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1	Exercise training reduces reward for high-fat food in adults with overweight/obesity
2	
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18	
19	Abbreviations: CI, confidence interval; HCHO, high-carbohydrate; HFAT, high-fat; HR _{max} ,
20	heart rate maximum, ITT, intent-to-treat; LFPQ, Leeds Food Preference Questionnaire; $M_{\Delta Pre-}$
21	$_{Post,}$ estimated marginal mean differences from baseline to post-intervention; $M_{\Delta\!Ex\text{-}C}$
22	estimated marginal mean differences between Exercisers and Controls; $M_{\Delta HF-HC}$, estimated
23	marginal mean differences between HFAT and HCHO; $M_{\Delta H-Fed}$, estimated marginal mean
24	differences from hungry to fed states; MCID, minimum clinically important difference;
25	VO _{2max} , maximal aerobic capacity.

26 Abstract

27 Purpose: There is increasing evidence that exercise training may facilitate weight management 28 via improvements in homeostatic appetite control, but little is known about how exercise 29 training affects food reward and susceptibility to overeating.

30 Methods: This study examined changes in food reward and eating behavior traits after a 31 supervised 12-week exercise intervention (10.5 MJ/week) in inactive individuals with overweight/obesity (Exercisers; n=46, 16 males/30 females; BMI=30.6 (SD 3.8) kg/m² and 32 age=43.2 (SD 7.5) years compared to non-exercising Controls (n=15; 6 males/9 females; 33 BMI=31.4 (SD 3.7) kg/m² and age=41.4 (SD 10.7) years). Liking and wanting scores for high-34 35 fat relative to low-fat foods was assessed with the Leeds Food Preference Questionnaire before 36 and after consumption of an isoenergetic high-fat (HFAT) or high-carbohydrate (HCHO) 37 lunch. Eating behavior traits were assessed using the Three-Factor Eating Questionnaire and 38 Binge Eating Scale.

Results: A week by group interaction indicated that wanting scores decreased from baseline to post-intervention in Exercisers only ($M_{\Delta Pre-Post}$ = -4.1, p=0.03, η_p^2 =0.09, 95%CI= -7.8 to -0.4), but there was no exercise effect on liking. There was also a week by group interaction for binge eating, which decreased in Exercisers only ($M_{\Delta Pre-Post}$ = -1.5, p=0.01, η_p^2 =0.11, 95%CI= -2.7 to -0.4). A small reduction in disinhibition was also apparent in Exercisers ($M_{\Delta Pre-Post}$ = -0.7, p=0.02, η_p^2 =0.10, 95%CI= -1.3 to -0.1).

45 **Conclusion:** This study showed that 12 weeks of exercise training reduced wanting scores for 46 high-fat foods and trait markers of overeating in individuals with overweight/obesity compared 47 to non-exercising Controls. Further research is needed to elucidate the mechanisms behind 48 these exercise-induced changes in food reward.

49

50 Keywords: food reward; eating behavior traits; appetite control; liking and wanting; physical
51 activity

52

53 Introduction

54 Physical activity is widely recommended as a strategy for weight management and exercise 55 interventions improve body composition in both men and women (1). In addition to potential effects on body weight via increased energy expenditure, it is becoming apparent that habitual 56 57 physical activity and exercise training improve markers of appetite control, such as increased satiety response to food and gastric emptying (2, 3). However, variability in the inter-individual 58 59 weight loss response to exercise interventions has been reported (4). This variability suggests 60 that some individuals may compensate for an increase in physical activity (and energy 61 expenditure) through changes in meal size, frequency or food choice, attenuating or even reversing the effect of exercise on weight loss. 62

63 Liking and wanting components of food reward may be heightened for palatable food in individuals with overweight and obesity compared to individuals who are lean (5). Food 64 65 reward is also potentially influenced by physical activity, but evidence has been inconsistent, and as highlighted by a recent systematic review on weight management interventions (6), 66 findings to date offer limited evidence for the impact of exercise interventions on food reward. 67 68 We have shown that an acute post-exercise increase (both at baseline and post-intervention) in 69 food liking and wanting (particularly of high-fat foods), was present in those with a smaller 70 than expected reduction in body weight during a 12-week exercise intervention (7). No overall 71 changes in food reward in individuals with obesity were found following 12 weeks of moderate 72 continuous or high-intensity interval training (8); however, we have previously reported a trend for a decrease in implicit wanting measured in the hungry state in response to 12 weeks of 73

structured exercise training (9). How meal consumption or macronutrient composition
influences these responses has yet to be explored.

76 In terms of eating behavior traits, studies have shown that with exercise-induced weight 77 loss, greater changes in restraint were associated with greater weight loss (10). Exercise 78 training has also been shown to decrease disinhibition in individuals with overweight and 79 obesity (10). A recent systematic review suggested that physical activity may reduce binge eating through potential effects of physical activity on the reward system as they may share 80 81 similar brain pathways (11). Other proposed mechanisms include changes in negative affect, 82 homeostatic appetite control and/or body composition (11). Few studies have assessed the 83 impact of exercise training on food reward and eating behaviors together. One study found 84 reductions in the neuronal responses to visual food cues using functional magnetic resonance 85 imaging but no changes in restraint or disinhibition following a 6-month exercise intervention (12). Whether changes in eating behaviors are associated with changes in food reward in 86 87 response to exercise remains to be elucidated.

Overeating traits and food reward states interact with the fat content of food with the potential to enhance or undermine appetite control (13). Disinhibition and binge eating have both been linked to greater intake and preference for high-fat or high-fat/sweet foods (14). Indeed, we have previously shown that food reward was reduced after consumption of a fixed energy low-fat meal but not after an energy-matched high-fat meal (15). Whether exercise training interacts with the fat content of the diet has gained interest in recent years and has relevance for weight management (2).

