Title: Aerobic exercise reduces neuronal responses in food reward brain regions

Authors:
Nero Evero¹, Laura C. Hackett¹, Robert D. Clark¹, Suzanne Phelan¹, Todd A. Hagobian¹

Authors Contribution:
NE - design, recruiting, data collection, interpretation, writing, editing; LCH - recruiting, data
collection, interpretation, editing; RDC - interpretation, editing; SP – design, interpretation,
editing; TAH - design, recruiting, data collection, interpretation, writing, editing

Affiliations:
¹Kinesiology Department, California Polytechnic State University, San Luis Obispo, CA

Running head: Exercise and neuronal response in food reward brain regions

Corresponding Author:
Todd A. Hagobian
Kinesiology Department
California Polytechnic State University
1 Grand Avenue
San Luis Obispo, CA 93407
Phone: (805) 756-7511
Fax: (805) 756-7273
Email: thagobia@calpoly.edu
Abstract

Acute exercise suppresses *ad libitum* energy intake, but little is known about the effects of exercise on food reward brain regions. After an overnight fast, 30 (17M, 13W), healthy, habitually active (Age = 22.2 ± 0.7 yr, BMI = 23.6 ± 0.4 kg/m², VO₂ peak = 44.2 ± 1.5 ml/kg-min) individuals completed 60 minutes of exercise on a cycle ergometer or 60 minutes of rest (no-exercise) in a counterbalanced, cross-over fashion. After each condition, blood oxygen level-dependent responses to high-energy food, low-energy food, and control visual cues, were measured by fMRI. Exercise, compared to no-exercise, significantly (P<0.005) reduced the neuronal response to food (high and low-food) cues vs. control cues in the insula (-0.37 ± 0.13% vs. +0.07 ± 0.18%), putamen (-0.39 ± 0.10% vs. -0.10 ± 0.09%), and rolandic operculum (-0.37 ± 0.17% vs. 0.17 ± 0.12%). Exercise alone significantly (P<0.005) reduced the neuronal response to high food vs. control and low food vs. control cues in the inferior orbitofrontal cortex (-0.94± 0.33%), insula (-0.37±0.13%), and putamen (-0.41±0.10%). No-exercise alone significantly (P<0.005) reduced the neuronal response to high vs. control and low vs. control cues in the middle (-0.47 ± 0.15%) and inferior occipital gyrus (-1.00 ± 0.23%). Exercise reduced neuronal responses in brain regions consistent with reduced pleasure of food, reduced incentive motivation to eat, and reduced anticipation and consumption of food. Reduced neuronal response in these food reward brain regions after exercise is in line with the paradigm that acute exercise suppresses subsequent energy intake.

Keywords: brain activity, food intake, visual attention, food reward, inhibitory control
Introduction

The current obesity epidemic is largely due to a gradual but progressive gain in body weight over time (31), which is related to an increased risk for Type-2 diabetes, cardiovascular disease, and other complications (1, 11, 39). Regular physical activity is widely regarded as playing an important role in obesity prevention efforts, including the prevention of body weight gain and body weight loss maintenance (7, 9, 60). Both observational and clinical trial data suggest that physically active individuals gain less body weight over-time compared to sedentary individuals (20, 21, 26, 47). Physical activity, in the form of 30-60 minutes of daily structured exercise, minimizes body weight gain because it directly raises energy expenditure and resting energy expenditure (7, 21).

Emerging research has also documented an impact of acute exercise on energy intake. Previous studies have shown that exercise suppresses *ad libitum* relative energy intake (4, 36, 54). We and others have focused on appetite-regulating hormones (e.g. ghrelin, insulin, leptin, etc.) to explain this phenomenon (4, 28, 29, 36). In general, these data suggest that appetite-stimulating hormones and perceptions of hunger are suppressed in responses to exercise, even when energy balance is maintained. Alternatively, to explain suppressed energy intake after exercise, other interpretations include altered body temperature, gastric motility, and dehydration. Westerterp-Plantenga et al. (59) showed that exercise and exposure to a sauna, which both presumably increased body temperature, altered taste perception and subsequent macronutrient intake (i.e. lower fat and higher carbohydrate intake) at an *ad libitum* meal. Others have found that gastric motility is a primary mediator of appetite, with stomach distention relaying a message to brain regions that regulate energy intake (33).
Surprisingly, little is known about how acute exercise affects food reward regions in the brain. With advancements in spatial and temporal resolution in neuroimaging, specifically functional Magnetic Resonance Imaging (fMRI), it is possible to monitor dynamic processes ongoing in the brain using blood oxygen level-dependent (BOLD) signals as a measure of neural activity (56). A recent study (13) using fMRI observed that 6 months of exercise training significantly reduced the neuronal response in the insula (food reward region). Furthermore, the change in the insula was positively correlated to change in body weight suggesting a reduced neuronal response in the insula was related to greater body weight loss. Also, Van Rensburg et al. (32) found that exercise significantly reduced the neuronal response to smoking cues in a reward (i.e. orbitofrontal cortex) brain region, while also reducing subjective perception of craving. These data provide preliminary evidence that exercise reduces neuronal responses, however no published study to date has comprehensively examined the effects of acute exercise on neuronal response in food reward brain regions.

