



## Prospective associations between dietary patterns, screen and outdoor play times at 2 years and age at adiposity rebound: The EDEN mother-child cohort

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### ARTICLE INFO

#### Keywords:

Adiposity rebound  
Diet  
Physical activity  
Screen time  
Preschoolers

### ABSTRACT

Although an early adiposity rebound (AR) is an established risk factor for later obesity, little is known regarding its determinants, especially modifiable ones. Using data from the French EDEN mother-child cohort (1903 children born in 2003–2006), we aimed to examine the association between diet and activity-related behaviors at 2 years of age and the timing of the AR. Two-year-old children ( $n = 1138$ ) with parent-reported data on their foods/drinks intake, TV/DVD watching time, outdoor playtime, and with an estimated (via growth modelling) age at AR were included in the present study. Two dietary patterns, labelled 'Nutrient-dense foods' and 'Processed and fast foods', were identified in a previous study. Multivariable linear and logistic regression models were used to assess the association between dietary patterns and activity-related behaviors and, respectively, the age at AR (continuous) and the likelihood of having a very early AR (before 3.6 years for girls and 3.8 years for boys, i.e., below the 10th percentile of sex-specific distribution). A higher score on the 'Processed and fast foods' dietary pattern was associated with a higher likelihood of having a very early AR (OR = 1.23; 95% CI: 1.00 to 1.50). No significant association was observed between the 'Nutrient-dense foods' dietary pattern, TV/DVD watching and outdoor playing times and the timing of the AR. This finding emphasizes the importance of reducing nutrient-dense and processed foods from the early years of life, and provides further support for early interventions aimed at helping parents establish healthy eating habits for their growing child from the complementary period.

### 1. Introduction

Typically, body mass index (BMI) increases rapidly during the first year of life, then decreases and reaches a nadir around 6 years of age, before increasing again until the end of growth. This second rise is called the adiposity rebound (AR) (Rolland-Cachera et al., 1984). An early age of occurrence of the AR (before 5 years) is an established risk factor for obesity in adolescence and adulthood (Whitaker et al., 1998; Rolland-Cachera et al., 2005), as well as for impaired glucose tolerance and

type 2 diabetes mellitus as an adult (Péneau et al., 2016). The hypothesized mechanisms underlying these observed associations refer to the theory of the developmental origins of health and diseases (DOHaD) and the concept of 'early life programming' (Rolland-Cachera et al., 2005; Rolland-Cachera et al., 2016). In particular, the 'first 1,000 days' - from conception to 24 months - have been considered as a critical period of development during which environmental factors such as nutritional exposures may operate, modifying BMI trajectories, altering body composition and programming later metabolic diseases such as obesity,

*Abbreviations:* AR, Adiposity Rebound; EBRBs, Energy Balance-Related Behaviors; BMI, Body Mass Index.

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<https://doi.org/10.1016/j.pmedr.2021.101666>

Received 11 July 2021; Received in revised form 8 December 2021; Accepted 12 December 2021

Available online 13 December 2021

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with epigenetic modifications likely to be involved (Koletzko et al., 2014; Godfrey et al., 2010). However, the most relevant critical periods of early life with regard to the timing of the AR and specific mechanisms underlying its association with later obesity risk remain to be elucidated (Rolland-Cachera and Cole, 2019; Dietz, 1997).

