fMRI of glucose ingestion

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TARGET AUDIENCE: Neuroscientists, obesity researchers, fMRI of food ingestion, physiologists.

PURPOSE Dysfunction of neural circuitries controlling food intake has been implicated in eating disorders such as obesity and anorexia. The majority of studies to date used fMRI of visual food cues to map neural circuitries involved in satiety. This approach activates many cognitive components of satiety regulation but not the physiological effects of food ingestion. Few have investigated the satiety circuitry associated with food ingestion per se and most of these studies reported changes only in the hypothalamus. The goal of this study was to use fMRI to investigate the neural networks responding to ingestion of a standardized glucose solution while the subjects were in the MRI scanner.

METHODS Healthy lean subjects (4 M, 3 F, 20-35 yo, BMI = 18-25 kg/m^2) fasted overnight for a period of eight hours. None of the subjects were on any diet program or recently lost weight. Whole-brain fMRI was acquired using EPI at 3T with TR = 3000ms, TE = 30 ms, 1.7 x 1.7 mm, 5-mm sagittal slices. The total scan lasted 65 mins with an initial 10-min period of baseline of pre-glucose ingestion acquisition, followed by 55 mins of post-glucose ingestion acquisition. Subjects ingested a standard glucola solution (75 g of glucose, 296 ml) in a self-pace manner over 4.5 ± 0.75 min via a peroral rubber tube. Blood glucose were measured every 10 min. Correlation analysis of the fMRI signals with blood glucose temporal profile was performed using the FSL software (FEAT tool).

RESULTS The basal blood glucose was 90 ± 10 mg/dL. The mean blood glucose started to elevate 15 mins after glucose ingestion, peaked 30 mins after glucose ingestion, and remained elevated during the entire fMRI study (**Figure 1**). The temporal profile of blood glucose peaking about 30 mins post glucose ingestion is consistent with previous findings[1].

The activated brain structures that showed correlation with blood glucose measurements were (**Figure 2**): the hypothalamus, caudate, orbitofrontal cortex (BA 47), medial frontal gyrus (BA 6), cerebellum, thalamus, cingulate gyrus (BA 31), precuneus (BA 7) and insula (BA 13).

DISCUSSION Hypothalamus, widely implicated in food intake, was activated, in agreement with previous fMRI studies of glucose ingestion[2,3]. However, these studies did not report other activated structures.

By contrast, we detected activated structures in the reward circuitries, including caudate[4], orbitofrontal cortex, which projects to hypothalamus[5] and has been implicated in reward value assessment and reward prediction errors[6], Insula, which has been implicated in reward and craving[7-8] and cingulate gyrus has been reported in anticipatory food reward tasks[9]. Activation of medial frontal gyrus, a cognitive structure, has been associated with decision-making based on emotional and integrative control of food intake[10]. The cerebellum is believed to activate when the brain is monitoring its sensory systems[11]. The thalamus, known to receive input from sensory, visceral and gustatory systems[12], was also correlated. Precuneus activation has been reported when changes in gastric distension occurred[13].

A limitation of this study is that it correlated only with blood glucose profile. It is possible that other neural activities associated with satiety differed from the blood glucose pattern and thus might not have been detected. Nonetheless, this approach identified many brain regions known to be involved in satiety regulation, suggesting this approach likely offers highly relevant physiological and functional information.

In conclusion, we found glucose ingestion evoked a large neural network that regulates satiety. This approach offers a reliable method to study neural circuitries involving food intake. Future studies will examine subjects with eating disorders and correlate with temporal profiles of other blood markers (such as c-peptide) and behavioral data of satiety.

Figure 1. Average blood glucose measurements.

Figure 2. fMRI responses to glucose ingestion

REFERENCES (1) Tschrtter et al. 2003. (2) Vidardottiret al. 2007. (3) Liu Y et al. 2000. (4) Alexander G.E. et al. 1990. (5) Nioche et al. 2000. (6) Pelchat et al. 1999. (7) Dreher et al 2012. (8) Small et al. 2010. (9) Stice et al. 2009. (10) Dreher et al. 2012. (11) Rosenbaum et al. 2000. (12) Del Parigi et al. 2002. (13) Edw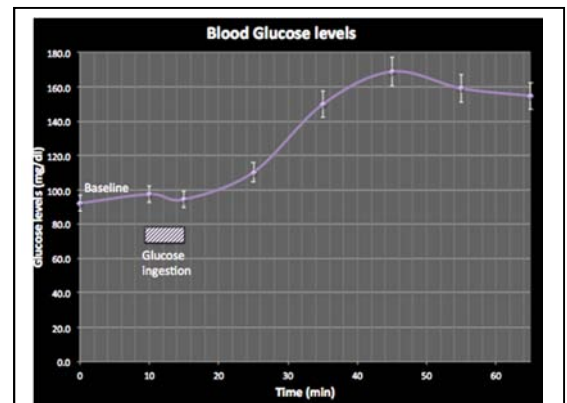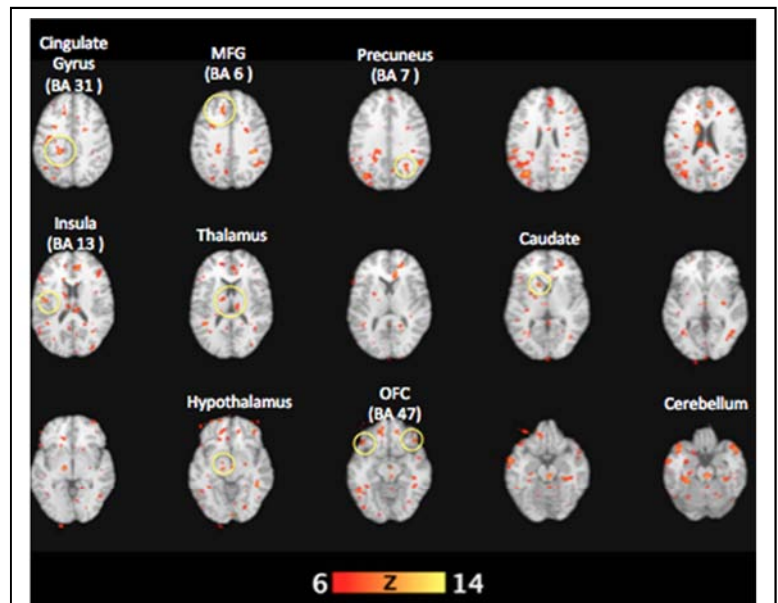ard et al. 2007. (14) Wang et al. 2007.