Therefore, the main objective of this study was to investigate the effect of a supervised 12-week exercise intervention on reward for high-fat food and eating behavior traits in inactive individuals with overweight and obesity compared to non-exercising Controls. This was examined during exposure to high-fat (HFAT) and high-carbohydrate (HCHO) feeding 99 conditions. A secondary aim was to examine relationships among changes in eating behavior100 traits, food reward and body composition.

101

102 Methods

103 **Participants**

104 Men and women with overweight and obesity aged 18-55 years were recruited via poster advertisements and email lists at the University of Leeds, UK and surrounding areas. 105 106 Participants were screened on the following inclusion criteria: BMI between 26.0-38.0 kg/m², non-smoker, inactive (≤ 2 h per week of exercise over the previous 6 months), weight stable 107 108 $(\pm 2 \text{ kg for previous 3 months})$, not currently dieting or participating in a weight loss regime, 109 no history of eating disorders, not taking any medication known to affect metabolism or 110 appetite, and acceptance of the study foods. Participants were asked to keep lifestyle habits and activities constant throughout the study. The study was approved by the Leeds West NHS 111 112 Research Ethics Committee (09/H1307/7). Participants provided written informed consent prior to taking part. The study was registered under international standard trials approval 113 114 (ISRCTN47291569).

115

116 Study design

Forty-six participants (Exercisers; 16 males/30 females) completed a 12-week exercise intervention in which they exercised 5 days per week under supervision of research staff in the Human Appetite Research Unit, University of Leeds, UK between November 2011 and July 2013. Aspects of these data have been previously reported (9, 15-17).

121 Fifteen control participants (Controls; 6 males/9 females) completed 12 weeks of 122 maintaining current low activity levels between July 2012 and July 2013. The non-exercising 123 Controls were not made aware of the exercise arm of the study; participants were requested not 124 to change their dietary or exercise patterns for the duration of the study.

At baseline and post-intervention, food reward and eating behavior variables were assessed (described below). Food reward was measured during HFAT and HCHO probe days before and after a fixed energy meal. These days were separated by at least one day and in a randomized crossover order. Prior to each laboratory session, participants were instructed to maintain their usual diet, not to engage in physical activity for 24 hours, refrain from consuming alcohol for 24 hours and fast overnight (10-12 hours).

131

132 Measurements

133 Anthropometrics and body composition. At baseline and post-intervention, participants 134 completed a measurement day. Anthropometrics and body composition measures were taken whilst participants were wearing tight fitting clothing and a swim cap. Standing height without 135 shoes was measured to the nearest 0.1 cm using a stadiometer (Leicester height measure, 136 137 SECA, UK). Body weight was measured using an electronic balance and recorded to the 138 nearest 0.1 kg (BodPod, Life Measurement, Inc., Concord, USA). Fat mass, fat-free mass and percentage body fat were estimated via air displacement plethysmography (BodPod) following 139 140 the manufacturer's instructions.

141

Eating behavior questionnaires. Psychometric questionnaires were completed following the body composition measures. The Three-Factor Eating Questionnaire is a validated 51-item instrument that measures three dimensions of eating behavior: cognitive control of restraint (i.e. concern over weight gain and the strategies adopted to prevent this), disinhibition of eating (i.e. tendency of an individual to overeat and to eat opportunistically in the obesogenic environment), and susceptibility to hunger (i.e. extent to which feelings of hunger are perceived 148 and how these sensations result in food intake) (18). The Binge Eating Scale is a validated 16-149 item questionnaire that assesses the severity of binge eating (19). The questions are based upon 150 both behavioral characteristics (e.g. amount of food consumed) and the emotional, cognitive 151 response (e.g. guilt or shame).

152

153 Test meals. At baseline and post-intervention, participants completed two separate probe meal days in which they consumed foods that were either HFAT or HCHO. The ingredients of the 154 155 foods provided during the meal days were covertly manipulated to be HFAT: 10.4 (SD 1.1) kJ/g, 37.7% carbohydrate, 54.4% fat and 7.9% protein; or HCHO: 6.6 (SD 0.8) kJ/g, 72.4% 156 157 carbohydrate, 19.3% fat and 8.3% protein. Four hours after a standardized breakfast (ad libitum 158 on baseline probe day and quantities consumed replicated on post-intervention probe day; see 159 meal details in Supplemental Table 1), the participants consumed a fixed-energy lunch composed of food items providing 3347 kJ (matched for weight across HFAT and HCHO; see 160 161 meal details in Supplemental Table 2). Foods were designed to be similar in appearance and 162 palatability between conditions.

163

Food reward. The Leeds Food Preference Questionnaire (LFPQ; 20) was administered during the HFAT and HCHO meal days pre- and post-fixed-lunch consumption (3347 kJ) to assess food reward behaviors (liking and wanting) in the hungry and fed states. The LFPQ computes scores of implicit wanting and explicit liking for high-fat (>50% energy) and low-fat (<20% energy) foods images matched for familiarity, sweetness, protein, and acceptability.

Prior to the procedure, screening of the images used in the task was completed by each participant to improve internal validity. If a participant did not know or recognize, or would never/rarely eat a particular food item used in the study, replacement images were chosen from a database of images of similar composition. 173 The LFPQ is composed of two tasks: one based on subjective ratings (explicit liking) 174 and the other based on a forced-choice task (implicit wanting). During the measure of explicit liking, participants were presented with one food image at a time, in a randomized order, and 175 176 rated the extent to which they like each food (How pleasant would it be to taste this food now?). 177 Participants made their ratings using a 100-mm visual analogue scale. Implicit wanting was 178 assessed by asking participants to select as fast as possible between successive pairs of foods from specific categories the food "they most want to eat now". Scores for implicit wanting 179 180 were computed from mean response times adjusted for frequency (21). To calculate liking and 181 wanting fat appeal bias as a measure of hedonic preference for high-fat relative to low-fat foods, 182 low-fat scores were subtracted from high-fat scores, thus a positive score indicates greater 183 explicit liking / implicit wanting towards high-fat compared to low-fat foods. The LFPQ has 184 been validated in a wide range of research (e.g. 22).

