SUPPLEMENTARY MATERIAL

Sociodemographic and clinical data

A self-reported survey was used to collect sociodemographic (i.e., age, professional status, educational level) and clinical (i.e., medical problems or issues that might condition the inclusion of the subjects in the study, history of cardiovascular risk markers or disease in subject's family) data. All subjects were provided with continuous instructions on how to complete the survey.

Cardiometabolic profile

Glycemic and lipids markers, HOMA index and C-reactive protein

Serum glucose, total cholesterol, high density lipoprotein-cholesterol and triglycerides were assessed following standard methods using an AU5832 automated analyzer (Beckman Coulter Inc., Brea CA, USA). Low density lipoprotein-cholesterol was estimated as: [total cholesterol – HDL-C – (triglycerides/5)], with all units in mg/dL (Friedewald, Levy, & Fredrickson, 1972). Serum insulin was measured using the Access Ultrasensitive Insulin chemiluminescent immunoassay kit (Beckman Coulter Inc., Brea CA, USA). The HOMA index was calculated as *(insulin (µU/mL) x glucose (mmol/L)/22.5* (Matthews et al., 1985). C-reactive protein was measured by immunoturbidimetric assay, employing the same automated analyzer as above.

Systolic and diastolic blood pressure

An Omron M6 upper arm blood pressure monitor (Omron Healthcare Europe B.V. Hoofddorp, The Netherlands) was used to determine the systolic and diastolic blood pressure, with subjects seated and relaxed. Measurements were taken at three time points, and the mean determined for use in later analyses.

Muscular strength

Handgrip strength was assessed as a proxy of muscular strength on a different day to when the cooling experiments and PET/CT scan were performed. Briefly, handgrip strength was determined using an adjustable grip TKK 5101 Grip - D hand dynamometer (Takei, Tokyo Japan). Subjects were asked to squeeze gradually and continuously for a few seconds, and were encouraged to do their best when performing the tests. All tests were performed using the optimal grip-span (Ruiz-Ruiz, Mesa, Gutiérrez, & Castillo, 2002). Each subject performed two attempts with each hand, with the arm fully extended and maintaining the trunk erect. The maximum score for each hand was recorded in kilograms and the mean score of the left and right hand used in analyses.

Cardiorespiratory fitness

Subjects' maximum oxygen consumption ($VO_{2\ max}$) was determined via a maximum exercise test using a Pulsar treadmill (H/P/Cosmos Sport & Medical GMBH, Nußdorf, Germany), based on the modified Balke protocol (Balke & Ware, 1959). O_2 consumption and CO_2 production were measured by indirect calorimetry (CPX Ultima CardiO_2, Medical Graphics Corp, St Paul, USA) using an Model 7400 oronasal mask (Hans Rudolph Inc., Kansas City, MO, USA) equipped with a Prevent™ metabolic flow sensor (Medgraphics Corp., St. Paul, MN, USA). The criteria for achieving $VO_{2\ max}$ were: a respiratory exchange ratio ≥1.1, a plateau in VO_2 (change of <100 mL/min in the last three consecutive 60 s stages), and a heart rate within 10 beats/min of the age-predicted maximum (208–0.7 x age) (Pallarés & Morán-Navarro, 2012). When no plateau in VO_2 was reached, $VO_{2\ peak}$ was measured.

Prevalence of metabolic syndrome

Specific cardiometabolic risk factors were recorded and the prevalence of metabolic syndrome then determined based on two classifications: i) the National Cholesterol

Education Program Adult Treatment Panel III (ATP III) criteria (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001), and ii) the International Diabetes Federation criteria (IDF, 2005). For (i), subjects were deemed to have metabolic syndrome when they had three or more of the following risk factors: waist circumference (WC) ≥102 cm for men and 88 cm for women; triglycerides ≥150 mg/dL; HDL-cholesterol <40 mg/dL for men and <50 mg/dL for women; systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg; plasma glucose >110 mg/dL. For (ii to have metabolic syndrome when they had central obesity plus at least two of the following risk factors: waist circumference (WC) ≥94 cm for men and ≥80 cm for women; triglycerides ≥150 mg/dL; HDL-cholesterol <40 mg/dL for men and <50 mg/dL for women; systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg; plasma glucose ≥100 mg/dL.

