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Plasticity of heart rate signaling and complexity with exercise training in obese individuals with and without type 2 diabetes

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Abstract

Objective—To examine the responsiveness of cardiac autonomic function and baroreflex sensitivity (BRS) to exercise training in obese individuals without (OB) and with type 2 diabetes (ObT2D).

Design—Subjects were tested in the supine position and in response to a sympathetic challenge before and after a 16 week aerobic training program. All testing was conducted in the morning following a 12-hour fast.

Subjects—34 OB and 22 ObT2D men and women (40-60 yr)

Measurements—Heart rate variability (HRV) was measured at rest via continuous ECG (spectral analysis with the autoregressive approach) and in response to upright tilt. The dynamics of heart rate complexity were analyzed with sample entropy and Lempel-Ziv entropy, and BRS was determined via the sequence technique. Subjects were aerobically trained 4x/wk for 30-45 min for 16 wks.

Results—Resting HR decreased and total power (lnTP, msec^2) of HRV increased in response to exercise training ($P<0.05$). High frequency power (lnHF) increased in OB subjects but not in OBT2D, and no changes occurred in ln low frequency/HF power with training. Upright tilt decreased lnTP and lnHF and increased LF/HF ($P<0.01$) but there were no group differences in the magnitude of these changes nor were they altered with training in either group. Tilt also decreased complexity (sample entropy and Lempel-Ziv; $P<0.001$), but there was no group or training effect on complexity. BRS decreased with upright tilt ($P<0.01$) but did not change with training. Compared to OB subjects the ObT2D had less tilt-induced changes in BRS.

Conclusion—Exercise training improved HRV and parasympathetic modulation (lnHF) in OB subjects but not in ObT2D, indicating plasticity in the autonomic nervous system in response to

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this weight-neutral exercise program only in the absence of diabetes. HR complexity and BRS were not altered by 16 wk of training in either OB or ObT2D individuals.

Introduction

Cardiac autonomic neuropathy (CAN) and abnormalities in vascular dynamics are frequently observed with obesity and with type 2 diabetes (T2D), and these alterations are associated with exercise intolerance, orthostatic hypotension, asymptomatic ischemia, myocardial infarction and increased risk of mortality (1). Reduced R-R interval variation (heart rate variability (HRV)) is an early indicator of CAN and is frequently observed in obese individuals and those with T2D. Chronic hyperinsulinemia, which is observed with obesity, is associated with a high output, low-resistance hemodynamic state (2). Low HRV is also associated with lower fitness levels and increased mortality (3; 4). In non-obese individuals, aerobic exercise training has been associated with increases in total HRV (5-8). However, there are conflicting reports on the effects of exercise training in obese individuals (OB) with some investigators reporting no change in HRV (9; 10) while others showing improvement (11; 12). While, the data appears equivocal with regards to standard HRV and exercise training, it is possible that HR complexity, which is a newer analysis technique of the non-linear component signal, may be more sensitive to training effects. Alterations in CAN may be reflected in the non-linear component of the HR signal (HR complexity). Complexity is the randomness or entropy of the time series. Since both arms of the autonomic nervous system (ANS) contribute to the non-linear oscillations, more variability or irregularity in the HR signal is considered beneficial and demonstrates more flexibility in the system (13). Aging (13), as well as cardiovascular and metabolic diseases, result in an attenuation of HR complexity (15) (16), but the impact of obesity and T2D on HR complexity have only been documented on a few occasions (16).

Although numerous studies have shown that exercise training can improve cardiac autonomic function (17-20) in healthy young and obese individuals, few studies have examined the effect of exercise training on HRV or HR complexity in obese individuals with (ObT2D) or without T2D. Since obesity and T2D are associated with metabolic and cardiovascular abnormalities (21), the ANS may respond differently to exercise training in these populations due to reduced plasticity. Zoppini et al (10) showed that 6 mo of moderate intensity exercise did not improve resting HRV in ObT2D subjects, but did improve the autonomic reflexive response to standing. This suggests that exercise training may affect reflex autonomic responses, with no apparent changes in resting supine autonomic function. More research is needed to understand the potential changes in these reflex responses in obese populations.

