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±0.13ng/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
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