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Timing of Adiposity Rebound and Adiposity in Adolescence

WHAT’S KNOWN ON THIS SUBJECT: Earlier adiposity rebound may increase fatness in later life; however, there is limited evidence from large cohorts of contemporary children with direct measures of fatness in adolescence or adulthood.

WHAT THIS STUDY ADDS: Early adiposity rebound is strongly associated with increased BMI and fatness in adolescence. Future preventive interventions should consider targeting early childhood to delay timing of adiposity rebound.

abstract

OBJECTIVES: To investigate associations between timing of adiposity rebound (AR; the period in childhood where BMI begins to increase from its nadir) and adiposity (BMI, fat mass) at age 15 years in the Avon Longitudinal Study of Parents and Children (ALSPAC).

METHODS: The sample consisted of 546 children with AR derived in childhood and BMI and fat mass index (FMI; fat mass measured by dual-energy radiograph absorptiometry/height in m²) measured at 15 years. Multivariable linear regression models were based on standardized residuals of log BMI and log FMI to allow comparison of regression coefficients across outcomes.

RESULTS: There were strong dose-response associations between timing of AR and both adiposity outcomes at 15 years independent of confounders. BMI was markedly higher in adolescence for those with very early AR (by 3.5 years; $\beta = 0.70$; 95% confidence interval [CI]: 0.33–1.07; $P = .001$) and was also higher for those with early AR (between 3.5 and 5 years; $\beta = 0.34$; 95% CI: 0.08–0.59; $P = .009$) compared with those with later AR (>5 years) after full adjustment for a range of potential confounders. Similar magnitudes of association were found for FMI after full adjustment for confounders (compared with later AR: very early AR $\beta = 0.74$; 95% CI: 0.34–1.15; $P = .001$; early AR $\beta = 0.35$; 95% CI: 0.07–0.63; $P = .02$).

CONCLUSIONS: Early AR is strongly associated with increased BMI and FMI in adolescence. Preventive interventions should consider targeting modifiable factors in early childhood to delay timing of AR. Pediatrics 2014;134:e1354–e1361

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KEY WORDS: adiposity rebound, early childhood, adolescents, obesity, adiposity. BMI, ALSPAC

ABBREVIATIONS

ALSPAC—Avon Longitudinal Study of Parents and Children AR—adiposity rebound CIf—Children in Focus FMI—fat mass index

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Adiposity rebound (AR), the period in childhood in which BMI begins to increase from a nadir, historically occurred between 5 and 7 years. There is some evidence that early AR (defined as younger age at onset) predicts substantially increased risk of obesity in later life as defined by BMI and other proxies for fat mass (waist circumference and skinfold thickness). However, the literature on timing of AR and later risk of obesity is limited in many respects, consisting largely of older studies conducted before the pediatric obesity epidemic and/or of small studies with relatively short follow-up or with a limited range of outcomes (usually only proxies for obesity). Few studies have examined the influence of timing of AR on directly measured fat mass in adolescence or adulthood. A recent study by Ohlsson et al found that early age at AR (<5.4 years of age) was associated with higher BMI and fat mass (measured by dual-energy radiograph absorptiometry) in young men (n = 573). However, these findings are limited to men, timing of AR was determined from retrospective childhood data, and the analyses did not adjust for factors that may confound the relationship between AR timing and later fatness. Overall, no studies have provided a definitive test of the influence of timing of AR on obesity and fatness in adolescence or adulthood.

The primary aim of the current study was therefore to investigate associations between timing of AR in early childhood and measures of adiposity (BMI-for-age and directly measured fat mass) at age 15 years in a large cohort of contemporary children studied after the pediatric obesity epidemic was underway in the United Kingdom.

METHODS

We used data from the Avon Longitudinal Study of Parents and Children (ALSPAC; http://www.bris.ac.uk/alspac), which is an ongoing population-based study investigating a wide range of influences on health and development of children. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. ALSPAC recruited 14,541 pregnant women residing in Avon, United Kingdom, with expected dates of delivery April 1, 1991, to December 31, 1992. A total of 14,541 is the initial number of pregnancies for which the mother enrolled in the ALSPAC study and had either returned at least 1 questionnaire or attended a “Children in Focus” (CiF) clinic by July 19, 1999. Of these initial pregnancies, there was a total of 14,676 fetuses, resulting in 14,062 live births and 13,988 children who were alive at 1 year of age. A 10% sample of the ALSPAC cohort, known as the CiF group, attended clinics at the University of Bristol at various time intervals between 4 and 61 months of age.

