

Cortisol is associated with thinner cortical gray matter in 512 elderly ADNI participants

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Introduction

Cortisol, a stress-related hormone, is linked to cognitive decline, raising concerns about how stress affects the brain throughout life. Many different environmental 'stressors' – both internal and external - stimulate corticosteroid secretion, leading to varying levels of cortisol in the brain [1]. Depending on other genetic and environmental factors, this can be harmful to brain structure and function [2-4]. To understand how stress hormones relate to the structure of the cerebral cortex in the elderly, we tested whether people with higher cortisol levels have thinner cortical gray matter using a vertex-wise approach across the cortical surface.

Methods

Subjects

512 participants (108 with Alzheimer's disease (AD), 351 with mild cognitive impairment (MCI), 53 healthy elderly; mean age: 75 ± 7 years) received a 1.5T anatomical brain MRI and cognitive evaluation as part of the Alzheimer's Disease Neuroimaging Initiative (ADNI). The cohort was predominantly Caucasian, so we restricted our analysis to Caucasians (n=738; mean age: 75.5 ± 6.8 years) to avoid population stratification effects.

Cortisol Measurements

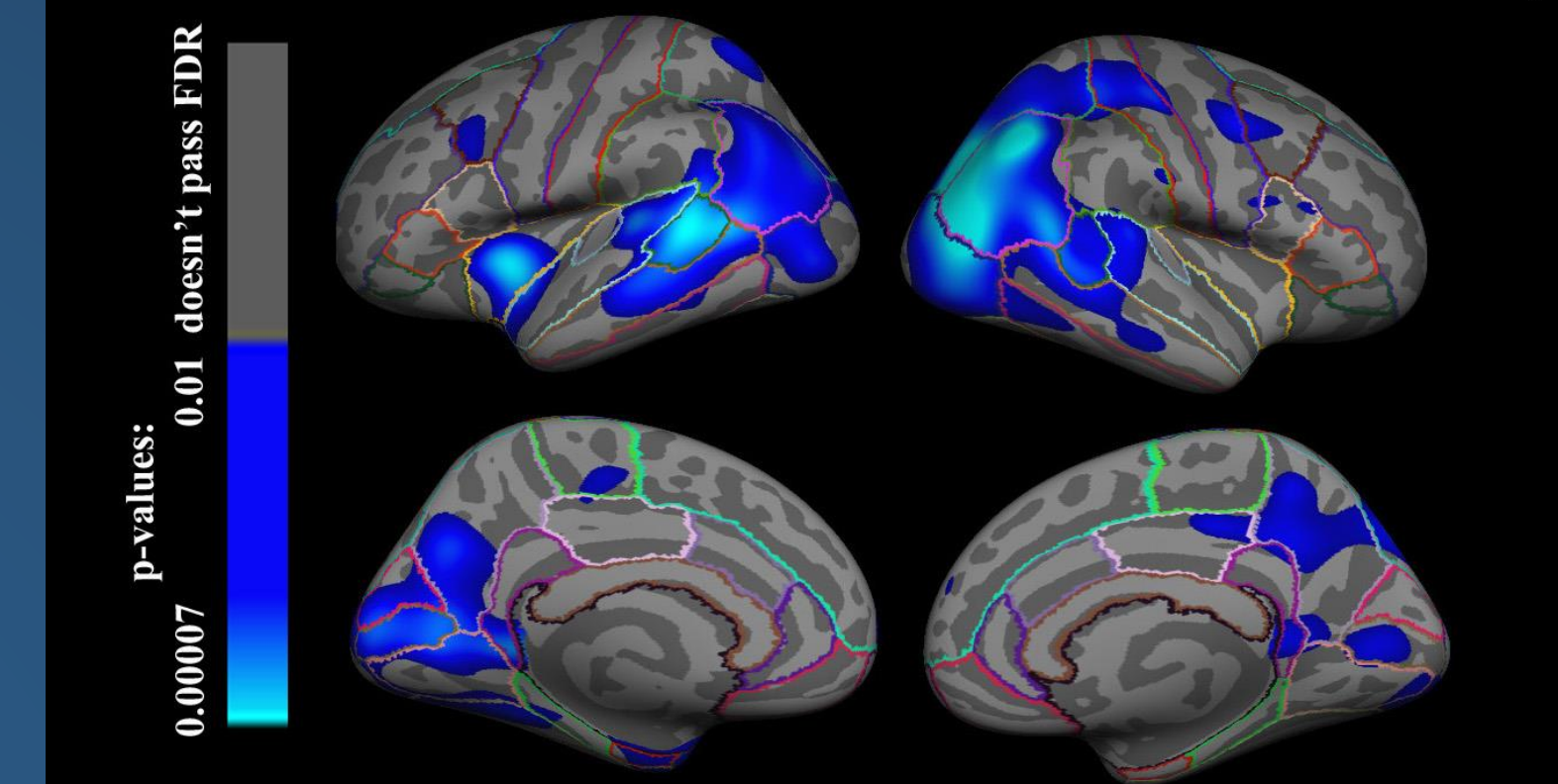
Plasma cortisol (mean: 2.17 ± 0.13 ng/ml) was measured from blood samples collected at the time of MRI acquisition after an overnight fast, using the 'Human Discovery Multi-Analyte Profile' platform by Rules-Based Medicine (RBM, Austin, TX). The quantification methods are described in the document: 'Biomarkers Consortium ADNI Plasma Targeted Proteomics Project – Data Primer' (available at <http://adni.loni.usc.edu>).

Cortical Thickness Analysis

Vertex-wise cortical thickness was obtained using the FreeSurfer image analysis suite (v5.0.0; <http://surfer.nmr.mgh.harvard.edu/>) as described previously [5, 6]. Five subjects were excluded from the study because the cortical surface reconstruction did not pass visual inspection.

Results

Cortical thickness and cortisol levels in N=512 elderly



3D *p*-value maps show significant associations of thinner cortical gray matter bilaterally with higher levels of cortisol, after controlling for age and sex (FDR critical *p*-value: 0.01).

In a *post hoc* analysis, we also adjusted for diagnostic group (AD, MCI, and controls) and *APOE4* status, in addition to age and sex. Cortisol remained significantly associated with thinner cortical gray matter; associations were detected in the right hemisphere, in the inferior and superior parietal and lateral occipital gyri (FDR critical *p*-value: 0.002).

Discussion

As far as we know, this is the first study to identify a 3D profile of thinner cortical gray related to higher stress hormone levels across a broad cognitive spectrum in the elderly. Significant associations were detected in temporal, parietal, medial, and occipital brain regions.

We did not detect a relationship with higher cortisol and reduced cortical GM in the anterior cingulate or prefrontal cortex that has been reported for chronically stressed adolescent or adult populations [7-9] and for middle-aged men [10], which are quite different populations than the elderly sample analyzed here.

References

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