Exercise training and weight loss, not always a happy marriage: single blind exercise trials in females with diverse BMI

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Abstract

Individuals show high variability in body weight responses to exercise training. Expectations and motivation towards effects of exercise on body weight might influence eating behaviour and could conceal regulatory mechanisms. We conducted two single-blind exercise trials (4 weeks (study 1) and 8 weeks (study 2)) with concealed objectives and exclusion of individuals with weight loss intention. Circuit exercise training programs (3 times a week (45-90 min), intensity 50-90% VO_2peak, for 4 and 8 weeks) were conducted. 34 females finished the 4 weeks intervention and 36 females the 8 weeks intervention. Overweight/obese (OV/OB) and lean (L) female participants´ weight/body composition responses were assessed and fasting and postprandial appetite hormone levels (PYY, insulin, amylin, leptin, ghrelin) were measured pre and post intervention for understanding potential contribution to individuals' body weight response to exercise training (study 2). Exercise training in both studies did not lead to a significant reduction of weight/BMI in the participants' groups, however, lean participants gained muscle mass. Appetite hormones levels were significantly ($p<0.05$) altered in the OV/OB group affecting fasting (-24%) and postprandial amylin (-14%) levels. Investigation of individuals' BMI responses using multiple regression analysis revealed that levels of fasting leptin, postprandial amylin increase, and BMI were significant predictors of BMI change explaining about 43% of the variance. In conclusion, tested exercise training did not lead to weight loss in female participants, while a considerable proportion of variance in body weight response to training could be explained by individuals' appetite hormone levels and BMI.

Keywords: Exercise, obesity, body mass maintenance, energy regulation, hormones

Introduction

Exercise is often prescribed for weight loss (Donnelly et al. 2009). However, although weight loss is often reported (Ross et al. 2000, 2004), exercise training does not always result in weight loss and often reveals high individual variability in body weight changes (King et al. 2007, 2008, Barwell et al. 2009). Possible causes of less than expected weight outcomes are suggested to be modified appetite, perceived reinforcement value of food and altered unstructured physical activity (Blundell et al. 2003, King et al. 2007, Church et al. 2009). Accordingly, the concept of compensators and non-compensators of negative energy balance has been established, although causes for individuals' responses are still debated (Finlayson et al. 2009). Energy balance, and therefore body weight, is regulated by mediators released from gastrointestinal apparatus, pancreas and fat tissue, as well as nutrients. Tonic and phasic signals provide important information about the energy status to the brain. Leptin and insulin, as well as possibly amylin, providing tonic information about energy status; ghrelin, as well as PYY (1-36, 3-36), GLP-1, CCK, and again amylin and insulin providing phasic signals direct to the hypothalamus but also to the hind brain (Suzuki et al. 2010). Moreover, the levels of response to hormonal changes are not restricted to satiety and hunger but expand to neuronal systems connected to hedonic responses, like the mesolimbic dopamine neurons towards leptin and insulin (Figlewicz 2003, Figlewicz and Benoit 2009) or ghrelin's involvement in reward processing (Jerlhag et al. 2007). Alterations on hormonal levels are shown to contribute to the regulation of energy balance if challenged by exercise training (Stensel 2010); with training PYY and ghrelin are more consistently found to be altered then others (Broom et al. 2009, Ueda et al. 2009, Kawano et al. 2013). A possible influencing factor in exercise training studies is the control of motivation and intention of individuals to restrain their food intake, even if this may not be wanted by the experimenters. It is possible that some studies are biased towards weight loss based on the recruitment of participants who may be motivated to lose weight and not naïve towards study aims and objectives. To investigate possible mediators influencing individuals' weight loss response to exercise we conducted two single blind exercise training studies, one lasting 4 weeks (study 1) and

the other lasting 8 weeks (study 2). Group-based circuit training exercises were performed at 50-95% VO2peak, 3 times a week, for 45-90 min. Energy intake was *ad libitum* in both studies, which were designed with the intention of avoiding the formerly mentioned influence of motivation to lose weight. Thus, aims and objectives were concealed from the participants and spurious objectives were provided. Females over a wide range of BMI were recruited as participants and individuals who expressed an intention to lose weight were excluded. In the first study (4 weeks), a randomized control design was used and body characteristics and composition, as well as cardiovascular fitness were measured pre and post training. In the second study (8 weeks), fasting and postprandial blood samples were taken for measurements of appetite hormones and metabolites, body composition, cardiovascular fitness, and resting metabolic rate assessed pre and post intervention. We hypothesized that a) females with overweight/obesity and leanness would regulate their body weight successfully leading to no weight/BMI changes after the training interventions; b) measured appetite hormones levels (PYY, insulin, amylin, leptin, ghrelin) could be used to explain individuals' variance in BMI changes; c) hormone levels would be affected by exercise training leading to reduced levels of appetite suppressing hormones.

