The Joint Winter Meeting between the Nutrition Society and the Royal Society of Medicine held at The Royal Society of Medicine, London on 8–9 December 2015

Conference on 'Roles of sleep and circadian rhythms in the origin and nutritional management of obesity and metabolic disease'
Cuthbertson Medal Lecture

Is breakfast the most important meal of the day?

James A. Betts[1]*†, Enhad A. Chowdhury[1]†, Javier T. Gonzalez[1], Judith D. Richardson[1], Kostas Tsintzas[2] and Dylan Thompson[1]

[1]*Department for Health, University of Bath, Bath BA2 7AY, UK*
[2]*School of Life Sciences, Queen's Medical Centre, University of Nottingham, Nottingham NG7 2UH, UK*

The Bath Breakfast Project is a series of randomised controlled trials exploring the effects of extended morning fasting on energy balance and health. These trials were categorically not designed to answer whether or not breakfast is the most important meal of the day. However, this review will philosophise about the meaning of that question and about what questions we should be asking to better understand the effects of breakfast, before summarising how individual components of energy balance and health respond to breakfast *v.* fasting in lean and obese adults. Current evidence does not support a clear effect of regularly consuming or skipping breakfast on body mass/composition, metabolic rate or diet-induced thermogenesis. Findings regarding energy intake are variable, although the balance of evidence indicates some degree of compensatory feeding later in the day such that overall energy intake is either unaffected or slightly lower when breakfast is omitted from the diet. However, even if net energy intake is reduced, extended morning fasting may not result in expected weight loss due to compensatory adjustments in physical activity thermogenesis. Specifically, we report that both lean and obese adults expended less energy during the morning when remaining in the fasted state than when consuming a prescribed breakfast. Further research is required to examine whether particular health markers may be responsive to breakfast-induced responses of individual components of energy balance irrespective of their net effect on energy balance and therefore body mass.

Fasting: Energy balance: Health: Thermogenesis

The broad field of nutrition and health is rife with myths, misconceptions and frequently posed yet seemingly fundamental questions that we intuitively feel should have simple answers. Is a calorie a calorie? Is obesity due to eating too much or doing too little? Is breakfast the most important meal of the day? Often there are simple answers, the first two being central to the themes considered in the present review and both absolutely 'yes' (just as a second is a second, one thermochemical calorie is simply a unit of measurement equivalent to 4·18 J). The third is not so easily answered and there can be no correct response until we refine that question; 'If you wish to converse with me' said Voltaire 'define your terms'. In this case, we must define both what is

---

meant by breakfast and what is meant by important (i.e. important for what?).

Framing our question in terms of whether breakfast is the most important meal of the day also implies some inherent value in comparing breakfast with other daily eating occasions. Why should the potential benefits of breakfast and therefore our decision about breakfast consumption depend on the relative importance of lunch or dinner? For example, breakfast consumption is unlikely to be more important for our general health than physical exercise or not smoking but that does not discount that breakfast may be sufficiently important to form part of a wider healthy lifestyle[1–4]. Indeed, markers of a healthy lifestyle are associated with frequent breakfast consumption, which confounds interpretation of causal links between breakfast and good health.

The true question to be explored in the present review therefore concerns our daily decision about when to interrupt an extended period of fasting (e.g. overnight). Whether what might then be defined as breakfast and has the potential to cause meaningful effects on various health markers across different populations and contexts can then be considered. While this approach is unlikely to fit the false dichotomy through which the media obsessively brand any given health strategy as universally good or bad, the truth is understandably less extreme or consistent (i.e. breakfast is probably more or less important for some outcomes/people per day than for others).

What do we mean by 'Breakfast'?

One issue contributing to the apparently conflicting findings in this area is that there is no universally accepted definition of breakfast[5]; and why should there be? Without thinking about this too hard, it might at first seem logical simply to define breakfast as the first meal of the day. This is then consistent with the etymology to 'break' the 'fast' and may work for some as a general description of breakfast but is logically flawed and not overly helpful as a scientific definition. Consider an individual who breaks their fast shortly after waking by ingesting energy from carbohydrate, protein and fat in the form of coffee with milk and sugar, then nothing else until early-afternoon when the same mixed-macronutrients (plus alcohol) are consumed but this time in the form of spaghetti Bolognese and wine. Opinions may now be divided about whether this person had breakfast at all and, if so, whether it was coffee and/or spaghetti and wine. Can we count a cup of coffee as a meal? Was the spaghetti consumed in the fasted-state (i.e. post-absorptive)? What if we learn that this person woke at midday?

These differences of opinion become problematic when scientific investigations have surveyed breakfast habits or recommended breakfast consumption but allowed individual interpretation regarding what constitutes breakfast. This can be informative from a sociological perspective but it is helpful when considering physiological health effects to employ a more precise and consistent operational definition. Taking the earlier example, some studies have included only solid foods as breakfast irrespective of the many highly calorific beverages available, yet (notwithstanding differences in gastric emptying rate and metabolic response to different nutrients in solid v. liquid form[6]), our net energy balance does not discriminate between absorbed nutrients or calories depending on whether they required chewing; 'a calorie is a calorie'.

While in the future it might become possible to justify a rationale for defining meals based on a certain mixture of nutrients, a logical starting point to define the essential conditions of breakfast per se would be based on the quantity and timing of energy consumed. We propose that a quantity of 209·2 kJ (50 kcal) represents an appropriate arbitrary threshold to exclude common ingestive behaviours that would neither be recognised as a meal by the majority of people nor meaningfully shift our physiology towards the fed-state, a marker of which could be a detectable perturbation in exogenous and/or endogenous substrate utilisation (thus one standard tea/coffee would be unlikely to meet this criterion).

The issue of timing is more complex and can be considered relative to time of day, time of waking and/or the intervals that distinguish separate eating occasions. A universal definition of breakfast as morning feeding based purely on light–dark cycles (i.e. clock time) independent of sleep–wakes cycles (or vice versa) is complicated by variance in these very cycles due to geographical/seasonal differences in daylight hours or cultural/vocational differences in sleeping patterns (e.g. night-shift workers). A nominal period of 2 h after waking is also often applied to the definition of the breakfast meal, with separate meals in turn having been distinguished from snacks by a cut-off quantity of approximately 1087·8 kJ (260 kcal) and distinct eating occasions isolated on the basis of a 45 min interval[7]. On balance, it therefore seems reasonable for a working definition of breakfast to represent the first meal consumed within 2 h after the longest sleep in any 24 h period, thus normally also reflecting the longest daily duration spent in the fasted-state and the only time most of us are genuinely post-absorptive[8].

According to the earlier rationale, our research involved approximately 70 lean and obese adults, of whom none worked night-shifts and approximately one-third habitually consumed <209·2 kJ (50 kcal) within 2 h of waking on most days, so might be classified as breakfast skippers. These individuals kindly participated in a series of experiments known as the Bath Breakfast Project, in which we allocated the habitual breakfast consumers and skippers equally into groups who for 6 weeks either: extended their overnight fast (0 kJ) until midday everyday; consumed 1464·4 kJ (350 kcal) within 2 h of waking and at least 2928·8 kJ (700 kcal) before 11.00 hours everyday; or maintained their usual lifestyles for 6 weeks[9].

