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Association between Eating Behaviour and 13-year Cardiovascular Damage in the Initially Healthy STANISLAS Cohort.

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Short running head: Eating behaviour and cardiovascular damages.

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Abstract (234 words)

Background: Several dimensions of eating behaviour, such as restrained eating, appear to be cross-sectionally associated with certain cardiovascular diseases and metabolic risk factors although little is known regarding longitudinal associations.

Aim: This study aimed to assess the associations between eating behaviour and cardiovascular damage or metabolic syndrome after 13 years, in initially healthy individuals.

Methods: This study included 1109 participants from the familial STANISLAS cohort study. Emotional eating (EmE), restrained eating (RE), and external eating (ExE) were assessed using the Dutch Eating Behaviour Questionnaire. Metabolic syndrome and cardiovascular damages such as carotid-femoral pulse-wave velocity (cfPWV), left ventricular mass, carotid intima-media thickness, and diastolic dysfunction (DD) were measured after a period of 13 years. Mixed model analysis with a family random effect and adjustment for age, sex, education, temporal gap and metabolic factors at baseline and mediation analysis were performed in adults and adolescents separately.

Results: Among adults, EmE was associated with a 38 % increased risk of DD 13 years later (OR=1.38 [1.05; 1.83]). Stress level mediated 31.9% of this association (p=0.01). EmE was positively associated with cfPWV ($\beta=0.02$ [0.01; 0.04]). ExE was slightly associated with lower cfPWV ($\beta=-0.03$ [-0.05; -0.01]). No associations were observed between eating behaviour dimensions and metabolic syndrome. Energy intake was not found to be a mediator of any associations.

Conclusion: Our results suggest that cardiovascular prevention should also take into account eating behaviour and include emotion regulation skills teaching.

Lay summary

The association of 3 dimensions of eating behaviour (emotional eating, restrained eating, external eating) with 13 year later cardiovascular damages have been investigated in the initially healthy STANISLAS cohort.

- Emotional eating was associated with higher pulse wave velocity and an increased risk of diastolic dysfunction. External eating was associated with lower pulse wave velocity.

- Stress level was found to be a mediator of the association found between emotional eating and diastolic dysfunction.

Keywords

Eating behaviour, cardiovascular damage, metabolic syndrome, mediation analysis

Introduction

Diet plays an important role in the development of a number of chronic diseases such as cardiovascular disease (CVD) (1), which is the most common cause of death in Europe (2). The current environment can be considered as "obesogenic", with a decrease in physical activity and changes in eating habits toward a western diet. Our environment is marked by the wide availability of high-fat, high-sweet and energy-dense foods in supermarkets and public places, as well as by promotion through advertising and marketing (3). Food availability and accessibility can influence people food choice (4). However, the emerging question is why, in this obesogenic environment, some people can maintain their energy balance and stay healthy for years, while others become obese and/or develop chronic diseases. Food choices are the result of a combination of multiple factors such as environmental, economic, hedonic and individual factors (5), and can be influenced by certain psychological dimensions of eating behaviour (6,7). The regulation of eating behaviour can be influenced by different factors such as exposure to food signals, cognitive and emotional state, personal and cultural attitudes.

Three common psychological dimensions have been proposed. Emotional eating is the tendency to overeat in response to negative emotional states, such as sadness or anxiety. It is based on the psychosomatic theory proposed by Bruch and Kaplan (8,9), which suggests that some individuals have difficulty in differentiating between internal states of excitement and hunger, which is associated with eating in response to emotions. External eating, based on the externality theory developed by Schechter and Rodin (10), states that eating occurs in response to external food cues such as the smell of food, the presence of food or of others persons eating in the environment regardless of the internal state of hunger and satiety. Restrained eating is based on the theory of cognitive restriction developed by Polivy and Herman (11), and corresponds to the tendency to consciously limit food intake to control weight.

Emotional and restrained eating have been found to be associated with CVD risk factors (12,13). Indeed, the risk of obesity, type 2 diabetes, and hypertension increased around 2-fold in participants with high emotional eating score among 578 adult Latinos (12). While in another cohort study of 2053 Czech participants, restrained eating has been associated with the risk of dyslipidaemia, obesity, and type 2 diabetes (all regression coefficient < 0.1) (13). To date, only 2 studies have examined the association between eating behaviour and CVD or

surrogate endpoints (13,14). Restrained eating was found to be cross-sectionally associated with a higher prevalence of hypertension and cardiovascular disease (ischaemic heart disease and cerebrovascular disease) independently of BMI (13). In a clinical trial carried out in 36 Romanian students, emotional eating was found correlated with pulse wave velocity in sedentary students ($R^2=0.25$). This was not the case for trained students who exercised 3 or more times per week. However, this study focused on young people and did not investigate the dimensions of restriction and externality (14).

Because of previous findings, we hypothesised that emotional eating and/or restrained eating dimensions of eating behaviour are positively associated with cardiovascular damages, as well as with cardiovascular risk factors, such as metabolic syndrome. The primary objective of this study was to assess the associations between three dimensions of eating behaviours and cardiovascular damages, measured after a period of 13 years. The secondary objective was to assess the cross-sectional and longitudinal associations between eating behaviours and cardiovascular risk factors, such as metabolic syndrome. The third objective was to perform a mediation analysis to identify mediators of the relationship between eating behaviours and cardiovascular damages.

Subjects and Methods

Population

The STANISLAS (Suivi Temporaire Annuel Non-Invasif de la Santé des Lorrains Assurés Sociaux) cohort is a longitudinal single-centre familial study of 4598 participants (1006 families) from the Lorraine region (north-east of France), recruited between 1993-1995 at the Centre for Preventive Medicine during a yearly routine examination, under the coverage of the Caisse Nationale d'Assurance Maladie (CNAM) (15). To be recruited into the STANISLAS cohort, families had to be of French origin, have at least two parents and two biological children aged over 6 years. Family members had to be free of known serious and/or chronic diseases declared by the subject.

