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Exercise and diet effects on delay discounting and related neurobiology in adults with overweight/obesity: A randomized trial

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Abstract

Objective: This study compared effects of exercise training and diet on impulsivity-related behaviors as measured by delay discounting and related neurobiology in adults with overweight/obesity. We hypothesized exercise versus diet would be associated with reduced delay discounting propensity (k) and increased response in brain regions involved in cognitive control (medial prefrontal cortex, anterior cingulate cortex [ACC], and bilateral anterior insulae).

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Methods: Participants ($N=40$) were randomized to 12 weeks of exercise training or diet intervention. At baseline and post-intervention, they completed a delay discounting task during functional magnetic resonance imaging in fasted and fed (post-meal) conditions. Linear mixed effects models assessed fasted-fed intervention effects on k and brain response in regions of interest. Exploratory analyses assessed whole-brain, satiety-state-specific, and reaction time (RT) effects.

Results: Across groups, k and RT during delay discounting and weight decreased post-intervention ($ps \leq 0.010$). In exploratory fed-state whole-brain analyses, a group*session effect was observed in right dorsolateral prefrontal cortex ($p < 0.005$), driven by exercise-associated changes. A similar group*session interaction effect was observed in ACC ($p = 0.006$), also driven by reductions in fed-state responses.

Conclusions: Both interventions altered delay discounting behaviors. Exercise training was associated with reduced fed-state engagement of brain regions involved in self-referential processing and regulation during decision-making.

Keywords

Delay discounting; fMRI; overweight/obesity; exercise training; diet intervention

Introduction

Obesity is associated with a variety of negative health outcomes, including diabetes and cardiovascular disease (1). As such, identifying effective weight-loss/maintenance interventions is greatly needed. Examining cognitive and neurobiological mechanisms contributing to overweight and obesity can inform targeted intervention development (2). It has been posited that challenges with impulsive decision-making and, more broadly, cognitive control (i.e., higher-order cognitive processes supporting goal-directed behavior) may impede ability to adhere to weight-loss interventions (3). Additionally, overweight/obesity is associated with alterations in neural networks supporting cognitive control (4). However, further study is needed to determine whether weight-loss/maintenance approaches, such as exercise and diet, alter cognitive control processes and associated neuronal function in overweight/obesity.

Delay discounting (DD) may provide a useful framework for assessing cognitive effects of weight-loss interventions. DD is associated with impulsivity and refers to the tendency to prefer smaller, immediate rewards over larger, delayed rewards (5). Higher DD rates are linked to more impulsive reward-based decisions, which can impact everyday decision-making and lead to prioritizing short-term gains over long-term benefits (e.g., consuming convenient high-calorie foods despite weight-loss goals) (6). DD applies to a variety of rewards (e.g., monetary, food, substances) and can be measured in real or hypothetical contexts. Previous work suggests DD propensity, or k , is generally consistent across different DD task contexts and reward types (7, 8). Although some studies suggest k is a stable trait (8), others suggest it can be altered by environmental and physical characteristics (e.g., obesity) as well as behavioral interventions (9).

In those with overweight/obesity, relative to those without, greater DD has been consistently observed (10, 11). Greater DD is also associated with higher percent body fat (12) and body mass index (BMI) (13). Neurobiologically, recent meta-analyses indicate that DD tasks consistently engage frontoparietal and salience regions of the brain (e.g., middle frontal gyrus, anterior cingulate cortex [ACC], and bilateral insula) (14, 15), which support cognitive control (16), emotion processing, and identification and valuation of rewarding stimuli (17). These processes may be disrupted, however, in overweight/obesity. In women with obesity, lower response in left anterior insula (18) and frontoparietal regions, such as middle and frontal gyri (19), during DD tasks is associated with higher k (i.e., greater impulsivity) and predictive of future weight gain (20). These studies suggest that less frontoparietal and salience engagement during DD decision-making may lead to more impulsive choices that can impact long-term health outcomes.

Some studies have begun investigating how DD relates to behavioral weight-loss/maintenance interventions such as diet and exercise. Weygandt et al. (21) found that a lower discounting rate (k) during a DD task was associated with greater subsequent weight loss following a 12-week dietary intervention in adults with obesity. The study also found greater right superior frontal gyrus response during the task predicted better weight maintenance one-year post-intervention (22). However, how exercise affects DD behavior and related neurobiology is not well understood. In rodent models, animals engaging in wheel running (vs. sedentary controls) are less sensitive to both reward amounts and delay periods during DD tasks (23). One preliminary study of exercise training effects on DD in humans found a seven-week running program was associated with reduced k in 12 women with varying BMIs (24). To our knowledge, however, no previous studies have examined how exercise training affects DD-related functional neurobiology. Further, no study has compared exercise to caloric restriction.

To address this, the present study compared effects of 12 weeks of exercise training to a 12-week dietary intervention on impulsive decision-making as measured by a DD task and related neurobiology in adults with overweight/obesity. Though preliminary studies indicate both interventions may be associated with improved DD behavior (21, 24), previous work suggests beneficial effects of exercise on broader executive function abilities (25, 26), likely conferred by modifying underlying neurobiological processes. For instance, exercise training has been linked to altered frontoparietal response during cognitive tasks, which was associated with enhanced performance (27). Effects on cognitive function, particularly impulsivity, could be a mechanism supporting the positive effects of exercise on weight-loss maintenance. We therefore hypothesized that exercise training, compared to a diet control, would be associated with reduced DD propensity (i.e., lower impulsivity as indexed by k). We also hypothesized greater neuronal response during DD following exercise, compared to diet, in regions involved in cognitive control and reward valuation that have previously been implicated in DD (medial prefrontal cortex [mPFC], ACC, and anterior insula [AI]) (14, 15). Satiety state may also impact DD behavior, but this is not well understood. Some studies measure DD in a fasted state (21), while others do not assess or control for satiety (24). Previous studies by our group and others have observed altered neuronal response to a meal (i.e., change from fasted to fed states) in individuals with overweight/obesity, compared to those without, when viewing food cues, with dampened response attenuation

from fasted to fed states in prefrontal cortex, ACC, and insula (29–31). In the present study, we examined DD behavior and associated functional neurobiology in both fasted and fed states, hypothesizing exercise-associated improvements in response to a meal (fasted-fed).

