The Journal of Nutrition
Nutrition and Disease

Maternal Pregnancy Diet Quality Is Directly Associated with Autonomic Nervous System Function in 6-Month-Old Offspring

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ABSTRACT

Background: Many pregnant women are consuming diets of poor overall quality. Although many studies have linked poor prenatal diet quality to an increased risk of specific diseases in offspring, it is not known if exposure to poor prenatal diet affects core neurophysiological regulatory systems in offspring known to lie upstream of multiple diseases.

Objective: We aimed to examine the association between prenatal diet quality and autonomic nervous system (ANS) function in infants at 6 mo of age.

Methods: Data from 400 women (aged >18 y, with uncomplicated pregnancies) and their infants participating in the Maternal-Infant Research on Environmental Chemicals-Infant Development cohort were used to investigate links between prenatal diet quality and infant ANS function at 6 mo of age. Prenatal diet quality was assessed using the Healthy Eating Index (2010), calculated from a validated FFQ completed by women during the first trimester. Infant ANS function was measured using 2 assessments of heart rate variability (HRV) including root mean square of successive differences (RMSSD) and SD of N-N intervals (SDNN). Associations were analyzed before and after adjustment for socioeconomic status, maternal depression symptoms, maternal cardiometabolic dysfunction, breastfeeding, and prenatal smoking.

Results: Poorer prenatal diet quality was associated with lower infant HRV assessed using RMSSD (B: 0.07; 95% CI: 0.01, 0.13; $R^2 = 0.013$) and SDNN (B: 0.18; 95% CI: 0.02, 0.35; $R^2 = 0.011$). These associations remained significant after adjustment for confounding variables [RMSSD: B: 0.09; 95% CI: 0.003, 0.18; squared semipartial correlation (sp^2) = 0.14 and SDNN B: 0.24; 95% CI: 0.0, 0.49; $sp^2 = 0.13$].

Conclusions: In a large cohort study, poorer prenatal diet quality was associated with lower offspring HRV, a marker of decreased capacity of the ANS to respond adaptively to challenge. Therefore, poor prenatal diet may play a significant role in the programming of multiple organ systems and could increase general susceptibility to disease in offspring. *J Nutr* 2020;150:267–275.

Keywords: prenatal programming, maternal diet, neuropsychiatric disorders, developmental origins of health and disease, biomarkers, pregnancy, diet quality

Introduction

Approximately half of all adults consume diets of poor overall quality [such as a Western-style diet, low in nutrients, and high in fats and sugars (1–3)], which can contribute to an increased risk of a range of noncommunicable diseases (1, 2). Women of childbearing age are no exception, because the majority enter pregnancy consuming a diet of suboptimal overall quality (4–6). Because organ systems rapidly develop prenatally, fetal exposure to poor prenatal diet has the potential to alter the development of these systems and increase offspring disease susceptibility (7, 8).

The developmental origins of health and disease hypothesis posits that prenatal and early postnatal environments affect health and disease risk throughout life (9, 10). Studies in humans have consistently reported links between poor prenatal diet and increased risk of adverse offspring outcomes including obesity (11), cardiometabolic problems (12–14), and psychopathology

Manuscript received July 15, 2019. Initial review completed August 15, 2019. Revision accepted August 28, 2019.
First published online October 1, 2019; doi: https://doi.org/10.1093/jn/nxz228.

(15, 16) in children ≤6 y of age. Factors associated with a poor prenatal diet, including maternal obesity, have also been linked to a host of offspring health problems in adulthood (14, 17, 18).

Studies in nonhuman animal models suggest that exposure to a diet low in nutrients and high in fats and sugars during pregnancy has detrimental effects on offspring cardiac morphology (19, 20), metabolic functioning (21, 22), and neurodevelopment (23–25). This research has also noted alterations in set-points within systems that coordinate hormonal and inflammatory responses to stressors, which can affect the functioning of multiple organ systems and increase the risk of a variety of chronic diseases (23, 26–28).

