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The Effect of Time of Day of Chronic Exercise on Neural Response to Visual Food Cues

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ABSTRACT

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This study examined the effect of an 8-week, progressive exercise intervention on neural responses, specifically N2 amplitude as a measure of inhibitory control, to pictures of food. Healthy women ages 18-44 years were randomized to a morning (AM) exercise group or evening (PM) exercise group. The AM group did moderate-to-vigorous intensity exercise on 4 days per week between 6:30 and 9:30 a.m. while the PM group had the identical volume of exercise between 6:30 and 9:30 p.m. Neural responses, eating behaviors, cardiovascular fitness outcomes, and body weight/composition were measured at baseline and after the 8-week intervention. The N2 amplitude in response to pictures of high- and low-calorie foods was assessed using electroencephalography during a go/no-go task. Dietary restraint, emotional eating, and external eating were assessed using the Dutch Eating Behavior Questionnaire. VO_{2peak}, HR_{max}, and time to completion were measured during a maximal treadmill test. Body weight was measured on a digital scale, and body composition was measured using dual-energy x-ray absorptiometry.

There was not a significant task (go, no-go) × group (AM, PM) × period (baseline, 8 weeks) interaction ($F = 0.18$; $p = 0.677$), but there was a main effect of exercise over 8 weeks ($F = 6.26$; $p = 0.017$) with increased N2 amplitude following the intervention. There was not a significant interaction as a function of picture type (high-calorie, low-calorie), task, group, and period ($F = 0.52$; $p = 0.478$). Changes in body weight and neural outcomes were not significantly associated with changes in eating behaviors for either group (*ps* > 0.05). There was a significant group × period interaction for body weight ($F = 4.90$; $p = 0.032$). Body weight increased by 0.79 ± 1.16 kg in the AM group and decreased by 0.21 ± 1.46 kg in the PM group (effect size = 0.77; CI = 0.15-1.35). There was not a significant group × period interaction for body fat percentage, total body fat or fat-free mass (*ps* > 0.05). When examining the main effect of exercise on cardiovascular fitness outcomes, VO_{2peak} was not different ($F = 1.80$; $p = 0.187$), time-to-completion on treadmill increased ($F = 6.51$; $p = 0.014$), and HR_{max} during the treadmill test was significantly lower ($F = 5.49$; $p = 0.025$).

This study suggests that 8 weeks of exercise training may increase the inhibitory response to pictures of both high- and low-calorie foods. However, time of day of exercise did not influence this response. Eight weeks of exercise training did not change self-reported dietary restraint, external eating, or emotional eating, and there was no correlation between these eating behaviors and inhibitory control. However, evening exercise was more beneficial for body weight than morning exercise. Given the novelty of this study and its results, additional studies on the influence of time of day of exercise on weight management are needed.

Keywords: electroencephalography, event-related potential, N2 waveform, go/no-go task, inhibitory control, dietary restraint, emotional eating, external eating

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Introduction

Consistent exercise has been shown to lower the risk of early death,[1,2] coronary heart disease,[3,4] stroke,[5-7] high blood pressure,[8-11] type 2 diabetes,[12-14] and several forms of cancer.[15-17] Exercise may also assist in body weight management[18-20] by increasing energy expenditure, thereby correcting for small energy imbalances resulting from excess energy intake.[21] Recently, however, there has been increased interest in the role of exercise not only for energy expenditure but also energy intake.[22-27]

Any attempt to describe or predict human eating behavior is difficult due to the large number of potential contributing factors. Nevertheless, a series of recent studies have focused on the brain; specifically, on neural responses to visual food cues[28-30] as potential correlates of energy intake or as predictors of weight management.[31,32] These studies indicate that the human brain may respond differently to pictures of food than to neutral pictures (e.g., flowers or office furniture), or to pictures of high-calorie foods than to pictures of low-calorie foods.[33-35] Combined with the knowledge that visual/external cues can influence eating,[36,37] these studies show promise to better understand how the neural responses to specific food cues may be associated with eating behavior. However, whether or not this relationship is influenced by exercise has received little attention.[38-40]

One method of determining neural responses to visual food cues is by using electroencephalography (EEG). EEG objectively detects the electrical potentials generated by apical dendrites in the brain[41] and can be reduced to provide a stimulus- or response-locked measure called an event-related potential (ERP). Specifically, an ERP represents brain activity time-locked to the presentation of a visual, aural, or response cue (i.e., the event). Typically,

ERPs are the average neural response to multiple similar visual cues (such as high-calorie food pictures).[41]

The ERP of interest in the present study is the N2 waveform which is a measure of inhibitory control.[42] Donkers et al. described inhibitory control as "the ability to deliberately suppress dominant, automatic, or prepotent responses."[43] The N2 is often measured during a go/no-go task in which participants must respond quickly to one kind of stimulus (go) and withhold a response from another, less frequent, type of stimulus (no-go). The N2 is highest after a no-go stimulus when the participants must suppress the preferred response.[42] One recent study suggests that the N2, as a measure of inhibitory control, may be correlated with self-reported eating behaviors[44] though more studies are needed to confirm this association.

An advantage of assessing ERPs associated with pictures of food is the objectivity of the assessment. At present, related studies have attempted to measure appetite, hunger, and motivation to eat[45,46] based on visual analog or related scales which are typically subjectively determined.[47-50] While use of subjective measurements can provide important information, objective assessments, such as ERPs, may produce superior and more meaningful data.[51]

There is currently a body of literature in which the effects of exercise on appetite and hunger have been studied.[22,23,27,52] Unfortunately, the data are mixed with some studies suggesting exercise increases appetite or hunger while others suggest exercise decreases or has a neutral effect on appetite or hunger.[53,54] It is possible that the mixed data are partially due to the subjective measurements. Similarly, in a recent review of the effect of exercise on energy intake, Donnelly et al., suggested that the majority of existing exercise studies do not show an influence of exercise on energy intake though they found that exercise may modestly lower dietary fat intake.[52] Therefore, it is presently unclear to what extent exercise influences eating-related

outcomes. However, several recent studies have shown that acute exercise reduces neural responses (measured via fMRI and EEG) to pictures of food.[40,55-57] Unfortunately, there are no studies on adults testing the long-term or adaptive effects of exercise on neural responses to pictures of food.

