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ORIGINAL ARTICLE

Association between habitual physical activity and brown adipose tissue activity in individuals undergoing PET-CT scan

Petros C. Dinas*, Alexandra Nikaki†, Athanasios Z. Jamurtas‡, Vassilios Prassopoulos†, Roxani Efthymiadou†, Yiannis Koutedakis‡,§, Panagiotis Georgoulias¶ and Andreas D. Flouris*

**FAME Laboratory, Department of Exercise Science, University of Thessaly, Trikala, †Nuclear Medicine Department and Positron Emission Tomography/Computed Tomography Department, "DTCA HYGEIA" Hospital, Athens, ‡School of Physical Education and Exercise Science, University of Thessaly, Trikala, Greece, §Faculty of Education, Health and Wellbeing, University of Wolverhampton, Wolverhampton, UK and ¶Nuclear Medicine Laboratory, Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece*

Summary

Objective Augmented brown adipose tissue (BAT) mass and activity lead to higher basic metabolic rate which is beneficial against obesity. Our aim was to investigate whether habitual (i.e. usual weekly participation) physical activity is linked with BAT activity and mass in humans, in a group of patients undergoing ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) scanning.

Design Cross-sectional study.

Patients Forty patients with cancer [26 male; 14 female; age 52·7 ± 17·5; body mass index (BMI) 26·4 ± 4·5].

Measurements Patients completed the 'usual week' form of the International Physical Activity Questionnaire and underwent assessment of BAT activity/mass via ^{18}F-fluorodeoxyglucose PET/CT.

Results We detected a significant association between habitual physical activity (METs-minute/week) and BAT activity [normalized by body weight (BW) ($\tau = 0{\cdot}28$, $P = 0{\cdot}02$), body surface area (BSA) ($\tau = 0{\cdot}29$, $P = 0{\cdot}02$) and lean body mass (LBM) ($\tau = 0{\cdot}38$, $P = 0{\cdot}002$)]. We also found a significant negative relationship between BMI and BAT activity [normalized by BW ($\tau = -0{\cdot}30$, $P = 0{\cdot}006$), BSA ($\tau = -0{\cdot}31$, $P = 0{\cdot}004$) and LBM ($\tau = -0{\cdot}45$, $P = 0{\cdot}001$)] as well as a significant negative relationship between age and BAT activity [normalized by LBM ($\tau = -0{\cdot}28$, $P = 0{\cdot}01$)]. The results also indicate significant differences between low/moderate/high levels of habitual physical activity and BAT activity ($P < 0{\cdot}05$). Moreover, BAT activity was different across the BMI categories (normal/overweight/obese) in both sexes ($P < 0{\cdot}05$). Finally, BAT activity was greater in women than in men ($P < 0{\cdot}05$).

Conclusions Increased participation in habitual physical activity is associated with higher BAT activity. Moreover, individuals with normal BMI demonstrate higher BAT activity compared to overweight and obese individuals. Finally, age is inversely linked with BAT activity, while women demonstrate higher BAT activity than men.

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Correspondence: Andreas D. Flouris, FAME Laboratory, School of Physical Education and Exercise Science, University of Thessaly, Karies, Trikala, 42100, Greece. Tel.: +302431500601, Fax: +302431063191; E-mail: andreasflouris@gmail.com

Introduction

The mammalian brown adipose tissue (BAT) plays a key role in energy balance through nonshivering thermogenesis,[1,2] a process that – in humans – occurs in BAT and skeletal muscle.[1,3] The BAT cells are found mainly in the supraclavicular and perirenal areas and display high mitochondrial and capillary content as well as presence of uncoupling protein one.[1] The prevailing hypothesis to date is that BAT is activated during cold exposures in an effort to maintain body temperature which, as a consequence, leads to excess energy expenditure.[1,2] As such, BAT has been proposed as a promising candidate to reduce the extent of the obesity epidemic.[2–4] Indeed, data summarized in a recent review showed that nonshivering thermogenesis represents up to 20% of the average daily metabolic rate.[3] Frequent stimulation of nonshivering thermogenesis (and thus, BAT) irrevocably increases basic metabolic rate, resulting in reduced body weight and fat stored.[1] On the other hand, attenuated BAT activity is linked with increased body mass index (BMI) and total body fat,[4] while BAT mass is inversely correlated with BMI.[5]

