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Longitudinal and cross-sectional evidence that daily resting and activity energy expenditures are independent in humans

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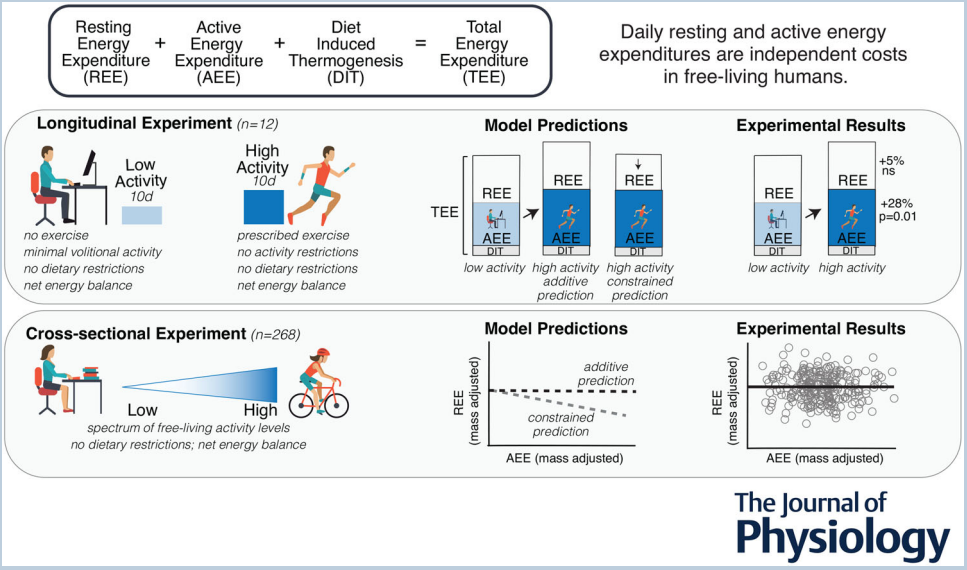

Abstract figure legend Two models of human energy expenditure were tested. The additive model predicts independent resting and activity costs, while the constrained model predicts a tradeoff between resting and active expenditure. Both longitudinal and cross-sectional experiments support the additive model, with no tradeoffs between resting and active energy expenditures.

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Abstract Total energy expenditure (TEE) is commonly modelled as the sum of resting energy expenditure (REE), activity energy expenditure (AEE), and diet-induced thermogenesis (DIT). This additive model has recently been challenged by the constrained energy balance model, which proposes that reductions in mass-adjusted REE compensate to some extent for increases in AEE, rendering mass-adjusted TEE effectively invariant. We tested these competing models using two complementary approaches. First, we conducted a short-term longitudinal, repeated-measures experiment in 12 adults who completed 10-day periods of high and low physical activity separated by a washout period. TEE was measured with doubly labelled water, AEE with wearable sensors, and REE with indirect calorimetry as well as anthropometric equations. Second, we analysed a cross-sectional sample of 268 adults from the Pennington Centre Longitudinal Study that measured TEE and REE independently. In both studies, metabolic rates were analysed using size-adjusted regression models. In the longitudinal experiment, a ∼28% increase in AEE (∼250 kcal/day) increased TEE by 10% (272 kcal/day) without reducing mass-adjusted REE, contradicting predictions of metabolic compensation. In the cross-sectional study, mass-adjusted REE and AEE were statistically independent, with no evidence for metabolic compensation. These results support the additive model of energy expenditure and indicate that increased physical activity does not suppress REE, contradicting the hypothesis that metabolic compensation thwarts the effects of physical activity on weight management.

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Key points

- There is a debate over whether active activity expenditure (AEE) is independent of resting energy expenditure (REE) corrected for body mass and composition or causes decreases in REE through metabolic compensation.
- We tested AEE's effects on REE using both a repeated measures longitudinal study and a cross-sectional study. In both studies, AEE and REE were measured independently, and metabolic rates were analysed using regression models.
- In the longitudinal study, a 28% increase in AEE had no effect on mass-adjusted REE, contradicting predictions of metabolic compensation. In the cross-sectional study, mass-adjusted REE and AEE were statistically independent with no evidence for metabolic compensation.
- These results indicate that increased physical activity does not suppress mass-adjusted REE, supporting the additive model of energy expenditure.

Introduction

At the organismic level of metabolism, energy balance (neither gaining nor losing weight over several days) can be quantified as TEE = REE + AEE + DIT, where TEE is total energy expenditure per day, REE is resting energy expenditure per day, AEE is activity energy expenditure per day, and DIT is diet-induced thermogenesis per day. Longstanding assumptions of this additive model, illustrated in Fig. 1, are that DIT is approximately 10% of TEE (Westerterp, 2004), and that REE and AEE are mostly independent, hence additive. A well-studied partial exception to the independence of REE and AEE is the phenomenon of excess post-exercise oxidative consumption (EPOC) (Gaesser & Brooks, 1984). Numerous studies show that physical activity (PA) can cause an immediate short-term rise in REE that rapidly declines and may be followed by a prolonged phase of slightly elevated REE that usually lasts just a few hours, but can potentially last up to 24 h depending on the dose and type of PA. In addition, long-term increases in AEE can increase muscle mass thus increasing REE (Speakman & Selman, 2003). Because of these effects, resting metabolic rates such as REE should be standardized by fat-free mass (FFM), and basal energy expenditure (BEE; also known as basal metabolic rate) should be measured a minimum of 24 h and ideally 48 h following physical activity. Sleeping metabolic rate may be an even better measure

but is challenging to measure in free range participants (Norman et al., 2026).

The additive model of REE and AEE, which assumes these variables are independent apart from EPOC, has recently been challenged following several studies that use doubly labelled water (DLW) to measure TEE and that sometimes also employ wearable sensors to estimate AEE. According to the resulting constrained energy balance or metabolic compensation model, whose predictions Fig. 1 also illustrates, increases in AEE cause long-term compensatory decreases in REE and thus can leave TEE per unit FFM invariant or only partly reduced (Pontzer et al., 2016). A corollary prediction of the model is that decreased levels of PA should increase levels of REE. Note that here we focus solely on metabolic compensation, which differs from behavioural forms of compensation, especially decreases in non-exercise physical activity (also known as non-exercise activity thermogenesis, NEAT) following increased levels of exercise (Halsey, 2021). How much and over what time period metabolic compensation occurs is debated. If metabolic compensation is 100%, then an additional expenditure of 300 kcal/day on PA would be offset by 300 kcal decrease in mass-adjusted REE, keeping TEE constant. Some studies, however, suggest that metabolic compensation is partial, on the order of 28% (Careau et al., 2021). In addition, Pontzer (2025) has suggested there may be a time lag between increased levels of PA and metabolic compensation but does not specify or test by what mechanisms and over what time period there is a delay between changes in AEE and REE (see below).