Materials and methods

The two studies were approved by Bangor University ethics committee and the North Wales Research Ethics Committee – West (Betsi Cadwaladr University Health Board – REC No 11/WA/0321 and 12/WA/0118). All participants were given written and verbal information and participants provided written informed consent.

Participants and studies design

For both studies, sedentary females were recruited. In study 1, 40 females were recruited for a 4 weeks training intervention, with 34 finishing the study. Participants were randomly allocated to an

exercise training group or a control group. In study 2**,** 56 females were recruited for an 8 weeks training intervention with 36 females completing. For both studies, recruitment was performed using emails to students and employees of Bangor University and posters in the Bangor area. To conceal the aims and objectives of the research, potential participants were informed that the study investigated *the influence of exercise training on cognitive performance and cardiovascular fitness*. In study 2, an incentive for taking part was the reimbursement for effort with a pair of trainers up to £100 value. The element of deception in both studies was achieved using a computer based cognitive sorting task for measuring reaction times in recognising combinations of pictures and words. Participant information sheets were written according to the spurious objectives, and any questions arising were answered by researchers accordingly. Participants were debriefed after the intervention.

Potential participants were selected to take part in the study based on their responses to a pre-screening questionnaire assessing health, physical activity, general diet habits (i.e. restrictive diet). To avoid participants' bias towards weight loss and potential dieting, we used Aizen's theory of planned behaviour (Ajzen 1991) as a framework for including/excluding participants based on current intention to lose weight (Sørensen et al. 2005). Participants were aged between 18 and 40; BMI categories were lean (L) < 25 kg/m^2 and overweight/obese (OV/OB) > 25 kg/m^2; healthy; sedentary; not following any type of specialised diet; and having not stated an intention to lose weight.

Exercise sessions were circuit based (e.g.running on the spot, lunges, star jumps, sit-ups, press-ups and squats) for both studies and completed 3 times a week. Length of sessions was 60 minutes in study 1, and between 40 – 90 minutes in study 2, dependent upon the intensity of exercise required to achieve equal exercise energy expenditure across two training groups (descriptions follows). All sessions were completed in small training groups (5-10 participants) and supervised by 3 members of the research team. Participants trained in groups according to their BMI group (L or OV/OB). In

study 1, after randomized distribution into control and exercise group, individuals trained on a target heart rate representing 70-80% of their heart rate at $\dot{V}O_2$peak. The control group did not take part in any exercise training. In study 2, to include the influence of exercise intensity into the design, participants were randomly assigned to two exercise intensities moderate (50-60% $\dot{V}O_2$peak) (L and OV/OB) and high intensity (80-90% $\dot{V}O_2$peak) (L and OV/OB) training groups. Exercise intensity was used as a continuous variable based on heart rate recordings as well as a covariate in the statistical analysis due to high variability of achieved target heart rates in the groups. Heart rate was continuously recorded throughout all sessions and an approximation of energy expenditure was calculated based on $\dot{V}O_2$peak assessment. Training intensity was controlled by a telemetric heart rate monitoring system (Activio, Activio Sport System, Sweden) displaying the live heart rates of each participant. HR data were analysed to calculate mean exercise intensity and estimates of energy expenditure throughout the 8 weeks training (study 2) to achieve a matched total exercise energy expenditure across groups.

Anthropometry

Body mass and composition were measured using a beam scale (Seca, Germany) and dual-energy x-ray absorptiometry (DXA; QDR 4500, Hologic, Bedford, MA, USA).

Resting metabolic measurements

In study 2, after 12 hour overnight fast participants, having refrained from exercise for 48 hours, resting metabolic rate (kcal.min^{-1}) and respiratory exchange ratio (RER; $\dot{V}CO_2/\dot{V}O_2$) were measured by indirect calorimetry (Oxycon Pro, Erich Jaegar, Germany) in a supine position for 30 minutes; heart rate (Polar RS800CX, Polar Electro Oy, Kempele, Finland) was also recorded.

Blood sampling and analysis

In study 2, under both overnight-fasting and postprandial conditions 12ml of venous blood was collected from the antecubital vein. Glucose was measured by the Accu-Chek Aviva glucose meter

(Accu-Chek® Aviva, Mannheim, Germany). For further measurements, plasma was aliquoted, frozen and stored at -80°C. Hormone measurements were carried out by enzyme-linked immunosorbent assay (ELISA) and plate reader (Fluostar Omega, BMG Labtech, Germany). ELISAs were carried out to measure amylin (Millipore, St. Charles, MO, USA) (intra assay CV: 12%), insulin (Mercodia, Uppsala, Sweden) (intra assay CV: 7%), leptin (BioVendor Research and Diagnostic Products, BioVendor – Laboratorni medicina a.s., Czech Republic) (intra assay CV: 7%), total ghrelin (Millipore; St. Charles, MO, USA) (intra assay CV: 4%), and PYY (Millipore Corporation, Billerica, MA, USA) (intra assay CV: 12%). The Homeostasis Model Assessment version 2 (HOMA2) (www.dtu.ox.ac.uk/homacalculator/) was used to calculate beta cell function, insulin resistance and insulin sensitivity. All samples were batch analysed and assayed in duplicate.