Despite these findings, studies in humans have focused mainly on links between exposure to poor prenatal diet quality and risk of pathology in individual organ systems or single diseases. This work has generally overlooked the comorbid nature of many chronic diseases (e.g., cardiovascular disease and depression) as well as the impact of prenatal diet on the development of the more basic neurophysiological regulatory systems that lie upstream of *multiple* chronic diseases in offspring.

Investigating how prenatal diet quality affects the development of physiological regulatory systems can provide a more complete understanding of the role of prenatal diet in offspring disease propensity in general and move the field closer to an understanding of the mechanisms through which poor prenatal diet may affect offspring development in humans.

The autonomic nervous system (ANS) is a core regulatory system that functions to maintain homeostasis across organ systems by coordinating adaptive responses to external environmental and internal physiological demands (29). ANS function can be assessed by measuring the variability between interbeat intervals of the heart, or heart rate variability (HRV) (30, 31). Greater HRV reflects a more flexible ANS capable of coordinating adaptive responses to a range of environmental challenges (29, 32). Conversely, low HRV is suggestive of a more rigid system with a limited physiological capacity to respond to stressors (33, 34).

Given its central role in homeostatic maintenance, autonomic dysfunction is linked to a host of diseases and comorbid conditions across the life span (35). Indeed, low HRV is linked to poorer regulatory capacity in infants and toddlers (36, 37), cardiovascular and mental health problems in children (38, 39), precedes future cardiovascular events in adults (40), is directly related to disease severity (41), and is a key risk factor for all-cause mortality (35).

The development of the ANS begins early in the first trimester and autonomic innervation of organ systems progresses rapidly throughout gestation (36, 42). Although ANS development appears to be sensitive to intrauterine conditions associated with maternal stress [see e.g., (43) for a review], no studies have examined associations between overall prenatal diet quality and offspring ANS development. The few studies that have examined dietary influences and offspring HRV have examined individual nutrients in isolation [vitamin B-12 (44), zinc (45), or omega-3 fatty acids (46)], and have used small or highly selected samples (43, 44).

Given this background, investigating whether a modifiable exposure such as prenatal diet is linked to an objective measure of ANS activity in offspring is important to our understanding of the mechanisms underlying links between adverse prenatal exposures and disease risk. We set out to examine the link between overall prenatal diet quality and HRV, an important predictor of disease risk and a well-validated, objective biomarker of ANS function, in a population-based cohort of Canadian mothers and their infants.

Methods

Sample

The Maternal-Infant Research on Environmental Chemicals (MIREC) study is a population-based longitudinal pregnancy cohort that recruited pregnant women from prenatal clinics (mean ± SD gestational age at recruitment 11.99 ± 1.5 wk) between 2008 and 2011 from across Canada (Vancouver, Edmonton, Winnipeg, Sudbury, Toronto, Hamilton, Kingston, Ottawa, Montreal, and Halifax). Women were eligible to participate if they were fluent in English or French, >18 y of age, planned to deliver locally, and agreed to provide a cord blood sample. Women were excluded if they were carrying a fetus with a known abnormality, had any medical complications, or reported any history of recreational drug use (47).

The current study is a longitudinal cohort study that used outcome data from the MIREC-Infant Development (MIREC-ID) substudy (an in-depth clinical assessment of $n = 400$ infants), which was designed to follow-up and assess development in the 6-mo-old infants (mean ± SD age: 6.7 ± 0.83 mo) of women that participated in the original MIREC study. MIREC infants were eligible to participate in the MIREC-ID substudy if they were a singleton and free of congenital birth defects or neurological disorders (for demographic comparison of MIREC and MIREC-ID infants, see **Supplemental Table 1**). Women provided written consent before participation and study procedures were approved by research ethics boards at Health Canada and all testing sites.

Measures

Predictor: prenatal diet quality.

The assessment of overall prenatal diet quality involved 2 steps. First, an FFQ (48) asked women to report on serving sizes and frequency of foods consumed in the past month. Second, the Healthy Eating Index-2010 (HEI) (49) used information obtained from the FFQ to calculate an overall diet quality score.

