CARIDIOVASCULAR AND AUTONOMIC RESPONSES TO RESISTANCE TRAINING IN INDIVIDUALS WITH DOWN SYNDROME

By

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Abstract

Down syndrome (DS), also referred to as Trisomy 21, is a genetic disorder caused by a partial or full extra copy of the chromosome 21. Studies show that physical activity levels in individuals with DS are much lower than individuals without DS. Individuals with DS have different responses to maximal and submaximal dynamic exercise, as well as other autonomic stimuli. The purpose of this research project was to investigate the cardio-autonomic responses in individuals with DS following resistance training and compare these responses to controls of similar age with no disabilities. Six healthy subjects (3 with DS, 3 controls without disabilities) aged 18 to 40 years participated in the study. There were two women and 1 male in both the experimental and control groups. The subjects underwent a 4 week resistance training protocol utilizing 8 different resistance machines (3 days per week). Body composition, BP, central arterial stiffness, HRV measurements were all taken prior to the intervention and following the 4 week training. Due to the exploratory nature and low n of the study, all results are presented as individual and group means per grouping area. Our data showed that individuals with DS exhibit divergent responses to resistance training compared to individuals without DS. These findings indicate further research investigating the cardio-autonomic responses to resistance training in individuals with DS is necessary.

INTRODUCTION

Down syndrome (DS) is the most common genetic chromosomal disorder to cause intellectual disability (American Academy of Pediatrics, 2001). Nondisjunction during cell division can lead to individuals having an extra copy of the 21st chromosome, which causes DS. In most children with DS, the condition is caused by nonfamilial Trisomy 21, but DS can also occur from unbalanced translocation (American Academy of Pediatrics, 2001). The lifespan of individuals with DS is much shorter, by approximately 20 years, than that of individuals without DS. Individuals with DS often exhibit numerous secondary conditions, such as congenital heart disease, leukemia, Alzheimer's, and hypothyroidism (American Academy of Pediatrics, 2001). Previously, a major cause of early mortality in this population was congenital heart disease, however with advancements in medical technology their lifespans have increased (Day SM, Strauss DJ, Shavelle RM, Reynolds RJ, 2005). Due to this increase in longevity, more individuals with Down syndrome will need greater levels of support. Exercise may be advantageous in preventing or treating deleterious changes in the cardiovascular system.

Studies show that physical activity levels in individuals with DS are much lower than individuals without DS (Whitt-Glover M.C., O'Neill K.L., Stettler N., 2009). Furthermore, low levels of physical activity constitute a sedentary lifestyle, which is associated with obesity and a higher risk of morbidity and mortality (Warren T.Y., et al., 2010). Individuals with DS exhibit a marked attenuation of heart rate (HR) during maximal and submaximal dynamic exercise compared to individuals without DS (Sang Ouk W, et al., 2014). Chronotropic incompetence has been linked to reduced peak oxygen consumption values and diminished work capacity in individuals with DS

(Guerra M, Llorens N, Fernhall B, 2003). Additionally, chronotropic incompetence is associated with mortality and morbidity in nondisabled populations (Brubaker PH, Kitzman DW, 2011). Even with great improvements in longevity through modern medicine, low levels of aerobic capacity remains a serious detriment to health and well being among individuals with DS.

During short term, low intensity static handgrip exercises, attenuated HR and systolic blood pressure (SBP) responses are seen in individuals with DS (Heffernan KS, et al., 2005). These findings suggest an impaired baroreflex, or a blunted parasympathetic withdrawal. In this study, cardio-autonomic function was assessed by monitoring heart rate, blood pressure, and heart rate variability responses during tilt table testing prior to and post intervention. The literature response in non-disabled healthy individuals to a tilt table test is an increase in heart rate and a drop in systolic blood pressure. Individuals with DS have a reduced response to passive tilt (Fernhall, et al., 2005). This blunted response to postural changes may be due to an inherent increase in arterial stiffness in individuals with DS, which decreases baroreceptor sensitivity.