Although metabolic compensation may be less than 100% (see below) and not immediate, a controversial implication of the constrained energy balance model is that PA may be ineffective for weight loss or preventing weight gain. Because this implication is consequential for evaluating the efficacy of exercise for weight management – a major, global public health issue – it is valuable to test both the additive and constrained models rigorously and conservatively.

Most analyses supporting metabolic compensation predicted by the constrained energy balance model are based on inferences from cross-sectional studies. One influential cross-sectional study found that a sample of 30 Hadza hunter-gatherers from Tanzania have FFM-adjusted TEEs similar to a sample of 239 Americans despite being approximately ten times more physically active (Pontzer et al., 2012). The study did not measure REE, but the authors inferred that the lack of difference in mass-specific TEE was a function of decreased REE. Other cross-sectional studies reported no difference in TEE relative to FFM when comparing large samples of individuals from industrial, high-income countries and less industrialized, low-income countries with presumably higher levels of AEE (Dugas et al., 2011; Luke et al., 2009). Although these studies did not compare REE *vs.* AEE, metabolic compensation was inferred to explain the invariance of TEE relative to FFM (Pontzer et al., 2016). Another study of children in a forager-hunter population from Ecuador found no difference in FFM-adjusted TEE compared to children from the US and UK but higher

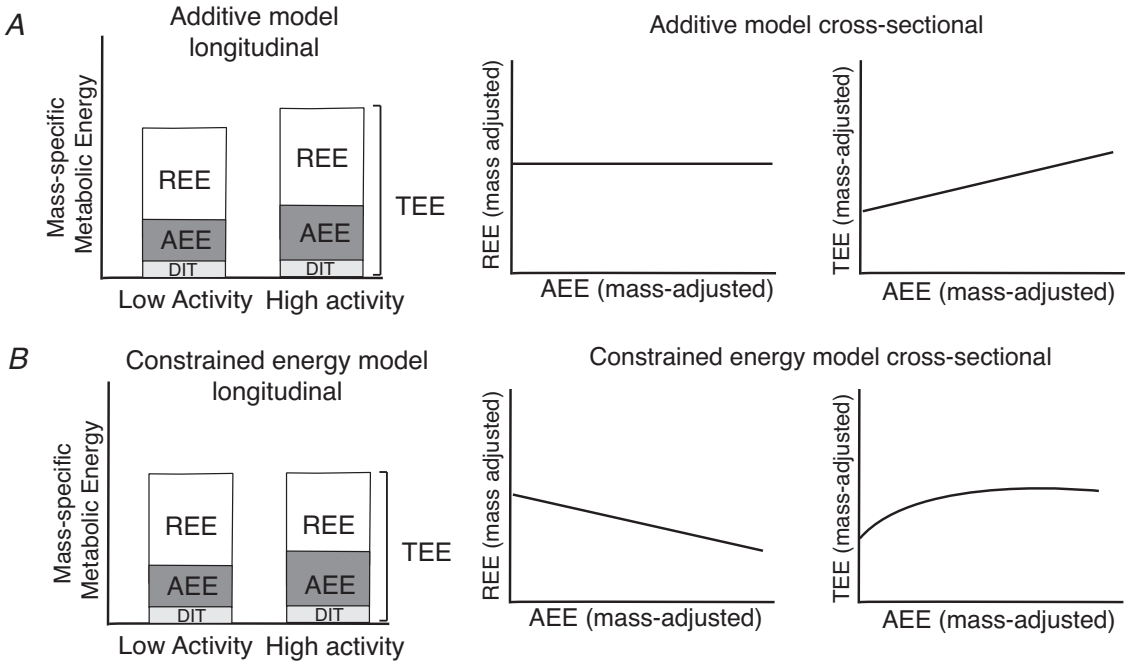

Figure 1. Model predictions
*L*ongitudinal (*A*, left) and cross-sectional (*B*, right) predictions of additive *versus* constrained energy models.

levels of REE combined with lower levels of AEE despite higher accelerometry counts (Urlacher et al., 2019, 2021). Because the higher REEs of the forager children were inferred to reflect increased immune costs from a greater infectious disease burden, the researchers reasoned that these children decreased their non-exercise PA levels to maintain similar TEE levels per FFM. Finally, Careau et al. (2021) analysed metabolic rates from 1,756 elderly adults whose TEE was measured using DLW, REE was measured using respirometry, and AEE was calculated as 0.9TEE − REE. On the basis of the significant negative association between AEE and REE after accounting for FFM, fat mass, and age, the authors inferred that decreases in REE compensate for 28% of the additional calories normal weight individuals spend on PA.

Although cross-sectional studies can take advantage of large sample sizes, not all such studies support evidence for metabolic compensation. For example, no evidence for compensation was reported from a cross-sectional study of 75 individuals including runners whose PA levels were measured with accelerometry and compared to TEE measured via DLW and REE measured repeatedly with indirect calorimetry (Howard et al., 2025). In addition, cross-sectional studies can have several drawbacks for testing the additive *versus* constrained energy balance hypotheses. One problem is the need to separate the effects of metabolic compensation, defined here as decreasing REE in response to increased AEE, from behavioral compensation which is typically caused by decreased levels of non-exercise PA that also lowers TEE (Halsey, 2021). An additional challenge with cross-sectional studies is controlling for covariates that affect REE and TEE independently or differently from their effects on AEE, such as body mass, body composition, environmental temperature, age, sex, fitness, and genetics. In addition, these models sometimes estimate energy compensation by regressing REE (or BEE) against AEE or TEE, but regressing non-independent variables such as these can cause spurious negative slopes driven by collinear measurement error that can be misinterpreted as evidence for compensation (Gonzalez et al., 2023; Lieberman et al., 2026). Instead, when observed metabolic rates are compared against metabolic rates predicted from an independent reference sample of mammals, mass-adjusted levels of AEE of highly active subsistence populations are 32%–206% higher than a sample of sedentary Americans, with no significant difference in levels of mass-adjusted REE (Yegian et al., 2024). Despite a wide range of variation in PA levels, Yegian et al. (2024) found no negative correlation between AEE and REE adjusted for FFM.

Controlled longitudinal studies are inherently a better experimental design to test alternative models of the effects of AEE on REE. Several longitudinal studies of the metabolic effects of increased PA levels have been argued to support the constrained energy balance model by reporting less than expected increases in TEE following increases in prescribed levels of exercise. Westerterp et al. (1992) trained 32 normal weight adult individuals (16 men, 16 women) for a half marathon over 44 weeks, leading to an average decline in BEE of 112 kcal/day associated with average decreases in fat mass of 3.8 kg and 2.0 kg in men and women, respectively, but increases in FFM of 1.6 kg and 1.2 kg in men and women. Careau's (2017) reanalysis of these data found that individuals with higher self-reported daily energy intake (DEI) had higher BMRs, but there was a negative relationship between BMR and estimated energy surplus (DEI − BMR), indicating compensation. Unfortunately, self-reported DEI is subject to considerable error, and this study did not analyse relationships between physical activity and BMR and thus cannot explain why some individuals had evidence for apparent compensation and whether the cause was behavioural or metabolic from changes in body composition or independent of FFM. In addition, Thurber et al. (2019) claimed that metabolic compensation was evident in a sample of 6 adults who ran across the USA, completing approximately 6 marathons per week over 20 weeks. These runners' TEEs declined by an average of ∼600 kcal/day during the race, but their measured REEs increased by approximately 6% despite an average weight loss of 4 kg, suggesting that observed decreases in the marathoners' TEE resulted from decreases in NEAT, which was not measured (Halsey, 2021).