In contrast to the wealth of evidence contrasting different types or amounts of breakfast foods, this is the first randomised controlled trial to compare a treatment involving breakfast with the complete absence of morning feeding in relation to all components of energy balance. Whilst the project therefore ostensibly concerns breakfast (indeed, you may only be reading the present paper due to a shared interest in that meal), our intervention from a basic science perspective is in fact the fasting treatment, with morning

feeding serving as a control (Bath Extended Morning Fasting Project did not seem so catchy). On that basis, the precise composition of breakfast prescribed was less important at this stage than simply ensuring that whatever was ingested differed sufficiently from fasting that meaningful effects would be detectable should they exist. The added practical benefits of this initial approach are that any significant effects could be generalised more broadly as responses to fasting as opposed to the presence or absence of specific foods consumed at breakfast; whereas none could argue that these treatments fail to polarise the contrast and meet all but the most extreme and unusual definitions of breakfast.

What do we mean by 'Important'?

If you are hungry upon waking and personally prefer to promptly satiate your hunger, then breakfast is undoubtedly the most important (i.e. only) meal suited to that purpose. Similarly, if your morning will involve physical exercise with performance on that day a priority, then consuming a carbohydrate-rich breakfast is the most important meal to achieve your immediate goals[10]. However, if we place importance on long-term health outcomes, these generally do not respond acutely to a single food or meal but instead require sustained exposure to a consistent dietary pattern. In this case, we are asking whether regular daily breakfast has a chronic effect on energy balance and associated health outcomes.

The present review will sequentially consider the effects of breakfast *v.* extended morning fasting on the various individual components of energy balance and health. For each outcome, we will first summarise the state of evidence linking breakfast to energy balance prior to our recent randomised controlled trial. That is the evidence upon which the pervasive societal beliefs about breakfast rested[11], despite being almost entirely cross-sectional in nature. The vast and diverse populations surveyed are a legitimate strength of these epidemiological studies but are also responsible for misconceptions amongst a public (and media) ill-equipped to evaluate research design, measurement error or controls, so who are inclined only to believe the findings (or headlines) from studies perceived to be large (again, define your terms). Conversely, other studies are too often discounted for being small irrespective of accuracy and precision in measurement (for a primer see How big does my sample need to be?[12]), which means we sometimes miss the opportunity to complement epidemiology with causal evidence from focused, tightly controlled and properly powered experiments (i.e. research where interventions and controls are directly manipulated). We will therefore set-out here how our understanding of causality specific to each outcome has been advanced by our recent series of randomised controlled trials; the Bath Breakfast Project.

Body mass/composition

As recently reviewed, although the extent to which the mere association between breakfast omission and obesity has been verified can be described as gratuitous, confirmatory studies continue to emerge even today despite the stated relationship confirmed by meta-analysis at a confidence level of $P = 0.001$ almost 20 years ago (rising to $P < 10^{-42}$ at the most recent cut-off in 2011)[11]. There can be little doubt, therefore, that individuals who more frequently consume breakfast tend to be leaner and that this pattern hardly varies across a diverse range of human populations. However, no matter how strong these correlations may be, they cannot be used to draw a causal inference and so cannot inform evidence-based recommendations either encouraging or discouraging breakfast for the purposes of weight-management.

The Bath Breakfast Project was designed primarily to examine individual components of energy balance as opposed to long-term weight-change, as evident in the fact that the intervention was applied for only 6 weeks with direct prescription and adherence to the treatments (i.e. a completers-only analysis)[9]. In this sense, our examination of body mass changes as an indication of net energy (im)balance better reflects an efficacy trial and nicely complements the results of a concurrent effectiveness trial which reported no significant difference in weight-loss over 16 weeks with a recommendation to eat or skip breakfast (i.e. an intention-to-treat analysis)[13]. Our data are consistent with this conclusion in that there was no significant difference in total body mass change between breakfast *v.* fasting amongst individuals who were either lean[14] or obese[15], although it is interesting to contrast the pattern of changes in dual-energy x-ray absorptiometry-derived body composition between groups across both levels of adiposity (Fig. 1).

As can be seen, despite the absence of differences between groups according to the breakfast intervention, there were significant within-group changes from baseline but with the pattern reversed according to adiposity and treatment group. Specifically working from left to right across Fig. 1, lean individuals in the fasting group did not compensate for the energy 'missed' at breakfast, hence there is a significant reduction in body mass (mostly from fat loss); whereas lean individuals in the breakfast group certainly do not gain weight despite the relatively large prescription of at least 2928·8 kJ (700 kcal) by 11.00 hours daily for 6 weeks[14]. In contrast, it was the fasting group in the obese population who exhibited the greatest compensation, with avoidance of weight-loss despite consuming not a single calorie until midday every day for 6 weeks; whereas the obese individuals in the breakfast group clearly did not compensate by expending the prescribed energy intake (or reducing subsequent energy intake sufficiently) and so increased energy storage in the form of adipose tissue[15].

The net effect of the earlier pattern is that, whether fed or fasted in the mornings, lean individuals may favour a more negative energy balance and obese individuals a more positive energy balance. This could mean that an individual's natural propensity to compensate is what determines the extent of adiposity and/or could equally mean that the extent of adiposity determines compensation. Whichever is the case, we begin to question both whether breakfast recommendations should vary
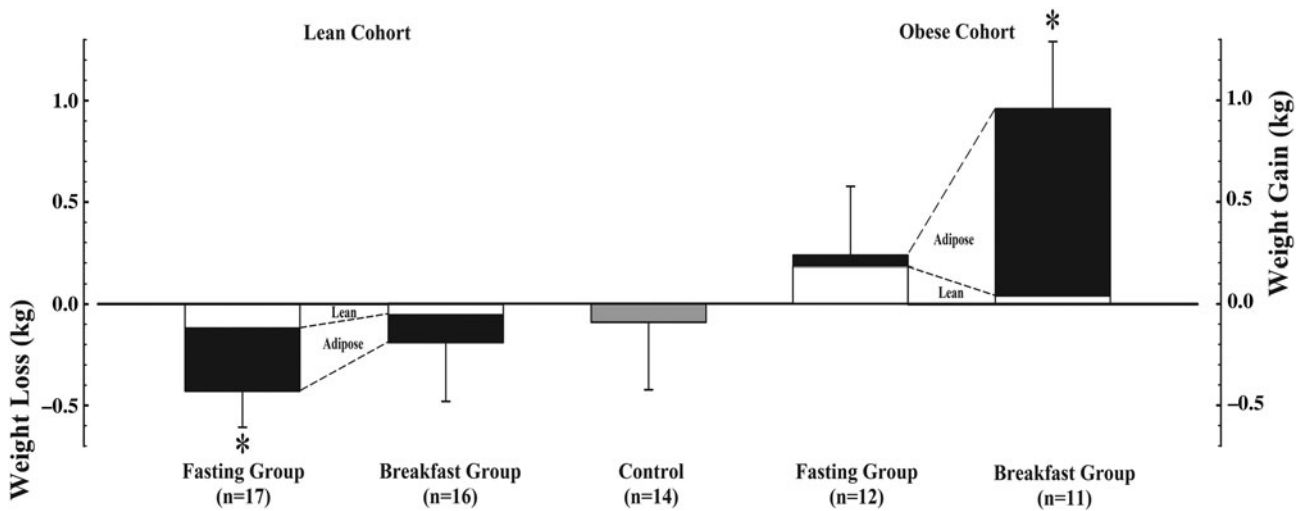
Fig. 1. Changes in dual-energy x-ray absorptiometry-derived body composition amongst lean[14] and obese[15] adults over 6 weeks with either ingestion of ≥2928·8 kJ (700 kcal) before 11.00 hours daily (Breakfast group), abstinence from all energy-providing nutrients until at least 12.00 hours daily (Fasting group) or lifestyle maintenance (Control). Data are means with SE bars and * denotes a significant within group change from baseline ($P < 0.05$).

according to adiposity and what mechanisms are involved in compensation (i.e. which components of energy balance are responsible)?