The primary purpose of this study was to determine whether acute exercise would alter neuronal responses to visual food cues assessed by fMRI. We hypothesized that a single bout of exercise, compared to a no-exercise resting condition, would reduce neuronal responses in food reward regions of the brain.
Methods and Procedures

Overview

Using a counterbalanced, crossover, within study design, subjects completed 60 minutes of rest (no-exercise) or 60 minutes of high-intensity exercise on a cycle ergometer. Blood oxygen level dependent (BOLD) levels in response to rewarding food images were immediately measured after both conditions.

Subjects

Thirty healthy, habitually active (> 3 hours of physical activity/week) adults were recruited through advertisement and fliers from the local community of San Luis Obispo, CA (Table 1). All subjects were right hand dominant, non-smoking, free of any metabolic or chronic disease, and physically capable of performing one hour of exercise on a stationary cycle ergometer, assessed by Health and Fitness History and Physical Activity Readiness questionnaires (PAR-Q). Exclusion criteria included, standard MRI contraindications (e.g. metal and/or electronic implants, claustrophobia, and pregnant or trying to become pregnant), neurologic or psychiatric conditions, unsafe dieting practices, body mass index (BMI) >30 kg/m², body fat >30%, peak oxygen consumption (VO₂peak) < 35 ml/kg-min, and any orthopedic or health problem that may have prohibited physical activity. Four of the thirteen women were on a triphasic birth control regimen that was maintained during the study. Women were tested in the early follicular phase (1 to 4 days after menstruation) of the menstrual cycle. The study was approved by the Human Subjects Committee at California Polytechnic State University, and verbal and written consent was obtained from all subjects.
Preliminary Testing

Height was measured by stadiometer (Ellaard Instrumentation LTD., Monroe, WA), body weight by balance scale (Continental Scale Corporation, Bridgeview, IL), and body fat percentage by bioelectrical impedance (Omron HBF-301, Vernon Hills, IL). All subjects were asked to adequately hydrate (at least 1 L of water 2 hours prior to testing) to allow for an accurate measurement of body fat percentage. Peak oxygen consumption (VO$_{2\text{peak}}$) was assessed using the Astrand Bicycle Ergometer Maximal Test Protocol (30). During the VO$_{2\text{peak}}$ test, expired air was connected to an online metabolic system (ParvoMedics Truemax 2400, Salt Lake City, UT), and VO$_{2\text{peak}}$ was determined as the highest 30-second value obtained. Throughout the VO$_{2\text{peak}}$ test, heart rate (HR) was continuously monitored using a HR monitor (Polar Electro, Lake Success, NY). VO$_{2\text{peak}}$, peak watts and HR was used to determine the appropriate level of physical work during the exercise condition (see below).

Procedures

Subjects were asked to refrain from exercise, alcohol, and caffeine for 24 hours prior to all trials. After an 8-12 hour overnight fast, subjects arrived at Templeton Imaging Medical Corporation (Templeton, CA), and completed a subjective appetite questionnaire using a visual analog scale as previously described (22). Subjects then either rested for 60 minutes (no-exercise) or exercised for 60 minutes in a counterbalanced, crossover fashion. There was a minimum of one week between conditions. In the exercise condition, subjects exercised at 83 ± 1.0% of heart rate max for 60 minutes on a cycle ergometer (estimated VO$_2$ = 29.3 ± 0.9 mL/kg-min; estimated energy expenditure = 2680 ± 108 kJ; power output = 140 ± 6.9 watts). Average HR (bpm), and power output (W) were recorded and relative oxygen consumption (ml/kg-min)
and total exercise energy expenditure was estimated (42) as; VO2 (mL/min) = (kgm/min*1.9 mL/kgm) + (3.5 mL/kg*kg of body weight) + (260 mL/min). Water intake during exercise was standardized, as all subjects consumed 1 L of water.

