A cross-over experiment to investigate possible mechanisms for lower BMIs in people who habitually eat breakfast

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BACKGROUND/OBJECTIVES: The body mass index (BMI) of breakfast eaters is frequently reported to be lower compared with that of breakfast skippers. This is not explained by differences in energy intakes, indicating there may be other mechanisms serving to drive this paradoxical association between breakfast and BMI. This study aimed to investigate the effect of eating breakfast versus morning fasting on measures predominantly of metabolism in lean and overweight participants who habitually eat or skip breakfast. SUBJECTS/METHODS: Participants (n=37) were recruited into four groups on the basis of BMI (lean and overweight) and breakfast habit (breakfast eater and breakfast skipper). Participants were randomly assigned to a breakfast experimental condition, breakfast eating or no breakfast, for 7 days and then completed the alternative condition. At the end of each breakfast experimental condition, measurements were made before and after a high carbohydrate breakfast of 2274 ± 777 kJ or a rest period. Resting metabolic rate, thermic effect of food (TEF), blood glucose, insulin and leptin levels were recorded. Hunger and 'morningness' were assessed and pedometers worn. RESULTS: Lean participants had lower fasting insulin levels (P = 0.045) and higher insulin concentrations following breakfast (P = 0.001). BMI and breakfast habit did not interact with the experimental breakfast condition, with the exception of hunger ratings; breakfast eaters were hungrier in the mornings compared with breakfast skippers in the no breakfast condition (P = 0.001). CONCLUSIONS: There is little evidence from this study for a metabolic-based mechanism to explain lower BMIs in breakfast eaters.

INTRODUCTION

Body mass index (BMI) is frequently reported to be lower in adults who habitually eat breakfast than in people who typically skip breakfast.1–5 However, a mechanism explaining this possible difference has not been established.6 Contenders for a mechanism include differences in food intakes4,7 and/or energy expenditure (EE).8 However, there is now evidence that eating breakfast may actually increase energy intakes,9 as also reported by the participants from this study who ate 671 ± 1808 kJ/day more when eating breakfast compared with not eating breakfast.10 This makes the difference in BMI even more unexpected and emphasises the need to investigate other potential mechanisms. Skipping breakfast has been shown to elevate blood glucose levels and alter metabolism including the resting metabolic rate (RMR) and the thermic effect of food (TEF) of people with a range of BMIs,11 and this could also have a role in establishing metabolic differences between breakfast eaters and breakfast skippers as both contribute to EE. Furthermore, leptin, an important peripheral regulator of energy metabolism, has a role in maintaining energy balance and correlates with body fat mass and the BMI.12

Farschi et al.13,14 described differences in post-prandial thermogenesis following regular and irregular meals in lean and obese women, reporting a lower TEF following irregular meal frequency that could contribute to weight gain in the long term, and impaired post-prandial insulin sensitivity in lean women after omitting breakfast.15 However, some research14,16 did not report the participants' breakfast habits, and this could be of relevance as differences in BMI between breakfast eaters and skippers are possibly associated with differing morning habits.17 Such habits may in turn be linked to a preference for early or late rising and being more active earlier or later in the day, respectively; these patterns have been considered by researchers by reference to the concept of 'morningness',18 and these time of day preferences may be linked to caffeine intakes. Several studies19,20 have shown that people who prefer to be active in the evening consume more caffeine compared with those who are morning active. Caffeine not only increases alertness and wakefulness but may also increase daily EE and reduce appetite.21,22 There is some evidence of greater weight loss in obese women who switch their usual morning routines from either eating breakfast to skipping breakfast or vice versa.23 However, a more recent randomised controlled trial where healthy adults were instructed to eat or skip breakfast found no noticeable effects of breakfast regime on weight loss.24

At present the available evidence is unable to clarify a mechanism that links BMI with the frequency of breakfast consumption; thus, studies aimed at explaining the underlying differences between breakfast eaters and breakfast skippers who are lean and overweight are required.6 Given the role of personal daily routines associated with morning eating, such a study should consider usual breakfast habits and morningness. Therefore, the present study investigated the effect of eating breakfast and morning fasting on measures of metabolism including postprandial TEF, activity levels, glucose, insulin and leptin levels, along with morningness, caffeine intake and pedometer scores in lean and overweight healthy people who habitually eat or skip breakfast.