Previous research has shown high intensity resistance training increases arterial stiffness in individuals without DS (Yoon ES, et al., 2010). Vascular remodeling following the resistance-training program in our study was assessed using pulse wave analysis and pulse wave velocity. This research will lend additional data to a population that may already present with decreased arterial distensibility leading to deleterious changes in vascular function and autonomic responses.

Resistance training is a technique used to investigate autonomic and vascular responses, since this form of exercise mitigates several autonomic and arterial changes.

To this author's knowledge, there are no studies that have examined the effects of resistance training on vessel remodeling and cardio-autonomic function in individuals with DS. Any mode of exercise is usually viewed in a positive light through the community lens. However, the purpose of this research project was to investigate the autonomic and vascular changes in individuals with Down syndrome (DS) following resistance training and compare these responses to controls of similar age with no disabilities.

All tests performed are non-invasive, and the exercises are simple to understand and execute. By performing this study, the scientific community will have a better understanding of how individuals with DS may respond differently to physiological stimulation than individuals without DS.

METHODS

Participants

Six healthy subjects (3 with DS, 3 controls without disabilities) aged 18 to 40 years volunteered for the study. There were two women and 1 male in both the experimental and control groups. Subjects in both groups were either sedentary or moderately active, but none of the subjects regularly resistance trained. Participants with Down syndrome were recruited from the local community and support groups. All Down syndrome participants either lived at home or in community group settings. Exclusion criteria were: congenital heart disease, current smoker, BMI >40 kg/m^2, blood pressure greater than 140/90 mmHg, diabetes (fasting glucose >110 mg/dL).

Study Design

The Appalachian State University Institutional Review Board approved all experimental procedures. All instrumentation and protocols were thoroughly explained prior to testing. Participants were familiarized with all testing procedures before data collection began. Each participant's measures were taken at baseline and following the four-week resistance training protocol. The measures include: anthropometrics, central and peripheral arterial stiffness, and tilt table testing.

Anthropometrics

Whole-body plethysmography (Bod Pod; Life Measurement Inc., Concord, CA, USA) was used to measure body composition, and body weight was measured using the Bod Pod scale. Height was measured using a stadiometer.

Central Arterial Stiffness

Pulse wave velocity and pulse wave analysis measurements were obtained using an applanation tonometer, Sphygmacor XCEL (Atcor Medical, Itasca, Illinois). Seated blood pressure measurements were taken using the Sphygmacor XCEL. The pulse wave was obtained between the right common carotid artery and the left femoral artery. A cuff was placed on the left femoral artery to occlude flow. Measurements, using a basic tape measure, were taken from the carotid artery to the sternal notch, from the sternal notch to the cuff, and then from the femoral artery to the cuff. These measurements were entered into the Sphygmacor XCEL, and used to calculated pulse wave velocity.

Tilt Table Testing

Subjects rested in a supine position for 5 minutes before head-up tilt was initiated, and data collection began. The subject was then tilted to 80° for five minutes. Beat-to-beat blood pressure was monitored using finger plethysmography (COMPANY) with the finger at heart level during data collection. Heart rate, Heart Rate Variability (HRV), low frequency (LF), high frequency (HF), and low frequency to high frequency ratio (LF/HF) was measured using single lead electrocardiogram modified CM5 configuration (COMPANY). Following the five-minute tilt period, the subject was returned to the supine position for five more minutes.

Resistance Training Program

The resistance training intervention included four weeks of training three days a week. During each session, the participant performed 3 sets of 15 repetitions at approximately 60% of their 1-rep max value using different resistance machines. Each subject's 10-rep max was determined, and from their 1-rep max was calculated. There were eight different resistance machines utilized, which consisted of leg extension, leg curl, chest press, shoulder press, bicep curl, tricep press, abdominal crunch and back extensions.

Statistical Analysis

Due to small sample size, we have described the data as means ± standard error. All grouped data (DS versus control subjects) was analyzed as percent change pre post training. Box and whisker will be employed to visually describe each data set by grouping variables.

