Current Biology
Supplemental Information

Constrained Total Energy Expenditure and Metabolic Adaptation to Physical Activity in Adult Humans

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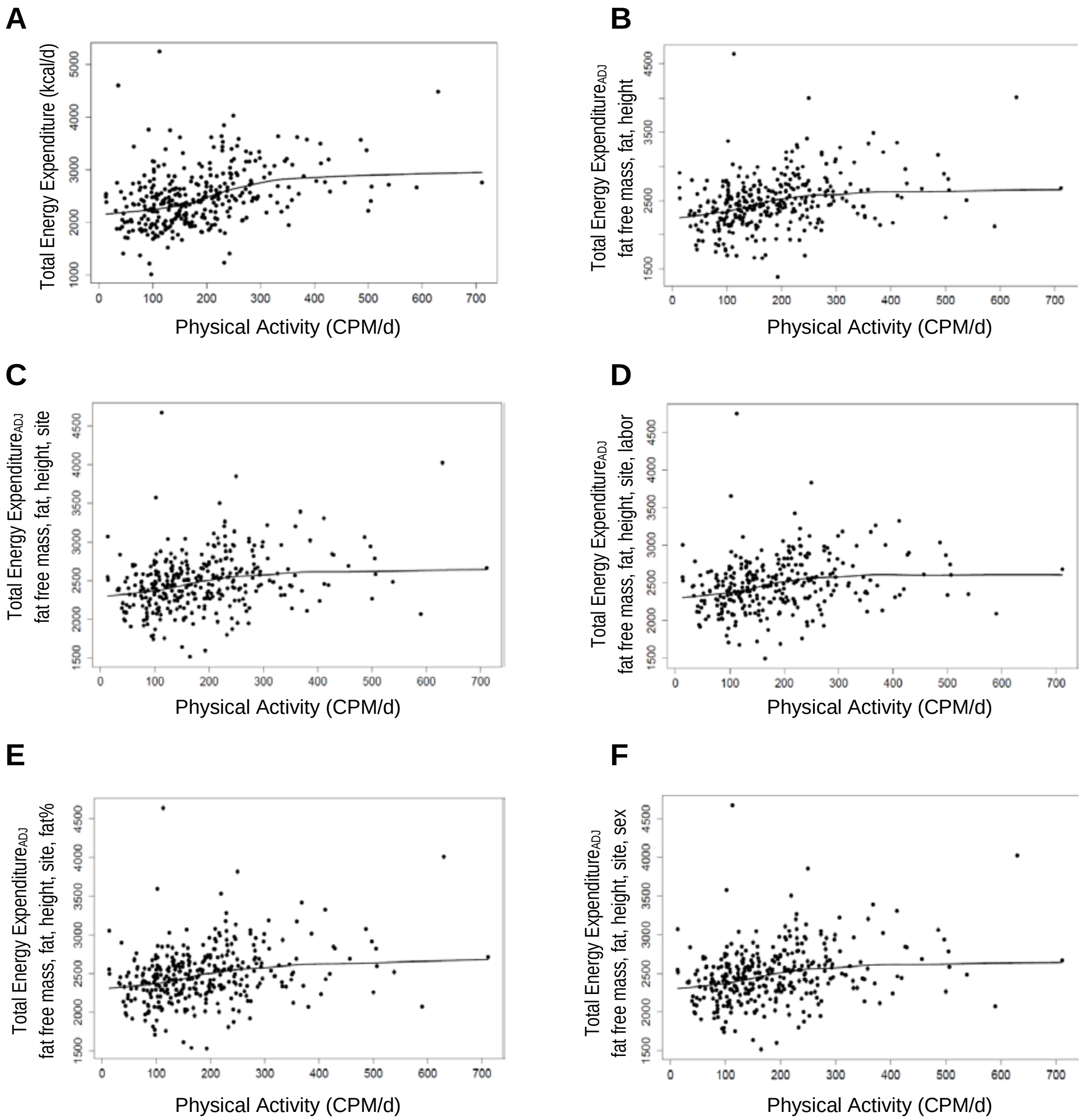