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MATERIALS AND METHODS

Participants

The study set out to recruit participants who could be divided into the following four groups: (1) lean breakfast eaters, (2) lean breakfast skippers, (3) overweight breakfast eaters and (4) overweight breakfast skippers. The lean groups were defined by the participants having a BMI under 25 kg/m2 and the overweight groups a BMI over 25 kg/m2 (three participants in each
of the overweight groups could be classified as obese). In terms of breakfast habit, an habitual 'breakfast eater' was defined as someone who considered themselves to eat breakfast regularly and had eaten breakfast ⩾5 days in the last week, which had consisted of 4418 kJ.25 An habitual 'breakfast skipper' was someone who considered themselves not to be a regular breakfast eater and had eaten breakfast on 2 days or less in the past week.

A minimum total sample size of n=34 was determined on the basis of presumed and practically important differences in energy intake equivalent to a medium effect size of d = 0.50, power of 80% and a two-tailed alpha of 0.05 using G*Power v3.1.15,26 Thirty-seven healthy male and female participants (32.9 ± 13.5 years) were recruited and completed the study (Table 1). Exclusion criteria included dieting, diabetes, symptoms such as dizziness, fainting and blackouts, high blood pressure or cholesterol medication. Female participants with a hysterectomy or on hormone replacement therapy were excluded. In menstruating women, all
measurements were made during the luteal phase of the menstrual cycle.

Design

The study employed a randomised cross-over design consisting of two 7-day experimental periods plus a minimum of a 1-week wash-out in between. Participants were randomly assigned to either the breakfast eating (BE) condition, where they consumed breakfast within an hour of waking in the morning, or the no breakfast (NB) condition, where they were asked to refrain from eating until midday; then following the washout period, participants took part in the alternate experimental condition. Participants attended the laboratory on the first morning of each breakfast condition and the morning after the final day of each test condition for assessment. Ethical clearance for the study was granted by the University of Roehampton Ethics Committee (Ref: LSC 11/ 010). All participants completed a health screen questionnaire and gave written informed consent before participating.

At a familiarisation session, participants answered questions related to breakfast habits, completed the composite morningness questionnaire18 and a questionnaire to measure caffeine intake (EL Gibson, unpublished, questionnaire analysis conducted using Food Standards Agency data).27 Anthropometric data are reported in Table 1.

Table 1. Participant characteristics (*n* or mean ± s.d.)

Weight	*Lean*		*Overweight*	
Breakfast habit	*Eater*	*Skipper*	*Eater*	*Skipper*
n	9	9	10	9
Male/female (*n*)	4/5	5/4	3/7	4/5
Age (years)	30.0 ± 7.9	29.0 ± 8.4	36.2 ± 15.6	36.1 ± 18.0
Body mass index (kg/m^2)	21.6 ± 1.3	21.1 ± 2.2	30.5 ± 6.7	28.7 ± 3.3
Body weight (kg)	66.7 ± 5.9	60.7 ± 8.4	91.2 ± 25.1	81.9 ± 10.7
Height (m)	1.76 ± 0.09	1.70 ± 0.09	1.72 ± 0.11	1.69 ± 0.06
Waist circumference (cm)	79.4 ± 5.6	75.4 ± 6.4	97.7 ± 18.0	89.3 ± 12.0

Free-living procedures

Physical activity data. Participants were required to wear a pedometer (Yamax Digiwalker SW-200, Tokyo, Japan) for the duration of the study and eport the total daily step count it recorded. Participants were requested to attach the pedometer to the waist band of their clothing as soon as they arose in the morning and remove it when they went to bed.

Laboratory procedures

*Protocol of laboratory visit*s. Participants were asked to arrive at the laboratory at 0800 h for each testing session having fasted from 2200 h the evening before and avoided strenuous exercise for the previous 24 h. After at least 10 min rest in the supine position, baseline data recording commenced. RMR and whole blood glucose were measured and blood samples were taken to measure insulin and leptin levels. This was then followed by a 30-min intervention period during which participants either consumed breakfast or rested. Immediately after completion of the breakfast meal or rest period, participants underwent the first of a series of six repeated measurement sessions. During this time the participants remained in the laboratory under controlled conditions. For each

measurement session, hunger, EE and whole blood glucose were measured. At the fifth of the six repeated test measurements (2 h post intervention), additional blood samples for insulin were taken.