(1) *FFQ:* A validated semiquantitative short FFQ was used by women to report on the intake of 46 food items across 6 subgroups (vegetables; fruits; meat, poultry, fish, and alternatives; dairy products; grain products; and other foods) (48). The FFQ was administered between 16 and 21 weeks of gestation. Previous studies have shown that short-form FFQs are valid in assessing overall diet quality (50–52) and FFQs with a similar number of items have previously been used by the HEI to calculate total diet quality (53).

(2) *HEI:* Based on the dietary intake information obtained from the FFQ, the HEI was used to estimate total diet quality (54)

Supported by Canadian Institutes of Health Research grant MOP-81285. The MIREC Research Platform is supported by the Chemicals Management Plan of Health Canada and the Ontario Ministry of the Environment. JEK is supported by the Vanier Graduate Scholarship Program.
Author disclosures: JEK, KB, TEA, GM, NP, JRS, LAF, CS, BA, NM, and RJVL, no conflicts of interest.
Supplemental Tables 1 and 2 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/jn/.
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Abbreviations used: ANS, autonomic nervous system; B, unstandardized β; ECG, electrocardiogram; HEI, Healthy Eating Index-2010; HRV, heart rate variability; MIREC, Maternal-Infant Research on Environmental Chemicals; MIREC-ID, Maternal-Infant Research on Environmental Chemicals-Infant Development; RMSSD, root mean square of successive differences; SDNN, SD of N-N intervals; sp^2, squared semipartial correlation; VIF, variance inflation factor.

[see (55) for the methods used to convert FFQ data to HEI scores]. We used the HEI scoring algorithm method because it is the recommended method to use when the goal is to examine the association between HEI diet scores based on dietary data from an FFQ and "another health outcome variable." The HEI assesses diet quality according to national dietary guidelines and has been validated in pregnant women (54). The HEI calculates 9 "adequacy" subcomponents (total fruit, whole fruit, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, and fatty acids). The HEI also contains 3 subcomponents comprised of foods that should be consumed in moderation [refined grains, sodium, and empty calories (from saturated fats and added sugars)]. These items are reverse-scored and so higher scores indicate less consumption of these "moderation" components. The sum of all subcomponents yields an HEI total score (maximum score = 100). Higher overall scores indicate greater consumption of adequacy components and less consumption of the moderation components. The HEI total score was used in our analyses. Our HEI total scores were consistent with those from other samples of pregnant women (56, 57).

Outcome: ANS function: time-domain HRV.

HRV is a measure of the variability between adjacent normal R waves (N-N intervals) acquired from an electrocardiogram (ECG). Seven electrodes were placed on the infant's chest at the following locations: *1*) right clavicle, lateral to the sternum; *2*) left clavicle, lateral to the sternum; *3*) left clavicle, at the mid-clavicular line; *4*) lower right chest wall; *5*) fourth intercostal space, at the right sternal edge; *6*) sixth rib, at the left mid-clavicular line; and *7*) fifth intercostal space, at the left axillary line. HRV was obtained during a short anthropometric assessment and throughout 2 validated tasks [tilt procedure (58) and arm restraint task (59), see **Supplemental Table 2** for protocols] that are commonly used to invoke fluctuations in HRV. HRV was averaged across tasks to obtain a global measure of HRV reactivity. Therefore, lower HRV throughout the challenges reflects maladaptive, diminished autonomic flexibility (33, 60, 61). Recordings were obtained using the MARS ambulatory ECG system (GE Healthcare) and the mean ± SD ECG recording length was 43 ± 21.3 min.

The 2 most utilized time-series measures of HRV—the SD of all N-N intervals (SDNN) and the root mean square of successive differences (RMSSD) (62)—were used in analyses. SDNN assesses reactions to environmental stimulation and is considered a gold-standard index of the cardiovascular response to changing demands (63). RMSSD reflects the beat-to-beat variance in heart rate and is the primary time-domain measure of parasympathetically mediated vagal tone (60). All ECGs were examined for artifacts by a cardiologist. Data were excluded if >2% of the recordings had noise (n = 10 excluded—no significant differences were observed on any of our demographic variables between the 390 dyads who were analyzed and the 10 that were excluded).

Confounding variables.

