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Is hunger important to model in fMRI visual food-cue reactivity paradigms in adults with obesity and how should this be done?

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ABSTRACT

We considered 1) influence of self-reported hunger in behavioral and fMRI food-cue reactivity (fMRI-FCR) 2) optimal methods to model this.

Adults ($N = 32$; 19–60 years; $F = 21$; BMI 30–39.9 kg/m^2) participated in an fMRI-FCR task that required rating 240 images of food and matched objects for ‘appeal’. Hunger, satiety, thirst, fullness and emptiness were measured pre- and post-scan (visual analogue scales). Hunger, satiety, fullness and emptiness were combined to form a latent factor (appetite). Post-vs. pre-scores were compared using paired t-tests. In mixed-effects models, appeal/fMRI-FCR responses were regressed on image (i.e. food/objects), with random intercepts and slopes of image for functional runs nested within subjects. Each of hunger, satiety, thirst, fullness, emptiness and appetite were added as covariates in 4 forms (separate models): 1) change; 2) post- and pre-mean; 3) pre-; 4) change and pre-.

Satiety decreased ($\Delta = -13.39$, $p = 0.001$) and thirst increased ($\Delta = 11.78$, $p = 0.006$) during the scan. Changes in other constructs were not significant (p’s > 0.05). Including covariates did not influence food vs. object contrast of appeal ratings/fMRI-FCR. Significant image X covariate interactions were observed in some fMRI models. However, including these constructs did not improve the overall model fit.

While some subjective, self-reported hunger, satiety and related constructs may be moderating fMRI-FCR, these constructs do not appear to be salient influences on appeal/fMRI-FCR in people with obesity undergoing fMRI.

1. Introduction

Neurobiological processes that link internal signals to external cues influence eating behavior and obesity (Dagher, 2012). Individuals experience external food-cues in several forms and exposure to certain types (e.g. visual) of food-cues has been linked to increased food intake in adults (Cornell, Rodin, & Weingarten, 1989; van den Akker, Jansen, Frentz, & Havermans, 2013; Coelho, Polivy, Herman, & Pliner, 2009; Ferriday & Brunstrom, 2008; Jansen et al., 2008; Wonderlich-Tierney, Wenzel, Vander Wal, & Wang-Hall, 2013). Rogers and Hill demonstrated that exposure to food-cues increased self-reported hunger and desire to eat in healthy volunteers (Rogers & Hill, 1989). Similarly, Lambert et al. showed that exposure to visual stimuli of chocolates significantly increased participants’ desire to eat compared to a group who only received a description of chocolates and a control group (Lambert, Neal, Noyes, Parker, & Worrel, 1991).

Recently, our understanding of how the brain responds to food cues has been advanced through the application of functional magnetic resonance imaging (fMRI) (Tataranni & DelParigi, 2003). In these fMRI Food Cue Reactivity (fMRI-FCR) paradigms subjects are typically presented with visual stimuli (pictures of food vs. non-food objects) and changes in BOLD (blood oxygen level-dependent) response in the brain are measured to determine the degree of involvement of various brain regions of interest in response to

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Abbreviations

AIC	Akaike information criterion
β	regression coefficient
BIC	Bayesian information criterion
BOLD	blood oxygen level-dependent
Δ	standardized post-vs. pre-scan change
fMRI	functional magnetic resonance imaging
fMRI-FCR	fMRI food-cue reactivity
H	hunger
ICC	intra-class correlation coefficient
μ	standardized mean of post- and pre-scan scores
Pre-	standardized pre-scan score
VAS	Visual analogue scales

food-vs. nonfood-cues (Kahathuduwa, Boyd, Davis, O'Boyle, & Binks, 2016). This has become a valuable tool in advancing our understanding of the brain's involvement in processing food cues in the environment. Furthermore, these types of brain responses in ingestion-related regions have been shown to predict eating behavior and weight gain (Boswell & Kober, 2016).

1.1. *Modeling hunger in fMRI studies*

Subjective hunger influences the reactivity of an individual to food-cues (Dagher, 2012; LaBar et al., 2001), and the brain is highly sensitive to food stimuli (Wang et al., 2004). Several studies have demonstrated influences on brain reactivity in the fasted vs. sated states (Del Parigi et al., 2002; Fuhrer, Zysset, & Stumvoll, 2008; Morris & Dolan, 2001; Tataranni et al., 1999). Thus it has been considered advisable, when designing well-controlled fMRI-FCR studies, that hunger be measured and modeled to account for these effects. This strategy is inconsistently undertaken with some studies including hunger measurement and others failing to do so. In those that do include measurement of hunger in their fMRI-FCR paradigms, and subsequent analyses, there is variability in how hunger is modeled, yet there appears to be no available empirical basis to inform these decisions. In addition, several different approaches tend to be used with some studies including pre-scan hunger (García-García et al., 2013a, 2013b; Gearhardt, Yokum, Stice, Harris, & Brownell, 2014; Giuliani & Pfeifer, 2015), others change in hunger (i.e. the difference between the pre- and post-scan hunger) (Yokum, Gearhardt, Harris, Brownell, & Stice, 2014) and still others, a combination of both pre- and/or post-hunger (Smeets, Kroese, Evers, & de Ridder, 2013).

