Body Mass Index as a Determinant of Brown Adipose Tissue Function in Healthy Children

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Objective To determine whether body mass index (BMI) percentile and ethnicity influence skin temperature overlying brown adipose tissue (BAT) depots in the supraclavicular region in healthy children.

Study design Infrared thermography measured supraclavicular region temperature (T_{SCR}) at baseline and after exposure to a mild cool stimulus (single hand immersion in water at 20.1°C) for 5 minutes in children aged 6-11 years (n = 55). The studies were undertaken in a normal school environment.

Results BMI percentile and ethnicity were significant predictors of baseline T_{SCR}, with an inverse relationship between BMI percentile persisting after adjustment for ethnicity. Twenty-four children demonstrated a significant rise in T_{SCR} after exposure to the cool stimulus. BMI percentile was a significant predictor of T_{SCR} response, although there was no effect of ethnicity on T_{SCR} change after exposure to the cool stimulus.

Conclusion We have demonstrated a negative relationship between BMI percentile and both baseline T_{SCR}, colocating with the primary region of BAT, and the change in T_{SCR} in response to the cool stimulus. Future studies aimed at determining the primary factors regulating BAT function in healthy children should be targeted at the goal of maintaining a healthy BMI trajectory during childhood. *(J Pediatr 2014;164:318-22)*.

Brown adipose tissue (BAT) is a highly metabolic, thermogenic tissue characterized by the unique uncoupling protein UCP1,[1] which was previously considered to disappear during infancy but is now known to persist into adulthood.[1-3] It has been estimated that only 40-50 g of BAT maximally stimulated could contribute up to 20% of daily energy expenditure.[4] In children and adults subjected to cold exposure, significant UCP1-positive adipose tissue depots have been demonstrated in the pericardial region,[5] supraclavicular region (SCR),[6] and mediastinal and perirenal regions[7,8] using tissue biopsy and/or radiolabeled ^{18}F-fluorodeoxyglucose positron-emission tomography with computed tomography (PET-CT).

The precise roles of BAT in human metabolism and energy balance have yet to be fully elucidated, especially for children. Nonetheless, a clear link exists between obesity and BAT dysfunction in adults.[9,10] Understanding the developmental physiology of BAT is crucial in determining whether this is a causative association, although some major limitations of PET-CT imaging prevent its use as a gold standard imaging technique in healthy children. We have recently demonstrated the feasibility of using infrared thermography as a safe, reproducible, and robust technique for measuring the temperature of the skin overlying BAT depots in the SCR (SCR temperature [T_{SCR}]) and quantifying thermogenesis induced by a mild cold.[11] This technique has demonstrated that BAT function is greatest in young children, although its primary regulators remain to be determined.

The main objective of the present study was to perform infrared thermography in a cohort of healthy children while in their normal school environment to test the hypothesis that a high body mass index (BMI) percentile is associated with a lower T_{SCR}. Because infrared thermography permits measurements in real time, we performed measurements under both basal and stimulated conditions; the latter is the norm for other modalities of BAT function in which it is not feasible to directly follow dynamic changes in function.[6] Secondary objectives included evaluating whether age, sex, ethnicity, and ambient room temperature are additional independent predictors of T_{SCR}.

Methods

Sixty-eight children aged 6-11 years were recruited from 2 inner-city schools in Nottingham, United Kingdom, between November 2011 and January 2012. There were no major exclusion criteria. Parents and children were given an information leaflet at school inviting any child who wished to do so to participate in the study, to ensure a representative sample of healthy volunteer children. The children expressing interest in the study were enrolled after receipt of written

BAT	Brown adipose tissue
BMI	Body mass index
PET-CT	Positron-emission tomography with computed tomography
SCR	Supraclavicular region
T_{SCR}	Supraclavicular region temperature

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informed parental consent. Additional verbal assent was obtained from each child on the day of study. Before participant recruitment, the study was approved by the University of Nottingham Medical School Ethics Committee.

The study was undertaken in the school environment, in a specifically designated area that provided adequate privacy for thermal imaging and assessment of BMI. To ensure adequate exposure of the neck and upper thorax for thermal imaging, the children were provided with standard cotton T-shirts to wear on their allocated day of study. The images of children who did not attend in suitable clothing (n = 10) were not processed and were not used for quantification of T_{SCR}, owing to inadequate exposure of the SCR to the thermal imager.

Children attended the study in pairs and before imaging were introduced to the research team and familiarized with the equipment and study protocol. Date of birth and sex were recorded, along with an assessment of ethnicity based on skin color, with each child classified as Caucasian or non-Caucasian. Because we did not have ethical approval to ascertain the detailed ethnicity of parents and grandparents, no further information was available for this aspect of the investigation.

