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Running head

Child BMI trajectories and adult metabolic outcome

Abbreviations

BMI, body mass index; CECA, child growth and cardiometabolic outcome at adulthood; DXA, dual X-ray absorptiometry; EPICES, evaluation of deprivation and inequalities of health in healthcare centers; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; JIS, Joint Interim Statement; LDL-c, low density lipoprotein cholesterol; MS, metabolic syndrome; NHANES, National Health and Nutrition Examination Survey; PAP, peroxidase, anti-peroxidase; SD, standard deviation; TC, total cholesterol; WC, waist circumference.

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Abstract

Background: Growth trajectories have shown to be related to obesity and metabolic risks in later life, however body mass index (BMI) trajectories according to the presence or absence of metabolic syndrome (MS) and its parameters in adulthood are scarce in literature. **Objectives:** To investigate BMI trajectories during childhood in relation to MS and its parameters in adult age. **Methods:** A total of 1,919 subjects (43.4% male, 20-60y) participated in this retrospective cohort study. Height, weight, waist circumference (WC), blood glucose, HDL-cholesterol, triglycerides and blood pressure were measured at adulthood. Childhood weight and height were collected retrospectively from health booklets. Differences between BMI growth curves of subjects with and without MS were assessed using mixed models for correlated data. **Results:** BMI trajectories differed according to the presence or not of MS at adulthood, from the age of 4 years forward (all $P<0.05$), to the presence or not of hypertriglyceridemia from 1.5 years forward (all $P<0.05$), and to WC >94cm (men) / 80cm (women) compared to lower WC, at all ages (all $P<0.05$). **Conclusions:** BMI growth curves differ according to the presence or not of MS at adulthood but differences only appeared after the age of 4 years. Changes vary according to the MS parameters considered. Deviation of the MS-associated BMI curve from normal pattern could correspond to alteration in body composition. These differences in BMI trajectories during childhood support the theory of an early origin of the MS, justifying early prevention.

Keywords: body mass index, metabolic syndrome, obesity, developmental growth, retrospective cohort study

Introduction

Overweight is nowadays one of the most prevalent health concerns all over the world. The worldwide prevalence of obesity nearly doubled between 1980 and 2014 (ref. 1), and is frequently associated with chronic diseases including metabolic syndrome (MS)[2-6], whose prevalence is also increasing[7]. MS is characterized by a cluster of risk factors (hypertension, hypertriglyceridemia, reduced high-density lipoprotein (HDL) cholesterol, hyperglycemia and central obesity) in which three abnormal findings out of five qualify a person for this condition[3].

Infancy and childhood are important periods of life in which highly active body alterations occur, and studies have shown that some development patterns in early life caused by inadequate nutrition can promote an adaptive metabolism that leads to permanent changes in metabolic pathways and have relevant health implications in adulthood[8-11]. Body mass index (BMI)-for-age trajectories in childhood have shown to be satisfactory for estimating the degree of adiposity among children, once they characterize changes in body weight over time[12,13]. Therefore, the development of BMI during growth has been a useful parameter to estimate cardiometabolic and obesity risks in later life stages[2,14]. Growth trajectories most associated with risk in later life stages have been identified through several different criteria, such as age at adiposity rebound[10,13-18], growth velocity[8,9,14,19,20], weight status changes[6,21-24] and group-based modelled trajectories[25-27]. However, BMI trajectories in infancy and childhood according to the presence or not of metabolic syndrome in adulthood have been little explored so far. Fall et al.[28] have shown that men and women with metabolic syndrome had more rapid BMI gain throughout infancy, childhood, and adolescence compared to the rest of the cohort, in a study including 1,492 Indian young adults. Studies regarding this subject are of great interest for helping the identification of individuals at risk before the development of chronic diseases and metabolic dysregulations as well as the age when it

becomes evident. It could therefore be a useful tool to public policies and clinical efforts willing to improve preventive strategies starting in early life stages.