The purpose of this study was to examine the plasticity of cardiac autonomic modulation and reflex autonomic function in obese men and women with and without T2D in response to exercise training. We hypothesized that: 1) obese individuals with T2D would have reduced HRV (lnTP) and parasympathetic modulation (lnHF) compared to OB individuals prior to training; 2) exercise training would improve HRV and HR complexity in both groups, but with less improvement in T2D individuals and 3) that reflex autonomic function in response to upright tilt would be attenuated in ObT2D compared to OB subjects but

would improve with exercise training. To provide a more complete picture of the plasticity, we also measured sensitivity of the baroreflex (BRS), since BRS is known to be altered with T2D and obesity independently and reduced BRS is associated with increased cardiovascular risk (21).

Methods

Subjects

Sixty-four obese men and women (age 40-60 yr) were enrolled in this study, and sixty subjects completed all aspects of the testing. Fifty-six obese subjects with and without T2D were included in the data analysis; 4 subjects were excluded because of missing data points or ectopic heart beats. Subjects were classified into two groups based on their body mass index (BMI) and metabolic status: OB (BMI ≥ 30 kg/m^2, fasting glucose < 100 mg/dL, n=21 women, 13 men), and ObT2D (BMI ≥ 30 kg/m^2, fasting glucose ≥ 126 mg/dL, and 2 hour OGTT glucose ≥ 200 mg/dL, n=12 women, 10 men). All subjects were physically inactive and had not been involved in any regular exercise during the past 6 months. Subjects were nonsmokers, had no signs or history of peripheral neuropathy or overt heart disease verified by a physician-supervised maximal exercise stress test. Both pre- and post-menopausal women were included in the study, but those women having irregular menstrual periods were excluded. Premenopausal women were studied in the first 10 days of their menstrual cycle. Of the post—menopausal women, only 5 were on hormone therapy. No subject was taking beta-blockers or any medication that could alter their HR or blood pressure (BP) responses (Table 1). The Institutional Review Boards at Syracuse University and SUNY Upstate Medical University approved the protocol and written informed consent was obtained from all subjects prior to any testing.

Experimental design

Subjects were tested in the supine position and during upright tilt (reflexive response) before and after a 16 wk aerobic training program. All testing was conducted in the morning following a 12-hour fast.

Exercise Training

Subjects participated in a supervised home-based program for 16 weeks and trained at 65% of their respective oxygen consumption ($\dot{V}O_2$ peak). The initial training workload was determined via measurement of $\dot{V}O_2$ on the first training day; HR and ratings of perceived exertion were subsequently used to assist the subject in identifying the workload on their own. Subjects were expected to walk for 30 min/d, 4 d/ wk for the first 8 wks. One day/wk the subjects were required to walk in a one-on-one supervised setting where they were instructed on how to monitor their workload. On the other 3 d/wk, subjects were allowed to use either a treadmill for their walking or be outdoors, as long as they achieved the appropriate intensity. By 8 wks, the duration of exercise increased gradually to 45 minutes so that for the last 6 wks subjects walked for 45 min/d at least 4 d/wk. Subjects completed exercise logs weekly, and their exercise compliance/progression was discussed with them weekly. We found ~90% compliance rate with this program and had only 4 dropouts.

The testing procedures below have been previously described (22), and will be presented briefly.

Anthropometric testing

Height and weight were taken and body mass index (BMI) was calculated. Waist circumference was also measured at the umbilicus. The Bod Pod (Life Measurements Inc., Concord, CA) was used to measure body density and percent body fat was calculated.

$\dot{V}O_2$ peak

$\dot{V}O_2$ was determined using a continuous treadmill protocol as previously described (23). The protocol started at 2.5 mph and the speed was increased by 0.5 mph every 2 min until 3.5 mph and then treadmill grade was increase 2% every 2 min until volitional fatigue. Throughout the test, oxygen consumption was also measured using indirect calorimetry (Cosmed Quark b^2, Rome, Italy). $\dot{V}O_2$ peak was selected as the highest O_2 consumption attained, as well as HR approaching age-predicted max, respiratory exchange ration >1.1 and RPE >16 (24). All exercise tests were evaluated by a cardiologist. Subjects completed this test both prior to and upon completion of the exercise training.

Oral glucose tolerance test

At 0700 h, a venous catheter was inserted into an antecubital vein (prior to any testing) and kept patent with normal saline. Baseline samples were drawn. Upon completion of the fasting measures of autonomic function (∼45 min), a 75 g dextrose drink (NERL Diagnostics, East Providence, RI) was consumed and a 5 ml blood sample was drawn every 30 minutes for 4 hours. Blood samples were analyzed for glucose and insulin as previously described (22).