Pontzer and Trexler's (2026) meta-analysis of longitudinal studies that prescribed aerobic exercise to human participants, mostly weight loss studies, reported evidence for partial (≈30%) metabolic compensation. However, this analysis did not test the relationship between AEE *vs*. REE but instead compared predicted *versus* observed changes in TEE relative to changes in physical activity levels and thus, by definition, cannot test whether any observed compensation (partial or full) is metabolic or behavioural. In addition, Pontzer and Trexler (2026) quantified expected *vs*. observed compensation as ΔTEE/ΔAEE, but since ΔAEE in many of these intervention studies is close to zero, the ratio can spuriously inflate estimates of compensation when in fact none may have occurred. For example, one of the trials Pontzer and Trexler (2026) analysed was the E-MECHANIC study, which randomized 198 adults to a no-exercise control group or two groups who exercised under supervision at either 8 or 20 kcal/kg body weight, and measured REE, TEE and AEE independently. After 24 weeks, the only evidence for compensation in the exercise groups was increased energy intake with no significant change in REE adjusted for body mass and composition (Flanagan et al., 2024; Martin et al., 2019). Although this was a randomized control study, inter-individual

variation in levels and types of compensation are a possible confound.

Here we present the results of two additional and different experimental tests of the relationship between AEE and REE in humans. The first (see Methods) is a short-term longitudinal, repeated measures experiment to assess how changes in AEE affect REE and TEE in 12 individuals who underwent 10-day long periods of high and low physical activity separated by a 60-day washout period. TEE was measured with DLW; REE was measured with respirometry and also estimated using anthropometric data; AEE was measured using both wearable sensors as well as by subtracting REE from 0.9 × TEE. While the additive model predicts REE to be independent of AEE, the constrained model predicts individuals' REEs to be significantly lower during the period of higher PA.

The second test is a cross-sectional analysis of 274 participants enrolled in the Pennington Centre Longitudinal Study (see Methods; Dorling et al., 2025; Falkenhain et al., 2025; Ravussin et al., 2015; Redman et al., 2014; Yegian et al., 2024;). TEE was measured using DLW and REE was measured using respirometry under controlled conditions. The additive model predicts mass-adjusted AEE and REE to be independent across individuals in the sample but a positive relationship between AEE and TEE; in contrast the constrained model predicts a negative relationship between AEE and REE, but no association between TEE and AEE. As discussed previously (Gonzalez et al., 2023), regression dilution in TEE *vs*. REE and correlated uncertainty in REE *vs*. AEE appears as compensation in regression models. Therefore, we focused our analysis on the added explanatory power of regression compared to the null additive model. To do so we calculated ΔR^2:

$$\Delta R^2 = {R^2}_{\text{reg}} - {R^2}_{\text{add}},$$

where ${R^2}_{\text{reg}}$ is the coefficient of determination from the simple linear regression model of REE *vs*. AEE or TEE *vs*. AEE and ${R^2}_{\text{add}}$ is the coefficient of determination from the additive model, which assumes resting and activity metabolic rates are independent.

Note that to control for the effect of body size on metabolic rates, the cross-sectional study used a standard multivariate linear regression to analyse AEE, REE, and TEE residuals controlled for FFM, FM, age, and sex. To be conservative, the Appendix includes a complementary analysis using metabolic quotients, defined as the ratio of measured metabolic rates (AEE, REE, TEE) relative to predicted values from an independent reference sample of mammals, and which have been validated to correct for size within humans (Yegian et al., 2024).

Methods

Ethical approval

We report results from two studies. The first is a short-term experiment in which authorization was provided by the Harvard IRB (IRB 21–1639). All participants gave informed consent before participating in the study which conformed to the standards set by the latest version of the *Declaration of Helsinki*. The second is an analysis of cross-sectional data from the Pennington Centre Longitudinal Study. Procedures for this study were reviewed by the Pennington Biomedical Research Centre Institutional Review Board (PBRC311EX). This data set comes from a compilation of studies conducted at Pennington since 1985, all of which were IRB approved and in which enrolled participants provided written, informed consent in accordance with the latest version of the *Declaration of Helsinki* except for registration in a database.

Short-term longitudinal study

Participants. For this study, which lasted 4 months, 12 participants (4 male; 8 female) were recruited from the Harvard community as summarized in Table 1. Mean age was 23.8 ± 3.5 (SD); mean BMI was 24.5 ± 2.7 (SD). Exclusion criteria were any musculoskeletal injuries, being pregnant, or having participated in weight loss for three months prior to the study. One additional participant was removed *post hoc* from the analysis because of erroneous TEE data.

Study interventions. Participants completed two 10-day intervention periods, one high activity (HA) and one low activity (LA) separated by an 8-week interim washout period to allow isotope ratios to return to baseline. Participants were dosed with DLW (see below) at the start of each intervention and provided daily saliva samples during both the HA and LA periods. REE was measured in a fasted resting state in the morning prior to the start of each intervention and then every 3 days at the same time of day. Finally, participants wore Fitbit Inspire 2 activity trackers (FitBit Inc., San Francisco, CA, USA) to measure overall activity levels.

Prior to the study, participants were interviewed to estimate their baseline average weekly physical activity in MET-minutes using standardized values from the literature (Jetté et al., 1990). During the HA period, participants were instructed to increase daily activity to at least 135 MET-min/day if they were not already at that threshold with their baseline activity level (which was then verified *post hoc* using wearable sensors). Participants were given a table adapted from Jetté et al. (1990) as a reference and were allowed to choose their activity types

Table 1. Participant characteristics and mean energetic values for the high activity and low activity periods of the longitudinal experiment

		Low activity	High activity	P^*
BMI	kg/m^2	24.2 ± 2.2	24.1 ± 2.7	0.930
Body mass	kg	71.2 ± 15.1	70.7 ± 14.7	0.213
Fat	%	20.7 ± 14.7	22.2 ± 14.7	0.247
TEE	kcal	2815 ± 746	3087 ± 582	0.017
REE$_{meas}$	kcal	1870 ± 385	1894 ± 389	0.645
REE$_{pred}$	kcal	1594 ± 156	1591 ± 154	0.392
AEE$_{meas}$	kcal	663 ± 447	885 ± 297	0.061
AEE$_{pred}$	kcal	939 ± 611	1187 ± 450	0.016

*Significance calculated using paired *t* tests (all variables passed Shapiro-Wilks tests for normality).

freely. For the LA period participants were told to avoid physical activity as much as possible, including exercise, locomotion, and other daily tasks.