At the individual level, regular monitoring of children's BMI growth curves is recommended to identify children with an early AR as soon as possible, so that measures aimed at preventing obesity can be rapidly instigated; a strategy that should be particularly useful for children with a very early rebound (i.e., before 3–4 years) who are at highest risk of adverse health consequences (Rolland-Cachera et al., 2005; Taylor et al., 2005). Knowledge of the determinants of an early AR, in particular modifiable ones, is also important to prevent the occurrence of early rebounds, which might increase the overall effectiveness of childhood obesity prevention efforts. However, the environmental and behavioral factors that influence the timing of the AR remain unclear (Taylor et al., 2005). Epidemiological studies have consistently reported that children who have at least one obese parent are more likely to have an earlier AR (Whitaker et al., 1998; Péneau et al., 2016; Dorosty and Emmett, 2000; Ip et al., 2017). These findings suggest that heritability may be important, and recent studies have confirmed that genetic susceptibility to adult obesity plays a role in the timing of the AR (Meyre et al., 2004; Couto Alves et al., 2019; Cissé et al., 2021). Parental BMI is also likely to reflect a shared familial environment that influences the early establishment of behaviors influencing the child's energy balance – that is diet and activity-related behaviors (physical activity and sedentary behavior) (Dietz, 1997). However, only a few prospective studies have analyzed the association between 'energy balance-related behaviors' (EBRBs) in the early years of life and the age at AR, and their results are inconclusive (Dorosty and Emmett, 2000; Ip et al., 2017; Taylor et al., 2004; Rolland-Cachera et al., 1995; Günther et al., 2006; Moore et al., 2003; Taylor et al., 2011). Several methodological shortcomings may explain such differences, including insufficient follow-up length to reliably estimate the age at AR, differences in the age of behavioral assessments, variability in EBRBs' definitions and measurements, and small sample size (Taylor et al., 2005). The majority of studies focused on macronutrients intake, in particular protein intake in children younger than 2 years at the time of exposure, with no or insufficient consideration of behaviors on the other side of the energy balance (Dorosty and Emmett, 2000; Taylor et al., 2004; Rolland-Cachera et al., 1995; Günther et al., 2006; Moore et al., 2003; Taylor et al., 2011). Empirically-derived dietary patterns are considered relevant not only for assessing the association between total diet and health indicators, but also because they can easily be translated into dietary recommendations (Ambrosini, 2014; Emmett and Jones, 2015). However, to the best of our knowledge, no study has analyzed the association between dietary patterns and age at AR. Early childhood is important because it is when particular dietary habits and sedentary behavior patterns become established (Reilly, 2008). However, few studies examined simultaneously screen-related sedentary behaviors, physical activity and diet in early childhood with regard to the timing of the AR (Ip et al., 2017).

We aimed to analyze the independent associations of TV/DVD watching time, outdoor playtime, and dietary patterns at 2 years (identified in a previous analysis<sup>24</sup>) with the age at AR (continuous trait) and a very early age at AR (below the 10th percentile of sex-specific distributions), respectively. We hypothesized that higher outdoor playtime and higher adherence to a healthy dietary pattern (labelled 'Nutrient-dense foods') would favor a later age at AR, whereas higher TV/DVD watching time and higher adherence to a suboptimal dietary pattern characterized by higher intakes of energy-dense and nutrient-poor food items (labelled 'Processed and fast foods') would favor an earlier age at AR.

## 2. Methods

### 2.1. Subjects

The EDEN mother–child study is a prospective cohort designed to assess pre- and postnatal determinants of child health and development (Heude et al., 2016). In brief, 2002 pregnant women (<24-weeks' gestation) aged 18–44 years were recruited between 2003 and 2006 in two university hospitals located in Nancy and Poitiers, France. Exclusion criteria were multiple pregnancies, history of diabetes, illiteracy and any plan to move out of the region within the next 3 years. Approval for the study was obtained from the relevant ethics committee (ID 0270 of 12 December 2012) and the French Data Protection Authority (CNIL, ID 902,267 of 12 December 2012). Written consents were obtained from both parents.

A total of 1138 children with data on diet and activity-related behaviors at 2 years and an estimated age at AR were included in the present study. Details of children's selection are presented in Fig. 1.

### 2.2. Age at adiposity rebound

BMI was assessed using weight and height measurements collected from the child's health-care booklet and at the clinical examinations undertaken at the university clinics at ages 1, 3 and 5 years. The age of occurrence of the AR was estimated via growth modelling, as described in details elsewhere (Cissé et al., 2021). Briefly, children had on average 10 BMI values available (interquartile range 6–14) from age 18 months to 13 years (children with <3 BMI measurements were excluded). Individual growth curves were obtained by using mixed-effects cubic models separately for girls and boys. The method for growth modelling of age at AR was inspired by the one previously described by Sovio et al. (2011). We considered age at AR both as a continuous variable (in days) and a dichotomic variable corresponding to a very early age at adiposity rebound (yes/no). For this latter variable, the threshold was set at the 10th percentile of the sex-specific distributions, i.e., 3.8 years in boys and 3.6 years in girls. These age thresholds were deemed relevant in clinical practice for early detection of children at higher risk of developing overweight-obesity, and is also consistent with the ones used in previous studies (Dorosty and Emmett, 2000; Ip et al., 2017; Rolland-Cachera et al., 1995).