Autonomic Measurements

Prior to any measurements, subjects rested in the supine position for 20 minutes. During 5 min of quiet rest with spontaneous breathing, beat-to-beat HR and hemodynamic data were measured, followed by 5 min of paced breathing (12 breaths/min (0.2 Hz) using a metronome), then 5 min of 80° head-up tilt with paced breathing. Head-up tilt was performed using an automatic tilt table where the subjects were secured with straps. Subjects were instructed not to move their hands or feet throughout the testing, and they were encouraged to remain quiet. Only the data collected during paced breathing was used in this analysis.

Electrocardiographic R-R intervals were continuously recorded with a modified CM5 lead interfaced with a digital acquisition system (Biopac Santa Barbara, CA), and data were sampled at 1000 Hz (22). Beat-by-beat finger plethysmographic arterial pressure (Portapres, TNO Biomedical Instrumentation, Amsterdam, The Netherlands) was also collected using a finger cuff, with the hand supported at the heart level (sampling rate of 100 Hz). Both the R-R intervals and beat-by-beat arterial pressure were measured in the supine position at rest and during tilt.

Data Analysis

Data were analyzed as previously described (22) and are described below briefly.

Heart Rate Variability

HRV data were analyzed in 5 min epochs, using the Heart Signal software (Oulu, Finland). The ECG signal was filtered via visual and automatic editing and only periods with no ectopic beats were analyzed. The procedures of Huikuri were followed (25). Initially, the R-R intervals were filtered through automatic editing to eliminate undesirable noise and premature beats. Any R-R interval that deviated more than 30% from the previous interval was considered premature (26). An average of accepted R-R intervals in the local neighborhood was computed and was used as a new value for the premature R-R intervals. This filtering technique has been suggested to remove abrupt temporary changes in R-R interval sequence and make the data more stationary (26). Huikuri et al. have shown that reliable measurements of spectral power densities of HRV can be achieved (<5% error) by eliminating randomly different numbers of R-R internals and re-computing them by average R-R intervals. In this study, only recordings with >98% qualified beats (less than 2% of beats were filtered) were included in the analysis. An autoregressive model (order of 10) was used to estimate the power spectral densities of the R-R interval variability. Power spectra was estimated by measuring the area in three frequency bands: very low frequency (VLF)=0.005-0.04 Hz; low frequency (LF)=0.040-0.150 Hz; and high frequency (HF)=0.150-0.400 Hz. The ratio between LF and HF spectra was calculated. High frequency and LF power spectral densities were calculated in both absolute and normalized units. Normalized units were calculated by dividing the power of a given component by the total power, from which the VLF power was subtracted, and multiplying by 100. All data analyses were carried out according to the standards put forth by the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (3).

HR complexity

Complexity refers to the irregularity of a dynamic process (13) and can be measured quantitatively by assessment of the uncertainty of patterns reoccurring within a time event series (13). Sample entropy (SampEn) and Lempel-Ziv entropy (LZEn) were used to quantify the complexity of the RRI time event series and calculated using nonlinear dynamics (WinCPRS, Absolute Aliens Oy, Turku, Finland) as previously described (27; 28). SampEn determines the probability of finding specific patterns or matches in a short time series, and ranges from 0-2. In a highly irregular signal, the value is ∼2, while the predictive or regular signal will have a value ∼0 (28). The embedding dimension m (length of sequences to be compared) was set at 2, while the range of tolerance for accepting matches was set at 20% of the standard deviation of the time series (29; 30). For this analysis we analyzed >200 consecutive stable and ectopic free data points, as has been previously recommended (27). The same number of beats was used for all within subject analysis pre and post training.

Using the same data points for calculating SampEn, we also calculated LZEn (WinCPRS). This measure counts the number of different and repeating patterns, from short to long,

based on Kolmogorov estimates (31). A string of symbols using binary coding is assigned such that if a value is above the mean then '1' is assigned, and a value below the mean results in a '0' is assigned. Thus insertion of symbol(s) forms a subque (a sequence of 0s and 1s) and then this subque is copied (27), creating a binary sequence. LZEn is computed on the basis of the number of such insertion and copying operations needed to generate the original sequence (27; 31). Similar to SampEn, an LZEn value near zero means that the signal is regular, whereas higher values reflect increased randomness of the signal.