In recent years, the connection between BAT and muscle cells is becoming increasingly evident. For instance, the expression of PGC1-α, a powerful transcriptional coactivator regulating mammalian mitochondrial biogenesis, is augmented in both BAT and oxidative muscle (type I and type IIa) cells and it is further increased by exercise.[6] Moreover, a recent study demonstrated that classical BAT (located in the supraclavicular and perirenal areas), unlike the brite/beige adipocytes resident within white fat, is derived from the same lineage as skeletal muscle.[7] Suppressing the PRDM16 molecule switches the fate of BAT precursor cells into skeletal muscle cells, while PRDM16 expression converts myoblasts into BAT cells.[7] In this light, analysis of the role of exercise in stimulating the activity of BAT is heavily warranted. Recent animal research showed that exercise can increase BAT mass and activity.[8] However, the potential link between participation in habitual physical activity and BAT mass/activity in humans has not been investigated to date. Our aim in this cross-sectional study was to investigate whether habitual (i.e. usual weekly participation) physical activity is linked with BAT activity and mass in humans, in a group of patients undergoing ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) scanning.

Methods

Participants

The study conformed to the standards set by the Declaration of Helsinki and was approved from the Ethics Committees at the University of Thessaly and the Hygeia Hospital. A minimum required sample size of 20 participants was determined (statistical power: 0·95; α error probability: 0·05) based on data from a recent study.[4] We obtained written informed consent from 26 male and 14 female adults [age 52·7 ± 17·5, BMI 26·4 ± 4·5, body surface area (BSA) 1·9 ± 0·2, lean body mass (LBM) 57·3 ± 11·6] undergoing ^{18}F-FDG PET/CT scanning. The large majority of scans were for cancer detection. The participants' characteristics are displayed in Table 1. We divided the participants in three categories according to their BMI using standard criteria (normal: <25; overweight: 25–29·9; obese: >30).[9] According to standardized methodology,[10] we excluded patients who underwent chemotherapy during the past 14 days, patients who took medications known to affect metabolism or were diagnosed with diabetes mellitus and/or other hypermetabolic diseases, patients with blood glucose >150 mg/dl on the day of the examination, and cases where the examined area was comprised by cancerous tumours or other pathologic hypermetabolic tissues.

Experimental design

All assessments were performed between September 2012 and April 2013, as this period shows the highest probability of observing ^{18}F-FDG BAT in Mediterranean climates such as Greece's.[11] Participants arrived at the hospital between 8:15 and 13:00 following ≥6 h of fasting. They provided medical history, completed the International Physical Activity Questionnaire (IPAQ) and underwent measurements for anthropometry, blood pressure and plasma glucose using standard methods.[12] Subsequently, we administered intravenously 5 mg of diazepam (stedon) to avoid excessive muscle activity during the examination[13] and 40 mg of furosemide (lasix) to reduce excretory system activity in participants with systolic blood pressure >110 mmHg.[14] Thereafter, we administered 358 ± 21·9 mega Becquerel of ^{18}F-FDG intravenously according to each participant's body weight following standard methodology.[15] Finally, we performed the PET/CT examination 1 h thereafter. All procedures were performed in a 22–24 °C environment. As previously,[11] subjects were neither warmed nor instructed to avoid cold before the PET/CT examinations.

Brown adipose tissue measurements

A Biograph LSO 16-slice device (Siemens AG, Munich, Germany) was used to obtain images from the base of the skull to the upper third of the thigh. Measurements of BAT were obtained from the left and the right side of the supraclavicular area and along the spine area. All ^{18}F-FDG PET/CT scans were interpreted by two independent experienced physicians. We calculated averages for each area from the maximum values for BAT volume (cm^3) and BAT activity [standardized uptake value (SUV)][16] and summed them to estimate the total values for each participant. As previously, BAT activity SUV was transformed to kilo Becquerel (KBq) units,[17] and values for BAT mass/activity were normalized by body weight (BW), BSA and LBM.[18,19]

