Carbohydrate ingestion induces sex-specific cardiac vagal inhibition, but not vascular sympathetic modulation, in healthy older women

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Cao L, Graham SL, Pilowsky PM. Carbohydrate ingestion induces sex-specific cardiac vagal inhibition, but not vascular sympathetic modulation, in healthy older women. Am J Physiol Regul Integr Comp Physiol 311: R49–R56, 2016. First published May 4, 2016; doi:10.1152/ajpregu.00486.2015.—The role of vagal function in cardiovascular risk in older women remains unclear. Autonomic modulation following carbohydrate ingestion (CI) and postural stress (PS) were investigated in 14 healthy men and 21 age-matched postmenopausal women (age: 65.0 ± 2.1 vs. 64.1 ± 1.6 years), with normal and comparable insulin sensitivity. Continuous noninvasive finger arterial pressure and ECG were recorded in the lying and the standing positions before and after ingestion of a carbohydrate-rich meal (600 kcal, carbohydrate 78%, protein 13%, and fat 8%). Low-frequency power of systolic blood pressure variability (SBP LF power), and the sequence method for spontaneous baroreflex sensitivity (BRS, ms/mmHg) were used to quantify autonomic modulation. In response to CI and PS, mean arterial pressure remained stable, and heart rate increased in women and men in the lying and standing positions. Following CI (60, 90, and 120 min postprandially) in the standing position, SBP LF power increased by 40% in men (P = 0.02), with unchanged HRV parameters; in contrast, in women, HRV HF power halved (P = 0.02), with unaltered SBP LF power. During PS before and after CI, similar magnitude of SBP LF power, HRV, and BRS changes was observed in men and women. In conclusion, CI induces sex-specific vascular sympathetic activation in healthy older men, and cardiac vagal inhibition in healthy older women; this CI-mediated efferent vagal inhibition may suggest differential cardiovascular risk factors in women, irrespective of insulin resistance, and impairment of autonomic control.

Inhibition of vagal (parasympathetic) modulation increases the incidence of coronary artery disease (CAD) (58), correlates with severity of CAD (17, 19), precedes daily activity-induced ischemic events in patients with stable CAD (24), and predicts cardiac death in postmyocardial infarction patients (25). Vagal enhancement is reported in women following acute coronary occlusion (1), which may counteract malignant ventricular arrhythmia (7, 14, 42). The role of vagal function in the development and protection of cardiovascular disease is underestimated (7, 14, 42, 55, 63), in particular, in women (1, 22, 59).

Dietary carbohydrate consumption, which is commonly underreported by women (6, 34), adversely influences vagal function (16) and worsens the progression of coronary atherosclerosis in postmenopausal women (41). Carbohydrate ingestion, in healthy young subjects, evokes acute hyperinsulinemia and sympathetic activation (4, 11, 67), with unaltered vagal modulation (11). Acute hyperinsulinemia-mediated sympathetic overactivation is found in those who are susceptible to the development of cardiovascular disorders (29, 37, 54). Sex differences in autonomic modulation have been reported previously, with women tending to exhibit less sympathetic vasoconstrictor effect to daily stressors (13, 50, 62). Sex differences in vagal modulation, on the other hand, are also associated with significant cardiovascular risks (25, 26), in women, in particular (1, 22). Whether or not dietary carbohydrate consumption, as a daily stressor and significant cardiovascular risk factor, may lead to adverse vagal or sympathetic modulation in women, is less clear, and is the subject of this investigation.

We hypothesized that, healthy older men and women, with normal insulin sensitivity (53, 64), and comparable responsiveness to postural stress (28), may exhibit distinctive features of autonomic modulation following carbohydrate ingestion, i.e., vagal inhibition, but not sympathetic activation, in women. Therefore, the present study aimed to evaluate sympathetic and vagal responses to both carbohydrate-rich meal ingestion and postural stress in healthy older men and women with normal comparable insulin sensitivity.

Power spectral analysis of blood pressure variability (43) and heart rate variability (35) was used to estimate autonomic modulation. Low-frequency power of systolic blood pressure variability (SBP LF) served as a surrogate marker of sympathetic modulation to the entire peripheral vasculature (43, 44), heart rate variability high-frequency (HRV HF) power served as a marker of cardiac vagal modulation (35), and HRV LF/HF ratio served as an index of sympathovagal balance (35, 36). Spontaneous heart rate baroreflex response to blood pressure (BP) change was calculated to estimate baroreflex sensitivity (26).