Potential confounding variables were included in our adjusted model if previous empirical evidence existed linking this variable to both our predictor and our outcome.

Maternal cardiometabolic dysfunction. To assess prenatal exposure to maternal metabolic dysfunction we used prepregnancy BMI (64). Maternal prepregnancy BMI (in kg/m^2) was calculated at the first-trimester visit by dividing self-reported prepregnancy weight by height squared obtained from medical charts. BMI was examined categorically (underweight: BMI $\leq$ 18.5; normal: 18.5 $<$ BMI $\leq$ 25; overweight: 25 $<$ BMI $\leq$ 29; obese: BMI $>$ 30) (65).

Maternal depression symptoms. Depressive symptoms were assessed when offspring were 6 mo of age using the 10-item Center for Epidemiologic Studies–Depression (short-form) scale. Women rated depressive symptoms experienced during the previous week using a 4-point scale (0 = "rarely" to 3 = "all of the time"), with higher scores representing more symptoms of depression (66).

Household income. Women self-reported their total household income before tax on a 10-point scale: "less than $10,000" and increases in $10,000 increments to >$90,000 (Canadian dollars).

Prenatal smoking. Self-reported smoking was captured at the third prenatal visit and was defined categorically: never smoked, former smoker, or smoke currently/quit in pregnancy.

Sex. Offspring sex was included as a confounder because programming effects of prenatal exposure to poor diet may differ depending on sex (67). Sex was also examined as a moderator of these links.

Breastfeeding. Breastfeeding was assessed at the 6-mo follow-up visit. It is recommended that healthy term infants should be breastfed exclusively for the first 6 mo (68). Therefore, a variable that dichotomized infants into those that were not breastfed or breastfed for <6 mo and those that were breastfed exclusively for 6 mo was included as a confounding variable.

Recording duration. Because of the variability in recording length, this was also adjusted for as a confounding variable.

Statistical analyses

Differences between women participating in MIREC compared with the MIREC-ID substudy were examined using independent-sample t tests and chi-squared tests. Two linear regression models were used to examine associations between the predictor (overall prenatal diet quality) and each outcome variable (RMSSD, SDNN). We also tested an offspring sex × prenatal diet quality interaction. Multivariable linear regression models were used to examine associations assessed in our unadjusted models with the addition of each confounding variable. The unique contribution of each variable (the predictor and each confounding variable) to our outcomes in the fully adjusted models was examined using squared semipartial correlations. All statistical tests were 2-tailed and statistical significance was set at $\alpha = 0.05$. Variance inflation factors (VIFs) were examined in the adjusted models to check for multicollinearity. VIF values were <10, therefore no multicollinearity was observed between our variables. To assess the impact of a 1-point change in diet on HRV, we present unstandardized β (B) values. Hypotheses were tested using 2-tailed significance tests ($P < 0.05$). All analyses were conducted using SPSS version 23 (IBM).

Results

Sample characteristics

The characteristics of the MIREC-ID study sample are presented in **Table 1**. Table 1 includes information for all dyads with infant HRV data (n = 400); however, 10 dyads had to be excluded from further analyses owing to excessive noise in the ECG trace, therefore analyses are conducted for n = 390 dyads. The mean ± SD age of mothers was 32 ± 4.7 y and 41% had an overweight/obese prepregnancy BMI. Mean ± SD maternal prenatal diet quality (HEI) score was 72.1 ± 8.1 (min = 42.9, max = 89.0) and 75.1% of women in our sample had scores in the "average" prenatal diet quality range for pregnant women [(60.0–79.9), scores >80 are considered "adequate" (57)]. The majority of women in this sample were married (n = 382, 95.2%) and were college/university educated (n = 384, 87.4%). Infants were born at mean ± SD 39.2 ± 1.4 weeks of gestation and tested at 6.7 ± 0.83 mo. Demographic characteristics of women participating in MIREC-ID were also similar to those of women participating in the nationally representative

TABLE 1 Socioeconomic characteristics of women and their infants from the Maternal-Infant Research on Environmental Chemicals-Infant Development sample and infant RMSSD and SDNN for each characteristic[1]