RESULTS

Table 1. Descriptive Statistics

Variable	PreRE DS Subject 1	PostRE DS Subject 1	PreRE DS Subject 2	PostRE DS Subject 2	PreRE DS Subject 3	PostRE DS Subject 3
Height (cm)	151.9	151.9	150.9	150.9	141.9	141.9
Mass (kg)	93.795	93.076	54.951	53.068	69.968	67.215
Body Fat (%)	44.2	42.8	18.5	28	41.8	47.1
SBP (mmHg)	126	122	136	120	120	115
DBP (mmHg)	70	82	71	69	66	72
SP (mmHg)	108	111	117	104	105	103
PP (mmHg)	37	27	46	35	39	29

Pre Resistance Exercise statistics for Down syndrome subject (PreRE DS), Post Resistance Exercise statistics for Down syndrome subject (PostRE DS).
Height; centimeters, Mass; kilograms, Body Fat; Percent, Systolic Blood Pressure (SBP); millimeters of mercury, Diastolic Blood Pressure (DBP); millimeters of mercury, Central Aortic Systolic Pressure (SP); millimeters of mercury, Central Aortic Pulse Pressure (PP); millimeters of mercury.

Table 2. Descriptive Characteristics

Variable	PreRE CTRL Subject 1	PostRE CTRL Subject 1	PreRE CTRL Subject 2	PostRE CTRL Subject 2	PreRE CTRL Subject 3	PostRE CTRL Subject 3
Height (cm)	170.8	170.8	174	174	171	171
Mass (kg)	81.705	79.78	71.628	70.81	72.407	71.891
Body Fat (%)	25.7	24.2	28.4	23.4	26.5	24.4
SBP (mmHg)	132	130	119	126	121	112
DBP (mmHg)	83	77	65	81	78	74
SP (mmHg)	114	111	100	112	104	99
PP (mmHg)	28	33	34	30	25	25

Pre Resistance Exercise statistics for Control subject (PreRE CTRL), Post Resistance Exercise statistics for Control subject (PostRE CTRL).
Height; centimeters, Mass; kilograms, Body Fat; Percent, Systolic Blood Pressure (SBP); millimeters of mercury, Diastolic Blood Pressure (DBP); millimeters of mercury, Central Aortic Systolic Pressure (SP); millimeters of mercury, Central Aortic Pulse Pressure (PP); millimeters of mercury.

From baseline to post intervention, DS Subject 1 saw a 15.8% increase in pulse wave velocity. Where as DS Subjects 2 and 3 saw an 8.33% and 4.30% decrease respectively. CTRL Subject 2 was the only control to see a rise in pulse wave velocity following intervention with an 8.25% increase. CTRL Subject 3 had an 11.6% decrease, and CTRL Subject 1 had a 6.74% decrease.