DLW protocol. On the first day of each intervention period participants provided a baseline saliva sample and then were given DLW doses of 1.8 g 10% ^{18}O and 0.12 g 99.9% ^{2}H per kilogram of body mass. Saliva samples from days 1, 4, 7, and 10 were analysed by the Stable Isotope Laboratory at the Children's Nutrition Research Centre, Baylor College of Medicine (Houston, Texas) following published methods (Wong and Clarke, 2012, 2015). FFM was calculated from body water estimates via isotope enrichment, and FM was the difference between FFM and BM, while TEE (kcal/day) was calculated from the rate of isotope depletion (Speakman et al., 2021). To validate the effectiveness of the 8-week washout period, baseline ^{2}H and ^{18}O samples from the start of HA and LA periods were compared, and confirmed to be not significantly different.

REE protocol. Three measurements of REE were taken 3 days apart during each intervention period. Participants came to the lab at the same time of the morning on each of the three days. Prior to their visit, participants were instructed to fast for 12 h and refrain from doing any physical activity that morning. During each lab visit, participants lay semi-reclined on cots for 35 min in a quiet state. After the first 25 min they were fitted with a mouthpiece and nose clip connected to a one-way valve and a Douglass Bag (AD Instruments, Colorado Springs, CO, USA). Flow rate through the valve was measured using a spirometer (AD Instruments, San Jose, CA, USA). After 5 min to allow for adjustment, flow was directed into the Douglass Bag and expired air was collected for 5 min. Expired gas was scrubbed of water vapor and analysed for O_2 and CO_2 content (PA-10 and CA-10 analysers, Sable Systems, Las Vegas, NV, USA). Flow was corrected to STP using room temperature and barometric pressure values, and $\dot{V}_{O_2}$ was calculated using the equation of Withers (1977). $\dot{V}_{O_2}$ was converted to energy using a standard conversion rate of 4.86 kcal/L of O_2 assuming an RQ of 0.85.

In addition to the average measured value via respirometry (REE$_{meas}$, kcal/day), we estimated average REE costs under basal conditions using the Mifflin-St Jeor equations (Mifflin et al., 1990) for males and females (REE$_{pred}$):

$$\mathrm{REE} = 10 \times \mathrm{weight}\,(\mathrm{kg}) + 6.25 \times \mathrm{height}\,(\mathrm{cm}) - 5 \times \mathrm{age}\,(\mathrm{years}) + 5 \text{ for males,}$$

$$\mathrm{REE} = 10 \times \mathrm{weight(kg)} + 6.25 \times \mathrm{height(cm)} - 5 \times \mathrm{age}\,(\mathrm{years}) - 1615 \text{ for females.}$$

Accelerometry. Participants were instructed to wear a Fitbit Inspire 2 accelerometer and heart rate monitor during all waking hours, and to charge their activity trackers when asleep. Wear time validation using heart rate data showed >85% wear time for all participants during each period. MET-minutes were extracted using the Fitbit API in time series at the resolution of one minute and then summed over the period in order to calculate a daily average of MET-min/day.

Data analysis. AEE was calculated as 0.9 × TEE-REE$_{pred}$ thus assuming that DIT is ∼10% of TEE (Westerterp, 2004). Note that we used REE$_{pred}$ rather than REE$_{meas}$ to avoid potential error from EPOC and DIT in REE$_{meas}$ (Speakman & Pontzer, 2023). Each variable passed a Shapiro-Wilks test for normality, so simple paired sample *t* tests were used to compare the HA and LA periods. Data are presented as means ± 1 standard deviation (SD).

Long-term cross-sectional study

Participants. We tested the relationships between AEE, REE, and TEE in a cross-sectional sample of 268

individuals (134 male, 134 female) previously described by Yegian et al. (2024) using cross-sectional data from the Pennington Centre Longitudinal Study. Participants in this population sample a wide range of activity levels, from extremely sedentary to highly active (see below). Included adult participants are those having 14-day DLW data, body composition (DXA, various instruments) and resting metabolic rate (Deltatrac II, ventilated hood metabolic cart) collected within a 30 day period as a baseline test (i.e. prior to an intervention). Briefly, average age was 38.5 ± 16.0 years (SD; range 18–74). Average BMI was 28.2 ± 6.0 kg/m^2 (SD; range 18.5–49.2). Of the 274 individuals in the sample of Yegian et al. (2024), 6 were removed from this analysis because they had negative AEE values (calculated by subtracting REE from 0.9TEE).

Intervention. Participant data represented only the baseline period prior to any intervention.

Measurements. During the baseline period energetic and body composition data collection followed standard operating procedures of the Pennington Biomedical Clinical Research Unit. TEE was measured over 2 weeks using DLW in the Mass Spectrometry Core. Two baseline urine samples were collected prior to administering an oral dose (∼1.5 g/kg body weight) that contained 1 part deuterium (99.9% enriched) and 19 parts ^{18}O (10% enriched). Baseline enrichments were subtracted from the post-dose sample enrichments, and isotope elimination rates were calculated using linear regression. CO_2 production rate was calculated using the equations of Schoeller (1998) as modified by Racette et al. (1994). TEE was calculated by multiplying the rate of CO_2 production (rCO_2) by the energy equivalent of CO_2 based on the estimated food quotient of the diet (0.866) and estimated changes in body energy stores. REE was measured in the morning following an overnight fast and no PA for the past 24 h using a portable metabolic cart and ventilated hood. Each test was at least 30 min in duration and followed a 30-minute rest. Percentage body fat was measured in the Bioimaging Core using dual energy X-ray absorptiometry (DXA).

Analysis. As with the longitudinal study described above, AEE was calculated as 0.9 × TEE-REE_{meas}, and we used simple linear regression to compare observed slope values to the known slopes of the additive models (REE *v*. AEE slope of 0; TEE *v*. REE slope of 1.0), as well as to compare the R^2 of the regression models to R^2 from the additive models as:

$$\Delta R^2 = {R^2}_{\text{reg}} - {R^2}_{\text{add}},$$

where ${R^2}_{\text{reg}}$ is the coefficient of determination from regression, and ${R^2}_{\text{add}}$ is the same for the additive model.

Results

Short-term longitudinal experiment

Among the 12 participants summarized in Table 1, PA levels measured using Fitbit trackers as MET-minutes, shown in Fig. 2*A*, were 35% higher during the HA than LA periods (HA: 1179 MET-min; LA: 869 MET-min; $P = 0.005$). AEE_{pred}, quantified as 0.9TEE − REE_{pred}, was 26% higher (HA: 1187 ± 450 kcal (SD); LA: 939 ± 611 kcal (SD); $P = 0.016$); AEE_{meas} was quantified as 0.9TEE − REE_{meas} was 33% higher (HA 885 ± 297 (SD); LA 663 ± 447 (SD); $P = 0.602$). Finally, when quantified using metabolic quotients, (Fig. 2*B*), activity levels were approximately 28% higher in the HA *vs*. LA periods as assessed by AMQ (HA: 1.01 ± 0.31 (SD); LA: 0.79 ± 0.51 (SD); $P = 0.015$). In addition, there were no significant changes in body mass ($P = 0.215$) or body fat percentage ($P = 0.243$) between the HA and LA periods (Table 1), and there was no significant difference in REE_{meas} calculated from three RMR measurements taken across each 10-day period (HA: 1894 ± 389 kcal (SD); LA: 1870 ± 385 kcal (SD); $P = 0.641$) as well as REE_{pred} calculated using the Mifflin-St. Joer equation (HA: 1591 ± 154 kcal (SD); LA: 1594 ± 156 kcal (SD); $P = 0.393$; Table 1). Note that as expected, REE_{meas} was 18% greater than REE_{pred} for both HA and LA periods by the Mifflin-St Joer equation, which predicts BMR not REE. This is expected since REE is often thought to be at least 10% higher than BMR. The complementary analysis of metabolic quotients produced the same results (see Appendix).