185

186 **12-week exercise intervention**

During the 12-week supervised exercise intervention (5 days/week), each exercise session was 187 188 individually prescribed to expend 2092 kJ at an intensity of 70% of age-predicted heart rate 189 maximum (HR_{max}), and to ensure compliance to the exercise prescription, the duration and 190 intensity of each exercise session was recorded (Polar RS400, Polar, Finland). A selection of 191 aerobic exercise equipment was available (i.e. treadmill, rower, cycle ergometer, and elliptical) 192 from which the participants were free to choose and change within each session as long as they 193 met the energy expenditure requirements. The duration needed to expend 2092 kJ at 70% 194 HR_{max} at baseline was calculated based on the relationship between heart rate, VO₂, and VCO₂ 195 for each individual during an incremental maximal aerobic capacity (VO_{2max}) test. This test 196 was also performed at week 6 of the intervention to account for changes in energy metabolism, 197 and post-intervention to assess overall changes in cardiorespiratory fitness with the

intervention. Total exercise-induced energy expenditure during the intervention was 116.98 ± 15.56 MJ, which represented >98% of the prescribed exercise-induced energy expenditure. VO_{2max} was not measured in the Controls.

201

202 Statistical analyses

203 Data are presented as mean (standard deviation), unless specified otherwise. Data were 204 analyzed using the statistical package SPSS version 21. Data were checked for outliers prior to 205 statistical analyses, and one of the Controls had a change score (baseline to post-intervention) 206 in both liking and wanting that was 5 SD below the mean; therefore, this participant was 207 excluded from the analysis. Independent sample t-tests were used to evaluate differences in 208 participant characteristics at baseline. Repeated measures ANOVA with group (Exercisers, 209 Controls), week (baseline, post-intervention), condition (HFAT, HCHO) and state (hungry, fed) where appropriate, were used to assess changes in outcome variables. Where appropriate, 210 211 Greenhouse-Geisser probability levels were used to adjust for non-sphericity, and post hoc 212 analyses were performed using the Bonferroni adjustment for multiple comparisons. Where 213 missing data were present, completers and intent-to-treat analyses (ITT) were conducted with 214 the last observation carried forward method. To assess the associations among changes in food 215 reward (overall mean of the 2 conditions and 2 states), eating behavior traits and body 216 composition, Pearson's correlations were conducted in the whole group and in Exercisers and 217 Controls separately.

The magnitude of the mean weight change (Exercisers – Controls) was interpreted against a minimum clinically important difference (MCID) of 2.5 kg (23), where a small clinically important effect was defined between 2.5-7.5 kg (3×2.5 kg), a moderate effect between 7.5-15 kg (6×2.5 kg) and a large effect >15 kg (24). The magnitude of the mean waist circumference change was interpreted against a MCID of 2 cm (4, 25), where a small clinically important effect was defined between 2-6 cm, a moderate effect between 6-9 cm and a large
effect >9cm (24).

Following the American Statistical Association's policy statement on p-values (26), all 225 p-values from specified statistical models were reported along with effect size and confidence 226 227 intervals to help determine compatibility of the data with the interpretation of findings. We have avoided referring to any outcome as 'statistically significant' on the basis of a particular 228 p-value. Estimated marginal mean differences (M_{Δ}) are reported ($M_{\Delta Ex-C}$, Exercisers – Controls; 229 230 $M_{\Delta Pre-Post}$, Post-intervention – Baseline; $M_{\Delta HF-HC}$, HFAT – HCHO; $M_{\Delta H-Fed}$, Fed – Hungry), as well as effect sizes as partial eta squared (η_p^2) and 95% confidence intervals of the mean 231 232 difference (95%CI). Because there are no benchmark values for partial eta squared in the 233 context of repeated measures designs (27), the effect sizes were interpreted cautiously 234 alongside the mean differences within the field of human appetite.

Based on G*Power (v3.1), in order to detect an interaction in liking or wanting ($\eta_p^2=0.03$) between 2 groups and 2 repeated measurements (r ≈ 0.8 , based on prior data from our research group (9)) with $\alpha=0.05$ and $1-\beta=0.8$, a total sample size of 28 was required.

238

239 Results

240 **Participant characteristics**

241 Participant characteristics at baseline and post-intervention are described in Table 1. Baseline 242 characteristics of Exercisers and Controls were similar (p>0.13 for all). There were interactions 243 between week and group for BMI, total mass, body fat percentage, fat mass and waist 244 circumference (all p<0.001, $\eta_p^2 \ge 0.19$). The week by group interaction for fat-free mass was 245 weaker (p=0.22, $\eta_p^2 = 0.03$).