Components of energy balance

Energy intake

Cross-sectional observations. Omission of breakfast results in an energy intake deficit at the beginning of the day relative to breakfast consumption. Whether this deficit is maintained will depend on the existence/ magnitude of compensatory feeding throughout the remainder of the day. Cross-sectional evidence predominantly suggests lower energy intake in those that skip breakfast[16–19], with a recent within person analysis from The National Health and Nutrition Examination Survey showing that energy intake is 1033·4 kJ (247 (95 % CI 121, 373) kcal) lower for men and 782·4 kJ (187 (95 % CI 121, 253) kcal) lower for women on days when breakfast was omitted (both $P < 0.001$)[20]. However, this observation has not been consistent across all studies[3], with work categorising individuals by graded breakfast frequency reporting no difference despite varying category definitions[2,4,21].

Acute laboratory studies. Experimental research has examined energy intake in both tightly-controlled acute settings in the laboratory and with chronic exposure to different morning feeding interventions under free-living conditions (i.e. people studied in their usual environment). The nature of laboratory investigations allows precise control and measurement of actual intake, yet it is that same tight control and elimination of external influences that presents a limitation when generalising to 'real world' behaviours[22]. However, laboratory investigations allow measurement of other relevant variables such as concurrent metabolic measurements, subjective responses and appetite regulatory hormones, which can provide valuable mechanistic insight[23]. The majority of appetite regulatory hormones previously measured are related to satiety and satiation (e.g. peptide tyrosine-tyrosine (PYY), glucagon-like peptide-1, leptin) but ghrelin acts as an appetite stimulant[24]. As would be expected, there are clear differences between morning fasting and breakfast consumption during the morning, with a postprandial reduction in ghrelin and increased PYY in response to breakfast consumption[25,26], thus reflecting an anorexigenic response evidenced by subjective measures of appetite, as recently reviewed in this Journal[27].

Lunchtime feeding also elicits a PYY response that persists throughout the afternoon[25,26], suggesting that this hormone reflects total cumulative intake as opposed to the energy content of the most recent meal. In contrast, both Clayton *et al.*[28] and our recent studies in lean[25] and obese[26] individuals suggest that, paradoxically, acylated ghrelin remains elevated during the afternoon in those that have consumed a carbohydrate-rich breakfast and lunch. This may be related to the reduced insulinaemic response to the lunchtime meal due to the second-meal effect[29]. While these findings for hormonal appetite regulatory mechanisms and results of subjective appetite assessments are informative, it is important to acknowledge that numerous factors contribute to appetite regulation[30]. We have also shown in obese individuals that the pattern of appetite regulatory hormones and subjective appetite ratings does not necessarily predict *ad libitum* intake[26].

Studies investigating acute appetite regulation following breakfast omission fall into two main categories: those that have examined subsequent *ad libitum* energy intake following an unbroken overnight fast; and those where prior to lunch a pre-lunch snack (i.e. preload) was provided in both breakfast consumption/omission

conditions such that lunch was always consumed in a fed state. In studies of lean individuals where lunch was consumed *ad libitum*, most but not all[31,32] indicate energy intake is increased at the lunch meal, both when fasted[25,28,31] and after a morning preload[33]. Of these studies, Astbury *et al.* report the energy deficit from breakfast was abolished by the increase in energy intake at lunch. This was not the case in our work in lean individuals[25], for whom total intake was greater in the breakfast condition. Notably the breakfast provided by Astbury *et al.* was relatively small (about 1046·0 kJ (250 kcal)) in comparison with those provided in most other investigations (typically >1673·6 kJ (400 kcal)). With this in mind, it is a logical suggestion that the energy content of larger breakfasts is less likely to be fully compensated in the next meal alone. Studies that have examined energy intake at both lunch and then dinner[28] or meals plus snacks[31] have not revealed increased intake after morning fasting, refuting the possibility that further compensation occurs throughout the day. This view is also supported by findings of similar energy intake during evening snacks and meals when comparing morning feeding *v.* fasting followed by a standardised lunch[34].

The balance of evidence from controlled studies therefore suggests that breakfast omission results in some compensation at the next meal in lean individuals but that this next-meal effect is relatively transient with little evidence of more sustained compensatory feeding mechanisms. Interestingly, our work in obese individuals indicated similar energy intake at lunch independent of morning fasting or breakfast consumption[26]. To our knowledge, this is the first report of *ad libitum* intake amongst obese adults after breakfast omission and subsequent investigations should attempt to determine if dietary compensation occurs at later feeding occasions in this population.

Intervention studies. Intervention studies attempting to quantify the response to chronic breakfast consumption or omission do not provide such clear evidence as laboratory investigations for the effect of breakfast omission upon energy intake. Early work in which feeding frequency was regimented throughout the day suggested that breakfast omission leads to greater energy intake than breakfast consumption[35]. Two recent studies both from the same research group using similar cross-over designs of 1-week duration provide further data in this regard. In the first investigation, Halsey *et al.*[36] reported no difference in energy intake when participants either fasted or consumed an *ad libitum* high-carbohydrate breakfast under supervised laboratory conditions. In a subsequent investigation, participants were asked to consume a freely chosen breakfast within 1 h of waking for 1 week, relative to fasting until midday; omission of breakfast reduced daily energy intake by 669·4 kJ (160 kcal) relative to a mean energy intake of about 1673·6–2092·0 kJ (400–500 kcal) prior to midday when breakfast was consumed[37].

Our recent investigations did not impose any dietary limitations on the participants in either group other than maintaining the morning fast until noon or consuming ≥2928·8 kJ (700 kcal) by 11.00 hours, with at least half of this consumed within 2 h of waking[9]. In lean individuals we found evidence for limited dietary compensation, with the breakfast group consuming 2255·1 kJ/d (539 (95 % CI 157, 920) kcal/d) more than those in the fasting group[14]. However, in the obese cohort energy intake was not significantly different between the breakfast and fasting groups, with those assigned breakfast intake consuming 1414·1 kJ/d (338 (95 % CI −313, 988) kcal/d) more[15]. This finding in obese individuals is consistent with the findings of Reeves *et al.*[37], where the difference between breakfast and fasting groups was a pooled effect of lean (about 1108·7 kJ (265 kcal) higher) and obese individuals (about 251·04 kJ (60 kcal) higher), suggestive that obese individuals may compensate more for a morning energy deficit than lean individuals under free-living conditions. Interestingly, in our experiments the same obese individuals undertook both the acute investigation described earlier (where there was no compensation observed at lunch) and the free-living assessments (where there was no difference in daily intake between groups)[15,26]. This is in contrast to the equivalent lean individuals who displayed limited compensation for breakfast omission both inside and outside the laboratory[14,25]. The discord between these two groups of individuals suggests either that lean and obese people respond differently to the study designs employed or that energy intake may be more strongly influenced by environmental factors with increasing adiposity[38]. For example, the energy intake compensation evident in the obese cohort may be due to food choices and frequency, as opposed to the quantity consumed at single homogenous meals provided in an artificial laboratory setting.

