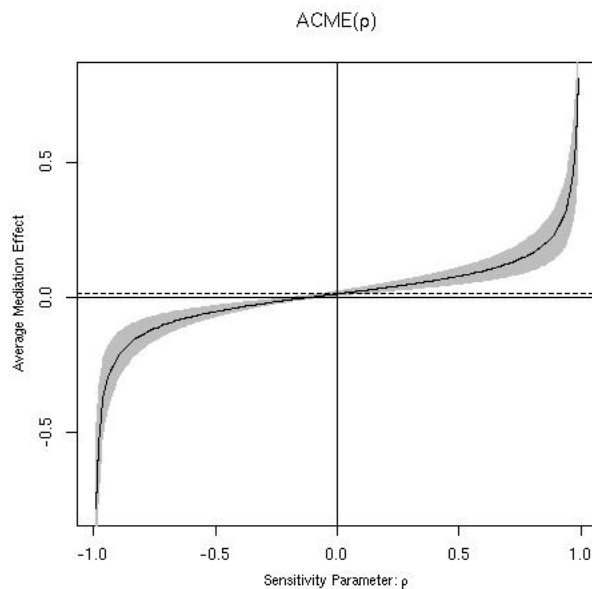
Supplemental Information



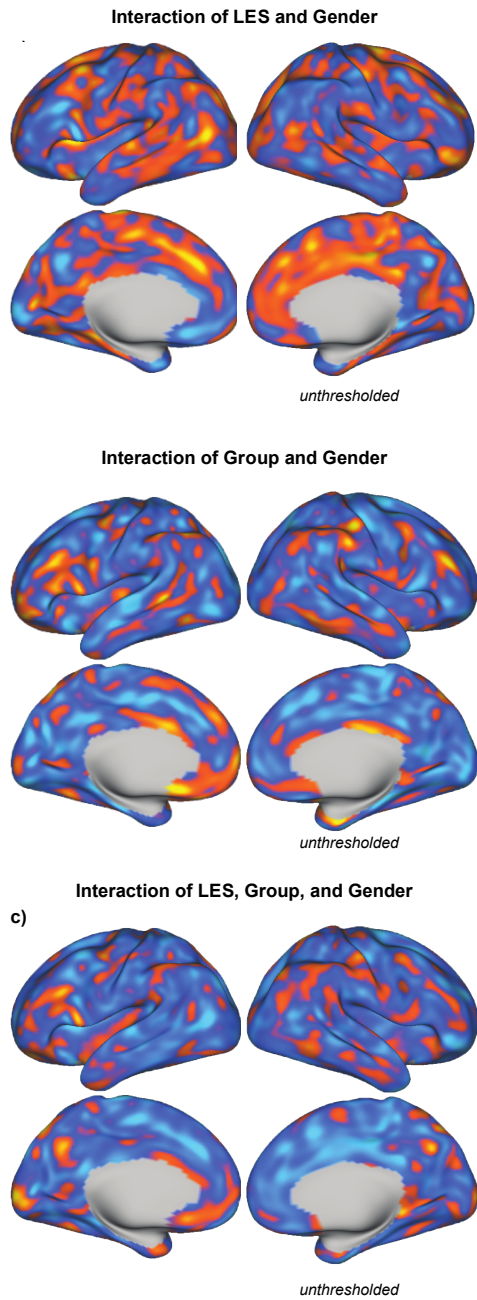
Supplemental Figure S1. **A)** Age is inversely associated with thickness across cortex ($\beta = -.36 - -.03$, t_{fce} $f_{wep} < 0.05$). **B)** Female gender is associated with thicker cortex, particularly in aspects of frontal cortex ($\beta = .06 - .21$, t_{fce} $f_{wep} < 0.05$), as well as thinner cortex in a small portion of bilateral temporal cortex ($\beta = -.25 - -.09$, t_{fce} $f_{wep} < 0.05$). Maps indicate effects of age and gender on thickness after accounting for scanner. f_{wep} = family wise error corrected p -value; t_{fce} = threshold free cluster enhancement.

