Moderate weight loss improves heart rate variability in overweight and obese adults with type 2 diabetes

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Sjoberg N, Brinkworth GD, Wycherley TP, Noakes M, Saint DA. Moderate weight loss improves heart rate variability in overweight and obese adults with type 2 diabetes. J Appl Physiol 110: 1060–1064, 2011. First published January 6, 2011; doi:10.1152/japplphysiol.01329.2010.—The objective of this study was to determine the effects of weight loss on heart rate variability (HRV) and its association with traditional cardiovascular disease risk factors in overweight and obese patients with type 2 diabetes. Forty-five patients [body mass index (BMI) 35.4 ± 0.7 kg/m2; age 56.5 ± 1.1 yr] with type 2 diabetes followed an energy-restricted diet (6–7 MJ/day) for 16 wk. Body weight, blood pressure, glucose, insulin, insulin resistance [homeostasis model assessment index 2 (HOMA2)], glycosylated hemoglobin (HbA1c), total cholesterol, low-density lipoproteins (LDL), high-density lipoproteins (HDL), triglycerides, resting HR, and HRV were measured before and after the intervention period. Mean reduction in body weight was 11.1 ± 1.0 kg (10%), with significant reductions in blood pressure (−10%), total cholesterol (−15.9%), LDL (−17.7%), HDL (−7.5%), triglycerides (−21.2%), glucose (−23.4%), insulin (−37.6%), HOMA2 (−40.1%), and HbA1c (−14.5%) (P < 0.05 for all variables). There were increases in several HRV components, including total power (1,370 ± 280 to 2,045 ± 280 ms2), low-frequency power (345 ± 70 to 600 ± 108 ms2), SD of normal to normal intervals (SDNN; 35.0 ± 2.5 to 43.0 ± 2.7 s), and square root of the mean squared differences of successive normal to normal intervals (RMSSD; 23.0 ± 3.5 to 32.0 ± 3.1 s), and a decrease in HR (69.0 ± 1.3 to 60.0 ± 1.2 beats/min) (P < 0.03 for all variables). Changes in HR, SDNN, total power, and low-frequency power correlated with change in BMI (P < 0.05). In addition to improvements in traditional cardiovascular and metabolic risk factors, weight loss improves HRV in overweight and obese patients with type 2 diabetes.

Diabetic autonomic neuropathy is a common and severe complication of type 2 diabetes, causing a dysregulation of autonomic control of the cardiovascular system known as cardiac autonomic neuropathy (8, 22). Cardiac autonomic neuropathy and related conditions are characterized by accelerated reductions in HRV during disease progression compared with what would be considered a normal rate of reduction based on age, sex, and other unmodifiable factors (10, 28). Obesity is a key risk factor for the development of type 2 diabetes, with the majority of patients with type 2 diabetes being either overweight or obese (11). Obesity itself has been shown to alter autonomic nervous system activity and weight gain decreases HRV (6–7, 10). Conversely, weight loss via dieting or gastroplasty has been shown to improve cardiac autonomic function and enhance HRV via increased cardiac vagal modulation in normal, otherwise healthy, obese individuals (4, 12, 17, 19). Such an improvement in HRV with weight loss in diabetic subjects could be an important indicator of reduced cardiovascular risk. Of concern, therefore, is the possibility that alteration of autonomic responsiveness in diabetic subjects may preclude such a beneficial effect. However, no studies to date have evaluated the effects of weight loss alone on HRV in overweight or obese patients with type 2 diabetes. This study therefore aimed to determine whether weight loss following a hypocaloric diet can improve HRV in overweight and obese adults with type 2 diabetes.

METHODS

Participants. Forty-five overweight and obese participants with type 2 diabetes were recruited via public advertisement. Participants completed a health-screening questionnaire and were not eligible to participate if they had known proteinuria, a malignancy, a history of liver, kidney, cardiovascular, respiratory or gastrointestinal disease, uncontrolled hypertension, or were pregnant, lactating, a smoker or were using insulin. All experimental procedures were approved by the Human Research Ethics Committees of the University of Adelaide and Commonwealth Scientific and Industrial Research Organisation (CSIRO). Written informed consent was obtained from all participants before commencement. The participants had a mean age of 56.5 ± 1.1 yr and body mass index (BMI) of 35.4 ± 0.7 kg/m2. Twenty-five of the subjects were taking metformin. Their baseline characteristics are presented in Table 1.