Assessment of physical activity participation

We assessed physical activity participation via the 'usual week' form of the IPAQ, which has been validated in Greek healthy[20] and clinical populations.[21] This questionnaire is self-reported and was completed by each participant at the clinic waiting room. Prior to completing the questionnaire, a researcher read each question clearly and provided explanations to ensure that participants understood what was asked. In addition, a researcher was available continuously, in case a participant needed further explanations. No time limits were set for the completion of the questionnaire. According to IPAQ guidelines,[22] the obtained data were transformed into weekly metabolic equivalents (METs-minute/week) based on low, moderate and vigorous physical activity intensity, number of days/week and minutes/day of their physical activity participation. More specifically, the following equations were used: (i) Low level (walking) = 3·3 METs*minutes of walking*days of activity, (ii) Moderate intensity level = 4 METs *minutes of walking*days of activity and (iii) High (vigorous) intensity level = 8 METs*minutes of walking*days of activity. The total METs-minute/week for each participant were calculated according to the equation: MET-minutes/week = Low (METs*min*days) + Moderate (METs*min*days) + High [(vigorous) (METs*min*days)].[22]

Physical activity categories were created based on the number of days/week, minutes/day and number of METs-minute/week of physical activity.[22] Specifically, a 'high' physical activity level was assigned to participants who reported: (i) vigorous-intensity activity on at least three days/week with a

Table 1. Patient characteristics

Patient	Sex	Age (years)	BMI	BSA (m^2)	LBM (kg)	Glc (mg/dl)	Blood pressure	Injected ^{18}F-FDG (kbq·10^3)	Disease	Disease stage
1	M	31	22·4	1·73	53·19	115	95/65	352	HD	Rest.
2	F	26	20·39	1·45	37·63	83	90/60	355	HD	Rest.
3	M	65	25·82	1·96	64·29	150	140/80	340	Colon cancer	Rest.
4	M	74	24·97	1·75	59·79	123	150/80	358	Neuroendocrine tumour	Rest.
5	F	77	28·47	1·74	46·69	107	100/60	320	Lung and pancreatic cancer	Rest.
6	M	67	31·79	2·22	74·01	103	140/80	390	Melanoma	Initial
7	M	66	26·07	1·79	55·88	127	125/70	350	Head and Neck (tongue)	Rest.
8	M	68	27·35	1·92	61·73	107	130/85	340	Lung cancer	Rest.
9	M	36	24·91	2·16	71·29	93	110/60	370	Infection	Invest.
10	F	58	24·22	1·81	49·80	78	105/65	355	Mediastinal mass	Invest.
11	M	39	24·41	1·88	59·69	98	120/70	360	NHL	Rest.
12	F	39	26·53	1·83	50·12	112	120/75	350	NHL	Initial
13	M	62	29·39	2·04	66·50	148	135/70	360	Lung cancer	Initial
14	F	33	18·25	1·63	43·19	115	125/75	356	HD	Rest.
15	M	20	25·72	1·91	60·92	90	140/75	357	Thyroid cancer	Rest.
16	F	74	23·45	1·4	36·14	110	120/70	340	Colon cancer and SPN	Rest.
17	M	71	24·15	1·79	55·89	112	155/80	280	Pancreatic cancer	Initial
18	M	64	25·94	2·06	67·04	103	120/70	340	NHL	Rest.
19	M	38	25·4	2·09	68·38	106	125/75	366	Seminoma	Initial
20	M	80	38·57	2·02	63·70	121	120/70	310	SPN	Invest.
21	F	50	18·51	1·48	38·20	121	95/70	354	Breast cancer	Rest.
22	F	63	35·65	1·67	41·21	111	120/70	350	UP	Rest.
23	F	37	28·71	1·94	53·53	127	120/70	356	Uterine cervix cancer	Initial
24	M	27	33·95	2·28	76·18	106	115/70	350	NHL	Rest.
25	M	60	27·47	2·05	67·03	109	110/65	384	UP	Initial
26	F	59	22·94	1·59	42·36	122	95/65	372	Lung cancer	Initial
27	M	61	27·16	2·09	68·88	90	120/70	380	SPN	Invest.
28	M	62	22·05	1·72	52·62	115	115/65	380	Lung cancer	Rest.
29	M	64	34·33	2·27	75·68	80	135/80	350	Lung cancer	Initial
30	F	54	25·71	1·77	48·26	100	110/75	370	Lung cancer	Rest.
31	F	23	25·07	1·68	45·43	94	110/75	373	NHL	Rest.
32	M	66	30·1	1·98	64·27	93	130/80	370	Mediastinal mass	Initial
33	F	31	24·65	1·59	42·31	115	110/70	350	Vaginal cancer	Rest.
34	M	62	24·22	1·81	56·65	120	120/70	380	HD	Rest.
35	M	66	29·61	2·15	71·03	111	130/65	376	Kidney cancer and SPN	Rest.
36	M	24	19·92	1·85	56·82	107	110/70	380	HD	Rest.
37	M	72	25·26	1·84	58·17	111	120/70	373	Lung cancer	Rest.
38	M	34	29·06	2·05	66·86	96	110/75	384	HD	Rest.
39	F	63	22·31	1·65	44·39	83	130/65	355	Colon cancer	Rest.
40	M	45	33·95	2·28	76·18	98	130/70	400	SPN	Invest.