In Exercisers, the training intervention led to reductions in BMI ($M_{\Delta Pre-Post}$ = -0.6 kg/m², p<0.001, η_p^2 =0.25, 95%CI= -0.9 to -0.3 kg/m²), total mass ($M_{\Delta Pre-Post}$ = -1.8 kg, p<0.001, 248 $\eta_p^2 = 0.27, 95\%$ CI= -2.6 to -1.0 kg), body fat percentage ($M_{\Delta Pre-Post} = -1.9\%$, p<0.001, $\eta_p^2 = 0.42$, 249 95%CI= -2.5 to -1.3%), fat mass ($M_{\Delta Pre-Post} = -2.2$ kg, p<0.001, $\eta_p^2 = 0.37, 95\%$ CI= -3.0 to -1.5 250 kg) and waist circumference ($M_{\Delta Pre-Post} = -3.7$ cm, p<0.001, $\eta_p^2 = 0.57, 95\%$ CI= -4.5 to -2.9 cm). 251 There were also increases in fat-free mass ($M_{\Delta Pre-Post} = 0.4$ kg, p=0.01, $\eta_p^2 = 0.10, 95\%$ CI=0.1 to 252 0.8 kg) and VO_{2max} ($M_{\Delta Pre-Post} = 5.7$ mL/kg/min, p<0.001, $\eta_p^2 = 0.43, 95\%$ CI= 3.7 to 7.6 253 mL/kg/min; not measured in Controls).

In Controls, there were increases in BMI ($M_{\Delta Pre-Post}=0.4 \text{ kg/m}^2$, p=0.08, $\eta_p^2=0.05$, 95%CI= -0.1 to 0.9 kg/m²), total mass ($M_{\Delta Pre-Post}=1.3 \text{ kg}$, p=0.06, $\eta_p^2=0.06$, 95%CI= -0.04 to 2.7 kg), body fat percentage ($M_{\Delta Pre-Post}=0.8$ %, p=0.15, $\eta_p^2=0.04$, 95%CI= -0.3 to 1.8 %), fat mass ($M_{\Delta Pre-Post}=1.3 \text{ kg}$, p=0.06, $\eta_p^2=0.06$, 95%CI= -0.1 to 2.6 kg) and waist circumference ($M_{\Delta Pre-Post}=2.1 \text{ cm}$, p=0.005, $\eta_p^2=0.12$, 95%CI= 0.6 to 3.6 cm).

The 12-week intervention produced a mean group (Exercisers – Controls) body weight difference of -3.1 kg (95% CI= -4.3 to -1.9 kg) and waist circumference difference of -5.8 cm(95% CI= -7.5 to -4.1 cm).

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263 [Table 1 here]
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265 Food reward
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266 Completers data were available in 38 Exercisers and 14 Controls (with the outlier removed).

For liking scores, Exercisers had a lower liking than Controls overall ($M_{\Delta Ex-C}$ = -6.0 mm, p=0.15, η_p^2 =0.04, 95%CI= -14.2 to 2.2 mm; ITT $M_{\Delta Ex-C}$ = -7.6 mm, p=0.06, η_p^2 =0.06, 95%CI= -15.5 to 0.2 mm). A week by group interaction was not apparent (p=0.75, η_p^2 =0.002; ITT p=0.87, η_p^2 =0.00) and there were no changes from baseline to post-intervention in both groups ($M_{\Delta Pre-Post}$ = -1.1 mm, p=0.24, η_p^2 =0.03, 95%CI= -3.0 to 0.79 mm; ITT $M_{\Delta Pre-Post}$ = -1.3 mm, 272 p=0.15, η_p^2 =0.04, 95%CI= -3.1 to 0.5 mm). Figure 1A shows only the main effect of the 273 intervention on liking within each group, for clarity.

On comparison across test meal conditions (main effect of HFAT vs. HCHO), liking 274 275 was greater in HFAT relative to HCHO ($M_{\Delta HF-HC}$ = 1.9 mm, p=0.06, η_p^2 =0.07, 95%CI= -0.1 to 3.9 mm; ITT M_{ΔHF-HC}= 1.9 mm, p=0.05, η_p^2 =0.06, 95%CI= -0.02 to 3.7 mm). The interaction 276 effect between condition and state (p=0.02, η_p^2 =0.11; ITT p=0.04, η_p^2 =0.07) showed minimal 277 differences in liking between HFAT and HCHO in the hungry state ($M_{\Delta HF-HC} = 0.3$ mm, p=0.81, 278 $\eta_p^2 = 0.001, 95\%$ CI= -2.2 to 2.8 mm; ITT M_{AHF-HC}= 0.4 mm, p=0.73, $\eta_p^2 = 0.002, 95\%$ CI= -2.1 279 to 2.9 mm), but liking was greater in HFAT relative to HCHO in the fed state ($M_{\Delta HF-HC}$ = 3.5 280 281 mm, p=0.003, η_p^2 =0.17, 95%CI= 1.3 to 5.7 mm; ITT M_{ΔHF-HC}= 3.3 mm, p=0.003, η_p^2 =0.14, 282 95%CI= 1.2 to 5.4 mm). There were no other apparent effects or interactions.

283 For wanting scores, Exercisers had lower wanting than Controls overall ($M_{\Delta Ex-C}$ =-11.1, p=0.17, η_p^2 =0.04, 95%CI= -27.2 to 4.9; ITT M_{ΔEx-C}= -15.4, p=0.06, η_p^2 =0.06, 95%CI= -31.3 284 to 0.5). The week by group interaction effect (p=0.08, η_p^2 =0.06; ITT p=0.06, η_p^2 =0.06), showed 285 that Exercisers reduced wanting from baseline to post-intervention ($M_{\Delta Pre-Post}$ = -4.1, p=0.03, 286 $\eta_p^2 = 0.09, 95\%$ CI= -7.8 to -0.4; ITT M_{\Delta Pre-Post}= -4.4, p=0.01, $\eta_p^2 = 0.10, 95\%$ CI= -7.7 to -1.0) 287 but not Controls ($M_{\Delta Pre-Post}=2.3$, p=0.45, $\eta_p^2=0.01$, 95%CI= -3.8 to 8.3; ITT $M_{\Delta Pre-Post}=2.3$, 288 289 p=0.46, η_p^2 =0.01, 95%CI= -3.8 to 8.4). Exercisers also had a lower wanting than Controls postintervention (M_{Δ Ex-C}= -14.3, p=0.07, η_p^2 =0.06, 95%CI= -30.0 to 1.4; ITT M_{Δ Ex-C}= -18.7, 290 291 p=0.02, η_p^2 =0.09, 95%CI= -34.4 to -3.1). Figure 1B shows only the main effect of the 292 intervention on wanting within each group, for clarity.