A related but separate body of literature has recently attempted to understand the effect that time of day has on eating behaviors.[30,58] This emerging body of literature suggests that eating tends to be greatest in the evening[59] and that nutrients/food may be processed in the body differently at different times of the day.[60,61] In addition, it is known that appetite-related hormone levels, such as leptin, may change throughout the day, thereby, potentially influencing eating.[62] The suggestion that time of day can influence eating behavior is indirectly supported by studies showing that night workers (who have irregular diet and sleep patterns) are at high risk for weight gain and obesity.[63-65] Also, other research has shown that restricting feeding to a certain time of the day (e.g., not eating at night) influences energy intake and weight gain.[66] The concept that time of day of exercise may influence eating behaviors has received very little scientific consideration relative to the larger body of exercise research.[25,67,68] This is surprising given the common lay recommendation that morning exercise has metabolic effects that may enhance weight management.

Currently, little is known about the influence of time of day of exercise on eating behaviors and nothing about the effect of time of day of exercise on neural responses to visual food cues. This novel study was designed to objectively explore the impact of time of day of exercise training on neural responses to food pictures and whether this relates to real eating behaviors. Therefore, the specific aims of this randomized study were:

1. To compare the effect of 8 weeks of morning exercise to 8 weeks of evening exercise on the neural response to visual food cues as measured by the N2 ERP waveform.
2. To determine the interaction between exercise training and the inhibitory neural response to high-calorie or low-calorie foods. In other words, to determine if 8 weeks of exercise training influences N2 response to pictures of high-calorie foods differently than pictures of low-calorie foods.
3. To determine the effect of 8 weeks of morning or evening exercise training on key eating behaviors including dietary restraint, external eating, and emotional eating using the Dutch Eating Behavior Questionnaire (DEBQ) and to determine their association with body weight and the N2 neural response to pictures of high-calorie or low-calorie foods during the go/no-go task.

We hypothesized that the 8-week exercise intervention (regardless of time of day of exercise) would result in a significant increase in the inhibitory response (i.e., greater inhibitory control) to pictures of high-calorie foods but not low-calorie foods. In addition, given that people tend to eat more in the evening[59] and that exercise may diminish neural responses to pictures of food,[40,55-57] we hypothesized that the increased inhibitory response to pictures of high-calorie foods would be greater in the evening exercise group compared to the morning exercise group. Finally, we hypothesized that 8 weeks of evening exercise training would improve eating behaviors (increase dietary restraint, reduce external eating, and reduce emotional eating) to a greater extent than 8 weeks of morning exercise, and would be significantly associated with the N2 neural response during viewing of pictures of high-calorie foods; therefore, body weight and/or body composition outcomes would be superior in the evening exercise group.

Methods

Participants

After approval from the university's Institutional Review Board (IRB), 56 participants were recruited. All participants were healthy, premenopausal women aged 18-44 years who were weight stable (no more than ± 2.27 kg [5 lbs.] over the previous 6 months). Participants were excluded from the study if they were underweight (BMI < 18.5 kg/m^2), morbidly obese (BMI 40 kg/m^2 or greater), or had a chronic disease (cardiovascular disease, cancer, diabetes, etc.), recent abnormal diet or eating disorder (e.g., participation in a weight loss diet, food allergies, anorexia, bulimia, binge eating disorder, etc.), neurological disorder (traumatic brain injury, seizure disorder, stroke, etc.), ADHD, or alcohol or substance abuse within the past year. Additionally, participants were excluded if they used tobacco products, were pregnant or lactating, or participated in exercise training using the following parameters: > 3 days of moderate intensity physical activity for > 30 minutes per day or > 3 days per week of vigorous intensity physical activity for > 15 minutes per day. Eligibility was determined by participant self-report during a phone interview with a research assistant.

In addition, each participant was screened to ensure she was healthy enough for exercise using a Physical Activity Readiness Questionnaire (PAR-Q).[69] Participants were excluded if they answered positively to any questions on the PAR-Q. Further, participants were excluded if they were considered "high risk" for physical activity according to criteria from the American College of Sports Medicine.[70] Those who were at "moderate risk" were required to obtain permission from a physician before participating. However, this applied to only one participant.

Study Design

Each participant completed two pretraining laboratory sessions at which baseline data for eating behaviors, neural response to visual food cues, cardiovascular fitness, and body composition were obtained. Participants were then randomized to exercise in the morning (AM) group (6:30-9:30 a.m.) or the evening (PM) group (6:30-9:30 p.m.). Each participant completed an 8-week progressive exercise intervention according to her group assignment. Afterward, two posttraining laboratory sessions were completed to obtain postintervention data. Figure 1 outlines the study design.

Pretraining Laboratory Session 1

Participants refrained from consuming caffeine or participating in vigorous exercise for 24 hours before the first pretraining laboratory session. They began fasting at 9:00 p.m. the evening before the session and got at least 7 hours of sleep. Upon arrival to the lab between 6:30 a.m. and 8:45 a.m., participants completed a written informed consent, medical history, demographics questionnaire, and DEBQ. After sitting for 5 minutes, participants were measured for their resting heart rate (HR_{rest}), using a digital blood pressure cuff, and fitted with an EEG net. Immediately before beginning the EEG, participants filled out a visual analog scale (VAS) to assess hunger and fullness levels, and then the EEG was performed. EEG data were recorded from 128 scalp sites through the geodesic sensor net and Electrical Geodesics, Inc., (EGI; Eugene, OR) amplifier system (20K gain, nominal bandpass = 10-100Hz). Impedances were maintained below 50 KΩ per the recommendation of the manufacturer. Data were referenced to the vertex electrode during data collection.

Pretraining Laboratory Session 2

For the second laboratory session, participants once again refrained from consuming caffeine or participating in vigorous exercise for 24 hours prior, and they slept for 7 or more hours the night before. Participants fasted for 12 hours before arriving at the lab between 6:30 a.m. and 8:45 a.m.

Participants were weighed on a digital scale, and height was measured using a digital stadiometer. Body composition was assessed using dual-energy x-ray absorptiometry (DXA) (Lunar iDXA; General Electric Company; Chicago, IL). Lastly, participants completed a maximal treadmill test on a Trackmaster treadmill (Full Vision, Inc.; Newton, KS) following a graded exercise protocol developed by George et al.[71] Maximal oxygen consumption (VO_{2peak}) and maximal heart rate (HR_{max}) were measured using the Cosmed Quark CPET system (Rome, Italy) and Cosmed heart rate monitor, respectively. At the end of the second laboratory session each participant was told to which group she had been randomized (AM or PM).