BMI, body mass index; BSA, body surface area; LBM, lean body mass; Glc, fasting blood glucose; ^{18}F-FDG, ^{18}F-fluorodeoxyglucose; Blood pressure, systolic/diastolic; M, male; F, female; Rest, restaging; Invest, investigation; HD, Hodgkin disease; NHL, non-Hodgkin lymphoma; SPN, solitary pulmonary nodule; UP, Unknown Primary.

minimum total physical activity of at least 1500 METs-minute/week, or (ii) 7 days/week of any combination of low, moderate or vigorous-intensity activities with a minimum total physical activity of at least 3000 METs-minute/week. A 'moderate' physical activity level was assigned to participants who reported: (i) three or more days of vigorous-intensity activity of at least 20 min/day, or (ii) five or more days of moderate intensity activity and/or low activity of at least 30 min/day or (iii) five or more days of any combination of low, moderate or vigorous-intensity activities with a minimum total physical activity of at least 600 METs-minute/week. Finally, a 'low' physical activity level was assigned to participants who did not meet the criteria for 'moderate' and/or 'high' levels of physical activity.

Environmental temperature

Given the reported link between environmental temperature and the probability of observing ^{18}F-FDG BAT in PET/CT scans conducted in Mediterranean climates such as

Greece's,[11] we obtained data for daily air temperature from the Hellenic National Meteorological Service. The data covered the entire study period and were collected every 6 h at a weather station located in Elliniko, which is approximately 18 km away from the Hygeia Hospital. The 6-h air temperature data were used to calculate average daily air temperature for the dates when the BAT measurements were obtained.

Statistical analysis

Nonparametric tests were used throughout. We investigated the associations between physical activity (total METs-minute/week), BMI, BAT mass, BAT activity and age using Kendall's tau-b correlation coefficient. We used Kruskal–Wallis analysis of variance with *post hoc* Mann–Whitney *U* tests to assess differences in BAT mass and activity due to variation in: (i) physical activity levels (i.e. low/moderate/high) and (ii) BMI categories (i.e. normal/overweight/obese). We also used Mann–Whitney *U* tests to assess sex differences. As previously suggested,[23] the data analyses were repeated after removal of all outliers (i.e. observations that were at a distance of more than two standard deviations from the mean of the distribution) to confirm the validity of our results. The results of the latter analysis are presented in an Online Data Supplement and confirmed that the outliers did not influence our findings. Finally, we investigated the associations between environmental temperature, BAT activity and BAT mass using Kendall's tau-b correlation coefficient. All analyses were conducted with PASW Statistics (version 18; SPSS Inc., Chicago, IL, USA) and a $P \leq 0{\cdot}05$ level of significance.

Results

Based on the aforementioned physical activity categories, 45·5% of the participants reported low levels of participation, while 30·3% and 24·2% reported moderate and high levels, respectively ($P < 0{\cdot}05$). We detected a significant association between total energy expenditure in METs-minute/week and BAT activity [normalized by BW ($\tau = 0{\cdot}28$, $P = 0{\cdot}02$; Fig. 1a), BSA ($\tau = 0{\cdot}29$, $P = 0{\cdot}02$; Fig. 1b) and LBM ($\tau = 0{\cdot}38$, $P = 0{\cdot}002$; Fig. 1c). We also found significant inverse correlations between BMI and BAT activity [normalized by BW ($\tau = -0{\cdot}30$, $P = 0{\cdot}006$; Fig. 2a), BSA ($\tau = -0{\cdot}31$, $P = 0{\cdot}004$; Fig. 2b) and LBM ($\tau = -0{\cdot}45$, $P = 0{\cdot}001$; Fig. 2c). No significant associations were observed for BAT mass ($P > 0{\cdot}05$). Interestingly, age was also inversely correlated with BAT activity normalized by LBM ($\tau = -0{\cdot}28$, $P = 0{\cdot}01$).