Methods

Participants

Participants were recruited via word-of-mouth, flyers, email blasts, and University-based recruitment websites in Aurora, CO between December 2014 and March 2019. Eligibility criteria included being 21–55 years old and sedentary (<2 hours planned weekly physical activity), with BMI 27–40 kg/m² and weight stability within 5% in the previous six months. Full inclusion criteria and information regarding sample size determination are provided in Supporting Information 1.0. Of the 67 participants enrolled, 12 withdrew before completing baseline measures/randomization, 11 withdrew during the intervention period, and four were excluded from analyses due to technical issues or excessive motion during scanning (median framewise displacement >0.5mm across runs). As such, 40 participants were included in analyses (exercise group $n=21$; diet group $n=19$; demographic information in Table 1; flow diagram in Figure S1).

Study design

Study activities were completed at the University of Colorado Anschutz Medical Campus in Aurora, CO. Participants provided written informed consent. Procedures were conducted in accordance with the Declaration of Helsinki and approved by the Colorado Multiple Institutional Review Board (COMIRB; Protocol #13–3252). This study was registered with [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02047721) (NCT02047721). The primary study outcome was neuronal response during a visual food cues task (data to be published separately), with blood oxygen level-dependent (BOLD) response during a DD task as a secondary outcome.

Immediately prior to the baseline fMRI study day, participants completed a three-day, macronutrient-controlled, eucaloric run-in diet (50% carbohydrate, 30% fat, 20% protein). After baseline assessments, participants completed either a 12-week exercise program or 12-week diet intervention, after which another three-day eucaloric diet period preceded a post-intervention study day to repeat assessments completed at baseline (see Figure 1 for study design overview). Random assignment to exercise or diet used simple randomization, stratified by sex. This was determined by a random number sequence generated by KTL, who did not interact with participants. Additional procedural details are in Supporting Information 2.0.

fMRI study day

On the two fMRI study days, participants arrived in the morning after an overnight fast of ≥ 10 hours. Participants completed an anatomical scan, followed by fMRI during rest, a visual food cues task (data to be published separately), and a DD task (details below). After the fasting fMRI session, a standardized breakfast meal was consumed over ≤ 20 min (30% estimated total daily energy intake requirements; macronutrient composition matching run-in diet). Approximately 40 minutes post-breakfast, participants repeated the resting-state

scan, visual food cues task, and DD task during fMRI (i.e., in the fed state). Eating behavior measures were also collected but outside the scope of the current study.

Interventions

Exercise and diet intervention details are in Supporting Information 3.0. Briefly, those assigned to exercise were prescribed aerobic exercise sessions at least 4 times/week for 12 weeks. Individualized exercise prescriptions were developed using age-predicted maximum heart rate ($220 - \text{age}$; HR_{max}). Sessions were preceded by a 2–5-minute warm-up at heart rate corresponding to 50–60% HR_{max}. Sessions started as 15 minutes at 60–65% HR_{max} at baseline and gradually increased to 45-minute sessions at 75–80% HR_{max} by weeks 11 and 12. Those assigned to the diet intervention attended 12 weeks of once-weekly instructional meetings with a registered dietitian or trained research staff member. During these meetings, participants were instructed on a variety of dietary practices to support the goal of reducing energy intake by ~2,000 kcal/week but asked to maintain typical physical activity behaviors during the intervention period.

MRI data acquisition

Imaging was performed using a Siemens Skyra 3.0 T MR system with a 20-channel head coil. A T1-weighted magnetization-prepared rapid acquisition gradient-echo (MPRAGE) anatomical image was acquired for each participant, then functional images were acquired with an echo planar T2* BOLD sequence (details in Supporting Information 4.1). Visual stimuli were presented using E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA) and an MR-compatible goggle system (Resonance Technology, Inc., Northridge, CA).

Delay discounting fMRI task

The DD task procedures have been described previously (32). Additional details are included in Supporting Information 4.2, but briefly, we used a monetary DD task to examine intertemporal choice behavior. All choices were hypothetical and customized based on each participant's estimated discounting parameter (k) or "decision point" (33), determined during a brief practice session prior to scanning. This initial estimate of k was used to customize choice options during the task. During fMRI, participants were visually presented with two monetary reward options: a smaller reward sooner or a larger reward later. They were asked to select one of these options via button press. To avoid repeating the same options across many trials, three levels of potential reward (small, medium, and large), three levels of time for the sooner choice (today, 2 weeks, 1 month), and two levels of time separating sooner and delayed choices (2 weeks, 1 month) were used. "Difficult" trials presented immediate rewards within 5% of the predicted reversal point, which made decisions more challenging, while "Easy" trials presented more straightforward choices. As such, there are four task conditions based on choice difficulty (Easy or Difficult) and participant choice (Sooner or Later): Easy Sooner, Difficult Sooner, Easy Later, and Difficult Later. Analyses focused on the contrast between Difficult and Easy trials (i.e., averaged across participant Sooner/Later choice).

MRI data preprocessing

MRI preprocessing was performed with the fMRIPrep 22.0.2 pipeline (34) (additional details in Supporting Information 4.3). Visual inspection of normalized structural and functional data for template overlap was performed for each subject. Additional preprocessing and first-level analyses of BOLD data were conducted with SPM12 (<http://www.fil.ion.ucl.ac.uk/spm>) in MATLAB 2019b (MathWorks, Natick, MA; Supporting Information 4.3).