Immediately (168 ± 9 seconds) following the 60 minutes of rest or exercise, subjects completed another appetite questionnaire and then proceeded to the magnetic resonance imaging (MRI) machine. Subjects were then instructed to lie supine on the MRI scanner table to be fitted with headphones and head coil by the MRI technician. Visual stimuli were presented from a laptop computer (Dell Latitude E5410) onto a 32-inch monitor (Vizio, Irvine, CA) using E-Prime software (Psychology Software Tools Inc., Pittsburgh, PA). Changes in BOLD signals to high- and low-energy food cues using fMRI were assessed (see below). Subjects viewed the images on a 32-inch monitor through a 2-way mirror mounted to the head coil. After the scan, subjects were given a final appetite questionnaire and completed a 24-hour dietary recall.

Visual Food Cue Paradigm

The food cue paradigm was adapted from Kilgore et al. (35) 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 foods, and 2) control images and high-energy foods. Control images consisted of non-food objects with similar visual complexity, texture and color (e.g. trees, shrubs, flowers, etc.). Low-energy food pictures included images depicting fresh fruits and vegetables, whole-grain cereal, garden salads, etc. High-energy food pictures included images depicting cheeseburgers, hot dogs, french fries, ice cream sundaes, chocolate chip cookies, barbecued chicken, pasta with meat sauce, etc. Each paradigm lasted for 180s and consisted of three 30s
control blocks which alternated with three 30s stimulation blocks. Each block consisted of 10 images (2 dummy + 8 control/stimulation) being presented for 3s each. The two dummy images (i.e. images of utensils) were used to provide transition from control to stimulation images.

MRI Data Acquisition

Functional neuroimaging data were acquired in two runs on a 1.5-T Siemens Symphony MRI scanner (Siemens, New York, NY) equipped with a standard head coil. For anatomical localization, matched T1-weighted high-resolution images were collected of the entire brain (256 × 256 matrix, field of view = 256 mm, 1-mm slice thickness) in the sagittal plane as a reference for 5 minutes. Functional imaging was collected using a whole-brain imaging sequence (TR=3000ms, TE=56ms, field of view = 200 mm², 64² acquisition matrix, 30 axial slices, and 3.5-mm slice thickness). BOLD data were collected during 12 blocks in one 12-minute session.

fMRI Data Processing and Statistical Analysis

Functional imaging data were processed and analyzed in SPM8 (Wellcome Trust Centre for Neuroimaging, UK) within the context of the General Linear Model on a voxel by voxel basis (24). Images were corrected for motion using an intrarun realignment algorithm, convolved into the standard Montreal Neurological Institute (MNI) space (using the EPI template found within SPM8) (23), and smoothed using an isotropic Gaussian kernel (full width half-maximum=7mm) and resliced to 2 x 2 x 2 mm.

As adapted from Stoeckel et al. (53), a two-stage procedure was used for the statistical analysis of a mixed-effects design. At the first level (fixed effects), the fMRI data from each subject was used to generate statistical contrasts maps to compare brain activation to: 1) control
vs. high-energy foods and 2) control vs. low-energy foods. These contrasts were then entered into a second level (random effects) analysis to compare the exercise and no-exercise conditions in response to the visual food cues, using a repeated measure ANOVA. In a separate repeated measure ANOVA analysis, we treated both the high-energy and low-energy food cues as the same (labeled “food” in results) and compared this to control cues. Given that no previous study has comprehensively examined brain responses to visual food cues after a single bout of exercise, *a priori* regions of interest (ROI) that have previously been reported in the regulation of food intake were used (i.e. dorsolateral prefrontal cortex (DLPFC), orbitofrontal cortex (OFC), insula and hypothalamus) \(12, 14, 35, 44\). ROI clusters were created using the Wake Forest University PickAtlas \(41\) and the MarsBaR toolbox \(6\) in addition to the Anatomic Automatically Labeling toolbox \(57\) to determine the anatomical location of each locus. As activation within these search territories was predicted to differ between exercise vs. no-exercise, the ROI analysis was conducted using the MarsBaR toolbox \(6\). To correct for multiple comparisons in the ROI approach, a Bonferroni correction was applied to the ROI’s. An \(\alpha<0.05\) was considered significant. In our analyses, we started with a whole brain analysis and were able to determine the ROIs from the whole brain activity.

