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Activity Energy Expenditure is an Independent Predictor of Energy Intake in Humans

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Abbreviations

AEE, activity energy expenditure; FFM, fat-free mass; FM, fat mass; RMR, resting metabolic rate; EI, energy intake; EE, energy expenditure; TEF, thermic effect of food.

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Abstract

Background: There is evidence that the energetic demand of metabolically active tissue is associated with day-to-day food intake (EI). However, the extent to which behavioural components of total daily energy expenditure (EE) such as activity energy expenditure (AEE) are also associated with EI is unknown. Therefore, the present study examined the cross-sectional associations between body composition, resting metabolic rate (RMR), AEE and EI.

Methods: Data for 242 individuals (114 males; 128 females; BMI = 25.7 ± 4.9 kg/m^2) were collated from the baseline control conditions of five studies employing common measures of body composition (air displacement plethysmography) and RMR (indirect calorimetry). EI (weighed-dietary records) and EE (FLEX heart rate) were measured daily over 6-7 days, and AEE was calculated as total daily EE minus RMR.

Results: Linear regression indicated that RMR (ß = 0.39; P < 0.001), fat mass (ß = -0.26; P < 0.001) and AEE (ß = 0.18; P = 0.002) were independent predictors of mean daily EI, with AEE adding ≈3 % of variance to the model after controlling for age, sex and study ($F_{(10, 231)}$ = 18.532, P < 0.001; R^2 = 0.445). Path analyses indicated that the effect of FFM on mean daily EI was mediated by RMR (P < 0.05), while direct (β = 0.19; P < 0.001) and indirect (β = 0.20; P = 0.001) associations between AEE and mean daily EI were observed.

Conclusions: When physical activity was allowed to vary under free-living conditions, AEE was associated with mean daily EI independently of other biological determinants of EI arising from body composition and RMR. These data suggest that EE per se exerts influence over daily food intake, with both metabolic (RMR) and behavioral (AEE) components of total daily EE potentially influencing EI via their contribution to daily energy requirements.

Key Words

Energy intake, fat mass, fat-free mass, resting metabolic rate, activity energy expenditure, total daily energy expenditure.

INTRODUCTION

It is well established in the farm animal literature,[1] and assumed in the literature on human energy requirements,[2] that metabolic body size and energy expenditure (EE) influence energy intake (EI). Until recently, evidence linking EE in humans to day-to-day feeding patterns has however been limited,[3] and the mechanisms that translate EE into a functional drive to eat are poorly defined.[4] Evidence is now accumulating, primarily from cross-sectional analyses, to indicate that the EE of metabolically active tissue is associated with daily EI in individuals not undergoing significant changes in body weight or composition, with studies reporting strong positive asscoiations between fat-free mass (FFM) and ad libitum EI.[5-9] These associations appear to reflect the energetic contribution that FFM makes to total daily EE, as the effect of FFM on EI has been reported to be mediated by resting metabolic rate (RMR)[10, 11] and 24-hour EE.[12] These studies suggest that EE per se is exerting influence on daily EI, and it has recently been hypothesized that together, RMR and activity energy expenditure (AEE) may act as key biological drivers of EI.[13] However, since AEE is typically more variable day-to-day and makes a smaller contribution to total daily EE than RMR,[14] any effect may be more difficult to determine in a free living state close to conditions of energy balance.

When exercise has been used to acutely manipulate AEE and total daily EE, a loose coupling between the EE of exercise and EI has been reported.[15, 16] This coupling may become stronger when energy balance is systematically manipulated using exercise over longer periods of time,[17-20] or in those with high habitual physical activity levels.[21-23] Previous studies have looked at associations between total daily EE and EI, but EE is often measured during confinement in a metabolic chamber.[12] Based on cross-sectional data in weight stable individuals, we have previously shown that total daily EE failed to explain any further variance in daily EI after accounting for RMR.[10] However, this study was conducted during a

14-day residential stay in a metabolic unit, a condition under which variability in physical activity may have been constrained. Therefore, the present study examined the cross-sectional associations between mean daily EI and individual components of total daily EE weight stable individuals under conditions where total daily EE was allowed to vary as a function of physical activity. Given its contribution to total daily EE, it was hypothesised that AEE would be associated with EI alongside components of body composition and RMR.