Methods

Study participants. The study was approved by the Ethics Committee at Macquarie University, New South Wales, Australia. All subjects provided written informed consent.

All participants (14 older male and 21 older female subjects) were recruited from communities through local newspaper advertisements and fulfilled inclusion criteria: age of 50–80 yr (older men 50–75 yr, older women 54–80 yr); all women were postmenopausal (defined as at least one entire year since last menstruation and not taking hormone replacement therapy). There was no history of heart disease, metabolic syndrome, or diabetes. Subjects were not prescribed vasodilatory medications (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, α- or β-adrenergic blocker, calcium channel blocker, and diuretics). Exclusion criteria were cardiac arrhythmia...
identified during the experiment, e.g., atrial fibrillation and/or frequent ectopic beats.

Subjects were instructed not to drink water 1.5 h prior to experiments, and to abstain from caffeinated beverages and food for 12 h, alcohol for 24 h, and moderate or strenuous physical activity for 48 h prior to the experiment.

**Measurements.** Fasting blood sample from each subject was collected on the day of study for measures of renal function, lipid profile, glucose level, and insulin level. General clinical profile of each subject was obtained by the study investigator (L. C.) prior to experiment.

The homeostasis model assessment (HOMA) [HOMA = (fasting glucose mg/dl × fasting insulin μU/ml)/405] and the quantitative insulin sensitivity check index (QUICKI): QUICKI = 1 / [log(fasting insulin μU/ml) + log(fasting glucose mg/dl)] were calculated as accurate surrogate markers used for evaluating insulin sensitivity (23, 38).

As previously described (11), electrocardiogram (ECG) and BP (finger photoplethysmography; Finometer Pro, Ohmeda, Amsterdam, Netherlands) were measured continuously. ECG was sampled at 1,000 Hz and stored for off-line analysis (LabChart 7.2 and PowerLab8/30, ADInstruments, Bella Vista, Sydney, NSW, Australia). BP waveform files were recorded at a sampling rate of 200 Hz for further power spectral analysis. The subject’s left arm was placed with the left hand (testing hand) at the level of the heart at all times (the testing hand was maintained at the heart level while standing up by a 90° elbow flexion). Brachial arterial blood pressure was recorded from the right arm with an automated sphygmomanometer (Microlife A100 PLUS, AG, 9443 Widnau, Switzerland) to confirm the hemodynamic equilibration, data were recorded again for 5 min. Each time interval incorporates 12-min recording time (5 min lying and 7 min standing) followed by 18 min in the supine resting state [see a diagram (Fig. 1) in our previous study (11)].

**Data analysis.** Power spectral analysis of RR interval was calculated with the HRV module in the commercial software of LabChart (LabChart 7.2, ADInstruments, Bella Vista, Sydney, NSW, Australia). The food formula is a 600-kcal carbohydrate-rich mixed meal (semi-liquid): 118 g carbohydrate (including 85 g sugar) (78%), 20 g protein (13%), 6 g fat (8%), and 300 mg sodium. The carbohydrate-rich meal was consumed within 10 and 12 min in a normal sitting position. The first 30-min time interval was defined as starting from the first mouthful of food intake (10–12 min of eating time), with subsequent 18–20 min postprandial supine resting state. Postprandial recordings were then conducted and repeated at each beginning of 30-min time-interval for a further 2 h. Each time interval incorporates 12-min recording time (5 min lying and 7 min standing) followed by 18 min in the supine resting state [see a diagram (Fig. 1) in our previous study (11)].