293 The week by state interaction effect (p=0.04, η_p^2 =0.08; ITT p=0.06, η_p^2 =0.06), 294 suggested reductions in wanting from hungry to fed post-intervention (M_{ΔH-Fed}= -5.3, p=0.10, 295 η_p^2 =0.05, 95%CI=-11.7 to 1.0; ITT M_{ΔH-Fed}= -5.3, p=0.08, η_p^2 =0.05, 95%CI=-11.3 to 0.7) and from baseline to post-intervention in the fed state ($M_{\Delta Pre-Post}$ = -3.3, p=0.10, η_p^2 =0.05, 95%CI= -7.2 to 0.6; ITT $M_{\Delta Pre-Post}$ = -3.2, p=0.10, η_p^2 =0.05, 95%CI= -7.1 to 0.6).

The main effect of condition showed that wanting was greater in HFAT relative to 298 299 HCHO (M_{Δ HF-HC}= 3.0, p=0.03, η_p^2 =0.09, 95%CI= 0.2 to 5.8; ITT M_{Δ}= 2.9, p=0.03, η_p^2 =0.08, 300 95%CI= 0.3 to 5.4). The interaction effect between condition, state and group (p=0.08, $\eta_p^2 = 0.06$; ITT p=0.09, $\eta_p^2 = 0.05$) suggested lower wanting in Exercisers than Controls when 301 hungry in HFAT ($M_{\Delta Ex-C}$ = -13.2, p=0.11, η_p^2 =0.05, 95%CI= -29.6 to 3.3; ITT $M_{\Delta Ex-C}$ = -17.5, 302 p=0.04, η_p^2 =0.07, 95%CI= -34.1 to -0.9) and HCHO (M_{\Delta Ex-C}= -13.7, p=0.12, η_p^2 =0.05, 303 95%CI= -31.2 to 3.8; ITT M_{Δ Ex-C}= -17.7, p=0.05, η_p^2 =0.07, 95%CI= -35.2 to -0.1), and when 304 305 fed in HFAT (M_{ΔEx-C}= -12.0, p=0.17, η_p^2 =0.04, 95%CI= -29.5 to 5.5; ITT M_{ΔEx-C}= -16.5, 306 p=0.06, η_p^2 =0.06, 95%CI= -33.7 to 0.6). Controls also had greater wanting after HFAT compared to HCHO in the fed state ($M_{\Delta HF-HC} = 7.3$, p=0.01, $\eta_p^2 = 0.12$, 95%CI= 1.6 to 13.1; ITT 307 $M_{\Delta HF-HC} = 7.3$, p=0.009, $\eta_p^2 = 0.11$, 95% CI= 1.9 to 12.8). There were no other apparent effects 308 309 or interactions.

310

311 [Figure 1 here]

312

313 Eating behavior traits

Completers' data were available for 46 Exercisers (45 for binge eating) and 12 Controls, and ITT for 14 Controls. As shown in Table 2, baseline scores for Exercisers and Controls were similar (p>0.15 for all).

317 For restraint, there were minimal differences from baseline to post-intervention across 318 groups ($M_{\Delta Pre-Post}$ = -0.5, p=0.37, η_p^2 =0.01, 95%CI= -1.5 to 0.6; ITT $M_{\Delta Pre-Post}$ = -0.4, p=0.38,

319 $\eta_p^2=0.01, 95\%$ CI= -1.4 to 0.5), between groups (M_{AEx-C}= -1.2, p=0.32, $\eta_p^2=0.02, 95\%$ CI= -3.6

320 to 1.2; ITT M_{Δ Ex-C}= -1.2, p=0.31, η_p^2 =0.02, 95%CI= -3.5 to 1.1), and no apparent week by 321 group interaction (p=0.89, η_p^2 =0.00; ITT p=0.94, η_p^2 =0.00).

322 For disinhibition, there were minimal differences between groups (M_{ΔEx-C}= -0.6, 323 p=0.60, η_p^2 =0.005, 95%CI= -2.8 to 1.6; ITT M_{ΔEx-C}= -0.9, p=0.40, η_p^2 =0.01, 95%CI= -2.9 to 324 1.2). The interaction effect between week and group (p=0.23, η_p^2 =0.03; ITT p=0.20, η_p^2 =0.03), 325 suggested a decrease in disinhibition from baseline to post-intervention in Exercisers (M_{ΔPre-} 326 Post= -0.7, p=0.02, η_p^2 =0.10, 95%CI= -1.3 to -0.1; ITT M_{ΔPre-Post}= -0.7, p=0.01, η_p^2 = 0.10, 327 95%CI= -1.2 to -0.1) but not in Controls (M_{ΔPre-Post}= 0.04, p=0.94, η_p^2 =0.0, 95%CI= -1.1 to 328 1.1; ITT M_{ΔPre-Post}= 0.04, p=0.94, η_p^2 =0.0, 95%CI= -1.0 to 1.0).