### 2.3. Energy balanced-related behaviors

#### 2.3.1. Sedentary behavior and physical activity

Postal questionnaires were sent to parents and completed, primarily by mothers, when the children were aged 2 years (mean 2.03 years, SD 0.09). As time spent in both indoor and outdoor leisure activities is likely to differ according to contextual factors, such as the day of the week (Brooke et al., 2014; Berglind and Tynelius, 2018), average time spent watching TV/DVD and playing outdoor were assessed from the responses to three questions regarding the time (in min per day) that the child spent in both activities on a typical weekday (excluding Wednesday), Wednesday (which was an off-school day at the time of the study) and weekend days, and described in detail elsewhere (Saldanha-Gomes et al., 2017). TV/DVD watching time was split into three categories: ≤15 min per day, >15 min per day to < 1 h per day and ≥1h per day, which corresponded to tertiles in our population. There is evidence of seasonal variations in outdoor physical activity, especially for the time children spend playing outdoors (Carson and Spence, 2010). Hence, outdoor playtime was categorized into season-specific tertiles (low, intermediate and high).

#### 2.3.2. Dietary patterns

Children dietary intake at the age of 2 years was collected using a food frequency questionnaire included in the postal questionnaire and described in detail elsewhere (Lioret et al., 2015). A previous analysis of

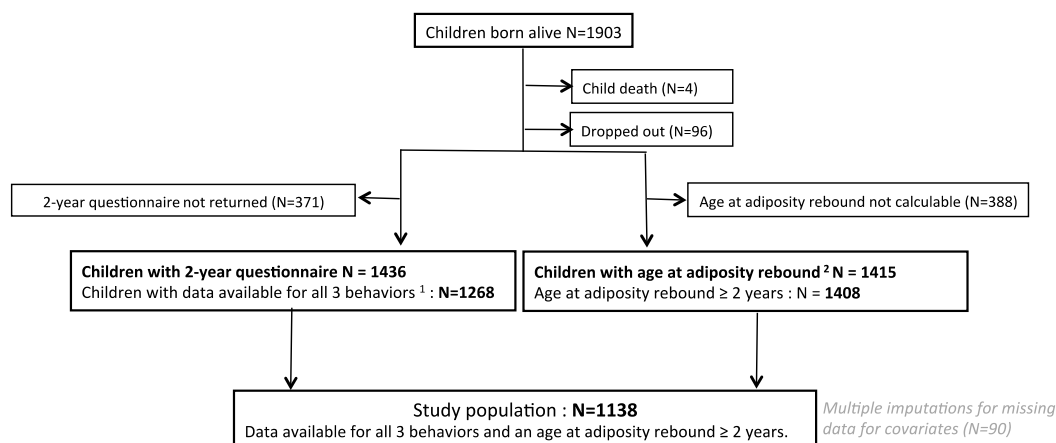


Fig. 1. Flow diagram for selection of children. 1 (Saldanha-Gomes et al., 2017). 2 (Cissé et al., 2021)

these data (Lioret et al., 2015), using principal component analysis, identified two dietary patterns, which accounted for 19.8% of the explained variance. The first pattern, labeled 'Processed and fast foods', was positively correlated with intake of French fries, processed meat, carbonated soft drinks, crisps, biscuits, pizzas, fruit juices, dairy puddings and ice cream, legumes and bread (by descending order of factor loadings) and inversely correlated with the intake of cooked vegetables. The second pattern, labeled 'Nutrient-dense foods', closer to dietary guidelines, was mainly characterized by high intake of cooked vegetables, rice, fruits, raw vegetables, low fat fish, potatoes, ham, compotes, meat and bread. Scores for each pattern were calculated at the individual level by summing the observed standardized frequencies of consumption of food groups, weighted according to the principal component analysis loadings. The overall measure of sampling adequacy from the Kaiser-Meyer-Olkin was 0.71. The Bartlett's test of Sphericity confirmed the correlation matrix of the 27 dietary items included in the PCA was statistically different ( $p < 0.001$ ) from an identity matrix that contained zero correlations. The dataset was therefore deemed suitable for PCA as it met the assumptions of these tests.

#### 2.4. Covariates

We considered variables that have been found to be associated with the age at adiposity rebound and at least one EBRB. Maternal and paternal BMIs were considered as 2 continuous variables from measured or, if unavailable, reported parental weight and height. Maternal education, measured at inclusion in the cohort, was used as a proxy of socioeconomic position and defined by the highest diploma obtained: less than high school, high school diploma, 2-year university degree and  $\geq 3$ -year university degree. Birth weight (in grams) and maternal age at the child's birth were considered as continuous variables.