**Table 1. Baseline profile of older men and older women**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Older Men (n = 14)</th>
<th>Older Women (n = 21)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Profile</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>65.00 ± 2.10</td>
<td>64.05 ± 1.65</td>
<td>0.722</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24.73 ± 0.75</td>
<td>25.34 ± 1.29</td>
<td>0.724</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.96 ± 0.01</td>
<td>0.86 ± 0.01</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Total cholesterol, mmol/l</td>
<td>5.03 ± 0.21</td>
<td>5.72 ± 0.19</td>
<td>0.023*</td>
</tr>
<tr>
<td>Fasting blood glucose level, mmol/l</td>
<td>5.36 ± 0.16</td>
<td>5.22 ± 0.10</td>
<td>0.456</td>
</tr>
<tr>
<td>Fasting serum Insulin level, μU/l</td>
<td>6.71 ± 0.87</td>
<td>6.81 ± 0.79</td>
<td>0.938</td>
</tr>
<tr>
<td>Quantitative insulin sensitivity check index (QUICKI)</td>
<td>0.36 ± 0.01</td>
<td>0.37 ± 0.01</td>
<td>0.845</td>
</tr>
<tr>
<td>Homeostatic model assessment (HOMA)</td>
<td>1.64 ± 0.25</td>
<td>1.61 ± 0.21</td>
<td>0.934</td>
</tr>
<tr>
<td>Corrected glomerular filtration rate (cGFR), ml-min⁻¹·1.73m⁻²</td>
<td>86.23 ± 7.32</td>
<td>86.08 ± 4.91</td>
<td>0.986</td>
</tr>
<tr>
<td><strong>Resting hemodynamic parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>127.40 ± 3.53</td>
<td>120.80 ± 3.18</td>
<td>0.177</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>78.29 ± 2.36</td>
<td>70.67 ± 1.75</td>
<td>0.012*</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>94.67 ± 2.58</td>
<td>87.37 ± 2.10</td>
<td>0.035*</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>58.57 ± 1.90</td>
<td>61.48 ± 1.49</td>
<td>0.228</td>
</tr>
<tr>
<td><strong>Resting autonomic parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP LF power, mmHg²</td>
<td>10.51 ± 2.18</td>
<td>4.62 ± 0.53</td>
<td>0.008**</td>
</tr>
<tr>
<td>HRV LF power, ms²</td>
<td>972.04 ± 366.28</td>
<td>452.30 ± 99.06</td>
<td>0.115</td>
</tr>
<tr>
<td>HRV LF power nu</td>
<td>60.73 ± 6.32</td>
<td>47.21 ± 4.51</td>
<td>0.082</td>
</tr>
<tr>
<td>HRV HF power, ms²</td>
<td>396.65 ± 149.57</td>
<td>450.60 ± 118.80</td>
<td>0.760</td>
</tr>
<tr>
<td>HRV HF power nu</td>
<td>31.81 ± 3.61</td>
<td>47.85 ± 4.05</td>
<td>0.009**</td>
</tr>
<tr>
<td>HRV LF/HF ratio</td>
<td>2.49 ± 0.41</td>
<td>1.38 ± 0.25</td>
<td>0.021*</td>
</tr>
<tr>
<td>BRS, ms/mmHg</td>
<td>13.06 ± 1.75</td>
<td>16.08 ± 2.70</td>
<td>0.395</td>
</tr>
</tbody>
</table>

Data values are expressed as means ± SE; unpaired t-test between sex groups; two-tailed P value (*P < 0.05, **P < 0.01).
Spontaneous baroreceptor reflex sensitivity (RR interval to systolic BP) was evaluated with HemoLab software: http://haraldstauss.com/HemoLab/HemoLab.php, using the sequence method that identifies sequences of four or more heartbeats, where BP and pulse interval change in the same direction; for example, rises in BP correspond with increases in pulse intervals, with minimal SBP (1 mmHg) and pulse interval (6 ms) as threshold changes in humans (5, 45). Only sequences with a coefficient of determination ($R^2$) $\geq 0.8$ were included in the sequence method for baroreflex sensitivity (sBRS) analysis. A delay of 0 – 2 physiological beat cycle(s) between systolic blood pressure and pulse interval was used to provide the most representative estimates of sBRS. In a very small number of cases, in particular, following meal ingestion at 30-min time point, while hemodynamic perturbation peaks (52), a delay of 3–5 beats (in both study groups) was used to achieve a larger number of slopes for optimal estimates of sBRS (9, 30, 66).