For susceptibility to hunger, Exercisers had lower scores than Controls overall ($M_{\Delta Ex}$ -330 c= -1.5, p=0.18, η_p^2 =0.03, 95%CI= -3.7 to 0.7; ITT $M_{\Delta Ex}$ -c= -1.9, p=0.07, η_p^2 =0.06, 95%CI= -331 4.0 to 0.1). The week by group interaction (p=0.33, η_p^2 =0.02; ITT p=0.35, η_p^2 =0.02) suggested 332 that Exercisers had lower scores than Controls post-intervention ($M_{\Delta Ex}$ -c= -1.9, p=0.11, 333 η_p^2 =0.04, 95%CI= -4.2 to 0.5; ITT $M_{\Delta Ex}$ -c= -2.2, p=0.04, η_p^2 =0.07, 95%CI= -4.4 to -0.01).

334For binge eating score, differences between groups were minimal ($M_{\Delta Ex-C}$ = -1.8,335p=0.46, η_p²=0.01, 95%CI= -6.4 to 2.9; ITT $M_{\Delta Ex-C}$ = -2.5, p=0.25, η_p²=0.02, 95%CI= -6.9 to3361.8). The interaction between week and group (p=0.06, η_p²=0.06; ITT p=0.06, η_p²=0.06)337revealed a decrease in Exercisers ($M_{\Delta Pre-Post}$ = -1.5, p=0.01, η_p²=0.11, 95%CI= -2.7 to -0.4; ITT338 $M_{\Delta Pre-Post}$ = -1.5, p=0.01, η_p²=0.11, 95%CI= -2.6 to -0.4), but not in Controls ($M_{\Delta Pre-Post}$ = 0.9,339p=0.44, η_p²=0.01, 95%CI= -1.4 to 3.1; ITT $M_{\Delta Pre-Post}$ = 0.8, p=0.46, η_p²=0.009, 95%CI= -1.3 to3402.8).

341

342 [Table 2 here]

343

Relationship between changes in food reward, eating behavior traits and body weight and composition

As shown in Supplemental Digital Content Tables 3-5, in the whole sample and in Controls, changes in wanting scores were weakly associated with changes in binge eating, and weakened further in Exercisers alone. In the whole sample, changes in body weight, fat mass and, more weakly, body fat percentage, were associated with changes in eating behavior traits but not with changes in food reward. These associations were weaker in the Exercisers alone and not apparent in the Controls alone, except for disinhibition.

352

353 **Discussion**

354 This study examined the impact of a 12-week supervised exercise intervention on state 355 measures of food reward and trait characteristics of susceptibility to overeating in inactive individuals with overweight and obesity compared to non-exercising Controls under conditions 356 357 of HFAT and HCHO feeding. The 12-week intervention led to improvements in body composition and fitness in Exercisers, whereas there was a small increase in adiposity in 358 359 Controls. The mean group (Exercisers - Controls) differences in body weight and waist circumference were small but clinically meaningful according to agreed guidelines on obesity 360 361 management (23). In Exercisers, there was a reduction in food reward (specifically wanting) 362 that was accompanied by improvements in eating behavior traits (clearly for binge eating and weakly for disinhibition), whereas no changes were apparent in Controls. 363

364

365 The impact of exercise training on food reward

366 In the current study, a 12-week exercise intervention led to a small reduction in wanting scores 367 for high-fat relative to low-fat foods in Exercisers compared to Controls, but no differences in 368 liking were found. Differences in food reward between Exercisers and Controls suggested that 369 liking and wanting were generally lower in Exercisers than Controls but this effect was small 370 and the variability was high. The group differences were more apparent in the ITT analyses, where a larger sample size and power strengthened the analysis. The changes in wanting in the 371 372 Exercisers from positive towards negative values indicated a greater wanting scores for low-373 fat relative to high-fat foods after the exercise intervention. While this reduction in wanting 374 scores for high-fat foods was accompanied by a small reduction in intake at an ad libitum dinner test meal in the HFAT condition (~130 kcal, data not reported in the current manuscript) (28), 375 376 overall HFAT daily intake, remained unchanged after the exercise intervention. The reduction 377 in wanting observed in the current study may not have been large enough to elicit meaningful 378 changes in food intake, but provides insight for a potential mechanistic influence of exercise 379 (with modest weight loss) on food reward, specifically wanting. It's also important to consider 380 that the design of the probe meal days 1) contained 2 fixed meals, thus if all test meals had been ad libitum perhaps larger effects on energy intake may have been observed (given that a 381 382 small reduction was seen at the dinner meal); and 2) did not allow for choices between high-383 fat and low-fat foods to be made, as each probe day was specifically designed to contain either 384 high-fat or low-fat foods. Therefore, future studies assessing reward for high-fat vs. low-fat (or 385 sweet vs. savory/non-sweet) foods in response to exercise should also include a food choice 386 component to the assessment of food intake with ad libitum test meals including foods varying 387 in fat content/taste.

Furthermore, on an individual-level, we have shown that an increase in food liking and wanting (particularly of high-fat foods) in response to acute exercise led to less than expected weight loss during a prior 12-week exercise intervention (7). This suggests a role for food reward in the compensatory eating response to exercise. Indeed, this may be related to changes in between-network connectivity occurring in the brain, specifically between the posterior cingulate cortex and a visuospatial network, with chronic exercise, as these have been found tobe associated with changes in susceptibility to hunger assessed by the TFEQ (29).

We have recently shown in a systematic review that reward for high-fat/energy food generally decreases following weight management interventions including a range of modes of weight loss (6). The review found limited available evidence on exercise interventions; therefore, this study adds to the sparse literature in this area. Future studies could examine characteristics of exercise interventions (e.g. frequency, intensity, type, duration, and timing) that could potentially have a larger effect on reward, eating behavior and food intake/choices than the effects demonstrated in the current study.