Results from the Kruskal–Wallis analysis of variance and *post hoc* Mann–Whitney *U* tests appear in Fig. 3. BAT activity (BW normalization: $P = 0{\cdot}02$; BSA normalization: $P = 0{\cdot}01$; LBM normalization: $P = 0{\cdot}02$) varied significantly between low/moderate/high levels of habitual physical activity participation. *Post hoc* tests showed that BAT activity was higher in participants with high levels of habitual physical activity compared to those with moderate (normalized by BSA) and low [normalized by BW, BSA and LBM ($P < 0{\cdot}05$); Fig. 3a] levels. In contrast, we did not observe any statistically significant effects for BAT mass ($P > 0{\cdot}05$).

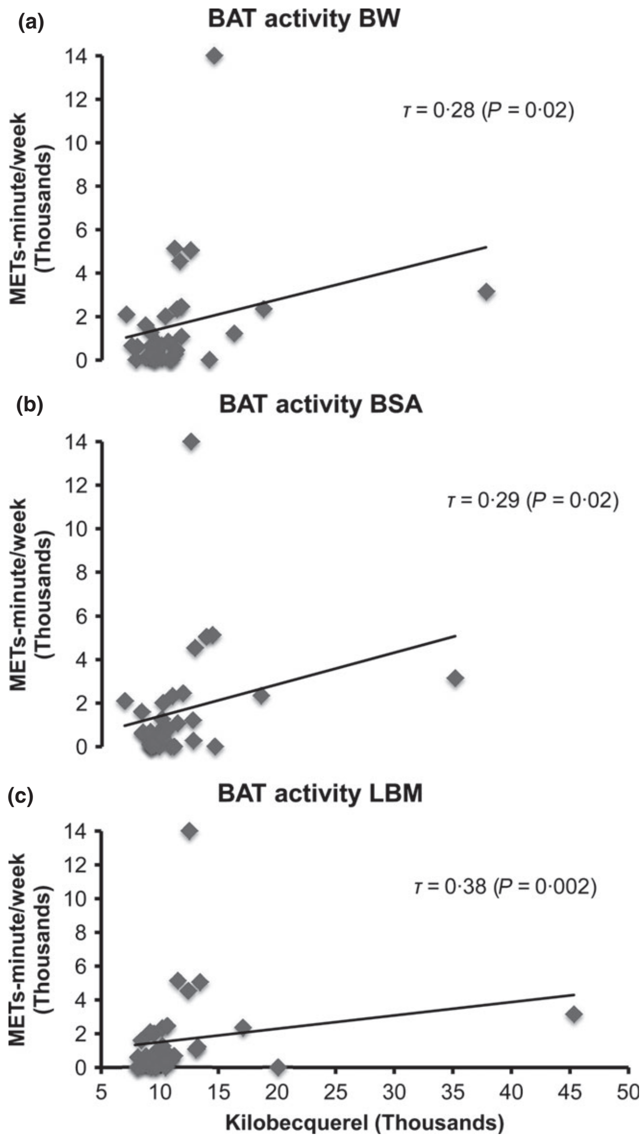

Fig. 1 Correlations between habitual physical activity (METs-minute/week) and brown adipose tissue activity normalized by body weight (a), body surface area (b) and lean body mass (c). Note: BAT = brown adipose tissue; BW = body weight; BSA = body surface area; LBM = lean body mass.

The BAT activity [normalized by BW ($P = 0{\cdot}01$), BSA ($P = 0{\cdot}03$) and LBM ($P = 0{\cdot}003$)] was different across the BMI categories in both sexes, with normal BMI participants showing higher BAT activity than their overweight and obese counterparts ($P < 0{\cdot}05$; Fig. 3b). Interestingly, we also found that BAT activity [normalized by BW ($P = 0{\cdot}02$), BSA ($P = 0{\cdot}02$) and LBM ($P = 0{\cdot}005$)] was greater in women than in men (Fig. 3c).