The aim of this study is to compare BMI trajectories from birth to 10 years old among adults with and without metabolic syndrome, and also with each of its parameters (hypertension, hypertriglyceridemia, reduced HDL cholesterol, hyperglycemia and central obesity), exploring whether there are specific ages when differences in BMI are particularly associated with later cardiovascular risk factors.

Methods

Population

The sample was selected from the pool of 24,574 adults attending one of the health examination centers in the central/western part of France (parts of 3 regions: Centre, Pays de la Loire and Normandie) from September 2008 to July 2009. All individuals affiliated with the French national health insurance system (corresponding to about 85% of the French population) are able to benefit from a free medical and laboratory check-up every 5 years. The population is generally aware of this possibility and practical information is publicly available. All adults attending the health centers traditionally complete a set of questionnaires that focus on diet, physical activity, lifestyle, socio-economic conditions and health status. In addition, a clinical examination and blood sampling was performed. Subjects participating in the Child Growth and Cardiometabolic Outcome at Adulthood (CECA) study were asked to fill in an additional growth questionnaire that included information on parental silhouette, nutrition in early life and weight and height data during childhood, and to bring their health booklets containing growth data to the medical check-up. In order to be included in the study, subjects should have brought the health booklet at the examination and completed the growth questionnaire. Data collection by the examination centers was approved by the *Comité*

National Informatique et Liberté (CNIL number 26674) and all subjects signed an informed consent.

Data collection

Socio-economic and lifestyle characteristics

Self-administered questionnaires were completed by participants and verified by the physician performing the health examination interview. Sex, age, physical activity (<10 min/day, 10 to 30 min/day, 31 to 60 min/day, >60 min/day) and occupational category (managerial staff, intermediate profession, employee or manual worker, unemployed, never employed and retired) were provided. The deprivation level of each participant was assessed using the "Evaluation of Deprivation and Inequalities of Health in Healthcare Centers" score (EPICES)[29]. The EPICES score is calculated based on answers to 11 questions (e.g. "Are there periods in the month when you have real financial difficulties to face your needs (food, rent, electricity)?"), and varies from 0 to 100, from the least deprived to the most deprived situation. Gestational age (months), birth weight (grams) and nutrition when leaving the maternity ward (exclusive or partial breastfeeding, formula feeding) were collected using data from the health booklets when available. Breastfeeding was defined as any kind of breastfeeding, including partial breastfeeding, whatever the duration. Parental silhouette was estimated using nine figural stimuli[30]. Subjects were asked to choose the silhouettes that most closely resembled that of their mothers and fathers at the maximal BMI attained during their lifetime.

Growth measurements during childhood

Data were obtained from health booklets, instruments that have been distributed by the Ministry of Health to parents of all newborns in France since 1945. They are intended to record anthropometry, measured by health practitioners, and health events during childhood,

from birth on. Subjects were asked to report weight and height data at birth and at specific periods during childhood: one measurement of weight and length/height at around 1 month, 3 months, 6 months and 9 months of age; two measurements between 1 and 2 years, between 2 and 3 years and between 3 and 4 years; and finally, one measurement at around 5 years, 6 years, 7 years, 8 years, 9 years and 10 years. Subjects were also asked to report the exact date and/or age at each reported measurement. These data were reported on a questionnaire, which was subsequently checked by medical staff at the Health center. Subjects with less than 5 height or weight measurements were not included in the analysis. Body mass index was calculated as weight (kg) divided by squared height (m^2) for each data point. Collected information provided the changes in BMI over many different points of age, starting at birth until the end of childhood (at 10 years old).