Exercise Training

Participants then followed a progressive, moderate-to-vigorous intensity exercise program. The progression of the exercise training is shown in Figure 2. On week 1, participants exercised 3 times for 30 minutes; on week 2, they exercised 4 times for 30 minutes; on weeks 3-8, participants exercised 4 times for 45 minutes. Weeks 1-6 were at moderate intensity. Weeks 7-8 included 15 minutes of moderate intensity, then 15 minutes of vigorous intensity, then another 15 minutes of moderate intensity for each exercise session. Moderate intensity was defined as 40-59% of heart rate reserve (HRR) and vigorous intensity as 60-89% HRR.[72] Heart rate ranges were calculated using the Karvonen method[73] with the HR_{rest} and HR_{max} values that were obtained during pretraining laboratory visits 1 and 2.

Three of the four exercise sessions each week were supervised in the lab and the mode of exercise was treadmill walking or jogging. One of four exercise sessions each week was unsupervised and walking/jogging was the encouraged mode of exercise. The AM group was advised to complete all exercise sessions, supervised and unsupervised, between 6:30 a.m. and 9:30 a.m. and the PM group between 6:30 p.m. and 9:30 p.m. Participants were instructed to avoid planned exercise outside of the assigned time window.

At the beginning of all supervised exercise sessions, participants were fitted with a Polar heart rate monitor (Polar Electro; Kempele, Finland) to ensure they stayed in the appropriate heart rate zone (40-59% HRR for moderate intensity or 60-89% HRR for vigorous intensity), and they were supervised throughout by a trained research assistant. At the end of each session a research assistant recorded the participants' treadmill speed and average rating of perceived exertion (RPE) on a scale from 6-20 (20 being maximal exertion).

During unsupervised sessions, participants were asked to follow the exercise intensity and duration prescribed for each week. Participants monitored their intensity using the RPE scale. They were told that an RPE of 11-14 corresponds to moderate intensity, and an RPE of 14 or greater corresponds to vigorous intensity. Following each unsupervised session, participants recorded their exercise time, mode, and RPE on an exercise record, which was checked weekly by a research assistant.

Posttraining Laboratory Sessions

Following 8 weeks of exercise training, each participant completed posttraining laboratory sessions 1 and 2. The procedures for these sessions were identical to those used for the pretraining laboratory sessions. Participants refrained from exercise for at least 24 hours before each laboratory session.

Eating Behaviors

Three eating behaviors—dietary restraint, external eating, and emotional eating—were assessed subjectively using the DEBQ, which consists of 33 questions. The DEBQ is a frequently utilized measure of eating behaviors and is considered a valid measurement.[74,75]

Hunger and Fullness

To ensure that all participants began the EEG with the same appetite level, hunger and fullness were assessed using visual analog scales (VAS). A VAS is a question paired with a 10 cm line representing a continuum between two polar statements. For example, the VAS assessing hunger asked the question, "How hungry do you feel right now?" The 10 cm line below it said "not at all" on the left end and "extremely" on the right end. Participants were asked to mark a vertical line along the continuum representing how they felt at the time. The distance from the left end of the line to the participant's vertical mark was measured with a standard ruler to the nearest 0.5 mm. VAS is a valid and reliable approach for determining hunger and fullness.[48]

Neural Responses to Visual Food Cues

Neural responses to visual food cues were assessed using the N2 ERP. For ERP data collection, participants were seated approximately 17 inches in front of a 17-inch digital display and shown 100 pictures of food, each for 100 milliseconds (ms) in random order. The pictures were used in a previous study by Killgore et al.[76] High-calorie foods included candy, baked goods, ice cream, and high fat restaurant foods. Low-calorie foods included vegetables, fruits, fish, and whole grains (Figure 3).

During the EEG, two similar go/no-go conditions were completed in random order. During condition A, participants were shown 70 pictures of low-calorie food and 30 pictures of high-calorie food. They responded to the low-calorie food pictures by pressing a button on a

keyboard with their right index finger (go task). They were told not to press the button (withhold their response) when presented with a picture of a high-calorie food (no-go task). For condition B, participants were shown 70 pictures of high-calorie food and 30 pictures of low-calorie food. They pushed the button during the high-calorie pictures (go-task) and withheld during the low-calorie pictures (no-go task).

The epoch for the N2 was collected from 200 ms prior to picture presentation to 400 ms after picture presentation and was baseline adjusted using the 200 ms pre-presentation period. Off-line, data were average-referenced and digitally low-pass filtered at 30Hz. Eye blinks were removed using independent components analysis (ICA) in the ERP PCA Toolkit.[77,78] Channels were defined as bad if the fast average amplitude exceeded 100 microvolts (μV) or if the differential average amplitude exceeded 50μV. Bad channels were interpolated using a nearest-neighbor interpolation. If 20% or more of a participant's channels were bad, then the participant was excluded.

N2 amplitudes were extracted as the mean amplitude between 200 and 300 ms.[79] In order to improve signal reliability relative to using a single electrode,[80] we used a region-of-interest (ROI) approach wherein mean N2 amplitude was averaged across four frontocentral electrode sites (6, 7, 107, and Cz; see Larson, Farrer, & Clayson, 2011 for electrode montage)[81] chosen *a priori.*

Body Composition

Participants were weighed on a digital scale and height was measured using a digital stadiometer. Fat mass, fat-free mass, and body fat percentage were measured using the DXA. The DXA has been shown to be a valid measure of body composition.[82]

Cardiovascular Fitness Outcomes

Maximal oxygen consumption (VO_{2peak}) was determined via a graded exercise test on a Trackmaster treadmill and indirect calorimetry using the Cosmed Quark CPET system. Prior to beginning the test, a Cosmed heart rate monitor was strapped around the participant's chest and synced with the Quark CPET software to provide continuous heart rate data during the test.