Table 1. Type 2 diabetes status. If a participant had been previously diagnosed with type 2 diabetes and was on hypoglycemic medication, diabetes status was accepted. If the participant was not on hypoglycemic medication, HbA1c was used to confirm diabetes status (HbA1c > 7%). If there was no recent previous HbA1c result provided, a venous blood sample was taken at screening for analysis of HbA1c. Mean diabetes duration was 6 ± 5 yr.

Study design. Participants followed a 16-wk energy-restricted diet (6–7 MJ/day) based on a prescriptive fixed menu plan with a primary...
Table 1. Baseline characteristics and changes after a 16-wk weight loss intervention (n = 45)

<table>
<thead>
<tr>
<th>Physiological parameters</th>
<th>Baseline</th>
<th>Week 16</th>
<th>%Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>56.5 ± 1.1</td>
<td>64.1 ± 2.1</td>
<td>−12.2†</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>103.4 ± 2.4</td>
<td>89.1 ± 1.9</td>
<td>−10.9‡</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>35.4 ± 0.7</td>
<td>31.6 ± 0.6</td>
<td>−10.7†</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>112.0 ± 1.8</td>
<td>101.7 ± 1.7</td>
<td>−9.2‡</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>137.3 ± 1.7</td>
<td>123.6 ± 1.9</td>
<td>−10.0†</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>82.9 ± 1.2</td>
<td>73.5 ± 1.1</td>
<td>−11.3‡</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>7.4 ± 0.2</td>
<td>6.3 ± 0.2</td>
<td>−14.5†</td>
</tr>
<tr>
<td>Total cholesterol, mmol/l</td>
<td>4.8 ± 0.2</td>
<td>4.0 ± 0.2</td>
<td>−15.9†</td>
</tr>
<tr>
<td>LDL, mmol/l</td>
<td>2.8 ± 0.2</td>
<td>2.3 ± 0.1</td>
<td>−17.7†</td>
</tr>
<tr>
<td>HDL, mmol/l</td>
<td>1.2 ± 0.04</td>
<td>1.1 ± 0.04</td>
<td>−7.5‡</td>
</tr>
<tr>
<td>Triglycerides, mmol/l</td>
<td>1.9 ± 0.1</td>
<td>1.5 ± 0.2</td>
<td>−21.2†</td>
</tr>
<tr>
<td>Glucose, mmol/l</td>
<td>8.9 ± 0.4</td>
<td>6.8 ± 0.2</td>
<td>−23.4†</td>
</tr>
<tr>
<td>Insulin, mU/l</td>
<td>14.2 ± 1.4</td>
<td>8.9 ± 1.0</td>
<td>−40.1†</td>
</tr>
<tr>
<td>Insulin resistance (HOMA2)</td>
<td>1.75 ± 0.15</td>
<td>1.05 ± 0.11</td>
<td>0.00‡</td>
</tr>
</tbody>
</table>

**HRV parameters**

| Heart rate, beats/min                          | 68.7 ± 1.3     | 60.3 ± 1.2    | −12.2†  |
| Total power, ms²                                | 1,370.8 ± 278.8| 2,043.9 ± 277.9| 49.1‡   |
| Low-frequency power, ms²                        | 343.2 ± 70.0   | 601.4 ± 108.0| 75.2‡   |
| High-frequency power, ms²                       | 343.3 ± 171.7  | 446.9 ± 87.7  | 30.2    |
| Low frequency, nu                               | 58.5 ± 2.8     | 55.4 ± 2.8    | −5.3    |
| High frequency, nu                              | 35.0 ± 2.4     | 39.3 ± 2.5    | 12.2    |
| Low frequency/high frequency (ratio)            | 2.5 ± 0.3      | 2.3 ± 0.4     | −9.5    |
| SDNN, ms                                       | 35.0 ± 2.5     | 42.9 ± 2.7    | 22.6‡   |
| RMSSD, ms                                      | 23.4 ± 3.5     | 32.2 ± 3.1    | 37.6†   |

HRV, heart rate variability; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HOMA2, homeostasis model assessment index 2; SDNN, SD of the normal to normal mean; RMSSD, the square root of the mean squared differences of successive normal to normal intervals. *P < 0.05, †P < 0.01, baseline values significantly different from values at week 16.