Biological and biometric data and anthropometry at adulthood

Weight, height and waist circumference (WC) were measured in the health examination centers by trained nurses, with participants wearing only underwear, according to standardized procedures[31]. WC was measured to the nearest 0.5 cm by a physician, as the smallest horizontal circumference between the costal margin (lower edge of the chest formed by the bottom edge of the rib cage) and the iliac crests (superior border of the ilium). Height was measured to the nearest 0.1 cm with a Seca® stadiometer (Seca GmbH & Co. KG, Hamburg, Germany). Weight was measured to the nearest 0.1 kg with a Seca® scale (Seca GmbH & Co. KG, Hamburg, Germany). Sitting diastolic and systolic blood pressures were measured by an OMRON® automatic tensiometer (Omron HEM-705CP; Omron Healthcare/DuPont Medical, Frouard, France) in subjects who had been lying down for at least five minutes.

Blood samples were collected in the morning after at least 8-hour fasting. All samples were assayed using a C8000 Architect Abbott analyzer (Rungis, France). Plasma glucose was

assayed by the hexokinase procedure (Architect Abbott, Rungis, France). HDL-cholesterol and triglycerides concentrations were assayed by an enzymatic method (Architect Abbott, Rungis, France). Total cholesterol (TC) concentration was assessed by a peroxidase, anti-peroxidase (PAP) antibody method (Architect Abbott, Rungis, France). LDL-cholesterol concentration was calculated with the Friedewald equation in which [LDL-c] = [TC] – [HDL-c] – [triglycerides] / 5 (ref. 32). Metabolic syndrome was defined according to the sets of criteria proposed by the Joint Interim Statement (JIS)[3]. Individuals had to present at least three of the following criteria: 1) waist circumference ≥ 94 cm (men) or ≥ 80 cm (women); 2) fasting plasma glucose ≥ 100 mg/dL (5.6 mmol/L) or use of antidiabetic medication; 3) triglycerides ≥ 150 mg/dL (1.7 mmol/L) or use of medication for elevated triglycerides; 4) HDL-cholesterol < 40 mg/dL (1.03 mmol/L) men) or < 50 mg/dL (1.29 mmol/L) (women) or use of medication for reduced HDL-cholesterol; 5) blood pressure ≥130/85 mmHg or use of blood-pressure lowering medication. Information on medication use was collected by physicians.

Statistical analysis

Characteristics of subjects at childhood and adulthood are presented as frequencies for categorical variables and means and standard deviation for continuous variables. Comparisons between groups were performed using Pearson's chi-square tests for categorical variables and the Student's t-test for continuous variables. BMI patterns were created from individual measures of BMI in each age. Differences in BMI at each age period (birth-1 year, 1.5-3 years, 4-6 years, 7-10 years) according to characteristics at adulthood (diagnosis of metabolic syndrome and each of its parameters – hypertension, hypertriglyceridemia, reduced HDL-c, hyperglycemia and central obesity) were estimated by mixed models for correlated data adjusted for potential confounders identified in the literature (age, sex, physical activity, EPICES score, gestational age, birth weight, mother's and father's silhouettes). P-values were

two-sided and significance was set at 5%. All analyses were performed using SAS software (version 9.3; SAS Institute Inc).

Results

Characteristics of the sample

A total of 2,549 consultants at the health centers completed the growth questionnaire and brought their health booklets to the medical checkup. From those, 14 were excluded due to missing anthropometric data at adulthood and 28 women were excluded for being pregnant at the time of examination. In addition, 427 subjects were excluded for having fewer than 5 weight or height data between birth and 10 years, and 161 for missing any of metabolic syndrome parameters. Thus, 1,919 subjects were included in this study (43.4% male). Compared with excluded subjects, included subjects were younger (30.7 ± 8.0 years vs 38.1 ± 9.0, $P < 0.0001$), had higher EPICES score (20.9 ± 18.2 vs 19.0 ± 18.5, $P = 0.029$), lower prevalence of MS (10.4% vs 15.7%, $P = 0.0007$), lower BMI at adulthood (23.5 kg/m² ± 4.1 vs 24.1 kg/m² ± 4.0, $P = 0.004$), lower waist circumference (80.4 cm ± 11.5 vs 83.3 ± 11.8, $P < 0.0001$), lower triglycerides (99.8 mg/dL ± 55.7 vs 105.0 ±55.4, $P = 0.05$), total cholesterol (192.9 mg/dL ± 36.5 vs 206.1 ± 36.3, $P < 0.0001$), HDL-c (54.9 mg/dL ± 12.5 vs 56.7 ±13.9, $P = 0.004$), LDL-c (117.8 mg/dL ± 32.0 vs 128.4 ± 32.8, $P < 0.0001$), glucose concentrations (87.7 mg/dL ± 9.6 vs 89.1 ± 8.7, $P = 0.002$), systolic (123.8 mmHg ± 12.6 vs 125.5 ± 14.3, $P = 0.007$) and diastolic blood pressure (74.4 mmHg ± 8.7 vs 77.2 ± 9.8, $P < 0.0001$). Excluded and included subjects showed no statistically significant differences in sex ratio and physical activity practice (all $P > 0.05$).

Characteristics of the study sample overall and according to sex are shown in **Table 1**. According to JIS classification, 10% of the studied sample had the diagnostic of metabolic syndrome, 7% were hyperglycemic, 12% presented hypertriglyceridemia, 21% had low HDL-

c concentrations, 27% presented high waist circumference and 35% presented high blood pressure. Men compared to women were older (P = 0.007), belonged to a higher-level occupational category, were more active and presented lower HDL-c and higher BMI, waist circumference, LDL-c, triglycerides, glycemia, systolic and diastolic blood pressure, birth weight (P < 0.0001 for all) and parental silhouette scores (P < 0.05). Prevalence of MS was also higher among men compared with women (13.9% vs 7.7%, P < 0.0001).

Growth curves and metabolic syndrome parameters

BMI trajectories according to the presence or not of MS (according to JIS) and each parameter used to classify MS are presented in Figure 1. Subjects with MS at adulthood presented higher BMI trajectories, from the age of 4 years on compared to subjects without MS (P-global < 0.001; 4-6 years: P = 0.014; 7-10 years: P < 0.0001). Subjects with WC > 94 cm (men) or 80 cm (women) presented higher BMI trajectories at all ages, compared to subjects with lower WC (P-global < 0.0001; birth-1 year: P = 0.029; 1.5-3 years: P = 0.0001; 4-6 years: P < 0.0001; 7-10 years: P < 0.0001). Differences in BMI curves were also observed among subjects with triglycerides concentrations ≥ 150 mg/dl starting at 1.5 years old and forward (P-global = 0.001; 1.5-3 years: P = 0.012; 4-6 years: P = 0.02; 7-10 years: P < 0.0001). BMI trajectories did not differ according to the presence of low HDL-c (< 40 mg/dL for men and < 50 mg/dL for women), hyperglycemia (≥ 100 mg/dl) or elevated blood pressure (≥ 130/85 mmHg) in adult age (P-global = 0.62, 0.23 and 0.18, respectively).

Discussion

Our study has shown that BMI trajectories in childhood are related to metabolic syndrome at adult age. The BMI trajectory that is associated with MS at adulthood starts similar to the trajectory from subjects that do not develop SM at adult age, and remains alike until 4 years old where it starts deviating. More specifically, BMI trajectories of waist

circumference deviated from birth and BMI trajectories of triglycerides from 1.5 years. No significant difference was observed for trajectories of the other MS parametres (HDL-c, glucose and blood pressure). The risk of developing metabolic syndrome therefore becomes apparent at 4 years, although it is probable that risk factors have operated earlier in life, corroborating findings related to risk trajectories from literature.