Breakfast consumption. On the experimental test day at the end of the BE week, the meal was eaten in the food laboratory and consisted of some or all of cereal, toast, fruit juice, tea, coffee, fruit and yoghurt. Participants served themselves and were permitted to eat as much as they wanted of the foods provided within 30 min. The mean energy consumed during breakfast on the experimental test days was 2274 ± 777 kJ. There was no evidence for differences in the amounts eaten at breakfast between groups. Participants in the NB condition rested in the physiology laboratory for the 30-min period. Energy expenditure: RMR and TEF. Baseline RMR was measured using the Douglas Bag technique while the participants were lying supine. Post intervention (BE or NB) EE was also measured using the Douglas bag technique as part of the six repeated measurement sessions. RMR and EE were calculated using the Weir equation.28 The TEF was calculated as the area under the curve (AUC) using the trapezoid method as absolute EE above baseline RMR for 150 min after the breakfast intervention.29

Blood sampling and analysis. Blood samples obtained from finger pricks were collected into microvettes that contained heparin fluoride for glucose sampling and clot activator for insulin and leptin. Blood glucose was measured immediately using an YSI 2300 Stat Plus blood glucose analyser (Fleet, UK). For blood glucose, baseline concentrations were recorded and the AUC from 0 to 150 min was calculated for post-intervention readings, using the trapezoid method.30 Blood samples for insulin and leptin were left to clot at room temperature for 30 min before being centrifuged at 1000 g (2500 r.p.m.) for 5 min at 20 °C. The serum was extracted and stored at − 20 °C. Insulin concentrations were later measured using a DRG Insulin ELISA kit (DRG Instruments, Marbury, Germany). Insulin concentrations at baseline and 2 h post intervention were reported, and insulin resistance was determined using the following formula. Homeostasis model assessment for insulin resistance (HOMA-IR) = fasting serum insulin μIU/ml x fasting blood glucose (mmol/l)/22.5.31 Leptin concentrations were tested using a Quantikine Human Leptin Immunoassay (R&D Systems, Oxford, UK). Manufacturers specified an intraassay coefficient of variation of 3.0–3.3% and an inter-assay coefficient of variation of 3.5–5.4%.

Hunger ratings. Subjective hunger ratings were assessed using the visual analogue scale, which consisted of a 100-mm line with words at each end to describe the two extreme hunger scenarios.32 The data were analysed as the baseline reading (taken on arrival at the lab) and the mean of the six post-breakfast intervention readings.

Statistical analysis

IBM SPSS Statistics 19 (IBM UK Ltd, Portsmouth, UK) and Microsoft Excel 2007 were used for statistical analysis. Normality of data was evaluated on the basis of Shapiro–Wilk's test and histograms; equality of variances was assessed using Levene's test. ANOVA models with two between-subject factors (BMI and breakfast habit) were generated to investigate the effects of the repeated measures test condition (breakfast versus no breakfast). 2 × 2 factorial ANOVAs were used to compare effects of BMI and breakfast
habit on TEF, caffeine intake and morningness. Summary statistics are reported in tables as means ± s.d.'s and in figures as means ± one s.e., unless otherwise indicated. Treating the P-value as a continuous variable, analyses were deemed to provide good evidence for an effect when P$<$0.05, whereas P-values$\leqslant$ 0.10 were considered to provide some evidence of an effect.33,34

RESULTS

The analysis did not indicate any large effects of the experimental conditions, except for expected differences in hunger ratings, glucose and insulin levels, following the consumption of breakfast. The controlled confounds BMI and breakfast habit did not interact with the experimental test condition; with the exception of the hunger ratings, there was no evidence for an effect of any of the two-way interactions between experimental condition, BMI and breakfast habit.

Physical activity

Participating in the BE condition as opposed to the NB condition had no effect on pedometer scores as assessed by step count averaged over the 7 days spent in each breakfast condition (P = 0.57); similarly, there was no evidence for interactions between experimental test condition and BMI (P = 0.28), test condition and breakfast habit (P=0.99) and the 3-way interaction between all three variables and step count data (P = 0.87). BMI or breakfast habit alone did not affect step count (P = 0.83 and 0.39, respectively); however, there was good evidence for an interaction between BMI and breakfast habit on mean daily step count (P = 0.005): overweight breakfast skippers had a mean daily step count of 10 465 ± 3263 steps and lean skippers 7743 ± 2969 steps. Lean habitual breakfast eaters had a mean step count of 9563 ± 2012 steps and overweight habitual breakfast eaters 7209 ± 2344 steps.