As might be expected, the data from free-living investigations are inherently more varied than controlled laboratory investigations and the limitations of self-reported energy intake have recently been detailed elsewhere[39]. While these factors contribute towards systematic and random error and so impact both validity and reliability, there is little reason to believe that comparisons between experimental groups would be systematically biased by such limitations[7]. Nonetheless, methods to assess diet remain challenging under free-living conditions and there are currently no viable alternatives to dietary records in some form if specific nutrient profiles and/or feeding patterns are of interest. However, from a pure energy-balance perspective, it is possible to estimate total energy intake with relative accuracy using the intake-balance method[40,41], which exploits the energy-balance equation to derive energy entering the system as the sum of the change in energy storage and objectively measured energy expenditure[42]. The latter may itself be responsive to altered feeding patterns and the following sections will address this possibility with specific reference to each individual component of energy expenditure.

Resting metabolic rate

RMR is for a large proportion of individuals the greatest contributor to energy expenditure[43]. Decreases in mass adjusted RMR have been demonstrated in both

starvation and hypoenergetic dieting[44–46] but evidence for a modifying effect of chronic morning feeding pattern upon RMR is not apparent. Three past studies have measured changes in RMR in response to a sustained morning feeding intervention[35,47,48]. Of these, Schlundt et al.[47] demonstrated that weight loss induced by caloric restriction in obese women resulted in similar reductions in RMR whether consuming breakfast or fasting during the morning. In accordance, the 2-week crossover intervention of Farshchi et al. found no difference in RMR (or weight/body composition) following breakfast consumption or skipping regimens in lean women[35]. In a crossover study design involving groups of lean and overweight individuals, 1 week of breakfast consumption or fasting until noon also had no effect upon RMR[48].

The results of our 6-week interventions in both lean[14] and obese[15] individuals over 6 weeks of daily breakfast or morning fasting indicated that RMR was unaffected by morning feeding pattern (all groups stable within 62·8 kJ/d (15 kcal/d)). Therefore, the evidence uniformly shows that consistently extending the overnight fast does not directly affect RMR beyond the predicted change associated with possible changes in body mass/composition.

Diet-induced thermogenesis

Diet-induced thermogenesis (DIT) is the smallest component of energy expenditure under most circumstances and reflects the obligatory energy expended for the processing and digestion of food. Different macronutrients induce varying levels of thermogenesis[49,50], but DIT is only ever a fraction of the energy content of the foods ingested and typically only about 10 % of intake when consuming a normal mixed diet[51]. Only one intervention study has examined the effect of a sustained morning feeding intervention on DIT, with no effect on the thermic effect of a mixed macronutrient test drink after breakfast skipping or consumption for 2 weeks[35].

There is some evidence that DIT is greater in the morning than later in the day[52,53] and the thermogenic effect of breakfast is necessarily greater than morning fasting. Indeed, when consuming breakfast and an ad libitum lunch, both lean and obese participants expend greater energy through DIT during the morning and afternoon than when omitting breakfast (276·1 (SD 138·1) kJ (66 (SD 33) kcal) v. 205·0 (SD 121·3) kJ (49 (SD 29) kcal) in lean and 284·5 (SD 125·5) kJ (68 (SD 33) kcal) v. 167·4 (SD 96·2) kJ (40 (SD 23) kcal) in obese; Chowdhury et al., unpublished results). In studies where a fixed lunch meal has been provided following morning fasting/feeding, DIT during the afternoon was greater following breakfast[34] or not different relative to fasting when measured 1 and 4 h after lunch[28]. Where energy intake has been matched across 24 h following breakfast omission by increasing intake at subsequent meals, no difference in 24 h energy expenditure was observed[54]. This suggests little modifying effect of morning feeding pattern on DIT. Future studies should determine the effect of chronic breakfast omission upon DIT in response to feeding (i.e. a chronic adaptation in

the acute response). However, any potential effect of breakfast consumption per se on overall DIT will be quantitatively small and inexorably outweighed by the energy intake required to elicit that DIT.

Physical activity thermogenesis

Of the components contributing to total energy expenditure, physical activity thermogenesis is undoubtedly the most modifiable component yet has received surprisingly little attention in the literature regarding breakfast. Higher physical activity levels assessed by questionnaire are cross-sectionally associated with regular breakfast consumption[1–3,21,55–57]. However, this relationship has not been explained by causal data from experimental studies, with the few that are available having employed a wide variety of methodologies of varied sensitivity and specificity. Several studies have investigated the effect of varying feeding frequencies upon overall energy expenditure measured using a whole body calorimeter[58–60], which understandably places severe restrictions upon natural physical activity patterns that might be responsive to breakfast outside the laboratory.

Other past studies have attempted to quantify aspects of physical activity behaviour in response to breakfast in particular or altered daily meal frequency in general using a variety of approaches. Physical movements have been estimated using hip-worn monitors, pedometers or accelerometers but have failed to detect any difference in step counts during 1 week of either breakfast or fasting[36,48] or any difference in accelerometer counts when comparing a three-meal feeding pattern with a single evening-meal for 8 weeks[61]. However, natural adjustments in overall activity may have been masked in the latter study because participants were 'encouraged to maintain their normal exercise throughout the day'. In addition, such measurement tools may also lack both reliability and sensitivity when applied to subtle changes across all aspects of physical activity thermogenesis[62]. While the issues of reliability and sensitivity have been overcome using doubly-labelled water to verify no difference in total energy expenditure between a two- v. seven-meal daily feeding pattern[63], that finding is neither specific to breakfast or physical activity thermogenesis per se, nor does the technique reveal temporal patterns of activity.

We employed combined heart-rate accelerometry as a validated tool to quantify physical activity thermogenesis on a minute-by-minute basis under free-living conditions in response to our daily breakfast v. fasting intervention. This instrument is particularly sensitive to the low-to-moderate intensity, spontaneous lifestyle activities that we hypothesised might be most responsive to breakfast[9,62]. Our investigation in lean individuals demonstrated that daily physical activity thermogenesis was substantially greater amongst those consuming breakfast than those fasting (1849·3 (95% CI 142·3, 3560·6) kJ/d (442 (95% CI 34, 851) kcal/d)), with a particular difference between groups apparent for the morning period and for light intensity activities[14]. The obese individuals subsequently studied were less active overall and did not

display such a difference between groups in total daily physical activity thermogenesis (1138·0 (95% CI 1309·6, 4133·8) kJ/d (272 (95% CI −313, 988) kcal/d)) although, like their lean counterparts, an effect on morning energy expenditure was apparent (786·6 (95% CI 167·4, 1401·6) kJ/d (188 (95% CI 40, 335) kcal/d))[15]. This suggests that modifying feeding patterns can affect physical activity, with the most pronounced response during the time period of energy restriction/breakfast consumption. The reasons for this are not immediately clear but might be related to perceptions of lethargy, expectations relating to physical activity readiness or that reduced availability of exogenous substrate and/or systemic metabolites may limit engagement in non-essential physical exertion.