Not many studies have evaluated the relationship between BMI trajectories in childhood and metabolic parameters in later life stages, especially until adulthood. Differences between statistical methods and choices of outcome variables are also relevant, turning it delicate to make comparisons with previous publications. A study using group-based trajectory modelling demonstrated that an early persistent obesity trajectory was related to elevated blood pressure at 18 years[27]. Other studies, using mixture modelling identified that specific trajectories were related to increased insulin resistance at age 14 (ref. 26), and to higher values for WC, total cholesterol, LDL-c, fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), triglycerides, and blood pressure at age 15 (ref. 25). In agreement with our findings, a study has found that BMI changes between 8.5 and 10 years were strongly associated with increased fat mass and also with a range of cardiovascular risk factors at age 15 (ref. 23). Other studies showed that greater BMI growth between birth and 9 years of age was related to a higher score used to predict metabolic syndrome risk (MetS score)[6], and that large relative increases in weight from ages 2 to 7 years were associated with greater adiposity and MS at age 16 (ref. 24). A systematic review that analyzed 15 studies (summing a total of 731,337 participants) concluded that high BMI from age 7 onwards was associated with an increased risk of coronary heart disease in later life[4].

Differences in BMI patterns according to metabolic risks could be explained by changes in body composition at different periods of growth. Rapid gain in BMI in early life is mainly associated with higher development of lean body mass, whereas rapid gain in BMI starting in later childhood results in relatively larger increase in fat mass[33,34]. At all ages, high

lean and fat masses are typical characteristics of childhood obesity[35]. However, the present study shows that the BMI trajectory associated with the MS displays average BMI values during the first years of life followed by later increase. Compared with always high BMI[36], the trajectory associated with MS seams to mainly reflect an increase in fat mass rather than lean tissue[34], thus limiting the beneficial effect of muscle mass such as improvement of insulin sensitivity[14,34,36]. Then, the BMI trajectory associated with MS could reflect an altered body composition. This pattern is consistent with the trajectory of a low BMI followed by an increase only at later age in subjects at risk of metabolic diseases such as cardiovascular diseases or diabetes[14].

Other indicators of fat patterns predicting later risks can be used. The occurrence of an early adiposity rebound (the moment when a second rise in body mass index trajectory occurs, after birth), has also been shown as a predictor of obesity[10,15,37] and metabolic syndrome[17,18] in later life stages. An early adiposity rebound (before 5 years old) is usually preceded by average or even low BMI and followed by an increase mainly reflecting changes in body fat[34]. This pattern could be the consequence of an unbalanced diet currently recorded in infancy[38-40]. The child's diet of young children is often characterized by a high protein and low fat content[41]. Such imbalanced diet is in large part attributable to restriction of fat intakes, mainly due to the use of low fat dairy products[42]. It has been suggested that low fat intake in early life (particularly during the period of large energy needs) may trigger a "low fat programming", in which fat restrictions could decrease leptin concentration and activate adaptive mechanisms to prevent underweight, thus increasing the susceptibility to later overweight and metabolic diseases[38,41].

Other hypotheses relate early life exposures to later health outcomes[43]. An early growth restraint in infancy has been proposed to induce a metabolic profile that becomes more susceptible to weight excess, to insulin resistance and to components of metabolic syndrome later in life[9,19]. Another growth pattern of risk includes slow fetal growth, small birth size and

thinness through infancy, followed by catch-up growth[8,14,20,21,44], which is characterized by a disproportionately higher rate of fat gain than lean mass gain[33,45]. In this situation, potential impaired development of organs and tissues could occur, predisposing future chronic diseases such as dyslipidemia, coronary heart disease, hepatic insulin resistance and type 2 diabetes. In agreement, a systematic review reported that early growth is indeed associated with the prevalence of obesity later in life[46].