Statistical analysis. All statistical analyses were performed using GraphPad Prism software (version 6). Subject profiles, baseline autonomic, and hemodynamic data were evaluated by using unpaired $t$-tests (two-tailed $P$ value) between two sex groups. Carbohydrate ingestion effects over the postprandial time points in the supine position and in the standing position in each sex group were evaluated using one-way ANOVA, followed by Greenhouse-Geisser corrections; further comparisons of autonomic responses (SBP LF power and HRV HF power) to carbohydrate ingestion in men and women were performed using paired $t$-tests [from fasting state to the later phase of the postprandial state (60, 90, and 120 min)], in the supine and the equilibrated standing positions, respectively. Statistical significance for hemodynamic and autonomic responses to carbohydrate ingestion and postural challenge was evaluated using two-way repeated-measures ANOVA, followed by Bonferroni post hoc corrections (i.e., meal ingestion effects over time in both lying and standing positions). Power calculations were undertaken to ensure that biologically important differences between the means could be detected at the 80% confidence limit. A $P$ value $< 0.05$ was regarded as statistically significant. Data are presented as means $\pm$ SE in figures and tables.

RESULTS

General profile. Females and males were of similar age and body mass index (BMI). Males showed a higher waist/hip ratio, and lower total blood cholesterol level, compared with females. Similar glomerular filtration rate and normal renal function were noted in the two study groups. With respect to
glucose metabolism, older men and women showed comparable fasting blood glucose level and insulin level, as well as markers indicative of insulin sensitivity (i.e., using QUICKI and HOMA) (Table 1).

Baseline autonomic and hemodynamic parameters. In resting state (preingestion and lying position), SBP and heart rate (HR) were similar between older men and women. Diastolic blood pressure (DBP) and mean arterial pressure (MAP) were higher in older men than women, albeit within a normal range (Table 1).

Baseline SBP LF power was higher in older men than women. HRV parameters were similar in the two groups, except for a higher HRV HF power nu in older women, and a greater HRV LF/HF ratio in older men. BRS was comparable in the two groups (Table 1).

Hemodynamic and autonomic responses to carbohydrate ingestion. Following carbohydrate ingestion, MAP remained unchanged, and HR increased in both the supine and the standing position in older men and women (Fig. 1). SBP LF power was markedly enhanced in the standing position over

Table 2. HRV changes in response to carbohydrate ingestion and postural stress

<table>
<thead>
<tr>
<th>Value (Ingestion)</th>
<th>0 min</th>
<th>30 min</th>
<th>60 min</th>
<th>90 min</th>
<th>120 min</th>
<th>P Value (Position)</th>
<th>P Value (Ingestion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRV LF power, ms²</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Lying</td>
<td>607.70 ± 230.35</td>
<td>521.27 ± 175.43</td>
<td>446.51 ± 130.31</td>
<td>530.16 ± 146.05</td>
<td>1226.59 ± 797.67</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Standing</td>
<td>396.65 ± 149.57</td>
<td>303.62 ± 102.26</td>
<td>359.95 ± 191.04</td>
<td>273.90 ± 153.51</td>
<td>284.06 ± 104.61</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>HRV HF power, ms²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lying</td>
<td>797.67 NS</td>
<td>149.18 NS</td>
<td>20.62 #</td>
<td>3.06 ##</td>
<td>3.29 **</td>
<td>0.0073 NS</td>
<td>0.0079 **</td>
</tr>
<tr>
<td>Standing</td>
<td>452.28 ± 99.06</td>
<td>957.06 ± 506.60</td>
<td>481.51 ± 127.73</td>
<td>360.14 ± 79.07</td>
<td>357.67 ± 65.65</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>HRV LF/HF ratio</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lying</td>
<td>52.97 ± 5.18</td>
<td>59.37 ± 4.49</td>
<td>62.12 ± 4.51</td>
<td>56.10 ± 3.84</td>
<td>65.20 ± 4.10</td>
<td>0.018 NS</td>
<td>0.0073 NS</td>
</tr>
<tr>
<td>Standing</td>
<td>47.21 ± 4.51</td>
<td>54.78 ± 4.38</td>
<td>52.95 ± 4.90</td>
<td>47.67 ± 4.33</td>
<td>54.62 ± 4.51</td>
<td>**P = 0.0075</td>
<td>NS</td>
</tr>
<tr>
<td>HRV HF power, ms²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lying</td>
<td>463.04 ± 108.59</td>
<td>302.55 ± 51.67</td>
<td>286.62 ± 72.64</td>
<td>228.69 ± 32.61</td>
<td>326.14 ± 69.82</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Standing</td>
<td>450.64 ± 118.81</td>
<td>616.54 ± 297.69</td>
<td>469.86 ± 173.05</td>
<td>308.96 ± 59.84</td>
<td>253.03 ± 62.23</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data values are expressed as means ± SE. *P < 0.05, **P < 0.01, effect of carbohydrate ingestion from preingestion (fasting) state to later in the postprandial state (60, 90, and 120 min) using one-way ANOVA. *P < 0.05, **P < 0.01, effect of postural change before and after carbohydrate ingestion using two-way ANOVA.
time in the postprandial state in older men, but not in older women (Fig. 2). BRS decreased in the supine position following carbohydrate ingestion in older women, and this remained unaltered in older men (Fig. 3). Following carbohydrate ingestion, HRV parameters remained unchanged in older men, whereas in older women, HRV HF power, and HRV HF power significantly reduced in both the lying and standing positions (Table 2).