Statistical analyses

Hypotheses and analytic plans were pre-registered prior to analyses on Open Science Framework (35). Chi-square and t-tests were used to evaluate group differences in categorical and continuous measures of participant characteristics, respectively (Table 1). Linear mixed effects models (LMEs) conducted in R statistical software (36) were used to examine intervention-related changes in DD behavior and associated neuronal response (details below). Degrees of freedom were estimated using Satterthwaite approximation. Tukey's HSD post-hoc tests were conducted to further characterize effects (post-hoc test p -values include correction for multiple comparisons [p_{corr}]). Primary outcomes focused on response to a meal (change from fasted to fed states; fasted-fed), with exploratory tests of state-specific effects (fasted and fed states separately). When outcomes had significant outliers (determined using Grubbs' test (37), $\alpha=0.05$), analyses were run with and without outliers (results reported in Supporting Information 5.0).

To test effects on the behavioral measure of DD (k), an LME was run with k as the outcome (response to a meal; fasted-fed), group (exercise vs. diet) and session (baseline vs. post-intervention) as fixed effects, and subject as a random effect, with $\alpha=0.05$. We calculated k using a logistic regression approach, as in Wileyto et al. (33). Higher k values indicated a greater discounting rate. Natural log transformation of k was conducted prior to analysis, as distribution is known not to be normal (33) and was positively skewed in our sample (skewness=2.15). One participant had negative k values at post-intervention, so their data at this timepoint could not be transformed and was not included in analyses of $\ln(k)$. An LME exploring intervention effects on average reaction time (RT) during DD trials was also conducted. Descriptive statistics for $\ln(k)$ and RT are in Table 2.

For fMRI analyses, analogous LMEs were run with response in each region of interest (ROIs; mPFC, ACC, and left and right AI) as outcomes. Average percent signal change (PSC) for each ROI was extracted from each participant's first-level analysis contrasting Difficult>Easy trials (in fasted>fed states) using Marsbar (<https://marsbar-toolbox.github.io>). ROI masks were derived from the Brainnetome atlas (38) (additional information in Supporting Information 6.0 and Figure S2). Average PSC for each ROI was used as the dependent variable in second-level LMEs, with group (exercise vs. diet) and session (baseline vs. post-intervention) as fixed effects and subject as a random effect, with $\alpha=0.0125$ (Bonferroni correction for four ROIs). Median framewise displacement was included as a covariate to control for possible motion effects.

We also explored task-related response (Difficult>Easy trials) across the whole brain using the 3dLME function within AFNI (39) to investigate potential effects outside hypothesized ROIs. Fixed effects included group and session. Subject was a random effect, with median framewise displacement included as a covariate. Additional details regarding cluster correction for whole-brain analyses are in Supporting Information 7.0. Briefly, at a voxelwise threshold of $p<0.005$ and cluster-size corrected $\alpha=0.05$, cluster threshold was 45 voxels. We also explored brain-behavior relationships by repeating fMRI analyses, including behavioral measures (k and RT) as covariates.

Results

Weight was significantly reduced following both exercise (-1.73 ± 2.91 kg, $p<0.001$) and diet (-3.19 ± 3.00 kg, $p<0.001$), with a group*session interaction ($\beta=-3.22$, $t_{118}=-2.75$, $p=0.007$) suggesting greater loss post-diet. Percent body fat was also significantly reduced in both groups (exercise: $-0.92 \pm 1.63\%$, $p<0.001$; diet: -1.02 ± 1.56 , $p<0.001$; group*session interaction not observed, $\beta=-1.03$, $t_{116}=0.35$, $p=0.726$).

Intervention effects on DD behavior

A significant session effect on $\ln(k)$ was observed ($p=0.010$; Table 3; Figure 2A), with decreased DD propensity from baseline to post-intervention across both groups. This effect remained in a model including weight change as a covariate ($p=0.010$), suggesting the observed decrease in $\ln(k)$ was not due to weight loss. No significant group or group*session effects on $\ln(k)$ were observed in the primary analysis ($p>0.081$). After removing an outlier, the session effect remained ($\beta=-0.25$, $t_{111}=-2.75$, $p=0.007$), and the group*session interaction was significant ($\beta=0.34$, $t_{113}=2.67$, $p=0.009$; see Supporting Information 5.1). In this analysis, effects appeared driven by reductions following diet ($t_{114}=-2.75$, $p_{\text{corr}}=0.035$) rather than exercise ($t_{118}=-1.02$, $p_{\text{corr}}=0.741$). No significant results were observed in exploratory models examining intervention effects on $\ln(k)$ in fasted and fed states separately ($p>0.080$; Tables S1 and S2). Thus, observed $\ln(k)$ effects were specific to measurement in the context of meal responsivity.

Exploratory analyses found significant RT reductions from baseline to post-intervention across both groups ($p<0.001$), with no significant group or group*session effects ($p>0.128$; Table 3; Figure 2B). The session effect remained when weight change was included as a covariate ($p<0.001$), again suggesting the effect was not due to weight loss. Satiety-state-specific analyses identified significantly reduced RT across groups in the fasted ($\beta=-106.32$, $t_{38}=-2.08$, $p=0.044$) but not fed state ($\beta=9.67$, $t_{38}=0.20$, $p=0.843$), suggesting effects observed in the context of meal responsivity were driven by fasted-state effects. There were no significant group or group*session effects observed in models assessing fasted and fed states separately ($p>0.153$; Tables S3 and S4).