Test meal

In study 2, to analyse potential influence of chronic and phasic appetite hormone changes on individual BMI alterations, participants were given a liquid test meal (Resource® Energy Vanilla 200ml, Nestle, Switzerland) following overnight fast according to a modified protocol by Kraemer et al. (2011). The meal provided 300kcal of which 55% was carbohydrate, 30% fat and 15% protein. This test meal was chosen to avoid variability in intake composition and processing known from more complex meals. Blood samples were taken prior to the test meal at fasting state and precisely 1 hour after consumption. Timing of blood sampling was chosen due to former experiments selecting the time point with the strongest correlation between appetite hormone levels and BMI-based body type. Significant ($p<0.05$) correlations between BMI and appetite hormone levels at fasting (F), postprandial (PP) levels and alterations (CH) were found for insulin (F, *rho*= 0.49; PP, *rho*= 0.37), amylin (F, *rho*= 0.49; CH, *rho*= -0.48), PYY (CH, *rho*= -0.33), ghrelin (CH, *rho*=0.43), leptin (F, *rho*= 0.59).

Peak oxygen consumption

For both studies, peak oxygen uptake ($\dot{V}O_{2PEAK}$; $ml.kg^{-1}.min^{-1}$) was measured on a cycle ergometer (Corival 400, Lode, Groningen, Netherlands) using a graded exercise protocol with 1 minute stages (20 watts steps), until exhaustion. Oxygen and carbon dioxide were measured by a metabolic cart (Oxycon Pro, Erich Jaegar, Germany). Heart rate (Polar RS800CX, Polar Electro Oy, Kempele, Finland) and ratings of perceived exertion (Borg 1973) were collected at the end of every stage and at point of exhaustion. $\dot{V}O_{2PEAK}$ was achieved when one of three criteria was met: RER greater than 1.1, RPE of 20 or cycling cadence less than 60rpm. Control subjects in study 1 were not tested for $\dot{V}O_{2PEAK}$.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics 20. Data were analysed either by one-way ANOVA (baseline characteristics), ANCOVA using exercise intensity as a covariate or by mixed model ANOVA and appropriate post hoc analysis, after assumptions had been met and outliers removed. Pearson's and Spearman's rho correlations were used to analyse relationships between variables. Multiple regression analyses using the enter and backward methods were performed on variables of interest. All data are reported as means and ± standard deviation. Statistical significance was set at $p<0.05$.

Results

In the first study, 34 female participants of the 40 recruited finished the intervention. Mixed model ANOVA with repeated measures revealed that there were no significant alterations in weight/BMI after the 4 weeks, neither in the exercise training group nor in the non-exercising control group (Table 1). Consequently, exercise related energy expenditure was compensated and body weight/BMI was maintained. Further analysis of body composition showed that there was a significant reduction in body fat [%] in the exercise group, however, this effect was only seen in the lean participants who lost about 0.5 kg fat (significant effect of time ($p=0.018$), interaction of time x

194 trial (control/exercise) (p=0.041), and interaction of time x baseline body fat [%] (p=0.046)), (Table
195 1). Moreover, an increase in lean mass (kg) was significant only in the lean participants of the
196 exercise group, who gained about 1 kg lean mass (increase of lean mass over time (p=0.009),
197 interaction of time x baseline fat percentage [%] (p=0.028) and time x trial (control/exercise)
198 (p=0.05)), (Table 1). Individual alterations in body characteristics over the 4 weeks intervention
199 period are depicted in Figure 1; positive effects on body composition were restricted to lean
200 participants of the exercise group but without alteration of weight/BMI.

201 The second study used principally the same experimental design but omitting a non-exercising
202 group; the training program was performed for 8 weeks. Additionally, exercise energy expenditure
203 was matched across participants using a wider range of training intensities (50-90%VO2peak).
204 Training intensity was implemented as a covariate to investigate its possible influence on weight and
205 body composition. This was suggested based on outcomes of study 1 where body composition
206 changes were restricted to lean participants who trained on higher absolute intensity. Moreover,
207 fasting and postprandial blood samples were collected for the analysis of appetite hormones and
208 metabolites pre and post intervention. The design was chosen to confirm outcomes of study 1 with a
209 further focus on the investigation of underlying factors responsible for individual weight/BMI
210 responses to exercise in lean and overweight/obese females.