The average value of SBP LF power and HRV HF power in the later phase of postprandial state (60, 90, and 120 min) was calculated to represent the postingestion variables, i.e., SBP LF power (mean of 60+90+120) and HRV HF power (mean of 60+90+120). SBP LF power and HRV HF power from fasting to postingestion state were compared. Following carbohydrate ingestion, in the supine position, SBP LF power increased and BRS decreased in both older men and women (Figs. 2 and 3); HRV HF power remained unchanged. In the standing position postprandially, SBP LF power markedly increased in older men, whereas in older women, HRV HF power halved (\( P < 0.05, \# P < 0.01 \), effect of carbohydrate ingestion; paired \( t \)-test).


time interaction of MAP in women (\( P = 0.015 \)).

In response to postural change over time before and after carbohydrate ingestion, SBP LF power increased and BRS decreased in both older men and women (Figs. 2 and 3); HRV LF power nu increased, HRV HF power nu reduced, and HRV LF/HF ratio increased in both men and women (Table 2).

**DISCUSSION**

The principal new finding of the present study is that, on the basis of the decreases in HRV HF power and BRS with an unaltered SBP LF power, carbohydrate ingestion induces cardiac vagal withdrawal in healthy older women without apparent vascular sympathetic activation to maintain mean arterial pressure. This finding is in contrast to age-matched healthy older men, irrespective of insulin resistance, and any impairments of autonomic control.

Following carbohydrate ingestion, hyperinsulinemia has a vasodilating role in facilitating glucose uptake (2); failure or impairment of this physiological function results in insulin resistance (27). Enhanced sympathetic nerve activity counteracts this physiological challenge and stabilizes hemodynamic homeostasis (8). This carbohydrate ingestion-induced hyperinsulinemia and associated sympathetic activation is known to occur in healthy young males (11, 67). The present study showed that, following carbohydrate ingestion, there is a steadily enhanced sympathetic modulation in healthy older
CARBOHYDRATE INGESTION INDUCES VAGAL INHIBITION IN WOMEN

men, similar to that demonstrated in healthy young men (11), which is crucial in compensating for any hemodynamic perturbation (60, 61) and stabilizing BP in the postprandial state. Failure of this sympathetic response may cause postprandial hypotension and potentially jeopardize organ perfusion (15, 33).

The present study enrolled healthy older men and women, who were matched for age, BMI, fasting blood glucose level, and insulin level, and who had normal insulin sensitivity (53, 64). Hyperinsulinemia-mediated sympathetic overactivation is unlikely to be present in our study groups (29, 37, 54). Autonomic modulation in these women is not different from men, as demonstrated in the current study, in that in response to postural stress, the increased vascular sympathetic outflow and HRV changes are of comparable magnitude in both groups (28). However, following carbohydrate ingestion, older women showed less favorable vascular sympathetic modulation (13, 62). Instead, we found that cardiac vagal reduction is evident in these apparently healthy older women. The corresponding beat-to-beat BP response to central sympathetic outflow is more attenuated in older women than in men (62); the current findings extend this earlier work by demonstrating that vagal inhibition may counteract this attenuation of sympathetic vasoconstrictor effect in older women and play a role in stabilizing BP. The distinctive sympathetic and vagal responses in older women may be explained by sex-specific baroreceptor afferent pathway (32, 47), provoked by different hemodynamic perturbation following carbohydrate ingestion, and during postural stress.

