Effects of Exercise on Brain Activation In Response to Visual Food Cues

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INTRODUCTION

Obesity has become a global epidemic, especially in the United States within the last ten years (9). Along with decreased quality of life, obesity leads to serious health complications and heightens chronic disease risk in affected individuals. Direct links have been confirmed to obesity as a major risk factor for cardiovascular disease and type-2 diabetes (26). Lifestyle changes have been recommended for reducing these risks; one of the major changes involving physical activity levels.

Physical activity plays an important role in weight management because it uniquely influences both energy intake and energy expenditure. Studies have shown that single bouts of exercise influence energy intake (20, 3) by altering concentrations of appetite regulating hormones (e.g. increased insulin, decreased ghrelin) during and shortly following exercise, thus suppressing hunger. Further studies have revealed that a single bout of exercise did not lead to compensatory caloric intake (29). Taken together, the data suggests that physical activity may temporarily suppress appetite.

While many studies have explored the relationships between physical activity, hormones, and appetite, none have explored the association between exercise and appetite-regulating regions of the brain. The brain plays an integral role in interpreting internal (e.g. hormones, etc.) and external stimuli (e.g. smell, taste, etc.), and regulating hunger and satiety responses. The question remains how the brain regions of appetite regulation are influenced by exercise when exposed to visual food cues. Known reward centers of the brain include the hypothalamus, orbitofrontal cortex, and left insular cortex (8, 27, 28, 12) while the dorsolateral prefrontal cortex is associated with inhibition of hunger (8, 22). These reward and inhibition regions are influenced by exercise to visual food cues via neuroimaging.

The purpose of this study was to determine if brain regions of interest were activated or suppressed following exercise when presented with visual food cues. We hypothesized that a single bout of moderate physical activity would suppress the reward regions and activate the inhibitory regions when presented with high-calorie food images.

METHODS

APPROACH

The purpose of this study was to determine if a single bout of exercise influences specific regions of the brain involved in inhibition and reward related to high-energy food stimuli and hunger. Using a counterbalanced, cross-over study design, in which subjects served as their own controls, each subject completed an exercise and no-exercise (rest) condition. Immediately after each condition a functional magnetic resonance imaging (fMRI) scan occurred. Blood oxygen level demands (BOLD) in response to food images were measured after each condition and compared among brain regions.

SUBJECTS

30 (17 male and 13 female) subjects were recruited using flyers and advertisements throughout the city of San Luis Obispo. All subjects were healthy, moderately active, right-handed, and between the ages 18-40 (see Table 1). Inclusion criteria was; non-smoking, free of chronic or metabolic diseases, and physically able to perform one hour of physical activity on a stationary cycle ergometer as determined by a Health and Fitness History and Physical Activity

Readiness Questionnaire (PAR-Q) and preliminary testing. Exclusion criteria included typical MRI contraindications (e.g. metal and/or electronic implants, claustrophobia, and pregnancy), neurologic and psychiatric conditions,

unsafe dieting practices, health problems prohibiting physical activity, and a body mass index (BMI) > 30

Variable	Mean ± SD	Range		
N (M,W)	30 (17,13)	N/A		
Age (years)	22.0 ± 3.8	18-34		
Weight (kg)	71.4 ± 12.2	50.9-100		
Height (cm)	173.6 ± 10.3	156-198.9		
BMI (kg/m ²)	23.6 ± 2.4	19.13-28.60		
Body Fat (%)	16.7 ± 7.0	6.5-29.3		
VO ₂ max	42.3 ± 8.2	29.6-65.7		

TABLE 1: Subject Characteristics – Mean values of number of subjects, subject age, weight, height, body mass index (BMI), percent body fat, and VO₂ max with standard deviation and entire value range.

kg/m². This study was approved by the Human Subjects Committee at California Polytechnic State University and written and verbal informed consent was obtained by each volunteer.