211 From the 56 recruited females for the 8 weeks training program, 36 females finished the study.
212 Baseline body characteristics and blood parameters of the participants are given in Table 2. OV/OB
213 participants had higher ($p < 0.05$) levels of BMI, weight, fat mass, lean mass, and RMR as well as
214 lower relative VO_2peak compared with L individuals (Table 2).

215 Training compliance was ~85 % across the training groups with no difference between groups; heart
216 rate based estimates of total exercise energy expenditure, amounting to ~3400 kcal after 8 weeks,
217 and was matched across the groups (Table 3). Moreover, mean training intensity in percent heart
218 rate reserve was about 65% with no difference between lean and OV/OB groups (Table 3).

Mixed model ANOVA with body type (BMI groups) as between factor and training intensity as covariate revealed that 8 weeks training did not lead to significant alterations of BMI/weight in either group (no significant main effect of time, or interactions of time x group) (Table 3); hence, both groups compensated the exercise energy expenditure over the training period confirming outcomes of study 1. In terms of body composition changes, females of the lean group lost body fat while participants of the OV/OB group remained unaltered after the training period (no significant time effect was reported for body fat [%] change but a significant (p=0.008) interaction of time x body type). Moreover, lean mass (kg) was not affected (non-significant time effect) but there was a significant interaction time x training intensity (p=0.025) supporting the hypothesis that lean mass changes have been influenced by training intensity (Table 3). A further splitting of the data (Table 4) in moderate and high intensity training groups without consideration of BMI shows that the higher intensity group tended to gain more lean mass than the moderate exercise group. Moreover, a significant correlation (R=0.458; p=0.006) between training intensity and $\dot{V}O_{2PEAK}$ showed that individuals with higher cardiovascular fitness tended to train harder.

In summary, the second study confirmed that lean and OV/OB females compensate exercise induced energy expenditure without losing weight but positive body composition changes were more apparent in lean participants being possibly related to training intensity.

To further investigate individuals' weight/BMI response to training (individuals' post intervention changes in BMI and body composition are shown in Figure 2), we analysed fasting and postprandial blood samples.

ANOVA analysis of pre intervention levels of the two groups revealed significant differences in fasting levels for leptin, PYY, insulin, and amylin between groups (Table 5). Moreover, postprandial increases in amylin and PYY were significantly different between L and OV/OB groups (Table 5). After 8 weeks exercise training, fasting and postprandial levels of amylin were significantly reduced in the OV/OB group but not in the L group (no significant main effect of time, significant interaction of time

x body type, p<0.001 for fasting and postprandial levels, p=0.004) (Table 5). The postprandial increase of amylin, which was significantly different between groups, was unaltered after the training revealing an unchanged higher increase of amylin after the test meal in L group females compared with females of the OV/OB group (Table 5). Multiple regression analysis showed that postprandial amylin levels after the intervention were determined (R^2=0.34, p=0.002, n=33) by fasting glucose levels (β=0.35, p=0.027) and postprandial increase in glucose (β=0.50, p=0.002). Fasting and postprandial levels of insulin, leptin, PYY, total ghrelin were unchanged after exercise training (no significant main effect and interactions) (Table 5).

To further associate hormonal levels with individuals' BMI response to exercise (see also figure 2), we performed multiple regression analysis (enter method) using appetite hormone levels as predictor variables and body characteristics for post intervention BMI changes. Analysis led to a significant model for the BMI change of participants who finished the training; the model used post intervention levels of leptin (β=0.59, p=0.002) and postprandial amylin change (β=-0.37, p=0.03), and pre-intervention BMI (β=-0.44, p=0.02) as predictor variables. The three variables explain 43% of the variance of the BMI alterations (R^2=0.43, p=0.002, n=30) after training. Other hormone parameters did not lead to significant model improvements.

Metabolic alterations

There were significantly higher levels in insulin sensitivity, beta cell function and lower insulin resistance in the L- than in the OV/OB group. However, comparisons of HOMA 2 parameters revealed no significant alterations after 8 weeks training. Additionally, $\dot{V}O_2$peak, RER, RMR, and fasting glucose levels were not significantly changed (Table 3).

Discussion

We conducted two exercise training interventions with sedentary females with concealed aims and objectives of the study and excluding participants who expressed an intention to lose weight. To our knowledge, this is the first exercise training study which tried to achieve *ad libitum* conditions for participants whilst avoiding the influence of explicit motivation towards weight loss. Both interventions did not lead to significant weight loss/BMI change in both OV/OB and L groups after 4 and 8 weeks training. This finding is consistent with our first hypothesis and we interpret this as indicative of intact weight regulation over the periods of the exercise training, even in females with high BMI (e.g. overweight/obesity). This outcome, considering the mean weight changes, as well as individual weight responses to exercise, is dissimilar to results published earlier (King et al. 2007, 2008). For example, King et al. (2008) reported considerable weight loss with high variability amongst overweight/obese participants and outcomes were skewed towards weight loss. This suggests that BMI/weight alterations in comparable training studies might be partially driven by participants' intention to lose weight with concomitant consequences for eating behaviour rather than a singular effect of exercise. Additionally, recent work showed that the window for a satisfactory increase in total energy expenditure is narrow; in a large, diverse population sample it was shown that only about 7-9% of the variance in total energy expenditure was explained by physical activity (Pontzer et al. 2016). These authors assume that homeostatic regulation not only affects weight but also total energy expenditure.

Our study results on group level (i.e. no weight change over time), though, do not explain the individuals' weight response to training which varied strongly from considerable weight loss to weight gain, a consistent finding in studies which lead to the concept of compensators and non-compensators (King et al. 2008). As mentioned before, body weight is influenced by homeostatic and hedonic mechanisms, with some authors suggesting that humans are more prone to be driven by hedonic regulation (Berthoud 2011). Indeed, exercise energy depletion could increase the incentive salience of food, like it is known from fasting (Berthoud 2011) and increasing hunger levels have previously been reported following exercise training (King et al. 2009). However, it was suggested

293 that alterations in food reward after exercise bouts are not influenced by exercise training and the
294 reward response seems to be more trait-like. Finlayson et al. (2011) did not find alterations in
295 wanting and liking of foods after 12 weeks training but participants who lost weight (responders)
296 had a lesser increase in food reward after a bout of exercise than participants who reduced weight
297 less than predicted (non-responders). Additionally, in our study, participants, not having the
298 objective to lose weight, could have responded to the exhaustion and sensation of effort related to
299 exercise in a self-rewarding manner with the selection of high palatable foods. Furthermore, poor
300 judgement of caloric expenditure could have reduced existing diet restrain. Clearly, these possible
301 factors might have contributed to the variance in the weight outcomes in our study. However, due
302 to our study design we were not able to collect data about any alterations in food reward. On the
303 other hand, it is known that both regulatory processes are heavily interlinked and difficult to
304 separate; in particular appetite hormones are repeatedly shown to influence 'liking' and 'wanting' or
305 reward perception, as well as influencing energy intake and energy metabolism (Volkow et al. 2011).
306 While we gathered no information about the individuals' motives of eating in our study, we still
307 gathered information about appetite hormones responses at fasting and postprandial levels to
308 analyse their possible contribution to the variability of weight/BMI changes after the exercise
309 training intervention. Post intervention, most of the tested appetite hormones revealed no
310 alterations in both groups maintaining the differences detected at baseline. Nonetheless, we found
311 significant alterations of amylin at fasting and postprandial levels in the OV/OB group, while the L
312 group revealed no changes after the 8 weeks training intervention. Reports about alterations in
313 amylin levels in response to exercise training are sparse; Izadpanah et al. (Izadpanah et al. 2012) and
314 Roberts at al. (2013) reported a reduction of amylin in response to a combined diet exercise
315 intervention in children with obesity for 14 days. Additionally, acute responses to exercise bouts
316 with a reduction of amylin after prolonged exercise bouts (Kraemer et al. 2011) and increase in
317 higher intensity bouts (Kraemer et al. 2002) were recently shown. Mechanistically, amylin expression
318 in beta cells was recently shown to respond directly to glucose availability via carbohydrate-

response-element-binding-protein (ChREBP) and thioredoxin-interacting-protein (TXNIP) (Jing et al. 2014). Indeed, our data revealed that amylin levels were significantly influenced by fasting levels and postprandial increase of glucose supporting this possible connection between amylin levels and altered glucose availability. Moreover, a positive associations between postprandial amylin levels and fasting glucose levels at post intervention was particular strong ($r=0.625$, $p=0.02$) in OV/OB group which highlights a possible connection between glucose availability and amylin levels. Clearly, fasting glucose levels can be influenced via sugar/carbohydrate intake (Sartor et al. 2013) as well as exercise (Sartor et al. 2010). Theoretically, a stronger depletion in glycogen storage during exercise in OV/OB individuals who might have more preferred carbohydrate utilization during exercise could have reduced glucose availability and could have led to reduced amylin levels with consequences for appetite and possible compensatory food intake.

Participation in exercise is often driven by a desire to lose weight (Teixeira et al. 2012). However, individual physiological differences may confound attempts to lose weight. In our study, observed amylin alterations contributed to the individual weight outcomes after the intervention. Indeed, our multiple regression analysis showed that hormone levels of leptin and postprandial amylin increase were best predictors for BMI changes (about 43% of BMI change variance explained). Leptin is known to be the most important tonic signal of fatness and mainly sensed in the hypothalamus for the intrinsic drive to eat and consequently for the regulation of body weight and energy expenditure (Blundell and Gillett 2001); therefore the contribution of leptin levels in the model is not unexpected. Additionally, leptin's links towards perceptual response to food was recently established identifying fasting leptin levels as a determinant of food reward (Hopkins et al. 2014). However, the strong contribution of amylin for the model is noteworthy. Amylin is known to play a role as a satiogenic signal, inhibits gastric emptying, and possesses glucoregulatory functions; agonists are well established in supporting weight loss in people with obesity (Smith et al. 2007). Moreover, amylin and leptin are shown to share important functions in the hindbrain and hypothalamus; it is suggested that amylin enhances leptin signalling and lead to transient alteration

of leptin responsiveness threshold (Trevaskis et al. 2010). Decreased amylin levels (postprandial and fasting) could increase leptin responsiveness threshold and could have led to increased energy intake in response to exercise training. Consequently, participants who displayed a combination of high levels of leptin and low postprandial increase in amylin were more prone to weight gain during exercise training. However, further work needs to support this interpretation.

Our work has several limitation; firstly, the selection of appetite hormones measured in this study does not exclude the importance and possible contribution of other hormones to the weight response in our study. Clearly, other hormones are consistently shown to be affected by training. Exercise training type, intensity, and duration are certainly factors that could influence outcomes in studies; besides the involvement of restricted dieting. Moreover, knowledge about altered food preference over the training period in terms of caloric density, macronutrient amounts and composition would have supported the interpretation of results largely. However, the need for not disclosing objectives of our study excluded the recording of precise food diaries and assessments of food liking, wanting and preference. *H*owever, our study used an ecological training programme which includes exercises and intensities commonly used in leisure centres or gyms. Finally, we used females only; consequently, we can't extrapolate findings towards males.

In summary, we have shown that under *ad libitum* condition 4 and 8 weeks exercise training did not result in weight loss in females over a wide range of BMI. Appetite hormone responses revealed decrease in amylin at fasting and postprandial levels, however this was restricted to overweight/obese participants. A large proportion of variance in BMI changes after training could be explained by postprandial amylin increase and leptin levels, pointing towards an important influence of amylin for weight regulation during exercise training.

Perspective

Exercise training is often performed with the objective of losing weight. However, individuals may face less than expected weight loss or even weight gain over an exercise training period. Clearly,

370 unrealistic expectations about the response of an individual to exercise training impairs exercise
371 participation, in particular in population groups who could largely benefit on many other health
372 levels other than weight loss. In our single blind exercise training study, excluding participants with
373 weight loss intentions, females within a wide range of BMI, did not lose weight on group levels.
374 However, individual weight gains or losses could be explained by appetite hormone levels. In
375 particular, levels of amylin and leptin could explain a significant proportion (43%) of the variance in
376 BMI changes post training. Our results highlight the need for individualized interventions tailored
377 also to the physiological and not only to psychological characteristics of clients in weight loss
378 programs.

379

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383

384 **Conflict of interest**

385 The authors declare no conflict of interest.

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508 Table 1: Participants characteristic pre and post 4 weeks exercise training (study 1)

	L Exercise (n = 10)		OV/OB Exercise (n = 7)		L Control (n = 10)		OV/OB Control (n = 7)	
Parameter (units)	Pre	Post	Pre	Pre	Post	Post	Pre	Post
Age (years)	22.4 ± 4.6		26.9 ± 3.9		22.5 ± 2.2		27.0 ± 4.8	
Weight (kg)	58.13 ± 6.27	58.66 ± 5.73	77.00 ± 9.85	77.2 ± 10.95	57.34 ± 9.78	58.22 ± 10.10	84.03 ± 5.26	83.53 ± 6.47
BMI (kg/m^2)	22.70 ± 2.14	22.92 ± 2.09	31.12 ± 5.60	31.21 ± 5.99	21.22 ± 2.46	21.55 ± 2.70	30.67 ± 2.09	30.67 ± 1.95
Fat percentage (%)	32.60 ± 5.91	31.39 ± 5.84*	43.93 ± 6.43	42.54 ± 7.05	29.90 + 4.09	29.80 ± 4.54	37.26 ± 2.51	37.20 ± 4.00
Lean mass (kg)	37.49 ± 3.67	38.56 ± 3.85*	42.30 ± 4.81	42.51 ± 4.67	38.59 ± 6.08	39.19 ± 6.26	52.63 ± 1.92	52.28 ± 2.51
VO_{2PEAK} (L/min)	1.87 ± 0.47	1.87 ± 0.36	2.07 ± 0.65	1.99 ± 0.51				
VO_{2PEAK} (ml/kg/min)	32.47 ± 8.34	31.85 ± 6.33	26.63 ± 7.15	25.31 ± 6.26				