#### 2.5. Statistical analyses

The study population was compared with the EDEN population not selected for this study (i.e., families enrolled in the cohort with live born children for whom any of the EBRBs or the age at AR were not available) for infant birth characteristics and parental sociodemographic characteristics. Two-sided  $\chi^2$  and Student *t* tests were used for categorical and continuous variables, respectively. We studied the associations between EBRBs and age at AR considered as a continuous or dichotomic variable with multivariable sex-adjusted linear and logistic regression analyses, respectively. These two sets of analyses were conducted in three steps. First, TV/DVD watching time, outdoor playtime and dietary patterns, were each included in separate models. Then, the three EBRBs were included simultaneously in a single model, named combined model

hereafter. Finally, this model was further adjusted for parental BMI, maternal age, maternal education, and birth weight, referred as the fully-adjusted model; we checked the absence of multicollinearity, assessed with the variance inflation factor criterion ( $VIF < 5$ ) (Rogerson, 2001).

Analyses were conducted with multiple imputations to deal with missing data for maternal BMI ( $N = 21$ ) and paternal BMI ( $n = 74$ ). Missingness of each variable was  $< 6.5\%$  (1.8% for maternal BMI; 6.5% for paternal BMI; and 0% for all other variables of interest). On the assumption that data were missing at random, 10 independent datasets were generated with the fully conditional specification method (MI procedure, FCS statement, NIMPUTE option; SAS software ("SAS [computer program]," 2013)) and pooled effect estimates were then calculated (MIANALYSE procedure; SAS software ("SAS [computer program]," 2013)). The imputation models included all variables of interest after they were ranked in ascending order of missing data. Continuous variables were imputed with predictive mean matching.

Statistical analysis was performed with SAS software ("SAS [computer program]," 2013) and the level of significance set at  $P < 0.05$ .

### 3. Results and discussion

The characteristics of the study population are summarized in Table 1.

Compared with the children included in the EDEN cohort but not in the present study ( $n = 765$ ), the 1138 children comprising the study population were born to an older mother (28.8 (SD 5.1) vs 30.0 (SD 4.7) years,  $P < 10^{-4}$ ), with a higher education level (20% with education  $\geq 3$ -year university degree vs. 39%,  $P < 10^{-4}$ ), and a lower pre-pregnancy BMI (23.6 (SD 0.2) vs. 23.0 (SD 0.2)  $\text{kg/m}^2$ ,  $P = 0.008$ ). Selected children also had a higher birth weight (3249 (SD 530) vs. 3298 (SD 499) g,  $P = 0.04$ ).

The associations between EBRBs and the likelihood of having a very early AR – that is an adiposity rebound occurring between 2 years of age and, respectively, 3.6 years for girls and 3.8 years for boys - are shown in Table 2. In the separate models (bivariable analyses), only the 'Processed and fast foods' dietary pattern was associated with increased odds of having a very early rebound. The magnitude of the regression coefficient decreased slightly with successive adjustments, but the association remained significant in the fully-adjusted model: each point increase (equivalent to + 1SD) on the 'Processed and fast foods' dietary score was associated with a 23% increase in the odds of having a very early adiposity rebound (95% CI: 1.00 to 1.50). No other EBRB predicted the occurrence of a very early AR.

The associations between EBRBs at 2 years and the age at AR considered as a continuous trait are shown in Table 3. In the separate models (bivariable analyses), the 'Processed and fast foods' dietary

**Table 1**

Characteristics of the study population (values are % yes or means (SD), N = 1138). The EDEN mother–child cohort.

Characteristics of study population	N (%) or mean (sd)
<b>Parental characteristics</b>	
<b>Maternal education</b>	
Did not complete high school	18.9
High school diploma	17.5
2-Year university degree	24.2
≥ 3-Year university Degree	39.4
Maternal age at Delivery (years)	30.0 (4.7)
Maternal BMI (Kg m <sup>-2</sup> )	23.0 (0.02)
Paternal BMI (Kg m <sup>-2</sup> )	25.0 (0.02)
<b>Child characteristics</b>	
Birth weight (g)	3298 (499)
<b>TV/DVD watching time at the age of 2 years</b>	
≤15 min per day	33.7
>15 To < 60 min per day	31.6
≥60 min per day	34.7
<b>Outdoor play time at the age of 2 years<sup>a</sup></b>	
Low	33.6
Medium	33.3
High	33.1
<b>Dietary pattern scores</b>	
'Processed and fast foods'	−0.04 (0.95)
'Nutrient-dense foods'	0.05 (0.96)
BMI at the age of 2 years (kg/m <sup>-2</sup> ) <sup>b</sup>	16.1 (1.1)
Prevalence of overweight (including obesity) at the age of 2 years <sup>c</sup>	3.3
Age at adiposity Rebound (year)	5.5 (1.4)

Abbreviations: SD Standard Deviation. BMI Body Mass Index. IOTF International Obesity Task Force.