Although the constrained model predicts no difference in TEE between the HA and LA periods, Table 1 and Fig. 2*B* also show that mean TEE was on average 272 kcal higher for the HA period, a difference of 10% (3087 ± 582 kcal (SD) *vs*. 2815 ± 746 kcal (SD); 0.017).

Long-term cross-sectional test

In order to assess effects of variations in AEE from the large sample of individuals ($n = 268$) in the Pennington Centre Longitudinal Study, Fig. 3*A* plots REE residuals against AEE residuals. Note that this population samples considerable variation in AEE (range from 107 kcal to 1943 kcal). Also shown is the slope of 0 predicted by the additive model. Linear regression of REE *vs*. AEE residuals yields a statistically significant but small negative slope (−0.012 ± 0.045 95%CI) as expected from error. However, ΔR^2 was 0.001 compared to the null hypothesis of 0 predicted by the additive model.

Since TEE = REE + AEE + DIT, Fig. 3*C* shows additional tests of the two competing models by plotting TEE residuals against REE residuals in the cross-sectional sample; also included is the additive model with an intercept of 0 and slope of 1.0 As expected due to

regression dilution, linear regression on the residuals yields a lower slope (0.91 ± 0.32 95%CI) and greater intercept (24.6 ± 42.5 95%CI) compared to the additive model. However, the added explanatory power from regression, ΔR^2, was only 0.007 ($R_{reg}{}^2 = 0.104$, $R_{add}{}^2 = 0.097$), indicating a trivial difference between the additive null hypothesis and the regression model. Furthermore, R^2 of the additive model (0.104) and the regression model (0.097) were both small, showing that REE has trivial explanatory power for TEE overall.

Discussion

While it has long been assumed that the metabolic cost of physical activity, usually quantified as AEE, is independent of REE, several recent studies have proposed that TEE is constrained, and that increases in AEE lead to compensatory decreases in REE (Careau et al., 2021; McGrosky et al., 2025; Pontzer, 2018; Pontzer et al., 2016). If so, then increased levels of AEE from exercise are potentially ineffective for preventing or reversing weight gain because decreases in

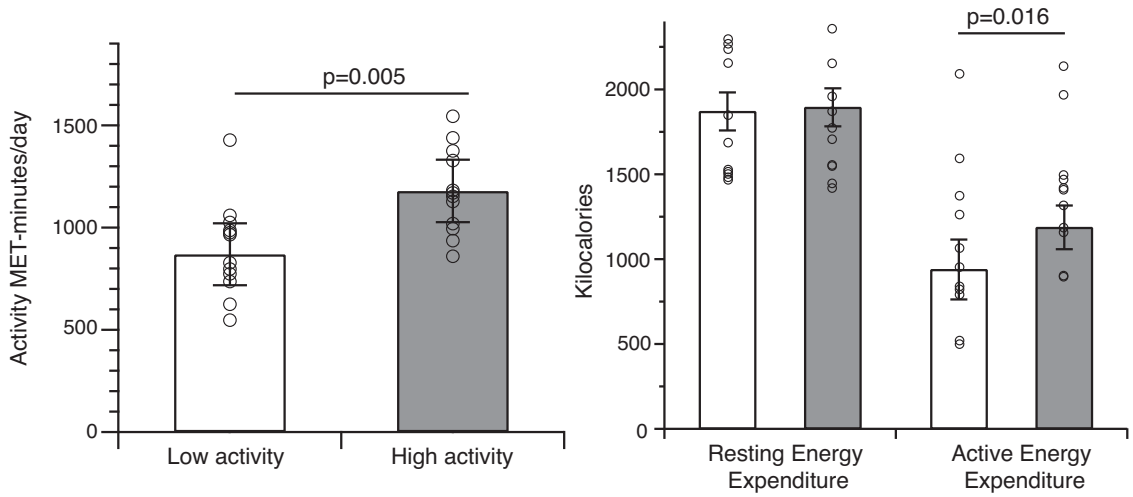

Figure 2. Results of longitudinal experiment
A, activity tracker estimates of physical activity (high activity period, filled bars; low activity period, open bars) in MET-minutes. Error bars are the 95% confidence intervals of the means. *B*, resting and active metabolic energy expenditures in the high activity and low activity periods. In both panels, significant differences were assessed by paired sample *t* tests.

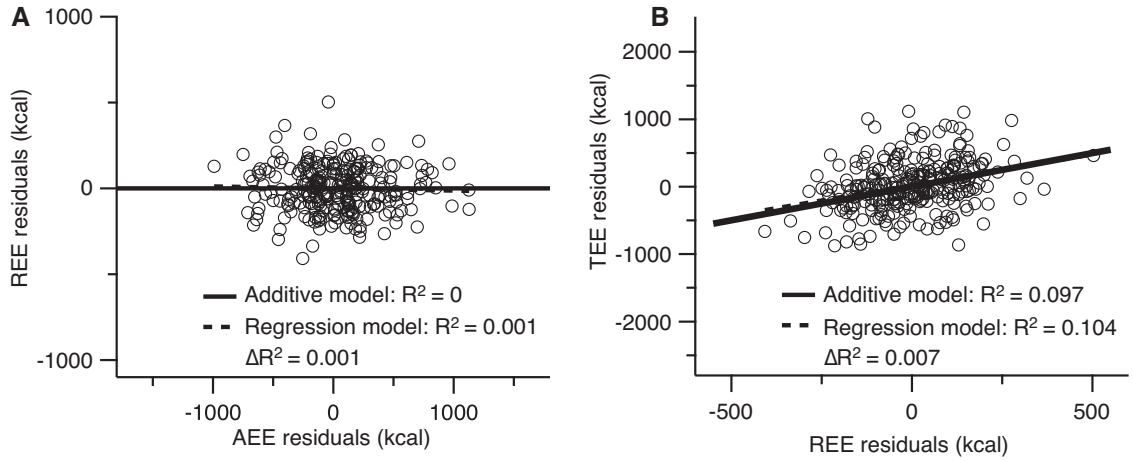

Figure 3. Results from cross-sectional experiment
Multivariate regression residuals of active energy expenditure (AEE) *versus* resting energy expenditure (REE) (*A*), and resting energy expenditure *versus* total energy expenditure (TEE) (*B*), with the additive model (i.e. null hypothesis of no relationship) plotted by the continuous line; the dashed line plots the linear regression through the data.