Timing of AR in Childhood (Exposure)

Timing of AR was determined by using the “gold standard” method, which involved visual inspection of individual childhood data and the analyses did not adjust for factors that may confound the relationship between AR timing and later fatness. Overall, no studies have provided a definitive test of the influence of timing of AR on obesity and fatness in adolescence or adulthood.

Outcome Measures at 15 Years

Two indices of adiposity were used as outcome measures: BMI-for-age and fat mass index (FMI). A high BMI-for-age has high sensitivity and very high specificity as a means of identifying individuals with excessive fat mass. Fat mass is a more direct measure of adiposity that provides greater sensitivity and power and was measured by using a Lunar Prodigy dual-energy radiograph.
absorptiometry scanner (GE Medical Systems, UK), as described previously. FMI was calculated as fat mass (kg)/height (m²). Potential Confounders

A number of potential confounders were included, as follows: child age at the 15-year clinic, gender, parity, gestation, birth weight, socioeconomic position on the basis of maternal education (none/Certificate of Secondary Education to university degree or above) and household social class (I [professional/managerial] to V [unskilled manual workers] as classified by the 1991 UK Office of Population Census and Surveys, having at least 1 obese parent (on the basis of maternal and paternal self-reported BMI prepregnancy), maternal smoking in pregnancy (on the basis of questionnaire responses from all 3 trimesters), and pubertal status (1 [least advanced] to 5 [most advanced] on the basis of Tanner pubic hair development for males and most advanced stage for pubic hair and breast development for females assessed at the 15-year clinic. Full details of how these variables were assessed are provided in the Supplemental Information.

Statistical Power

Power was fixed by the size of the subsample and so no formal power calculation was carried out. However, the sample size available at follow-up is 1 of the largest studies to date on the long-term outcome of timing of AR. Previous studies have found associations between timing of AR and obesity in smaller samples, in part because of the strength of the associations between timing of AR and later obesity. Statistical Analyses

Means and SDs were calculated for continuous variables that were approximately normally distributed, medians and interquartile ranges for skewed variables, and proportions for categorical variables. Adiposity measures at 15 years (BMI z score, fat mass [kg], FMI, percentage of body fat, and weight status) were described by AR category. BMI and FMI at 15 years were treated as continuous variables, which were logged because of their skewed distribution, and further analysis by using multivariable linear regression (described below) was based on standardized residuals of log BMI and log FMI to allow comparison of regression coefficients across outcome measures. From this point onward we refer to standardized residuals of log BMI and log FMI as BMI and FMI.

Modeling Strategy

Associations between timing of AR (exposure variable) and outcomes (on the basis of measures of BMI and FMI at 15 years) were tested by using multivariable linear regression models. We formally tested the association between timing of AR and outcomes for an interaction with gender. There were no interactions (P > .3 for BMI and FMI); therefore, all models were fitted for boys and girls together. A series of models were used to explore the extent of the attenuation of the association between timing of AR and outcomes. Model 1 (minimally adjusted) was adjusted for age at the 15-year clinic and gender. Model 2 adjusted for variables in model 1 plus parity, maternal education, household social class, at least 1 obese parent, any smoking in pregnancy, gestational age, and birth weight. The final model (model 3) adjusted for the variables in model 2 plus pubertal status at age 15. Pubertal stage was added separately because this variable had a large amount of missing data.

The impact of missing data was assessed by comparing character-istics between participants who provided BMI data at the age 15-year clinic and those who did not attend the clinic or those who attended but did not provide BMI data. To assess whether any change in regression coefficients in models 2 and 3 was due to the confounders rather than due to bias relating to missing data, model 1 (minimally adjusted) was repeated restricting to only those participants who had complete data in model 3 (complete confounder information). SPSS version 20 (IBM SPSS Statistics, IBM Corporation, Armonk, NY) was used for all analyses.

RESULTS

The timing of AR was derived for 907 children; 6.9% (n = 63) of children had experienced “very early AR” (by 43 months), 20.3% (n = 184) had experienced “early AR” (between 44 and 61 months), and 72.8% (n = 660) had rebounded later (>61 months). The majority of characteristics were similar across AR categories (see Table 1). BMI z scores were similar across AR categories at 37 months (ie, before the rebound had occurred) but were higher in the very early and early AR categories at 61 months and 7 years, respectively (ie, after rebound had occurred in these categories; see Fig 1). All adiposity measures at 15 years (ie, BMI z score, fat mass [kg], FMI, percentage body fat, and weight status) were substantially higher in those with very early AR than in those with early AR and later AR (see Table 2 and Fig 1).