In our analyses, waist circumference was the MS parameter most associated with the general BMI trajectories in childhood. Accordingly, Börnhorst et al.[6] found waist circumference to be related to rates of BMI change during infancy and childhood. Positive associations between weight gain during infancy or childhood and waist circumference in later life were also found by others[22,24,47]. Elevated triglycerides concentrations were also associated with BMI trajectories in our study. Differences in growth trajectories between adults with hypertriglyceridemia compared to adults with normal concentrations were observed from 1.5 years on. On the other hand, subjects with low HDL-c concentrations compared to subjects with normal HDL-c showed overall no significant differences in BMI patterns. Few studies have investigated the relationships between BMI trajectories or weight gain during childhood and lipid levels in later life stages, and findings are not consistent. Howe et al.[23] found greater increases in BMI from age 8.5 to 10 years to be strongly associated with triglycerides and HDL-c concentrations at age 15. On the other hand, a study evaluating subjects from birth to 17 years observed rapid weight gain during infancy (0 to 6 months) but not during early childhood (3 to 6 years) to be related to fasting triglycerides and HDL-c at age 17 (ref. 22). Leunissen et al.[47] observed rapid growth only the first three months of life to be positively associated with triglycerides and negatively associated with HDL-c concentrations in adulthood. Finally, lipid levels during late childhood were related to BMI growth during infancy (0 to 9 months) and early childhood (9 months to 6 years) – but not during late childhood, in a subgroup of participants (older than 6 years) of the study from

Börnhorst et al.[6], while no such association was found among the younger age group. In the same study, blood pressure was positively associated with rates of BMI change during infancy, early childhood and late childhood, but solely among the subgroup of subjects older than 6 years. Such finding may partly result from the smaller sample in the younger group, leading to reduced statistical power.

In our study, comparison of BMI trajectories among subjects with elevated fasting glucose concentrations versus euglycemic subjects and those with high blood pressure versus normotense subjects showed no difference overall. In the case of glucose, the low proportion of subjects with elevated fasting concentrations in our sample (7%) may have contributed to the lack of association. In accordance with our findings, Howe et al.[23] showed that BMI changes in childhood were only weakly associated with fasting glucose and diastolic blood pressure among adolescents aged 15 years. Moreover, a cross-sectional study with subjects 6-17 years from the National Health and Nutrition Examination Survey (NHANES) 2001–2006 have found higher fasting glucose concentrations only among subjects in the 99th percentile of BMI-for-age, and consistent significant increases in the prevalence of high or borderline systolic and diastolic blood pressure, respectively, in the 90th and 95th percentile[48]. Such results suggest that those specific risk factors become significant only among subjects at the highest BMI-for-age percentiles, or could be affected in a minor or slower degree compared to the other parameters.

Strengths and limitations of the study

One strength of our study lies in data collection over a long period in a large sample of individuals, and in having many biochemical and cardiometabolic indicators available at adult age. Growth trajectories were determined from several weight and length measurements between birth and 10 years old for each participant (the mean of around 10 for each variable)

and, to ensure the quality of trajectories, individuals with less than 5 measures were not included in the study.

One of the limitations of our study was the fact that anthropometric data in childhood were recorded retrospectively in health booklets, but such measurements were performed and recorded by physicians, limiting potential bias. In addition, modelling growth trajectories using BMI as a measure of adiposity in childhood may be discussed, since such measure does not distinguish fat mass from lean mass. A persistent high BMI likely corresponds to both high lean and fat masses[35,36], however, rapid changes in the BMI trajectories (e.g. changes according to early vs late AR) appear to mainly reflect variations in fat rather than lean mass[34]. It has also been shown in a study using dual X-ray absorptiometry (DXA) that differences in BMI among children between 5 and 9 years old were caused specifically by alteration in body fat rather than by alterations in lean mass content[49]. In addition, rapid gain in BMI after 2 years old, despite the concurrent rise in lean mass, was shown to be associated with larger increases in fat mass[33]. Furthermore, evidence from a cohort that included 7,589 participants showed that BMI, waist circumference and total fat mass (assessed by DXA) were similarly associated to cardiovascular risk factors in childhood[50], suggesting that BMI may adequately assess adiposity in children. Other limitation lies on study participation rate, which was relatively low due to individuals forgetting to bring their growth questionnaire or health booklet and to those that have lost their booklet, those that have never received one, and still others who had no data in their health booklets. Thus, results cannot be generalized to all populations and need to be replicated in different contexts. However, our sample showed an obesity prevalence (BMI ≥30 kg/m^2; 7.3% in included subjects and 7.5% in excluded subjects) similar to that of the whole sample of subjects who went to the examination center after standardization with the French age distribution (8.9% in men vs 8.6% in women) in 2005 (ref. 51). Finally, although a wide range of potential confounders was considered in the

analyses, we cannot exclude the possibility that other important confounders were not taken into account.

