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A low resting metabolic rate in late childhood is associated with weight gain in adolescence☆

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ABSTRACT

Background and objectives: Lower total energy expenditure (TEE) and resting metabolic rate (RMR) are associated with greater weight gain in Native American adults. Whether these effects exist in childhood is unclear. We hypothesized that lower energy expenditure measured in childhood would predict greater relative change in body mass index (BMI) during adolescence.
Methods: Measurements of height, weight, body composition, RMR and TEE were completed in 181 Native American children at exams done at age 5 and 10 years, with 126 children having biennial follow-up assessments of weight and height after age 10 years until age 20 years. TEE and RMR were adjusted for age, sex, height, fat mass and fat free mass. BMI-change was assessed using population specific and Center for Disease Control (CDC) BMI z-scores and change in the relative difference to the 95th BMI-centile.
Results: Lower adjusted RMR at age 10 years was associated with greater increase in population-specific and CDC BMI z-scores, greater increase in the relative difference to the 95th BMI-centile and greater weight gain (all $r \le -0.22$, $p \le 0.01$). However, no association was found with adjusted RMR at age 5 years and with adjusted TEE and physical activity level assessed at age 5 or 10 years.
Conclusions: Lower adjusted RMR at age 10 years predicted greater change in adolescent BMI z-score indicating that the effects of relatively low metabolic rate on future weight gain in this population may begin in late childhood.

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1. Introduction

Children who are obese tend to become obese adults, so risk factors for weight gain are likely present in childhood and adolescence [1–4]. As in adults, weight gain in childhood is due to an imbalance between energy expenditure (EE) and energy intake such that intake exceeds energy requirements including metabolic rate and growth. In terms of EE, our group and others have shown that a lower relative 24-hour EE and resting metabolic rate predict weight gain in adults [5–8]. However, others have reported opposing effects [9] or no effect at all [10,11], which could be explained by varying effects of ethnicity. It is unclear, whether this relationship also exists in childhood.

It was shown that children born to obese or overweight biological mothers had a lower EE in infancy compared to children born to mothers with normal weight during pregnancy [12] and that a lower total EE (TEE) at age 3 months was associated with greater risk of overweight at age one year [13]. However, prior studies failed to show any relationship between EE and weight gain in later childhood [14,15] and thus could not determine at which time point a lower metabolic rate begins to increase the risk of subsequent weight gain.

One recent study found that the resting metabolic rate (RMR) relative to body size decreased after the age of 10 years, possibly due to puberty associated energy conservation, identifying this age as a possible transition for EE in regards to its association with weight gain [16]. Based on this evidence, we hypothesized that an effect of RMR would emerge in later childhood. Thus, in children examined at both age 5 and 10 years, we investigated total EE and RMR as predictors of weight change during adolescence.

Abbreviations: AEE, activity energy expenditure; BMI, body mass index; CDC, Centers for Disease Control and Prevention; DXA, dual-energy x-ray absorptiometry; EE, energy expenditure; FFM, fat free mass; FM, fat mass; GH, Growth hormone; IGF-1, Insulin-like growth factor 1; IQR, interquartile range; LMS, lambda-mu-sigma; NIH, National Institutes of Health; PAL, physical activity level; RMR, resting metabolic rate; RQ, respiratory quotient; TEE, total energy expenditure; %BMI/95P, BMI as relative difference to the 95th BMI-centile.

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2. Methods

From 1992 to 1996, 181 5-year-old Native American children of southwestern heritage participated in a study conducted either at the National Institutes of Health (NIH) Field Clinic located in the Gila River Indian Community in Sacaton, Arizona or at the NIH clinical research unit in Phoenix, Arizona, and returned to one of these facilities 5 years later (at age 10 years). The purpose of this study was the determination of EE measures at the age of 5 and 10 years.

Some children also participated in a longitudinal study of health in Native Americans of southwestern heritage (NCT00339482). In this study conducted from 1965 to 2007, volunteers were invited to participate in study examinations as frequently as every two years. We used data from this study to obtain follow-up measurements of weight and height during adolescence from the children who participated in the first study.