REE offset energy spent on PA. Because this proposed compensation has implications for medical and public health recommendations regarding exercise and adiposity, it is valuable to evaluate rigorously these claims against the null hypothesis of no metabolic compensation (note that behavioural compensation such as decreasing levels of non-exercise PA is a different matter). Although repeated measure short-term longitudinal studies which quantify the effect of changes in AEE on REE are a useful way to test these competing models while controlling for confounding effects such as age, sex, fitness, a potential problem is that some as yet unspecified amount of time, possibly weeks, may be needed for changes in REE to compensate for shifts in AEE (Pontzer, 2025). How or why such lags occur on an individual level is unclear. Changes in REE can occur either from changes in body composition, endocrine regulation (especially thyroid hormones), or from the central nervous system, primarily hypothalamic/autonomic regulation. If hormone levels or homeostatic regulation by the hypothalamus change over more extended time scales in response to changes in PA levels, such changes and their underlying mechanisms need to be tested with long-term repeated measures studies. However, the null hypothesis is that metabolic responses to PA occur in the short term, and it is reasonable to assume that large cross-sectional samples of individuals with varying, long-term habitual PA levels are metabolically stable. Put differently, these data are unlikely to be confounded by time-lags on the order of weeks or months between changes in PA levels and compensation by REE. Therefore, this study complements a short-term repeated measures experiment with a cross-sectional study that did not include an intervention. We also use this study to evaluate the confounding effects of measurement error on regressions between AEE and REE.

In terms of the short-term controlled longitudinal study, when participants increased their level of PA by an average of 248 kcal/day their REE did not decrease whether measured directly in fasted condition on three separate mornings in each treatment period or as estimated from body composition. These results, which complement the results of Martin et al. (2019) and Flanagan et al. (2024), support the additive model and contradict the constrained energy model. Note that we used REE_{pred} not REE_{meas} to calculate AEE because the added uncertainty of DIT and EPOC during respirometry estimates of REE produce large errors in AEE (see Speakman & Pontzer, 2023). Note that because of the negative dependency between AEE and REE, errors in REE_{meas} will make the slope more negative, potentially leading to spurious inferences of compensation (Gonzalez et al., 2023).

While the lack of any significant association between AEE and REE in this repeated measures study fits the additive model, we also found that measured resting metabolic rates – all taken in the morning in a fasted thermoneutral condition after 35 min of rest – were on average approximately 18% higher than those predicted by the Miflin-St Joer equation for BMR. These differences presumably reflect the effects of some combination of circadian effects, EPOC, DIT, and measurement error as shown by other studies (see Heymsfield et al., 2019, 2021; Seidler et al., 2023; Speakman & Pontzer, 2023).

Even though the repeated measures longitudinal experiment presented here finds no negative effect of PA on REE as predicted by the energy compensation model, it is possible that more than 10 days might be required for compensation to occur (Pontzer, 2025). As noted above, it is unclear what biological mechanism could cause such a time lag, and our cross-sectional analysis shows that individuals with substantial long-term differences in PA levels do not vary in their mass-adjusted REEs. In particular, there was no positive association between the degree of physical activity (measured as mass-adjusted AEE) in mass-adjusted REE among this sample of individuals, who varied substantially in PA levels. We have high confidence in these results because the REE measurements were made under strictly controlled conditions and then used in the regression models described above. Additionally, in these regressions, mass-adjusted REE was independent of mass-adjusted TEE, which was measured with DLW, and AEE was estimated by subtracting REE_{pred} from TEE, thus avoiding collinearity from subtracting REE_{avg} from TEE. Altogether, REE is a negligible determinant of variation in TEE. Similar results from a cross-sectional analysis of runners with varying levels of PA also found no effect of variations in AEE on REE adjusted for fat-free mass (Howard et al., 2025).

Another result to note is that the correlations between TEE and REE were weak in both the additive model ($R^2 = 0.104$) and linear regression ($R^2 = 0.097$). Although REE fluctuates within and between days, its average value has essentially no effect on average TEE. Because TEE = REE + AEE + DIT, and since we have no reason to believe there is strong daily variation in DIT, then variations in activity expenditure must be the major cause of cross-sectional variations in TEE. This evidence strongly supports the additive model's assumption of independence between REE and AEE, which makes sense since REE is primarily determined by tissue composition (Heymsfield et al., 2019) and AEE is primarily determined by PA behaviours.

Given the potential effects of error on regressions, another result to highlight is that the slope of the regression of REE against AEE in the cross-sectional analysis was less (−0.012) than the slope of 0.0 predicted by the additive model. As described previously by Gonzalez and colleagues (2023), one expects a negative dependency between these two variables because of

error. Since our dataset came from a single study with strictly controlled REE measurements, the error was likely small, thus leading to a very small negative slope in the regression model. These errors are an important concern because uncertainty in REE measurements may arise from respirometry measurement error and time of day, variations in mitochondrial efficiency, and error from potential contributions of EPOC and DIT on REE (for reviews, see Lieberman et al., 2026; Speakman & Pontzer, 2023). While instantaneous respirometry measurements can be collected under controlled resting conditions with modest error (usually less than 3%), REE is an estimate of energy spent per day calculated by multiplying a given measured resting metabolic rate by usually more than an order of magnitude (e.g. 48× for a 30-minute measurement). This is potentially consequential because these measurements can include error not only from technical and instrumental effects, but also from normal diurnal and day-to-day variation, and methodological and protocol factors such as fasting duration, rest period prior to measurement, posture and fidgeting, previous caffeine intake, stress, and sleep quality, that together result in coefficients of variation of ≈10% (Compher et al., 2006). Extrapolating short-term measures of RME as 24-h REE estimates can thus amplify the magnitude of small variations. Compiling REE data from multiple studies, such as via the IAEA DLW Database, also introduces uncertainty from heterogeneity among studies. Ideally, linear models on such datasets should use study-level random effects to avoid issues with dependent clustering of data (Harrison et al., 2018; Schielzeth & Nakagawa, 2013). Altogether, while there is error involved in individual respirometry measurements that can be minimized with proper experimental controls, REE error is likely substantially greater, especially when multiple studies are compiled.

This study has several limitations. While the longitudinal experiment presented here has the advantage of being a repeated measures study in which individuals served as their own controls thus removing the need to control for factors such as body mass and composition, age, sex, fitness, and genetics, the sample size is small, and the duration of the two treatment periods was only 10 days. In addition, while we measured AEE and were able to quantify how much AEE differed between the HA and LA periods, the exercise was not supervised and we did not control how much of this difference was from exercise and other forms of PA, nor did we quantify the dose of added PA in terms of intensity and duration. In addition, the washout period of 60 days was intended to prevent DLW from the first treatment period affecting the TEE measurements of the second treatment period, but lifestyle shifts over the two months between treatment periods could have biased the results. In addition, while REE_{meas} was measured at the same time in the morning on three occasions in a fasted state following 35 min of rest in thermoneutral conditions, as with all measurements of REE, it is impossible to eliminate error from circadian effects and other uncontrolled factors due to the fact that these were free-living individuals.