Intervention effects on neuronal response during DD

A significant group*session interaction was observed in ACC ($p=0.006$; Table 3; Figure 3A). Post-hoc tests were null, suggesting no significant changes in ACC response within exercise or diet groups ($p_{\text{corr}}>0.080$). Exploratory satiety-state-specific analyses identified a fed-state

group*session interaction ($\beta=-0.31$, $t[38]=-2.12$, $p=0.041$; Figure 4B; Table S6), although this did not survive multiple comparisons correction. Post-hoc tests examining within-group (exercise and diet) changes in the fed state were also non-significant ($p_{\text{corr}} > 0.188$). No significant effects were observed in the fasted state ($p > 0.779$; Figure 4A; Table S5), suggesting fed-state effects drove the interaction observed in the primary analysis.

Similarly, a group*session interaction was observed in mPFC, although this did not survive multiple comparisons correction ($p=0.013$; Table 3; Figure 3B). As with ACC, post-hoc tests were non-significant ($p_{\text{corr}} > 0.063$). There were also no significant findings from mPFC satiety-state-specific analyses ($p > 0.055$; Tables S7 and S8).

No significant effects were observed for left or right AI ($p > 0.050$), though directionality was similar to ACC and mPFC findings (Table 3; Figures 3C and 3D). There were also no significant effects observed in satiety-state-specific analyses for left or right AI ($p > 0.057$; Tables S9–S12).

No significant clusters were observed in the exploratory whole-brain analysis (fasted-fed). In satiety-state-specific whole-brain analyses, however, a significant fed-state group*session interaction was observed in right dorsolateral prefrontal cortex (dlPFC; peak $F=18.06$; voxelwise $p < 0.005$; peak MNI coordinates for dlPFC cluster: $x=30$, $y=57$, $z=21$; Figure 5). To further characterize this effect, average PSC was extracted from this cluster, with post-hoc tests run to examine within-group effects. This revealed that the interaction was driven by reduced fed-state dlPFC response following exercise ($t[38]=-5.24$, $p_{\text{corr}} < 0.001$) but not diet ($t[38]=0.87$, $p_{\text{corr}}=0.818$), an effect not observed in the fasted state (voxelwise $p > 0.005$).

In investigations of relationships between behavioral and imaging outcomes, $\ln(k)$ was not associated with brain response in ROI or whole-brain analyses ($p > 0.152$). Significant relationships were observed, however, between RT and right AI response both in ROI ($\beta=0.0003$, $t[73]=2.62$, $p=0.011$) and whole-brain analyses (peak $F=13.23$; voxelwise $p < 0.005$; peak MNI coordinates for right AI cluster: $x=42$, $y=27$, $z=-9$).

Discussion

This study aimed to compare effects of 12 weeks of exercise and a diet control intervention on delay discounting behavior and related neuronal response in adults with overweight/obesity. This is the first study to our knowledge to examine the impact of exercise on brain response during DD decision-making and the first to compare effects of different weight-loss/maintenance interventions on DD. Weight and percent body fat were reduced after both exercise and diet, although with greater weight reduction post-diet. Both interventions altered DD behaviors, with reduced k (i.e., less impulsivity) and RT during DD decisions observed across both groups, with some indication that effects may be more pronounced following diet. These findings suggest weight-loss/maintenance interventions, particularly diet, may impact impulsive decision-making, which could have important implications for health-related behaviors (e.g., making healthy food choices in the moment to support longer-term weight-loss goals). Consistent with our hypotheses, exercise training may elicit

unique effects on DD-related neurobiology. Exercise was associated with patterns of altered response to a meal during DD in right dlPFC, which appeared to be driven by decreased fed-state response. A similar fed-state-specific effect was also observed in ACC. Together, these findings provide novel insights into the impact of behavioral weight-loss interventions on DD processes and potential mechanisms by which they may influence health behaviors and outcomes in individuals with overweight/obesity. Though additional work is needed to further explore these associations, our findings suggest there may be distinct neural processes underlying exercise and diet intervention effects on DD behaviors.

That decreased k was observed across both groups was somewhat surprising. We expected more substantial declines in k following exercise given previously demonstrated effects of physical activity on k (24) and cognitive performance more broadly (25, 26). Yet, our findings suggest diet conferred similar, and potentially even greater, benefits on DD propensity compared to exercise. Although no previous studies to our knowledge have examined diet-related changes in k , prior work found lower baseline k was associated with subsequent diet-related weight loss (21, 22). The present findings also support that k is modifiable (9) and that relatively brief behavioral interventions can reduce DD propensity in adults with overweight/obesity. Overall, findings underscore the potential effectiveness of both exercise training and dietary interventions in modifying DD processes, which has broader implications for understanding behavioral effects of such interventions on impulsivity and decision-making. As we did not observe k associations with neuronal response during DD, it is possible that behavioral changes occurred independent of alterations in neurobiology as measured in the study. It is also possible that such changes are related but occur on different time scales requiring a longer study to investigate.

We also observed reduced RT during DD (i.e., faster decision-making) across both groups, which appears driven by changes in the fasted rather than fed state. Longer RTs during DD decisions often indicate being at an indifference point, suggesting increased cognitive effort in choosing between sooner and delayed rewards (40). Although speculative, this finding could suggest improved decision-making efficiency post-intervention. Across groups and sessions, RT was positively associated with response in right AI. This is consistent with prior studies demonstrating positive associations between RT and brain response in task-positive regions (e.g., AI) during cognitive tasks, thought to reflect learning as task familiarity increases (41).

We found exercise training, compared to diet, was associated with increased response (i.e., a greater reduction) following a meal in right dlPFC during the DD task. Similar patterns were also observed in ACC and mPFC, although the mPFC finding did not pass multiple comparisons correction. Additionally, ACC and mPFC effects should be interpreted with caution, as within-group effects did not reach significance. The observed changes in dlPFC response appeared to be driven by effects in the fed state, with patterns of decreased fed-state response following exercise but increased response following diet. The divergent effects between fasted and fed states support the importance of considering satiety state when investigating DD. The decreased fed-state response following exercise was somewhat unexpected, as we anticipated exercise training would be associated with *increased* response in ROIs during DD. Previous cross-sectional studies in women with obesity found reduced

response in frontoparietal and salience regions during DD was associated with increased impulsivity (18, 19), although satiety state was not reported. The current findings may suggest that the observed impulsivity decrease following exercise reduced the need to engage brain regions associated with self-regulation and processing during decision-making in a fed state. As such, reduced fed-state dlPFC response during DD could reflect decreased need for attentional and cognitive control strategies during reward-based decisions post-meal, which could be particularly meaningful in eating without hunger (3). Of note, behavioral effects on RT were more prominent in the fasted state, further demonstrating need to consider satiety state in future studies of DD.