Physical activity level

The DST daily rhythm can be masked by several factors, including physical activity (Sarabia, Rol, Mendiola, & Madrid, 2008). This is partially explained by the fact that those people who perform exercise or physical activity generally have a higher average skin temperature during exercise. This could lead to variations in the DST and its daily rhythm. To avoid any confounding effect, physical activity was objectively measured using a wrist-worn GT3X+ accelerometer (ActiGraph, Pensacola, FL, US) for 7 consecutive days (24 h/day) (Sanchez-Delgado et al., 2015), and adjusted for when examining the association between the DST daily rhythm and BAT ^{18}F-FDG uptake. The subjects were given detailed information on how to wear the accelerometer. Once the recording was finished and the raw data processed and analyzed (described extensively in Acosta et al. [2018]), an overall indicator of physical activity (mG)

during time awake was established using the ENMO (Euclidean Norm Minus One) metric.

Chronotype

Alignment between the biological and social clocks is important for the management of obesity (Roenneberg, Allebrandt, Merrow, & Vetter, 2012). Indeed, the central circadian clock, which harmonizes all the processes ranging from cellular to whole-body physiology with environmental cues, is often influenced by social obligations (for instance, humans align their sleep and wake times to their work schedule or social events). To quantitatively characterize these individual differences in daily schedule, several variables related to subject chronotype were recorded: i) midsleep timepoint (the midpoint between sleep onset and waking up); ii) chronotype (the midsleep timepoint corrected for the sleep deficit on free days); and iii) social jetlag (the difference between midsleep timepoints on free days and on workdays). All these variables were calculated using the Munich Chronotype Questionnaire, employing the formula proposed by Roennerberg et al. (2012). Sleep onset was recorded for workdays (Sunday to Thursday) and free days (Friday and Saturday), and the sleep offset for workdays (Monday to Friday) and weekends (Saturday and Sunday), from the sleep diaries the subjects completed over the days they wore the DST sensor.

Table S1. Distal skin temperature (DST), personal environmental temperature (personal-ET; see Methods and Materials), and ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET/CT scan variables, by evaluation wave.

	Wave 1 (n=18)*		**Wave 2 (n=21)**		**Wave 3 (n=18)**		**Wave 4 (n=20)**		**P-value**
DST variables									
IS	0.38	(0.13)	0.42	(0.14)	0.50	(0.09)	0.51	(0.11)	**0.004**
IV	0.23	(0.11)	0.22	(0.10)	0.12	(0.05)	0.15	(0.10)	**0.002**
RA	0.02	(0.01)	0.03	(0.01)	0.04	(0.02)	0.04	(0.02)	**<0.001**
TL10 (hh:mm)	15:26	(03:43)	15:13	(02:33)	18:01	(02:09)	17:04	(02:15)	**0.005**
TM5 (hh:mm)	04:35	(03:07)	03:49	(00:50)	05:04	(01:43)	04:25	(01:33)	0.25
L10 (ºC)	33.91	(0.66)	33.37	(0.70)	32.34	(1.14)	32.34	(1.21)	**<0.001**
M5 (ºC)	35.36	(0.60)	35.21	(0.60)	35.38	(0.69)	35.29	(0.92)	0.88
Personal-ET variables									
IS	0.30	(0.10)	0.31	(0.11)	0.31	(0.14)	0.27	(0.12)	0.63
IV	0.27	(0.09)	0.22	(0.10)	0.23	(0.10)	0.25	(0.11)	0.47
RA	0.05	(0.02)	0.07	(0.03)	0.12	(0.05)	0.09	(0.04)	**<0.001**
TL10 (hh:mm)	06:07	(01:54)	05:36	(01:40)	06:52	(04:16)	07:45	(04:51)	0.23
TM5 (hh:mm)	16:32	(02:37)	16:43	(02:39)	18:19	(03:58)	19:02	(05:14)	0.12
L10 (ºC)	24.83	(1.21)	22.25	(1.14)	18.53	(2.16)	19.15	(2.95)	**<0.001**
M5 (ºC)	27.42	(1.24)	25.71	(1.78)	23.51	(3.08)	23.10	(4.09)	**<0.001**
^{18}F-FDG PET/CT variables									
BAT radiodensity (HU)	-61.86	(16.78)	-56.14	(10.21)	-58.63	(9.72)	-58.39	(10.52)	0.55
BAT volume (mL)	15.08	(29.16)	61.42	(48.29)	104.12	(50.64)	95.89	(69.70)	**<0.001**
BAT SUV_{mean}	2.02	(1.45)	3.60	(1.64)	4.80	(1.78)	4.37	(1.59)	**<0.001**
BAT SUV_{peak}	3.55	(3.85)	9.81	(6.90)	17.14	(9.37)	13.64	(6.88)	**<0.001**
Superficial muscle SUV_{peak}	0.56	(0.11)	0.60	(0.15)	0.66	(0.22)	0.61	(0.09)	0.23
Deep muscle SUV_{peak}	0.89	(0.18)	1.14	(0.38)	1.25	(0.38)	1.18	(0.25)	**0.005**
All muscle SUV_{peak}	0.72	(0.14)	0.86	(0.25)	0.94	(0.26)	0.89	(0.13)	**0.01**
Descending aorta SUV_{peak}	1.48	(0.26)	1.70	(0.46)	1.59	(0.33)	1.62	(0.29)	0.29