Figure S1. Related to Figure 2A and 3A. Total energy expenditure and total energy expenditure$_{ADJ}$ plotted against physical activity (CPM/d) for **A**. measured total energy expenditure values, **B**. total energy expenditure$_{ADJ}$ using fat free mass, fat mass, and height, **C**. total energy expenditure$_{ADJ}$ calculated using fat free mass, fat mass, height, and study site, **D**. total energy expenditure$_{ADJ}$ calculated using FFM, fat mass, height, study site, and employment in manual labor, and **E**. total energy expenditure$_{ADJ}$ calculated using fat free mass, fat, height, study site, and body fat percentage, **F**. total energy expenditure$_{ADJ}$ calculated using fat free mass, fat, height, study site, and sex. All approaches give similar results, but due to the covariation of PA with fat free mass, fat mass, and study site ($r^2=0.25$, $p<0.001$), unadjusted total energy expenditure (shown in **A**) exhibits plateau point at greater physical activity (CPM/d). Regressions fit using the lowess function in R [S1], with f=2/3, iter=5.

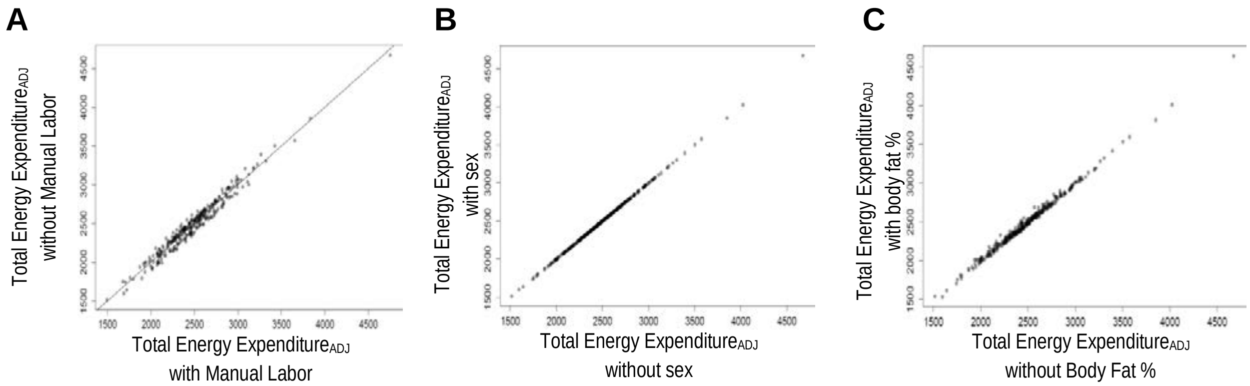

Figure S2. Related to Table 1. Different models for total energy expenditure$_{ADJ}$ are highly correlated. Total energy expenditure$_{ADJ}$ for **A.** employment in manual labor, **B.** sex, and **C.** body fat percentage. For each comparison, slope = 1.0 and r^2 is 0.97 or greater.

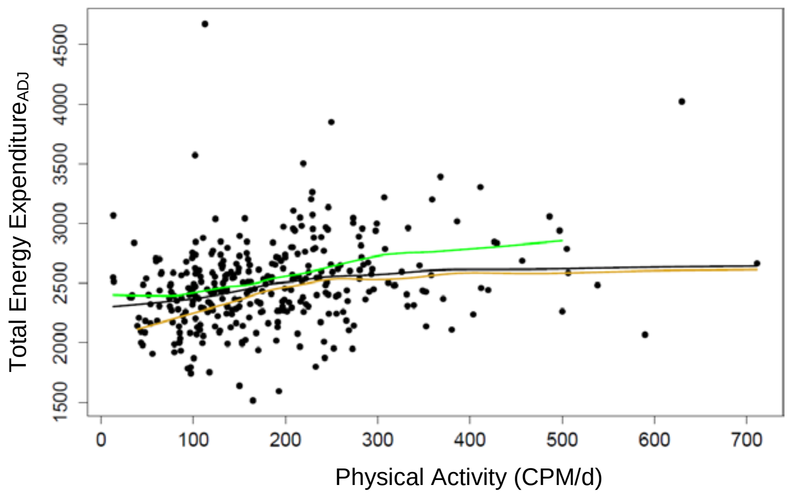

Figure S3. Related to Table 1 and Figures 2A and 3A. Total energy expenditure$_{ADJ}$ versus physical activity (CPM/d) for different fat percentages. Green line: lowess regression for subjects with body fat percentage above the median value for this dataset. Yellow line: lowess regression body fat percentage below the median. Black line: all subjects. Lowess regressions fit using the lowess function in R [S1], with f=2/3, iter=5.