The following graded exercise test protocol developed by George et al.[71] was utilized: 1) each participant walked at a self-selected speed and 5% incline for a 3-minute warm-up, 2) each participant increased her speed to a walk or jog that could be maintained for ~5-10 minutes, 3) after three minutes at this intensity, the incline was increased by 1.5% every minute thereafter until maximal exertion was reached.[71]

At each 1-minute interval during the test the participant indicated her RPE. Criteria for maximal effort was based on recommendations from the American Thoracic Society/American College of Chest Physicians (ATS/ACCP) which instruct that 1 or more of 5 specific criteria should be met.[83] In addition, based on recommendations from the ATS/ACCP for analyzing breath-by-breath oxygen consumption data, the last 30 seconds of each test was averaged together to determine VO_{2peak}.[83]

Statistics

The statistical software program SAS, version 9.4 (Cary, NC) was used to analyze the data. An alpha level of < 0.05 was set to determine statistical significance. To determine differences in inhibitory control (N2 magnitude) in response to pictures of high-calorie food or pictures of low-calorie food and exercise training, a trial type (go, no-go) × group (AM, PM) × period (baseline, 8 weeks) interaction was determined using repeated measures ANOVA (see Aim 1). Similarly, to determine the extent to which exercise training in the morning or evening

influences N2 responses to high-calorie foods differently than low-calorie foods (see Aim 2), repeated measures ANOVA was used. Where significant, main effects and interactions were reported. We also used ANOVA to determine interactions for eating behavior and for cardiovascular fitness outcomes using completer-only and intent-to-treat analyses. Pearson correlations were utilized to determine the relationship between neural outcomes, body composition, and eating behaviors (see Aim 3).

Results

Five hundred thirty-one adults initially expressed interest in the study; 475 were excluded; 64 were enrolled in the study; 56 initiated the study; and 53 completed baseline testing and were randomized to either the AM or PM group (see Figure 4). Of these, 46 participants completed the study requirements, 21 from the AM group (78% completion rate) and 25 from the PM group (86% completion rate). However, only 38 participants had usable EEG data (8 participants were excluded for either too few trials to calculate reliable ERPs or missing data due to data of insufficient quality in one or more sessions); thus, for the N2 outcomes, only n = 38 are reported. As shown in Table 1, there was not a significant difference between groups at baseline for age, weight, BMI or VO_{2peak} (*ps* > 0.05). However, body fat percentage was significantly higher at baseline in the AM group than the PM group (F = 4.09; $p = 0.049$) (Table 1).

Exercise Training

Participants who completed the study had a high level of compliance to the number of exercise sessions prescribed (94.8%). For completers, the average treadmill speed per exercise session was 3.80 ± 0.50 mph at baseline and progressed to 4.25 ± 0.52 mph at 8 weeks. Specifically, the AM group averaged 3.72 ± 0.34 mph at baseline and progressed to 4.16 ± 0.53

mph at 8 weeks and the PM group averaged 3.91 ± 0.66 mph at baseline and progressed to 4.33 ± 0.50 mph at 8 weeks. Overall, RPE was 11.67 ± 1.35 at baseline and progressed to 13.20 ± 1.48 at 8 weeks. Specifically, the AM group averaged an RPE of 11.71 ± 1.36 at baseline and progressed to 13.29 ± 1.43 at 8 weeks; whereas, the PM group averaged an RPE of 11.63 ± 1.08 at baseline and progressed to 13.11 ± 1.52 at 8 weeks.

Eating Behaviors

For the AM group, dietary restraint was 2.46 ± 0.67 at baseline and 2.52 ± 0.65 after 8 weeks ($F = 0.21$; $p = 0.646$), external eating was 3.38 ± 0.62 at baseline and 3.14 ± 0.60 after 8 weeks ($F = 1.96$; $p = 0.171$), and emotional eating was 2.64 ± 1.02 at baseline and 2.58 ± 0.93 after 8 weeks ($F = 0.03$; $p = 0.870$). For the PM group dietary restraint was 2.18 ± 0.71 at baseline and 2.17 ± 0.78 after 8 weeks ($F = 0.02$; $p = 0.896$), external eating was 3.16 ± 0.62 at baseline and 3.14 ± 0.56 after 8 weeks ($F = 0.14$; $p = 0.711$), and emotional eating was 2.62 ± 0.76 at baseline and 2.54 ± 0.73 at 8 weeks ($F = 0.36$; $p = 0.552$). There was not a group × period interaction for either completer-only or intent-to-treat analyses for any of these eating behavior variables ($ps > 0.05$).

Hunger and Fullness

As expected, among completers there was not a difference between the AM and PM groups in subjectively determined hunger ($F = 1.30$; $p = 0.260$) or fullness ($F = 0.03$; $p = 0.870$) as measured by VAS prior to baseline neural measurements. Similarly, at 8 weeks there was also no difference in subjectively determined hunger ($F = 1.73$; $p = 0.196$) or fullness ($F = 0.91$; $p = 0.346$) prior to neural measurements.

N2 Responses to Pictures of Food

To accomplish the first aim of this study, we performed the following analyses for the N2 ERP: 1) a task (go, no-go) × group (AM, PM) × period (baseline, 8 weeks) interaction with pictures combined, 2) the main effect of period (baseline, 8 weeks) with pictures combined, 3) the main effect of task (go, no-go) with pictures combined. First, there was not a task × group × period interaction ($F = 0.18$; $p = 0.677$) indicating that the difference in the go and no-go tasks was not a function of group or period with consideration of all pictures combined. Second, there was a main effect of the exercise intervention over the 8 weeks ($F = 6.26$; $p = 0.017$) indicating a stronger N2 response to all pictures at 8 weeks than at baseline. Third, there was a main effect of task ($F = 13.85$; $p < 0.001$) indicating a stronger N2 response to all pictures (more negative) for the no-go task compared to the go task.

To accomplish the second aim of this study, which differentiated responses by picture type, we performed the following analyses for the N2 ERP: 1) a picture type (high-calorie, low-calorie) × task (go, no-go) × group (AM, PM) × period (baseline, 8 weeks) interaction, 2) a task (go, no-go) × group (AM, PM) × period (baseline, 8 weeks) interaction for the high-calorie pictures and the low-calorie pictures separately, along with go or no-go specific interactions as a function of group and period (Table 2), and 3) several additional interactions and main effects by picture type (high-calorie, low-calorie).