Four medical visits were organised from 1993 to 2016 with one every 5 to 10 years. The detailed description of the STANISLAS cohort has been published elsewhere (16). From the 4598 included participants, 1704 attended to both visits 2 and 4: the second visit (V2), where eating behaviour was assessed, and the fourth visit (V4), where cardiovascular phenotyping was performed, and for whom data on eating behaviour (EB) were complete. After excluding

483 participants with missing or incomplete data regarding EB, and 112 with missing data on health outcomes or covariates, the present analysis included 1109 participants, 916 of whom were adults and 193 adolescents (Supplementary figure 1).

Data collection

Eating behaviour

Eating behaviour was assessed once during the second visit (1998-2000) by using the validated French version (17) of the Dutch Eating Behaviour Questionnaire (DEBQ), which is a valid and reliable tool for assessing EB in adult and adolescent (18,19). The questionnaire consists of 33 items, which measure three dimensions of EB: emotional eating (EmE, 13 items), restrained eating (RE, 10 items), and external eating (ExE, 10 items). Each question has five possible answers, scored from 1 to 5 points, consisting of never (1 point), rarely (2 points), sometimes (3 points), often (4 points), and very often (5 points). For each scale, a score was calculated as the mean of all items included in the scale. DEBQ scales have high internal consistency, and high convergent and discriminant validity (20). In the present population, Cronbach's α coefficients were 0.93 in adults and 0.90 in adolescents for the emotional eating scale, 0.92 in adults and 0.91 in adolescents for the restrained eating scale, and 0.83 in adults and 0.78 in adolescents for the external eating scale.

Cardiovascular damages

The primary endpoints were cardiovascular (CV) damages measured at the fourth visit (V4).

Carotid-femoral pulse-wave velocity

Carotid-femoral pulse-wave velocity (cfPWV) was assessed with the Complior® device (ALAM Medical, France), which simultaneously records arterial pulse waves at carotid and femoral sites, according to the recommendations of the European Network for Noninvasive Investigation of Large Arteries (21). Two sensors were placed simultaneously on the carotid artery and femoral artery. Two measurements were made, with cfPWV calculated as their mean. If the 2 measurements differed by >0.5 m/s, a third measurement was made, and the cfPWV was then calculated as the median of the 3 measurements. The onboard foot-to-foot algorithm based on the second-derivative waveforms was used to determine the transit time. The carotid-to-femoral, carotid-to-sternal-notch, and sternal-notch-to-carotid distances were

measured with a measuring tape, and cfPWV (m/s) was obtained by the formula $cfPWV = D \times 0.8/(t)$.

Left ventricular mass

Echocardiographic examinations of the subject in the left lateral decubitus position were performed by an experienced echocardiographer using a commercially available standard ultrasound scanner (Vivid E9, General Electric Medical Systems, Horten, Norway) with a 2.5-MHz phased-array transducer (M5S). The echo/Doppler examinations included exhaustive examinations in parasternal long- and short-axis views and in the standard apical views (22). All acquired images and media were stored on a secured network server as digital videos with unique identification numbers, and analysed on a dedicated workstation (EchoPAC PC, version 110.1.0, GE Healthcare). The septal wall thickness, posterior wall thickness, and left ventricular internal diastolic diameter from the parasternal 2-dimensional long-axis view were measured. Intra-class correlation coefficients were good for both: Intra-observer 0.98 (0.97-0.99); inter-observer 0.95 (0.91-0.97) (22). These measurements were subsequently used in the cube-function formula of the American Society of Echocardiography guidelines to calculate left ventricular mass (LVM) (23), which was then indexed for height to the 2.7 power (24).

Carotid intima-media thickness

Carotid intima-media thickness (cIMT) measurements were routinely performed by high-resolution echo-tracking in a controlled environment at 22 ± 1 °C after 10 minutes of rest in the supine position as described elsewhere (25). Carotid diameter, distension and intima-media thickness were measured on the right common carotid artery. Four measurements were obtained per patient. Examinations were performed with the wall track system (WTS, ESOATE, Maastricht, The Netherlands) and the ART.LAB (ESAOTE, Maastricht, The Netherlands) in immediate succession. Both inter-device reproducibility and measurement agreement were excellent (26).

Diastolic dysfunction

Assessment of left ventricular diastolic dysfunction (DD) was performed according to the recommendations of the American Society of Echocardiography and the Committee of the European Association of Echocardiography (22,27), using the following grading scheme:

mild or grade I (impaired relaxation pattern), moderate or grade II (pseudonormal filling) and severe (restrictive filling) or grade III. Due to the relatively small number of subjects (n=3) with grade III diastolic dysfunction (DD) in our population, it was decided to consider the variable as no DD, grade I and grade II/III.

Metabolic syndrome

Metabolic syndrome (MetS) was defined according to the National Cholesterol Education Program Adult Treatment Panel 3 (NCEP ATP 3) (28). The ATP 3 concept is one of the most widely used for assessing metabolic syndrome. It requires the presence of at least 3 of the following defined criteria: waist circumference > 102 cm in men and > 88 cm in women; office blood pressure \geq 130/85 mm Hg or treated by hypertensive drugs; elevated triglycerides \geq 1.5 g/L or treated by lipid-lowering drugs; fasting blood glucose \geq 1.10 g/L or treated by antidiabetic drugs; reduced HDL cholesterol < 0.4 g/L in men, < 0.5 g/L in women.