The Pennington Centre Longitudinal Study benefits from the use of standardized protocols and procedures over time and it afforded a relatively large cohort having a wide range of age and body types. The dataset lacked accelerometry data to provide an added ability to quantify the PA during the 2-week DLW measurement. In addition, because the study was conducted and analysed prior to the publication of Speakman et al.'s (2021) revised equation for computed TEE, the DLW results underestimate TEE by 1%–2% (Falkenhain et al., 2026). This small underestimate, however, doesn't affect the results because the hypotheses are tested by regressing TEE against AEE and the TEE residuals against REE residuals.

Despite these limitations, the results of the longitudinal, cross-sectional, and error simulation studies presented support other analyses that question or contradict the hypothesis of compensation between REE and AEE (Flanagan et al., 2024; Gonzalez et al., 2023; Howard et al., 2025; Lieberman et al., 2026; Martin et al., 2019). Instead, the results support independence between these two major components of daily metabolism. We conclude that apart from the short-term and limited effects of EPOC, energy spent on physical activity has a negligeable influence on the energy spent on resting metabolism in the absence of changes in fat-free body mass. Since REE is generally similar among individuals after correcting for body mass, body composition, age, fitness and other such factors (Heymsfield et al., 2019), variation in individuals' mass- and body-composition-adjusted TEE is driven primarily by variations in physical activity. Further, although TEE is measured effectively by the DLW method, it is not an independent, actual physiological variable but instead the sum of the major components of an organism's metabolism. The inference that mass-adjusted TEE is constrained is thus conceptually questionable.

Another important conclusion of our study is that potentially erroneous inferences underlie the hypothesis of energy compensation because of the effects of measurement error and the lack of independence among some of the variables used in regression analyses. As previously emphasized (Gonzalez et al., 2023), errors associated with metabolic rate measurements can have major effects on the slopes of regressions, leading to artifactual inferences of compensation. For this reason, we urge caution in the use of compendium datasets that combine REE measures taken by different researchers at different times and different locations with different protocols. Although these datasets have the advantage of being large and diverse, they may be prone to artifactual results from measurement errors and from dependencies

among variables. The same concern also applies to smaller, experimental datasets that do not strictly control or precisely measure REE. Another problem to avoid are analyses of datasets that calculate AEE by subtracting REE from TEE and then regressing AEE against either REE or TEE, thus leading to false inferences that arise from autocorrelations. Instead, we recommend estimating AEE by subtracting REE predicted from anthropometric equations rather than measured REE. Using predicted REE values does not completely remove error dependency, but the errors from standard predictive equations are relatively small (Heymsfield et al., 2019) and quantitatively known from previous studies, while the error from compiling disparate data or uncontrolled RMR measures can be very large.

The most important conclusion of the analyses we present that combine longitudinal and cross-sectional experimental data is that normal doses of PA do not apparently reduce resting metabolism. This result contradicts the hypothesis that metabolic compensation from reduced REE levels makes it impossible for PA to influence adiposity independently of other forms of behavioural compensation from less non-exercise PA or increased food intake. If anything, PA temporarily but only modestly increases REE through the effects of EPOC. In addition, while numerous controlled and epidemiological studies have found that low levels of PA – including the 150 weekly minutes of moderate physical activity recommended by the WHO – have little to no effect on people's weight, higher doses of PA have been shown to help prevent weight gain and potentially also contribute to modest weight loss (Gordon-Larsen et al., 2009; Murtagh et al., 2015; Oppert et al., 2021; Thomas et al., 2012; Wu et al., 2009). While diet unquestionably has a much more substantial effect than exercise on weight gain and loss, exercise may also play some role in weight management, especially weight gain. Better understanding the metabolic effects of physical activity on metabolism thus matters because most diets fail not because dieters can't lose weight, but because they regain the weight after the diet is over (Anderson et al., 2001; Kraschnewski et al., 2010; Weiss et al., 2007; de Zwaan et al., 2008). According to many studies, moderate levels of exercise can be an effective way to help prevent weight regain following a diet (Jakicic et al., 2024; Lee et al., 2010; Pavlou et al., 1989; Schoeller et al., 1997; Thomas et al., 2014). Since exercise has manifold other health benefits, public health recommendations for weight management should thus include both diet and exercise.

Appendix 1

We present a complimentary analysis of the data using metabolic quotients as the scale for describing energy expenditures. Briefly, metabolic quotients (AMQ, RMQ, TMQ) were calculated as the ratio of observed metabolic rates to relative to the predicted rates for an average legged mammal of the same size and environmental temperature based on a multivariate scaling analysis of 476 species. Thus, a quotient value of 1.0 is equal to the predicted metabolic rate of an average mammal of the same size and body composition, and higher or lower values represent, respectively, higher or lower size-independent metabolic expenditure. MQs are conservative and generalizable because they are not dependent on any one sample. Metabolic quotients have been validated for comparisons of human populations and yield nearly identical to residuals from multivariate linear regression models controlling for FFM, FM, age and sex (see Yegian et al., 2024). As expected, results using quotients were mostly identical to those of the linear models.

In the longitudinal study, RMQ_{avg} was 5% but not significantly ($P = 0.126$) higher for the HA period (2.08 ± 0.20 (SD)) than the LA period (1.99 ± 0.21 (SD)), similar to the RMQ values predicted from anthropometry (1.77 ± 0.18 (SD) *vs.* 1.72 ± 0.17 (SD), $P = 0.274$, Table A1

Table A1. Participant characteristics and mean energetic values for the high activity and low activity periods of the longitudinal experiment including metabolic quotients

		Low activity	High activity	P^*
BMI	kg/m2	24.2 ± 2.2	24.1 ± 2.7	0.930
Body mass	kg	71.2 ± 15.1	70.7 ± 14.7	0.213
Fat	%	20.7 ± 14.7	22.2 ± 14.7	0.247
TEE	kcal	2815 ± 746	3087 ± 582	0.017
REE_{meas}	kcal	1870 ± 385	1894 ± 389	0.645
REE_{pred}	kcal	1594 ± 156	1591 ± 154	0.392
AEE_{meas}	kcal	663 ± 447	885 ± 297	0.061
AEE_{pred}	kcal	939 ± 611	1187 ± 450	0.016
RMQ_{avg}		1.98 ± 0.21	2.08 ± 0.20	0.124
RMQ_{pred}		1.72 ± 0.17	1.77 ± 0.18	0.084
AMQ		1.03 ± 0.51	1.28 ± 0.33	0.015

*Significance calculated using paired *t* tests (all variables passed Shapiro-Wilks tests for normality).

and Fig. A1). In the cross-sectional study, the slope of RMQ *vs*. AMQ was −0.08 ± 0.06 95%CI, and ΔR^2 was 0.019, confirming that REE and AEE are independent in this sample (Fig. A2). Analysis of TMQ *vs*. RMQ showed the same results, with a lower slope (0.27 ± 0.14 95%CI; *post hoc* $P = 0.047$) and greater intercept (0.77 ± 0.25 95%CI; *post hoc* $P = 0.031$) compared to the additive model (Fig. A3).