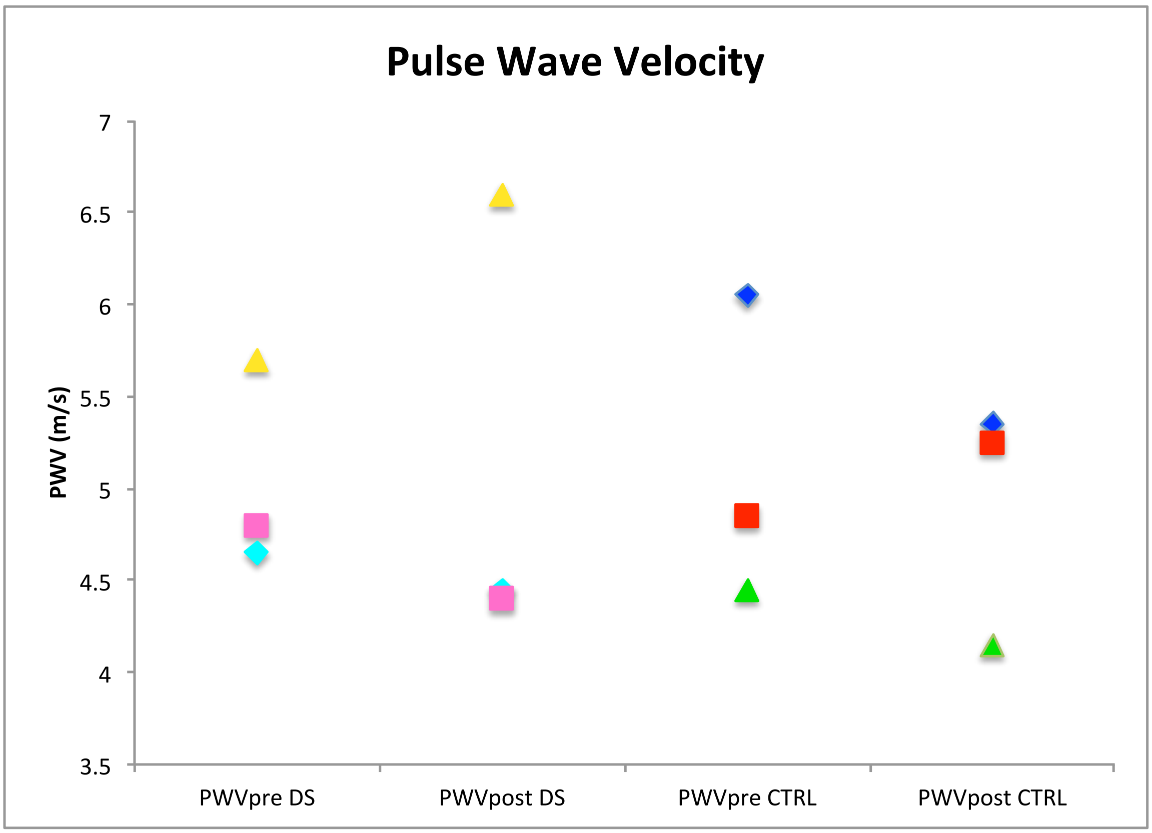

Figure 1. Changes in pulse wave velocity (PWV) from pre to post intervention in Down syndrome (DS) and Control (CTRL) subjects.

DS Subject 1 (yellow triangle), DS Subject 2 (pink square), DS Subject 3 (turquoise diamond), CTRL Subject 1 (green triangle), CTRL Subject 2 (red square), CTRL Subject 3 (blue diamond).