Arterial baroreflex sensitivity (BRS)

Systolic arterial pressure and R-R intervals obtained from finger arterial pressure waveform were used to determine the coupling between fluctuations in HR and SAP. BRS was determined via the sequence technique using the WinCPRS software. The WinCPRS program searches for runs of 3 or more consecutive beats characterized by a progressive increase or a decrease in SAP of at least 1 mmHg. Baroreflex sequences were selected from the changes in SAP if R-R intervals concurrently changed in the same direction with SAP for 3 or more consecutive beats for at least 4 msec. 'Up sequences" (Up-up) sequences are those of increasing SBP and R-R intervals, whereas decreasing SAP and R-R intervals were defined as 'down sequences' (Down-down). The slope of the regression line between SAP and R-R intervals was used to calculate BRS. Only sequences with correlations equal or greater than 0.80 were accepted (22).

Statistical Analysis

Data were screened for normality of distribution by creating a histogram of the data and checked for skewness. The variables TP, LF/HF and HF were significantly skewed and a log transformation was performed. The initial data analysis revealed that there were no gender differences for any of the primary outcome variables (e.g. lnTP, lnHF, complexity, etc), so the data were not separated by gender for the remainder of the analysis. The data were analyzed using a 3-way analysis of variance with repeated measures (group (OB vs. ObT2D) × position (supine vs. upright) × training (pre vs. post)). If significant interactions were found, we followed up with post hoc analyses examining the data across group or position. The Tukey test and Bonferroni corrections were applied to the post hoc analyses. We assumed significance with alpha =0.05, and used 2-tailed statistical analyses so that results in either direction could be interpreted. All data were analyzed using SPSS statistical software (ver 16, Chicago, IL) and are expressed as mean ± SE.

Results

Subject characteristics

There were no age differences between groups. The groups were similarly matched for BMI, percent body fat, VO_2 peak and waist circumference (Table 2). As expected the ObT2D individuals had a higher HbA1c and fasting glucose concentrations ($P<0.05$) than the OB subjects ($P<0.05$). Fasting insulin concentrations were not significantly greater in the ObT2D individuals than the OB individuals.

Effect of training

Resting HR decreased slightly, but not significantly with exercise training in both groups. Exercise training significantly increased VO_2 peak in both groups (*OB* pre: 23.1±0.7, post 26.5±0.8; *ObT2D* pre: 22.2±0.2, post 24.2±0.7 ml/kg/min; P<0.05) (Table 2). Resting mean arterial pressure (MAP) did not change significantly with training in the OB subjects (pre 82.3±1.9; post 84.4±1.7 mmHg), whereas in the ObT2D subjects MAP increased (P<0.05) over the training period (pre 81.6±1.7; post 87.5±2.2 mmHg). There was a trend (P=0.06) for fasting insulin concentrations to decrease in the obese subject but there was no change in insulin concentrations in the ObT2D subjects.

Training resulted in a significant increase in HRV total power (log transformed (ln) (lnTP, $msec^2$) in the OB group but not in the ObT2D group. In the obese group, lnTP increased from 6.7±0.1 pre training to 7.0±0.1 $msec^2$ post training, (P<0.05); while lnTP showed only a slight change in the ObT2D group (pre 6.5±0.2, post 6.58±0.2 $msec^2$) (Figure 1a). There was no significant difference in resting lnTP between groups. Resting lnHF was found to increase with training (P<0.05, Figure 1b) in the OB group, but not in the ObT2D group. lnLF/HF did not respond to training in either group. No group differences and no training effects were observed for lnLF/HF in these subjects (Figure 1c). HR complexity was also unaltered in response to training and was not different between groups, when analyzed as either SampEn or LZEn (Figure 2).

Upright tilt

Both groups showed an increase in HR with upright tilt (*OB*: supine 66±1, upright 80±2; Ob*T2D*: supine 70±2, upright 80±2 b/min). In response to tilt, lnTP decreased (P<0.01, Figure 1) in the OB subjects to levels approaching those observed in the ObT2D group, while the change in the ObT2D response was not significant. There was no upright tilt by training effect for lnTP. Further lnHF showed a significant decline (P<0.001) in both groups (∼40%) with upright tilt but there was no training effect on the response to tilt in either group. There was a significant tilt by group interaction for lnLF/HF (P<0.05), such that the OB individuals demonstrated larger increases in lnLF/HF balance with tilt (supine: 4.27±0.12, upright: 6.17±0.17) than the ObT2D individuals (supine: 4.35±0.15, upright: 5.73±0.20). There was no effect of training.