SUBJECTS AND METHODS

Subjects

In total, 242 subjects (114 males; 128 females; BMI = 25.6 ± 5.0 kg/m^2) were included in the present cross-sectional analyses (see Table 1), which combined data from the baseline, non-intervention control conditions of five previous studies employing common experimental procedures (Supplementary Figure 1).[24-29] These studies were originally designed to examine the effect of diet on body composition, eating behaviour and health, and had no a priori hypotheses about the effects of body composition or EE as determinants of food intake. All data were collected at the Rowett Institute, University of Aberdeen, United Kingdom between the dates of 1998 and 2007, and subjects were weight stable (weight change of <2 kg in the previous three months), free from disease and not taking medication known to influence metabolism or appetite. For each study, written informed consent was obtained, data were anonymised, and ethical approval was granted by the Grampian Research Ethics Committee. Secondary analyses of these data were retrospectively registered at clinicaltrials.gov (NCT03319615).

Table 1 here

Study Design

Data were aggregated from the non-intervention baseline control conditions of five studies employing common experimental measures of body composition (air displacement plethysmography), energy expenditure (indirect calorimetry and FLEX heart rate) and total daily EI (weighed dietary records).[11] Total daily EI and total daily EE were measured over 6 (n = 54) or 7 days (n = 188). Detailed descriptions of the procedures, repeatability of measurements and the assumptions and limitations associated with the measurement of daily EI, EE and energy balance in these data have previously been reported.[24, 25, 28, 30]

Anthropometry and Body Composition

Stature was measured to the nearest 0.5 cm using a portable stadiometer (Holtain Ltd., Crymych, Dyfed, Wales), while body weight was measured to the nearest 0.01 kg after voiding (DIGI DS-410 CMS Weighing Equipment, London, UK). The change in body weight over the 6 or 7-day period in which total daily EE & EI were estimated was also measured in 229 subjects. Air-displacement plethysmography was used to estimate a 2-compartment model of body composition in 233 participants (BOD POD Body Composition System, Life Measurement, Inc., Concord, USA). After voiding, subjects were weighed to the nearest 0.01 kg while wearing minimal clothing (e.g. swimwear and swim hat) and body composition was then estimated according to manufacturers' instructions (with thoracic gas volumes estimated using the manufacturer's software). Air-displacement plethysmography has been validated against underwater weighing in normal weight[31] and overweight and obese adults.[32] In nine subjects, body composition was estimated from skinfold thickness (Holtain Ltd., Dyfed, Wales, UK) and the equations of Durnin & Womersley[33] as measures of air-displacement plethysmography were unavailable. The inclusion of these subjects alongside those with estimates using air-displacement plethysmography did not alter the outcomes of any analyses.

Resting Metabolic Rate

RMR was measured over 30-40-minute period following a 12-hour fast in a thermo-neutral room using an indirect calorimeter fitted with a ventilated hood (Deltatrac II, MBM-200, Datex Instrumentarium Corporation, Finland). The first and last five minutes' measurements were excluded, and EE was calculated from minute-by-minute data, using the equations of Elia and Livesey,[34] and plotted. The mean of the first 15 consecutive minutes visually showing minimal variation in EE was calculated. Details of calibration burns and repeatability testing have been described elsewhere.[29]

Total Daily Energy Expenditure and Activity Energy Expenditure

Total daily EE was calculated using the modified FLEX heart rate method of Ceesay et al.[35] and the calorimetric equations of Elia and Livesey,[36] and was based on a minimum of 12 hours of heart rate data per day (Polar Sport Tester, Polar Electro Oy, Finland). Heart rate was averaged over 1-minute intervals throughout the waking day, with subjects recording the time at which they started and stopped wearing the heart rate monitors each day. To calculate total daily EE, a regression line of heart rate vs. EE was established for each subject by simultaneously measuring heart rate, breath-by-breath $\dot{V}O_2$ and $\dot{V}CO_2$ (averaged over 10-s intervals) at incremental workloads in the morning, after an overnight fast. The test comprised of a series of sedentary activities and an incremental exercise test on a bicycle ergometer in the following sequential steps with no break between them: 5 minutes sitting, 5 minutes standing up, 5 minutes cycling at the lowest possible resistance (55 W), and a further 3 × 5-minute blocks increasing resistance and maintaining 60 rpm.[37] The average of two calibration curves was used for calculation of EE. Total daily EE was estimated based on the following equation:[35, 38]