Taken collectively, these observations that physical activity levels are lower in response to fasting begin to explain why a resolution to start skipping breakfast may not predict the degree of weight loss one might expect. The shaping of our genome prior to the agricultural revolution ensured that individuals evolved mechanisms to protect against energy deficit during natural fed–fasted cycles on a daily basis (i.e. when almost every meal required initial 'investment' of energy). In this sense, it might be better to express the energy-balance equation not as Balance = Intake − Expenditure but instead Balance = −Expenditure + Intake. The net result is unchanged but this serves as a reminder that, in terms of survival, our investment of energy comes first and is inevitable, whereas food availability/procurement is uncertain and may be zero.

Strategies designed to improve human health by targeting energy balance must therefore integrate an appreciation of how compensatory feedback mechanisms can operate to defend against energy deficit. Conserving energy via reduced physical activity can be effective in the short term, but may not favour survival during a sustained food shortage, in which case more sedentary behaviours might be selected-out relative to the more proactive approach of competing for what limited resources are available early in the post-absorptive period. It therefore remains a possibility that more extreme or sustained exposure to extended daily fasting resulting in a chronically hypoenergetic diet could stimulate increased spontaneous physical activities, similar to the starvation-induced hyperactivity noted in rodents and patients with anorexia[64]. Of course, these elegantly evolved compensatory mechanisms have become somewhat obsolete (for most) in modern societies where food procurement is largely independent of any up-front investment of energy[65]. An effective intervention today will therefore need to target both sides of the energy-balance equation (e.g. diet and physical activity); hence, the following section will consider the arguably more natural scenario in which fasting is superimposed against a background of physical activity and/or exercise.

Exercise–fasting interactions

An important distinction should be made between physical activity thermogenesis and exercise-induced thermogenesis. Whilst both have an end result of increasing energy expenditure, the distinguishing factor is that the latter is defined by having a purpose. Accordingly, if structured exercise was already planned for as part of an individual's morning, then this is likely to prohibit the effect of breakfast consumption on physical activity thermogenesis, since energy expenditure is prescribed. The question then arises, what are the effects of breakfast consumption on metabolism for the morning exerciser?

The acute responses of exercise metabolism to prior feeding are well characterised. Total energy expenditure is almost entirely determined by the duration and intensity of the exercise bout, but substrate selection can be drastically shifted by nutritional status. Consumption of a mixed-macronutrient breakfast increases carbohydrate oxidation and suppresses fat oxidation during exercise[32,66], which is largely driven by the type and quantity of carbohydrate in the meal[67]. This is predominantly due to the insulin-induced suppression of plasma NEFA availability; insulin concentrations after a mixed-macronutrient carbohydrate-rich breakfast remain elevated sufficient to all but maximally suppress palmitate appearance[68]. Interestingly, the breakfast-induced suppression of fatty acid availability during exercise is not due to a reduction in lipolysis (at least in the subcutaneous adipose tissue depot) but rather to an increase in re-esterification[69]. In addition, if the breakfast has a particularly high glycaemic index, then an elevated pre-exercise muscle glycogen concentration[70] can also contribute to a further suppression of fat oxidation in both men[71] and women[72].

The omission of breakfast prior to exercise (or delaying breakfast consumption until after exercise) also appears to have unique consequences for acute whole-body substrate balance. Physical exercise does not invoke the same acute energy intake response to breakfast omission/delay presented earlier (i.e. energy intake at lunch and dinner is largely either unaltered[32,73,74] or does not fully compensate for breakfast omission[28]). Instead, the increase in energy expenditure due to exercise, combined with the shift in substrate utilisation towards greater lipid oxidation with breakfast omission, results in a less positive (more negative) fat balance in both lean[32] and overweight men[74]. This has also been observed over a full 24-h period with room calorimetry and fixed energy intake[75]. Given the importance of endogenous carbohydrate stores for exercise tolerance[76–78], the preservation of whole-body carbohydrate balance in the presence of a negative fat balance[32,74] could be an attractive metabolic milieu for the regular exerciser.

The chronic effect of breakfast–exercise interactions is much less clear. An emerging theme in exercise physiology is the augmentation of endurance-type training adaptations through manipulation of substrate availability. Methods such as multiple bouts of exercise[79,80], reductions in dietary carbohydrate intake and timing of dietary carbohydrate intake[81,82] all serve to reduce endogenous or exogenous carbohydrate availability, consequently elevating fatty acid availability. Whilst (to the authors knowledge) no studies are available on the effect of breakfast on endurance training adaptation *per se*,

there is evidence to suggest that consumption of a carbohydrate-rich breakfast prior to training, in addition to carbohydrate intake during every exercise training session can impair some endurance-type training adaptations. Specifically, compared to extending the overnight fast until after exercise, carbohydrate consumption before and during exercise can attenuate and/or abolish the increases in V_{O2max}[83] glucose tolerance, insulin sensitivity, resting muscle glycogen concentrations and GLUT4 content[84]. It should be noted however, that these effects are not consistent across all studies of fasted-state exercise training[85].

The energy balance and body composition responses to regular exercise training with breakfast consumption/omission are currently unknown. It therefore remains to be seen whether the Nobel Laureate and Exercise Physiologist A.V. Hill had a firm rationale for running a mile every morning prior to having breakfast[86].

Health outcomes

Much of the work examining different morning feeding patterns as described in the present review has focused on components of energy balance. Considering the severity of the growing issue of obesity[87] and the general pre-occupation of the public/media with the effects of diet upon weight, this is not surprising. However, it is important to keep in mind that the primary reason for the study of energy balance is not as an endpoint in itself, but because of our interest in the potential impact of an individual's energy (im)balance upon factors that may then affect their health. While chronic energy (im)balance is potentially an important contributor to negative health outcomes, specific components of energy balance such as physical activity can also impact disease and mortality risk independent of net energy surplus/deficit or changes in adiposity[88,89]. Therefore, it is perfectly plausible that the omission/consumption of breakfast might affect markers of health independent of energy balance.

While there is a wealth of evidence for increased disease risk in those that omit breakfast[1–4], randomised controlled trials that have provided causal mechanisms to explain these observations remain very limited. In the two prior studies where health markers have been measured, Stote et al.[61] report increased lipoproteins relative to a three-meal pattern (total, HDL and LDL) when individuals adhered to a one-meal a day regimen. In a less extreme model, Farshchi et al.[35] report when delaying morning intake until 10.30 hours each morning for 2 weeks that total and LDL-cholesterol and insulin response to a test drink increased (although other measures of insulin sensitivity remained unchanged), relative to a reduction when consuming breakfast daily. Our recent studies have extended this evidence by measuring several markers related to CVD risk and metabolic control. In lean individuals, only a modest increase in glucose variability in those fasting during the afternoon/evening was detected[14], with no effects for 24 h glycaemic control detected in obese individuals[15].