Values are means (standard deviation). *For the group of subjects assessed in evaluation wave 1, a few measurements of personal-ET and BAT radiodensity were missing (remaining n=17 and 16 respectively). One-way ANOVA was used to detect any difference among evaluation waves. Significant values (P<0.05) are shown in bold. IV:

intraday variability, L10: mean of the 10 consecutive hours with the lowest values and when they occurred (TL10), M5: mean of the five consecutive hours with the highest values and when they occurred (TM5), PET/CT: positron emission tomography combined with computed tomography, RA: relative amplitude.

Table S2. Association between distal skin temperature (DST) variables and brown adipose tissue (BAT) volume and standardized uptake values (SUV mean and peak), after adjusting for potential confounders (n=76).

	BAT volume (ml)			**BAT SUV_{mean}**			**BAT SUV_{peak}**		
	B	R^2	P	B	R^2	P	B	R^2	P
Model 1 (adjusted for sex, personal-ET_{L10}, and body mass index)									
IS	83.64	0.307	0.12	0.44	0.228	0.80	4.20	0.259	0.58
IV	-85.12	0.295	0.27	0.77	0.228	0.76	-8.92	0.263	0.41
RA	648.61	0.305	0.13	8.94	0.232	0.52	74.17	0.272	0.22
TL10 (hh:mm)	4.84	0.326	**0.04**	0.07	0.236	0.37	0.43	0.274	0.19
TM5 (hh:mm)	-1.53	0.285	0.67	-0.23	0.272	**0.04**	-0.78	0.282	0.12
L10 (ºC)	-9.33	0.306	0.13	-0.09	0.230	0.64	-1.18	0.275	0.17
M5 (ºC)	-0.90	0.283	0.93	0.07	0.228	0.82	-0.48	0.257	0.73
Model 2 (adjusted for sex, personal-ET_{L10}, and lean mass index)									
IS	62.77	0.280	0.24	-0.15	0.264	0.93	1.36	0.284	0.85
IV	-42.61	0.269	0.57	2.02	0.272	0.39	-2.22	0.284	0.83
RA	489.33	0.279	0.26	1.72	0.264	0.90	41.80	0.289	0.48
TL10 (hh:mm)	4.70	0.306	**0.05**	0.05	0.269	0.51	0.35	0.295	0.28
TM5 (hh:mm)	-1.70	0.268	0.64	-0.22	0.306	**0.04**	-0.75	0.308	0.12
L10 (ºC)	-7.69	0.282	0.22	-0.02	0.264	0.93	-0.83	0.293	0.33
M5 (ºC)	-2.10	0.267	0.84	0.02	0.264	0.94	-0.71	0.286	0.61
Model 3 (adjusted for sex, personal-ET_{L10}, and fat mass index)									
IS	85.44	0.310	0.11	0.92	0.226	0.60	6.03	0.263	0.43
IV	-83.39	0.297	0.27	-0.27	0.223	0.91	-12.52	0.270	0.24
RA	620.56	0.306	0.14	12.94	0.232	0.35	87.77	0.278	0.14
TL10 (hh:mm)	4.6	0.326	**0.04**	0.07	0.234	0.32	0.45	0.276	0.17
TM5 (hh:mm)	-1.44	0.287	0.68	-0.23	0.267	**0.04**	-0.77	0.281	0.12
L10 (ºC)	-9.02	0.307	0.14	-0.14	0.228	0.49	-1.32	0280	0.12
M5 (ºC)	-0.84	0.285	0.93	0.11	0.224	0.74	-0.35	0.257	0.80
Model 4 (adjusted for sex, personal-ET_{L10}, and body fat percentage)									
IS	85.64	0.321	0.10	1.48	0.245	0.38	8.18	0.284	0.27
IV	-72.55	0.305	0.31	-1.20	0.240	0.61	-14.97	0.294	0.14
RA	561.37	0.314	0.17	15.94	0.253	0.23	96.76	0.301	0.09
TL10 (hh:mm)	4.25	0.329	0.06	0.07	0.248	0.32	0.43	0.291	0.17
TM5 (hh:mm)	-1.54	0.297	0.66	-0.23	0.280	**0.04**	-0.76	0.296	0.12
L10 (ºC)	-8.36	0.315	0.16	-0.17	0.246	0.38	-1.42	0.301	0.09
M5 (ºC)	-0.73	0.295	0.94	0.15	0.240	0.64	-0.19	0.272	0.89