Also, whole brain, voxel-wise group contrasts were performed to identify differences in brain activity outside *a priori* ROI. Brain activation was evaluated at a threshold of \(P<0.005\) (uncorrected), with an extent threshold of 5 contiguous voxels, which is standard for exploratory fMRI studies given the relatively novel approach \(35\). A repeated-measure ANOVA was used to determine differences between conditions, visual food conditions and the interaction between conditions and visual food cues. BOLD percent signal changes of significantly active regions were measured using the MarsBar toolbox \(6\).
Exploratory analyses were also conducted in each condition separately to compare neuronal responses to high-energy food vs. control cues and low-energy food vs. control cues. A one-factor ANOVA was used to determine significantly activated/deactivated brain regions (P<0.005, uncorrected). This analysis was performed in order to get a sense of direction of the condition effects of each run (i.e. regions being activated or deactivated) in response to the visual food cues.

Minitab 16 Statistical Software (Minitab Inc., State College, PA) was used for statistical analyses of the subjective appetite ratings. A General Linear Model was used to determine differences in hunger, satiety, fullness and prospective food consumption between the exercise and no-exercise conditions. An $\alpha<0.05$ was considered significant, and a Bonferroni Simultaneous post-hoc test was applied. Pearson product moment correlations were used to assess the relationship between changes in BOLD signal and changes in appetite rating.
Results

ROI Analysis

Exercise, relative to no-exercise, significantly reduced (P<0.05; Table 2) the neuronal response to high food vs. control cues and food vs. control cues in the insula (-0.35 ± 0.13% vs. 0.05 ± 0.17% and -0.45 ± 0.10% vs. -0.06 ± 0.11%, respectively). Exercise, relative to no-exercise, increased the neuronal response to food vs. control cues in the hypothalamus but did not reach significance (P=0.064; Table 2). No other a priori ROI was significantly active (Table 2).

Whole Brain Analysis

Exercise, relative to no-exercise, significantly reduced the neuronal response to high food vs. control cues in the left and right insula (P<0.005, uncorrected; Table 3). Also, exercise, relative to no-exercise, significantly reduced the neuronal response to food vs. control cues in the left postcentral gyrus, right putamen, left insula, right rolandic operculum, and right supramarginal gyrus (P<0.005, uncorrected; Table 3, Figure 1). Exercise, relative to no-exercise, significantly reduced the neuronal response to low food vs. control cues in the left postcentral gyrus (P<0.005, uncorrected; Table 3). Figure 2 presents a brain view of the exercise and no-exercise conditions depicting the reduced neuronal response after exercise.

Exercise, relative to no-exercise, significantly increased the neuronal response to high food vs. control cues in the left precuneus (P<0.005, uncorrected; Table 3). No other brain region was significantly altered in exercise vs. no-exercise condition (Table 3).
Whole Brain Analysis for Exercise and No-exercise Alone

Exercise was associated with reduced neuronal response (deactivated) to high food vs. control cues in the left middle occipital gyrus, right inferior occipital gyrus, right inferior frontal gyrus (triangular part), left superior parietal gyrus, right putamen, left and right insula, and cerebellar vermis (P<0.005, uncorrected; Table 4), while significantly increased neuronal response (activation) in the right precuneus (P<0.005, uncorrected, Table 4). Similarly, exercise was associated with reduced neuronal response to low food vs. control cues in the right inferior occipital gyrus, left middle occipital gyrus, left inferior orbitofrontal cortex, left superior frontal gyrus (medial surface) and left precentral gyrus (P<0.005, uncorrected; Table 4).

In contrast, the no-exercise condition was associated with reduced neuronal response to high food vs. control and low food vs. control cues only in the right inferior occipital gyrus, and left middle occipital gyrus (P<0.005, uncorrected; Table 4), while significantly increased the neuronal response in the right lingual gyrus (P<0.005, uncorrected; Table 4).