- Total daily EE = sedentary EE + sleep EE + activity EE

Sleep EE was calculated as 95 % of measured RMR[39] and was applied to the time when the heart rate monitors were not worn (i.e. during sleep). Sedentary EE was assumed to be equal to the mean EE from RMR, sitting, and standing measurements during the calibration.[38] However, as these calibration measures were performed following an overnight fast, the thermic effect of food (TEF) would not have been accounted for in these calculations, and this would have likely resulted in an under-estimation of total daily EE in the present study. For heart rate exceeding FLEX heart rate, heart rate was calculated using the subject-specific heart rate: O_2 calibration regression equation for each individual. Zero values and heart rates that were considered to be outside of the physiological range (>220 beats/min), which may have occurred due to a loss or interference in the signal between the HR transmitter and receiver, were removed and replaced by the average of the previous and subsequent values.[40] In the present study, AEE was calculated as total daily EE minus RMR.

Total Daily Energy Intake

A weighed dietary record method was used to measure EI in which subjects were asked to record all foods and drinks consumed. Full written and verbal information on how to complete the record was given to all subjects, and each subject was provided with calibrated digital electronic scales with a resolution of 1 g (Soehnle model 820; Soehnle-Waagen GmbH & Co. KG, Murrhardt, Germany) and a food diary for recording a description of the food/drink consumed, time of consumption, weight of food, cooking method and any leftovers. Subjects were encouraged to record all recipe formulations and to keep all packaging for ready-to-eat food products. When scale use was difficult (i.e. when eating out), subjects were instructed to record as much information as possible about the quantity of the food they ate by using household measures.

Dietary data were analysed using Diet 5 (Robert Gordon University, Aberdeen), a computerised version of McCance and Widdowson composition of foods and supplements. The database of nutritional information was updated for unusual food products based on the food packaging provided by subjects. Standard portions sizes were used with missing weights or portion sizes, and to reduce investigator bias and inputting errors, all diets were cross-checked by at least one other trained member of staff. In the present paper, mean daily EI was calculated based on the average of a participant's intake over the 6 or 7-day measurement period.

Statistical Analysis

Data are reported as mean ± SD. A paired t-test was used to examine the change in body weight 6 or 7-day measurement period, and simple linear and segmental linear regression were used to examine the association the average weight change and energy balance over this period. The use of segmental linear regression allowed the association between energy balance and weight change to be different for positive and negative weight change by including in the regression an additional term which was the interaction between weight change and an indicator variable for positive changes. Based on previous findings,[5-8, 10, 41] a regression model was constructed using general linear modelling (IBM SPSS, Chicago, Illinois, Version 24) with mean daily EI as the dependent variable and fat mass (FM), FFM, RMR and AEE as independent variables. A 'study' term was also entered in the regression model to account for any heterogeneity introduced by the inclusion of aggregated data from separate studies, and given their known effect on RMR and EI, sex and age were also included. Multicollinearity was assessed using the variance inflation factor (VIF), which indicated that there were no violation in the model described (VIF < 5.5).[42]

Path analysis (IBM AMOS, Chicago, Illinois, Version 24) was also used to further examine the associations the standardised residual scores for FM, FFM, RMR, AEE and mean daily EI (after adjusting for study differences using residuals from a linear regression model which had a term for study only). A model was constructed that tested whether AEE had a direct effect on mean daily EI or indirect effects via FM, FFM and RMR.

A-priori power calculations indicated that for the number of observed (5) and unobserved (4) variables included in the model, the sample size exceeded the required N (137) to detect medium effect sizes (0.3) with a power of 0.80, and a probability level of $P \leq 0.05$.[43] The significance of the regression coefficients and fit statistics were calculated using the Maximum Likelihood estimation method. The following recommended goodness of fit indices were analysed to test for the adequacy of the mediation model: Chi-square (χ^2), Tucker Lewis Index (TLI), Comparative Fit Index (CFI), and Root-Mean Square Error of Approximation (RMSEA), with 95% confidence interval.[42, 44] Indirect effects were tested through the bootstrapping method, with 2000 Bootstrap samples and 95% bias-corrected confidence intervals (CI). Effects were significant when zero was not included in the CI lower and upper limits.[42, 44]