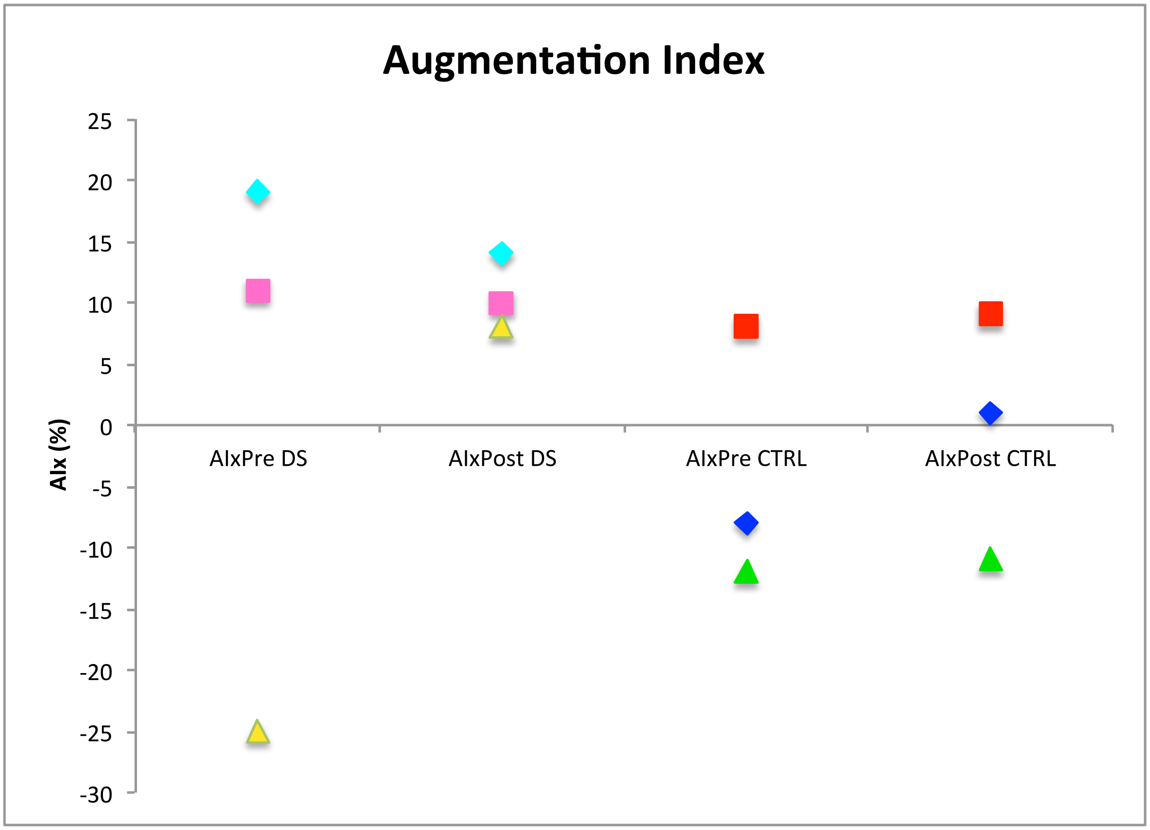

Figure 2. Changes in Augmentation Index from pre to post intervention in Down syndrome (DS) and Control (CTRL) subjects.

DS Subject 1 (yellow triangle), DS Subject 2 (pink square), DS Subject 3 (turquoise diamond), CTRL Subject 1 (green triangle), CTRL Subject 2 (red square), CTRL Subject 3 (blue diamond).