Covariates

At each visit, all participants underwent a full clinical examination, including weight, height, waist circumference and blood pressure measurements. Body mass index was calculated as weight (kg) divided by the square of height (m). Blood samples were also collected, and serum concentrations of the following biomarkers were measured: fasting blood glucose, HDL, LDL, and triglycerides. Self-reported socio-demographic and medical questionnaires were used to collect the participants' age, sex, education level (categorised into low, intermediate, or high), practice of a physical activity such as walk (>1h/day) or any sport (yes/no), onset of CV disease during follow-up (yes/no, regrouping heart failure, angina, myocardial infarction, cardiac rhythm disorder, valvulopathy, stroke, arteritis of lower limb) treatments. Level of stress was assessed during the fourth visit using a visual analogue scale from 0 to 10 points. Temporal gap was calculated between the two visits as the median age difference between V4 and V2.

The adolescents' education level at V2 was represented as the highest education level of their parents.

Ethics

The study was conducted in accordance with the Declaration of Helsinki. The protocol was approved by the local ethics committee (Comité de Protection des Personnes Est III, Nancy, France). All participants signed a written informed consent at each visit.

Statistical analysis

Participants' characteristics are described as mean and standard deviation for continuous variables in instances of normal distribution, and otherwise as median and quartiles. Categorical data are presented as numbers and percentages. The differences regarding baseline characteristics between included and non-included participants was assessed using the chi-square test for categorical variables or t-test or non-parametric Kruskal-Wallis test for continuous variables. Due to the significant interaction between the two generations and the eating behaviour scales in some of the adjusted models (see table 1) statistical analyses were run separately for adults and adolescents. The EB dimensions were compared between adults and adolescents using the Wilcoxon test. We also looked at the spearman correlations between each EB dimension.

The associations between each EB dimension and each cardiovascular damages were investigated using mixed linear models with random family effect for continuous variables and generalised linear mixed models with random family effect for categorical variables. The following variables LVM, PWV and IMT were log-transformed to obtain a better residual distribution. Ordinal logistic regression was performed for DD in order to take into account the different grades. Analyses were performed by controlling for the following adjustment variables: age, sex, education level, diabetes, hypertension, temporal gap, BMI, HDL, LDL, triglycerides, physical activity, the other dimensions of EB at the second visit and the onset of CV disease during follow-up. The same analyses were performed with MetS measured at V2 and V4, as outcome. An additional incremented model was run for these last analyses consisting in removing the component of metabolic syndrome.

A mediation analysis was next conducted to explore the causal pathways in case of significant association between eating behaviour dimensions and CV damages (Figure 1). To this end, several mediators related to response and explanatory variables were selected based on the findings of a literature review (29). We hypothesised that the association between EB dimensions and CV damages could be mediated by stress level or energy intake (30). SAS *PROC CAUSALMED* was used, which invokes the causal mediation analysis using regression adjustment methods. The factors adjusted in the mediation analyses were the same as in the main analyses. Three estimators were computed: 1) the direct effect, representing the association between EB dimension and the outcome that is not mediated, 2) the indirect effect, representing the association between EB dimension and the outcome mediated by the potential mediator, 3) the total effect, which is the sum of the direct and indirect effects. The

proportion mediated was calculated as the ratio of the indirect effect to the total effect, multiplied by 100 and was interpreted as mediation when positive or as suppressor when negative (31).

Analyses were performed using SAS (version 9.4, SAS Institute Inc.). A two-sided P-value of <0.05 was considered significant.

Results

Characteristics of the population

The included population consisted of 1109 participants, including 367 families with at least two family members. The included and non-included participants did not differ much appreciably with regard to baseline clinical and demographic characteristics (Supplementary Table 1). Compared to the non-included, the included adults were older, had higher education level and were less likely to smoke. The included adolescents were younger and more often female than non-included adolescents.

The characteristics of the participants at the second and fourth visits are summarised in Table 1. The median follow-up between the two visits was 13.4 years. Among the 916 adults, the median age at visit 2 was 44.7 years with an almost equal number of female and male participants. The adult group included 31.0% of participants with overweight, 7.9% with obesity, and 2.7% with underweight. 58% of the adults practiced a sport. In the adolescent group, there were 8.3% of participants with overweight and no cases with obesity or underweight. 39% of the adolescent practiced a sport. The adolescent group had a median age of 15.2 years and included a higher proportion of female than male participants, and their parents had a higher level of education than in the adult group. The median of the EmE score did not differ between adults and adolescents ($p=0.48$). However, adults had a higher median RE score ($p<0.0001$), and a lower median ExE score ($p=0.0003$) than adolescents. Emotional eating was correlated with restrained eating ($\rho=0.29$, $p<0.001$) and external eating ($\rho=0.43$, $p<0.001$). Restrained eating was not correlated to external eating ($\rho=-0.03$, $p=0.59$).

Longitudinal association between eating behaviour and cardiovascular damages in adults

The EmE was associated with a 38 % increased risk for DD (OR=1.38 [1.05; 1.83]) in the adjusted model in adults (Table 2). The EmE was positively associated with cfPWV ($\beta=0.02$ [0.01; 0.04]) and ExE negatively associated with cfPWV ($\beta=-0.03$ [-0.05; -0.01]).

Longitudinal association between eating behaviour and cardiovascular damages in adolescents

Only the association with the cardiovascular damages cfPWV, cIMT and LVM were assessed in adolescents at V2 due to the relatively low number of cases of DD and MetS at V4 (Table 1). The results presented in Table 2 show that none of EB dimensions was associated with CV damages in adolescents.

Cross-sectional and longitudinal association between eating behaviour and metabolic syndrome in adults

The results of the cross-sectional analysis performed among adults did not demonstrate any association between each of the three dimensions of EB and MetS evaluated at V2 or at V4 (Table 3).