All children were full heritage Native American. In both studies, children were always examined in the fasting state (10-hour overnight fast). All children were healthy as determined by medical history and physical examination. All volunteers and their parents were fully informed of the nature and purpose of the study. Children assented, and a parent or guardian provided written informed consent prior to participation. The experimental protocol was approved by the Institutional Review Board of the National Institute of Diabetes and Digestive and Kidney Diseases.

2.1. Anthropometry and body composition

At the 5- and 10-year visit, body weight was measured while the children were wearing light summer clothing. Height was measured without shoes. Mothers weight was recorded using self-reported weights. Body composition was assessed using the ^{18}O dilution space method [17], a way to assess body composition, in all children at the 5-year visit and in 71 children at the 10-year visit. Fat free mass (FFM) was quantified using the assumption that water is 74% of the FFM in boys and 75% in girls [18].

In all children at the 10-year visit, body composition was also measured using dual-energy x-ray absorptiometry (DXA), as previously described [19]. To compare the body composition data of the 110 children without ^{18}O measurement at the 10-year visit to all other ^{18}O measurements, we converted body fat measured by DXA to percentage of fat measured by ^{18}O using a previously validated regression equation [20].

During the initial study phase at age 5 years, all anthropometric measurements were taken twice (due to urine collections associated with the doubly-labeled water) during clinic admissions one week apart, and results are expressed as the mean of the two measurements. Due to a worldwide shortage of doubly-labeled water at the time of the 5-year follow-up [21], only 71 of the 10-year-old children were able to repeat the doubly-labeled water measures. Therefore, only a single measure of the anthropometric assessments was available for most of the 10-year visits and means were not calculated. This group of 71 subjects did not differ from the rest of the group in terms of anthropometric measurements.

2.2. Total energy expenditure and resting metabolic rate

In all children at the 5-year visit and in 71 children at the 10-year visit, TEE was assessed using the doubly-labeled water method. Volunteers provided a urine sample that they collected at home the evening before the dosing. Just after arriving at the clinic in the fasting state, a second baseline urine specimen was collected. Volunteers were then dosed with doubly labeled water as described previously [22]. The dose contained 2.508 g of 10% $H_2^{18}O$/kg total body weight and 0.132 g of 100% ^2H_2O/kg total body weight (Isotec, Inc., Miamisburg, OH). The dosing container was rinsed with 100 ml drinking water and the water was given to the volunteer to assure consumption of the entire dose. Urine was collected 1.5, 2.5, 3.5, and 4.5 h after dosing on day 1 and at 2 time points 1 h apart after 7 days. The sample collected after 1.5 h was discarded to ensure complete bladder emptying prior to tracer collection. Isotope concentrations of the two baseline urine samples were averaged to provide one baseline value to account for any background enrichment. Disappearance rates of the two stable isotopes were assessed as described previously [23] and a respiratory quotient of 0.866 was used to assess CO_2 production. After the dosing of the doubly-labeled water, volunteers rested comfortably on a bed for 10 min and then resting metabolic rate (RMR) was measured for 20 min using a ventilated hood (DeltaTrac Metabolic Monitor, SensorMedics Corp, Yorba Linda, CA) as previously described [14,24]. Children were carefully instructed about the testing procedure before the measurement began. During the assessment, a parent was nearby, and the children could watch a nonviolent cartoon video. The RMR measurement was repeated at the return visit 1 week later, and the results of the 2 measurements were averaged (coefficient of variation for these measures was 5.4% and intra-class correlation was 0.87 (95% CI: 0.83 to 0.90, $p < 0.001$).

In the remaining 110 children at the age 10 visit, RMR was measured only once using a ventilated hood. Carbon dioxide production and oxygen consumption were calculated for each minute of the 20- to 25-minute period and EE was calculated and then extrapolated to 24 h [14]. The fasting respiratory quotient (RQ), a proxy for the ratio of lipid to carbohydrate oxidation, was calculated as the ratio of mean carbon dioxide production to mean oxygen consumption. Energy used for physical activity was assessed using the following equations: 1) - activity energy expenditure (AEE) = TEE − (RMR + 0.1 × TEE) where 0.1 × TEE represents an estimate of the thermic effect of food [25] and 2) the ratio of TEE to RMR which represents the physical activity level (PAL) [22].