With upright tilt, there was a decrease in SampEn (P<0.001) and there was a group by tilt interaction (P<0.05) (Figure 2). This decrease in complexity was greater in the OB subjects (23%) than in the ObT2D subjects (12%) (P<0.05). Similarly there was a significant decrease in LZEn with tilt in both groups (P<0.05).

Both the OB and ObT2D subjects increased MAP (approximately 9 mmHg) with tilt with training (P<0.05). There was a training by upright tilt interaction (P<0.01) for both groups, such that post training the increase in MAP with upright tilt was considerably smaller (∼3 mmHg) than pre training (∼10 mmHg).

Baroreflex sensitivity decreased with upright tilt as expected both pre and post training (P<0.001) (Figure 3). For the down-down measure, there was a tilt by group interaction (P<0.01); the OB subjects (supine: 11.0±0.75; upright: 5.5±0.44 ms/mmHg) had a greater

magnitude of decrease ($P<0.01$) in the down-down component than in the ObT2D subjects (supine: 8.8±0.96; upright: 5.9±0.57 ms/mmHg). There was a significant effect of upright tilt in the up-up measure of BRS ($P<0.05$) but there were no group differences. We observed no effect of exercise training for the up-up measure for BRS.

Discussion

Although there is considerable research demonstrating that lower fitness levels are associated with lower HRV (4), there are only a few studies examining the plasticity of the autonomic nervous system with exercise training in an obese population. Utilizing a commonly recommended exercise program, with an intensity and duration that produced a significant increase in VO_2peak, there were 3 main findings: 1) exercise training improved total HRV and parasympathetic modulation in OB individuals while there was no improvement in the ObT2D subjects, 2) ObT2D individuals had attenuated tilt-induced BRS compared with OB individuals which was not altered with training, and 3) exercise training had no impact on HR complexity. From these results we concluded that there is a loss of plasticity of the ANS in middle-aged obese individuals with T2D.

Previous exercise training studies have demonstrated that exercise training augments total HRV in young individuals (6-8; 32), but only a few prospective studies have assessed the effects of exercise training in middle-aged obese individuals. Our exercise intervention resulted in an increase in total power (5%) and improvement in parasympathetic modulation in the OB individuals, but these improvements were not observed in the individuals with T2D. Our findings in the OB individuals parallel earlier work in young non-obese males that has shown that endurance training (6 wk (12) or 12 wk (11)) increased resting parasympathetic modulation after training. Together these studies suggested that there may be a reversibility of human ANS dysfunction with exercise training in OB individuals. Our study, as well as other recent studies (9; 10) in ObT2D individuals have noted no change in HRV with aerobic training suggesting a lack of responsiveness of the ANS in individuals with T2D implying that if obese individuals progress to T2D the autonomic dysfunction is either irreversible or a more aggressive training program is needed.

In the present study we did not observe substantial changes in body weight, but weight loss may also relate to potential changes in autonomic function. Vanninen et al. (33) noted improvements in HRV ($P<0.01$) compared to baseline variables in women with T2D following an intensive dietary and exercise intervention. Recent research (34) also indicates that changes in HRV will only occur with a minimal exercise intensity of 8 kcal/kg/week in women. Our study subjects exercised at a training load at or greater than 8 kcal/kg/week, thus in both our groups we would have expected improvements in autonomic function while changes were only observed in the OB group. In addition, the plasticity of the ANS in the OB subject may be linked to changes in fasting insulin concentrations. There was a trend for fasting insulin levels to decrease, which may also be linked to the improvements in total HRV and parasympathetic modulation in the OB group only. Likewise, Emdin (2) noted an improvement in hemodynamic and HRV changes in obese individuals with weight loss, and this was related to improvement in fasting insulin levels.

This is the first study to demonstrate that HR complexity is not different between the OB and ObT2D individuals at rest, and that exercise training did not alter HR complexity. This contrasts Heffernan et al (29), who in healthy young men (mean age 25 yr), noted significant increases in entropy measures of HR complexity with 6 wks of resistance training. The lack of change in complexity in our subjects compared to Heffernan (29), indicate these changes may be age-related, body composition related or may be dependent on exercise training mode.