Mediation analysis

In adults, the indirect effect (via stress level) of EmE on DD was significant ($\beta=0.01$, $p=0.005$) (Table 4), indicating that the association between EmE and DD was mediated by stress level. The percentage mediated was 31.9%. Nonetheless, the slight relation between EmE and PWV did not appear to be mediated by stress level.

None of the tested relation appear to be mediated by energy intake measured at V4.

Discussion

The present study showed for the first time that the presence of certain dimensions of EB in initially healthy participants may be associated with specific subclinical cardiovascular damage 13 year later in life, with results differing among adults and adolescents. In adults, EmE was associated with an increased 38% risk of DD 13 years later. Furthermore, stress level appeared to be a mediator of the relationship between EmE and DD. EmE was also positively associated with cfPWV. ExE was negatively associated with PWV but our analyses did not reveal any mediation effect. No associations between EB dimensions and CV damages were observed in adolescent.

Eating behaviour and CV damages

An emotion is a complex set of brain stimuli that affect behavioural response (32). Emotional eaters have a modified EB, characterised by increasing food consumption depending on emotional states. In cross-sectional studies, EmE has consistently been associated with weight

issues, such as overweight and obesity, and is known to be a CV risk factor (33–35). EmE has also been associated with other CV risk factors such as type 2 diabetes, hyperlipidaemia or hypertension (12). Our results, presented here in a longitudinal framework, extend previous findings from cross-sectional studies. Our findings showed a significant increased risk of DD 13 years later related to a higher EmE score. Mediation analysis further showed that stress level is a mediator of the relationship between EmE and DD, explaining 31.9% of this relationship. According to Godet et al. there is an effect of negative emotional situations and stress on the brain's responses to food, and this can influence food consumption (36). Indeed, stress level is associated with changes in appetite as well as food consumption, through activation of the hypothalamic-pituitary-adrenal axis upon increased glucocorticoid synthesis and glucose availability needed to fuel the metabolic demands of stress responses. This may lead to overconsumption, notably of a high-calorie diet, resulting in weight gain (9,37). The reward system may be particularly involved in emotional eating, where eating may reduce anxiety and eating comfort foods may blunt the response to acute stress (36). The emotion regulation interventions might hence prove fruitful in reducing its negative affect, which could in turn reduce the likelihood of overconsumption or binge eating (38). Conversely, there is a body of evidence indicating that EmE is not responsible for greater energy-dense dietary intake (39), likely explaining why high energy intake was not involved as a mediator in the association between EmE and DD in our analysis.

Regarding PWV, Sîrbu et al. (14) showed that arterial stiffness differed in young healthy students. Among those who were physically active on a regular basis, i.e., 3 to 5 times a week, PWV was lower than in the group of sedentary students. In their study, EmE was positively correlated with PWV in sedentary students but not in the group of trained students. In the present study, in our fully adjusted model, we also found a slight and positive relationship between EmE and cfPWV. Nonetheless, we were unable to find any mediators of this relationship. ExE appeared to be negatively associated with cfPWV in adults. This relationship could not be explained by a mediator such as energy intake. This could be due to the small effect size observed, or to the fact that other possible non-studied confusion factors or mediators such as psychological traits may potentially explain this result.

With regard to RE, two cross-sectional studies found that RE was associated with hypertension, CVD, and hyperlipidaemia (12,13). Despite these earlier findings, we were unable to show an association between RE and long-term cardiovascular damages in our

study. However, a limitation of the Hainer et al. study (13), including non-standardised reported morbidity, and the substantial difference in study design and low prevalence of CVD in our population, could explain the incongruity of these findings.

No association were observed between EB and CV damages in adolescents in the current study, this could be due to an insufficient temporal gap in detecting CV damages, as the majority of them were still healthy as young adults, and also the small size of the adolescent group, and therefore lacking power to detect a significant effect. Further research is needing to explore these associations in young people.

EB and MetS

In the Healthy Twin Study, the three dimensions of EB were longitudinally associated with increased risk of MetS (40). However, our study did not find any association between three dimensions of EB and MetS in adults in adjusted models in both long-term and cross-sectional analyses, despite current evidence from the literature. The discrepancies in MetS criteria ($WC \geq 90$ cm for men in the Song et al. study vs. $WC \geq 102$ cm for men in our study), and the difference in statistical analysis (the authors did not take into account the family random effect) may be the source of the disparity in the results.

These results are of interest for public health prevention strategies in cardiovascular diseases. Stress or psychological factors such as depression can predict hypertension, and clinical CV outcomes such as coronary heart disease, heart failure (41), and CV mortality (42). Nonetheless, it is less clear how psychological stress affects CV damages and other clinical outcomes, such as atrial fibrillation (43). Recent systematic reviews of international guidelines states that if screening of stress in patients at high CV risk patients are increasingly mentioned, only few guidelines actually recommend stress management (44,45). We can now assume that not only modulating stress levels but also EmE may be a potentially promising way to prevent the onset of DD later in life. The use of emotion regulation skills through mindfulness-based intervention, including cognitive, behavioural, psychological, and interpersonal therapies could be a good strategy for those patients at risk. Indeed, in current practice this kind of intervention has become widely used to modify EB in obesity (46). Further clinical trial testing strategies to address psychological factors would be worth undertaking.

Besides, since little is known about how EB is associated with long-term CVD, our study allows shedding new light on this topic. Further study on the longitudinal influence of different dimensions EB on cardiovascular outcomes are needed.