2.3. Follow-up measurements of weight and height

Of the 181 children that completed both measures of EE at age 5 and 10 years, 126 had available data for follow-up measurements of height and weight at an exam prior to age 20 years. If a participant developed type 2 diabetes, the last available visit prior to the diabetes diagnosis was used (n = 7). Paternal and maternal diabetes status was also obtained from this longitudinal study. Median follow-up time from the 5-year visit to the last available childhood (<age 20 years) study visit was 10.8 years (interquartile range [IQR]: 8.3, 12.3 years; range 6.1 to 14.8 years). Median follow-up time from the 10-year visit to the last available childhood (<age 20 years) study visit was 5.9 years (interquartile range [IQR]: 3.3, 7.4 years; range: 1.1 to 9.8 years).

BMI and weight were compared with the standards of the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics by creating z-scores, using the lambda-mu-sigma (LMS) method as described previously [26]. LMS parameters may be inaccurate at very high BMI values [27], therefore, we also expressed the BMI as relative difference to the 95th BMI-centile (%BMI/95P) as recommended by the CDC [27]. To account for average anthropometric differences between the CDC-based population and this southwestern Native American population, we also used population-specific z-scores calculated for weight and BMI. Z-scores for this Native American population were calculated using data from the longitudinal study of health mentioned above using all visits between ages ≥5 and ≤20 years (n = 20,619) at one-year intervals by sex. Follow-up was limited to visits at age <20 years as only few participants had available data after this age (n = 6) and CDC z-scores are only available until the age of 20 years.

2.4. Statistical methods

All statistical analyses were performed using software of the SAS Institute (Enterprise Guide V7.15 (7.100.5.5850), Cary, NC). Normally distributed data was expressed as mean ± standard deviation, whereas skewed data was expressed as median and interquartile range (IQR). Skewed variables were log transformed before being entered into the linear regression models to conform to the assumptions of linear regression. Measures of EE and RQ were analyzed using linear regression models to account for known determinants of EE including sex, age, fat-mass (FM), FFM and height. We included height in our regression models because it is a significant predictor of EE in children [28]. The measures were expressed as the difference-from-expected value based on the known determinants (i.e. the residual or relative value) and related to the annual change of z-scores of weight, BMI (based on CDC data and population-specific z-scores) and %BMI/95P (based on CDC data). Change in weight and BMI z-scores was assessed as follow: 1) from age 5 to 10 years, 2) from age 5 years to last exam prior to age 20 years and 3) from age 10 years to last follow-up exam prior to age 20 years. Given evidence that children born preterm or small for gestational age have differences in body composition and resting metabolic rate in later childhood [29,30], we also performed sensitivity analyses with the dataset limited to children born at term (>37th gestational week) with a birth weight >2500 g (n = 157 at 5- and 10-year visits and n = 111 at last visit).

3. Results

Anthropometric and EE measures for all subjects at age 5 years, 10 years and at the last follow-up visit are summarized in Table 1. Children with follow-up measures after the 10-year visit had similar anthropometric and EE measures compared to the entire baseline cohort. RMR at age 5 years (±SD) was 1018 ± 158 kcal in girls and 1105 ± 138 kcal in boys. RMR at age 10 years was 1482 ± 255 kcal in girls and 1545 ± 267 kcal in boys. We observed a strong positive relationship between 5-year RMR and 10-year RMR (r = 0.74, p < 0.001), such that the increase in RMR at 10 years was dependent and proportional to the RMR at age of 5 years (regression line slope = 1.27, 95% CI: 1.10, 1.44; Fig. 1).

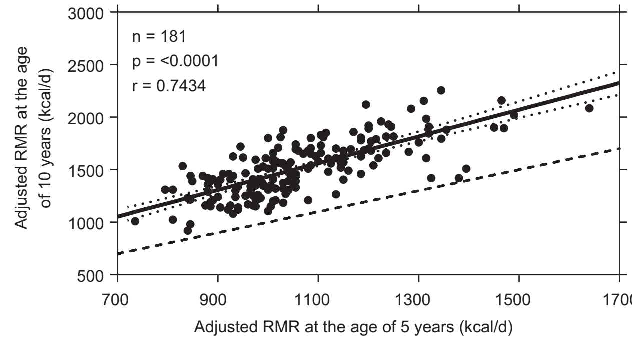

Fig. 1. Positive correlation of 5-year and 10-year RMR. The regression line has a slope of 1.27 with its 95% CI ranging from 1.10 to 1.44. Figure legend: Black line, regression line; Dashed line, Identity line; Abbreviations: RMR, Resting Metabolic Rate; CI, Confidence Interval.