Energy expenditure: RMR and TEF

RMR was not affected by the experimental test condition (P = 0.97), and there was no evidence that breakfast interacted with the intervention and BMI (all P -values$\geqslant$ 0.12) (Table 2). Figure 1 shows TEF post breakfast

consumption (0–150 min) for participants grouped by BMI and breakfast habit. There was some evidence that lean participants had a greater TEF (173.92 ± 69.54 kJ) compared with overweight participants (131.36 ± 75.65 kJ; P = 0.086), but breakfast habit was unrelated to TEF (breakfast eaters 147.87 ± 56.35 kJ had similar values to skippers 156.50 ± 92.07 kJ; P = 0.74).

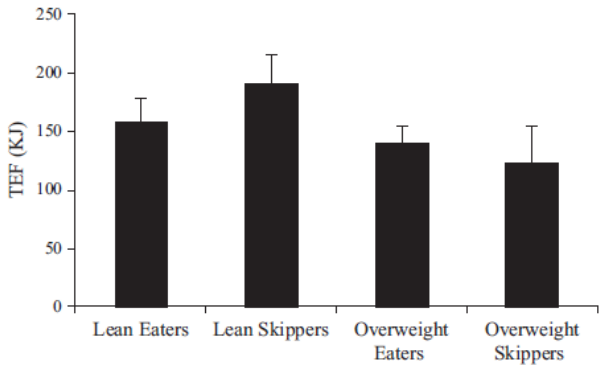

Figure 1. Mean TEF post breakfast (0–150 min), measured as iAUC of absolute EE above the absolute resting metabolic rate. Error bars represent ± one s.e.

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Table 2. Metabolic and blood measures in the two test conditions: breakfast eating (BE) and no breakfast (NB) (mean ± s.d.)

Group	*BE condition*				*NB condition*			
	Lean eaters	*Lean skippers*	*Overweight Overweight skippers*	*Overweight eaters*	*Lean eaters skippers*	*Lean skippers*	*Overweight*	*eaters*
RMR (kJ/day)	6867 ± 1242	6217 ± 1563	7377 ± 1763	7080 ± 1010	6749 ± 875	6791 ± 1493	7173 ± 1472	6850 ± 991
Glucose AUC 0–150 min (mmol · min/L)	833.8 ± 91.1	831.3 ± 94.4	880.5 ± 88.9	893.5 ± 123.5	662.1 ± 50.5	690.2 ± 37.5	676.1 ± 62.0	691.3 ± 74.4
HOMA-IR 2.50	1.80 ± 1.02	1.81 ± 0.59	2.53 ± 1.28	2.79 ± 1.02	1.63 ± 0.48	1.79 ± 0.50	2.31 ± 1.21	2.93 ±
Insulin concentration (μIU/ml)[a] 12.3	9.6 ± 5.2	8.4 ± 3.0	11.8 ± 5.7	13.0 ± 4.6	7.9 ± 2.1	8.5 ± 2.5	11.0 ± 5.5	13.7 ±
Insulin concentration (μIU/ml)[b]	24.7 ± 21.8	22.3 ± 17.9	36.6 ± 25.1	22.6 ± 13.8	6.4 ± 2.0	9.0 ± 3.5	9.7 ± 4.1	7.9 ± 2.0
Leptin: pre-breakfast intervention 12428 (pg/ml)[a]	10162 ± 5805	9691 ± 7462	29779 ± 27910	15335 ± 13894	9449 ± 4991	8347 ± 7254	26862 ± 19983	14100 ±

Abbreviations: AUC, area under the curve; HOMA-IR = Homeostasis model assessment for insulin resistance; RMR, resting metabolic rate. [a]Pre-breakfast intervention. [b]2 h post breakfast intervention.