Study strengths include the randomized controlled design, assessment in both fasted and fed states (including meal standardization prior to scanning), and integration of behavioral and neuroimaging measures. Limitations include the relatively small sample size, predominantly comprised of White, non-Hispanic females, which could impact generalizability. This also prohibited us from examining effects of sex. Future studies are warranted to investigate sex effects and to replicate findings in larger, more heterogeneous samples. Though prior studies suggest DD tasks are sensitive to within-subject changes and minimally impacted by practice effects (42, 43), the potential for order/practice effects is a limitation, so future studies should randomize fasted and fed scan order. Longer-term studies will also be necessary to assess sustainability of effects over time. Finally, the study focused on DD as a measure of impulsivity. Including self-report impulsivity questionnaires and a broader range of decision-making and cognitive control tasks in future studies could provide a more comprehensive understanding of neuronal and cognitive changes associated with weight-loss/maintenance interventions. Future studies should also explore associations between intervention-related effects on impulsivity and eating behaviors.

Conclusion

The current study suggests both exercise and diet interventions may improve DD behaviors in adults with overweight/obesity. Unique effects of exercise training on DD-related neurobiology may relate to decreased fed-state engagement of brain regions involved in cognitive control and self-referential processing, which was not observed following the diet intervention. These findings suggest distinct neural mechanisms underlying exercise and diet effects on DD. Findings also suggest the importance of considering satiety when investigating DD, as results may be satiety-state specific. Further research is warranted to investigate long-term intervention effects on decision-making behavior and their implications for health outcomes in individuals with overweight/obesity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Study Importance Questions

What is already known about this subject?

- Greater delay discounting (i.e., more impulsive, reward-based decision-making) has previously been associated with overweight/obesity.
- Delay discounting propensity may be associated with weight-loss/maintenance intervention outcomes, but no randomized controlled trials have explored the effects of exercise training on delay discounting behaviors and underlying functional neurobiology.

What are the new findings in your manuscript?

- Twelve weeks of either exercise training or diet intervention affected behavioral measures of impulsive decision-making in adults with overweight/obesity.
- Exercise training may uniquely affect the neurocircuitry supporting delay discounting, leading to decreased post-meal engagement of brain regions involved in cognitive control and self-referential processing during decision-making.

How might your results change the direction of research or the focus of clinical practice?

- Study findings suggest further research is warranted to investigate changes in cognitive processes, such as delay discounting and associated brain response, as potential mechanisms of weight-loss/maintenance interventions.
- Intervention effects were somewhat dependent on satiety state (fasted or fed), suggesting the importance of considering feeding state when assessing delay discounting propensity.

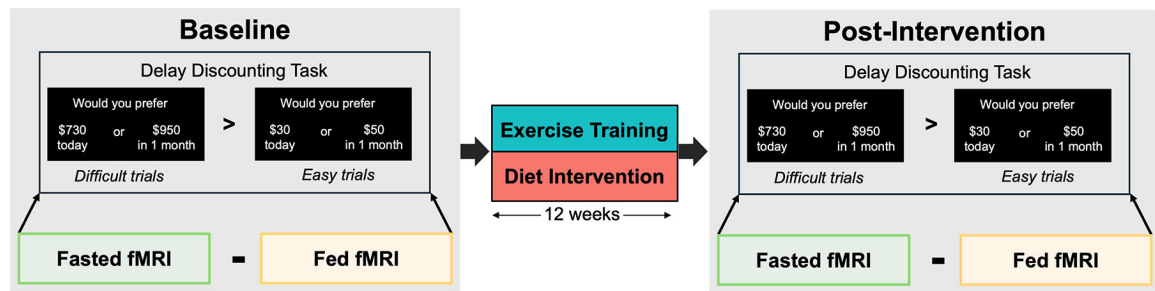


Figure 1. Overview of the study design.

Participants completed a monetary delay discounting task during fMRI, both after an overnight fast (fasted) and after a standardized meal (fed) at baseline and post-intervention (12 weeks of either exercise training or diet intervention). The figure depicts examples of “Difficult” and “Easy” trials in the delay discounting task, illustrating the types of choices participants were given during the experiment. Intervention effects on delay discounting behavior (delay discounting propensity [k] and reaction time) were assessed, as were effects on associated responses in brain regions of interest, which were measured as the difference between Difficult and Easy trials. Primary analyses focused on changes in these metrics in response to a meal (fasted-fed states), with exploratory analyses examining satiety-state-specific effects (fasted and fed separately).