However, there was an interaction effect for insulinaemic response to an oral glucose tolerance test in this population, with a reduction in those consuming breakfast relative to an increase in those fasting. Across both groups, the majority of health markers were unaffected by either regimen. Therefore, it appears that any effects of chronic morning fasting upon health in healthy individuals are either non-existent or not detectable over the relatively short time period examined. Evidence for a potential effect upon insulin sensitivity and glycaemic control is evident in the work of our group and others[14,15,35], and tallies somewhat with reports of improved glycaemic control with greater breakfast quantity in type-2 diabetics[90,91]. However, considering that not all measures of metabolic control demonstrated a deterioration with extended morning fasting in healthy individuals, it appears that any effects are subtle at best. Future studies could provide further insight by employing interventions of longer durations, over which potential effects upon markers of health might be more apparent.

Conclusions

The evidence reviewed suggests that breakfast omission affects some components of energy balance much more than others. There is no evidence to suggest that breakfast consumption per se affects RMR, or DIT of subsequent meals or over the day as a whole. Evidence that breakfast affects energy intake is compelling for laboratory studies, with the majority of studies showing energetic compensation at the next meal, but not sufficient to eliminate the deficit from morning fasting. In addition, designs where afternoon/evening feeding has been allowed do not demonstrate sustained compensation for breakfast omission. Experiments outside the laboratory understandably produce more varied results, with the balance of evidence suggesting that energy intake is either lower or similar when omitting breakfast. Our work in lean and obese groups would suggest that there are differences between groups in energy intake responses based on adiposity. The body of evidence taken together supports the concept that, in general, energy intake is reduced when breakfast is omitted, with limited support for the popular perception of greater overall energy intake after breakfast omission.

While much work has investigated energy intake in response to breakfast omission, there is a severe lack of studies investigating the most modifiable component of energy expenditure-physical activity energy expenditure, with some studies limited by measurement issues. Our work in both lean and obese individuals suggests that breakfast omission may lower physical activity energy expenditure, particularly during the morning, although this needs confirmation and the potential reasons for this phenomenon remain to be established. The majority of studies conducted to date have been of relatively short duration, but those that have examined the effect of breakfast omission upon body weight do not support the strongly established public perceptions and correlational evidence that omission of breakfast is associated with weight-gain.

Future investigations should focus on concurrently measuring all aspects of energy balance, to provide a fuller understanding of the effects of breakfast omission upon individual components (and importantly the interaction of these components). Longer-term studies are needed to conclusively establish the effects of breakfast omission upon health markers, with more studies required examining overweight and obese populations. Breakfast may or may not be the most important meal of the day, but it is certainly an important meal to investigate further.

Acknowledgements

Financial Support

Conflicts of Interest

None.

Authorship

References

1. Cahill LE, Chiuve SE, Mekary RA *et al.* (2013) Prospective study of breakfast eating and incident coronary heart disease in a cohort of male US health professionals. *Circulation* **128**, 337–343.
2. Mekary RA, Giovannucci E, Cahill L *et al.* (2013) Eating patterns and type 2 diabetes risk in older women: breakfast consumption and eating frequency. *Am J Clin Nutr* **98**, 436–443.
3. Mekary RA, Giovannucci E, Willett WC *et al.* (2012) Eating patterns and type 2 diabetes risk in men: breakfast omission, eating frequency, and snacking. *Am J Clin Nutr* **95**, 1182–1189.
4. Odegaard AO, Jacobs DR Jr, Steffen LM *et al.* (2013) Breakfast frequency and development of metabolic risk. *Diab Care* **36**, 3100–3106.
5. O'Neil CE, Byrd-Bredbenner C, Hayes D *et al.* (2014) The role of breakfast in health: definition and criteria for a quality breakfast. *J Acad Nutr Diet* **114**, Suppl. 12, S8–S26.
6. Berry MK, Russo A, Wishart JM *et al.* (2002) Effect of solid meal on gastric emptying of, and glycemic and cardiovascular responses to, liquid glucose in older subjects. *Am J Physiol* **284**, G655–G662.
7. de Castro JM (1994) Accommodation of particular foods or beverages into spontaneously ingested evening meals. *Appetite* **23**, 57–66.
8. Ruge T, Hodson L, Cheeseman J *et al.* (2009) Fasted to fed trafficking of Fatty acids in human adipose tissue reveals a novel regulatory step for enhanced fat storage. *J Clin Endocrinol Metab* **94**, 1781–1788.
9. Betts JA, Thompson D, Richardson JD *et al.* (2011) Bath Breakfast Project (BBP) – Examining the role of extended daily fasting in human energy balance and associated health outcomes: study protocol for a randomised controlled trial [ISRCTN31521726]. *Trials* **12**, 172.
10. Wright DA, Sherman A & Dernbach AR (1991) Carbohydrate feedings before, during, or in combination improve cycling performance. *J Appl Physiol* **71**, 1082–1088.
11. Brown AW, Bohan Brown MM & Allison DB (2013) Belief beyond the evidence: using the proposed effect of breakfast on obesity to show 2 practices that distort scientific evidence. *Am J Clin Nutr* **98**, 1298–1308.
12. Batterham AM & Atkinson G (2005) How big does my sample size need to be? A primer on the murky world of sample size estimation. *Phys Ther Sport* **6**, 153–163.
13. Dhurandhar EJ, Dawson J, Alcorn A *et al.* (2014) The effectiveness of breakfast recommendations on weight loss: a randomized controlled trial. *Am J Clin Nutr* **100**, 507–513.
14. Betts JA, Richardson JD, Chowdhury EA *et al.* (2014) The causal role of breakfast in energy balance and health: a randomized controlled trial in lean adults. *Am J Clin Nutr* **100**, 539–547.
15. Chowdhury EA, Richardson JD, Holman GD *et al.* (2016) The causal role of breakfast in energy balance and health: a randomized controlled trial in obese adults. *Am J Clin Nutr* **103**, 747–756.
16. Cho S, Dietrich M, Brown CJ *et al.* (2003) The effect of breakfast type on total daily energy intake and body mass index: results from the Third National Health and Nutrition Examination Survey (NHANES III). *J Am Coll Nutr* **22**, 296–302.
17. Deshmukh-Taskar PR, Nicklas TA, O'Neil CE *et al.* (2010) The relationship of breakfast skipping and type of breakfast consumption with nutrient intake and weight status in children and adolescents: the National Health and Nutrition Examination Survey 1999–2006. *J Am Diet Assoc* **110**, 869–878.
18. Nicklas TA, Myers L, Reger C *et al.* (1998) Impact of breakfast consumption on nutritional adequacy of the diets of young adults in Bogalusa, Louisiana: ethnic and gender contrasts. *J Am Diet Assoc* **98**, 1432–1438.
19. Nicklas TA, O'Neil CE & Berenson GS (1998) Nutrient contribution of breakfast, secular trends, and the role of ready-to-eat cereals: a review of data from the Bogalusa Heart Study. *Am J Clin Nutr* **67**, 757S–763S.
20. Kant AK & Graubard BI (2015) Within-person comparison of eating behaviors, time of eating, and dietary intake on days with and without breakfast: NHANES 2005–2010. *Am J Clin Nutr* **102**, 661–670.

21. Wyatt HR, Grunwald GK, Mosca CL *et al.* (2002) Long-term weight loss and breakfast in subjects in the National Weight Control Registry. *Obes Res* **10**, 78–82.