3.1. *Adjusted RMR at age 10 years but not 5 years was associated with weight gain in adolescence*

The average CDC BMI z-score change per year (±SD) from age 5 and 10 years to the last available follow-up visit in adolescence was 0.11 ± 0.15 and 0.04 ± 0.09, respectively. RMR measured at age 5 years and adjusted for sex, age, FM, FFM and height was not associated with CDC BMI z-score change per year (p = 0.9; Fig. 2A). In contrast, adjusted RMR at age 10 years was negatively associated with CDC BMI z-score change per year (r = −0.22, p = 0.01; Fig. 2B). In other words, children with a 200 kcal lower RMR at age 10 years had a 0.18 increased BMI z-score at age 15 years. The parameters of the linear models are presented in Supplemental Table 1.

Weight gain during adolescence was also assessed by change in the relative difference in relation to the 95th BMI-centile based on CDC population data (%BMI/95P). We used this parameter because BMI z-scores may be inaccurate at very high BMI values [27]. The average change in %BMI/95P per year from age 5 and 10 years to the last available follow-up visit was 1.69 ± 1.98 and 1.29 ± 2.76, respectively. Adjusted 5-year RMR was not associated with %BMI/95P change per year (p = 0.7; Fig. 2C). In contrast, adjusted 10-year RMR was negatively associated with %BMI/95P change per year (r = −0.30, p = 0.0008, Fig. 2D).

To account for anthropometric differences in our population of Native American children, we also assessed weight gain using population-specific BMI z-scores. The average population-specific BMI z-score change per year from age 5 and 10 years to the last available follow-up visit was 0.05 ± 0.13 and 0.03 ± 0.12, respectively. Adjusted 5-year RMR was not associated with population-specific BMI z-score change per year (p = 0.7; Fig. 2E). In contrast, adjusted 10-year RMR was negatively associated with population-specific BMI z-score change per year (r = −0.32, p = 0.0003; Fig. 2F).

Table 1
Demographic, anthropometric and metabolic characteristics of the study population with follow-up data.

	5-year visit (girls/boys)	10-year visit (girls/boys)	Last visit (girls/boys)
Number of subjects (girls/boys)	181 (91/90)	181 (91/90)	126 (61/65)
Age (years)	5.5 ± 0.3/5.6 ± 0.3	10.5 ± 0.3/10.5 ± 0.3	16.1 ± 2.2/16.0 ± 2.4
Birth weight (grams)	3449 ± 517/3545 ± 488	3449 ± 517/3545 ± 488	3442 ± 470/3517 ± 522
Number of subjects premature at birth	15 (8/7)	15 (8/7)	11 (6/5)
Weight (kg)	23.1 ± 5.7/23.7 ± 5.7	54.1 ± 15.0/52.1 ± 15.4	82.7 ± 21.5/91.1 ± 28.6
Height (cm)	114 ± 5.1/115 ± 4.9	147 ± 6.8/146 ± 6.4	160 ± 5.6/170 ± 8.5***
Percent body fat	31.4 ± 7.1/28.2 ± 7.2**	38.2 ± 9.3/34.3 ± 10.2**	N/A
Fat mass (kg)	7.6 ± 3.7/7.0 ± 3.7	20.4 ± 9.1/18.3 ± 9.8	N/A
Fat free mass (kg)	15.5 ± 2.3/16.6 ± 2.4**	29.0 ± 5.2/30.1 ± 5.1	N/A
BMI (kg/m^2)	17.6 ± 3.1/17.6 ± 3.2	24.6 ± 5.4/24.2 ± 5.8	31.9 ± 7.1/31.0 ± 8.2
BMI z-score (population-specific)	0.09 ± 0.87/0.14 ± 1.13	0.34 ± 0.96/0.38 ± 1.06	0.45 ± 1.01/0.56 ± 1.13
BMI z-score (CDC based)	0.96 ± 1.05/0.96 ± 1.28	1.55 ± 0.90/1.51 ± 0.94	1.64 ± 0.80/1.68 ± 1.07
Percent of 95th BMI-centile (CDC based)	95.2 ± 16.7/97.1 ± 17.6	105.2 ± 22.9/107.0 ± 25.7	109.0 ± 2.8/111.6 ± 3.1
RMR (kcal)	1018 ± 158/1105 ± 138***	1482 ± 255/1545 ± 267	N/A
RMR per kg weight (kcal)	45.1 ± 5.5/48.0 ± 6.2**	28.4 ± 4.0/30.9 ± 5.1**	N/A
RMR per kg FFM (kcal)	65.9 ± 5.7/66.8 ± 5.5	51.9 ± 10.2/51.6 ± 6.6	N/A
TEE (kcal)	1378 ± 228/1522 ± 256	2326 ± 392/2550 ± 566‡	N/A
TEE per kg weight (kcal)	102.1 ± 14.8/106.6 ± 27.4	44.6 ± 8.0/49.1 ± 12.5‡	N/A
TEE per kg FFM (kcal)	89.8 ± 10.2/91.5 ± 9.2	79.3 ± 8.8/82.1 ± 16.5‡	N/A
RQ (ratio)	0.88 ± 0.04/0.88 ± 0.03	0.87 ± 0.04/0.88 ± 0.05	N/A
PAL (ratio)	1.38 ± 0.16/1.38 ± 0.14	1.08 ± 0.16/1.03 ± 0.20‡	N/A