We also noted no changes in BRS with training. Employing a similar time frame of exercise training (5 months), Loimalla (9) also reported no change in BRS, yet their one year intervention study elicited improved baroreflex sensitivity in men with T2D (9). This suggests that a longer exercise stimulus may be needed to change the BRS in the OB population. Well-controlled longitudinal studies in patient populations with cardiovascular complications report improvements in BRS with exercise training (9; 35; 36). Physical inactivity decreases BRS as well as endothelial function, thus a long period of stimulation is possibly needed to induce changes in vascular structure. Paralleling the findings on BRS we found no change in MAP in the OB individuals but a small increase in MAP in ObT2D. This could be attributed to an increase in DAP in the ObT2D that was not observed in the OB group during this training period.

Reflex Autonomic Function

Upright tilt stimulates the sympathetic nervous system and induces vagal withdrawal, resulting in a displacement of blood to the lower body, distension of the venous system and stimulating a cascade of hemodynamic and autonomic adjustments associated with the responsiveness of the baroreflex loop (27). In the present study, all subjects demonstrated a normal response to upright tilt, with a~45% decrease in parasympathetic modulation. With tilt, lnLF/HF increased by 30% in the OB group, while there was only a 19% change in the ObT2D group, indicating the OB individuals have a better ability to shift the sympathovagal balance towards sympathetic predominance. Although tilt increased HR (11-14 beats/min), HR complexity was not as responsive to tilt in the ObT2D individuals compared to the OB individuals. These differences may be a reflection of early autonomic cardiovascular dysfunction. In contrast to our hypothesis, HR complexity did respond to tilt but no changes in response were found with training. More research related to HR complexity with training of longer duration and differing intensities is needed in obese populations.

Although we found no effects of training on BRS, we did observe that BRS decreased during upright tilt with the reduction being greater in the OB than in the ObT2D subjects. The lack of training effect on BRS may be because initially the subjects had an appropriate stimulus response, thus leaving minimal room for improvement. The ObT2D subjects had a 33% decrease in BRS with tilt and the OB subjects had a 49% decrease, indicating less sensitivity to the stimulus in those with T2D. Since training did not enhance the response in this group, aerobic exercise training of moderate intensity may not be sufficient to improve the response to upright tilt, or in the ObT2D individual structural changes may have occurred that are resistant to training effects.

Group differences

We did not observe differences in the linear or non-linear components of resting HR between the obese groups as anticipated. All subjects were untrained and were extensively screened for overt cardiovascular disease, which may have minimized the differences in HR modulation between groups. Our initial screening also excluded individuals with overt neuropathies. A previous study (12) noted that in ObT2D individuals without peripheral neuropathy the cardiac LF and HF components were similar to normal volunteers, while a more recent report (37) suggested that improvements in HRV with training in ObT2D subjects may depend on the degree of cardiac autonomic neuropathy such that subjects with definite cardiac autonomic neuropathy can realize more benefit.

A strength of the present study was that it employed a generally recommended exercise regimen (30 min/ d, ∼ 4 d/wk), but unlike many previous studies, our subjects exercised on their own 3 d/wk, which is a more ecological approach to exercise training. This training protocol increased VO_2 peak, yet this was not associated with improvement in autonomic function, BRS or in ObT2D. An additional strength is that potential changes in autonomic function were examined in obese individuals and compared those with and without T2D. Each subject's medication regimen was closely monitored, did not change during the study and subjects on beta blockers or any medications known to impact autonomic function or to cause syncope were excluded. This study therefore provides insight into the responses of the ANS to exercise training while individuals are using medications common in ObT2D.

In conclusion in obese individuals without T2D, exercise training results in a small improvement in HRV and parasympathetic modulation. These improvements were not observed in the obese subjects with T2D. Exercise training did not alter LF/HF, HR complexity or BRS. This suggests that in obese individuals the ANS has sufficient plasticity to adapt to a moderately intense training stimulus. More importantly this study reveals that ANS is not as plastic in individuals with T2D and with no overt cardiovascular disease. These individuals demonstrate inappropriate responses to reflex autonomic function, while their resting HR and BP responses appear similar to those of OB individuals. Short term (16 wk) exercise training without weight loss does not correct these differences in ObT2D. Additional studies are needed to investigate different approaches to help improve cardiovascular autonomic dysfunction in ObT2D.