22. Blundell J, de Graaf C, Hulshof T *et al.* (2010) Appetite control: methodological aspects of the evaluation of foods. *Obes Rev* **11**, 251–270.

23. Karra E & Batterham RL (2010) The role of gut hormones in the regulation of body weight and energy homeostasis. *Mol Cell Endocrinol* **316**, 120–128.

24. Cummings DE, Frayo RS, Marmonier C *et al.* (2004) Plasma ghrelin levels and hunger scores in humans initiating meals voluntarily without time- and food-related cues. *Am J Physiol Endocrinol Metab* **287**, E297–E304.

25. Chowdhury EA, Richardson JD, Tsintzas K *et al.* (2015) Carbohydrate-rich breakfast attenuates glycaemic, insulinaemic and ghrelin response to ad libitum lunch relative to morning fasting in lean adults. *Br J Nutr* **114**, 98–107.

26. Chowdhury EA, Richardson JD, Tsintzas K *et al.* (2016) Effect of extended morning fasting upon ad libitum lunch intake and associated metabolic and hormonal responses on obese adults. *Int J Obes*, **40**, 305–311.

27. Clayton DJ & James LJ (2015) The effect of breakfast on appetite regulation, energy balance and exercise performance. *Proc Nutr Soc* 1–9.

28. Clayton DJ, Barutcu A, Machin C *et al.* (2015) Effect of breakfast omission on energy intake and evening exercise performance. *Med Sci Sports Exerc* **47**, 2645–2652.

29. Hamman L & Hirschmann II (1919) Studies on blood sugar; IV. Effects upon the blood sugar of the repeated ingestion of glucose. *Johns Hopkins Hospital Bulletin* **30**, 306–307.

30. Berthoud HR & Morrison C (2008) The brain, appetite, and obesity. *Annu Rev Psychol* **59**, 55–92.

31. Levitsky DA & Pacanowski CR (2013) Effect of skipping breakfast on subsequent energy intake. *Physiol Behav* **119**, 9–16.

32. Gonzalez JT, Veasey RC, Rumbold PL *et al.* (2013) Breakfast and exercise contingently affect postprandial metabolism and energy balance in physically active males. *Br J Nutr* **110**, 721–732.

33. Astbury NM, Taylor MA & Macdonald IA (2011) Breakfast consumption affects appetite, energy intake, and the metabolic and endocrine responses to foods consumed later in the day in male habitual breakfast eaters. *J Nutr* **141**, 1381–1389.

34. Thomas EA, Higgins J, Bessesen DH *et al.* (2015) Usual breakfast eating habits affect response to breakfast skipping in overweight women. *Obesity* **23**, 750–759.

35. Farshchi HR, Taylor MA & Macdonald IA (2005) Deleterious effects of omitting breakfast on insulin sensitivity and fasting lipid profiles in healthy lean women. *Am J Clin Nutr* **81**, 388–396.

36. Halsey LG, Huber JW, Low T *et al.* (2011) Does consuming breakfast influence activity levels? An experiment into the effect of breakfast consumption on eating habits and energy expenditure. *Publ Health Nutr*, 1–8.

37. Reeves S, Huber JW, Halsey LG *et al.* (2014) Experimental manipulation of breakfast in normal and overweight/obese participants is associated with changes to nutrient and energy intake consumption patterns. *Physiol Behav* **133**, 130–135.

38. Mela DJ (2006) Eating for pleasure or just wanting to eat? Reconsidering sensory hedonic responses as a driver of obesity. *Appetite* **47**, 10–17.

39. Dhurandhar NV, Schoeller D, Brown AW *et al.* (2015) Energy balance measurement: when something is not better than nothing. *Int J Obes (Lond)* **39**, 1109–1113.

40. Gilmore LA, Ravussin E, Bray GA *et al.* (2014) An objective estimate of energy intake during weight gain using the intake-balance method. *Am J Clin Nutr* **100**, 806–812.

41. de Jonge L, DeLany JP, Nguyen T *et al.* (2007) Validation study of energy expenditure and intake during calorie restriction using doubly labeled water and changes in body composition. *Am J Clin Nutr* **85**, 73–79.

42. Racette SB, Das SK, Bhapkar M *et al.* (2012) Approaches for quantifying energy intake and %calorie restriction during calorie restriction interventions in humans: the multicenter CALERIE study. *Am J Physiol Endocrinol Metab* **302**, E441–E448.

43. Carpenter WH, Poehlman ET, O'Connell M *et al.* (1995) Influence of body composition and resting metabolic rate on variation in total energy expenditure: a meta-analysis. *Am J Clin Nutr* **61**, 4–10.

44. Doucet E, St-Pierre S, Almeras N *et al.* (2001) Evidence for the existence of adaptive thermogenesis during weight loss. *Br J Nutr* **85**, 715–723.

45. Dulloo AG & Jacquet J (1998) Adaptive reduction in basal metabolic rate in response to food deprivation in humans: a role for feedback signals from fat stores. *Am J Clin Nutr* **68**, 599–606.

46. Martin CK, Heilbronn LK, de Jonge L *et al.* (2007) Effect of calorie restriction on resting metabolic rate and spontaneous physical activity. *Obesity* **15**, 2964–2973.

47. Schlundt DG, Hill JO, Sbrocco T *et al.* (1992) The role of breakfast in the treatment of obesity: a randomized clinical trial. *Am J Clin Nutr* **55**, 645–651.

48. Reeves S, Huber JW, Halsey LG *et al.* (2015) A cross-over experiment to investigate possible mechanisms for lower BMIs in people who habitually eat breakfast. *Eur J Clin Nutr* **69**, 632–637.

49. Tappy L (1996) Thermic effect of food and sympathetic nervous system activity in humans. *Reprod Nutr Dev* **36**, 391–397.

50. Westerterp KR, Wilson SA & Rolland V (1999) Diet induced thermogenesis measured over 24 h in a respiration chamber: effect of diet composition. *Int J Obes Relat Metab Disord* **23**, 287–292.

51. Westerterp KR (2004) Diet induced thermogenesis. *Nutr Metab (Lond)* **1**, 5.

52. Bo S, Fadda M, Castiglione A *et al.* (2015) Is the timing of caloric intake associated with variation in diet-induced thermogenesis and in the metabolic pattern? A randomized cross-over study. *Int J Obes (Lond)* **39**, 1689–1695.

53. Romon M, Edme JL, Boulenguez C *et al.* (1993) Circadian variation of diet-induced thermogenesis. *Am J Clin Nutr* **57**, 476–480.

54. Kobayashi F, Ogata H, Omi N *et al.* (2014) Effect of breakfast skipping on diurnal variation of energy metabolism and blood glucose. *Obes Res Clin Pract* **8**, e201–e298.

55. Smith KJ, McNaughton SA, Cleland VJ *et al.* (2013) Health, behavioral, cognitive, and social correlates of breakfast skipping among women living in socioeconomically disadvantaged neighborhoods. *J Nutr* **143**, 1774–1784.

56. van der Heijden AA, Hu FB, Rimm EB *et al.* (2007) A prospective study of breakfast consumption and weight gain among U.S. men. *Obesity* **15**, 2463–2469.

57. Barr SI, DiFrancesco L & Fulgoni VL III (2013) Consumption of breakfast and the type of breakfast consumed are positively associated with nutrient intakes and adequacy of Canadian adults. *J Nutr* **143**, 86–92.