Blood measures

Figure 2 presents glucose concentrations at 30-min intervals post (Po0.001) on AUC glucose levels (150 min), with higher readings in the BE condition (BE: 860 ± 99.8 mmol _ min/L; NB: 680 ± 56.7 mmol _ min/L) (Table 2)Insulin data were based on 35 participants, because of the insufficient volume of blood samples taken from two participants in one of the test conditions. There was good evidence that BMI was related to baseline insulin concentration (P = 0.045); these were lower in lean compared with overweight participants. There was good evidence for an effect of breakfast condition on 2 h post meal insulin levels, with higher insulin concentrations reported for the BE than for the NB condition (Po0.001). No other interactions were reported for baseline or post breakfast insulin concentrations (P ⩾0.22); (Table 2). BMI and insulin resistance were linked; HOMAIR was higher for the overweight compared with the lean group (P = 0.024). There was no evidence for an effect of test condition or breakfast habit on HOMA-IR values (P-values⩾0.49). Leptin concentrations were available for 34 participants because of insufficient volumes of samples collected from 3 participants in one of the test conditions (Table 2). There was no evidence for an effect of test condition or breakfast habit on leptin concentration (P = 0.18 and 0.30, respectively). There was good evidence for an

association between BMI and leptin levels (P = 0.026), with the overweight group having greater leptin concentrations compared with the lean group.

Hunger

Hunger rating curves were very different for the BE and the NB conditions (Figure 3); there was good evidence for an effect of test condition (P = 0.042) and breakfast habit (Po0.001) on baseline hunger, whereby hunger scores were greater in the BE compared with NB condition, and habitual breakfast eaters were more hungry compared with habitual skippers. Also, there was good evidence for an interaction between BMI and breakfast habit (P = 0.008). Overweight habitual eaters were slightly hungrier at the start of the experimental day compared with overweight habitual skippers, whereas lean habitual breakfast eaters were the hungriest and lean habitual skippers the least hungry. As anticipated, higher mean hunger ratings were observed in the NB compared with BE condition (Po0.001), and habitual breakfast skippers had lower mean hunger ratings compared with habitual breakfast eaters (P = 0.004). There was also good evidence for an interaction between test condition and breakfast habit (Po0.001). In the BE test condition habitual breakfast eaters and skippers expressed similar mean levels of hunger, whereas habitual breakfast eaters were hungrier compared with habitual breakfast skippers in the NB condition.

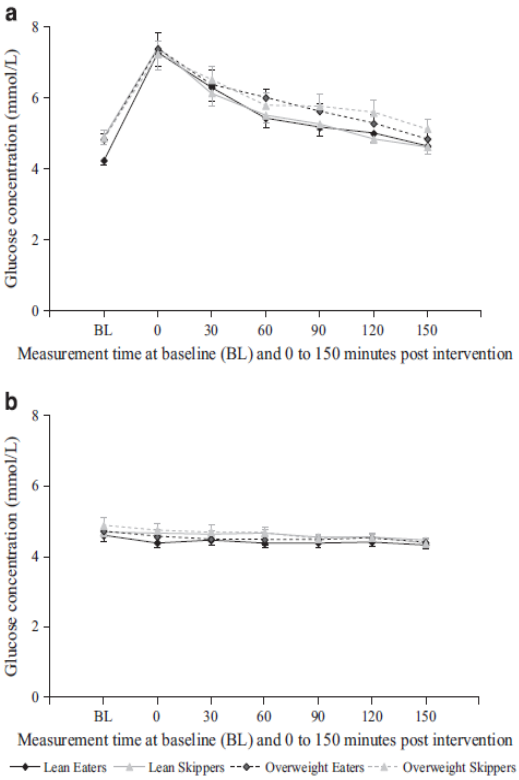

Figure 2. Response–time curves for glucose concentration at baseline (BL) and at 30-min intervals after the breakfast (**a**) and no breakfast (**b**) test conditions. Errors bars represent ± one s.e.