402 Cross-sectional differences in the reward value of foods (liking and wanting) have been observed in active compared to inactive males that differed in BMI (30), while in individuals 403 404 with similar BMI (healthy range), level of habitual physical activity did not appear to influence 405 food reward (31, 32). Other studies using functional magnetic resonance imaging have found 406 a reduction in the neural response to food cues with greater levels of habitual physical activity 407 (33) and after exercise training (12), with inconsistencies regarding the role of body fat loss or 408 status in the responses observed. In individuals with overweight and obesity, a 6-month 409 exercise training intervention was associated with attenuated neural response to food cues 410 despite no effect on behavioral measures of appetite, raising the question of whether exercise 411 could improve weight management through attenuated hedonic motivation to eat (12). 412 Interestingly, changes in the default mode network activity (reflecting an individual's internal 413 mental state) during this 6-month intervention was positively associated with changes in fat 414 mass as well as hunger (measured via TFEQ and in response to a test meal) (34).

In contrast to functional magnetic resonance imaging, the LFPQ methodology allows for a quantified behavioral assessment of food reward. Interestingly, in a study conducted in inactive individuals with overweight and obesity, 12 weeks of exercise training (523-1046 kJ, 418 3 days/week) did not affect liking or wanting scores measured by the LFPQ (8), whereas the 419 12-week intervention in the current study, at a higher dose of exercise (2092 kJ, 5 days/week), 420 reduced the wanting scores for high-fat food relative to non-exercising Controls. The potential 421 effects of exercise training dose (and other parameters of exercise such as those mentioned 422 above) on food reward warrant further investigation. Moreover, future studies combining the 423 LFPQ with measures of neural activation (12) and changes in food intake would provide 424 convincing evidence of the potency and specificity of exercise on food reward.

425 The major innovative aspect of this current study is that exercise training affected 426 wanting rather than liking for high-fat foods. However, this effect was small and the clinical relevance for weight management cannot be determined. Wanting may be interpreted as the 427 428 anticipatory reward (i.e. motivation or desire to eat before the consumption) while liking is the 429 pleasure to eat (35). It could be hypothesized that exercise affects wanting more than liking as exercise has an indirect effect on dietary habits, and rather affects cognition and executive 430 431 function (36). This strengthening of cognitive processes such as inhibitory control would be 432 expected to have an effect on wanting rather than liking for high-fat food (36). On the contrary, 433 diet interventions may have a greater effect on liking as they are directly manipulating food 434 patterns. In a recent systematic review, three dietary interventions reduced liking; however wanting was not measured in these studies (6). Our study demonstrates that, in assessing effects 435 436 on food reward, it is necessary to measure both liking and wanting as differing responses may 437 be seen. We show beneficial effects of exercise on the hedonic motivation to eat through a 438 small reduction in wanting scores for high-fat relative to low-fat foods, but not liking. Changes 439 in food reward did not appear to be associated with changes in body weight; however, associations between fasting leptin and food reward in response to exercise training have 440 441 previously been shown with or without controlling for body fat (9). It remains unknown 442 whether the influence of chronic exercise on wanting is due to improvements in cognitive

443 processes, to a modulation of the brain reward system or to other mechanisms. A better 444 understanding of the neurocognitive effect of exercise and its relationship with food reward 445 and eating behaviors is needed. It is also important to acknowledge, as shown in Figure 1, that 446 large individual variability in the food reward responses existed, and more studies should be 447 conducted to identify the reasons for such differences.

448

449 Exercise training and eating behaviors promoting overconsumption

Regarding the assessment of eating behavior traits, a week by group interaction showed that binge eating decreased in Exercisers in response to the exercise intervention, whereas no changes were observed in Controls. Disinhibition also showed a small decrease in Exercisers, with a weaker week by group interaction, but corroborates an earlier exercise training study from our group that also found a reduction in disinhibition (10). Interestingly, the changes in eating behaviors in that study were more pronounced in those who lost more weight compared to those who lost less weight in response to the exercise intervention (10).

457 Cross-sectional studies in lean individuals matched for BMI ranging in physical activity levels suggest little influence of physical activity on eating behavior traits (31, 32). However, 458 459 across a larger range of BMI, negative associations were observed between time spent in 460 moderate-to-vigorous physical activity and disinhibition and binge eating, but these weakened 461 after controlling for body fat (37), and also a study by Shook et al. found greater disinhibition 462 in their lowest quintile of moderate-to-vigorous physical activity but not when controlling for body weight (38). Further evidence examining the effects of exercise on other trait markers of 463 464 susceptibility to overeating are inconsistent, with a 6-month exercise training study reporting no effect on food cravings (12), while another study suggested that physical activity could 465 466 modulate craving control (39). This latter study showed that individuals who increased total 467 exercise time over a 1-year free-living period had a reduction in the difficulty to resist food468 cravings (39).

469 This could mean that the impact of chronic exercise and habitual physical activity on 470 trait measures of susceptibility to overeating may be more influenced by or dependent on body 471 weight/composition. Indeed, in the current study, changes in eating behaviors were associated 472 with changes in body weight (more strongly in the whole group than in the Exercisers alone). 473 In contrast, food liking and wanting are considered as more state-dependent, with acute 474 exercise able to modulate short-term food reward responses (7, 40), and did not appear to be 475 influenced by changes in body weight. The effects of chronic exercise and body 476 weight/composition on trait and state markers of overeating remain to be fully understood.

Furthermore, it has been suggested that chronic exercise may reduce binge eating through a mechanistic effect on the reward system (11). In the current study, correlational analyses suggested potential associations between changes in wanting and changes in trait binge eating in the whole sample; however, the uncertainty in our data do not allow for any conclusions to be made at this time regarding the effect of exercise on this relationship. Clearly more work is needed to elucidate the impact of chronic exercise on the food reward and neurocognitive systems as well as on psychological eating behavior traits.