Gender differences: ** = p < 0.01; *** = p < 0.001. ‡Data available from n = 71 (33 girls/38 boys). Abbreviations: BMI, Body Mass Index, Z-BMI, Standard Deviation of BMI adjusted for age and sex; CDC, Centers for Disease Control and Prevention; RMR, Resting Metabolic Rate; TEE, Total Energy Expenditure; RQ, Respiratory Coefficient; PAL, Physical Activity Level.

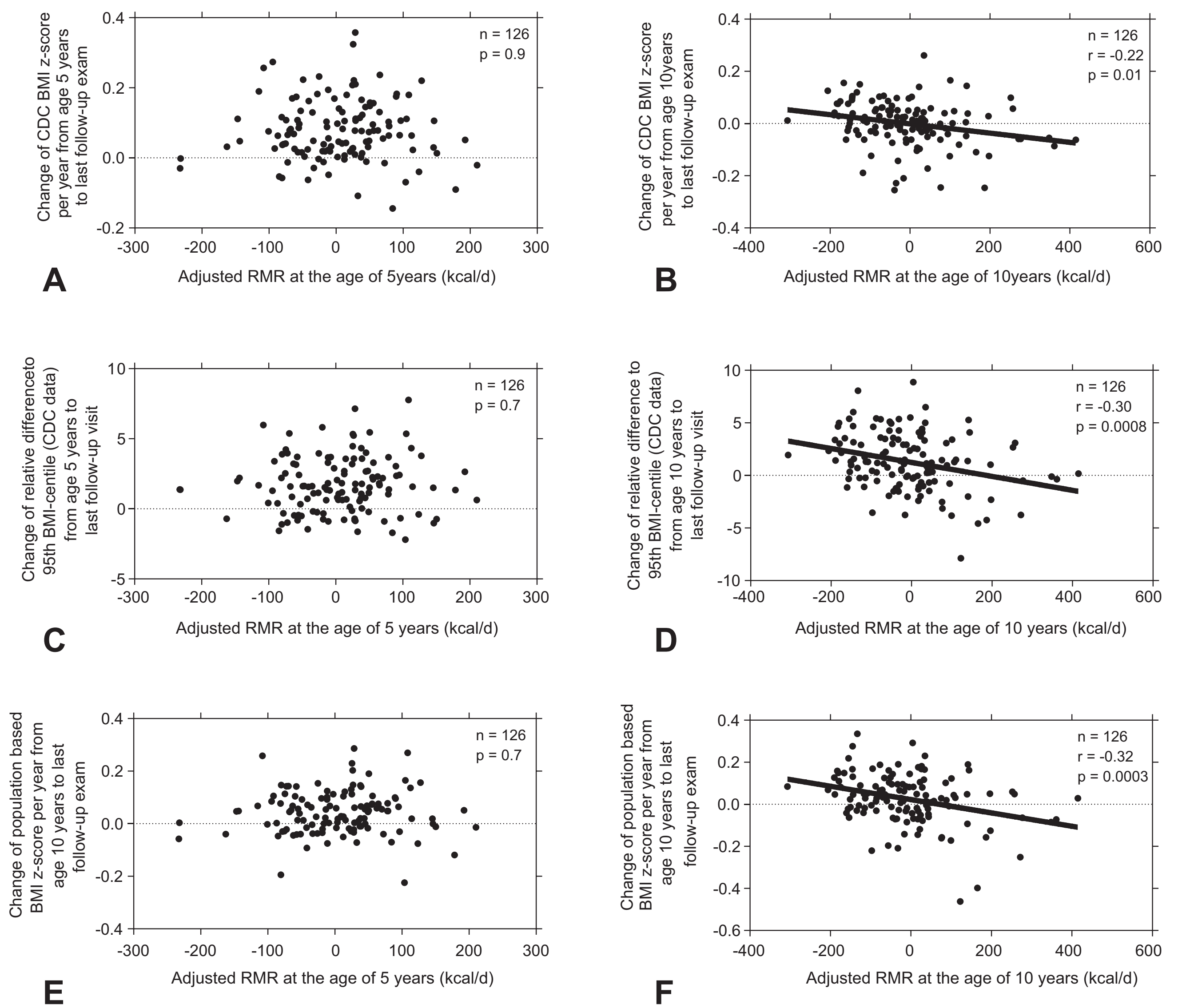

Fig. 2. Relationship of adjusted RMR at age 5 years and 10 years with measures of weight gain through last follow-up prior to age 20 years. Adjusted RMR at age 5 years was not associated with (A) BMI z-score change per year (based on CDC population data), (C) the relative difference to the 95th BMI-centile (based on CDC population data), and (E) BMI z-score change per year (based on Native American population-specific data). In contrast, adjusted RMR at age 10 years was inversely associated with (B) BMI z-score change per year (based on CDC population data), (D) the relative difference to the 95th BMI-centile (based on CDC population data), and (F) BMI z-score change per year (based on Native American population-specific data. RMR was adjusted for age, sex, height, FFM and FM at 10-year visit. Abbreviations: BMI, Body Mass Index; CDC, Centers for Disease Control and Prevention; RMR, Resting Metabolic Rate; FFM, Fat Free Mass; FM, Fat Mass.