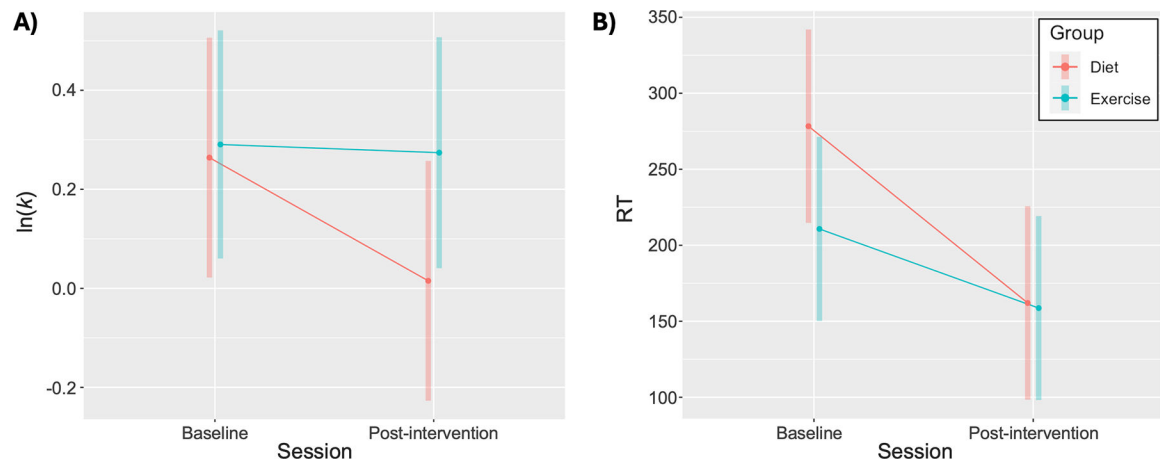


Figure 2. Decreased delay discounting propensity ($\ln(k)$) and average reaction time (RT) measured in response to a meal (fasted-fed) were observed across the exercise and diet groups. Plots depict estimated marginal means from linear mixed effects models used to assess intervention effects on behavioral delay discounting task outcomes. There was a significant decrease in *A*) $\ln(k)$ ($p=0.010$) and *B*) RT during delay discounting decisions ($p<0.001$) from baseline to post-intervention. Error bars represent 95% confidence intervals.

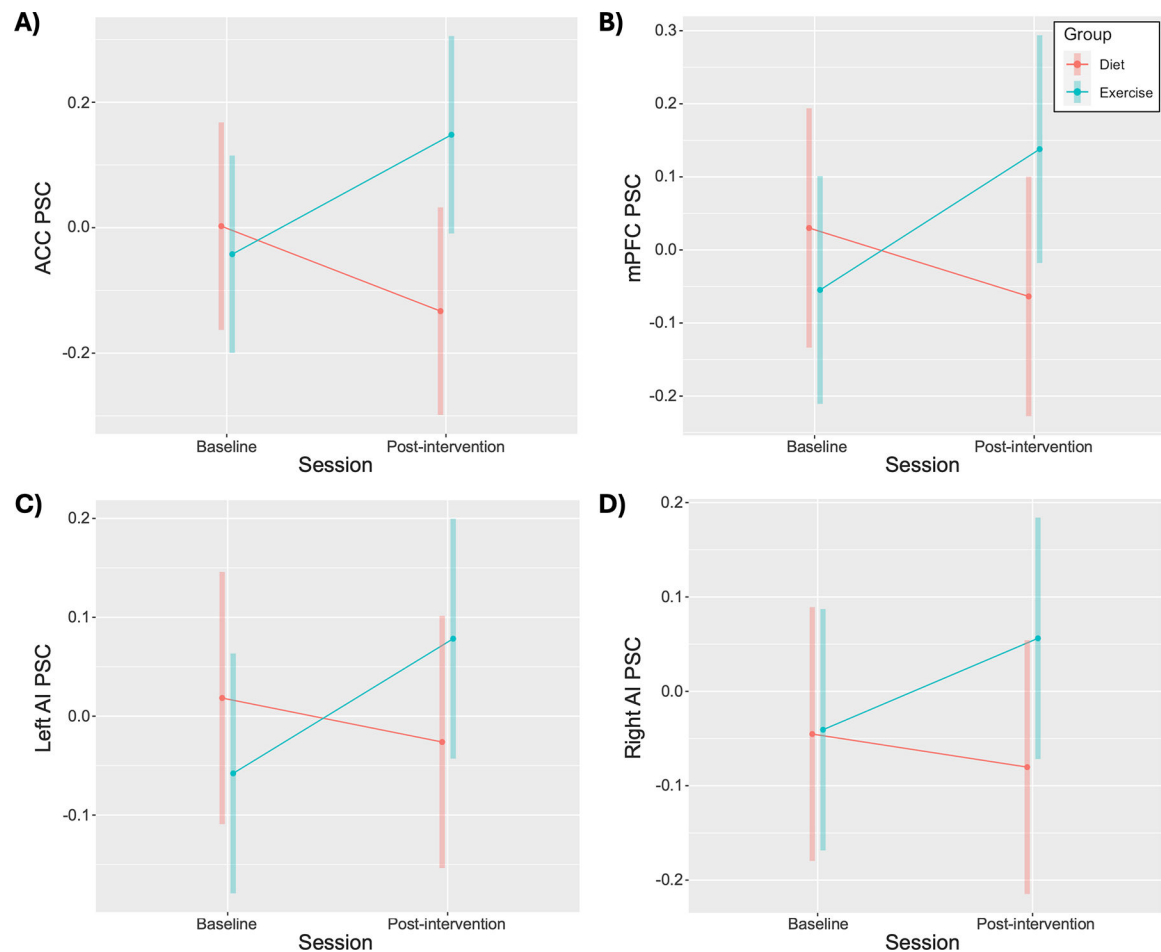


Figure 3. Twelve weeks of exercise training and diet intervention may have differential effects on neuronal response during a delay discounting task measured in response to a meal (fasted-fed).

Plots depict estimated marginal means from linear mixed effects models used to assess intervention effects on average percent signal change (PSC) in brain regions of interest. *A)* Significant group*session interaction in anterior cingulate cortex (ACC; $p=0.006$), with a similar trending effect in *B)* medial prefrontal cortex (mPFC; $p=0.013$). No significant effects were observed for *C)* left anterior insula ($p=0.055$) or *D)* right anterior insula ($p>0.121$). Error bars represent 95% confidence intervals.