Subjective Appetite Responses

Exercise, relative to no-exercise condition, significantly lowered ratings of hunger (P=0.02; Figure 3) and prospective food consumption (P<0.01; Figure 3), and significantly increased perceptions of satiety (P=0.02; data not shown) and fullness (P=0.02; data no shown). Most correlations between BOLD signal in brain regions and subjective appetite responses were weak and/or non-significant (P>0.05).
Discussion

In the current study, an acute bout of exercise altered the neuronal (or BOLD) response to food cues in brain regions important in food reward, visual attention, and inhibitory control. Specifically, in support of our hypotheses, we found that exercise resulted in a decreased responsiveness to food cues in food reward regions (i.e. insula, putamen, rolandic operculum) and near significant for hypothalamus. In follow-up exploratory analyses, we similarly showed that exercise reduced the neuronal response in two food reward regions (right inferior orbitofrontal cortex and bilateral insula), which have a central role in reward value (45, 46), expected reward value (25), regulation of food behavior (12, 14, 50, 51) and subjective pleasantness of food (40). Taken together, these data suggest that acute exercise reduces the neuronal response in food reward brain regions in a direction expected to decrease energy intake.

In the current study, we observed a clear effect of acute aerobic exercise on reducing neuronal responses to visual food cues. Acute exercise, relative to no-exercise, resulted in significantly reduced neuronal responses in the left and right insula, right putamen, right rolandic operculum and orbitofrontal cortex, all of which are consistent with reduced food reward (13, 48, 52). Furthermore, reduced activity in the orbitofrontal cortex is consistent with reduced decision-making and reduced pleasantry and palatability of food (61). To our knowledge, only two other published studies have evaluated the impact of exercise on brain activity using fMRI (13, 32). Recently, Cornier et al. (13) observed that 6 months of exercise training significantly reduced brain activity in a food reward region (i.e. insula) and other visual brain regions. Janse Van Rensberg et al. (32) found that 10 minutes of exercise significantly lowered activation in the orbitofrontal cortex and dorsolateral prefrontal cortex in response to visual smoking pictures, which is consistent with decreases in a food reward region and better inhibitory control,
respectively. Although not directly evaluating the impact of exercise on brain activity, others found that energy imbalance (12, 14, 15), a high-protein meal (43), and exogenous leptin (2) administration decreased activity in food reward regions (in particular the insula). Thus, our results are generally consistent with, and extend the results of, those previous studies showing decreased neuronal response in food reward regions (i.e. insula, putamen, rolandic operculum, orbitofrontal cortex) after acute exercise.

Food reward can be divided into two different components – liking (pleasure and palatability of food) and wanting (incentive motivation to eat) (3). Previous studies have shown that neuronal responses to liking and wanting may overlap or may be distinctly different (5, 25, 38, 49). Born et al. (5) found that liking task-related brain signaling was apparent in the insula, whereas wanting task-related brain signaling was in the cingulate cortex, thalamus, and putamen. Others found that the orbitofrontal cortex is a liking brain region (49). In the current study, even though we did not directly measure liking and wanting, we found that acute exercise reduced both liking (i.e. insula, orbitofrontal cortex) and wanting (i.e. putamen) specific brain regions. Moreover, we found that acute exercise reduced activity in the right rolandic operculum, which is consistent with reduced anticipation and consumption of food (52). Thus, our data are consistent with acute exercise reducing the pleasure of food (liking), incentive motivation to eat (wanting), and anticipation and consumption of food.

Interestingly, in exploratory analyses, we also found that exercise led to significantly reduced neuronal response in cortical brain regions associated with visual attention and processing (i.e. left middle occipital gyrus and right inferior occipital gyrus). These finding suggest that exercise may decrease the awareness and reward of external food cues, especially with the concomitant deactivation of prefrontal regions. This is in line with previous findings
(12–14, 32, 43) showing that energy imbalance, with or without exercise, alters visual processing brain centers. However, we also observed that exercise increased the neuronal response in the precuneus, which is consistent with reward anticipation. Interestingly, Van Rensburg et al. (32) found similar activation of the precuneus after 10 minutes of exercise. Emerging evidence indicates that the role of the precuneus is extremely complex, and in addition to being associated with a visual-processing center, may also play a role in spatial relations of body movement, motor imagery, and attention shift between objects (10). Thus, in the current study the increased activation of the precuneus in response to exercise may be related to higher-order cognitive functions and not necessary a heightened awareness to the visual food cues.

