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COMIRB Protocol

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Project Title (COMIRB): Effects of implicit priming on food cue responses
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I. Hypotheses and Specific Aims:

The development of novel strategies to promote weight loss and maintenance is critical, given the increasing prevalence of obesity in the United States. Greater responsivity to high-calorie foods may lead to greater intake of these foods, contributing to obesity. The main aim of the current pilot project is to inform the development of a potential weight loss tool by assessing how priming pictures of food affects ratings. To achieve this goal, participants will be assigned to either the (a) active group or (b) control group. In the active group, images of high- and low-calorie foods will be paired with implicitly presented (below perceptual threshold) images of either negative or positive valence (high-calorie paired with negative; low-calorie with positive). For example, an ice cream image primed with an image of a pizza with cockroaches on it, or a piece of fruit primed with an image of a smiling child. During this task, participants will not perceive these primed pictures (although they will be told that they are there), and will rate each food picture on whether the food is "healthy" or "not healthy". Those in the control group will be primed with neutral images. Brain responses to food pictures will be recorded before and after the priming task. Participants will rate pictures of foods before and after the priming task on how much they "desire to eat" each food. In addition, participants will eat a buffet-style breakfast and lunch after the priming task, to see how the task affects food intake.

II. Background and Significance:

The prevalence of obesity in the United States has drastically increased in recent decades[1], creating a significant health concern. Current estimates indicate that 34% of adults are obese and 68% are either overweight or obese[2]. Weight loss in obese individuals is associated with a reduction in comorbid conditions, such as cardiovascular disease and hypertension[3]. The development of novel and effective strategies that promote healthier eating habits could be helpful in weight maintenance.

Previous studies, including those from our laboratory, have found neuronal responses to visual food cues to be heightened in overweight/obese[4-7], reduced-obese[6, 8-10], and obese-prone[11] compared to lean individuals. Greater responsivity to high-calorie foods may lead to greater intake of these foods and subsequently, contribute to obesity. Supporting this, previous studies have found overweight/obese individuals to demonstrate greater activation to high-calorie food cues (compared to low-calorie food cues) in comparison to lean individuals[5]. Behavioral studies have found similar results: overweight/obese individuals have been found to rate high calorie foods as more appealing compared to lean individuals[5, 10], being overweight/obese has been associated with increased fat and sweet preferences[12, 13], and preference for snack foods has been associated with future weight gain[14]. Food preferences are thought to be largely learned responses[19] that develop via classical conditioning through repeated pairings with positively and negatively valenced stimuli[20], which can influence food preferences and intake[19]. Indeed, implicit (automatic) attitudes towards food have been associated with self-reported snack consumption and food choices[21, 22]. Thus, changing these automatic associations may alter food preferences and intake.

The proposed study is the first step in a larger goal to identify a technique to promote healthier eating that would neuronal responses to food cues and food intake behaviors. This pilot study will investigate an implicit priming task, in which positive or negative images are presented immediately prior to food images, but are not consciously perceived. This pilot study will identify whether implicit priming can alter ratings of food pictures on “desire to eat.” In addition, we will assess how priming alters brain responses to food and food intake. The results of this study will inform the development of a larger study to implement this approach as an intervention to promote healthier eating habits.

Previous studies have found implicitly pairing target pictures with pictures or words of positive/negative valence (e.g., pairing a flower picture with the word “stench”) lead to increased liking/disliking of the target picture[23]. These effects may be quite durable, as one study found alterations in ratings of target pictures to remain 2 months later[24]. As such, this approach has the potential to reduce the appeal of hedonic foods and increase the appeal of healthier foods, which could encourage reduced intake of high-calorie foods in favor of low-calorie foods, promoting weight loss and weight loss maintenance.

III. Preliminary Studies/Progress Report:

As this is a pilot study, there are no preliminary data to report. If the aims of the project are achieved, the next step would be to use the results to inform development of an intervention to promote healthy eating. The subsequent study will also investigate the effects of this intervention on neuronal responses and subsequent food intake.