The reduction in HR correlated with %weight loss (r = 0.32, P < 0.05), %weight loss (r = 0.34, P < 0.01), WC (r = 0.36, P < 0.05), and HOMA2 (r = 0.32, P < 0.05) as well as reductions in systolic blood pressure (r = 0.32, P < 0.05), diastolic blood pressure (r = 0.31, P < 0.05), total power (r = 0.32, P < 0.05), and RMSSD (r = 0.33, P < 0.05). All data are shown as means ± SE.

RESULTS

All individuals in the analysis lost weight (range −1.44 to −26.02 kg). Overall, the mean weight loss was 11.3 ± 2.1 kg (P < 0.01), which was accompanied by significant reductions in WC, blood pressure, total LDL and HDL cholesterol, triglycerides, glucose, insulin, HOMA2, and HbA1c (P < 0.05 for all variables). These results are shown in Table 1.

Representative power spectra from one individual are shown in Fig. 1. At week 16, HR was significantly reduced (P < 0.01). The reduction in HR correlated with %weight loss (r = 0.52, P < 0.01), and the reduction in BMI (r = 0.49, P < 0.01), WC (r = 0.50, P < 0.01), triglycerides (r = 0.35, P = 0.02), insulin (r = 0.31, P = 0.04), and HOMA2 (r=0.32, P = 0.04). The HRV components total power, LFP, SDNN, and RMSSD all increased after weight loss (P ≤ 0.03). HFP and LF/HR ratio did not change significantly during the intervention. The reduction in BMI was inversely correlated with the change in SDNN (r = −0.30, P = 0.05), total power (r = −0.32, P = 0.04), and LFP (r = −0.34, P = 0.03). Changes in LFP also correlated with %change in weight (r = −0.34, P = 0.02) and the change in WC (r = −0.31, P = 0.04). Although not significantly changed itself, changes in HFP correlated with change in BMI (r = −0.30, P = 0.05), WC (r = −0.36, P = 0.04), %weight loss (r = −0.31, P = 0.02), insulin (r = −0.37, P = 0.01), and insulin resistance (r = −0.38, P = 0.01). There was a correlation between LF/HF ratio and HOMA2 (r = 0.31, P = 0.04).
DISCUSSION

Many markers are used to assess cardiovascular health, and associated risk of cardiovascular adverse events, including endothelial function, pulse wave velocity, as well as the more established measures such as heart rate and blood pressure (9). In addition, HRV is also becoming an accepted marker of cardiovascular health, and lowered HRV has been shown to be associated with increased cardiovascular risk.

There is no doubt that overweight or obesity increases cardiovascular risk and previous studies have shown that increased BMI decreases HRV (attenuates SDNN) in normal, healthy individuals, and that HRV can be improved following exercise training or with dieting in the normal population (17, 19). Collectively, published data support a link between weight reduction and beneficial changes in the balance of sympathetic and parasympathetic activity. For example, weight loss following a hypocaloric diet has been shown to increase cardiac parasympathetic vagal tone in obese individuals (13, 20).

Type 2 diabetes is an independent risk factor for cardiovascular disease, and type 2 diabetes also reduces HRV, presumably reflecting a decrease in cardiac autonomic control (22). A worrying possibility, therefore, is that type 2 diabetes may attenuate or obviate the beneficial effects of weight reduction on HRV and other markers of cardiovascular health in those patients with this comorbidity. Encouragingly, the main finding of this study is that this is not so; HRV improved with modest (~10 kg) weight loss in obese and overweight patients with concomitant type 2 diabetes, indicating that weight loss through dietary intervention is producing beneficial effects on a range of cardiovascular risk factors in this group.