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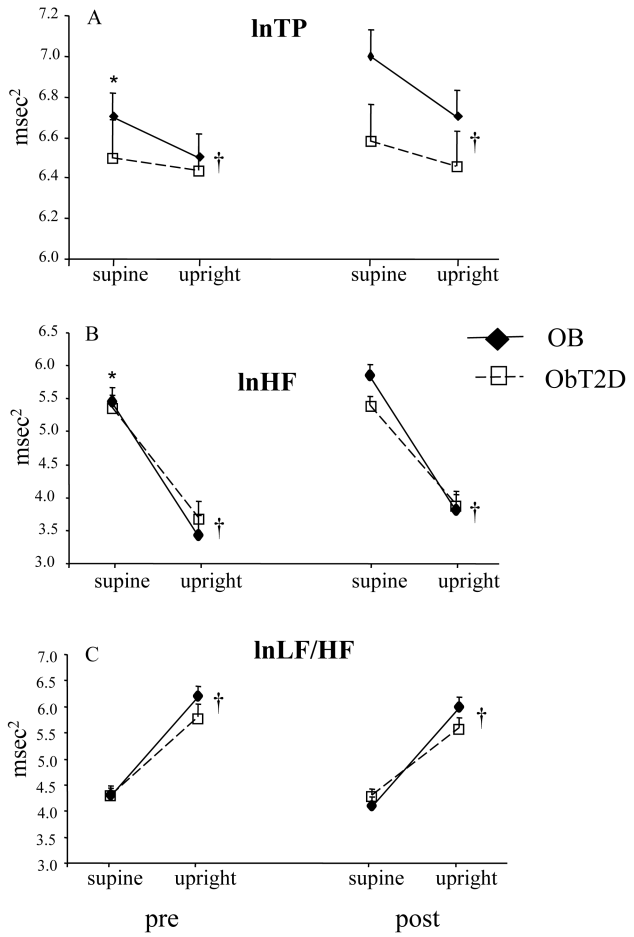

Figure 1.

The effects of upright tilt and pre/post training responses on total power (lnTP), high frequency (lnHF) and low frequency to high frequency ratio (lnLF/HF). *P<0.05 resting pre vs. post in obese (OB) individuals; †P<0.000 supine vs. upright. Obese individuals with type 2 diabetes (ObT2D)

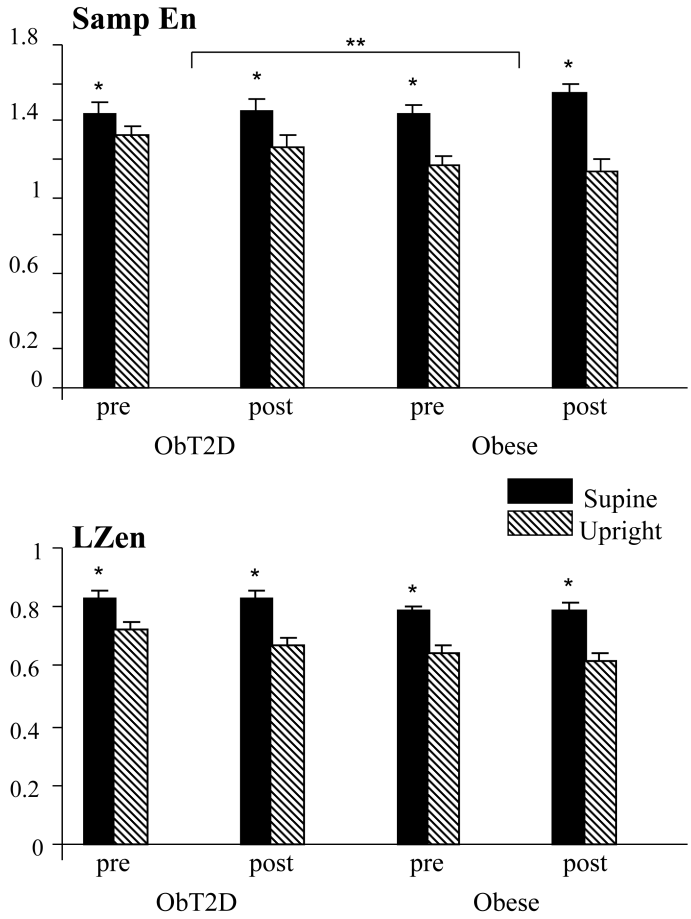

Figure 2.