IV. Research Methods

A. Outcome Measure(s):

Primary outcomes in this study will be:
1) Ratings of food pictures on “desire to eat”
2) Brain responses to food pictures
3) Food intake

B. Description of Population to be Enrolled:

The study will include adult participants between ages 21-65. Participants older than 65 years of age will not be included to avoid potential effects of aging on food perceptions.

Exclusion criteria include: history of major medical condition affecting weight/metabolism; medications affecting weight; pregnancy; bariatric surgery; history of psychiatric/eating disorder; current dieting; those following a vegan or vegetarian diet; and fMRI exclusions (claustrophobia, metal in body, weight>300 lbs). Those at risk for eating disorders (score >20 on the Eating Attitudes Test [EAT-26]) will also be excluded.

C. Study Design and Research Methods

Initially, subjects will be pre-screened over the phone to assess eligibility. Eligible and interested subjects will be asked to arrive to the screening visit in a fasted. Following informed consent and demographics, participants will undergo a screening day including baseline measures and a 1-day, run-in eucaloric diet, prior to the fMRI study day. The run-in diet’s caloric value will be determined through body composition measurements taken at baseline, using BodPod. Also during the initial baseline visit, participants will be asked to complete several food/eating-related questionnaires: Eating Attitudes Test (EAT-26), Disgust Scale -R, Three Factor Eating Questionnaire (TFEQ), Power of Food Scale (PFS), and Food Craving Inventory (FCQ). In addition, participants will complete two brief surveys, one in which they will rate food pictures on "desire to eat" and another in which they will categorize foods as "healthy" or "unhealthy." After baseline measurements, participants will be randomly assigned to either the (a) active group or (b) control group in a 1:1 ratio. In the active group, images of high- and low-calorie foods will be paired with implicitly presented (below perceptual threshold; presented for 20 ms) images of either negative or positive valence (high-calorie paired with negative; low-calorie with positive). During this task, participants will not perceive these primed pictures (although they will be told that they are there), and will rate each food picture on whether the food is "healthy" or "not healthy." Those in the control group will be primed with neutral images. The priming task will be completed during functional magnetic resonance imaging (fMRI), to assess brain responses during the task. Additionally, participants will view a series of food pictures during fMRI recording immediately before and after the priming task. Following the priming/categorization task, participants will again complete the food picture ratings outside the MRI. Following this, participants may stay for an additional 4 hours, across which they will consume a buffet-style lunch to measure food intake. Subjects will also complete visual analog scale (VAS) ratings on their subjective hunger, fullness, and prospective food consumption at baseline, prior to, and 30/60 minutes after each ad libitum meal. The entire session will take approximately 2-6 hours. Participants may also be asked to return 3-5 days later to complete the food picture ratings again, which will take approximately 10 minutes.

D. Description, Risks and Justification of Procedures and Data Collection Tools:

Ad-Libitum Food Intake: Ad-libitum intake will be measured during a lunch meal served after the fMRI priming task. The purpose of this method will be to use weigh and measure methods to quantify food intake and macronutrient content of the diet directly. Specifically, a research dietician will work with the subject to provide meals that replicate, to the extent practical/possible, usual meals consumed by the subject. Subjects will be asked to not consume any other food or beverages and to maintain usual activities. All meals will be prepared by the metabolic kitchen of the Anschutz Health and Wellness Center (AHWC) and will be offered with 30% more food than predicted requirements. Subjects will be instructed to eat what they want and that they can request more of any food. This design should neither restrict intake, nor encourage over consumption. Food intake and macronutrient composition will be determined by 'weigh and measure' methods by the dietary staff of the AHWC.

Body composition: Fat mass and fat-free body mass will be measured at baseline, prior to the fMRI study day, using BodPod at the AHWC. The BodPod system employs air displacement plethysmography to determine body composition, through calculating body volume and measuring body mass[33].