First, there was not a significant interaction as a function of picture type, task, group, and period ($F = 0.52$; $p = 0.478$) indicating that differences in task, group, and period were not a function of picture type. Second, for the high-calorie pictures only, there was not a significant task × group × period interaction ($F = 0.60$; $p = 0.442$) (see Table 2). Similarly, for the low-calorie pictures there was also not a significant task × group × period interaction ($F = 0.07$; $p =$

0.798) (see Table 2). However, for the high-calorie no-go task, there was a main effect of period ($F = 4.39$; $p = 0.0430$) indicating higher N2 responses on the no-go task at 8 weeks compared to baseline. Similarly, for the high-calorie no-go task, there was a main effect of group with the PM group showing higher N2 amplitudes on the no-go task ($F = 5.53$; $p = 0.024$). For the go task there was also a main effect of period for high-calorie ($F = 7.79$; $p = 0.008$) and low-calorie pictures ($F = 4.83$; $p = 0.034$) indicating N2 responses to the go task were higher at 8 weeks for both high- and low-calorie food pictures. No other interactions of main effects were significant ($p > 0.05$). Third, there was a significant task × picture type interaction ($F = 5.16$; $p = 0.029$) indicating the magnitude of the N2 difference between the go and no-go trials was larger for high-calorie pictures relative to low-calorie pictures. Additionally, there was a significant picture type × group interaction ($F = 7.10$; $p = 0.011$) indicating a stronger N2 response for the high-calorie pictures in the PM group compared to the AM group.

To address the third aim of the study, we examined correlations between changes in N2 variables and body weight and eating behaviors (dietary restraint, external eating, and emotional eating). Associations between neural outcomes, body weight, and eating behavior changes over the course of the study are reported in Table 3. For both the AM and PM group, change in body weight and neural outcomes were not significantly associated with change in eating behavior (*ps* > 0.05).

Body Composition

As shown in Table 4, there was a significant group × period interaction for body weight among completers ($F = 4.90$; $p = 0.032$). In the AM group 76% of participants gained weight while in the PM group 64% of participants lost weight. Among completers, body weight increased by 0.79 ± 1.16 kg in the AM group and decreased by 0.21 ± 1.46 kg in the PM group

(effect size = 0.77; CI = 0.15-1.35). This interaction remained significant with an intent-to-treat analysis (F = 5.12; p = 0.029). There was not a significant group × period interaction for body fat percentage, total body fat, or fat-free mass (*ps* > 0.05) (see Table 4).

Cardiovascular Fitness Outcomes

For cardiovascular fitness outcomes, there was not a group × period interaction for VO_{2peak}, time to completion on the treadmill, HR_{max} during the treadmill test, or RPE (*ps* > 0.05). This was also true with an intent-to-treat analysis (*ps* > 0.05). When examining the main effect of time (exercise groups combined), VO_{2peak} was not changed (F = 1.80; *p* = 0.187), time-to-completion on treadmill increased (F = 6.51; *p* = 0.014), HR_{max} during the treadmill test was significantly lower (F = 5.49; *p* = 0.025), and RPE was not different (F = 0.88; *p* = 0.354). Intent-to-treat analyses did not influence these results.

Discussion

We are confident that the 8-week exercise intervention was completed as designed. Participants who completed the study demonstrated excellent compliance to the exercise protocol (94.8%). Also, three quarters of the exercise sessions were supervised by a research assistant in the exercise laboratory (see Figure 2) and were verified. In addition, results from the maximal treadmill test indicate that participants' cardiovascular fitness trended toward improvement for all participants. There was a significant increase in performance duration from baseline to 8 weeks. In other words, participants could exercise longer, and at a greater incline, at 8 weeks than they could at baseline. We recognize that VO_{2peak} did not increase from baseline to 8 weeks, but this was not surprising with an exercise intervention of predominantly moderate-intensity exercise and of rather brief duration.

The first aim of the study was to compare the effect of 8 weeks of morning exercise to 8 weeks of evening exercise on the neural response to visual food cues as measured by the N2 ERP waveform. We found that the difference in N2 magnitude between the go and no-go tasks was not a function of group or period. In other words, time of day of exercise over 8 weeks does not appear to influence inhibitory control. However, when groups were combined, exercise training, regardless of time of day, increased N2 amplitude.

This was the first study to examine the effect of time of day of exercise on neural responses to visual food cues. While it appears that time of day of exercise has no effect on the N2 neural response, the main effect of exercise training on the N2 neural response is interesting. To our knowledge, the only other study to look at the impact of progressive exercise training on neural responses to visual food cues was conducted by Cornier et al.[55] However, the Cornier et al. study was in children. After 24 weeks of progressive treadmill walking, participants' neural responses (measured by fMRI) were attenuated in regions of the brain related to food regulation,[55] a beneficial response for weight management.

Our findings suggest that a prolonged exercise program increases inhibitory control. Whether or not greater N2 amplitude is a beneficial outcome for eating behaviors and weight management is unclear. Watson et al. reported a negative correlation between N2 amplitude and external eating.[44] That is, female participants who had a higher N2 response to food cues tended to have lower self-reported external eating scores. The Watson et al. findings suggest that higher N2 magnitude would be a beneficial adaptation.[44] However, we did not find a significant correlation between N2 amplitude and eating behaviors (discussed below) to support Watson's findings. In addition, there was no nonexercise control group. Thus, it is possible that increased

N2 amplitude occurred due to a second exposure to the same tasks, although this is unlikely given the duration of time between the two tasks.

The second aim of the study was to determine if 8 weeks of exercise training influenced N2 responses to high-calorie foods differently than low-calorie foods. We hypothesized that 8 weeks of exercise would result in a significant increase in the inhibitory response to pictures of high-calorie foods but not low-calorie foods. Our hypothesis was not supported as exercise, regardless of time of day, was also not responsible for the difference in the go and no-go tasks for either high-calorie or low-calorie pictures. In addition, we hypothesized that the increased inhibitory response to pictures of high-calorie foods that we were expecting would be greater in the evening exercise group compared to the morning exercise group. However, our data indicated that inhibitory control was not influenced as a function of time of day of exercise over 8 weeks for high-calorie pictures or low-calorie pictures.