The results were further confirmed by using weight z-score change per year adjusted for height z-score change per year based on either CDC or southwestern Native American population-specific data. Again, adjusted 10-year RMR was negatively associated with yearly weight gain during adolescence based on CDC z-scores ($r = -0.18$, $p < 0.05$) and population-specific z-scores ($r = -0.22$, $p = 0.01$), whereas adjusted 5-year RMR was not associated with yearly weight gain during adolescence (all $p > 0.7$).

All associations with RMR at the age of 10 years remained significant after additional adjustment for exposure to diabetes during pregnancy, presence of parental diabetes prior to conception or mother's weight at baseline. Results did also not differ between boys and girls and there was no interaction effect of sex by RMR in these linear models with the exception of that using yearly CDC BMI z-score change ($p = 0.01$ for interaction). A separate analysis of boys and girls demonstrated that adjusted 10-year RMR was a predictor of yearly CDC BMI z-score change in girls ($p = 0.006$), with an attenuated but similar trend observed in boys ($p = 0.06$).

Measures of adjusted TEE, RQ and PAL at age 5 and 10 years were not associated with BMI z-score, %BMI/95P, and weight z-score change per year in adolescence, based on either CDC or population-specific data (all $p > 0.09$). Excluding children born prematurely or with low birth weight (<2500 g) did not change the results.