In general, a single bout of exercise suppresses subsequent *ad libitum* energy intake (36). Previous studies have shown that exercise alters appetite hormones in a direction expected to suppress energy intake (8, 28, 29, 36), while others have focused on body temperature, dehydration, and gastric motility to suppress energy intake (33, 59). To our knowledge, few studies have examined the effects of brain activity on energy intake (15, 52), and none, including the present study, evaluated whether exercise-induced changes in brain activity alters *ad libitum* energy intake. The lack of prior data limits our ability to infer that reduced neuronal responses in food reward and visual attention brain regions would have suppressed actual energy intake in our exercise treatment.

Surprisingly, we did not find changes in the dorsolateral prefrontal cortex (a commonly recognized inhibitory region) in response to exercise and, in our exploratory analyses we found that exercise reduced activation in the superior frontal gyrus (medial surface), which is associated with an inhibitory control region. These data, coupled with our findings that activity in other frontal regions were decreased (right inferior OFC, right inferior frontal gyrus (triangular
part), are at least partially in line with the “Transient Hypofrontality” hypothesis (17, 18). The “Transient Hypofrontality” hypothesis proposes that aerobic exercise decreases neural activity to brain regions that are not necessary to the preservation of the exercise bout (18). These brain areas with decreased activity include the higher cognitive centers of the frontal lobe (19). During exercise the metabolic demands of the brain are increased (34), but blood flow to the cerebral cortex and other frontal brain regions, as a proportion of cardiac output, is reduced during high-intensity exercise (19, 55). Therefore, in response to exercise it becomes challenging to maintain neural activity to all brain structures and it seems that frontal lobe regions have decreased activity.

Consistent with the current brain findings, after exercise, participants reported lower self-perceptions of hunger and prospective food consumption. These results are consistent with most previous studies showing that exercise alters appetite ratings in a direction expected to suppress food intake (8, 36, 37). However, in the current study many correlations between brain activity and appetite ratings were weak and non-significant, which is in disagreement with a previous fMRI study (43). The lack of correlation in our data suggests a possible disconnect between appetite ratings and food reward brain activity. This is partially supported by a recent study (4) showing that appetite hormones and appetite ratings respond to different metabolic signals (i.e. changes in energy balance vs. meal size, respectively). Although we did not measure appetite-hormones in the current study, it is plausible that brain activity and appetite ratings are also responding to different metabolic signals, although this is highly speculative.

There are several limitations of the current pilot study. First, because all conditions occurred at our fMRI facilities not in our laboratory, we were unable to directly measure oxygen consumption and energy expenditure during exercise. We chose a similar dose of exercise (high-
intensity, 60 minutes) to previous studies showing robust changes in appetite hormones and
decreased energy intake (8, 36). Also, estimating oxygen consumption and energy expenditure
using the Latin et al. (42) equation has a high correlation with actual exercise energy
expenditure. Second, due to our convenient sample of healthy, habitually active students, the
generalizability to sedentary, clinical over-weight or obese groups is limited. Previous studies
(16, 44) have shown brain responses to visual food cues to differ between individuals of different
weight classifications, but further research is still needed to determine the impact of acute
exercise on brain responses in at risk, sedentary groups. Third, the strength of the fMRI machine
we used, a 1.5-Tesla, may not have been robust enough to detect differences in homeostatic and
hedonic control feeding centers deep within the brain, even though the hypothalamus approached
significance (P=0.06). Previous studies have shown increased activity in the hypothalamus and
other inner brain regions using a 1.5-Tesla (35), but more recent studies have shown greater
activity in inner brain regions using a more powerful 3.0-Tesla (14, 53). Fourth, we did not
assess body weight and body temperature in response to exercise, both of which may influence
subsequent energy intake (59). In our previous studies (27–29) using a similar dose of exercise,
we observed <0.45 kg change in body weight pre to post exercise, and it remains unclear the
impact of exercise-induced changes in weight and body temperature on brain activity. Fifth,
subjects were overnight fasted in both conditions, and it is possible that feeding subjects prior to
exercise may alter the brain activity patterns observed in the current study. To fully explore this,
future studies are needed to evaluate fed vs. fasted on exercise-induced brain activity. Finally, in
the no-exercise condition, we observed minimal changes in neuronal activity, which is in
disagreement with previous studies using similar normal-weight subjects (35). However, our
subjects were habitually active, and had moderate to high cardiorespiratory fitness levels, which may have had an independent effect on neuronal activity.