Demographic variables	Maternal/family characteristics ($n = 400$)	Infant RMSSD	Infant SDNN
Diet quality[2]	72.1 ± 8.1	—	—
Age, y	32 ± 4.7	—	—
Marital status			
Married/common law	382 (95.2)	15.2 ± 4.8	38.0 ± 15.5
Divorced/separated	3 (0.8)	14.5 ± 4.9	35.0 ± 15.1
Single	15 (3.8)	15.6 ± 3.7	37.9 ± 9.01
Household income,[3] $			
<50,000	71 (17.8)	15.6 ± 5.3	40.4 ± 17.1
50,001–100,000	186 (46.5)	15.1 ± 5.1	38.8 ± 14.2
>100,000	143 (35.8)	15.4 ± 4.3	38.7 ± 14.8
Education			
High school or less	50 (12.6)	15.9 ± 4.9	38.0 ± 13.1
College educated/university degree	348 (87.4)	15.1 ± 4.9	39.2 ± 15.3
Birth country			
Canada	349 (87.3)	15.2 ± 4.8	38.5 ± 14.9
Elsewhere	51 (12.7)	15.9 ± 5.4	42.6 ± 14.8
Breastfeeding			
Yes	380 (96.0)	15.3 ± 3.7	39.2 ± 15.1
Never or only once	16 (4.0)	14.3 ± 4.9	35.6 ± 11.9
Smoking			
Never	265 (66.3)	15.3 ± 4.9	39.1 ± 15.5
Former	102 (25.5)	15.5 ± 4.8	39.4 ± 13.3
Current/quit in pregnancy	33 (8.3)	14.3 ± 4.2	37.2 ± 15.8
Prepregnancy BMI, kg/m^2			
Underweight	7 (1.9)	15.4 ± 5.9	52.4 ± 27.5
Normal	210 (56.9)	15.2 ± 4.5	38.3 ± 13.5
Overweight	86 (23.3)	15.3 ± 4.9	39.1 ± 17.4
Obese	66 (17.9)	15.6 ± 5.3	38.9 ± 14.5
Depressive symptoms (CES-D10)[4]	6.0 ± 4.0	—	—
Infant characteristics			
Age, mo	6.7 ± 0.83	—	—
Heart rate	140.6 ± 10.4	—	—
RMSSD	15.3 ± 4.9	—	—
SDNN	39.0 ± 15.9	—	—
Birth weight, g	3497.7 ± 497.4	—	—
Gestational age, wk	39.2 ± 1.4	—	—
Male	205 (51.2)	—	—

[1]Values are *n* (%) or mean ± SD. Infant RMSSD or SDNN did not differ in relation to any of our demographic variables. CES-D10, Center for Epidemiologic Studies Depression scale (short form); RMSSD, root mean square of successive differences; SDNN, SD of N-N intervals.
[2]Diet quality scores between 60 and 79.99 are of "average" quality in pregnant women; in our sample 75.1% consumed a diet of average quality.
[3]Canadian dollars.
[4]Maximum possible score on the CES-D10 is 30 points. Eighty-nine percent of the sample had scores ≤ 0, and scores >10 are considered a cutoff for depression risk.

population-based Canadian Health Measures Survey (Cycle 1 2007–2009) (47).

Analyses

In unadjusted associations, a significant positive association between poor overall prenatal diet quality and lower HRV assessed using both RMSSD and SDNN measures (**Figure 1** and **Table 2**) was observed. Associations remained significant after adjustment for confounders (**Table 3**). Variance accounted for by prenatal diet did not change in adjusted models. The potential presence of heteroscedasticity was tested for using the Breusch–Pagan test and White's test. Both tests were nonsignificant ($P = 0.21$, $P = 0.38$), therefore there did not appear to be any violations of the homoscedasticity assumption. Finally, offspring sex did not modify these relations.

Discussion

In this large sample of Canadian mothers and their infants, maternal prenatal diet quality was associated with lower offspring HRV even after adjustment for known confounders. To our knowledge, this study is the first to observe a link between overall prenatal diet, a common and modifiable exposure, and HRV, a well-validated objective marker of ANS function and disease risk. These findings suggest that prenatal diet may play a role in the programming of multiple organ systems in offspring.