Conclusions

In this retrospective cohort study, we have shown that BMI growth curves differ according to the presence or not of the MS at adult age, suggesting that determinants of metabolic syndrome in adult life have operated during childhood. However, differences according to metabolic syndrome diagnosis only appeared from the age of 4 years. Before this age, BMI curves between people with MS compared to non-MS were similar, although such finding does not exclude the possibility that risk factors may have operated in the first years of life. Waist circumference and elevated triglycerides concentration were the parameters that mostly contributed to the body mass index trajectory associated with metabolic syndrome at adulthood. The BMI pattern associated with the metabolic syndrome could be due to an alteration in body composition, characterized by an increase in fat mass starting after several years of life without concurrent increase in lean mass. This trajectory is consistent with the trajectory of low followed by later BMI increase recorded in subjects at risk of metabolic diseases such as cardiovascular diseases or diabetes These observations confirm that the identification of BMI trajectory at risk during childhood may be of importance for the early prevention of chronic diseases, and turning researches towards the identification of factors responsible for the metabolic syndrome.

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Author contributions

The authors' responsibilities were as follows: KVG supervised statistical analyses, interpreted data and drafted the manuscript. M-FR-C designed the protocol, interpreted the data and critically revised the manuscript. GG, DG and OL collected the data and critically revised the manuscript. SH designed the protocol and critically revised the manuscript. SP designed the protocol, supervised statistical analyses, interpreted data and critically revised the manuscript.

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Figure legends

Figure 1. Body mass index trajectories from birth to 10 years old (lsmeans) estimated by mixed models for correlated data and adjusted for potential confounders (age, sex, physical activity, EPICES score, gestational age, birth weight, mother's and father's silhouettes) according to the diagnostic of metabolic syndrome (A) and to its parameters in adulthood: waist circumference (B), HDL-cholesterol concentrations (C), triglycerides concentrations (D), fasting glucose (E) and blood pressure (F) (N = 1919, CECA growth study, 2008-2009). * P<0.05; *** P<0.001; N.S., not significant.

Table 1. Characteristics of the studied sample according to sex (N = 1919, CECA growth study, 2008-2009).

	Total (n = 1919)		Male (n = 833)		Female (n = 1086)		P
	% or mean (SD)	N	% or mean (SD)	N	% or mean (SD)	N	
Adulthood information							
Age (years)	30.7(8.0)	1919	31.4(7.8)	833	30.2(8.2)	1086	**0.007**
Occupational category (%)							
Managerial staff	13.1	251	17.9	149	9.4	102	**<0.0001**
Intermediate professions	16.3	313	18.5	154	14.6	159	
Employees, manual workers	39.8	763	37.8	315	41.3	448	
Unemployed, never-employed, retired	30.3	581	25.2	210	34.2	371	
Missing data	0.6	11	0.6	5	0.6	6	
Body Mass Index (kg/m²)	23.5(4.1)	1919	24.0(3.6)	833	23.2(4.4)	1086	**<0.0001**
Nutritional status (%)							
Normal weight (< 25 kg/m²)	72.3	1388	67.2	560	76.2	828	**<0.0001**
Overweight (25 to 29.9 kg/m²)	20.4	391	26.4	220	15.7	171	
Obese (≥ 30 kg/m²)	7.3	140	6.4	53	8.0	87	
Waist circumference (cm)	80.4(11.5)	1919	85.1(10.2)	833	76.8(11.2)	1086	**<0.0001**
≥ 94 cm (male) or 80 cm (female)	26.8	514	19.0	158	32.8	356	**<0.0001**
≥ 102 cm (male) or 88 cm (female)	12.7	243	7.7	64	16.5	179	**<0.0001**
Physical activity (%)							
<10 min/d	16.5	316	13.3	111	18.9	205	**<0.0001**
10 to 30 min/d	37.6	722	32.8	273	41.3	449	
31 to 60min/d	21.2	407	21.6	180	20.9	227	
>60 min/d	20.9	402	28.3	236	15.3	166	
Missing value	3.8	72	4.0	33	3.6	39	
EPICES* score (0-100)	20.9(18.2)	1833	19.8(17.5)	787	21.8(18.8)	1046	**0.020**
Biochemistry							
Total cholesterol (mg/dL)	192.9(36.5)	1918	194.5(39.1)	832	191.6(34.2)	1086	0.093
HDL-c (mg/dL)	54.9(12.5)	1919	50.8(11.4)	833	58.1(12.3)	1086	**<0.0001**
≥ 40 (male) / 50 (female) mg/dL, %	20.9	401	15.5	129	25.0	272	**<0.0001**
<40 (male) / 50(female) mg/dL and/or treatment,%	21.4	410	16.0	133	25.5	277	**<0.0001**