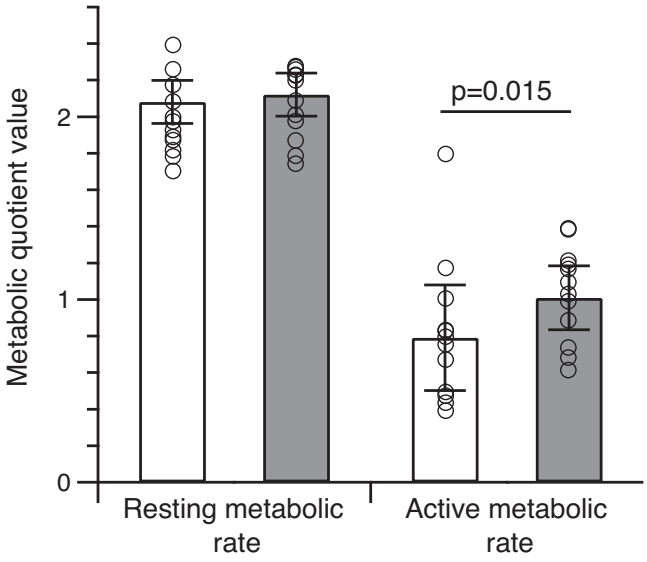

Figure A1. Resting and active metabolic quotients in the high activity (dark grey) and low activity (unfilled) periods of the longitudinal study
Significant differences were assessed by paired sample *t* tests.

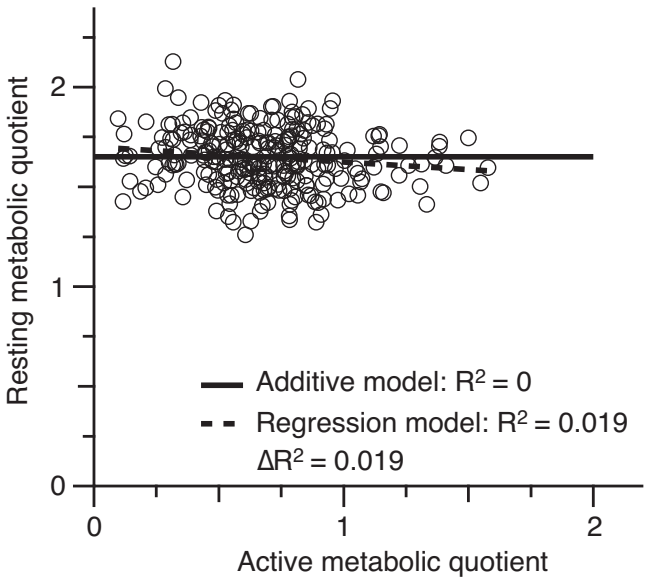

Figure A2. Resting metabolic quotients (RMQ) *vs*. active metabolic quotients (AMQ) in the cross-sectional study
Regression is indicated using a continuous line, with the additive model (slope = 0) indicated by a dashed line.

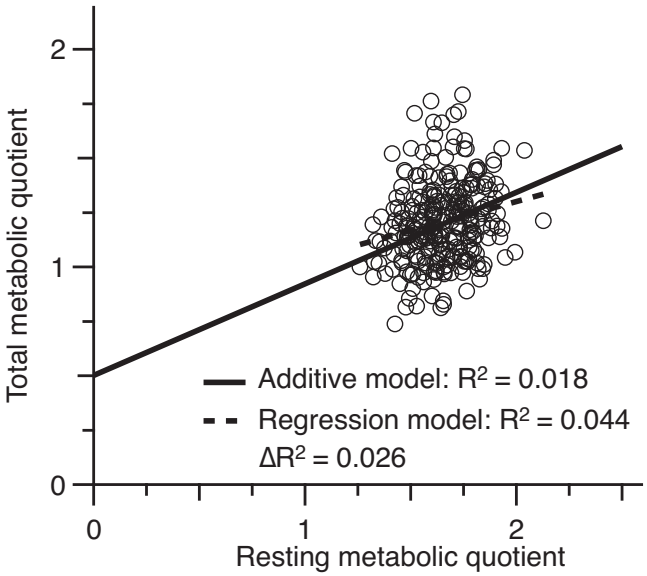

Figure A3. Total metabolic quotients (TMQ) *vs*. resting metabolic quotients (RMQ) in the cross-sectional study
Regression is indicated using a continuous line, with the additive model indicated by a dashed line (slope = 1.0).

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Additional information

Data availability statement

The data presented in this manuscript are available upon request from the authors.

Competing interests

S.K.C., A.R.H., D.E.L., L.M.R., W.W.W., and A.K.Y. declare no conflict of interest. S.B.H. serves on the Medical Advisory Boards of Tanita Corporation, Novo Nordisk, Lilly, Abbott, Regeneron, and Medifast.

Author contributions

Experiments were performed in the Department of Human Evolutionary Biology, Harvard University, Cambridge, MA 02138, and Pennington Biomedical Centre, University of Louisiana, Baton Rouge, LA, USA. Author contributions: D.E.L., L.M.R., A.K.Y. designed and conceptualized the study; all authors performed research and helped analyse data; A.K.Y. and D.E.L. wrote the original draft of the paper; all authors reviewed and edited the paper. All authors approved the final version of the manuscript, approved the final version of the manuscript, agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved, and all persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the HTML view of the article. Supporting information files available:

Peer Review History

Translational perspective

An individual's total metabolism over 24 h, termed their total energy expenditure (TEE) is the sum of their resting energy expenditure (REE), activity energy expenditure (AEE), and the cost of digesting food (termed diet-induced thermogenesis). Although AEE and REE are traditionally considered to be independent and thus additive, a recent hypothesis (the constrained energy balance model) proposes that increases in AEE cause decreases in REE. We tested these two alternative models using two complementary approaches. First, we conducted a short-term longitudinal experiment in 12 adults who completed 10-day periods of high and low physical activity separated by a 6-week washout period to avoid carry-over effects. Second, we analysed a cross-sectional sample of 268 adults. Both studies measured TEE, AEE and REE independently and adjusted metabolic rates for the effects of body size. In the longitudinal experiment, a nearly 30% increase in AEE (∼250 kcal/day) increased TEE by 10% (272 kcal/day) but did not reduce REE, contradicting predictions of metabolic compensation. In the cross-sectional study, REE and AEE were statistically independent after adjusting for the effects of body mass, also providing no evidence for metabolic compensation. These results support the additive model of energy expenditure and indicate that increased physical activity does not suppress REE, contradicting the hypothesis that metabolic compensation makes it impossible for physical activity to prevent weight gain or assist with weight loss.