We found a significant 12.2% reduction in resting HR, which correlated with a reduction in metabolic markers (insulin, insulin resistance, and triglycerides) and BMI. This is consistent with other studies that have also shown that weight loss can reduce HR in obese hypertensive patients (23). The HRV markers of cardiovascular health were also improved, although some measures demonstrated this more convincingly than others. The time domain measures SDNN and RMSSD are simple measures of the mathematical variance in the heart rate. These were both highly significantly increased (by 22.6% and 37.6%, respectively) by the intervention. The increase in SDNN was significantly correlated with the reduction of BMI. The changes in parameters derived from power spectral analysis of heart rate were also consistent, with one minor exception. Changes in all measures of HRV correlated with the change in BMI (and other measures of weight loss). Total power, LFP, and HFP were all increased substantially. Total power and LFP changes were significant at $P < 0.01$, but although HFP increased by over 30%, this was not statistically significant. It may be that HFP is less responsive to weight loss than the other measures, and that the weight loss in our study was not large enough to produce a statistically significant change in HFP. However, we note that other studies have attained significant improvements in HFP with a similar or lesser degree of weight loss (2, 17). It should be noted that breathing rate and depth can affect HRV, in the HF band, and so we cannot be sure that changes in HF (or lack thereof) were not due to changes in breathing mechanics. An alternative is that

![Figure 1: Representative spectra from 1 subject at baseline (A) and at week 16 (B). Vertical lines at 0.04, 0.15, and 0.4 Hz show the boundaries of the low-frequency and high-frequency bands.](http://jap.physiology.org/10.1152/japplphysiol.00110.2010)
our study lacked sufficient power to detect a significant change in HFP in particular, because of the high variability in this measure. A retrospective power calculation found the statistical power of the change in HFP with 45 subjects was 10%. Future studies should therefore increase the number of subjects in each trial to clearly demonstrate the significant change in HFP.

Total power and LFP are considered to represent the response to blood pressure fluctuations mediated by the baroreflex. Studies carried out using orthostatic and exercise challenges as well as pharmacological studies with beta blockers have shown the link between LFP and increase in efferent sympathetic activity, and have led to the use LFP as a marker of sympathetic activity (1, 21). The increased LFP amplitude after weight loss in the type 2 diabetes subjects in our study is thus most likely a reflection of improved baroreceptor-dependent control of the heart, consistent with other published studies (25).

Total cholesterol, HbA1c, and triglycerides, which are surrogate markers of global vascular health, also decreased after weight loss in our study group. These metabolic markers have previously been identified as independent markers of cardiovascular health (14).

In conclusion, weight loss via a hypocaloric diet improved HRV in overweight and obese patients with type 2 diabetes. Since cardiac autonomic dysfunction is an indicator of adverse cardiovascular risk, the improvement in HRV after weight loss should be considered beneficial and suggests improved cardiovascular health. Importantly, we show here that overweight or obese patients with type 2 diabetes appear to have increased sympathetic activity, which can be reversed by weight loss in a way similar to that seen in nondiabetic patients (25–26), despite the possible confounding factors of poor autonomic control resulting from the comorbidity of type 2 diabetes. This study therefore provides further support for the clinical importance of weight loss reducing the risk of adverse cardiovascular events in overweight diabetic patients.

ACKNOWLEDGMENTS

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The authors’ responsibilities were as follows. N. Sjoberg contributed to the design of the study, performed data analyses, interpreted the data, and coordinated the writing of the manuscript. G. D. Brinkworth was responsible for the design of the study, coordinated the study, and contributed to data interpretation and the writing of the manuscript. T. P. Wycherley was responsible for the design of the study, coordinated the study, and contributed to the writing of the manuscript. M. A. Saint contributed to the design of the study, data interpretation, and writing of the manuscript. All authors agreed on the final version of the manuscript.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES