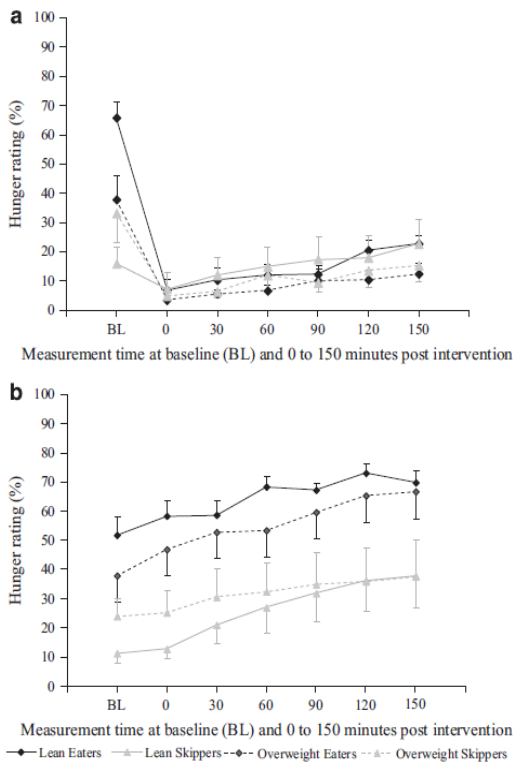

Figure 3. Mean hunger rating curves at baseline (BL) and at 30-min intervals (**a**) post breakfast and (**b**) no breakfast intervention. Error bars represent ± one s.e.

Morningness

Morningness scores were similar across all groups (Figure 4). Breakfast consumption was not linked to morningess (P = 0.15). Furthermore, BMI was not related to morningness (P = 0.58).

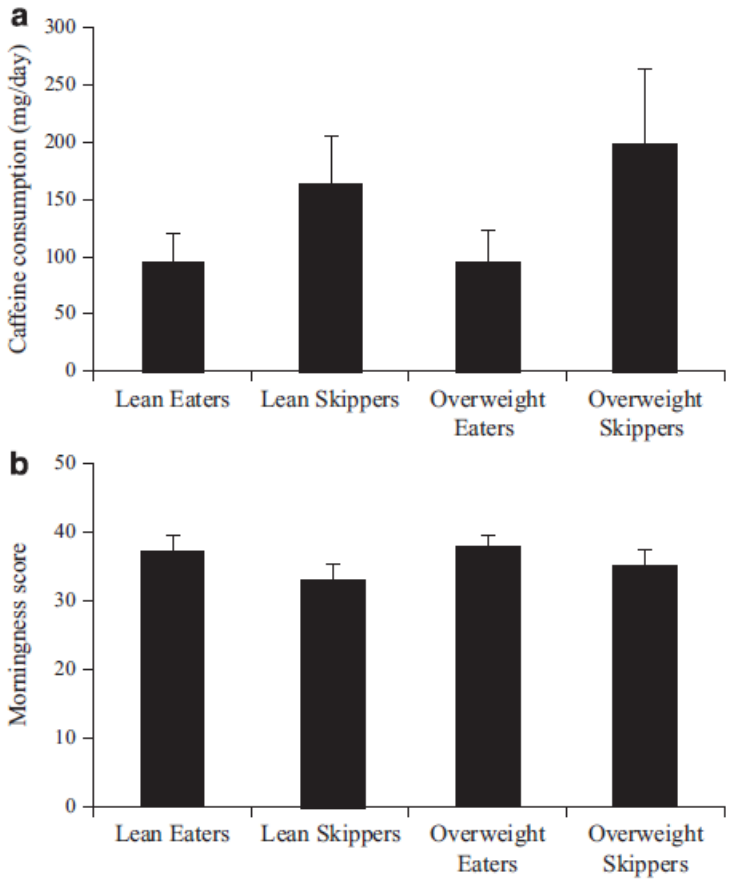

Figure 4. Mean total caffeine intake (**a**) and morningness scores (**b**). Error bars represent ± one s.e.

Caffeine

There was some evidence of an association between breakfast habit on caffeine intake (P = 0.052), with breakfast skippers consuming 181.50 ± 160.65 mg/day and breakfast eaters 95.49 ± 82.72 mg/day. Caffeine intake was unrelated to BMI and the interaction between BMI and breakfast habit (P-values40.65, see Figure 4).

DISCUSSION

Many cross-sectional studies[1,5,8] provide evidence that breakfast eaters are slimmer compared with breakfast skippers. Yet, it has also been shown that daily energy intakes may actually be higher when breakfast is consumed.[9,10] Furthermore, the present study offers no evidence that daily activity levels are associated with eating or not eating breakfast, supporting findings from a previous experiment.[17] If indeed apparent differences in BMI between breakfast eaters and skippers are not a result of differences in energy intakes or activity levels, other mechanisms that influence energy balance must be at play. Although glucose, insulin and hunger levels were affected by the breakfast intervention, there was a lack of interactions between the breakfast intervention and the potential confounders BMI and breakfast habit. Therefore,evidence for a mechanism to explain why breakfast eaters tend to be leaner compared with breakfast skippers was not forthcoming from the present experiments. The non-significant findings support the recent criticism of positive reporting bias in the field of breakfast research[6] and serve to refocus research towards alternative mechanistic explanations. In the present study, there was no evidence for an association between the breakfast condition and activity levels, represented by pedometer scores. Overweight habitual breakfast skippers recorded the highest mean daily step count and, although unreported, it is remotely possible that this group was increasing their activity as well as skipping breakfast in an attempt to lose weight, although participants were screened out during recruitment if they reported to be dieting. There were no methodological reasons why the overweight groups would have higher pedometer scores.[35] Future