*, significantly different to baseline

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517 Table 2: Anthropometric and metabolic parameters of participants at baseline (Study 2)

Parameters (units)	OV/OB (n=23)	L (n=11)
Age (years)	23.39 ± 5.70	24.55 ± 6.93
BMI (kg m^{-2})	30.27 ± 3.66 *	22.41 ± 2.14
Weight (kg)	82.78 ± 11.88 *	63.71 ± 5.60
Fat mass (%)	38.74 ± 4.88 *	29.32 ± 4.72
Lean mass (kg)	49.13 ± 5.44 *	43.32 ± 3.99
Fasting glucose (mmol l^{-1})	4.56 ± 0.42	4.51 ± 0.44
Total cholesterol (mmol l^{-1})	3.85 ± 0.83	3.59 ± 0.56
HDL (mmol l^{-1})	1.51 ± 0.47	1.68 ± 0.41
LDL (mmol l^{-1})	2.24 ± 0.71	1.75 ± 0.63
TG (mmol l^{-1})	1.06 ± 0.37	0. 80 ± 0.00
VO_2 peak (l min^{-1})	2.64 ± 0.49	2.92 ± 0.56
VO_2 peak (l $min^{-1}kg^{-1}$)	32.58 ± 6.27 *	45.89 ± 0.85
RMR (kcal d^{-1})	1619.2 ± 318.9 *	1361.4 ± 178.9
RER	0.77 ± 0.06	0.79 ± 0.07

* significant group difference $p<0.05$; High Density Lipoprotein, HDL; Low Density Lipoprotein, LDL; Triglycerides, TG; Resting Metabolic Rate, RMR; Respiratory Exchange Ratio, RER

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529 Table 3: Training parameters and alterations of anthropometric and metabolic characteristics of 8

530 weeks training study

Parameter (units)	OV/OB (n=23)	L (n=11)
Training Energy Expenditure (kcal)	3324.7 ± 1060.4	3194.2 ± 1344.0
Training intensity (Watt)	89.94 ± 36.13	78.84 ± 20.06
Training intensity (% Heart Rate Reserve)	60.47 ± 11.09	65.10 ± 11.98
Δ BMI (kg m^{-2})	0.15 ± 0.48	0.02 ± 0.33
Δ Weight (kg)	0.43 ± 1.69	0.08 ± 0.96
Δ Fat mass (%)	0.15 ± 1.43	-1.16 ± 1.12 #
Δ Lean mass (kg)	0.15 ± 1.23 †	0.61 ± 1.18 †
Δ Fasting glucose (mmol l^{-1})	0.08 ± 0.45	0.28 ± 0.40
Δ Total cholesterol (mmol l^{-1})	0.27 ± 0.64	0.23 ± 0.60
Δ HDL (mmol l^{-1})	-0.10 ± 0.23	0.05 ± 0.35
Δ LDL (mmol l^{-1})	0.25 ± 0.48	0.17 ± 0.50
Δ TG (mmol l^{-1})	0.12 ± 0.26	0.05 ± 0.18
Δ VO2peak (l min^{-1})	0.05 ± 0.41	-0.23 ± 0.32
Δ VO2peak (l $min^{-1}kg^{-1}$)	0.61 ± 5.10	-3.43 ± 4.74
Δ RMR (kcal d^{-1})	44.86 ± 250.95	116.57 ± 182.85
Δ RER	0.032 ± 0.08	0.024 ± 0.11

Δ represents changes from pre to post training; Significant ($p<0.05$) effect of group, *; significant ($p<0.05$) interaction (group x time), #; interaction (training intensity x time), †

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539 Table 4: Alterations in anthropometric and metabolic parameters after 8 weeks moderate and high

540 intensity exercise training

Parameters (units)	Moderate Intensity (n=16)	Change (post –pre intervention levels)	High Intensity (n=18)	Change (post –pre intervention levels)
Age (years)	23.06 ± 5.27		24.35 ± 6.74	
BMI (kg m^{-2})	27.14 ± 4.75	0.11 ± 0.61	28.11 ± 5.17	0.01 ± 0.62
Weight (kg)	74.13 ± 11.85	0.33 ± 1.64	78.83 ± 14.50	0.02 ± 1.76
Fat mass (%)	35.39 ± 6.44	0.04 ± 1.34	35.84 ± 6.84	-0.81 ± 1.74
Lean mass (kg)	45.84 ± 5.14	-0.01 ± 1.14	48.39 ± 6.50	0.55 ± 1.26
Fasting glucose (mmol l^{-1})	4.37 ± 0.39	0.30 ± 0.46†	4.75 ± 0.36	-0.02 ± 0.34†
Fasting cholesterol (mmol l^{-1})	3.81 ± 0.76	0.31 ± 0.74	3.71 ± 0.76	0.15 ± 0.49
HDL (mmol l^{-1})	1.72 ± 0.44	-0.14 ± 0.30	1.40 ± 0.40	0.03 ± 0.22
LDL (mmol l^{-1})	2.02 ± 0.61	0.30 ± 0.54	2.10 ± 0.80	0.10 ± 0.43
TG (mmol l^{-1})	0.90 ± 0.18	0.12 ± 0.26	1.04 ± 0.41	0.08 ± 0.24
VO_2peak (l min^{-1})	2.75 ± 0.53	-.0.84 ± 0.47	2.72 ± 0.52	0.02 ± 0.32
VO_2peak (l min^{-1} kg^{-1})	38.06 ± 8.39	- 1.18 ± 5.94	36.00 ± 9.52	0.02 ± 4.43
RMR (kcal d^{-1})	1460.3 ± 219.1	102.9 ± 187.7	1629.4 ± 356.9	19.8 ± 266.3
RER	0.78 ± 0.06	0.01 ± 0.10	0.77 ± 0.06	0.04 ± 0.07

† significant interaction (intensity * time) $p<0.05$; High Density Lipoprotein, HDL; Low Density Lipoprotein, LDL; Triglycerides, TG; Resting Metabolic Rate, RMR; Respiratory Exchange Ratio, RER

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547 Table 5: Appetite hormones and HOMA 2 parameters at baseline and after 8 weeks exercise training

	OV/OB (n=23)		L (n=11)	
	Pre	Post	Pre	Post
Fasting Leptin (ng ml^{-1})	36.25 ± 15.76 *	36.38 ± 16.40 *	16.00 ± 11.90	14.83 ± 12.52
Fasting Insulin (mU l^{-1})	7.52 ± 3.19 *	7.93 ± 3.69 *	4.34 ± 1.93	4.84 ± 2.61
Postprandial Insulin (mU l^{-1})	40.99 ± 19.43 *	47.48 ± 19.45 *	31.05 ± 17.35	38.15 ± 23.50
Postprandial Insulin Change (mU l^{-1})	33.46 ± 19.21	39.55 ± 19.41	26.27 ± 17.95	33.47 ± 23.59
Fasting Amylin (pg ml^{-1})	16.16 ± 3.85 *	12.25 ± 3.33 #	11.96 ± 6.20	11.66 ± 5.27
Postprandial Amylin (pmol l^{-1})	20.42 ± 3.64	17.55 ± 3.96 #	18.77 ± 7.89	20.96 ± 7.74
Postprandial Amylin Change (pmol l^{-1})	4.26 ± 2.76 *	5.35 ± 4.45 *	8.27 ± 4.69	9.64 ± 6.82
Fasting Ghrelin (pg ml^{-1})	677.0 ± 254.3	674.5 ± 244.8	797.4 ± 259.2	823.4 ± 321.7
Postprandial Ghrelin (pg ml^{-1})	452.3 ± 205.0	491.5 ± 216.4 #	566.3 ± 200.2	524.1 ± 179.2
Postprandial Ghrelin Change (pg ml^{-1})	-224.71 ± 126.72	-183.00 ± 93.74#	-231.13 ± 87.67	-299.32 ± 162.07
Fasting PYY (ng/ml)	146.85 ± 53.17	147.60 ± 64.92	118.70 ± 60.71	133.35 ± 50.89
Postprandial PYY (ng/ml)	206.73 ± 63.29	243.56 ± 54.90	227.38 ± 75.74	241.78 ± 81.36
Postprandial PYY Change (ng/ml)	62.87 ± 65.70*	95.96 ± 53.72	108.68 ± 40.30	108.43 ± 46.10
Beta Cell Function (%)	111.34 ± 31.14 *	109.91 ± 30.37 *	76.73 ± 22.90	73.33 ± 26.67
Insulin Sensitivity (%)	125.19 ± 55.43 *	118.19 ± 48.85 *	221.09 ± 113.02	200.09 ± 91.49
Insulin Resistance (IR)	0.95 ± 0.41 *	1.02 ± 0.48 *	0.55 ± 0.25	0.62 ± 0.34

Significant ($p<0.05$) effects of group, *, interaction (group x time), #

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Figure 1: Individual changes in body characteristics in control and exercise group after 4 weeks exercise training. Black bars depict changes of overweight/obese individuals and empty bars of lean individuals.

576 Figure 2: Individual changes in body characteristics after 8 weeks exercise training. Black bars depict

577 changes of overweight/obese (OV/OB) individuals and empty bars of lean individuals (L).