Table S1. Related to Table 1. Key sample characteristics (sample size *n*, mean, and standard deviation *sd*).

			Age (y)		**Height** (cm)		**Mass** (kg)		**Fat Free Mass** (kg)		**Total Energy Expenditure** (kcal/d)		**CPM/d**		**Resting Metabolic Rate** (kcal/d)		
Study Site	**Sex**	***n***	mean	*sd*	mean	*sd*	mean	*sd*	mean	*sd*	mean	*sd*	mean	*sd*	*n*	mean	*sd*
Ghana	M	27	35.9	*5.96*	168.6	*6.46*	62.6	*7.09*	54.2	*4.69*	2862	*414*	273.7	*79.5*	18	1598	*125*
	F	35	37.6	*5.80*	157.5	*5.27*	64.4	*15.96*	42.4	*5.72*	2363	*443*	177.6	*60.1*	29	1385	*140*
Jamaica	M	33	33.2	*5.74*	175.6	*5.97*	71.7	*18.05*	55.7	*8.70*	2457	*478*	162.9	*80.3*	-	-	-
	F	34	34.9	*5.61*	163.7	*6.24*	73.9	*15.94*	43.6	*6.02*	2110	*345*	125.0	*63.6*	-	-	-
S. Africa	M	28	32.9	*6.17*	168.3	*3.96*	62.5	*12.55*	47.9	*5.88*	2369	*391*	233.1	*96.0*	19	1556	*207*
	F	44	34.2	*6.00*	162.4	*6.84*	84.0	*26.38*	45.5	*9.28*	2317	*456*	123.5	*58.9*	38	1552	*228*
Seychelles	M	30	33.3	*5.09*	170.3	*5.83*	72.5	*11.54*	54.9	*5.08*	2902	*400*	301.6	*149.5*	22	1635	*174*
	F	36	31.8	*6.34*	162.9	*6.12*	75.4	*19.32*	43.6	*7.08*	2180	*391*	154.5	*66.1*	24	1346	*178*
US	M	33	33.5	*5.83*	178.9	*6.02*	91.9	*25.26*	64.6	*9.34*	3160	*705*	217.3	*132.0*	29	1778	*371*
	F	32	33.5	*5.38*	164.1	*5.64*	89.2	*18.60*	50.9	*6.06*	2310	*363*	148.1	*102.5*	25	1448	*286*

Table S2. Related to Table 1 and Figure 2A. Counts per minute and total energy expenditure$_{ADJ}$ for each decile of physical activity (CPM/d).

			total energy expenditure$_{ADJ}$		
Decile	***n***	**median CPM/d**	mean	*st.dev.*	median
1st	34	53	2384	*275*	2383
2nd	33	90	2254	*271*	2278
3rd	33	108	2471	*519*	2386
4th	33	131	2470	*241*	2464
5th	33	150	2451	*300*	2529
6th	34	183	2361	*296*	2384
7th	33	209	2599	*328*	2553
8th	33	239	2630	*435*	2598
9th	33	280	2582	*299*	2598
10th	33	386	2646	*418*	2556

Table S3. Related to Table 1. Additional parameters for energy expenditure prediction models.