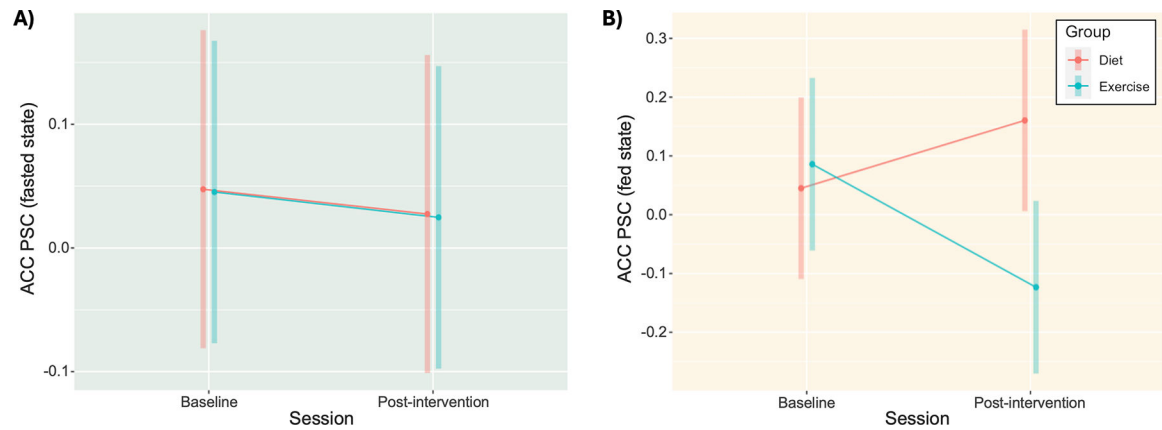


Figure 4. Intervention effects on anterior cingulate cortex (ACC) response during a delay discounting task may be driven by changes in the fed state rather than fasted state.

Plots depict estimated marginal means from linear mixed effects models used to assess satiety-state-specific intervention effects on average percent signal change (PSC) in ACC.

A) No significant fasted-state effects were observed ($p > 0.779$; green background), but B) a trending fed-state group*session interaction was observed ($p = 0.041$; tan background). Error bars represent 95% confidence intervals.

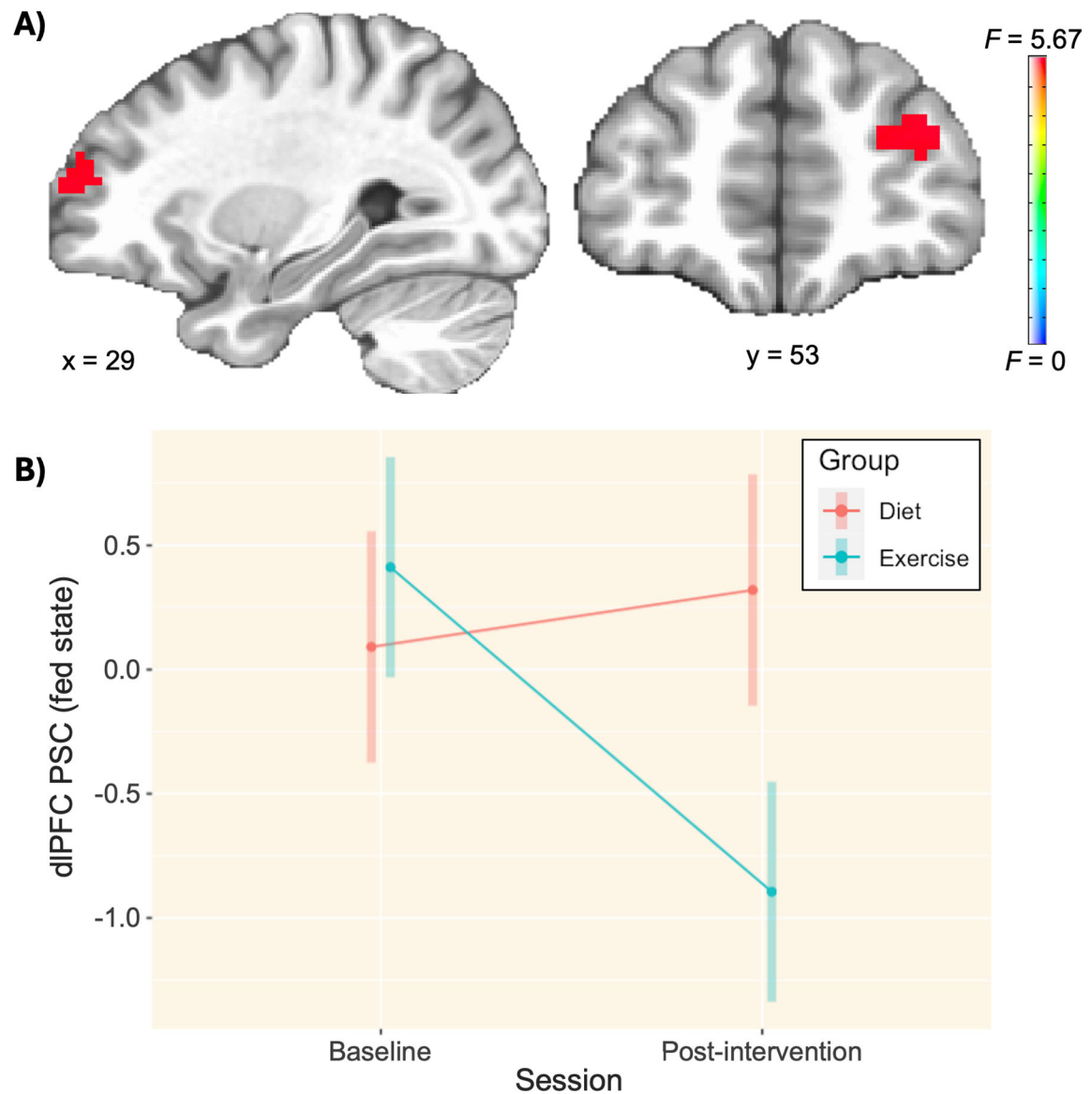


Figure 5. Exercise training was associated with decreased fed-state response in right dorsolateral prefrontal cortex (dlPFC) during a delay discounting task.