<sup>a</sup> Ranges for outdoor play time categories. Low (Tertile 1): spring (9 min to 1 h 23 min), summer (23 min to 1 h 58 min), autumn (4 min to 1 h 12 min) and winter (0 min to 50 min). Intermediate (Tertile 2): spring (1 h 24 min to 2 h 15 min), summer (1 h 59 min to 2 h 55 min), autumn (1 h 13 min to 1 h 58 min) and winter (51 min to 1 h 18 min). High (Tertile 3): spring (2 h 16 min to 6 h), summer (2 h 56 min to 6 h 34 min), autumn (1 h 59 min to 6 h) and winter (1 h 19 min to 4 h 09 min).

<sup>b</sup> Predicted BMI based on Jenness' nonlinear model (Carles et al., 2016).

<sup>c</sup> IOTF cutoff.

pattern score and higher TV/DVD watching time were negatively associated with age at AR. The magnitude of all the regression coefficients decreased after successive adjustments for several child and parental characteristics, including parental BMI and maternal educational attainment and, in the fully-adjusted model, no association remained.

The 'Processed and fast foods' pattern is reflective of an energy-dense and nutrient-poor diet, likely to favor a positive energy balance. Therefore, a high score on this pattern may promote a faster weight gain and subsequently contribute to advance the age of occurrence of the AR. This is all the more plausible since we have previously shown that this dietary pattern tracks from 2 to 5 years of age (Lioret et al., 2015), and an earlier AR is likely to partly result from continued exposure over time to less healthy foods, along with the cumulative adverse effect of a positive energy balance. Other studies showed that distinctive empirically-derived dietary patterns emerge during the complementary period, and then track from infancy into mid- and late-childhood, with tracking being stronger for the "least healthy" patterns (i.e., the energy-dense type of pattern) (Smithers et al., 2011; Luque et al., 2018; Emmett et al., 2015).

A few studies (Lioret et al., 2015; Emmett, 2016; Abraham et al., 2012), including our own previous analyses of the EDEN data<sup>24</sup> also found that feeding practices during infancy are associated with childhood dietary patterns, an important finding considering that dietary patterns track across childhood and energy-dense type of patterns have been associated with overweight and obesity in late childhood and adolescence (Ambrosini, 2014; Emmett et al., 2015; Ambrosini et al., 2015). In particular (Loret et al., 2015), we showed that a multi-time

**Table 2**

Associations between EBRBs at the age of 2 years and a very early age at adiposity rebound. The EDEN mother–child cohort.

Energy Balance Related behaviors	Very early age at adiposity rebound (N=113/1025) <sup>a</sup> Logistic regression Odds Ratio (95% CI)		
	Separate models <sup>b</sup>	Combined model <sup>c</sup>	Fully-adjusted model <sup>d</sup>
<b>TV/DVD watching time (min per day)</b>			
≤15	Ref.	Ref.	Ref.
>15–<60	1.30 (0.79, 2.13)	1.27 (0.77, 2.09)	1.08 (0.81, 1.44)
≥60	1.47 (0.91, 2.38)	1.33 (0.81, 2.17)	0.95 (0.71, 1.27)
P-value	0.28	0.49	0.86
<b>Outdoor play time<sup>d</sup></b>			
Low	Ref.	Ref.	Ref.
Medium	0.77 (0.47, 1.26)	0.73 (0.45, 1.20)	0.84 (0.62, 1.12)
High	1.00 (0.63, 1.59)	0.92 (0.57, 1.47)	1.00 (0.75, 1.33)
P-value	0.49	0.45	0.38
<b>Dietary pattern scores</b>			
'Processed and fast foods'	1.30 (1.08, 1.57)	1.28 (1.06, 1.56)	1.23 (1.00, 1.50)
P-value	0.006	0.01	0.05
'Nutrient-dense foods'	0.93 (0.76, 1.13)	0.93 (0.76, 1.14)	0.93 (0.76, 1.15)
P-value	0.45	0.49	0.51

Abbreviation: EBRBs Energy Balance Related Behaviors.