We observed no statistically meaningful associations between environmental temperature and BAT activity [normalized by BW ($\tau = -0{\cdot}14$, $P = 0{\cdot}212$), BSA ($\tau = -0{\cdot}11$, $P = 0{\cdot}338$) and

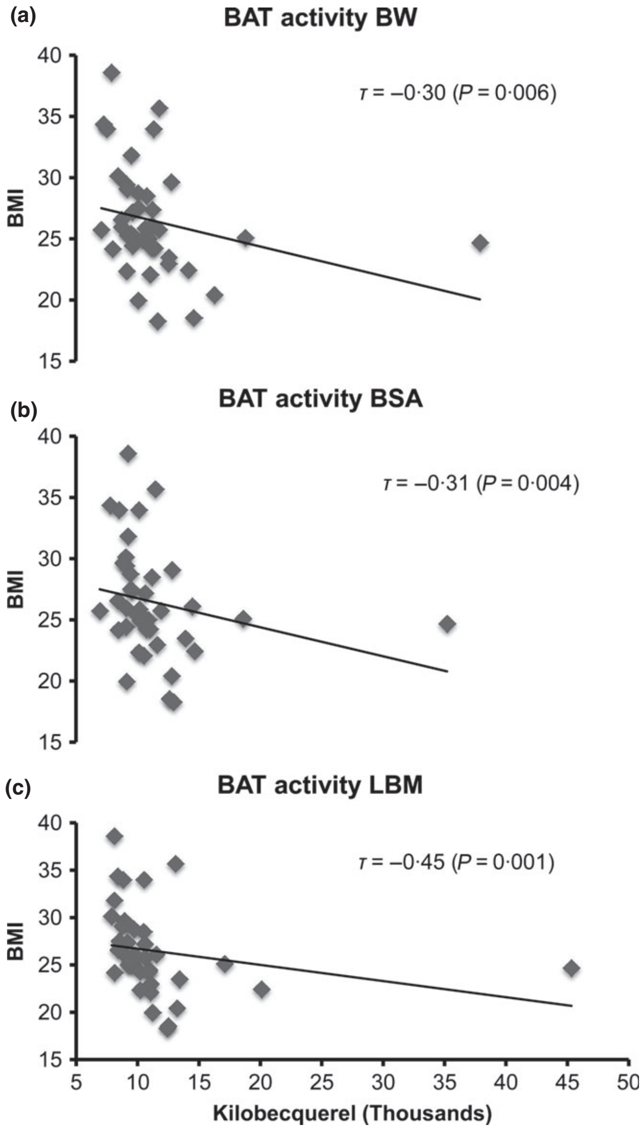

Fig. 2 Correlations between body mass index and brown adipose tissue activity normalized by body weight (a), body surface area (b) and lean body mass (c). Note: BAT = brown adipose tissue; BW = body weight; BMI = body mass index; BSA = body surface area; LBM = lean body mass.

LBM ($\tau = -0{\cdot}06$, $P = 0{\cdot}599$)]. We also found no statistically significant correlations between environmental temperature and BAT mass [normalized by BW ($\tau = -0{\cdot}12$, $P = 0{\cdot}277$), BSA ($\tau = -0{\cdot}10$, $P = 0{\cdot}350$) and LBM ($\tau = -0{\cdot}11$, $P = 0{\cdot}344$)]. Scatterplots illustrating these results are presented in Figure S5 (see Online Data Supplement).

Discussion

In recent years, BAT has been proposed as a promising candidate to reduce the spread of the obesity epidemic.[2,4] To our knowledge, this is the first study to investigate whether habitual (usual weekly participation) physical activity is linked with BAT activity and mass in humans. Our results suggest that BAT activity is positively linked with habitual physical activity in patients undergoing ^{18}F-FDG PET/CT scanning. On the other hand, we did not find an association between habitual physical activity participation and BAT mass. This may be explained by the high oxidative capacity of brown adipocytes that may display high BAT activity in a relative small amount of tissue's volume.[24]