484

485 Liking and wanting in response to HFAT and HCHO feeding conditions

Prior baseline analyses of the current study showed that not only are high-fat (and energydense) foods less satiating than high-carbohydrate foods (lower satiety quotient response) and lead to an overconsumption of energy, but that consumption of these foods modulates liking and wanting (15). In the present study, and in line with our previous findings (15), we show that regardless of the exercise intervention, liking and wanting scores for high-fat relative to 491 low-fat foods was dependent on the composition of the foods consumed. Moreover, the 492 composition of the food consumed interacted with the hunger state of the participants, showing 493 a greater liking and wanting scores for high-fat foods after consumption of high-fat foods 494 compared to high-carbohydrate foods (for wanting this effect was more prominent in the 495 Controls). However, food composition did not interact with the reward responses to exercise 496 training. This emphasizes the importance of the energy density of the diet in determining both 497 homeostatic (satiety and energy intake) and food reward (liking and wanting) responses. It also 498 suggests that exercise-induced improvements in appetite control are unlikely to (on their own) 499 overcome the overconsumption of energy typically seen with high-fat foods, as the palatable 500 nature of energy dense foods can offset homeostatic satiation and satiety signals (13).

501

502 Limitations

503 Despite the present study being among the few in this area to include a non-exercising control 504 group, the relatively small number of Controls compared to Exercisers adds some additional 505 uncertainty (i.e. increased size of confidence intervals) to the study outcomes. Additionally, 506 this study was not a randomized controlled trial; Exercisers and Controls were recruited 507 separately. While the exercise intervention in Exercisers was supervised and closely monitored 508 for adherence, no free-living exercise or food intake data were collected in the Controls to 509 confirm they hadn't changed their behavior during the 12 weeks. Furthermore, the menstrual 510 cycle of female participants was not considered and may have impacted on the appetite 511 responses. However, as the study was 12 weeks in duration, the female participants should have 512 been in the same phase of their cycle at both baseline and post-intervention measures days. The 513 interrelationships between exercise and changes in body composition make it difficult to tease 514 out specific contributors (whether direct or indirect) to the changes in appetite observed in the 515 current study. A future study design could attempt to control body weight during exercise

518

519 Conclusions

520 In inactive individuals with overweight and obesity, a 12-week exercise intervention reduced 521 wanting scores for high-fat foods and trait binge eating relative to non-exercising Controls. A reduction in trait disinhibition with exercise was apparent but to a lesser degree. The 522 523 intervention improved body composition in the Exercisers compared to the non-exercising 524 Controls. Taken together with previous work on the impact of physical activity on appetite, our 525 cautious interpretation is that exercise training, in general, enhances appetite control through 526 an impact on homeostatic and hedonic processes occurring around an eating episode, and has 527 an improved effect on more enduring eating behavior traits promoting overconsumption. Whether these trait effects are dependent upon changes in body weight/composition remains 528 529 to be fully understood. Furthermore, it cannot be claimed that such an improvement will be 530 seen in all people undertaking exercise. The effects of exercise on the body are complex and 531 involve simultaneous physiological adjustments. Effects should be treated cautiously, and our modest interpretation is that exercise has the potential to generate biological signals that cause 532 533 adaptation to the dietary environment; this will be greater in some individuals than in others. 534 Despite the degree of uncertainty in the outcomes, we feel it is important to continue to attempt 535 to understand a complicated situation, and to openly debate the findings.

536

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542

543 Authors' contributions

C. G., J. E. B., G. F. and P. C. contributed to the study design; M. H., C. G. and P. C. contributed
to the data collection; K.B. and G. F. contributed to the data analyses; K.B., M.H., C.G., P.O.,
J. E. B. and G. F. contributed to the interpretation of data and writing of the manuscript. All
authors read and approved the final version of the manuscript.

548

549 **Conflict of Interest**

550 The authors declare no conflicts of interest. The results of the present study do not constitute

551 endorsement by ACSM and are presented clearly, honestly, and without fabrication,

552 falsification, or inappropriate data manipulation.

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670

671 Supplemental Digital Content

- 672 Table 1. Food items and macronutrient composition of the ad libitum HFAT and HCHO
- 673 breakfast at baseline
- 674 Table 2. Food items and macronutrient composition of the fixed energy HFAT and HCHO675 lunches
- Table 3. Pearson correlation matrix of the associations among changes in food reward, eatingbehavior traits and body composition in the whole group
- 678 Table 4. Pearson correlation matrix of the associations among changes in food reward, eating
- 679 behavior traits and body composition in Exercisers
- Table 5. Pearson correlation matrix of the associations among changes in food reward, eating
 behavior traits and body composition in Controls
- 682

683 Figure Captions

684 Fig. 1. Liking (A) and wanting (B) for high-fat relative to low-fat foods in Exercisers (n=38) 685 and Controls (n=14) at baseline (B) and post-intervention (PI). For clarity, the overall mean of 686 HFAT and HCHO and pre-post lunch is presented. Individual values of food reward are 687 represented by the points and the descriptive statistics by boxplot with median. The figure 688 illustrates both the effect of exercise on food reward (difference between the 2 boxplots) and 689 the inter-individual variability in the changes. Repeated measures ANOVA were conducted 690 with post hoc Bonferroni adjustments. *Exercisers baseline vs. post-intervention (completers p=0.03, η_p^2 =0.09; ITT p=0.01, η_p^2 =0.10). *Exercisers vs. Controls post-intervention 691 (completers p=0.07, η_p^2 =0.06; ITT p=0.02, η_p^2 =0.09). 692