<sup>a</sup> age at adiposity rebound occurring before 3.8 years in boys and 3.6 years in girls. <sup>b</sup> TV/DVD watching time, outdoor play time and dietary patterns were included in three separate models with adjustment for sex. <sup>c</sup> The three EBRBs were included simultaneously in the same model with adjustment for sex. <sup>d</sup> Combined model further adjusted for parental BMI, maternal age at child's birth, maternal education and birth weight. <sup>e</sup> Ranges for outdoor play time categories. Low (Tertile 1): spring (9 min to 1 h 23 min), summer (23 min to 1 h 58 min), autumn (4 min to 1 h 12 min) and winter (0 min to 50 min). Intermediate (Tertile 2): spring (1 h 24 min to 2 h 15 min), summer (1 h 59 min to 2 h 55 min), autumn (1 h 13 min to 1 h 58 min) and winter (51 min to 1 h 18 min). High (Tertile 3): spring (2 h 16 min to 6 h), summer (2 h 56 min to 6 h 34 min), autumn (1 h 59 min to 6 h) and winter (1 h 19 min to 4 h 09 min).

point dietary pattern corresponding to continued exposure to processed and fast foods between 2 and 5 years of age was associated with suboptimal feeding patterns over the first year of life (PCA-derived patterns based on breast-feeding duration, age at introduction of 14 complementary foods and type of food used at 1 year of age, i.e., pre-packaged baby food, adult food, or homemade food (Betoko et al., 2013)). More specifically, higher adherence to the longitudinal (2–5 years) 'Processed and fast foods' pattern was inversely associated with a first-year feeding pattern characterized by longer breastfeeding, later main meal food introduction and use of home-made foods – that is the pattern closest to infant feeding guidelines – as well as with a pattern characterized by later dairy product introduction and use of ready-prepared baby foods; whereas it was positively associated with a pattern characterized by use of ready-prepared adult foods – that is a pattern suggestive of a less age-specific diet for the infant. Altogether, these findings lead to the idea that continued suboptimal feeding practices and food choices from infancy to early childhood may contribute to faster weight gain and increase the risk of later obesity, in part through advancing the age of occurrence of the AR.

Our results are difficult to compare with those of previous studies since none of them examined the association between early dietary patterns and the timing of the AR. A recent study (Ip et al., 2017), conducted by Ip et al in a sample of 248 children aged 2.5 to 3.5 years at baseline and living in Latino farmworker families in North Carolina (a population group supposedly at high risk of obesity), found that increased energy intake was associated with an earlier AR in multivariate longitudinal analysis. Older studies have focused on macronutrients

**Table 3**

Associations between EBRBs at the age of 2 years and age at adiposity rebound (in days). The EDEN mother-child cohort.

Energy Balance Related behaviors	Age at adiposity rebound in days (N=1138) Linear regression beta coefficients (95% CI)		
	Separate models <sup>a</sup>	Combined model <sup>b</sup>	Fully-adjusted model <sup>c</sup>
TV/DVD watching time			
≤15 min per day	Ref.	Ref.	Ref.
>15 to <60 min per day	-1 (-72, 70)	5 (-66, 76)	33 (-37, 103)
≥60 min per day	-94 (-164, -25)	-72 (-144, 1)	-15 (-87, 57)
P-value	0.01	0.06	0.40
Outdoor play time <sup>d</sup>			
Low	Ref.	Ref.	Ref.
Medium	-35 (-106, 36)	-27 (-98, 44)	-25 (-95, 44)
High	-86 (-157, -15)	0.16	0.22
P-value	0.06		
Dietary pattern scores			
'Processed and fast foods'	-45 (-75, -14)	-34 (-66, -3)	-24 (-55, 8)
P-value	0.004	0.03	0.14
'Nutrient-dense foods'	14 (-16, 44)	13 (-17, 43)	12 (-18, 42)
P-value	0.37	0.41	0.43