RESULTS

Mean daily EI, total daily EE, RMR, AEE and PAL can be seen in Table 2. There was a mean energy deficit of -1250 ± 3039 kJ/d during the measurement period, which resulted in a small but statistically significant loss of body weight (-0.49 ± 0.92 kg; P = 6.0602E-14). The intercept of the average weight change and energy balance (i.e. total daily EE minus total mean daily EI) was found to differ significantly from zero (coefficient = -0.401; SE = 0.064;

P = 2.0007E-9), indicating an underestimation of energy balance relative to that predicted from weight change. As the energy cost of weight gain and weight loss differ,[45, 46] segmented linear regression was also used to examine the association between weight change and energy balance and indicated that zero weight change occurred at an energy balance of -1121 kJ ($F_{(2, 226)}$ = 6.363, P = 0.002; R^2 = 0.05).

Table 2 here

Body Composition and Energy Expenditure as Predictors of Energy Intake

Figure 1 here

As can been seen in Figure 1, statistically significant positive bivariate associations were seen between EI and FFM (r = 0.541; P = 8.198E-20), RMR (r = 0.482; P = 1.8273E-15) and AEE (r = 0.364; P = 5.3458E-9), while a statistically significant negative association was seen between FM and mean daily EI (r = - 0.157; P = 0.014). To further examine these relationships between body composition, RMR, AEE and mean daily EI, a regression model was constructed using general linear modelling (Table 3). After accounting for sex (ß = 0.15; P = 0.561), age (ß = -0.09; P = 0.121) and study (P = 0.023 to P = 0.693), FM (ß = -0.26; P = 0.000402), RMR (ß = 0.39; P = 0.000431) and AEE (ß = 0.18; P = 0.002) were found to independently predict mean daily EI ($F_{(10, 231)}$ = 18.532, P = 9.4156E-25; R^2 = 0.445).

Table 3 here

To further explore the reported association between AEE and mean daily EI, a path analysis was conducted to test the direct and indirect effects of AEE on mean daily EI, through the effects of FM, FFM and RMR (Figure 2). The following path coefficients were non-significant and removed from the model: the direct effects of AEE on RMR (b_{AEE} = 0.00; SEb

= 0.04; Z = 0.12, P = 0.904), and the direct effect of FFM on mean daily EI (b_{FFM} = 0.12; SEb = 0.10; Z = 1.27, P = 0.204). The model with these nonsignificant paths removed revealed a good fit ($\chi^2_{(2)}$ = 1.63, P = 0.444; TLI = 1.00; CFI = 1.00; RMSEA = 0.00, P = 0.626). The predictors proposed in the theoretical model accounted for a total of 39% of the variance of EI and 75% of RMR variance. Overall, analyses indicated that, AEE had a direct effect on EI and also an indirect effect mediated by decreased FM and increased FFM. In turn, effects of FM and FFM on EI were found to be partially and fully mediated by RMR, respectively. AEE had a significant direct effect on FM (β = -0.15) and on FFM (β = 0.39). FM had a direct effect on mean daily EI (β = -0.35), and an indirect effect of 0.18 mediated by RMR (95% CI = 0.13, 0.24; P = 0.001). FFM had an indirect effect of 0.43 on mean daily EI mediated by RMR (95% CI = 0.34, 0.51; P = 0.001). AEE had a significant indirect effect on RMR of 0.26 (95% CI = 0.16, 0.35; P = 0.001) mediated by FM (βAEE.FM x βFM.RMR = -0.15 x 0.32 = -0.05) and by FFM (βAEE.FFM x βFFM.RMR = 0.39 x 0.77 = 0.30). AEE had a direct effect on mean daily EI (β = 0.19) and an indirect effect of 0.20 (95% CI = 0.14, 0.26; P = 0.001).

An alternative reversed model was examined which tested the effect of mean daily EI on AEE via FM, FFM and RMR. Results indicated that this model presented an unacceptable model fit ($\chi^2_{(2)}$ = 30.50, P = 0.001; TLI = 0.72; CFI = 0.94; RMSEA = 0.24, P = 0.001).

