Short-term hypercaloric diet decreases hypothalamic and brainstem functional connectivity in humans

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Hypothalamic and brainstem pathways, particularly the leptin melanocortin system, regulate energy balance through adjustments in autonomic efferent activity. Disordered regulation of the system predisposes to obesity and obesity-associated arterial hypertension. We applied high-resolution subcortical functional magnetic resonance imaging (fMRI) to test whether short-term increase in energy intake elicit functional connectivity changes between and within hypothalamus and brainstem nuclei in human beings.

We submitted 20 subjects (7 women, 26.7±8 years; 22.6±2 kg/m^2) to 5 days hypercaloric (25% increase of energy intake by fat) or normocaloric diets in a randomized crossover fashion with a washout period between interventions. We obtained high resolution brainstem and hypothalamus fMRI (3T PET/MRI, Siemens mMR Biograph). Then, we applied masked independent component analysis for resting state measurements and defined functional connectivity changes using dual regression between and within relevant regions.

We observed significantly decreased functional connectivity after hypercaloric compared to normocaloric diet. In particularly, connectivity decreased between hypothalamic regions involved in metabolic regulation such as ventromedial and arcuate nuclei, mamillary bodies, and lateral and posterior hypothalamic areas. In the brainstem, functional connectivity decreased between rostral ventrolateral medulla and the inferior olive; two regions involved in sympathetic regulation. Moreover, connectivity decreased between hypothalamus and brainstem involving several nuclei: ventromedial, arcuate and supraoptic nuclei in the hypothalamus; as well as the solitary, raphe and inferior olivary nuclei in the brainstem.

We conclude that several days hypercaloric dieting produces significant resting state functional connectivity changes within and between hypothalamus and brainstem areas known to regulate efferent autonomic activity. The methodology may have utility in elucidating how metabolic and cardiovascular autonomic control are integrated in human beings and how perturbed regulation contributes to cardiometabolic disease.