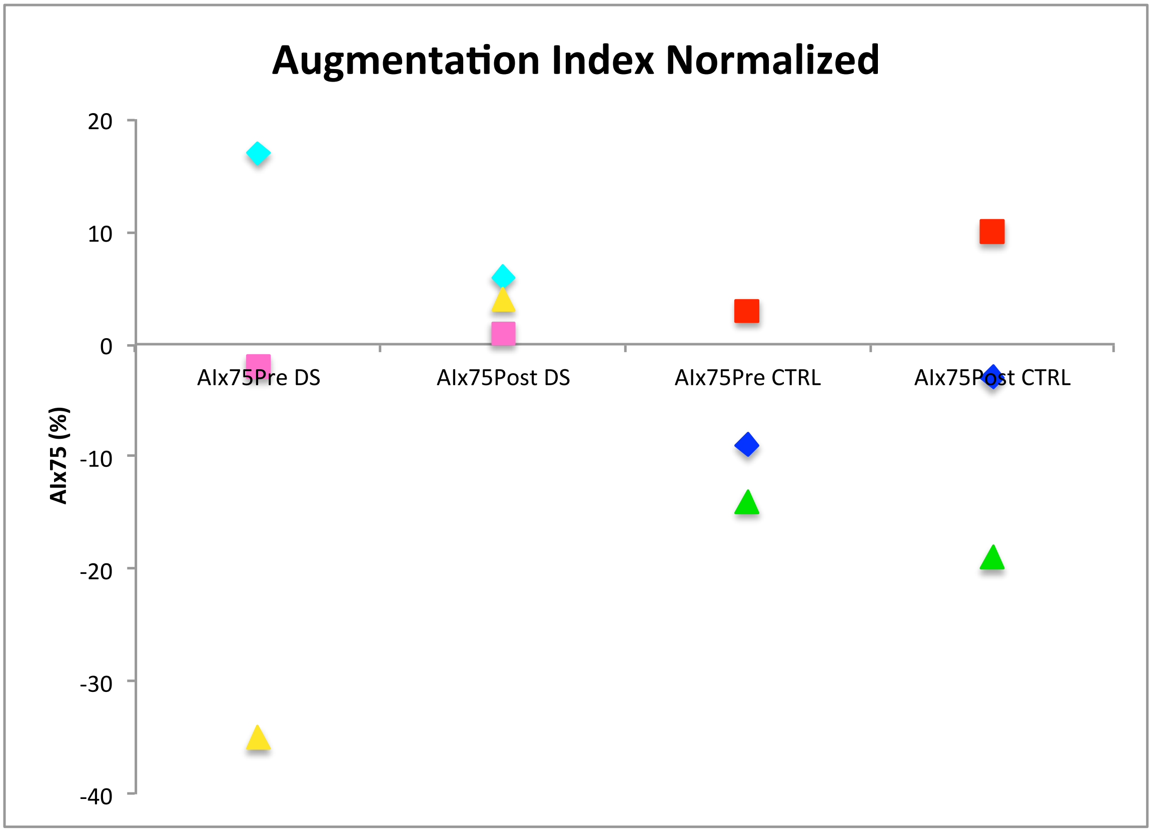

Figure 3. Changes in heart rate corrected Augmentation Index (AIx75) from pre to post intervention in Down syndrome (DS) and Control (CTRL) subjects.

DS Subject 1 (yellow triangle), DS Subject 2 (pink square), DS Subject 3 (turquoise diamond), CTRL Subject 1 (green triangle), CTRL Subject 2 (red square), CTRL Subject 3 (blue diamond).

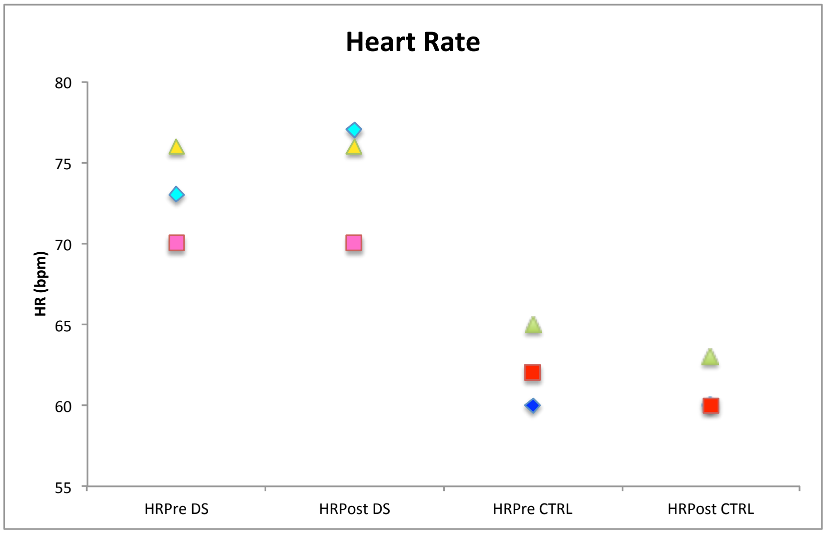

Figure 4. Average Heart Rate (HR) in beats per minute pre and post intervention for DS and CTRL groups

DS Subject 1 (yellow triangle), DS Subject 2 (pink square), DS Subject 3 (turquoise diamond), CTRL Subject 1 (green triangle), CTRL Subject 2 (red square), CTRL Subject 3 (blue diamond).

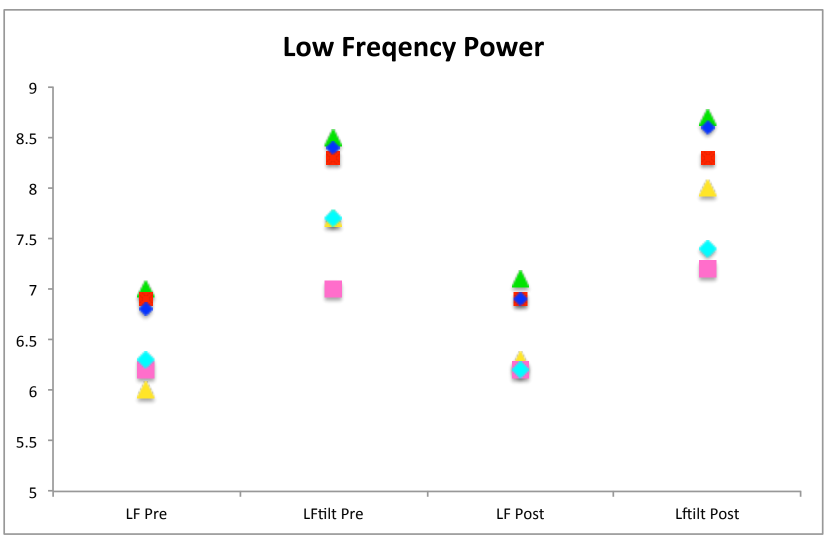

Figure 5. Low Frequency Power (LF) pre and post intervention for DS and CTRL groups

DS Subject 1 (yellow triangle), DS Subject 2 (pink square), DS Subject 3 (turquoise diamond), CTRL Subject 1 (green triangle), CTRL Subject 2 (red square), CTRL Subject 3 (blue diamond).