Strengths and limitations

The present study featured several strengths. First, the analyses were based on a relatively large, general, and initially healthy population-based cohort with the availability of complete data on eating behaviour, measured by the validated questionnaire with good internal validation in our population. Second, this study was based on quality data owing to the availability of detailed health information and an extensive cardiovascular phenotyping. Third, the prospective design of our study allowed us to investigate for the first time the longitudinal association between EB and CV damage. Some limitations of this study should be noted. First, due to the observational design of our study, it was not possible to address the question of causality. Second, stress level was assessed using a non-validated visual analogue scale, which elicits a subjective response of the stress level, based on a single question. This type of scale, widely used in clinical studies, was chosen in order not to multiply the already high number of questionnaires, to avoid a lassitude due to the completion of the questionnaire and a potential responses bias. Third, if in our analyses the practice of a physical activity was taken into account, we did not have information about the kind of work, thus we are not aware of the sedentary nature of the work. Fourth, this study included initially healthy individuals, and they were still relatively healthy 13 years later. A limited number of participants had hard CV outcomes, such as myocardial infarction . Therefore, we focused on the association between EB and surrogated endpoints, i.e. CV damages. Further studies should assess the magnitude of association with hard clinical endpoints. Fifth, as observed in many other longitudinal cohorts, attrition between the inclusion and the last follow-up may be a potential source of bias. If we did not observed differences between included and non-included participants regarding baseline biological data, it appear that the non-included were few years younger, had a lower level of education, and smoked more. Sixth, this study included individuals from the Lorraine region, one may wonder about the generalization of these results to other populations. Nonetheless, our participants had the same characteristics of another European cohort with the same range of age: the Malmo Preventive Project (47). If some comparable levels of biomarkers were observed between the STANISLAS cohort and the Framingham Heart study (48), the BMI was higher in the later study which could be due to the difference in dietary habits and metabolic factors between the European and North

American population. Even if the STANISLAS cohort population are similar to other cohorts, the results have to be validated in another context and larger cohort.

Conclusion

In summary, we were able to show a longitudinal association between certain dimensions of EB and several cardiovascular damages in adults. In particular, EmE was found to be associated with diastolic dysfunction. Interestingly, this association appeared to be mediated by stress level. EmE was also found to be positively associated with cfPWV. The present findings suggest that, in clinical practice, patients with this emotional eating behaviour should benefit from emotion regulation skills, such as cognitive, behavioural, psychological, and interpersonal therapies, already developed in other fields such as obesity, as well as pharmacological treatments. Those patients should be particularly monitored in order to prevent the development of CV damages later in life.

Author contributions

PR, NG, and JMB designed the fourth visit of the STANISLAS cohort. LM performed the data management of the data. EB and NG supervised the cardiovascular (arterial stiffness and thickness and echocardiography, respectively) assessments. SW, AS, PR, BdLG, JAN designed the present research. AS performed the statistical analysis. AS and SW drafted the manuscript. All authors were involved in the interpretation of the results and the critical review of the manuscript.

All gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

Data availability statement

The data underlying this article can be shared on reasonable request to the corresponding author.

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Table 1. Description of the studied population (n=1109) at visits 2 (V2) and 4 (V4).

	Adults		Adolescents at V2	
	V2	V4	V2	V4
n	916		193	
Age, y	44.7 (39.7-48.7)	58.0 (53.0-62.0)	15.2 (13.4-16.6)	29.0 (27.0-31.0)
Female, n (%)	455 (49.7)	455 (49.7)	111 (57.5)	111 (57.5)
BMI, (kg/m ²)	24.0 (21.7-26.6)	25.6 (23.0-28.6)	19.6 (17.6-21.3)	23.0 (21.1-26.0)
Education level, n (%)				
Low	530 (58.1)	269 (29.4)	85 (44.0)	88 (45.6)
Intermediate	272 (29.8)	463 (50.7)	77 (39.9)	21 (10.9)
High	110 (12.1)	182 (19.9)	31 (16.1)	84 (43.5)
Smokers, n (%)	144 (18.3)	143 (15.7)	19 (11.7)	61 (31.6)
WC, cm	80.0 (71.0-89.0)	90.0 (81.0-99.0)	67.0 (63.0-71.0)	82.0 (74.0-91.0)
LDL, g/L	1.3 ± 0.4	1.4 ± 0.3	1.0 ± 0.3	1.2 ± 0.3
HDL, g/L	0.6 ± 0.2	0.6 ± 0.1	0.6 ± 0.1	0.6 ± 0.1
Triglycerides, g/L	0.9 (0.6-1.2)	1.0 (0.7-1.3)	0.7 (0.5-0.9)	0.8 (0.6-1.1)
Fasting glucose, g/L	0.9 (0.8-1.0)	0.9 (0.8-1.0)	0.9 (0.8-0.9)	0.8 (0.8-0.9)
Diabetes mellitus, n (%)	10 (1.1)	54 (5.9)	0	1 (0.5)
Hypertension, n (%)	31 (3.4)	32 (3.5)	0	1 (0.5)
Onset of CV disease during follow-up, n (%)		146 (15.9)		11 (5.7)
MetS, n (%)	75 (8.2)	271 (29.7)	0	6 (3.1)
cIMT, µm		653.5 (566.4-748.0)		541.0 (499.5-541.0)
cfPWV, m/s		8.5 (7.7-9.8)		7.0 (6.6-7.8)
LVM, g/m ²		34.1 (28.9-41.4)		28.8 (24.6-33.1)
DD, n (%)		219 (23.9)		1 (0.5)
Emotional Eating score	1.6 (1.2-2.3)		1.5 (1.2-2.2)	
Restrained eating score	2.6 (1.8-3.3)		1.8 (1.2-2.6)	
External eating score	2.6 (2.2-3.0)		2.7 (2.4-3.2)	