In summary, we observed a clear difference in the way acute exercise alters neuronal responses to visual food cues. Exercise reduced neuronal responses in food reward and visual attention brain regions. This has implications for both our understanding of basic science (e.g. brain regions that alter energy intake), and practical perspective (e.g. exercise and body weight gain). In general, acute exercise suppresses subsequent relative energy intake. The results of the current study suggest at least one potential explanation.
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Disclosure:

There are no conflicts of interest to be reported.

Authors Contribution:

NE - design, recruiting, data collection, interpretation, writing, editing; LCH - recruiting, data collection, interpretation, editing; RDC - interpretation, editing; SP – design, interpretation, editing; TAH - design, recruiting, data collection, interpretation, writing, editing
References


Figure Captions

Figure 1. Mean BOLD percent signal change (± SEM) of significantly active clusters to food vs. control cues in exercise and no-exercise conditions. Exercise significantly different than no-exercise (P<0.05) in all brain regions.

Figure 2. Whole brain view of neuronal responses to high food cues vs. control cues (A) and food cues vs. control cues (B) in exercise and no-exercise conditions. Exercise, relative to no-exercise, significantly (P<0.005, uncorrected) reduced the neuronal response in the bilateral insular cortices and right putamen, and significantly increased (P<0.005, uncorrected) the neuronal response in the precuneus. Data are shown in neurological orientation (i.e. right hemisphere on right, left hemisphere on left). Color bar reflects suprathreshold value of the SPM{t} statistic for analysis.

Figure 3. Hunger and prospective food consumption ratings in exercise and no-exercise conditions.

*Significantly higher (P<0.05) than exercise.
Table Legends

Table 1. Subject Characteristics.

Table 2. ROI analysis in exercise and no-exercise conditions.
DLPFC, dorsolateral prefrontal cortex; OFC, orbitofrontal cortex

Table 3. Foci of significantly active clusters (P<0.005, uncorrected) for whole brain analysis in exercise and no-exercise conditions.
EX, exercise; NEX, no-exercise
*Stereotactic coordinates in Montreal Neurologic Institute space
†Cluster mass center not specified by atlas, used proximal region

Table 4. Foci of significantly active clusters (P<0.005, uncorrected) for whole brain analysis in exercise and no-exercise conditions alone.
EX, exercise; NEX, no-exercise
*Stereotactic coordinates in Montreal Neurologic Institute space
†Cluster mass center not specified by atlas, used proximal region
Exercise No-Exercise

Precuneus  Putamen  Insula

Exercise  No-Exercise
Table 1. Subject characteristics

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Table 2. ROI analysis in exercise and no-exercise conditions

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<td>OFC</td>
<td>1.540</td>
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<tr>
<td><strong>Exercise vs. No-Exercise</strong></td>
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<td></td>
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<tr>
<td>High vs. Con</td>
<td>DLPFC</td>
<td>0.930</td>
<td>0.540</td>
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<td>Hypothalamus</td>
<td>1.840</td>
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<tr>
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<td>Insula</td>
<td>-2.280</td>
<td>1.000</td>
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<tr>
<td></td>
<td>OFC</td>
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<td>Low vs. Con</td>
<td>DLPFC</td>
<td>-1.460</td>
<td>0.999</td>
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<td>Hypothalamus</td>
<td>1.290</td>
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<tr>
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<td>Insula</td>
<td>-1.340</td>
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<td>OFC</td>
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<td>1.000</td>
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<tr>
<td>Food vs. Con</td>
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<td>0.984</td>
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<td>Hypothalamus</td>
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<td>Insula</td>
<td>-2.490</td>
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<tr>
<td></td>
<td>OFC</td>
<td>-1.540</td>
<td>1.000</td>
</tr>
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</table>

