Calorie restriction reduces psychological stress reactivity and its association with brain volume and microstructure in aged rhesus monkeys.

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Authors: Willette, AA, Coe, CL, Colman, RJ, Bendlin, BB, Kastman, EK, Field, AS, Alexander, AL, Allison, DB, Weindruch, RH, Johnson, SC

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Abstract

BACKGROUND: Heightened stress reactivity is associated with hippocampal atrophy, age-related cognitive deficits, and increased risk for Alzheimer's disease. This temperament predisposition may aggravate age-associated brain pathology or be reflective of it. This association may be mediated through repeated activation of the stress hormone axis over time. Dietary interventions, such as calorie restriction (CR), affect stress biology and may moderate the pathogenic relationship between stress reactivity and brain in limbic and prefrontal regions.

METHODS: Rhesus monkeys (Macaca mulatta) aged 19-31 years consumed either a standard diet (N=18) or were maintained on 30% CR relative to baseline intake (N=26) for 13-19 years. Behavior was rated in both normative and aversive contexts. Urinary cortisol was collected. Animals underwent magnetic resonance imaging and diffusion tensor imaging (DTI) to acquire volumetric and tissue microstructure data respectively. Voxel-wise statistics regressed a global stress reactivity factor, cortisol, and their interaction on brain indices across and between dietary groups.

RESULTS: CR significantly reduced stress reactivity during aversive contexts without affecting activity, orientation, or attention behavior. Stress reactivity was associated with less volume and tissue density in areas important
for emotional regulation and the endocrine axis including prefrontal cortices, hippocampus, amygdala, and hypothalamus. CR reduced these relationships. A Cortisol by Stress Reactivity voxel-wise interaction indicated that only monkeys with high stress reactivity and high basal cortisol demonstrated lower brain volume and tissue density in prefrontal cortices, hippocampus, and amygdala.

CONCLUSIONS: High stress reactivity predicted lower volume and microstructural tissue density in regions involved in emotional processing and modulation. A CR diet reduced stress reactivity and regional associations with neural modalities. High levels of cortisol appear to mediate some of these relationships.

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