The high rates of consumption of diets of poor quality in women of childbearing age [~60% (5)] highlight the importance of investigating its link to core physiological regulatory systems in offspring such as the ANS. Despite the potentially modifiable nature of this exposure, only 4 studies to

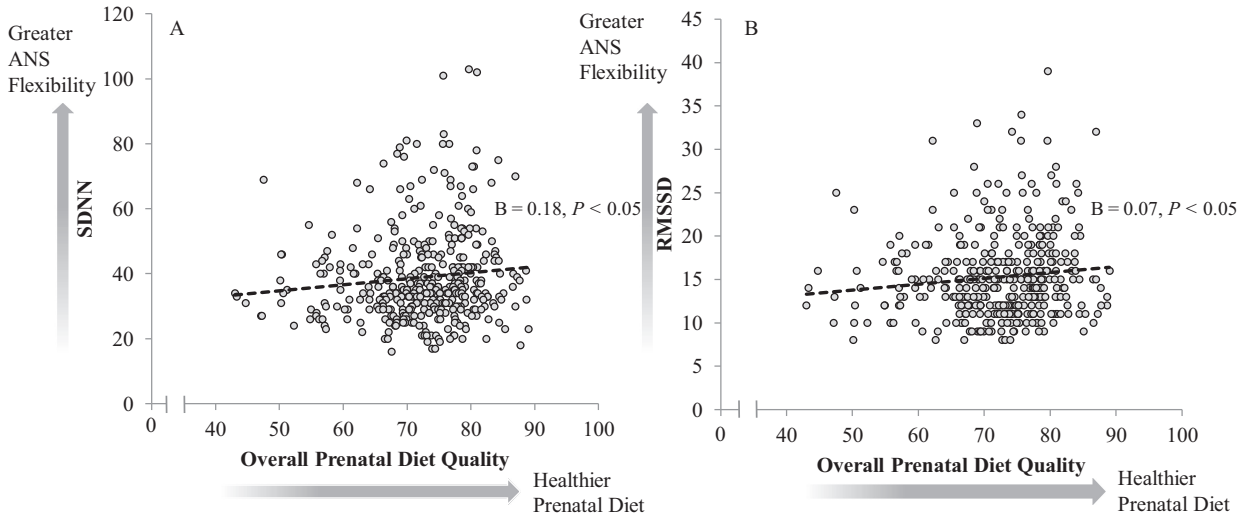

FIGURE 1 Unadjusted associations between overall prenatal diet quality and offspring SDNN (A) and offspring RMSSD (B). ANS, autonomic nervous system; B, unstandardized β; RMSSD, root mean square of successive differences; SDNN, SD of N-N intervals.

our knowledge have investigated associations between prenatal nutrition and diet exposures and offspring ANS function. Lower HRV measured during gestation was observed in the fetuses of adolescent mothers deficient in zinc in the third trimester (45). Lower HRV was also noted in 5-y-old children born to women low in vitamin B-12 during pregnancy from urban south India (44). Conversely, offspring of women that consumed healthier carbohydrates prenatally exhibited a trend toward higher HRV ($P = 0.06$) (69), and greater HRV was noted in the infants of women supplemented prenatally with ω-3 fatty acids (46). However, the utilization of small and highly selected samples or restriction to single macro- or micronutrient components limits the generalizability and clinical utility of these findings. In addition, because nutrients have synergistic effects on development, focusing on overall prenatal diet quality could reflect the effect of multiple nutrient imbalances on offspring ANS function (70).

ANS development appears to be sensitive to intrauterine conditions. Studies examining proxies of intrauterine adversity [e.g., survivors of very low birth weight (<1500 g)] have noted poorer autonomic functioning in offspring (71). Maternal prenatal mental disorders (72–77) and substance abuse (78–83) may also affect offspring HRV. However, the proportions of women with mood/anxiety disorders [affecting 12–15% of women prenatally (84, 85)], substance use problems [affecting 1–14% of women prenatally (86)], and who have very-low-birth-weight infants [<1% of births (87)] are much smaller than for those consuming diets of poor overall quality. In addition, the vast majority of these findings have been reported in neonates (72–75, 78, 80–83), and because ANS development continues throughout infancy (36) it has been unclear whether these associations persist beyond the neonatal period.