Linear regressions were performed to examine the association between DST variables and BAT volume, SUV_{mean}, and SUV_{peak}, after adjusting for sex, mean personal environmental temperature over the L10 period (personal-ET_{L10}), and body mass index (Model 1); for sex, personal-ET_{L10}, and lean mass index (Model 2); for sex, personal-ET_{L10}, and fat mass index

(Model 3), and for sex, personal-ET_{L10}, and body fat percentage (Model 4). Non-standardized B coefficient, adjusted R^2 and P values are provided. Significant values are shown in bold ($P \leq 0.05$). IS: interday stability, IV: intraday variability, L10: mean of the 10 consecutive hours with the lowest values and when they occurred (TL10), M5: mean of the five consecutive hours with the highest values and when they occurred (TM5), RA: relative amplitude.

Figure S1

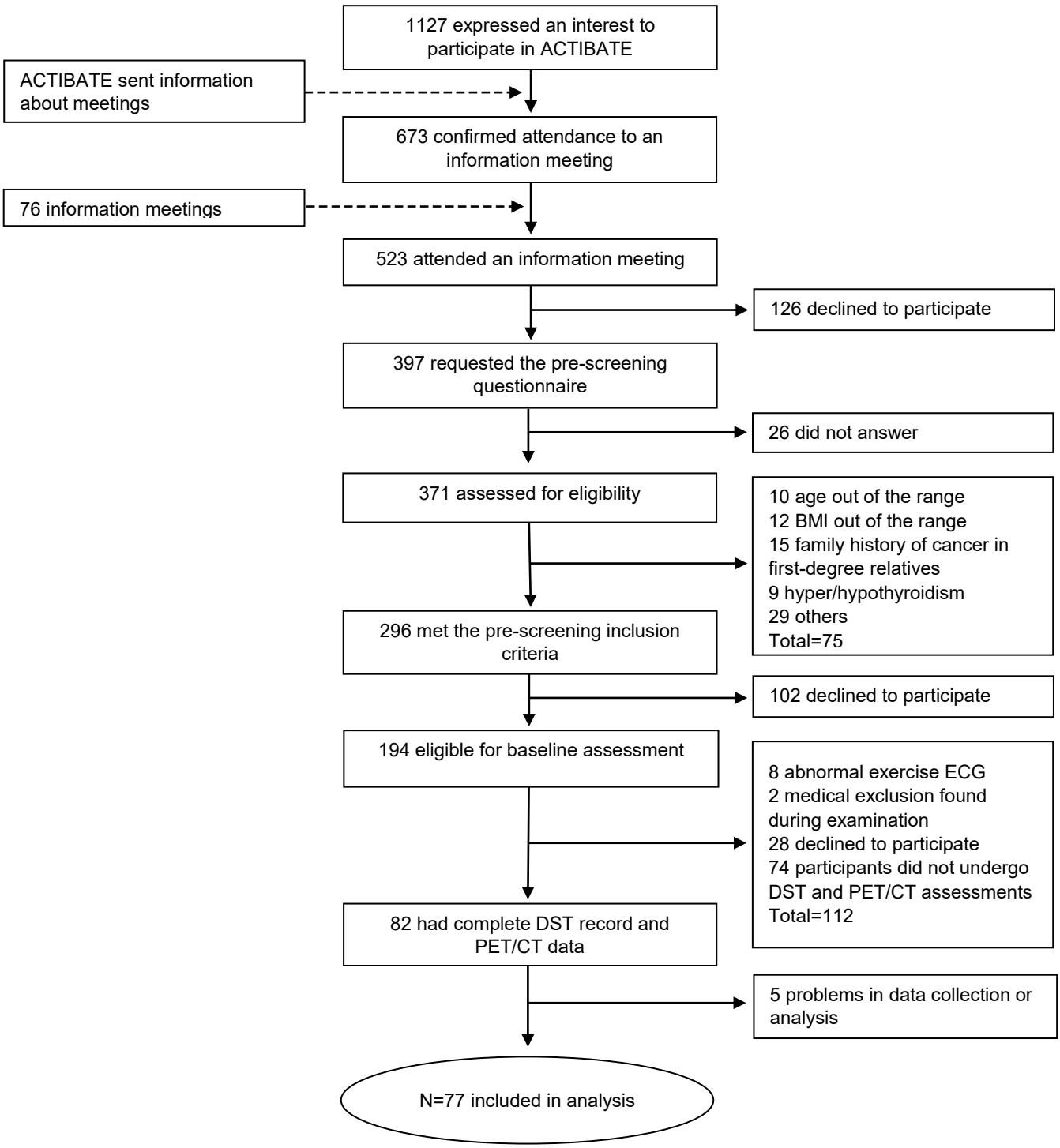