Children were dressed in their standard school uniform and their study T-shirt. Measurements of height and weight without shoes were performed following standard protocols. Height was measured to the nearest 0.1 cm using a stadiometer (Leicester height measure; Child Growth Foundation, Sutton Coldfield, United Kingdom), and weight was measured to the nearest 0.1 kg with a portable digital scale using standard methodology. Because BMI percentiles for children standardize BMI for age and sex, BMI was calculated for each child as weight (in kg)/height (in m^2), and individual sex- and age-specific percentiles were determined using an online calculator.[12]

The experimental protocol included a 7-minute baseline period, followed by exposure to a mild cool stimulus for another 5 minutes as established previously,[11] producing a decrease in hand temperature of 8.41 ± 1.99°C. The stimulus was immersion of the left hand in cool water. Images were obtained at 1-minute intervals with a thermal imaging camera (FLIR B425; FLIR Systems, Danderyd, Sweden) with a range limit of −20°C to 120°C. The child was positioned to provide an optimal view of the head, neck, and upper thorax seated 0.8-0.9 m from the thermal imaging camera with the arms adducted, right hand placed in the lap, and left hand placed in an empty 6-L receptacle. Before imaging, ambient room temperature, relative humidity, and perpendicular distance from the camera were recorded, and the camera was set up accordingly.

After acquisition of adequate baseline images, cool water (20.1°C) was poured into the bucket such that the whole hand was immersed to the level of the ulnar and radial styloid processes. Immersion was maintained for a total of 5 minutes; the child was free to remove his or her hand at any point during the study. Tympanic membrane temperature was measured immediately before and on cessation of thermal imaging in triplicate using a Braun Thermoscan Pro 4000 (Welch Allyn, Skaneanteles Falls, New York).

The infrared thermography images were downloaded onto a personal computer and analyzed using FLIR Researcher Pro 2.10 (FLIR Systems AB, Danderyd, Sweden). A region of interest was defined for the left and right SCR overlying known regions of BAT using the anatomic landmarks for the borders of the posterior triangle of the neck (sternocleidomastoid, trapezius, and clavicle) as described previously.[11] T_{SCR} was calculated as the median value of the hottest 25% of the defined region of interest. Skin surface temperature was determined from data obtained using iButtons (model DS1921H-F50; Maxim, Sunnyvale, California)[11] applied to a region not known to contain BAT on the chest wall (below the sternal notch).

Baseline T_{SCR} was calculated as a mean of the values measured at −2, −1, and 0 minutes before exposure to the cool stimulus. The peak T_{SCR} reached during the 5-minute period of hand immersion was recorded, and the change from baseline was defined as ΔT_{SCR}. Given that previous studies using PET-CT have shown that not all individuals have detectable BAT at thermoneutrality,[1-3] a priori we designated a rise of 2 SD of baseline T_{SCR} (0.09°C) as a likely biologically significant increase (maximal ΔT_{SCR}).

During the initial descriptive analysis, it became apparent that 3 subjects were extreme outliers on the basis of both body weight and baseline T_{SCR} (ie, >2 SDs from those children included in the analysis). These children, 2 Caucasian females and 1 Caucasian male, performed the study on different data collection days, were significantly obese (>98th percentile calculated BMI), close in age (7 years, 1 month to 7 years, 3 months), and had a T_{SCR} >2.5 SD from the mean value for their BMI group. These children were excluded from subsequent analysis; thus, data from 55 children were analyzed.

Data were entered using a simultaneous entry method and assessed for normality using the Kolmogorov-Smirnov normality test, and are presented as mean ± SD unless stated otherwise. Comparisons between left and right T_{SCR} were done using the paired *t* test. Pearson product moment correlation coefficients were calculated to determine the correlation between BMI percentile and T_{SCR} or ΔT_{SCR}. Multiple linear regression analyses were performed to assess associations of T_{SCR} with age, sex, ambient room temperature, and ethnicity, in addition to BMI percentile. This was undertaken to elucidate possible relationships taking into account the age, sex, ethnicity, and BMI range of the children participating in the study. Given the relatively small number of children who were classified as obese, multiple regression analysis permitted exploration of relationships between variables. Variables were selected a priori and were based on previous findings and the hypotheses of this study. Sex and ethnicity were entered as dummy variables. Data were analyzed using SPSS 19.0 (IBM, Armonk, New York), with statistical significance set at $P < .05$.

Results

The study sample consisted of children with a mean age of 101.1 ± 18.2 months and a mean BMI percentile of 58.8 ± 28.0, 6 of whom were overweight (defined as BMI ≥85th percentile but <95th percentile) and 5 of whom were obese (defined as BMI ≥95th percentile[13,14]). Characteristics of