Persistent vagal adaptation (inhibition) is not without adverse consequences. It is known that a long-term healthy diet may enhance vagal function and facilitate cardiovascular health in postmenopausal women (16). Dietary nutrients are sensed and signaled by the central nervous system (48, 49). Long-term efferent vagal inhibition may adversely influence cholinergic anti-inflammation pathways (56, 57). The precise mechanism of carbohydrate diet-mediated efferent vagal inhibition to cardiovascular risk remains to be determined.

In the present study, following carbohydrate ingestion, a lack of vascular sympathetic buffering effect and a decreased heart rate baroreflex response were observed in older women, but not in older men. The reduced baroreflex response may reflect baroreceptor resetting (47) to compensate for a lack of sympathetic modulation to the peripheral vasculature (51). Such a depressed BRS may be associated with increased cardiovascular risk (25, 26).

Limitations of the present study are largely related to the indirect nature of the measurements and include the following: 1) baseline DBP and SBP LF power in men is slightly higher than that of women (21). It is unlikely that an increased sympathetic response to carbohydrate ingestion in older men is due to the higher baseline DBP (31), because this increased vascular sympathetic response in the postprandial state is also observed in healthy young males (11, 67). 2) The present study recruited only postmenopausal women. The findings may not be generalized to women in younger age, but it is likely that premenopausal women share this diet-mediated sex-specific vagal inhibition that may lead to an increased cardiovascular risk (22). 3) In a very strict sense, to exclude the possibility of repetitive lying and standing effects on meal ingestion responses, nonfed male and female groups as controls may be needed. In fact, before each postprandial time point data recording, subjects were in a supine resting state for 20 min to minimize (or “wash out”) the effects from repetitive quiet standing [see experimental protocol diagram (Fig. 1.) in our previous study; Ref. 11]. In addition, subjects rested in the changed position for 2 min to allow for equilibration (4). The value of HRV LF power as a marker of sympathetic modulation remains unclear (20). In the current study, only HRV HF power reduction with an associated increase in HRV HF/LF ratio was used to interpret a sympathovagal balance shifting toward sympathetic predominance (35, 36). QT interval variability may be a better index for cardiac ventricular sympathetic modulation (3, 46) and prediction of malignant cardiac arrhythmias (18). 5) Nonlinear analysis of cardiovascular variabilities is an evolving valuable complementary mathematical approach in estimating autonomic response to daily stressors (12); additional data analysis for autonomic responses to meal ingestion is worthwhile.

Perspectives and Significance

Vagal inhibition increases risk of CAD (19) and is associated with cardiac death (25). Sex difference in vagal modulation is found in the development of cardiovascular diseases (22). Excessive dietary carbohydrate consumption is a recognized risk factor of metabolic syndrome and results in atherosclerotic diseases (41). The current study demonstrates for the first time that carbohydrate ingestion elicits sex-specific features of autonomic modulation in healthy older men and women. Older men exhibit increased sympathetic outflow to the peripheral vasculature, whereas the response in older postmenopausal women favors cardi vagal withdrawal, and an attenuated heart rate baroreflex response. This study provides new experimental evidence for sex-specific autonomic modulation following carbohydrate ingestion, irrespective of insulin resistance, and any impairments of autonomic control. We speculate that carbohydrate ingestion induced vagal inhibition may underlie the pathogenesis of cardiovascular diseases in women. Autonomic dysregulation following carbohydrate ingestion in women in the development and progression of cardiovascular disease warrants further investigation.

GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

L.C., S.L.G., and P.M.P. conception and design of research; L.C. and P.M.P. analyzed data; L.C. and P.M.P. interpretation of data; L.C. and P.M.P. dissemination of results; L.C. and P.M.P. prepared figures; L.C. and P.M.P. wrote the manuscript in a first version; L.C., S.L.G., and P.M.P. approved final version of manuscript.

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