LDL-c (mg/dL)	117.8(32.0)	1910	121.2(33.7)	825	115.3(30.4)	1085	**<0.0001**
Tryglycerides (mg/dL)	99.8(55.7)	1919	110.6(67.5)	833	91.5(42.7)	1086	**<0.0001**
≥ 150 mg/dL, %	12.1	233	17.0	142	8.4	91	**<0.0001**
≥ 150 mg/dL and/or treatment,%	12.7	243	17.5	146	8.9	97	**<0.0001**
Glucose (mg/dL)	87.7(9.6)	1919	90.6(8.6)	833	85.5(9.8)	1086	**<0.0001**
≥ 100 mg/dL, %	7.2	139	11.0	92	4.3	47	**<0.0001**
≥ 100 mg/dL and/or treatment,%	7.3	140	11.0	92	4.4	48	**<0.0001**
Blood pressure							
Systolic (mmHg)	123.8(12.6)	1919	130.1(11.2)	833	119.0(11.4)	1086	**<0.0001**
Diastolic (mmHg)	74.4(8.7)	1919	75.3(8.6)	833	73.7(8.7)	1086	**<0.0001**
Systolic ≥ 130 and/or diastolic ≥ 85 mmHg, %	34.9	670	52.3	436	21.5	234	**<0.0001**
Systolic ≥ 130 and/or diastolic ≥ 85 mmHg and/or treatment,%	35.9	689	52.5	437	23.2	252	**<0.0001**
Metabolic syndrome (JIS)** (%)	10.4	200	13.9	116	7.7	84	**<0.0001**
Childhood information							
Parental silhouette							
Mother's silhouette (range 1-9)***	5.0(1.4)	1855	5.0(1.4)	799	4.9(1.5)	1056	**0.031**
Father's silhouette (range 1-9)***	5.3(1.5)	1810	5.4(1.5)	787	5.2(1.5)	1023	**0.011**
Pregnancy duration (months)	8.9(0.4)	1065	8.9(0.4)	491	8.9(0.4)	574	0.50
≤ 8 months	8.7	93	7.5	37	9.8	56	0.20
> 8 months	91.3	972	92.5	454	90.2	518	
Birth weight (g)	3253(507.5)	1916	3343(514.7)	832	3185(491.1)	1084	**<0.0001**
< 2500 g	5.8	111	4.3	36	6.9	75	**0.016**
Early nutrition (%)							
Exclusive breastfeeding	35.1	609	34.0	249	35.8	360	0.060
Partial breastfeeding	5.5	95	7.0	51	4.4	44	
Formula feeding	59.5	1033	59.0	432	59.8	601	

* Evaluation of Deprivation and Inequalities of Health in Healthcare Centers) score. The score ranges from 0 to 100, from the least deprived to the most deprived situation. **Metabolic syndrome prevalence using the Joint Interim Statement (JIS) definition. ***Maximal parental silhouette attained during life as assessed using nine silhouettes (higher score corresponds to larger silhouette).