Continuous variables presented as mean ± SD or median (Q1 - Q3), as appropriate. Categorical variables are presented as number and percentage. BMI – body mass index; WC – waist circumference; LDL – low density lipoprotein; HDL – high density lipoprotein; MetS – metabolic syndrome; cIMT – carotid intima-media thickness; cfPWV – carotid-femoral pulse-wave velocity; LVM – left ventricular mass; DD – diastolic dysfunction

Table 2. Longitudinal association between the three dimensions of eating behaviour and cardiovascular damages in the adjusted model in adults (n=916) and in adolescents (n=193) at V2.

	cfPWV - β (95% CI)		cIMT - β (95% CI)		LVM - β (95% CI)		DD - OR (95% CI)
	Adults	Adolescents	Adults	Adolescents	Adults	Adolescents	Adults
Emotional eating	0.02 [0.01; 0.04] P=0.01	0.02 [-0.01;0.05] P=0.18	-0.007 [-0.03;0.01] P=0.47	0.01 [-0.02;0.05] P=0.46	0.02 [-0.005;0.04] P=0.12	0.02 [-0.04;0.08] P=0.59	1.38 [1.05;1.83] P=0.02
	P for interaction 0.84		P for interaction 0.45		P for interaction 0.08		-
Restrained eating	-0.007 [-0.02; 0.006] P=0.29	-0.01 [-0.04;0.015] P=0.37	0.003 [-0.01;0.02] P=0.73	-0.002 [-0.03;0.03] P=0.93	-0.02 [-0.04; 0.005] P=0.13	0.04 [-0.007;0.09] P=0.09	0.81 [0.64;1.83] P=0.07
	P for interaction 0.47		P for interaction 0.05		P for interaction 0.002		-
External eating	-0.03 [-0.05; -0.01] P<0.001	-0.03 [-0.08;0.01] P=0.11	0.01 [-0.01;0.03] P=0.41	0.03 [-0.02;0.07] P=0.30	0.02 [-0.02;0.05] P=0.32	-0.04 [-0.11;0.04] P=0.29	0.90 [0.62;1.31] P=0.58
	P for interaction 0.78		P for interaction 0.39		P for interaction 0.009		-

β – regression coefficient; OR – odds ratio; 95% CI – 95% confidence interval. cfPWV - carotid-femoral pulse-wave velocity; cIMT – carotid intima-media thickness; LVM – left ventricular mass; DD – diastolic dysfunction.

Model were adjusted for age, sex, education level, diabetes, hypertension, temporal gap, BMI, HDL, LDL, triglycerides, physical activity, and the other EB dimensions at the second visit, and the onset of CV disease during FUP.

Table 3. Cross-sectional and longitudinal association between the three dimensions of eating behaviour and metabolic syndrome (MetS) in adults (n=916): odds ratio (OR) 95% confidence interval (CI).

		Metabolic syndrome at V2 OR (95% CI) P	Metabolic syndrome at V4 OR (95% CI) P
Emotional eating	M1	0.87 [0.58 ; 1.31] P=0.74	1.21[0.91;1.6] P=0.19
	M2	1.17 [0.91 ; 1.51] P=0.50	1.17[0.91;1.51] p=0.23
Restrained eating	M1	1.08 [0.75 ; 1.57] P=0.68	1.05[0.84;1.31] P=0.66
	M2	1.11 [0.78 ; 1.57] P=0.55	1[0.81;1.24] P=0.97
External eating	M1	0.91 [0.63 ; 1.32] P=0.62	0.91 [0.63 ; 1.32] P=0.62
	M2	1.19 [0.69 ; 2.05] P=0.53	0.90 [0.65 ; 1.26] P=0.55

OR – odds ratio; 95% CI – 95% confidence interval.

Models 1 were adjusted for age, sex, education level, diabetes, hypertension, temporal gap, bmi, HDL, LDL, triglycerides, physical activity, the other dimensions of EB at the second visit, and the onset of CV disease during FUP.

Models 2 were models 1 after excluding criteria of metabolic syndrome.

Table 4. Mediation analysis of the association between eating behaviour and cardiovascular outcome in adults (n=916)

Mediator	Tested Association	Total Effect β (95% CI)	Natural Direct Effect β (95% CI)	Natural Indirect Effect β (95% CI)	Percentage Mediated (%)
Stress level	EmE - DD	0.04 [-0.001; 0.07] p=0.06	0.03 [-0.01; 0.06] p=0.19	0.01 [0.003; 0.02] p=0.005	31.9
Energy intake		0.03 [-0.01; 0.06] p=0.06	0.03 [-0.01; 0.06] p=0.06	0.002 [-0.001; 0.01] p=0.30	4.7
Stress level	EmE - cfPWV	0.006 [-0.008; 0.02] P=0.37	0.006 [-0.008; 0.02] P=0.37	0.002 [-0.001; 0.004] P=0.27	17.9
Energy intake		0.01 [-0.0006; 0.026] P=0.06	0.01 [-0.0006; 0.026] P=0.06	-0.0002 [-0.001; 0.0009] P=0.77	-1.3
Energy intake	ExE - cfPWV	-0.13 [-0.03; 0.004] p=0.14	-0.13 [-0.03; 0.004] p=0.14	0.0001 [-0.003; 0.003] p=0.93	-0.9

β – regression coefficient; 95% CI – 95% confidence interval. DD – diastolic dysfunction; cfPWV – carotid-femoral pulse-wave velocity; LVM – left ventricular mass.

¹ Model were adjusted for age, sex, education level, diabetes, hypertension, temporal gap, bmi, HDL, LDL, triglycerides, physical activity, the other dimensions of EB at the second visit, and the onset of CV disease during FUP.