58. Smeets AJ & Westerterp-Plantenga MS (2008) Acute effects on metabolism and appetite profile of one meal difference in the lower range of meal frequency. *Br J Nutr* **99**, 1316–1321.

59. Dallosso HM, Murgatroyd PR & James WP (1982) Feeding frequency and energy balance in adult males. *Hum Nutr Clin Nutr* **36C**, 25–39.

60. Taylor MA & Garrow JS (2001) Compared with nibbling, neither gorging nor a morning fast affect short-term energy balance in obese patients in a chamber calorimeter. *Int J Obes Relat Metab Disord* **25**, 519–528.

61. Stote KS, Baer DJ, Spears K *et al.* (2007) A controlled trial of reduced meal frequency without caloric restriction in healthy, normal-weight, middle-aged adults. *Am J Clin Nutr* **85**, 981–988.

62. Thompson D, Batterham AM, Bock S *et al.* (2006) Assessment of low-to-moderate intensity physical activity thermogenesis in young adults using synchronized heart rate and accelerometry with branched-equation modeling. *J Nutr* **136**, 1037–1042.

63. Verboeket-van de Venne WP, Westerterp KR & Kester AD (1993) Effect of the pattern of food intake on human energy metabolism. *Br J Nutr* **70**, 103–115.

64. Hebebrand J, Exner C, Hebebrand K *et al.* (2003) Hyperactivity in patients with anorexia nervosa and in semistarved rats: evidence for a pivotal role of hypoleptinemia. *Physiol Behav* **79**, 25–37.

65. Eaton SB & Eaton SB (2003) An evolutionary perspective on human physical activity: implications for health. *Comp Biochem Physiol* **136**, 153–159.

66. Wu CL & Williams C (2006) A low glycemic index meal before exercise improves endurance running capacity in men. *Int J Sport Nutr Exerc Metab* **16**, 510–527.

67. Wu CL, Nicholas C, Williams C *et al.* (2003) The influence of high-carbohydrate meals with different glycaemic indices on substrate utilisation during subsequent exercise. *Br J Nutr* **90**, 1049–1056.

68. Jensen MD, Caruso M, Heiling V *et al.* (1989) Insulin regulation of lipolysis in nondiabetic and IDDM subjects. *Diabetes* **38**, 1595–1601.

69. Enevoldsen LH, Simonsen L, Macdonald IA *et al.* (2004) The combined effects of exercise and food intake on adipose tissue and splanchnic metabolism. *J Physiol* **561**, Pt 3, 871–882.

70. Wee SL, Williams C, Tsintzas K *et al.* (2005) Ingestion of a high-glycemic index meal increases muscle glycogen storage at rest but augments its utilization during subsequent exercise. *J Appl Physiol* **99**, 707–714.

71. Wee SL, Williams C, Gray S *et al.* (1999) Influence of high and low glycaemic index meals on endurance running capacity. *Med Sci Sport Exerc* **31**, 393–399.

72. Stevenson E, Williams C, Nute M *et al.* (2008) Influence of the glycaemic index of an evening meal on substrate oxidation following breakfast and during exercise the next day in healthy women. *Eur J Clin Nutr* **62**, 608–616.

73. Deighton K, Zahra JC & Stensel DJ (2012) Appetite, energy intake and resting metabolic responses to 60 min treadmill running performed in a fasted versus a postprandial state. *Appetite* **58**, 946–954.

74. Farah NM & Gill JM (2013) Effects of exercise before or after meal ingestion on fat balance and postprandial metabolism in overweight men. *Br J Nutr* **109**, 2297–2307.

75. Shimada K, Yamamoto Y, Iwayama K *et al.* (2013) Effects of post-absorptive and postprandial exercise on 24 h fat oxidation. *Metabolism* **62**, 793–800.

76. Bergstrom J, Hermansen L, Hultman E *et al.* (1967) Diet, muscle glycogen and physical performance. *Acta Physiol Scand* **71**, 140–150.

77. Alghannam AF, Jedrzejewski D, Tweddle MG *et al.* (2016) Impact of muscle glycogen availability on the capacity for repeated exercise in man. *Med Sci Sports Exerc* **48**, 123–131.

78. Casey A, Short AH, Hultman E *et al.* (1995) Glycogen resynthesis in human muscle fibre types following exercise-induced glycogen depletion. *J Physiol (Lond)* **483**, 265–271.

79. Hansen AK, Fischer CP, Plomgaard P *et al.* (2005) Skeletal muscle adaptation: training twice every second day vs. training once daily. *J Appl Physiol (1985)* **98**, 93–99.

80. Yeo WK, McGee SL, Carey AL *et al.* (2010) Acute signalling responses to intense endurance training commenced with low or normal muscle glycogen. *Exp Physiol* **95**, 351–358.

81. Marquet LA, Brisswalter J, Louis J *et al.* (2016) Enhanced endurance performance by periodization of CHO Intake: 'sleep low' strategy. *Med Sci Sport Exerc* **48**, 663–672.

82. Van Proeyen K, Szlufcik K, Nielens H *et al.* (2011) Beneficial metabolic adaptations due to endurance exercise training in the fasted state. *J Appl Physiol (1985)* **110**, 236–245.

83. Stannard SR, Buckley AJ, Edge JA *et al.* (2010) Adaptations to skeletal muscle with endurance exercise training in the acutely fed versus overnight-fasted state. *J Sci Med Sport* **13**, 465–469.

84. Van Proeyen K, Szlufcik K, Nielens H *et al.* (2010) Training in the fasted state improves glucose tolerance during fat-rich diet. *J Physiol* **588**, Pt 21, 4289–4302.

85. De Bock K, Derave W, Eijnde BO *et al.* (2008) Effect of training in the fasted state on metabolic responses during exercise with carbohydrate intake. *J Appl Physiol (1985)* **104**, 1045–1055.

86. Hill AV & Lupton H (1923) Muscular exercise, lactic acid, and the supply and utilization of oxygen. *Q J Med* **16**, 135–171.

87. Wang YC, McPherson K, Marsh T *et al.* (2011) Health and economic burden of the projected obesity trends in the USA and the UK. *Lancet* **378**, 815–825.

88. Ekelund U, Ward HA, Norat T *et al.* (2015) Physical activity and all-cause mortality across levels of overall and abdominal adiposity in European men and women: the European Prospective Investigation into Cancer and Nutrition Study (EPIC). *Am J Clin Nutr* **101**, 613–621.

89. Walhin JP, Richardson JD, Betts JA, *et al.* (2013) Exercise counteracts the effects of short-term overfeeding and reduced physical activity independent of energy imbalance in healthy young men. *J Physiol* **591**, Pt 24, 6231–6243.

90. Jakubowicz D, Wainstein J, Ahren B, *et al.* (2015) Fasting until noon triggers increased postprandial hyperglycemia and impaired insulin response after lunch and dinner in individuals with type 2 diabetes: a randomized clinical trial. *Diabetes Care* **38**, 1820–1826.

91. Rabinovitz HR, Boaz M, Ganz T *et al.* (2014) Big breakfast rich in protein and fat improves glycemic control in type 2 diabetics. *Obesity* **22**, E46–E54.