total energy expenditure	**MODEL 1** Adjusted r^2=0.52 ±SE 383.7		df=326, p<0.001		**MODEL 2** Adjusted r^2=0.55 ±SE 368.2		df=322, p<0.001		**MODEL 3** Adjusted r^2=0.59 ±SE 349.1		df=292, p<0.001	
Variable	β	*±SE*	t	p	β	*±SE*	t	p	β	*±SE*	t	p
(Intercept)	1227.64	*622.04*	1.97	0.05	347.67	*628.65*	0.55	0.58	-37.06	*626.18*	-0.06	0.95
FFM (kg)	46.38	*4.67*	9.94	<0.001	42.15	*5.33*	7.91	<0.001	41.52	*5.25*	7.90	<0.001
Fat Mass (kg)	-4.98	*2.54*	-1.96	0.05	-2.10	*2.89*	-0.72	0.47	-0.86	*2.90*	-0.30	0.77
Height (cm)	-6.21	*3.68*	-1.69	0.09	1.34	*3.85*	0.35	0.73	1.38	*3.83*	0.36	0.72
Age (y)	2.72	*3.62*	0.75	0.45	1.84	*3.54*	0.52	0.60	0.13	*3.58*	0.04	0.97
Sex (1=M, 0=F)	6.52	*88.84*	0.07	0.94	-14.42	*95.15*	-0.15	0.88	60.18	*95.50*	0.63	0.53
Site: Ghana					-	-	-	-	-	-	-	-
Jamaica					-374.01	*73.57*	-5.08	<0.001	-269.22	*73.69*	-3.65	<0.001
S Africa					-164.00	*77.63*	-2.11	0.04	-122.49	*76.41*	-1.60	0.11
Seychelles					-100.81	*73.10*	-1.38	0.17	-39.70	*78.55*	-0.51	0.61
US					-245.56	*76.79*	-3.20	0.002	-181.05	*80.66*	-2.24	0.03
CPM/d									1.07	*0.22*	4.79	<0.001
Manual Labor									117.18	*47.11*	2.49	0.01

resting metabolic rate	Adjusted r^2=0.55 ±SE 178.1		df=198, p<0.001		Adjusted r^2=0.59 ±SE 171.0		df=195, p<0.001		Adjusted r^2=0.60 ±SE 163.6		df=172, p<0.001	
Variable	β	*±SE*	t	p	β	*±SE*	t	p	β	*±SE*	t	p
(Intercept)	145.92	*366.68*	0.40	0.69	-299.35	*369.87*	-0.81	0.42	-251.08	*376.40*	-0.67	0.51
FFM (kg)	9.87	*2.86*	3.45	<0.001	13.36	*3.32*	4.02	<0.001	15.64	*3.39*	4.62	<0.001
Fat Mass (kg)	5.54	*1.45*	3.82	<0.001	4.90	*1.73*	2.82	0.005	3.25	*1.80*	1.81	0.07
Height (cm)	5.31	*2.26*	2.35	0.02	7.20	*2.36*	3.05	0.003	6.30	*2.41*	2.61	0.009
Age (y)	1.42	*2.14*	0.67	0.51	-0.20	*2.13*	-0.09	0.93	-1.50	*2.23*	-0.67	0.50
Sex (1=M, 0=F)	-118.04	*51.27*	-2.30	0.02	-67.02	*56.05*	-1.2	0.23	-35.53	*57.58*	-0.62	0.54
Site: Ghana					-	-	-	-	-	-	-	-
S Africa					9.11	*43.87*	0.21	0.84	31.04	*44.29*	0.70	0.48
Seychelles					-65.02	*40.85*	-1.59	0.11	-25.37	*47.65*	-0.53	0.60
US					-144.33	*42.96*	-3.36	<0.001	-141.44	*47.15*	-3.00	0.003
CPM/d									-0.05	*0.13*	-0.41	0.68
Manual Labor									31.60	*30.79*	1.03	0.31

total energy expenditure$_{ADJ}$	**MODEL 5** df=330, adj. r^2=0.07 *±SE* 349.3, p<0.001				**MODEL 6** df=301, adj. r^2=0.08 *±SE* 349.3, p<0.001				**MODEL 7** df=300, adj. r^2=0.09 *±SE* 345.2, p<0.001			
	β	*±SE*	t	*p*	*β*	*±SE*	*t*	*p*	*β*	*±SE*	t	*p*
(Intercept)	2309.0	*38.4*	60.1	<0.001	2277.0	*45.1*	50.4	<0.001	2094.2	*84.9*	24.7	<0.001
CPM/d	0.94	*0.2*	5.3	<0.001	0.81	*0.2*	4.3	<0.001	1.0	*0.2*	5.0	<0.001
Manual Labor					100.5	*40.5*	2.5	0.01	104.4	*40.2*	2.6	0.01
Body Fat %									445.4	*2.5*	2.5	0.01