EXPERIMENTAL PROTOCOL

PRELIMINARY TESTING

Prior to starting the study, participants completed a Health and Fitness Questionnaire as well as a PAR-Q to determine their eligibility for participation. The Health and Fitness Questionnaire addressed issues such as current medications, mental and physical health conditions, and eating habits. Extreme diets, mental health disturbances, and physically limiting health problems excluded subjects from participating in the study. Upon qualification, subjects' height, weight, and percentage body fat were measured. Height was measured by stadiometer (Ellard Instrumentation LTD., Monroe, WA), weight by balance scale (Continental Scale Corporation, Bridgeview, IL), and body fat by bioelectrical impedance (Omron body fat analyzer HBF-301, Vernon Hills, IL). From these values, body mass index (BMI, kg/m²) and total daily energy expenditure (TDEE) were calculated. TDEE was calculated in accordance with the equation derived from Harris et al. (15) particular to males and females depicted below. Activity factor was determined based on responses from the Health and Fitness questionnaire.

Males: TDEE = 66.47 + 13.75(weight in kg) + 5.0(height in cm) - 6.76(age in years) * (activity factor) Females: TDEE = 655.1 + 9.56(weight in kg) + 1.85(height in cm) - 4.68(age in years) * (activity factor)

Peak oxygen consumption (VO₂ peak) was assessed using the Astrand Bicycle Ergometer Maximal Test Protocol (16). The protocol consisted of one 3minute rest stage followed by continuous 3-minute stages of increasing resistance on the stationary cycle ergometer (Lode Corival 400, Groningen, Nederland); with a constant cadence of 50 rpm. The initial power output was 50W for women and 100W for men. After the initial stage, 30W and 50W were added to each subsequent stage for women and men respectively. The test continued until three of the four following conditions were met: 1] Pedal cadence <50 rpm; 2] respiratory exchange ratio > 1.15; 3] the subject's heart rate was within 10 beats of age-predicted max; and 4] subject voluntarily stopped the test. During the VO₂ peak test, expired air was collected through a two-way breathing valve that was connected to an online metabolic system (ParvoMedics Truemax 2400, Salt Lake City, UT) that was calibrated prior to each test. VO_2 peak was determined by the highest 30-second value obtained and maximum wattage was calculated as the proportion of completed stage time over total time of stage achieved (3 minutes per stage) multiplied by the expected wattage for the given stage. For example, a female subject completes only 2 min (120s) of the 3 min (180s) stage, the percentage of the stage completed (120s/180s x 100%= 66%) will be multiplied by the total wattage of the stage (30W) to determine the wattage of her final stage (.66*30W=20W). Throughout the VO₂ peak test, heart rate (HR) was continuously monitored using a heart rate monitor (Polar Electro, Lake Success, NY) the subject wore. VO_2 peak, peak watts, and HR were used to determine the appropriate level of physical work during the exercise condition of the trial.

TEMPLETON DATA COLLECTION

All subjects reported to Templeton Imaging Medical Corporation (Templeton, CA) following an overnight (8-12 hour) fast and 24 hours without exercise, caffeine, or alcohol. Upon arrival, subjects completed an appetite questionnaire to assess subjective appetite responses using a visual analog scale (5). Subjects then were randomly split into two conditions, exercise and non-exercise. Exercise was performed for 60 minutes above 75% of their HR_{max} on a cycle ergometer. In the non-exercise condition, subjects rested for 60 minutes prior to the scan. The order of the conditions was counterbalanced and each subject completed both conditions. Within the first ten minutes of exercise, wattage was increased to reach 75% of agepredicted HR_{max}. Watts were maintained for an additional 50 minutes for a total of 60 minutes of exercise. HR and power (W) were continuously monitored in five-minute intervals and recorded for the duration of the exercise bout. Average HR (bpm), average power output (W), and relative oxygen consumption (mL/kg/min) were calculated from the last 30 minutes of steady-state cycling. Relative oxygen costs of cycle ergometry were predicted from a previously validated equation provided by Latin et al. as described below (21).