3.2. RMR at age 5 years was not associated with weight gain at age 10 years

RMR at the age of 5 years adjusted for sex, age, FM, FFM and height was not associated with change in BMI z-score per year or change in %BMI/95P per year at the age of 10 years using CDC population data ($p = 0.5$; Supplemental Fig. 1A, B) or population specific BMI z-scores ($p = 0.4$; Supplemental Fig. 1C). In addition, no association was seen for adjusted RMR measured at 5 years and weight z-score change per year adjusted for height z-score change per year based on CDC or southwestern Native American population-specific data at the age of 10 years ($r = 0.03$, $p = 0.7$ and $r = 0.08$, $p = 0.3$, respectively). Measures of adjusted TEE, PAL and RQ were not associated with annual change of BMI z-score (CDC and population-specific) or change in %BMI/95P until the age of 10 years (all p-values > 0.2; data not shown). Excluding children born prematurely or with low birth weight (<2500 g) did not change the results.

4. Discussion

We have previously shown that a relatively lower 24-h and resting EE are associated with increased future weight gain in adult Native Americans of southwestern heritage [7,8] and that there are different patterns of weight gain during childhood [31]. Here we show that in the same population, after accounting for the main determinants of EE in children including sex, age, height and body composition, a lower relative RMR at age 10 years, but not age 5 years, predicted future weight gain prior to age 20 years. These results were consistent whether weight gain was assessed by annual change in BMI z-scores or weight z-scores adjusted for change in height z-scores based on CDC or population-specific data. The results were also seen when weight gain was assessed by change in the relative difference in relation to the 95th BMI-centile (based on CDC data), which is a sensitive marker of weight gain in more overweight populations [27]. Adjustment for parental diabetes status prior to conception or exposure to diabetes in utero conditions did not change the results. This result can be of importance as the weight in young adulthood defines the future weight gain trajectory [32].

4.1. Energy expenditure is unlikely to influence weight gain before the age of 10 years

Only a small number of studies have so far investigated whether EE predicts future weight gain in children. One large study did not find an association between RMR at age 7 years and weight gain or changes in body composition at age 13 years [15]. Two other smaller studies also failed to show an association between RMR and weight change in children [33,34]. One study did demonstrate that lower RMR in girls with poor linear growth was associated with greater weight gain and fat mass accumulation [35]. However, all these studies share that baseline measurements of EE were performed before the age of 10 years. Indeed, the timing of the EE measurement might be crucial to explain our findings. We found that RMR at age 10, but not 5 years, was associated with weight change. We believe there are several potential explanations for this.

4.2. Distinct changes in resting metabolic rate at the age of 10 years

One of the most pertinent may be the apparent RMR changes that occur with approaching puberty [36]. Mostazir et al. measured yearly RMR in children from age 7 to 16 years [16]. They identified an increase of unadjusted RMR from age 7 to 11 years, as expected for growing children. However, the RMR plateaus and then even decreases from age 11 to 15 years. This was more apparent when RMR was adjusted for concomitant body composition in which case the RMR decrease was more pronounced from age 10 to 15 years. This indicates that RMR physiology appears to change at age 10 years. Mostazir et al. hypothesize that this may be part of an "energy conservation program" that occurs during puberty originating from times where nutrition was scarce to provide sufficient energy to allow pubertal development and hence eventually reproduction. The RMR data measured at age 10 years may have been at the cusp of this decline. We hypothesize that those who had a greater relative decline or a decline to a lower absolute level would be predisposed to greater weight gain. Altogether, this may explain the discrepancy in RMR association with weight gain at different ages.

4.3. Reduced physical activity after the age of 10 years

Another possible explanation for the divergence in the association of RMR measured at 5 years versus 10 years may be the relative contribution of physical activity to EE during childhood versus adolescence. In many populations, declines in physical activity are seen in early adolescence [16,37,38]. Thus, any effect of RMR at age 5 years may be diluted by greater overall physical activity in children of age 5 to 9 years. However, when EE for physical activity declines (as in early adolescence), RMR may then have a relative greater contribution to weight gain.