Sensitivity Analyses

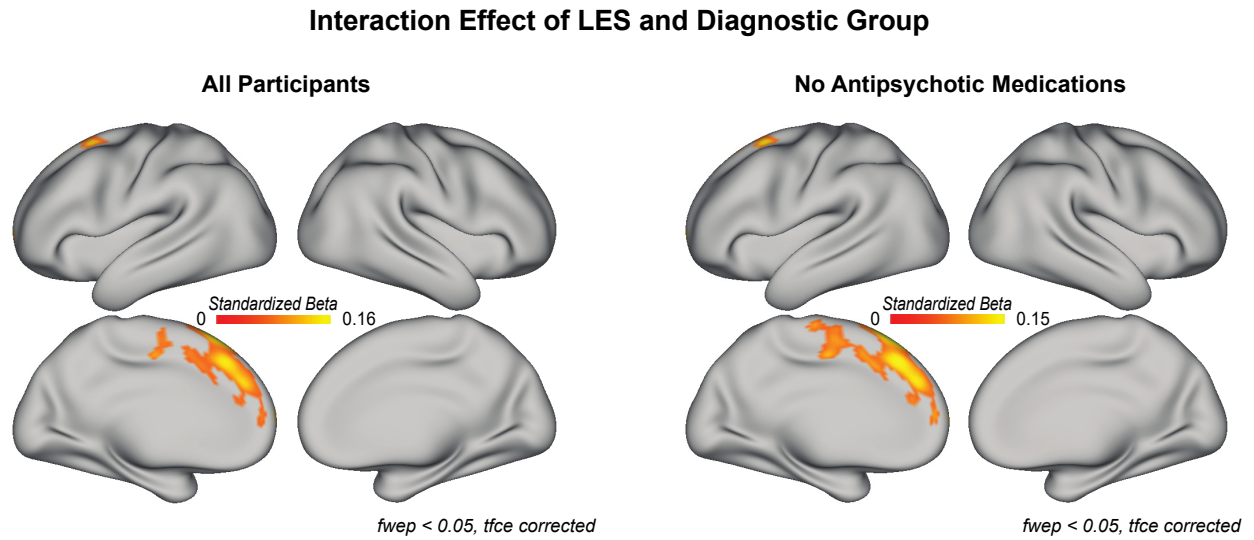
Sensitivity analyses of causal mediation effects were conducted to test for violations of the sequential ignorability assumption, using the *mediation* package in R, as there are limitations to conducting mediation analysis with cross-sectional data. Mediation analyses in this report were found to be highly sensitive (Figure S2). Specifically, we find that when sensitivity (p) equals $-.012$, the confidence intervals for the mediation effect include zero. Thus, the observed mediation finding is sensitive to a potential violation of sequential ignorability, meaning that a relatively small unobserved confound would overturn the results obtained. Assumptions of causality should be interpreted with caution, and future longitudinal work testing temporal precedence among LES, brain morphological changes, and clinical outcomes is needed.



Supplemental Figure S2: Mediation effects and sensitivity analyses. Figure indicates the estimated average mediation effects under different sensitivity thresholds (p). The gray shaded area represents the 95% confidence interval for the mediation effect at each p value, and the dashed line represents the estimated mediation effect for $p = 0$.



Supplemental Figure S3: Two and three-way interactions between gender, LES, and diagnostic group. The interaction between (a) gender and LES, (b) gender and diagnostic group, and (c) gender, LES, and diagnostic group is not significantly associated with cortical thickness in any vertices across cortex. Unthresholded maps indicate disparate patterns of positive and negative associations between each interaction term and cortical thickness.



Supplemental Figure S4. The interaction between LES and diagnostic group is associated with the thickness of left superior frontal cortex among all participants (left). When participants who were prescribed antipsychotic medications at baseline ($n = 6$) were removed from analyses, results remained largely consistent (right).