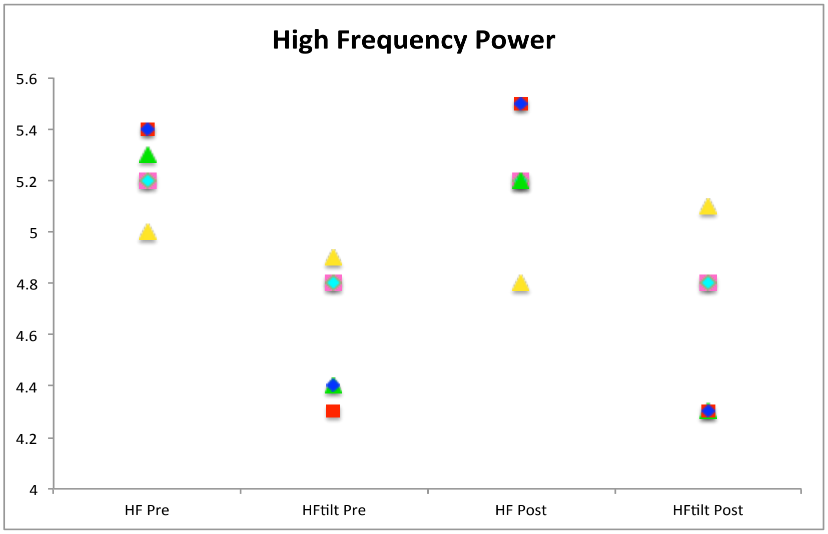

Figure 6. High Frequency Power (HF) pre and post intervention for DS and CTRL groups

DS Subject 1 (yellow triangle), DS Subject 2 (pink square), DS Subject 3 (turquoise diamond), CTRL Subject 1 (green triangle), CTRL Subject 2 (red square), CTRL Subject 3 (blue diamond).

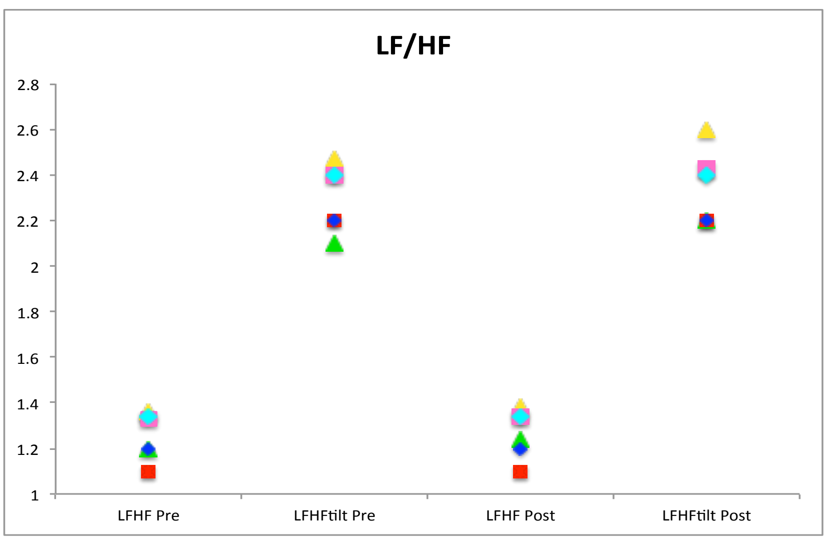

Figure 7. Low Frequency to High Frequency (LF/HF) pre and post intervention for DS and CTRL groups

DS Subject 1 (yellow triangle), DS Subject 2 (pink square), DS Subject 3 (turquoise diamond), CTRL Subject 1 (green triangle), CTRL Subject 2 (red square), CTRL Subject 3 (blue diamond).