Demographic measures: Participants will be asked to report their age, ethnicity, and body mass index (see "Demographics Form" attachment). A potential risk is discomfort at disclosing this information. It will be made clear that participants can choose not to disclose any of this information if they are not comfortable doing so.

Eating-Related Questionnaires: TFEQ to measure food-related behaviors including restraint, disinhibition, and hunger[29]; PFS to assess the drive to eat palatable foods in the absence of energy need or "hedonic hunger"[30]; FCQ to assess food-related cravings[31]; Disgust Scale-R to measure disgust; and EAT-26 to assess risk for eating disorders[32].

Food rating task: For the food ratings, images of foods will be rated for "desire to eat" on a visual analogue scale from 0-100 (with 0 indicating "no desire to eat" and 100 indicating "strong desire to eat"). The food rating task will be performed using the ImageRate program[28] and includes 90 food pictures, which takes approximately 10 minutes. This will be repeated both before and after the priming categorization task, and again 3-5 days following the initial session. A potential risk during this procedure could be fatigue. However, given that each iteration of this task is only 10 minutes, this risk is anticipated to be minimal. To mitigate this risk, participants are given a short break between each of the three 10-minute portions of the experiment.

Priming/categorization task: In the active group, images of high- and low-calorie foods will be paired with implicitly presented (below perceptual threshold; presented for 20 ms) images of either negative or positive valence (high-calorie paired with negative; low-calorie with positive). For example, an ice cream image primed with an image of cockroaches on food, or a piece of fruit primed with an image of a smiling child. The negative and positive images used for priming were taken from the International Affective Picture System (IAPS; csea.phhp.ufl.edu), which is a large set of standardized color photographs ranging across a wide variety of categories. These pictures have been rated for emotional valence. We will exclude the most emotionally arousing negative pictures to avoid using images that could make participants overly uncomfortable, so will only use those with an arousal rating of less than 7. During the task, participants will not perceive these primed pictures (although they will be told that they are there), and will rate each food picture on whether the food is "healthy" or "not healthy," as fast as possible. Those in the control group will be primed with neutral images and will also rate the food pictures as "healthy" or "not healthy." The task will be performed during fMRI recording using Eprime 2.0, which will allow us to collect reaction time and response data for the response to each picture. The entire task takes approximately 10 minutes. As with the rating task, a potential risk of this procedure is fatigue. As with the rating task, this task is also only 10 minutes, so minimal risk of fatigue is anticipated. To mitigate this risk, participants are given short breaks between portions of the experiment. In the unlikely event of a computer malfunction, there is a very small potential risk that the screen may pause on one of the priming images (which are usually not perceived). If this were to happen on an image of negative valence, there is potential for the participant to be uncomfortable if it were an image they found to be unpleasant (e.g., cockroaches on food). The computer used to present the stimuli has been tested extensively to ascertain that it is fast and powerful enough to complete the paradigm with no pauses. In 30 test runs, the computer has not once paused during picture presentation. We have also used a high-speed video camera (with slow motion playback) to ascertain that the computer being used is presenting the priming stimuli for 20 ms, as desired. There are no known risks to the types of magnetic fields and radio waves that are used in functional MRI studies. However, some types of metal may be moved or may heat up by the magnets in the MR scanner. The MRI machine is a small round tube. Subjects with claustrophobia may feel uncomfortable. Very rarely, some people experience warmth and reddening of the skin. This usually goes away after a few minutes. As such, we feel that the risks are minimal.

Run-In Diet: A 1-day eucaloric, run-in diet will be performed prior to the study day. The caloric value of the diet will be determined by taking into account measured resting energy expenditure (REE) and lean body mass (LBM; multiplying by a correction factor to adjust for physical activity) and will have a macronutrient composition of 50% carbohydrate, 30% fat, and 20% protein. This baseline dietary control period will ensure energy balance and weight maintenance prior to studies being performed. This approach has been used effectively by our group in a number of prior studies. All meals will be prepared by the metabolic kitchen of the AHWC.