A) Visual depiction of a significant fed-state group*session interaction observed in right dlPFC in exploratory whole-brain analyses (voxelwise $p < 0.005$). Data are shown in the neurological convention (left hemisphere on the left). *B)* Estimated marginal means from an exploratory post-hoc analysis of the group*session interaction in (A), for which average percent signal change (PSC) was extracted from the dlPFC cluster. This suggests the interaction depicted in (A) was driven by significantly reduced dlPFC response following exercise training ($p < 0.001$) that was not observed following diet ($p = 0.818$).

Table 1.

Participant demographics.

	Diet (n=19)	Exercise (n=21)		
	n (%)	n (%)	χ^2	p
Sex (Female)	15 (78.9%)	17 (81.0%)	0.03 (1)	0.874
Race			6.95 (3)	0.074
White	16 (84.2%)	17 (81.0%)		
Black/African American	3 (15.8%)	0		
Asian	0	2 (9.5%)		
Mixed Race	0	2 (9.5%)		
Ethnicity			2.48 (2)	0.290
Hispanic	5 (26.3%)	5 (23.8%)		
Not Hispanic	12 (63.2%)	16 (76.2%)		
Unknown/Not Reported	2 (10.5%)	0		
Level of Education			2.50 (5)	0.777
High School Diploma	1 (5.3%)	1 (4.7%)		
Vocational Degree	1 (5.3%)	1 (4.7%)		
College Degree	9 (47.4%)	7 (33.3%)		
Master's Degree	3 (15.8%)	4 (19.0%)		
PhD/Professional Degree	3 (15.8%)	2 (9.5%)		
Unknown/Not Reported	2 (10.2%)	6 (28.6%)		
Household Income			5.50 (4)	0.239
\$10,000–25,000	1 (5.3%)	0		
\$25,000–50,000	1 (5.3%)	1 (4.7%)		
\$50,000–75,000	4 (21.1%)	9 (42.9%)		
Over \$75,000	10 (52.6%)	5 (23.8%)		
Unknown/Not Reported	3 (15.8%)	6 (28.6%)		
	M (SD)	M (SD)	t (df)	p
Age	39.21 (10.05)	36.54 (8.54)	0.91 (38)	0.366
Body Mass Index (BMI; kg/m ²)				
Baseline	31.53 (3.57)	30.15 (2.83)	1.36 (38)	0.182
Post-Intervention	30.55 (3.95)	29.44 (2.90)		
Weight (lbs)				
Baseline	192.31 (27.18)	188.91 (32.73)	0.36 (38)	0.724
Post-Intervention	185.27 (25.72)	185.09 (33.73)		
Percent Body Fat				
Baseline	41.09 (6.28)	39.24 (7.06)	0.87 (38)	0.390
Post-Intervention	39.73 (6.65)	38.32 (6.39)		

Note. Statistical results presented herein (χ^2 , t , and p) reflect comparisons between the exercise and diet groups at baseline.

Table 2.

Descriptive statistics of DD propensity ($\ln[k]$) and reaction time (RT; measured in milliseconds) by group (diet or exercise), session (baseline or post-intervention), and satiety state (fasted or fed).

	Diet ($n=19$) M (SD)		Exercise ($n=21$) M (SD)	
	Baseline	Post-Intervention	Baseline	Post-Intervention
Fasted				
$\ln(k)$	-4.66 (0.77)	-4.93 (0.89)	-4.79 (0.97)	-4.72 (0.96)
RT	1,916.31 (227.92)	1,809.68 (283.04)	1,986.14 (299.46)	1,875.21 (287.64)
Fed				
$\ln(k)$	-4.92 (0.88)	-4.95 (0.84)	-5.08 (1.30)	-4.99 (1.12)
RT	1,637.99 (241.03)	1,647.65 (249.84)	1,775.41 (367.19)	1,716.54 (311.96)

Table 3.

Results from linear mixed effects models examining intervention effects (Session: baseline vs. post-intervention; Group: exercise $n=21$ vs. diet $n=19$) on delay discounting (DD) behaviors and average percent signal change in brain regions of interest (anterior cingulate cortex, medial prefrontal cortex, and bilateral anterior insula) during a delay discounting task measured in response to a meal (fasted-fed).

	β	SE	t (df)	p
DD Propensity (ln[k])				
Session	-0.25	0.10	-2.62 (116)	0.010
Group	0.03	0.17	0.16 (52)	0.874
Session*Group	0.23	0.13	1.75 (117)	0.082
Reaction Time				
Session	-116.30	32.02	-3.63 (118)	<0.001
Group	-67.59	43.99	-1.54 (66)	0.129
Session*Group	64.24	44.19	1.45 (118)	0.149
Anterior Cingulate Cortex				
Session	-0.13	0.08	-1.56 (118)	0.122
Group	0.00	0.12	0.01 (64)	0.992
Session*Group	0.31	0.11	2.79 (118)	0.006
Medial Prefrontal Cortex				
Session	-0.09	0.08	-1.13 (118)	0.262
Group	-0.07	0.12	-0.62 (64)	0.541
Session*Group	0.28	0.11	2.54 (118)	0.013
Left Anterior Insula				
Session	-0.04	0.07	-0.62 (118)	0.540
Group	-0.05	0.09	-0.60 (68)	0.553
Session*Group	0.17	0.09	1.94 (118)	0.055
Right Anterior Insula				
Session	-0.03	0.06	-0.56 (117)	0.574
Group	0.01	0.09	0.10 (58)	0.924
Session*Group	0.13	0.08	1.56 (117)	0.121

Note. Significant p -values that survive multiple comparison corrections are denoted in bold font.