Figure legend

Graphical abstract

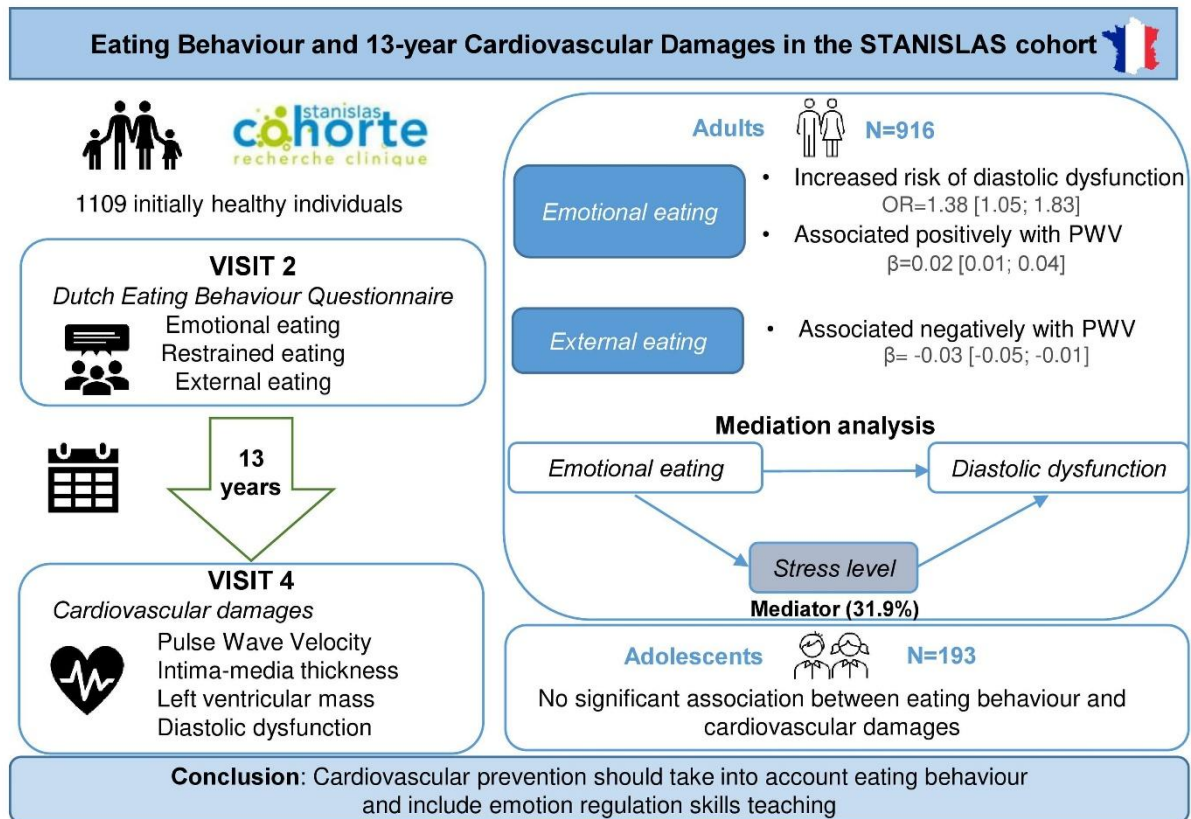
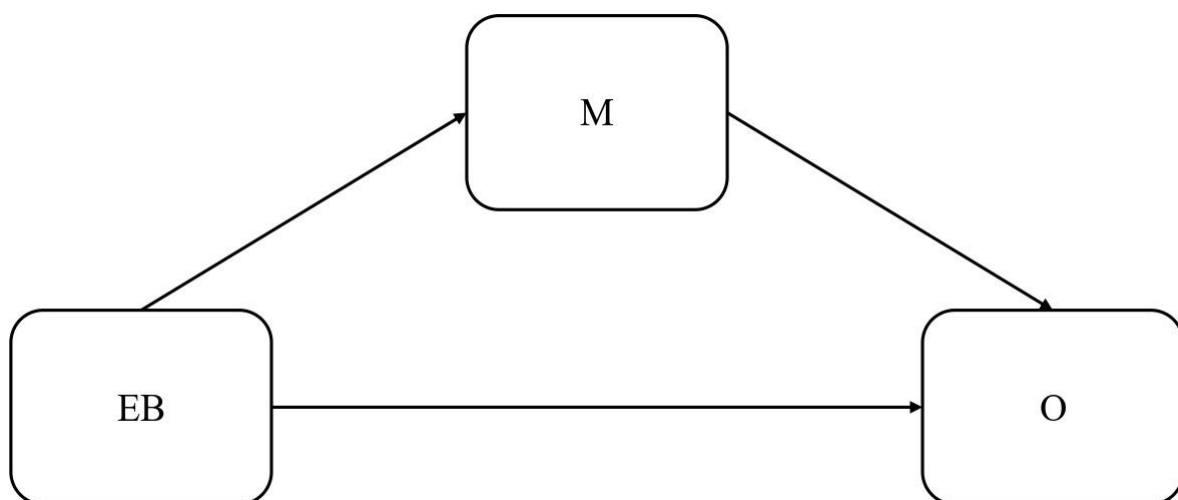
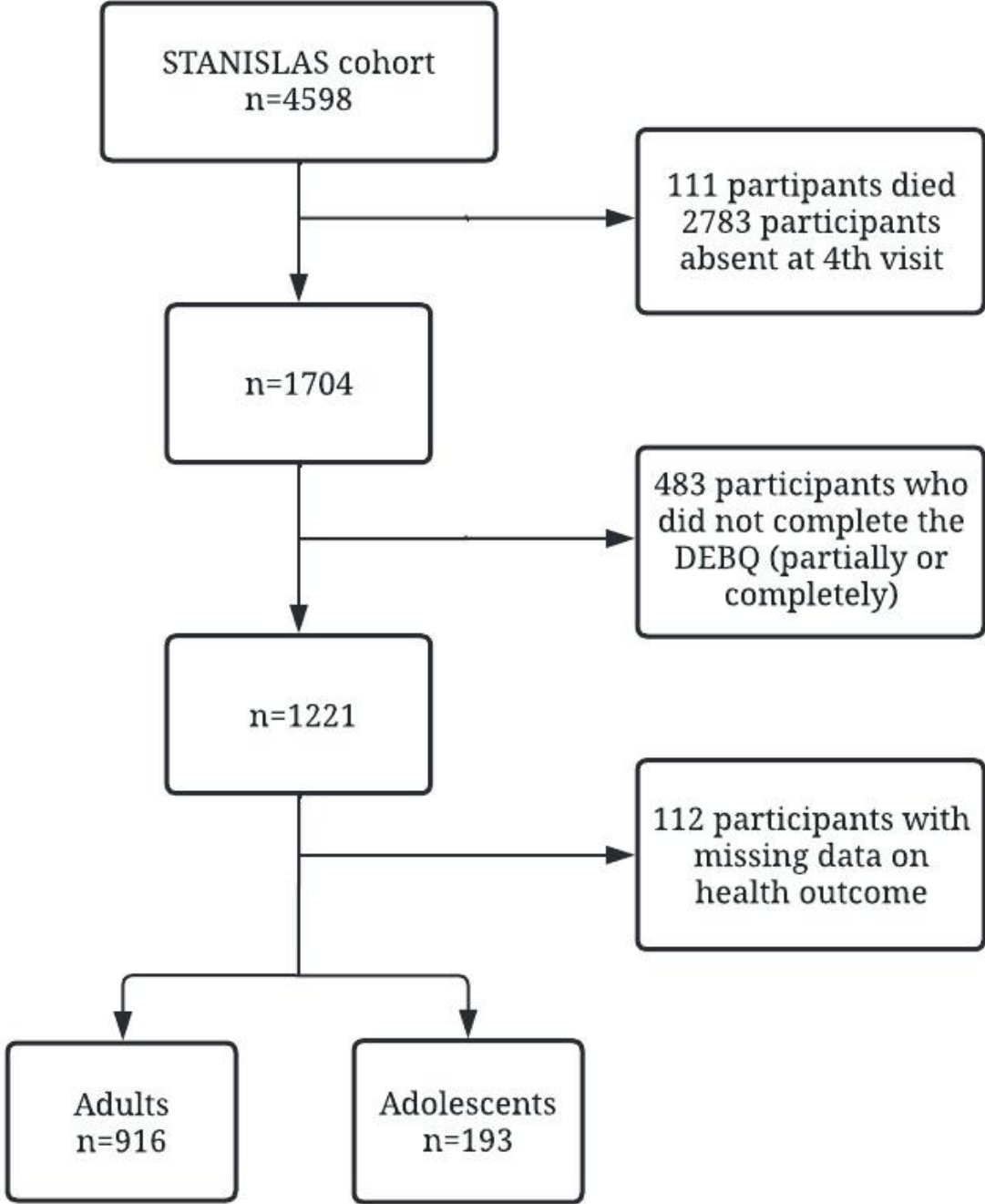