Figure S1. Enrollment flow-chart. BMI: body mass index, ECG: electrocardiogram, PET/CT: positron emission tomography combined with computed tomography, DST: distal skin temperature.

Figure S2

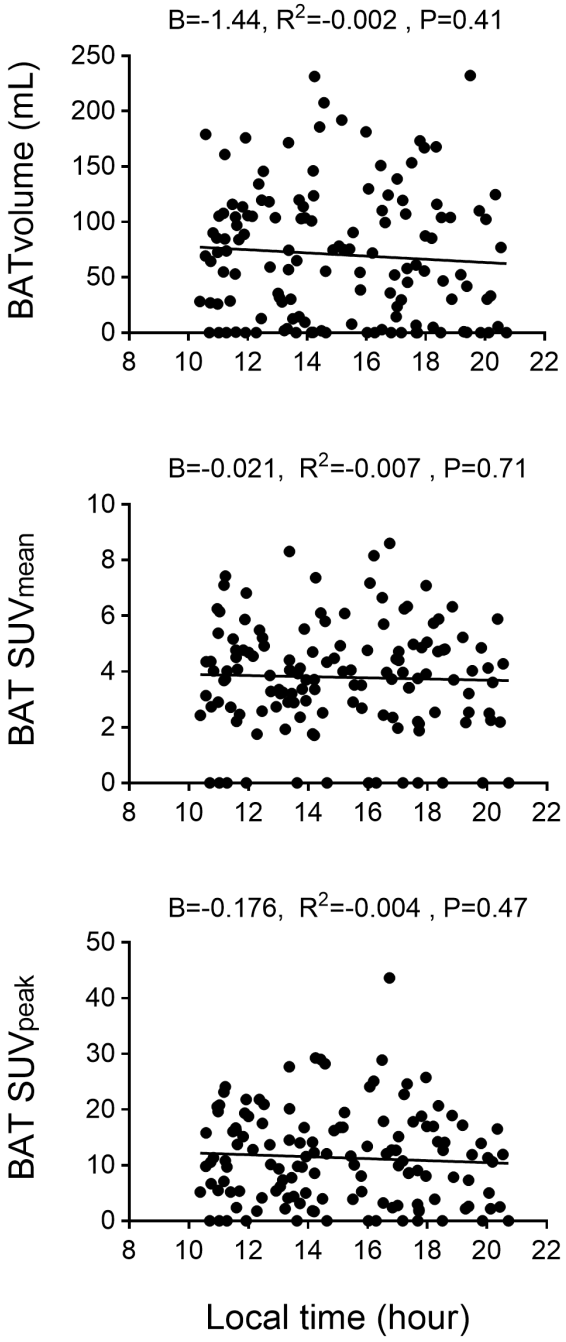

Figure S2. Association between brown adipose tissue (BAT) ^{18}F-fluordeoxyglucse uptake and the time of the day when it was assessed in young sedentary adults. Simple linear regressions were perfumed to examine the association between BAT volume (**Panel A)**, the mean standardized uptake value (SUV_{mean}, **Panel B**) and SUV_{peak} **(Panel**

C), with the time of the day when BAT was assessed. Non-standardized beta coefficient, adjusted R^2 and P values are provided. These analyses were performed with data from the complete study cohort of the ACTIBATE study (n=133, 88 women, 22±2 years old, body mass index: 24.9±4.8 kg/m^2).

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