Other studies have looked at the neural responses to different picture types. Focusing on two specific ERPs (the P3 and late positive potential), Nijs et al. found that the brain responds differently to pictures of food than it does to nonfood pictures.[29] The magnitude of both ERPs was greater when participants viewed food pictures compared to control pictures. In addition, Killgore et al. used EEG to determine how the brain responds to high-calorie and low-calorie pictures of food. They found that areas of the brain were activated differently in response to high-calorie pictures of food and low-calorie pictures of food.[76] In Killgore's study, the amygdala, hippocampus, peripheral cortex and part of the ventromedial prefrontal cortex were activated in response to all food pictures regardless of calorie content. However, there was significantly more activation in the medial and dorsolateral prefrontal cortex, medial dorsal thalamus, hypothalamus, corpus callosum, and cerebellum when participants were shown

pictures of high-calorie foods than when they were shown pictures of low-calorie foods. Njis and Killgore's findings demonstrate how the brain responds differently to different picture types. Our results were similar in that the difference in N2 magnitude between the go and no-go trials was significantly larger for high-calorie pictures relative to low-calorie pictures. However, we did not find that exercise influenced the response to high-calorie pictures differently than low-calorie pictures.

The third aim of the study was to determine the effect of 8 weeks of morning vs. evening exercise training on dietary restraint, external eating, and emotional eating and to determine their association with body weight and the N2 neural response to pictures of high-calorie vs. low-calorie foods during the go/no-go task. We hypothesized that 8-weeks of evening exercise would improve the above eating behaviors to a greater extent than 8-weeks of morning exercise. However, there was not a significant difference in eating behaviors from baseline to 8 weeks for either group, and time of day of exercise made no difference in the participants' self-reported eating behaviors.

Additionally, we hypothesized that changes in eating behaviors would be significantly associated with the N2 neural response during viewing of high-calorie food pictures. Contrary to our hypothesis, the correlations between the change in eating behaviors and the change in the inhibitory response to pictures of high-calorie foods were weak to moderate and none were significant ($ps > 0.05$). Our findings were not consistent with a previous study by Watson et al., which found a correlation between the difference in N2 magnitude (between food and nonfood pictures) and external eating.[44]

Changes in eating behaviors were also not associated with changes in body weight, although there was an effect of time of day on body weight. Morning exercisers tended to gain

weight while evening exercisers tended to lose weight. While the eating behaviors and neural responses measured in the present study did not account for the changes in body weight, it is plausible that other dietary or neural factors could explain the relationship between body weight and time of day of exercise. For example, a study by Masterson et al. found that the hemodynamic responses (measured by fMRI) to pictures of food were lower in the evening than in the morning in several regions of the brain. Additionally, they found that participants' preoccupation with food (measured subjectively with VAS) was higher in the evening.[84] It is possible that Masterson's findings, assuming they persist with exercise training, could correlate with body weight before and after exercise training.

Other studies have looked at the role of exercise in weight management and have found that exercise increases energy expenditure and improves weight management.[18-21] Another group of studies has investigated the effect of exercise on energy intake[22,24,26,27,85,86] to see if exercise can also alter the other component of the energy balance equation, and therefore aid in weight management. The most comprehensive review of this topic to date is a paper by Donnelly et al.[52] They conducted a review on 99 studies to assess the impact that exercise has on daily energy intake. Of the 24 randomized trials they reviewed, 75% showed no change in energy intake with exercise, 21% showed a decrease in energy intake, and 4% showed an increase in daily energy intake. Given the results of the present study, it is possible that the studies in Donnelly's review are inconsistent because the influence of exercise on energy intake is dependent on the time of day during which the exercise is performed.

Some recent studies have looked at appetite and energy intake in relation to time of day of exercise. Heden et al. looked at the timing of exercise in relation to meals and found that both premeal and postmeal resistance training aided in appetite regulation in individuals with type 2

diabetes.[86] O'Donoghue et al. conducted a randomized crossover study to determine the effect of time of day of exercise on acute energy intake in healthy men. They found no difference between morning and afternoon exercisers.[87] Maraki et al. found that a 60-minute exercise session increased appetite, but not energy intake, in women regardless of the time of the exercise (morning or evening).[67] Although these acute studies found no difference in the effects of morning and evening exercise, they are few in number, and their findings may not apply to prolonged exercise training. More investigation is needed to determine if appetite, energy intake, or other eating behaviors can explain why morning exercisers gained weight while evening exercisers lost weight in the present study.

Limitations

This study had several strengths, including a randomized design, unique research questions, objective and valid measurements, and a supervised exercise intervention. However, there are notable weaknesses. First, the sample size for this study was modest. A larger sample size may have brought about more significant results. Second, the majority of the participants began at a healthy body weight (Table 1). Had the sample included individuals with a higher BMI, the results might have been different. Third, the exercise intervention was just 8 weeks long and the exercise was primarily moderate intensity. A longer or more vigorous intervention might have influenced the results. Fourth, there was no nonexercise control group. Including a control group in the design would have increased our confidence that it was the intervention that brought about the results and not some other factor. Fifth, although the participants were randomized, there was a significant difference between groups for body fat percentage at baseline, though we doubt this influenced the results. Lastly, we note that the results of this study should not be generalized beyond healthy women between the ages of 18 and 44 years.

Conclusion

The results of this study suggest that exercise training increases the inhibitory response to pictures of food. However, time of day of exercise does not seem to have an effect on inhibitory response. Likewise, changes in inhibitory control before and after exercise training do not appear to be different for high- and low-calorie food pictures. Based on our findings, exercise does not change self-reported dietary restraint, external eating, or emotional eating. There is no correlation between these eating behaviors and changes in inhibitory control before and after an 8-week progressive exercise program. Overall, our results do not support the common lay recommendation that morning is the best time to exercise for weight management. In fact, evening exercisers were more likely to complete the exercise program and tended to lose weight while morning exercisers tended to gain weight.

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Table 1. Baseline participant characteristics (n = 53)

	AM Group (n = 25)	PM Group (n = 28)	F	*p*
Age	25.32 ± 4.11	25.35 ± 6.74	0.00	0.985
Weight (kg)	68.27 ± 13.52	66.55 ± 9.26	0.30	0.589
BMI (kg/m^2)	25.25 ± 4.71	23.53 ± 3.85	2.12	0.151
Body fat (%)	37.88 ± 7.59	34.07 ± 6.11	4.09	0.049
VO_{2peak} (ml/kg/min)	36.24 ± 4.80	37.86 ± 5.46	1.27	0.265

AM group exercised between 6:30 and 9:30 a.m.; PM group exercised between 6:30 and 9:30 p.m.