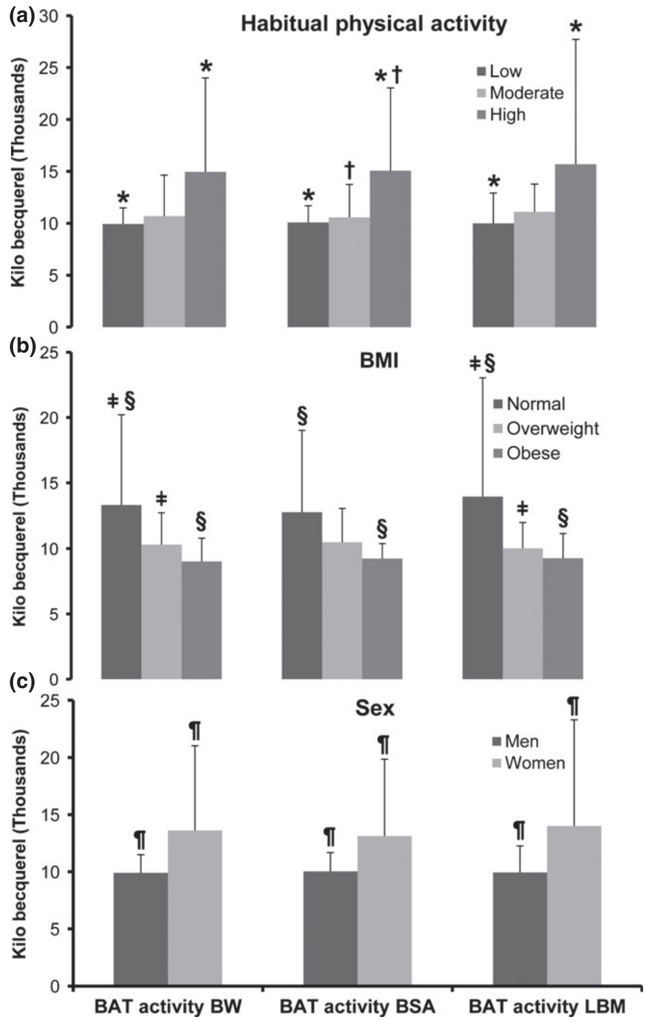

Fig. 3 Results from *post hoc* Mann–Whitney *U* tests for brown adipose tissue activity normalized by body weight, body surface area and lean body mass with respect to habitual physical activity (a), body mass index categories (b) and sex (c). Note: BMI = body mass index; BAT = brown adipose tissue; BW = body weight; BSA = body surface area; LBM = lean body mass. *Significant differences between low and high levels of habitual physical activity with respect to BAT activity normalized by BW ($P = 0{\cdot}002$), BSA ($P = 0{\cdot}003$) and LBM ($P = 0{\cdot}006$). †Significant differences between moderate and high levels of habitual physical activity with respect to BAT activity normalized by BSA ($P = 0{\cdot}03$). ‡Significant differences between normal and overweight individuals with respect to BAT activity normalized by BW ($P = 0{\cdot}02$) and LBM ($P = 0{\cdot}006$). §Significant differences between normal and obese individuals with respect to BAT activity normalized by BW ($P = 0{\cdot}01$), BSA ($P = 0{\cdot}02$) and LBM ($P = 0{\cdot}01$). ¶Significant differences between men and women with respect to BAT activity normalized by BW ($P = 0{\cdot}02$), BSA ($P = 0{\cdot}02$) and LBM ($P = 0{\cdot}005$).

The lack of previous human studies on this topic precludes conclusive inferences for the link shown here between habitual physical activity participation and increased classical (i.e. supraclavicular and perirenal) BAT activity. Animal studies have shown that acute exercise upregulates PGC-1α which, in turn, co-ordinates different physiological pathways that lead to mitochondrial biogenesis in BAT.[8,25,26] In addition to mRNA changes in mitochondrial biogenesis/function, chronic exercise leads to mRNA changes characteristic of fatty acid transport and metabolism that are linked with increased fat utilization and microscopic alterations in hepatocytes and brown adipocytes.[8,26] While these hypotheses are plausible and should be further examined in future studies, there is no evidence that the level of habitual physical activity in which our participants engaged in was sufficient to trigger the aforementioned mechanisms promoting BAT activity. Indeed, 30·3% and 24·2% of our participants reported moderate and high physical activity levels, respectively. This is difficult to compare to the 8-week running-based exercise programme for 40 min/day at a speed of 15 m/min for 5 days/week[8] or the 7-day running-based exercise programme for 60 min/day at 10 m/min[26] that have previously reported to promote BAT activity in mice. Previous human studies on this topic have used exercise protocols such as 20–35 min/day of cycling at 65% of maximal oxygen uptake for 4–5 sessions/week for 10 weeks.[27] However, the human studies published to date have not assessed the effects of these long-term exercise programmes on BAT activity and/or mass, thus precluding a direct comparison with the current data.