TABLE 2 Unadjusted associations between overall prenatal diet quality and offspring heart rate variability[1]

	B (95% CI)	
	RMSSD	SDNN
Prenatal diet quality	0.07 (0.01, 0.13)	0.18 (0.02, 0.35)
R^2	0.013	0.011

[1] B, unstandardized β; RMSSD, root mean square of successive differences; SDNN, SD of N-N intervals.

Although the mechanisms by which prenatal overall diet affects offspring autonomic function are not known, they could occur through fetal alterations in the development of central regulators of ANS activity. In nonhuman animal models, the periventricular nucleus of the hypothalamus, the mesocorticolimbic dopamine system (88, 89), and the prefrontal cortex (90), all of which mediate autonomic cardiovascular control (32), are adversely affected in offspring exposed to high-fat diets prenatally (21, 90, 91). Other studies have observed prenatal nutritional influences on epigenetic alterations in genes integral to ANS development. Indeed, *Mash1* mRNA was significantly reduced in the offspring of dams fed a high-fat diet prenatally (25). Alterations in genes laying the foundation for ANS development and adverse development of important brain areas known to modulate cardiovascular control could reflect a reduced capacity to adaptively modulate physiological resources in response to challenges. This is consistent with work that observed associations between prenatal adversity and ANS function when the latter was measured during tasks designed to induce adaptive changes in HRV. Prenatal adversity may program differences in regulatory physiology that are more likely to be detected when the system is challenged, relative to quiet rest (76, 91). Indeed, exposure to early-life adversity has been linked to a blunted stress response (92) and dysregulated stress reactivity predicts a host of health problems later in life (93). As a result, measuring ANS activity during exposure to stressors (as done in the current study) may be important because this could reflect a diminished capacity of the system to respond effectively to challenges.

Although the goal of the current study was to determine if a link exists between overall diet quality and offspring ANS function, specific nutrients that comprise healthier overall diets may act synergistically to promote optimal ANS development in offspring. Zinc, iron, choline, and long-chain PUFAs play a significant role in DNA synthesis, energy metabolism, neurotransmitter synthesis, myelination, and synaptogenesis and therefore are important components of fetal nervous system development (94). Pregnant women do not consume enough of these nutrients and physiological requirements of these nutrients increase during pregnancy (95). Consumption of an optimal

TABLE 3 Adjusted associations between overall prenatal diet quality and heart rate variability at 6 mo of age[1]

	RMSSD		SDNN	
	B (95% CI)	sp^2	B (95% CI)	sp^2
Prenatal diet quality	0.09 (0.003, 0.18)	0.14	0.24 (0.00, 0.49)	0.13
Maternal BMI	0.14 (−0.75, 1.02)	0.02	−0.40 (−2.87, 2.07)	−0.02
Infant age	0.22 (−0.66, 1.02)	0.03	1.09 (−1.37, 3.55)	0.06
Maternal smoking	−0.30 (−1.04, 0.44)	−0.06	−0.77 (−2.80, 1.30)	−0.05
Total household income	−0.04 (−0.37, 0.29)	−0.02	−0.20 (−1.12, 0.72)	−0.03
Maternal depressive symptoms	0.09 (−0.10, 0.27)	0.06	0.13 (−0.39, 0.64)	0.03
Recording duration	0.09 (0.06, 0.13)	0.32	0.37 (0.26, 0.48)	0.42
Sex	−0.03 (−1.40, 1.32)	−0.003	0.61 (−3.19, 4.41)	0.02
Exclusive breastfeeding	0.39 (−1.00, 1.80)	0.04	−0.06 (−3.95, 3.83)	−0.002
Adjusted R^2	0.14 ($P < 0.001$)		0.18 ($P < 0.001$)	

[1]B, unstandardized β; RMSSD, root mean square of successive differences; SDNN, SD of N-N intervals; sp^2, squared semipartial correlation—which indicates the amount of unique variance accounted for by each individual independent variable to the total variance of the dependent variable (RMSSD and SDNN).

healthy overall diet may decrease the likelihood of deficiencies in these important nutrients, therefore reducing the risk of adverse ANS development.