Supplemental Experimental Procedures

Our analyses focus on total energy expenditure$_{ADJ}$, resting metabolic rate$_{ADJ}$, and activity energy expenditure$_{ADJ}$ to determine the relationship between daily energy expenditure and physical activity. In any analysis of metabolic rates, body size, particularly fat free mass, is an important, potentially confounding, variable that must be considered. Additionally, other factors related to lifestyle might affect total energy expenditure, such as food intake, macronutrient intake, the type of activities engaged in, sex, and age. Controlling for these variables is necessary in order to examine the effect of physical activity, measured via accelerometry as mean counts per minute per day (CPM/d), without spurious effects of covariates affecting results.

We used residuals from multivariate linear regression to isolate the effect of physical activity on energy expenditure, such that total energy expenditure$_{ADJ}$ = residual total energy expenditure + mean total energy expenditure. Residual total energy expenditure was calculated in R version 3.1.0 [S1] as resid(lm(total energy expenditure~A+B+C…*i*)) for a set of *i* independent variables (A, B, C…*i*). Interactions between independent variables were not considered. The set of independent variables used for the analyses of total energy expenditure$_{ADJ}$ in the main text is given in Model 2 of Table 1: fat free mass, fat mass, height, age, sex, and study site location. Including other variables, such as body fat percentage and employment in manual labor, did not change the pattern of variation in total energy expenditure$_{ADJ}$ with respect to physical activity (CPM/d) (Figure S1) because different calculations of total energy expenditure$_{ADJ}$ were highly correlated, with slopes of 1.0 and determinants of relatedness of r^2 >0.95 (Figure S2).

Resting metabolic rate$_{ADJ}$ was calculated in a similar manner, using the same variables as for total energy expenditure$_{ADJ}$: fat free mass, fat mass, height, age, sex, and study site location. As with total energy expenditure$_{ADJ}$, alternative approaches for calculating resting metabolic rate$_{ADJ}$ gave similar results. Due to missing resting metabolic rate measurements for the Jamaican subjects and some others, sample size for resting metabolic rate and activity energy expenditure analyses is *n*=204. Adjusted activity energy expenditure was calculated activity energy expenditure$_{ADJ}$ = 0.9 total energy expenditure$_{ADJ}$ – resting metabolic rate$_{ADJ}$, which assumes that the thermic effect of food digestion is equal to 10% of TEE. As noted in the main text, activity energy expenditure$_{ADJ}$ exhibited a marked plateau point at physical activity = ~230 CPM/d, similar to total energy expenditure$_{ADJ}$, and had a significantly non-zero intercept. We found similar results when we calculated activity energy expenditure from unadjusted measurements of total energy expenditure and resting metabolic rate, with a marked plateau point in activity energy expenditure at physical activity ~230 CPM/d and highly significant, non-zero intercept for the activity energy expenditure vs physical activity regression. For the full dataset, activity energy expenditure was significantly correlated with physical activity ($t(202)=5.37$, $\beta=1.23\pm0.23$, $p<0.001$) but the intercept was significantly different from zero ($t(202)=10.1$, $\beta=503.0\pm49.6$, $p<0.001$). For all subjects below the physical activity = 230 CPM/d plateau, the effect of physical activity on activity energy expenditure was greater ($t(145)=2.43$, $\beta=1.45\pm0.60$, $p=0.02$), but the intercept remained significantly different from zero ($t(145)=5.27$, $\beta=456.6\pm86.7$, $p<0.001$).

Supplemental Reference

S1. Team, R.C. (2013). R: A Language and Environment for Statistical Computing (R Foundation for Statistical Computing, Vienna), Version 3.1.0.