Interestingly, we found that higher BMI is associated with lower BAT activity in both sexes, confirming recent studies.[4,28,29] In addition, we report for the first time that individuals of different BMI categories (normal, overweight and obese) demonstrate significantly different BAT activity levels, independently of sex. This supports our recent proposal that abnormalities in BAT function and development can lead to obesity phenotype, and that increasing BAT activity in overweight and obese individuals may be of therapeutic value.[1,2] We also detected a negative relationship between age and BAT activity, indicating that BAT levels decrease during ageing as previously reported.[30] Moreover, in line with recent data,[10,11] we show that women demonstrate higher BAT activity than men, a phenomenon that has been attributed to sex hormone variation.[2,31,32] Nevertheless, it is important to note that the current cross-sectional study demonstrates an association between habitual physical activity and BAT activity in humans. Whether a causal relationship exist between these two factors remains to be determined. For instance, it may well be that the augmented BAT activity of low BMI individuals is not mediated by physical activity but, instead, by the lower body mass that these individuals tend to have. As total body heat content is proportional to body mass,[33–35] overweight and obese individuals are in less need for nonshivering thermogenesis and, therefore, their lower BAT activity would be anticipated.

Moreover, while environmental temperature did not appear to influence our data, the current findings should be considered with some caution because our measurements were performed in individuals undergoing ^{18}F-FDG PET/CT scanning, the majority of which pertained to cancer detection. However, there was no association of BAT uptake with oncologic diagnoses in the current study. Patients with cancer have been recruited in several previous studies investigating potential links between BAT activity, cold exposure and age.[10,11,36] These studies considered the BAT mass and activity levels – assessed via ^{18}F-FDG PET/CT – valid, because the examined area did not include cancerous tumours or other pathologic hypermetabolic tissues. We adopted this screening methodology and further reinforced it using two independent experienced physicians who verified that all PET/CT results did not include cancerous tumours. Nevertheless, it is worthwhile to discuss potential physiological differences between patients with cancer and healthy subjects with respect to the present findings. In adult patients with cancer, the prevalence of BAT detection through ^{18}F-FDG PET/CT ranges from 1·9% [37] to 9·9%.[38] In healthy adults, the only study to assess BAT activity without cold exposure reported no ^{18}F-FDG uptake in BAT.[29] The prevalence of BAT detection through ^{18}F-FDG PET/CT after exposure to mild cold in healthy individuals ranges from 33%[29] to 96%.[4] In the current study, we did not use the usual detection threshold of 2·0 SUV [10] but, instead, considered all cases in our analysis as our purpose was to investigate the association between BAT activity and physical activity participation – not whether BAT was detected or not. As the assessments were conducted under routine clinical imaging conditions, we chose to conduct our study during the winter period that shows the highest probability of observing ^{18}F-FDG BAT in Mediterranean climates such as Greece's.[11]

Robust evidence has shown that there are few lifestyle differences between individuals with or without cancer history.[39,40] Regarding physical activity, the available data suggest that the probability to meet physical activity guidelines is similar in patients with cancer and healthy individuals.[40] This is confirmed by our data showing that 45·5% of the participants reported low levels of physical activity participation, while 30·3% and 24·2% reported moderate and high levels, respectively. These results are in line with recent data for the Greek healthy adult population.[41] In addition, it should be mentioned that the IPAQ is a well-known standardized questionnaire that has been used in a large number of studies around the world and has been validated for Greek healthy[20] and clinical populations.[21] Given the above, while including pedometer data would have strengthened our results, we are confident that our physical activity data represent those of the healthy Greek population.

In conclusion, we found that increased participation in habitual physical activity is associated with higher BAT activity. Moreover, individuals with normal BMI demonstrate higher BAT activity compared to overweight and obese individuals. Finally, age is inversely linked with BAT activity while women demonstrate higher BAT activity compared to men. Future studies should examine the effects of prescribed exercise interventions on BAT mass/activity in humans.

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