DLPFC, dorsolateral prefrontal cortex; OFC, orbitofrontal cortex
Table 3. Foci of significantly active clusters (P<0.005, uncorrected) for whole brain analysis in exercise and no-exercise conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Region</th>
<th>MNI coordinate*</th>
<th>t-statistic</th>
<th>Cluster Size</th>
<th>EX % Signal Change</th>
<th>NEX % Signal Change</th>
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</thead>
<tbody>
<tr>
<td>Exercise&lt;No-Exercise</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>High Food vs. Con</td>
<td>L Insula</td>
<td>-45 8 -8</td>
<td>3.98</td>
<td>81</td>
<td>-0.37 ± 0.13</td>
<td>0.07 ± 0.18</td>
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<tr>
<td></td>
<td>R Insula‡</td>
<td>42 5 -5</td>
<td>3.76</td>
<td>115</td>
<td>-0.31 ± 0.15</td>
<td>-0.03 ± 0.17</td>
</tr>
<tr>
<td>Low Food vs. Con</td>
<td>L Postcentral gyrus</td>
<td>-60 -4 25</td>
<td>3.56</td>
<td>71</td>
<td>-0.34 ± 0.20</td>
<td>0.40 ± 0.15</td>
</tr>
<tr>
<td>Food vs. Con</td>
<td>L Postcentral gyrus</td>
<td>-45 -7 28</td>
<td>4.32</td>
<td>315</td>
<td>-0.21 ± 0.10</td>
<td>0.31 ± 0.14</td>
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<tr>
<td></td>
<td>R Putamen</td>
<td>24 2 -5</td>
<td>3.91</td>
<td>64</td>
<td>-0.39 ± 0.10</td>
<td>-0.10 ± 0.09</td>
</tr>
<tr>
<td></td>
<td>R Insula‡</td>
<td>42 2 -11</td>
<td>3.78</td>
<td>74</td>
<td>-0.38 ± 0.10</td>
<td>-0.05 ± 0.10</td>
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<tr>
<td></td>
<td>R Rolandic Operculum</td>
<td>45 -22 13</td>
<td>3.78</td>
<td>90</td>
<td>-0.37 ± 0.17</td>
<td>0.17 ± 0.12</td>
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<td>R Supramarginal gyrus</td>
<td>48 -34 40</td>
<td>3.75</td>
<td>68</td>
<td>-0.23 ± 0.16</td>
<td>0.18 ± 0.15</td>
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<tr>
<td>Exercise&gt;No-Exercise</td>
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<tr>
<td>High Food vs. Con</td>
<td>L Precuneus</td>
<td>-6 -55 34</td>
<td>4.79</td>
<td>234</td>
<td>0.38 ± 0.23</td>
<td>-0.08 ± 0.26</td>
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<tr>
<td>Low Food vs. Con</td>
<td>No significant regions</td>
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<tr>
<td>Food vs. Con</td>
<td>No significant regions</td>
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</tr>
</tbody>
</table>

EX, exercise; NEX, no-exercise

*Stereotactic coordinates in Montreal Neurologic Institute space

‡Cluster mass center not specified by atlas, used proximal region

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Table 4. Foci of significantly active clusters (P<0.005, uncorrected) for whole brain analysis in exercise and no-exercise conditions alone

<table>
<thead>
<tr>
<th>Condition</th>
<th>Region</th>
<th>MNI coordinate*</th>
<th>t-statistic</th>
<th>Cluster Size</th>
<th>% Signal Change</th>
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<tbody>
<tr>
<td></td>
<td><strong>Activated</strong></td>
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<td><strong>Exercise</strong></td>
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<tr>
<td>High vs. Con</td>
<td></td>
<td></td>
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<td>R Precuneus</td>
<td>-12 -55 28</td>
<td>6.23</td>
<td>715</td>
<td>0.61 ± 0.20</td>
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<td></td>
<td>L Middle Occipital gyrus</td>
<td>-36 -55 -17</td>
<td>8.60</td>
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<td></td>
<td>R Inferior Occipital gyrus</td>
<td>42 -88 1</td>
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<tr>
<td></td>
<td>R Inferior Frontal gyrus (triangular part)</td>
<td>57 35 19</td>
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<td>L Superior Parietal gyrus</td>
<td>-24 -58 58</td>
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</tr>
<tr>
<td></td>
<td>R Putamen</td>
<td>27 -4 -20</td>
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<tr>
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<td>Cerebellar Vermis'</td>
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<td>High vs. Con</td>
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<td>R Lingual gyrus</td>
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<td>39 -91 10</td>
<td>4.31</td>
<td>141</td>
<td>-0.33 ± 0.28</td>
</tr>
</tbody>
</table>

*Stereotactic coordinates in Montreal Neurologic Institute space
‡Cluster mass center not specified by atlas, used proximal region