The following limitations of this study must also be considered. First, it should be acknowledged that some participants with high diet quality had infants with low HRV and some with poor diet quality had infants with high HRV. Because it is well known that HRV can change depending on state (e.g., strong, rapid increases in negative affectivity, increased drowsiness), HRV obtained from these few participants may have been affected by state-related changes before, or during, ECG acquisition. Unfortunately, we did not obtain information on infant state before the ECG recordings. In addition, unmeasured variables, such as shared genetics or prenatal exercise, may also have affected our findings for these dyads. Second, replicating this study using samples of pregnant women at elevated risk of poor diet consumption (such as those of lower socioeconomic status) and their offspring would be important to determine if a positive association between diet quality and offspring HRV can also be found in these populations. Indeed, MIREC only recruited healthy pregnant women and because diets of Canadian women are generally healthier than those of American women (75.1% of our sample consumed a diet of average quality) (56), this should be considered when generalizing findings to other populations. However, given the strong programming effects of prenatal diet on offspring development reported in both experimental animal model literature and epidemiological studies in humans (e.g., 15, 16, 24) we hypothesize that associations between diet and offspring HRV could be even stronger in samples that include more women at risk of poor diet consumption. Third, we are unable to examine whether low offspring HRV persists beyond 6 mo of age and if HRV in the infants in this study predicts later disease. Fourth, it is unclear whether offspring ANS functioning could be affected by diet specifically in pregnancy or by the woman's diet over the course of her life leading up to pregnancy. Because women are born with their lifetime complement of ova, a woman's diet across the life span may also play a role in offspring ANS development. Fifth, although short FFQs are valid in assessing overall diet quality (50–52), future studies could use more comprehensive measures to further investigate dietary patterns and offspring ANS functioning. Further, it should be acknowledged that FFQ-reported intakes themselves can be biased, which could have affected our HEI total scores. Finally, although our associations between prenatal diet and offspring HRV were significant, we acknowledge that they were small in magnitude. However, given that a 1% increase in HRV was linked to a 1% decrease in risk of cardiovascular disease (41), we believe that our findings could have significant public health implications.

In conclusion, although data in humans suggest that poor prenatal diet quality is associated with an increased risk of chronic diseases and their comorbidity in offspring, these studies have tended to examine risks of individual diseases in isolation and have not investigated mechanisms that might underlie broad chronic disease risk. The data from this large cohort study suggest that a common modifiable exposure, prenatal diet quality, may adversely affect offspring ANS function. These findings suggest that for some dyads, prenatal diet could play a role in altering this core physiological regulatory system known to underlie risk of multiple chronic conditions across the life span. As a result, our findings could have significant public health implications and could one day inform the development of interventions aimed at improving health for both women and their infants.

Acknowledgments

We acknowledge the site investigators for the MIREC-ID Study: Peter Von Dadelszen, University of British Columbia; Warren G Foster, McMaster University; Graeme Smith, Queen's University; Mark Walker, University of Ottawa; William Fraser, Universite de Sherbrooke; Linda Dodds, Dalhousie University. The authors' responsibilities were as follows—JEK, KB, TEA, and RJVL: conceptualized the idea for this study and its design, wrote the first draft of the manuscript, and incorporated subsequent edits and revisions; JEK, KB, TEA, RJVL, LAF, CS, BA, and NM: analyzed the data and interpreted the findings; GM, NP, and JRS: contributed to the design of the MIREC cohort study, interpreted the data, aided in interpretation of data acquisition procedures, provided feedback, and critically evaluated subsequent drafts of the manuscript; LAF, CS, BA, and NM: provided support for the intellectual content of the article and supported edits and subsequent drafts of the manuscript; and all authors: read and approved the final manuscript.

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