Values represent mean ± standard deviation.

BMI = body mass index.

Participants who did not complete baseline assessments were excluded from the analysis.

Table 2. N2 amplitude for the high-calorie and low-calorie pictures by group and period

	AM Group (n = 18)		**PM Group** (n = 20)		F	*p*
	Baseline	8 Weeks	Baseline	8 Weeks		
High-Calorie Pictures						
N2 no-go amplitude (μV)	0.139 ± 2.288	-1.233 ± 2.289	-1.872 ± 2.325	-2.250 ± 2.424	1.52	0.226
N2 go amplitude (μV)	0.324 ± 1.717	-0.856 ± 1.848	-1.256 ± 2.472	-1.733 ± 2.182	1.48	0.231
N2 difference amplitude (μV)	-0.185 ± 1.044	-0.377 ± 0.691	-0.615 ± 0.788	-0.517 ± 0.983	0.60	0.442
Low-Calorie Pictures						
N2 no-go amplitude (μV)	-0.865 ± 2.251	-1.583 ± 1.569	-1.391 ± 2.023	-1.859 ± 2.160	0.12	0.730
N2 go amplitude (μV)	-0.667 ± 1.880	-1.515 ± 1.583	-1.380 ± 2.199	-1.927 ± 2.011	0.22	0.639
N2 difference amplitude (μV)	-0.199 ± 0.801	-0.069 ± 0.709	0.025 ± 0.669	0.069 ± 0.963	0.07	0.798

AM group exercised between 6:30 and 9:30 a.m.; PM group exercised between 6:30 and 9:30 p.m.

Values represent mean ± standard deviation.

μV = microvolts.

N2 difference amplitude = no-go amplitude minus go amplitude.

F and P represent group by period interactions.

Table 3. Pearson correlations for change in body weight and N2 amplitudes and change in eating behaviors

	Δ Body Weight	Δ High-Calorie No-Go N2 Amplitude	Δ High-Calorie Go N2 Amplitude	Δ Low-Calorie No-Go N2 Amplitude	Δ Low-Calorie Go N2 Amplitude
AM Group (n = 18)					
Δ Dietary Restraint	-0.235	0.258	0.272	0.039	-0.048
Δ External Eating	-0.268	-0.289	-0.345	-0.169	-0.089
Δ Emotional Eating	-0.352	-0.402	-0.349	-0.104	0.001
PM Group (n = 20)					
Δ Dietary Restraint	0.200	0.323	0.195	0.411	0.225
Δ External Eating	0.182	0.145	0.068	0.302	0.306
Δ Emotional Eating	0.383	-0.022	-0.073	0.077	0.333

AM group exercised between 6:30 and 9:30 a.m.; PM group exercised between 6:30 and 9:30 p.m.

Δ = change in; i.e., the change from baseline to 8 weeks of the exercise program.

*None of the Pearson correlations were statistically significant.

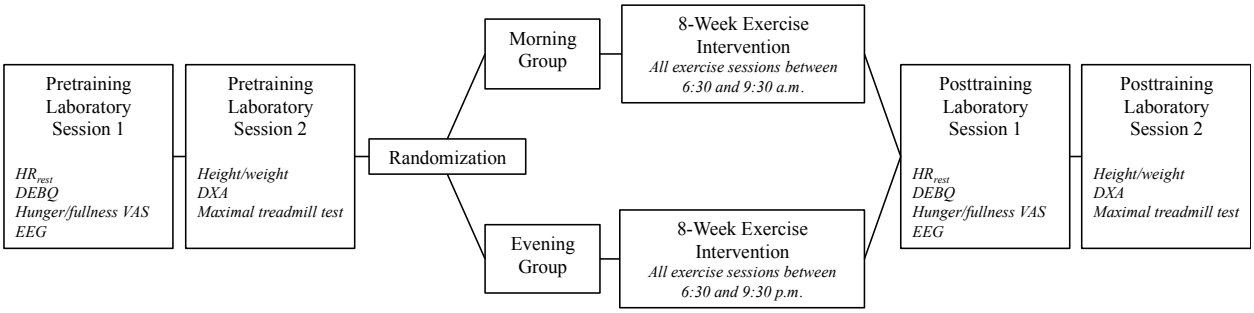
Table 4. Body composition at baseline and 8 weeks by group for finishers

	AM Group (n = 21)		**PM Group** (n = 25)			
	Baseline	8 Weeks	Baseline	8 weeks	F	P
Body weight (kg)	70.16 ± 13.575	70.96 ± 14.406	65.92 ± 9.071	65.71 ± 9.175	4.90	0.03
Body fat (%)	39.14 ± 7.243	39.03 ± 7.277	33.21 ± 5.491	33.03 ± 5.668	0.04	0.8354
Total body fat (g)	27102 ± 9949	27156 ± 10565	21245 ± 5821	21144 ± 5917	1.46	0.234
Fat free mass (g)	40468 ± 5100	40879 ± 5753	41912 ± 5079	41993 ± 4871	0.86	0.359

AM group exercised between 6:30 and 9:30 a.m.; PM group exercised between 6:30 and 9:30 p.m.

Values represent mean ± standard deviation.

F and p values represent the group by period interaction.