studies should consider using accelerometers to determine more accurate levels of physical activity as one study has shown that regular breakfasting may increase activities of light intensity during the morning in lean adults.[36]

Despite no differences in RMR between groups, there was some evidence for an association between BMI and TEF, with lean participants demonstrating higher TEF on average. However, therewas no effect of breakfast habit on TEF. Other studies have shown that skipping breakfast and/or irregular meal patterns can result in blunted TEF,[13] and blunted TEF could decrease overall EE, contribute to weight gain and increase insulin resistance.[37,38] Given that TEF is a key component of energy balance, and that energy balance may in some cases only be achieved over a period of weeks,[39] it is conceivable that a study with a longer time frame is required.

Other than as a result of eating breakfast, there was no evidence for differences in blood glucose levels between groups.There was good evidence for an effect of BMI on insulin resistance;lean participants had lower baseline insulin levels and higher insulin concentrations following breakfast than did overweight participants. Overweight participants may have had some insulin resistance as a result of their body weight and location of body fat.[40] Other studies have noted changes in insulin secretion following irregular meal patterns and have suggested that this could affect circadian secretions of insulin.[14,41] However, future studies should consider increasing the number of insulin measurements taken and investigating post-lunch effects. Leptin concentrations were higher in the overweight groups compared with the lean groups, similarly to the findings of other studies,[42] but did not vary between the different test conditions in this study. There are studies that have reported that leptin levels are affected by sleep and meal timing;[43] however, other research[44] has suggested that this hormone may not be involved in shortterm regulation of food intake but has a greater role when energy stores change, and thus a longer time frame would be required to investigate this.

Participants who were habitual breakfast eaters were hungrier in the mornings, and this was particularly pronounced in the lean breakfast eaters whose hunger ratings may reflect an habitual expectation to eat breakfast and the possibility of reduced food intake the night before.[10] There was also some evidence for greater consumption of caffeine in breakfast skippers compared with breakfast eaters. Caffeine could suppress the appetite or hunger[45] for breakfast, but equally this could be linked to personality type and associated with a degree of morningness as research has shown that evening types are more likely to consume greater amounts of caffeine[19,20] and are more likely to skip breakfast.[46] Other studies have shown that routine breakfast eaters are more likely to be morning active, that is, report high levels of morningness,[17,47,48] although our own data did not provide further evidence of this relationship.

Our data add to previous research indicating the lack of association between breakfasting behaviour and physical activity[17] and lower self-reported energy intakes when breakfast is not consumed.[9,10,49] Other potential mechanisms underlying a relationship between breakfasting frequency and BMI that are worth exploring include the role of molecular genetics and appetite hormones.[50,51] However, perhaps at present the most parsimonious explanation for observed cross-sectional associations between breakfast and BMI reported by other researchers [1–3]is that breakfast eaters are generally healthier and exhibit corresponding habits that include healthy eating. Thus, maybe eating breakfast is simply a marker for a healthy lifestyle,[48,52] and in turn psychosocial processes[53] that can potentially help elucidate the link between breakfast and BMI may also warrant further exploration.

In summary, our study represents an experimental manipulation, with a protocol of high ecological validity, to compare the predominantly physiological effects of breakfasting versus morning fasting in lean and overweight habitual breakfast eaters and skippers. The data suggest that the measured physiological differences that arise between breakfasting and fasting are at best small. Further research is required to expand the search for the putative causal link between breakfast consumption and BMI.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

JH, LH and SR contributed to study design; LH, JH, SR and TS contributed to study coordination; TS, LH, JH, SR, MVM and JE contributed to data collection; TS contributed to supervision of data collection; TS and JH contributed to data analyses, SR contributed to drafting of manuscript; all authors contributed to input on data and manuscript.

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