Our goal is to develop evidence-based guidance to inform both the value of and process for modeling hunger and related constructs in fMRI-FCR paradigms. Thus, the first aim of this study was to examine the effects of exposure to the fMRI-FCR paradigm along 5 subjective parameters (hunger, satiety, thirsty, and subjective fullness/emptiness of the stomach) in subjects with obesity. It was hypothesized that including hunger and related constructs would have an influence on behavioral appeal ratings obtained for images of food as compared to images of matched objects (i.e. behavioral food-cue reactivity) and also fMRI-FCR. We further hypothesized that exposure to the fMRI-FCR paradigm would increase subjective self-reported hunger and related constructs and decrease satiety and related constructs. Our subsequent goal of the study was to better understand, using both behavioral and fMRI data, the optimal approach for modeling hunger and related constructs when analyzing outcomes of fMRI-FCR paradigms.

2. Materials and methods

2.1. *Participants*

Data from thirty-two subjects with obesity (BMI 30–39.9 kg/m^2) aged 19–60 years who completed the initial assessment and baseline fMRI scanning sessions as part of a larger randomized clinical intervention/fMRI trial at Texas Tech University were included. Exclusion criteria for the larger trial were: having a motor, visual or hearing impairment or any contraindications for fMRI scanning (e.g. an implanted medical device, any ferrous metal in body); diagnosed diabetes mellitus, uncontrolled hypertension, history of ischemic heart disease, cerebrovascular accidents, neurological disease or current severe psychiatric illness. Female subjects were excluded if they had an irregular menstrual cycle, were pregnant or were attempting to conceive. The study was approved by the Human Research Protection Program of Texas Tech University (TTU IRB #505380; 9/11/2015), and all the procedures complied with the Helsinki Declaration amended in 2000 (WHO, 2001). All subjects provided informed consent before participating in the study.

2.2. *Procedures*

Potential subjects were first screened for eligibility by telephone. Then they attended a second in-person session. The first half allowed for further evaluation/determination of study eligibility following which informed consent was obtained from eligible subjects and additional study-related assessment conducted. For this study, data from eligible consented subjects enrolled in the larger study who completed the initial two study visits (i.e. assessment and fMRI scanning sessions) were extracted. Data from the assessment session included measured weight (TANITA BC-418 scale; TANITA Corporation of America Inc., IL, USA) and height (stadiometer) to calculate BMI. Participants completed a questionnaire package of health and weight history and additional study-related measures following which the second visit (fMRI scan) was scheduled. For female participants, the fMRI scanning session was scheduled in the second half of the follicular phase of menstrual cycle to eliminate the effects of menstrual cycle on cravings (Dye, Warner, & Bancroft, 1995) as a potential confounder.

To prepare for the fMRI scanning visit (total duration of visit approximately 1.5 h; scan time 45 min) at Texas Tech Neuroimaging Institute, subjects were instructed to refrain from alcohol, caffeine, and tobacco for 24 h and fast (no food; only non-caloric beverages) for 8 h. In the beginning of the scanning session, subjects received instructions for performing the fMRI-FCR task and had a 2-min practice run using a laptop computer to become familiar with the task. The practice run contained 60 images, which were not presented in the fMRI scanner. Visual analogue scales (VAS) using a 100 mm line were administrated to subjects before (pre-) and after (post-) the fMRI scan to measure self-reported hunger ('How hungry do you feel at this moment?'), satiety ('How satiated do you feel at this moment?'), thirst ('How thirsty do you feel at this moment?'), fullness ('How full does your stomach feel at this moment?'), and emptiness ('How empty does your stomach feel at this moment?'). In the scanner, images of 120 food and 120 matched non-food objects (examples are shown in Fig. 1a) were displayed on an LCD screen and projected via a mirror attached to the head coil for ease of viewing. The images were obtained from varied sources and all resized to 600 × 600 pixels. Image presentations were divided into 4 runs with each run containing 30 images of food and 30 images of matched non-food objects. The order of runs and order of images in each run were randomly presented without repeat. While in the scanner, subjects responded