HR_{rest} = resting heart rate
DEBQ = Dutch Eating Behavior Questionnaire
VAS = visual analog scale
EEG = electroencephalogram
DXA = dual-energy x-ray absorptiometry

Figure 1. Study design

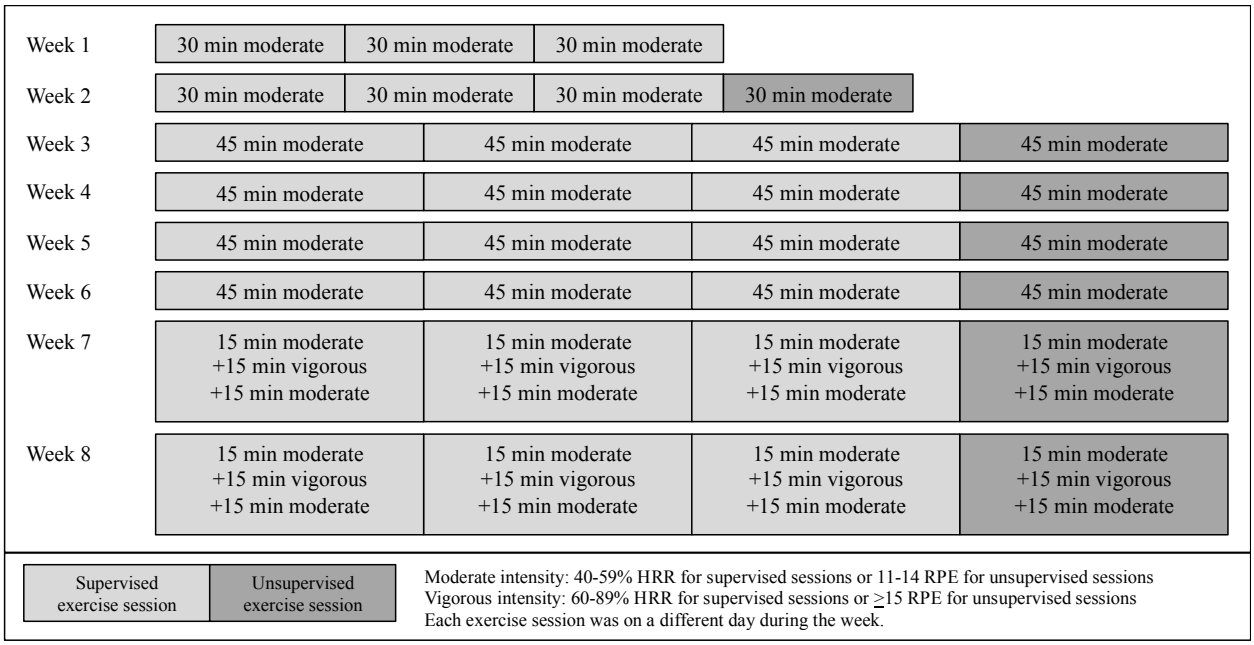


Figure 2. Progressive exercise program

3.1 High-calorie food pictures

3.2 Low-calorie food pictures

Figures 3.1-3.2. Examples of pictures of high-calorie and low-calorie foods

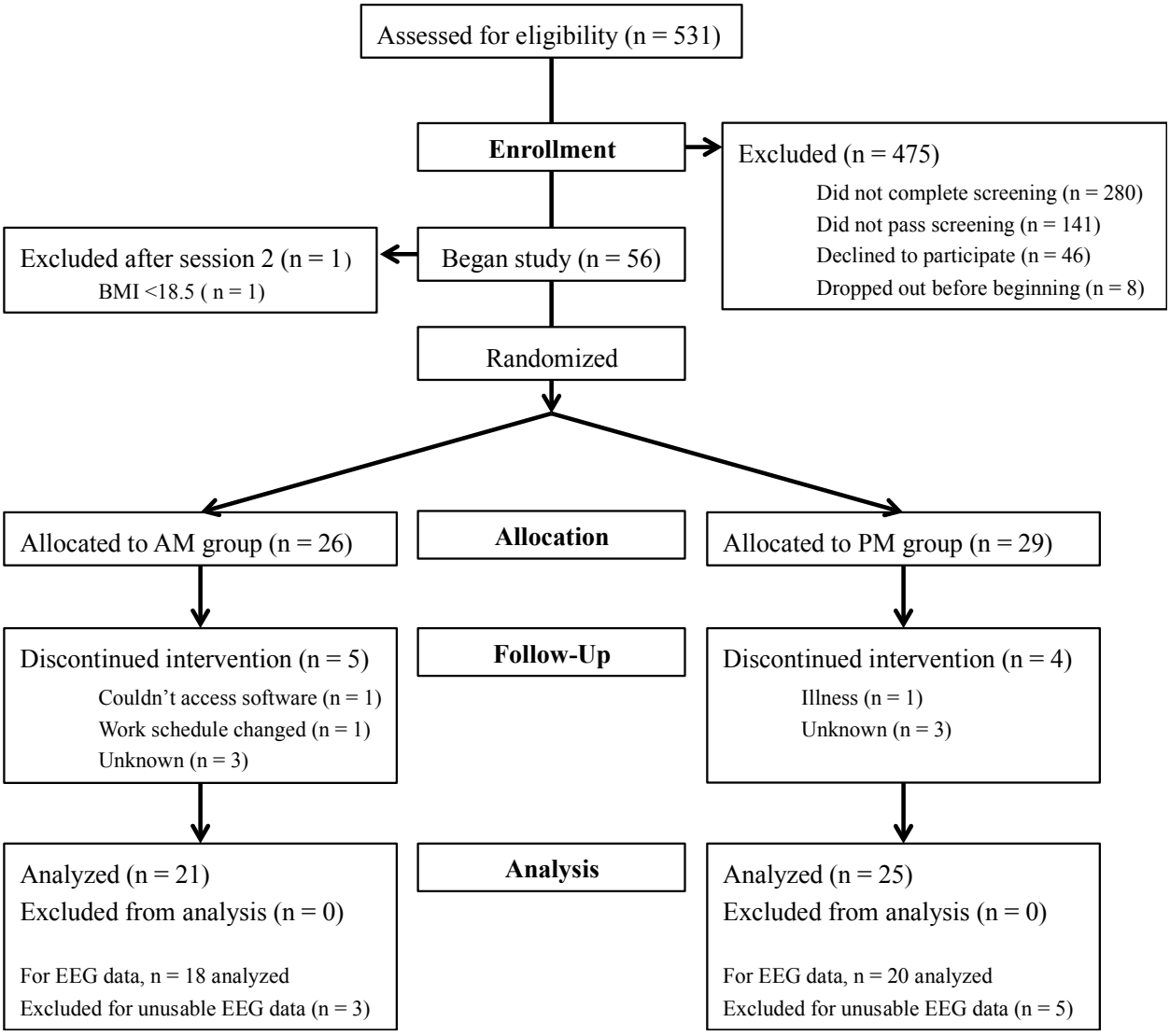


Figure 4. Eligibility flowchart.