Of the 907 children for whom AR was derived, 546 (60.2%) had BMI outcome data at age 15 and 520 (57.3%) had FMI outcome data. See Supplemental Tables 4 and 5 for comparison of characteristics between participants who provided BMI data at the 15-year research clinic and those who did not provide BMI data at 15 years.
Associations Between Timing of AR and Adiposity at Age 15 Years

Table 3 shows the associations between timing of AR and adiposity outcomes (on the basis of measures of BMI and FMI) at 15 years. In all models (models 1–3) BMI and FMI at age 15 were higher in children with very early and early AR compared with those with later AR (Table 3). In the minimally adjusted model, children who had experienced very early AR (by 43 months) had an almost 1-SD increase in BMI and FMI at age 15 when compared with those who experienced later AR (>61 months).

When all potential confounders were taken into account, this effect attenuated to two-thirds of a SD. Children who had experienced early AR (between 44 and 61 months) had an increase in the SD of one-third in BMI and FMI at age 15 compared with those who experienced later AR (>61 months) in the minimally adjusted model, and adjustment for all potential confounders did not change the regression coefficients. Further analysis revealed that the attenuation of the regression coefficients in the very early AR group were mainly due to having at least 1 obese parent, which was more prevalent in the very early group (28%) compared with the later group (13.9%).

We repeated model 1 in those with complete data on all confounders and the regression coefficients remained similar (see Supplemental Table 6).

**DISCUSSION**

In the current study, we found a strong “dose response” association between timing of AR and both adiposity outcomes at age 15 years, independent of a range of confounders, with similar magnitudes of association across BMI and FMI outcomes.
We observed large differences in adiposity outcomes at 15 years across AR categories, particularly between the very early group and the later AR group. BMI and FMI at 15 years were two-thirds of a SD higher for children with very early AR (by 3.5 years of age) compared with those with later AR (>5 years of age). Table 2 shows that mean BMI z score (externally derived) at 15 years was 1.27 (SD: 1.04) in the very early AR group (a BMI z score ≥1.33 defines clinical overweight in the United Kingdom) compared with 0.26 (SD: 1.07) in the later AR group. Fat mass and percentage of body fat were substantially higher (by >7 kg and 10%, respectively) among children with very early AR compared with those with later AR. The prevalence of overweight and obesity in adolescence was 58% in the very early AR group and 21% in the later AR group.

An interesting finding was the higher prevalence of parental obesity in the very early AR group (28%) compared with the early (19%) and later (14%) AR groups, suggesting that young children of obese parents are at greater risk of earlier AR and therefore could be targets for preventive interventions. A detailed discussion of the early-life environmental factors associated with timing of AR is beyond the scope of the current study but has been discussed elsewhere.\textsuperscript{2,5,24,25}

A number of generally smaller and/or older studies have suggested that earlier AR increases obesity risk, as reviewed by Taylor et al.\textsuperscript{2} A recent study by Koyama et al\textsuperscript{6} found that an earlier AR (4 years of age) was associated with a higher BMI and poorer cardiometabolic health at 12 years; however, the sample size was smaller than in the current study; BMI was measured at 12 years, whereas outcomes measured later in adolescence (as in the current study) are more likely to predict outcomes in adult life\textsuperscript{26}; and the influence of early AR on directly measured

![Figure 1](image-url) Mean BMI z score by timing of AR across childhood and adolescence. BMI z scores were calculated by using the UK 1990 population reference data.\textsuperscript{12}

<table>
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<th>Comparison of Adiposity Measures at the 15-Year Research Clinic Across AR Categories</th>
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\textsuperscript{a} BMI z scores calculated by using the UK 1990 population reference data.\textsuperscript{12}

\textsuperscript{b} Medians and IQRs are displayed for skewed variables.

\textsuperscript{c} FMI calculated as fat mass in kg/height in m\textsuperscript{2}.

\textsuperscript{d} Percentage body fat calculated as fat mass in kg/measured weight in kg.

\textsuperscript{e} The outcome measures on which the associations between timing of AR and outcomes were conducted.