Figure 2 here

DISCUSSION

The present study examined whether biological (e.g. body composition and RMR) and behavioural (e.g. AEE) components of total daily EE acted as independent determinants of mean daily EI in individuals not undergoing significant changes in body weight or composition. Consistent with our previous findings,[10, 11] FFM was associated with mean daily

EI but its effect on EI was mediated by RMR. Importantly, AEE was also found to predict mean daily EI alongside RMR and FM. These data therefore suggest that the energy expended through daily activity may also influence mean daily EI, albeit, under these conditions, not as strongly as other biological determinants such as body composition and RMR.

The Effect of Activity Energy Expenditure on Daily Energy Intake

As determinants of total daily EE, evidence is accumulating to suggest that FFM and RMR are associated with a drive to eat that reflects the energetic demands of metabolically active tissue.[5-8, 10, 41] It has previously been reported that FFM is positively associated with EI,[5, 9-11] but this association is mediated by RMR.[10, 11] In line with these findings, path analysis in the present study indicated that while FFM was associated with EI, its effect on mean daily EI was fully mediated by RMR. The present analyses extend our previous findings by accounting for the behavioural contribution of AEE to total daily EE. Importantly, AEE was found to independently predict mean daily EI alongside RMR and FM, with path analysis indicating a direct association between AEE and mean daily EI that was not accounted for by FM, FFM or RMR (alongside an indirect association- see below). Given previous findings,[5-8, 10, 41] it is plausible to suggest that AEE may influence EI via its contribution to total daily EE and that EE per se may exerts influence over food intake. However, as these data are cross-sectional and do not include a large array of potential explanatory variables, alternative explanations may exist. For example, it could be speculated that habitually active individuals conscious or subconscious alter food choice to increase EI. It should also be noted that the direct and indirect pathways reported here represent statistical associations, and therefore, causality should not be inferred and care should be taken when interpreting the direction of flow. An alternative 'reversed' model was tested that examined the effect of EI on AEE i.e. that increased EI was associated with greater FM, and in turn, lower AEE. However, this 'reverse' model failed to support this alternative hypothesis, and while it does not provide evidence of causality, it does help suggest the likely direction of flow in the model.

The amount of variance in mean daily EI accounted for by AEE was smaller than that seen for RMR and FM, with AEE explaining ≈3 % of the between-subject variance in mean daily EI after accounting for sex, age, body composition and RMR. The strength of the direct path between AEE and mean daily EI was also weaker than that seen between RMR and EI. However, the modest association between AEE and mean daily EI is consistent with the smaller proportion of total daily EE explained by AEE as compared to RMR.[29] Biologically mediated components of total daily EE such as FFM and RMR may also be more closely associated with EI as they typically display less between-day variability than AEE (which, in part, reflects the behavioral activities of daily living).[14, 29] It could therefore be argued that while FFM and RMR are well placed to exert stable influence over food intake, the contribution of AEE to daily food intake is likely to be weaker and more variable (and thus, harder to quantify). Errors in the measurement of total daily EE may have also contributed to modest association between AEE and mean daily EI. While FLEX heart rate provides valid estimates of total daily EE relative to doubly labelled water at the group level, higher levels of error are observed at the individual level.[47] The use of accelerometry is now more common place, but significant error in the individual estimates of EE are still observed with this technique.[48]

Although cross-sectional, the present findings may have implications for our understanding of how physical activity influences EI. Systematic increases in AEE may promote (modest) increases in EI over time as EI begins to partially track changes in total daily EE.[17-20] This interpretation fits with the loose coupling thought to exists between exercise-induced EE and EI,[49] and evidence indicating partial tracking of EI when exercise is used to manipulate energy balance over 7 to 14 day[17-19] and 12 week[20] periods. However, these data should not be interpreted to suggest that increases in physical activity or AEE will lead to overconsumption i.e. eating in excess of energy needs, as any increase in EI should be evaluated in the context of changes in total daily EE and energy balance. Indeed, a tighter coupling is thought to exist between EI and EE in individuals with high habitual activity levels that means day-to-day EI more closely matches daily energy requirements.[21-23] There appears to be two important features of this tighter coupling in active individuals; i) an increase in orexigenic drive that elevates EI in response to increased EE (although the increase in EI does not typically fully compensate for the increase in EE), and ii) a concomitant increase in the sensitivity to post-prandial hunger and satiety cues that helps 'tune' daily EI to daily energy requirements.[50] The present findings help provide insight into the mechanisms that lead to this increase in orexigenic drive, with greater EI in active individuals in part reflecting the increased contribution of AEE to total daily EE. This effect is likely modest when considered in isolation, but physical activity-induced changes in body composition (e.g. increased FFM and, in turn, RMR), may also contribute to an increased orexigenic drive. However, prospective longitudinal interventions that systemically manipulate AEE are needed to confirm (or refute) these suggestions.