Figure 1. Model depiction of hypotheses. EB – eating behaviour. O – outcome (cardiovascular damages here). M – Mediator.



Supplementary materials legend

Supplementary figure 1. Study flowchart.



Supplementary table 1. Baseline characteristics of the included and non-included participants

¹Compared by using chi-square, or t-test or Kruskal-Wallis test as appropriate.

	Adults		p-value ¹	Adolescents		p-value ¹
	Included (n=916)	Non included (n=1965)		Included (n=193)	Non included (n=1524)	
Age, y	40.2 (35.4 - 44)	37.7 (20.2- 42.1)	<0.001	11.1 (9.8- 12.2)	12.3 (10.4- 14.6)	<0.001
Male, %	50%	49%	0.46	42%	54%	0.003

*72% of the data are missing

BMI – Body Mass Index, WC – waist circumference, LDL – low density lipoprotein, HDL – high density lipoprotein;

BMI, (kg/m ²)	23.2 (20.9 – 25.8)	23.1 (20.7- 25.9)	0.72	16.7 (15.3- 18.5)	18.1 (16.2- 20.4)	<0.001
Education Level, %			0.01			0.20
Low	70%	74%		44%	57%	
Intermediate	21%	19%		40%	28%	
High	9%	7%		16%	15%	
Smokers, n (%)	13%	26%	<0.001	*	*	
WC, cm	78 (70-87)	77 (69-87)	0.40	58 (55-63)	63 (58-69)	<0.001
LDL, g/L	1.4 ± 0.4	1.4 ± 0.4	0.35	1.2 ± 0.3	1.2 ± 0.3	0.19
HDL, g/L	0.5 ± 0.1	0.5 ± 0.1	0.02	0.6 ± 0.1	0.5 ± 0.1	0.03
Triglycerides, g/L	0.8 (0.6-1.2)	0.8 (0.6-1.2)	0.03	0.6 (0.5- 0.9)	0.6 (0.5-0.9)	0.97
Fasting glucose, g/L	0.9 (0.8-0.9)	0.9 (0.8-0.9)	0.30	0.9 (0.8- 0.9)	0.9 (0.8-0.9)	0.75

Supplementary table 1. Baseline characteristics of the included and non-included participants

¹Compared by using chi-square, or t-test or Kruskal-Wallis test as appropriate.

*72% of the data are missing

BMI – Body Mass Index, WC – waist circumference, LDL – low density lipoprotein, HDL – high density lipoprotein;