Visual food cues task: Visual stimuli will be presented during fMRI recording using a projector and screen system. fMRI will be performed while subjects view food images (48 high-calorie, 48 low-calorie). Two runs each lasting approximately 6 minutes will be performed. Each run will consist of a blocked design with 6 blocks of high-calorie food images, 6 blocks of low-calorie images, and 6 blocks of non-food-related objects. Runs will also include 6 blocks of a low-level baseline fixation condition, consisting of 3 crosses centered in a black screen. This task will be completed before and after the intervention and will take approximately 8 minutes each time.

E. Potential Scientific Problems:

This is a pilot study designed to identify the feasibility of using implicit priming as an intervention to promote healthier eating. As study utilizes two simple behavioral measures, and fMRI measurement during a visual food cues task we have used in multiple previous studies, there are no anticipated scientific problems.

F. Data Analysis Plan:

Response and reaction time data for the response to each picture during the priming task will be collected via the presentation software (Eprime 2.0). These data will be imported into SPSS version 21 (IBM Corp., Armonk, NY). Responses will be split into high- and low-calorie foods, which will be compared using paired-samples t-tests. The food ratings are performed using the ImageRate program [28], which saves results in a spreadsheet. These ratings (for pre- and post-priming) will be imported into SPSS and split into high- and low-calorie foods. The change between session 1 and session 2 will be assessed for both high- and low-calorie foods using paired-samples t-tests. Group comparisons (control vs. active) will use independent-samples t-tests and the interaction between high- and low-calorie foods (difference in the change between each category) will also be tested.
fMRI data will be processed with Statistical Parametric Mapping (SPM8, Wellcome Dept. Cognitive Neurology) in Matlab 7.14. All data initially will be visually inspected for motion, field homogeneity and reconstruction errors, at least bi-weekly to ensure that scans with poor quality can be replaced. We typically observe excess movement (> 2 mm) in 1 out of every 15 scans. Data from each participant will be realigned, normalized to the Montreal Neurological Institute (MNI) template using a gray-matter-segmented IR-EPI as an intermediate, and smoothed with an 8-mm full width at half maximum Gaussian kernel to improve signal-to-noise ratio and account for non-independence on neighboring voxels. After preprocessing, a 128-second high-pass filter will be applied to remove low-frequency fluctuation in the BOLD signal. To account for intersubject/intrasubject variability, a random effects statistical model will be utilized. To generate this model in SPM8, statistical parametric maps will be generated for each subject using the general linear model to describe data variability on a voxel by voxel basis. The hemodynamic response will be modeled with a double gamma function, without temporal derivatives. Hypotheses expressed in terms of model parameters will be assessed at each voxel with univariate statistics, yielding an image whose voxel values comprise a statistical parametric map[47]. For visual food cues tasks (pre- and post-intervention), first-level parametric maps will be entered into a second-level repeated measures ANOVA, in which group effects (change in high-calorie>objects and basics>objects from pre- to post-intervention) will be examined with directional t-contrasts. For correlations noted above, % signal change reflecting activity for each participant will be extracted at the local maximum for each region of interest (insula/ventral

striatum). Relationships between change in neuronal response during the visual food cues task from pre- to post-intervention and (1) eating behaviors, (2) body composition, and (3) neuronal response during IP will be determined using correlations in SPSS version 21.0 (IBM Corp., Armonk, NY), as will the relationship between neuronal response during IP and subsequent eating behaviors. Differences in eating behavior measures between groups (IP vs. control) will be performed using independent samples t-tests in SPSS.

G. Summarize Knowledge to be Gained:

Obesity is a significant public health concern in the United States. Losing weight reduces the risk of comorbid diseases associated with obesity, such as cardiovascular disease and diabetes. The identification of successful techniques to encourage healthier eating would be greatly beneficial to obese individuals, in addition to lean individuals. The proposed pilot project aims to identify a potential technique to encourage healthier eating that will subsequently be developed into a larger intervention. The current project will inform the development of this intervention, and will investigate the effects of the intervention on neuronal responses and food intake.

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