Total energy expenditure (kcal) was also calculated for the entire 60 minute exercise bout (1).

Energy Expenditure (kcal•min) = VO₂ (L•min) * 5.0

Immediately following the exercise or non-exercise portion of the trial, subjects completed another appetite questionnaire (identical to the first), and proceeded to the magnetic resonance (MR) machine within a maximum of two minutes from completion of the first stage. Subjects were then instructed to lay supine on the MR scanner table and were fitted with headphones and a head coil by the MRI technician. Visual stimuli were presented via a laptop computer (Dell Latitude E5410) onto a 32" monitor (Vizio, Irvine, CA) outside the imaging room using E-Prime software (Psychology Software Tools Inc., Pittsburg, PA) which subjects could see via a mirror mounted to the head coil.

Changes in BOLD signals to high and low energy food pictures using fMRI were assessed. Immediately after the scans were complete, subjects were given a final appetite questionnaire and completed a 24 hour dietary recall. The dietary recall was conducted following all imaging procedures so as not to disrupt the typical brain activation by food images. There was a one-week washout period between all trials.

fMRI DATA ACQUISITION AND ANALYSIS

OVERVIEW

fMRI data was acquired throughout two stages. First, a five minute anatomical scan was conducted as a reference for BOLD data. Second, BOLD data was collected during blocks of visual food cue stimulation paradigm.

VISUAL FOOD CUES

The food cue paradigm was adapted from Killgore et al. (18) by using the high quality photographs obtained from the authors. During the fMRI scan, subjects completed two stimulation paradigms over two scanning runs in a counterbalanced

order: 1] control images and low-energy food images (see Figure 1) and 2] control images and high-energy food images (see Figure 2). Control photographs consisted of non-edible food objects with similar visual complexity, texture, and color including trees, shrubs, and flowers. Low-energy images depicted fresh fruits, vegetables, whole-grain cereal, and garden salads. High-energy photographs included images depicting cake, cheeseburgers, milkshakes, chocolate chip cookies, and pasta with meat sauce. Each paradigm lasted for 180s and consisted of three 30s control blocks which alternated with three 30s stimulation blocks. Each 30s block consisted of 10 images, either control or stimulation, which were presented for 3s each.

Condition	Time in 30s intervals					
Control						
Low-Energy						

FIGURE 1: Food Cue Paradigm – Low-Energy and Control

Condition	Time in 30s intervals					
Control						
High-Energy						
EIGURE 2: Eood Cup Paradiam		High Energy and Control				

FIGURE 2: Food Cue Paradigm – High-Energy and Control

DATA COLLECTION

Functional neuroimaging data was acquired in two runs on a 1.5-T-Siemens Magnetom MRI scanner (Siemens, New York, NY) equipped with a standard head coil. Functional imaging was collected by using a whole-brain imaging sequence (TR= 3000ms, TE = 56 ms, field of view = 200cm, 64^2 acquisition matrix, 30 axial slices, and 3.5mm slice thickness). BOLD data was collected during 12 blocks in one 12-minute session (see Figures 1 and 2). For anatomical localization, matched T1-weighted high-resolution images were collected of the entire brain (256•256 matrix, field of view = 256cm, 1mm slice thickness) in the sagittal plane as a reference.

DATA ANALYSIS

Functional imaging data was processed and analyzed in Spatial Parametric Mapping (SPM8; Wellcome Trust Centre for Neuroimaging, UK) (18). To maximize the saturation effect the first five scans were eliminated from each ten-scan block

within each condition. Images were corrected for motion using an intra run realignment algorithm, convolved into the standard Montreal Neurological Institute (MNI) space and smoothed using an isotropic Gaussian kernel (full width half-maximum = 10mm) and re-sliced to 2x2x2 mm. A statistical parametric map was generated for each subject using general linear models within SPM8 (10, 11). Group SPM contrast maps were created to determine mean suprathreshold for low and high-energy food relative to the control conditions plus to compare activation changes (i.e. at a whole brain level) associated with high-energy images versus low-energy images. Given that no previous study has examined the brain's response of normal-weight or over-weight individuals to visual food stimuli after a single bout of exercise, a whole brain scan was conducted.