Changes in HR complexity. A. SampEn, B. LZEn. *P<0.01 supine vs. upright tilt; ** P<0.01 position x group interaction, OB subjects had a greater decrease than the ObT2D; OB=obese, ObT2D=obese with type 2 diabetes.

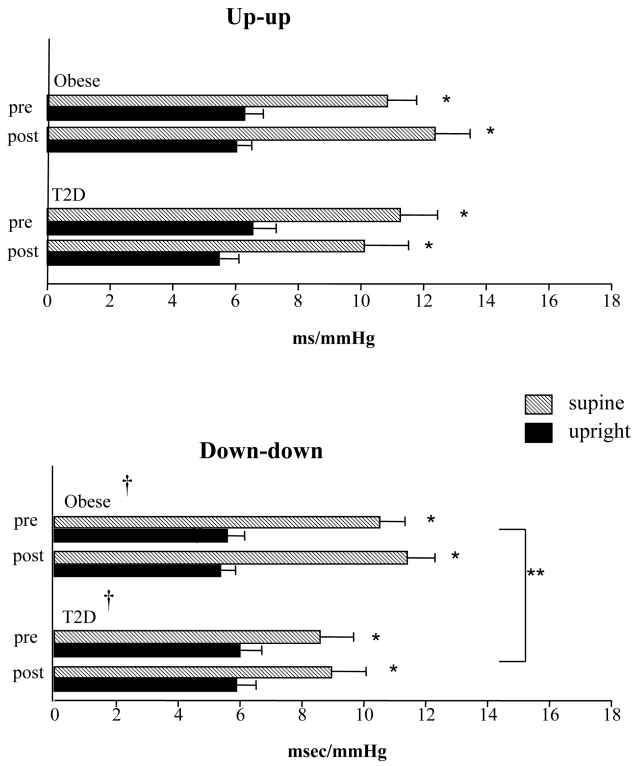

Figure 3.

Changes in baroreflex sensitivity with training and upright tilt in all groups. *P<0.01 supine vs. upright tilt; ** P<0.01 position x group interaction, OB subjects had a greater decrease than the ObT2D; †P<0.06 training effect on upright tilt; OB=obese, ObT2D=obese with type 2 diabetes.

Table 1

Subject Medications

	Obese with type 2 diabetes (n=22)	Obese without type 2 diabetes (n=34)
Glucose lowering drugs	26	0
Metformin	*17*	*0*
Sulfonylurea	*2*	*0*
TZD	*7*	*0*
Lipid lowering drugs	*8*	*9*
Statin	*8*	*7*
Fibrate	*0*	*1*
Other	*0*	*1*
Antihypertensives	*10*	*7*
HCTZ	*1*	*3*
ACE-I	*6*	*3*
Valsartan	*3*	*2*
Hormone replacement therapy	0	3
Antidepressants	6	4
Other drugs	14	19
No medications	2	12

TZD- Thiazolidinediones

HCTZ- Hydrochlorothiazide

ACE-I- Angiotensin Converting Enzyme Inhibitors

Table 2

Anthropometric and baseline measures in all subjects.

	ObT2D (n=22) Pre	Post	OB (n=34) Pre	Post
Age (yr)	50.0±1.6		49.0±0.9	
Height (cm)	170.0±1.8		168.4±1.4	
Weight (kg)**	110.0±4.1†	109.3±4.1	100.8±302	99.8±3.3
BMI (kg/m^2)**	37.5±1.0	37.2±1.1	35.7±0.8	35.0±0.9
Waist circumference (cm)**	120.7±2.7	117.1±2.6	109.4±2.1†	107.3±2.0†
% body fat	42.1±1.7	41.9±1.7	41.6±1.3	41.2±1.4
VO_2 peak (ml/kg/min)**	22.2±0.2	24.2±0.7	23.1±0.7	26.5±0.8
Hemoglobin A1c (%)	7.3±0.3	7.2±0.2	5.7±0.2†	5.3±0.1†
Fasting glucose (mmol/L)	7.2±0.2	6.9±0.3	5.1±0.2†	5.1±0.2†
Fasting insulin (pmol/L)	103.1±18.8	109.4±15.6	84.7±15.2	64.1±12.5

† P<0.05 vs. ObT2D

** P<0.05 vs. pre/post training: obese subjects (OB); obese subjects with T2D (ObT2D)