Indirect Effects of Activity Energy Expenditure on Energy Intake

In addition to its contribution to total daily EE, physical activity may influence EI via a number of other mechanisms, e.g. alterations in gastric emptying,[51] appetite-related hormones[52] or psychometric eating behaviour traits.[53] Indeed, path analysis in the present study also indicated an indirect effect of AEE on EI (mediated by body composition and RMR). This appears to arise from the effects of AEE on body composition, with higher AEE associated with higher FFM and lower FM in the present study. While it might be predicted that higher FFM would be associated with higher EI (due to a higher RMR), we have previously demonstrated that the influence of FM on EI is more complex. As previously reported,[11] FM appears to influence EI via two separate and opposing associations; a weak positive association between FM and mean daily EI that may reflect its energetic contribution to RMR, and a stronger a negative association that may reflect the inhibitory action of biological (e.g. leptin)[54] and/or psychological factors (e.g. dietary restraint).[11] It is the balance between these separate, and potentially opposing, effects of FM and FFM that determine their overall influence on EI. It is plausible to suggest that AEE may also indirectly influence EI by altering the balance between these associations via long-term changes in body composition.

Limitations

Mean daily EI was measured in the present paper using a self-reported weighed dietary record method, which is known to lead to an underestimation of EI.[55] Similarly, FLEX heart rate tends to underestimate EE relative to doubly labelled water,[35, 38, 56] although mean PAL in the present study was 1.69 x RMR (which is similar to population estimates for energy requirements in free-living subjects derived using doubly-labelled water).[57] These measurement issues may explain why a bias was seen in the relationship between weight change and energy balance. No adjustment for TEF was made in the calculation of AEE. As HR:$\dot{V}O_2$ curves were estimated in fasting subjects, TEF would not have been adequately accounted for in the calculation of total daily EE in the present study, and this would have likely resulted in an under-estimation of total daily EE (and AEE). Thus, deducting an arbitrary EE factor to account for TEF in the calculation of AEE in the present study would have improved our analysis. Furthermore, although TEF is commonly assumed to equal 10 % of EI,[58] applying a constant TEF value fails to recognise i) between-subject variability in the energy cost of digestion and storage/metabolism, and ii) differences in TEF following the ingestion of foods differing in macronutrient composition.[58] While the unique variance explained by AEE in these models was modest, this is not perhaps surprising given the multiple pathways through which AEE can influence EI, and the inter-individual variability typically seen in both AEE[29] and key appetite-related processes.[59]

CONCLUSIONS

These data indicate that AEE independently predicted mean daily EI alongside body composition and resting metabolism, albeit not as strongly. These findings are in agreement with the loose coupling previously reported between exercise-induced EE and EI,[49] and provide further support for the idea that EE and its metabolic (RMR) and behavioral (AEE) sub-components are associated with daily food intake in individuals who are not undergoing significant changes in body weight or composition.

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LEGENDS FOR FIGURES

Figure 1

Scatter plots and bivariate correlation coefficients illustrating the associations between mean daily energy intake and fat mass (A), fat-free mass (B), resting metabolic rate (C) and activity energy expenditure (D).

Figure 2

Path diagram with standardized parameter coefficients for the direct and indirect effects of the standardised residual scores of fat mass, fat-free mass, resting metabolic rate and activity energy expenditure (after adjusting for the influence of study differences using residuals from a linear regression model which had a term for study only) on mean daily energy intake, and the squared multiple correlations (R^2) for resting metabolic rate and energy intake. The mediation model indicates that the effect of fat-free mass on mean daily energy intake was fully mediated by resting metabolic rate, while activity energy expenditure had direct and indirect effects on mean daily energy intake. FM, fat mass; FFM, fat-free mass; RMR, resting metabolic rate; AEE, activity-energy expenditure; EI, energy intake.

ONLINE SUPPLEMENTARY MATERIAL

Supplementary Figure 1: Participant flow chart detailing the contribution from individual studies.