\textsuperscript{f} Overweight defined as BMI z score ≥1.04 and <1.64, equivalent to 85th–94th percentiles; obese defined as BMI z score ≥1.64, equivalent to ≥95th percentile.
fat mass was not explored. Only 1 study\textsuperscript{10} to date has explored the association between timing of AR and direct assessment of adiposity in adulthood and reported results consistent with our own. This study\textsuperscript{10} by Ohlsson et al found that age at AR was a strong predictor of young adult men BMI, fat mass, and percentage body fat, and the associations were maintained after adjustment for BMI at AR. Subjects with early age at AR (<5.4 years of age) had higher young adult BMI (+34%) and fat mass (+34%) compared with those with later age at AR. However, this study had several limitations, as discussed previously. Thus, the current study was the first to our knowledge to test for associations between timing of AR and 2 measures of adiposity in adolescence including direct assessment of fat mass, adjusting for a wide range of potential confounders and using a relatively large contemporary sample in whom timing of AR had been established with the use of prospective childhood growth measures made in a research clinic and visual inspection of BMI-for-age plots, the “gold standard” for defining timing of AR.\textsuperscript{1,12,16}

Early AR reflects excessive positive energy balance in early life\textsuperscript{2,5,24,25}; therefore, influencing health behaviors (eg, toddlers’ lifestyles) before the AR has occurred may reduce the risk of early AR and its sequelae. Our findings, together with evidence indicating that the AR occurs earlier now than in the past.\textsuperscript{2,5,25,27,28} provide a justification to policy makers and clinical practitioners to consider (1) more populationwide public health interventions in early childhood to delay timing of AR, (2) increased growth monitoring in early childhood to identify children at risk of early AR (eg, those with obese parents) or those who experienced early AR and are therefore in greatest need of preventive efforts, and (3) more clinical interventions directed at these “high risk” children and their families.

Studies\textsuperscript{28,30} have criticized the AR on the grounds that an early AR predicts later high fatness because it identifies children with a high BMI-for-age, and therefore BMI at or before the AR may be better predictors of later outcomes. However, these studies\textsuperscript{28,30} examined the association between age at AR and the BMI pattern of centile curves constructed cross-sectionally, which led to high BMIs at all ages on the high centiles, whereas studies\textsuperscript{5,10,24} using individual longitudinal assessment have shown that many children who rebound early have a normal or low BMI at or before the rebound followed by an increased BMI after the rebound. These findings are supported by our data (see Table 1 and Fig 1), which show that mean BMI z scores were within the healthy range and similar across AR categories at 37 months (ie, before the rebound had occurred) but were significantly higher in the very early and early AR categories after the rebound had occurred at 61 months and 7 years, respectively, in these children. Thus, this evidence highlights the importance of BMI trajectories in early childhood rather than focusing on a single measure of BMI at or before the AR. Concerns have also been raised whether an early AR reflects increased fat or lean mass and whether the increase in BMI observed in adolescents and adults who have experienced early rebound is due to an increase in body fat.\textsuperscript{26} Evidence\textsuperscript{1,5,8,24,31–34} indicates that early AR is attributable to an increase in body fatness (rather than alterations in lean mass) arising from “obesogenic” lifestyles in early life, and our results confirm that the high BMI observed in later life is due to increased fat mass.

The current study had some weaknesses. Loss to follow-up is inevitable in all cohort studies. Of the 907 children in whom AR was derived, 60.2% had BMI outcome data at age 15 and 57.3% had outcome data for FMI. Although slight differences in some maternal and social characteristics were observed between participants who provided BMI data at the 15-year research clinic and those who did not (see Supplemental Information), BMI z scores in childhood and pubertal status at the 15-year follow-up were similar between groups and so it seems likely that loss to follow-up at 15 years did not have a marked impact on study findings. In addition, restricting the minimally adjusted analyses to those with complete data on all confounders produced similar regression coefficients (see Supplemental Information).
Information), again suggesting that missing data did not bias results. In the current study, follow-up was undertaken at age 15 rather than in adult life, but adiposity outcomes at age 15 would be strongly predictive of outcomes in adult life.26 Furthermore, most participants were in pubertal stages 4 and 5 by the time of the 15-year research clinic and pubertal status was similar across the AR categories and did not alter associations between timing of AR and outcomes. Although the association between timing of AR and outcomes was only slighted attenuated after adjustment for a number of potential confounding factors, other potential confounders may have been missed (eg, gestational diabetes and more recent measures of socioeconomic position). Finally, generalizability of the current study findings to other ethnic groups and populations from different settings should also be considered with caution because the influence of timing of AR on later obesity might be different.

CONCLUSIONS

The current study suggests that early AR is strongly associated with increased BMI and fatness in adolescence. If modifiable, the timing of AR may be a novel target for future population-based preventive interventions by targeting modifiable factors in early life to delay timing of AR. Furthermore, routine identification of the timing of AR could identify young children at increased risk of obesity in later life and who are therefore in greatest need of preventive interventions.

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