STATISTICS

The resulting masks were used to spatially define regions of task-related activity within which a whole brain analysis was completed. Therefore, in the second level (between subject) analysis, the newly constructed contrast images were entered into an analysis of variance (ANOVA) to compare responses of exercise versus no exercise including both men and women after controlling for BMI, age, and percent body fat. Statistical Analysis Software Inc. (SAS Institute, Cary, North Carolina) was used for statistically analyzing the data. The data was compared for significance with a p-value < 0.005, uncorrected.

RESULTS

The exercise trial characteristics for all 30 subjects are presented in Table 2. Because duration of exercise was set at 60 minutes for all subjects, there was a significant difference in power and exercise energy expenditure between male and female participants. Total energy

Variable	Mean ± SD
Duration (min)	60 ± 0
Heart Rate (bpm)	157 ± 12.4
Power (W)	138 ± 37.7
EE (kcals)	640 ± 141.5

TABLE 2: Exercise Characteristics – Mean exercise bout duration, subject heart rate, power, and energy expenditure values with standard deviation.

expenditure (EE) was estimated using the calculation previously described.

Clusters of significant activation in two major groups during high-energy stimuli are presented in Figure 3. The mass center coordinates, cluster sizes, and levels of significance of all significant groups are listed in Table 3. Exercise showed significantly greater activation ($P \le 0.005$, uncorrected) in the precuneus, medial orbitofrontal cortex, sub temporal gyrus, fusiform gyrus, middle temporal gyrus, and superior medial frontal lobe. The only significant activation in the no-exercise condition was in the midbrain and fusiform gyrus. The largest clusters of cue-related effects across all conditions were observed in the precuneus and sub-temporal gyrus regions. There were no significant regions of activation for the no-exercise high-energy versus control or low-energy versus control conditions.

Condition	Region of Activation	X	У	Z	Cluster size	t-statistic
Exercise						
High vs. Control	Precuneus	6	-58	37	1938	6.37
-	Medial OFC	12	47	-2	476	3.98
Low vs. Control	Sub Temporal Gyrus	45	-58	22	1065	4.29
	Fusiform Gyrus (Parahipoocampus Gyrus)	-21	-43	-11	371	4.02
High vs. Low	Precuneus (limbic)	-12	-52	28	1272	6.05
	Middle Temporal Gyrus	-48	2	-32	427	4.45
	Superior Medial Frontal	0	62	28	919	4.11
No Exercise						
High vs. Low	Midbrain	12	-13	-11	363	4.65
	Fusiform Gyrus	-21	-79	-5	992	4.59

TABLE 3: Whole Brain Analysis – Clusters of significant activation in response to the high-calorie and low-calorie images (p<0.005) in various conditions as compared with control scans and between exercise and no-exercise treatments.



FIGURE 3: Brain Region Activation – Top Left: Sagittal Plane, Top Right: Coronal Plane, Bottom Left: Transverse Plane; Yellow and orange regions represent clusters of activation in brain regions in response to High-Calorie food images. The precuneus is a visuo-spatial attention region. The Superior Medial Frontal Gyrus is an inhibitory region.

DISCUSSION

The main goal of this study was to determine if a single bout of exercise influenced brain regions associated with reward and inhibitory control when presented with high and low calorie food images. We showed that with exercise 1] Inhibiting regions were highly activated 2] activation of visual attention regions increased and 3] one food reward region was activated. These results suggest that single bouts of physical activity suppress appetite through the activation of inhibition regions and increased visual attention toward food cues.

