OR20-2: Oxytocin Significantly Attenuates the Functional Connectivity between Food Motivation Brain Areas in Overweight and Obese Men Exposed to High Caloric Food Images

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Background: The hypothalamic neurohormone oxytocin (OXT), shown to decrease food intake in animal models and men, is a promising novel treatment for obesity. The mechanisms underlying OXT effects on caloric intake in humans are not well understood. We previously showed that in overweight and obese men, 24 IU intranasal (IN) OXT reduced fMRI activation in the ventral tegmental area (VTA), the origin of the mesolimbic dopaminergic reward system, in response to high-calorie food vs non-food visual stimuli. To provide further insight into the mechanisms by which OXT exerts its anorexigenic effects, we employed a dynamic method of fMRI analysis, functional connectivity, which refers explicitly to the influence that one neural system exerts over another in a context-dependent manner. We hypothesized that OXT would modulate the functional connectivity of the VTA with key brain areas known to be involved with food sensory and cognitive processing when participants viewed high-calorie foods compared to objects.

Methods: In this randomized, double-blind, placebo-controlled crossover study of 24 IU IN OXT, 10 overweight/obese (mean±SD BMI 28.9±0.8 kg/m2), otherwise healthy men age 31.4±1.8 years presented after a 10-h overnight fast. Sixty min after drug administration, subjects started an established fMRI food motivation paradigm that included images of high and low-calorie foods, household objects, and fixation stimuli. Using psychophysiological interaction analysis, the VTA was anatomically defined as the seed region to explore effects of OXT on functional connectivity.

Results: Following OXT administration, compared to placebo, participants showed significant attenuation of the functional connectivity between the VTA and insula, parietal operculum, amygdala, anterior and posterior cingulate, and hippocampus in response to viewing high-calorie food stimuli vs. objects ($Z \geq 3.1$, cluster corrected, $P=0.05$).

Conclusion: Here we have shown in overweight/obese men that OXT attenuates functional connectivity between the VTA and brain regions associated with the cognitive, sensory and emotional processing of food images. This is particularly relevant to obese individuals, since previous studies have shown greater activation to palatable food images in these areas (e.g., amygdala, hippocampus and insula), and it has been proposed that this hyperactivity of the dopaminergic reward circuit renders obese individuals prone to overeating. Attenuated functional connectivity findings reported here could partially explain the clinically-observed anorexigenic effect of OXT, providing insight into the mechanism through which OXT ameliorates food-cue-induced, CNS-mediated reward anticipation in obese patients. Additional studies are ongoing to further delineate the neural connections underlying the anorexigenic effect of OXT in human obesity.

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