Plasma cortisol is associated with accelerated brain atrophy: An Alzheimer's Disease Neuroimaging Initiative (ADNI) study

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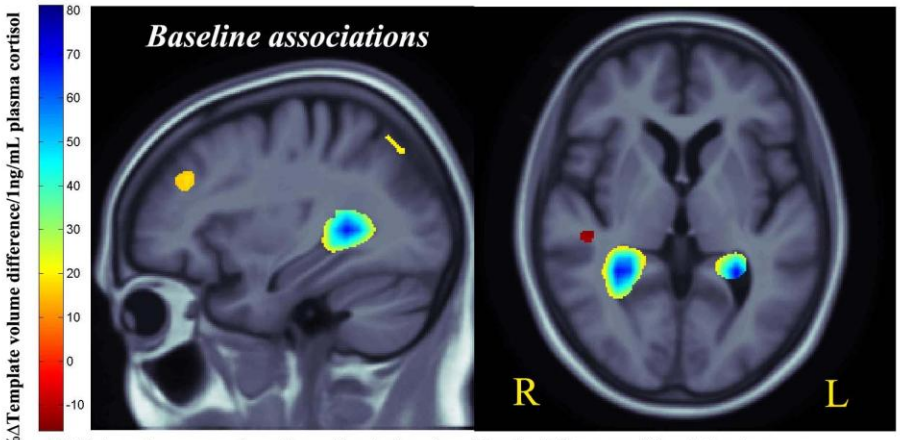
Introduction: Excess glucocorticoid exposure can potentiate electrophysiological imbalances and deleterious neuronal structural changes resulting in cognitive decline. Studies link elevated baseline plasma cortisol (blPC), with lower hippocampal volumes in Alzheimer's disease and in the healthy elderly; the hippocampus has a high density of glucocorticoid receptors. We hypothesized elevated blPC would be associated with lower brain volumes, higher rates of brain atrophy over time, and cognitive impairment.

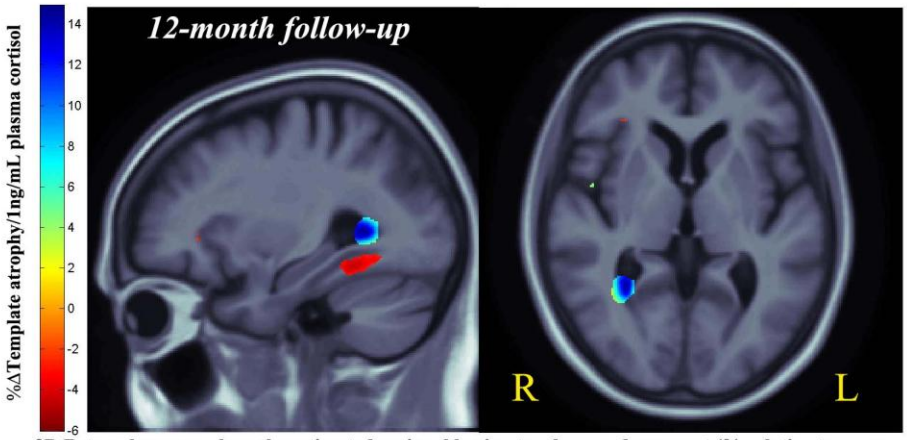
Methods: Overnight fasting blPC levels (mean:2.1±0.1ng/ml) were measured in 517 Caucasian subjects (110 AD, 354 MCI, 53 Controls; mean age: 75.2 ±7years) at baseline. These 517 and a subset of 440 subjects at 1-year follow-up were scanned with brain MRI at 1.5 Tesla and cognitively tested as part of ADNI. Using tensor-based morphometry, we computed 3D Jacobian maps of brain volume differences at baseline and annual atrophy rates, mapping subjects to a mean template. We carried out standard linear regression at every brain voxel, to associate blPC with 1) baseline brain volumes, 2) 1-year brain atrophy rates, 3) cognitive scores (MMSE,CDR); after adjusting for age, sex, and Geriatric Depression index (GDI). We corrected for multiple comparisons using standard false discovery rate at the 5% level. We also carried out a post-hoc test of blPC associations with ventricular shapes.

Results: With every 1ng/mL increase in blPC levels, we found up to 1) 80% ventricular expansion locally at baseline 2) 6% accelerated rate of brain atrophy in the temporo-occipital fusiform gyrus, and 14% accelerated rate of lateral ventricular enlargement at 1-year in the trigone; predominantly on the right side, relative to the mean template. Ventricular shape maps detail these associations. blPC levels negatively correlated with MMSE and CDR ($P<0.001$ at both time points), after adjusting for age, sex, diagnosis and GDI.

Conclusion: blPC levels influenced rates of brain atrophy and accelerated cognitive decline. To our knowledge, this study is the first to map blPC correlations with the rate of brain atrophy.

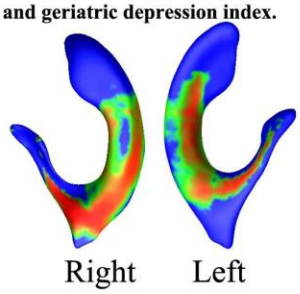


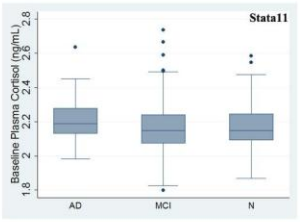
3D Beta-value maps show the estimated regional brain differences (% relative to mean template) at each significant voxel, per every 1ng/mL increase in the plasma cortisol levels.



3D Beta-value maps show the estimated regional brain atrophy or enlargement (% relative to mean template) at each significant voxel, per every 1ng/mL increase in the plasma cortisol levels.

Ventricular shape changes at baseline associated with 1 ng/mL increase in baseline plasma cortisol, irrespective of age, sex, diagnosis and geriatric depression index.





Ventricular shape changes at 12-month associated with 1 ng/mL increase in baseline plasma cortisol