Abbreviation: EBRBs Energy Balance Related Behaviors

<sup>a</sup> TV/DVD watching time, outdoor play and dietary patterns were included in three separate models adjusted by sex. <sup>b</sup> The three EBRBs were included simultaneously in the same model adjusted by sex. <sup>c</sup> Combined model further adjusted for parental BMI, maternal age at child's birth, maternal education and birth weight. <sup>d</sup> Ranges for outdoor play time categories. Low (Tertile 1): spring (9 min to 1 h 23 min), summer (23 min to 1 h 58 min), autumn (4 min to 1 h 12 min) and winter (0 min to 50 min). Intermediate (Tertile 2): spring (1 h 24 min to 2 h 15 min), summer (1 h 59 min to 2 h 55 min), autumn (1 h 13 min to 1 h 58 min) and winter (51 min to 1 h 18 min). High (Tertile 3): spring (2 h 16 min to 6 h), summer (2 h 56 min to 6 h 34 min), autumn (1 h 59 min to 6 h) and winter (1 h 19 min to 4 h 09 min).

intake during infancy, with the primary aim to test the 'early protein hypothesis'. According to this hypothesis excessive protein intake in the early years of life stimulates the secretion of insulin and insulin-like growth factor I, which enhances early growth and adipogenic activity, thereby leading to a premature AR and an increased risk of later obesity (Rolland-Cachera et al., 2016). Results of these studies are inconsistent: while the earlier study<sup>17</sup> found that higher protein intake (expressed as % of energy) at 2 years was associated with an earlier age at AR (<5.5 years), two later studies<sup>11</sup> (Günther et al., 2006), with nutrient intake measured at different times between 8 and 24 months could not replicate this finding.

We found no indication that activity-related behaviors at 2 years are related to the timing of the AR. This may be explained by the fact that, unlike dietary patterns that are generally established by 2 years of age, the activity behaviors considered here develop largely after 2 years of age, as the child gains in mobility and becomes increasingly attracted and exposed to screens. Hence the duration of exposure to these activity behaviors may not have been long enough to show an effect on the timing of the AR, especially for the earlier outcome, i.e., the likelihood of having a very early AR (<3.8 years). The lack of association may also be explained by the fact that physical activity is particularly difficult to assess by questionnaire in young children, since activities at this age are essentially unstructured and tend to occur in short and sudden bursts (Cardon et al., 2011; Cliff et al., 2009). The few studies that examined the longitudinal association between objective measures (e.g., using accelerometers) of physical activity or sedentary time and the age at AR are mixed (Ip et al., 2017; Moore et al., 2003; Taylor et al., 2011). Two studies<sup>12</sup> (Taylor et al., 2011), of children aged around 3 years at baseline and followed for 2–4 years found no significant difference in

physical activity levels or total sedentary behavior time between early and later rebounders in multivariate longitudinal analysis. By contrast, in a subsample of children from the Framingham Children's Study around 4 years of age at baseline and followed for 8 years, Moore et al. showed that the most active children from ages 4 to 11 years, i.e., those in the highest tertile of average daily total physical activity at each time point, reached the lowest point in their BMI curve about one year later than less active children (around 6 years versus 5 years of age) (Moore et al., 2003). They also had consistently smaller gains in BMI, triceps, and sum of five skinfolds throughout childhood.

It is worth to note that the 'Processed and fast foods' dietary pattern, like the activity-related behaviors, was not significantly associated with the age at the AR (continuous outcome), that occurred at 5.5 years on average in the study sample. A few studies (Saldanha-Gomes et al., 2020; Leech et al., 2015; Gubbels et al., 2012), including our own previous analysis of EDEN data (Saldanha-Gomes et al., 2020), used data-driven methods (e.g., PCA or clustering approaches) to investigate lifestyle patterns in young children. Their results show that, in 5- to 6-year-olds – that is around the period of the AR for most children – eating and activity behaviors combine in complex ways, that vary by gender and family's socio-economic position (Gubbels et al., 2013; D'Souza et al., 2020; Santos et al., 2020; Noethlings et al., 2003; Newby and Tucker, 2004; McPhie et al., 2014; Gebremariam et al., 2015; Leech et al., 2014). Furthermore, some patterns that combine several obesogenic behaviors (e.g., more TV, higher energy-dense foods/drinks or unhealthy eating habits) were associated with a higher percentage of body fat at 5 years (in girls) (Saldanha-Gomes et al., 2020) or a higher BMI at later ages (Leech et al., 2015; Gubbels et al., 2012). Further longitudinal studies based on large samples and using methods that allow to better assess the combined effect of diet, physical activity and screen-based sedentary behavior over time (Santos et al., 2020), would be useful to inform about the timing of formation of clusters of obesogenic behaviors and their evolution throughout childhood, and help better identify children at higher risk of earlier AR and later obesity.