In this study, exercise increased activation of inhibition regions of the brain, the superior medial frontal lobe and superior temporal gyrus. Even though this study is the first to evaluate brain activation in response to exercise, these findings are consistent with previous non-exercising studies including showing significant clusters of activation in the medial and dorsolateral prefrontal cortex when presented with high-calorie food stimuli suggesting a function of the prefrontal cortex as anticipating reward and monitoring behavioral responses (18). Del Parigi et al. found similar results while mapping brain responses following administration of a meal with hungry individuals demonstrating increased neuronal activity in the prefrontal cortex and decreased neuronal activity in regions including the orbitofrontal cortex (7). These results further associate the prefrontal cortex to inhibition of hunger and termination of energy intake and the orbitofrontal cortex with assessing reward values from food intake. A third study examined neuronal responses to smoking addiction and presented subjects following exercise or no-exercise conditions with images of individuals smoking (17). Similar to our study, they found that following a session of exercise, subjects' brain activity suggested a decline in cravings, theirs to cigarette smoking, and ours to high-calorie food intake.

Exercise also increased visual-attention processing regions of the brain. Specifically, we found significant activation of the precuneus, superior temporal gyrus, fusiform gyrus, and middle temporal gyrus. All of these areas have been linked to visual attention functions (4, 6, 13, 30). The precuneus is responsible for a number of complex processes, including both visuo-spatial processing and visual attention shift: this region is activated when tracking moving objects and when shifting

attention based on changing visual stimuli (4). McCaffery et al. found that successful weight-loss maintainers exhibited greater visual attention to food images than obese or unsuccessful weight-loss maintainers (25). Our data suggest that exercise increased attention to visual stimuli to high-calorie and low-calorie images. External visual cues have been shown to be important in the regulation of energy intake (6) and our results demonstrate that exercise increases attention to these cues.

Surprisingly, exercise increased food reward regions. We expected to see that the orbitofrontal cortex would be less activated following exercise; however these results may be due to the reward-processing function of the region, not the desire for reward as originally hypothesized. The orbitofrontal cortex is responsible for establishing connections between visual cues and reward or punishment stimuli related to those cues (27). The orbitofrontal cortex receives detailed information from visual processing and attention regions in order to evaluate reward related to various visual stimuli. One study found that higher BMI individuals experienced less orbitofrontal activity in response to high-calorie food images than lower BMI individuals (19); these results suggest not only that higher-BMI individuals have less evaluation of stimulus-reward contingencies, but that they also receive less assistance from this brain region on modifying goal-directed behavior.

The no-exercise condition yielded significant activation in only 2 brain regions, the midbrain and fusiform gyrus, which is in disagreement with previous studies. Differences may hinge on subject characteristics. For example, in the current study we chose habitually active individuals because we wanted to ensure that they could complete the high-intensity exercise, where as previous studies have not reported cardiorespiratory fitness levels (6, 8, 19). Previous research has shown that habitually active individuals have greater suppression of appetite due to regular bouts of physical activity as well as hormone changes as expected to lower appetite (3, 14). Because we did not have a "true" control group (sedentary), it remains unclear the full impact of cardiorespiratory fitness on brain activation and warrants future investigation.

A few limitations of this study need to be mentioned. First, a 1.5 T magnet used to obtain BOLD data was not as powerful as other magnets used in similar studies (6, 12). Second, the study was not powered to detect sex differences, a variable we would like to explore in the future. Finally, we did not directly measure VO_2 during the exercise bout, and we had to estimate the VO_2 and energy expenditure. However, the estimated energy expenditure based on wattage has a high correlation with indirect calorimetry (23, 24).

In conclusion, we found our data to be partially consistent with previous studies. Our results extend the notion that exercise increases the awareness of visual cues related to food as well as heightens the inhibitory and reward feedback loop that aids in suppressing compensation for energy deficits following exercise. Single bouts of exercise are effective in preventing compensatory eating following physical activity.

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