4.4. 10-year RMR predicts weight gain after growth spurt

Changes in hormone-mediated growth from childhood to puberty may also be a potential explanation for our findings. Between the ages of 10 to 12 years, pituitary growth hormone (GH) with subsequent hormone insulin-like growth factor 1 (IGF-1) secretion as well as thyroid hormones mainly control growth velocity. During the pubertal growth spurt phase after the age of 12 years, the sexual hormones testosterone and estradiol additionally influence GH secretion and determine the beginning and ending of growth spurt during adolescence [39]. During this phase, longitudinal growth temporary accelerates before considerably slowing down until final height is achieved [40]. All previous studies which investigated RMR in childhood share that follow-up measurements were performed when longitudinal growth velocity was still high, on average. Our final follow-up measures extended into the phase where longitudinal growth is slowing (i.e. beyond the "growth spurt") and where weight gain is not primarily driven by this longitudinal growth, which may explain why we detected an effect of relatively lower RMR at age 10 years on later weight gain. The lack of a relationship between 5-year RMR and later weight gain in this study might also be due to longitudinal growth as the predominant driver of relative weight gain in early childhood, thus minimizing an effect of RMR. Taken together, longitudinal growth mediated by different hormones might be a possible confounder, which has masked a possible correlation of RMR and later weight gain in other studies.

4.5. Limitations

Our report has several limitations. The results may only be relevant to Native American children. Due to the shortage of doubly labeled water at the time of the 10-year follow-up visit, only about a third of our subjects had measurements of TEE and PAL at that visit, limiting our power to detect an effect of TEE and PAL on weight gain. However, other studies, including studies from our research group, have failed to detect an effect of free living energy expenditure measurements on body weight changes [8,41–43]. Resting metabolic rate may be a more inherent and stable attribute and has less measurement variation than free-living TEE, as measured by doubly-labeled water, which also includes physical activity. Furthermore, the lack of association of PAL with weight change may also be due to the inherent imprecision of this measure based on assumptions from its calculation from the TEE assessment by doubly-labeled water. Another limitation is that children were not assessed for detailed pubertal status and that we did not have information on dietary habits or patterns. While decline in physical activity may play a role in weight gain, it is likely that increased food intake is of greater importance as food intake is one of the main determinants of weight gain [8,44]. We also do not have measures of hormone concentrations during childhood and adolescence.

5. Conclusion

This study shows that a lower relative RMR at age 10 years predicts weight gain in adolescence. This association remained consistent whether the analysis was performed using BMI z-scores or weight z-scores adjusted for change in height z-scores based on CDC or population specific data. The same results were observed when weight gain was assessed by change in the relative difference in relation to the 95th BMI-centile. This finding indicates that an individual's metabolic rate likely begins to affect weight gain after both active linear growth and physical activity (which may mask effects of resting metabolic rate) may have peaked [45]. These results need to be confirmed in larger more heterogeneous populations including hormonal and genetic measures to determine the mechanism of these differences. In this Native American population of southwestern heritage, resting metabolic rate exerts an effect on weight gain as early as age 10 years reflecting an inherent near life-long metabolic risk for excess adiposity. These findings might be useful for the understanding of the influence of resting metabolic rate on weight gain in early and late childhood and targeting those with relatively low RMR with more intensive lifestyle efforts.

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Potential conflicts of interest

The authors have no conflicts of interest relevant to this article to disclose.

Financial disclosure

The authors have no financial relationships relevant to this article to disclose.

Contributors' statement

Dr. Hohenadel designed the study, drafted the initial manuscript, carried out the initial analyses, interpreted the results and approved the final manuscript as submitted.

Dr. Hollstein carried out the initial analyses, interpreted the results, wrote the manuscript and approved the final manuscript as submitted.

Dr. Thearle contributed substantially to the study conception and design, interpreted the results, revised the manuscript, and approved the final manuscript as submitted.

Dr. Reinhardt contributed substantially to the study conception and design, interpreted the results, revised the manuscript, and approved the final manuscript as submitted.

Dr. Piaggi carried out the initial analyses, revised the manuscript, and approved the final manuscript as submitted.

Dr. Salbe contributed substantially to the study conception and design, revised the manuscript, and approved the final manuscript as submitted.

Dr. Krakoff contributed substantially to the study conception and design, critically reviewed the manuscript, and approved the final manuscript as submitted.

All authors read and approved the final manuscript. All authors agreed 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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.metabol.2018.12.008.

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