### 3.1. Study limitations and strengths

The sole reliance on parental report for all behavioral data is a limitation of our study. In particular, the lack of objective measures of physical activity and sedentary behavior may have limited our ability to show an association with the timing of the AR. Regarding diet, we acknowledge that the estimation of dietary intake would have been more precise with a quantitative food frequency questionnaire. Nevertheless, research shows that frequency of consumption is actually the major determinant of intake, whereas information of portion or serving size in food frequency questionnaires provides little additional data on food consumption variance (Noethlings et al., 2003). Therefore, frequencies of consumption have commonly been used to identify dietary patterns (Newby and Tucker, 2004). Second, the participants of the EDEN study are characterized by a higher socioeconomic position than the French population (Heude et al., 2016). Thus, they probably do not represent extreme values of EBRBs nor of parental and infant weight status. The non-representativeness of our sample compared to the general population, however, should not affect the validity of the observed association. We can hypothesize though that better representation of disadvantaged families would have provided more contrast and better statistical power to show higher effect sizes for the longitudinal effects of EBRBs on age at AR. This is particularly relevant for dietary patterns and TV/DVD watching time, which are known to be socially patterned from early childhood (McPhie et al., 2014; Gebremariam et al., 2015). A major strength of this study is to have considered behaviors on both sides of the energy balance simultaneously. Moreover, the relatively large sample size allowed to examine their association with a very early AR, specifically.

## 4. Conclusion

We found evidence that 2-year-old children who had a diet patterned by higher intake of energy-dense and nutrient-poor food items were more likely to have a very early AR. This finding emphasizes the importance of reducing nutrient-dense and processed foods from the early years of life, and provides further support for early interventions aimed at helping parents establish healthy eating habits for their growing child from the complementary period.

## CRedit authorship contribution statement

**Cécilia Saldanha-Gomes:** Conceptualization, Methodology, Software, Formal analysis, Writing – original draft. **Aminata Hallimat Cissé:** Software. **Alexandra Descarpentrie:** Software, Formal analysis. **Blandine de Lauzon-Guillain:** Writing – review & editing. **Anne Forhan:** Data curation. **Marie-Aline Charles:** Writing – review & editing. **Barbara Heude:** Methodology, Writing – review & editing. **Sandrine Lioret:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Patricia Dargent-Molina:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Supervision.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

We are extremely grateful to all the families who took part in this study, the midwives and psychologists who recruited and followed them, and the whole EDEN team, including research scientists, engineers, technicians and managers and especially Josiane Sahuquillo and Edith Lesieux for their commitment and their role in the success of the study. We also acknowledge the commitment of the EDEN mother-child cohort study group, whose members are: I. Annesi-Maesano, J.Y. Bernard, M.A. Charles, P. Dargent-Molina, B. de Lauzon-Guillain, P. Ducimetière, M. de Agostini, B. Foliguet, A. Forhan, X. Fritel, A. Germa, V. Goua, R. Hankard, B. Heude, M. Kaminski, B. Larroquey, N. Lelong, J. Lepeule, G. Magnin, L. Marchand, C. Nabet, F. Pierre, R. Slama, M.J. Saurel-Cubizolles, M. Schweitzer, and O. Thiebaugeorges.

## Funding

The EDEN study was supported by Foundation for medical research (FRM), National Agency for Research (ANR), National Institute for Research in Public health (IRESP: TGIR cohorte santé 2008 program), French Ministry of Health (DGS), French Ministry of Research, INSERM Bone and Joint Diseases National Research (PRO-A), and Human Nutrition National Research Programs, Paris-Sud University, Nestlé, French National Institute for Population Health Surveillance (InVS), French National Institute for Health Education (INPES), the European Union FP7 programmes (FP7/2007–2013, HELIX, ESCAPE, ENRIECO, Medall projects), Diabetes National Research Program (through a collaboration with the French Association of Diabetic Patients (AFD)), French Agency for Environmental Health Safety (now ANSES), Mutuelle Générale de l'Éducation Nationale a complementary health insurance (MGEN), French national agency for food security, French-speaking association for the study of diabetes and metabolism (ALFEDIAM).

The funding sources were not involved in the study design or in the collection, analysis and interpretation of data.

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