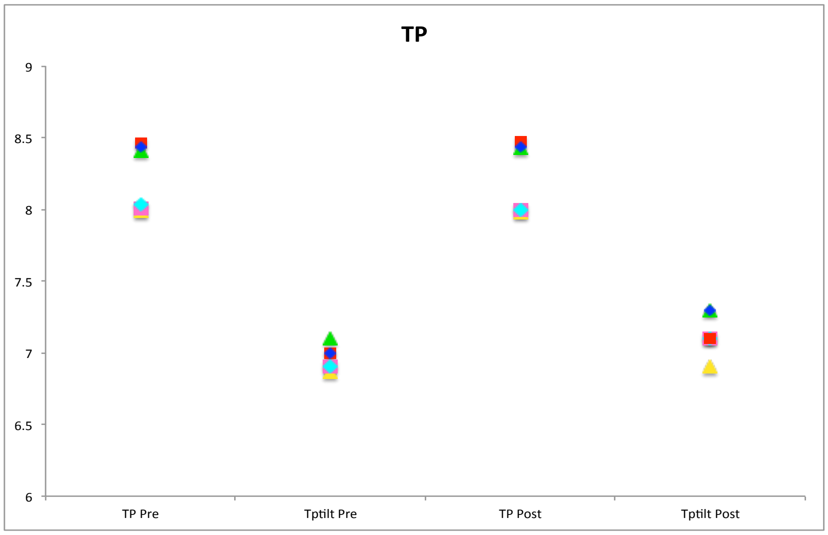

Figure 8. Total Power (TP) pre and post intervention for DS and CTRL groups

DS Subject 1 (yellow triangle), DS Subject 2 (pink square), DS Subject 3 (turquoise diamond), CTRL Subject 1 (green triangle), CTRL Subject 2 (red square), CTRL Subject 3 (blue diamond).

DISCUSSION

The present study aimed to investigate the autonomic and vascular changes seen after four weeks of resistance exercise training in individuals with DS. Previous studies have shown aerobic exercise and resistance exercise (RE) elicit different vascular and autonomic responses in individuals without DS (Yoon E.S., et al., 2009). Following an aerobic exercise program, previous research has shown an individual without DS will see a decrease in central pulse wave velocity (PWV) indicating an increase in the distensibility of the vessel (Collier S.R., et al., 2010). Decreases in central arterial distensibility have been associated with increased mortality and morbidity, which indicates aerobic exercise can potentially decrease cardiovascular risk in individuals without DS. Prior investigations have indicated that following an acute aerobic bout; individuals with DS show an attenuated arterial response compared with controls (Hu M., et al., 2013).

Resistance training has been shown to produce different physiological responses than aerobic exercise. The vascular responses to exercise are also dependent upon gender in individuals without DS. Arterial distensibility decreases in men following resistance exercise training, which causes increases in central PWV. Increases in central PWV are not generally seen in women indicating their arterial distensibility is not altered with RE. Although resistance training increases the central arteries stiffness in men, mean arterial pressure does not increase and vasodilatory capacity increases (Collier S.R., et al., 2010). This suggests the physiological adaptations following resistance training are not deleterious to individuals without DS.

Our main findings, with regards to vascular remodeling, were that most individuals with DS have similar responses to individuals without DS. **Figure 1** indicates DS Subject 1's PWV increased, whereas the other two DS subjects had slight decreases. These variances could possibly be due to sex differences, and are consistent with trends seen in individuals without DS. Although an increase is seen with DS Subject's PWV, SBP and DBP had no sizable changes (**Table 1**). The other DS subjects had only slight decreases in pulse wave velocity, which was similar to the control's responses.

Augmentation Index (AIx) is a measure of pulse wave reflection, and can be used as an indirect measure of arterial stiffness. The most noticeable difference in AIx was seen in DS Subject 1, where their AIx % increased considerably (**Figure 2**). This increase in AIx represents an increase in the reflected wave, which can cause adverse effects on cardiovascular functioning (Weber T., et al., 2004). This increase is also seen with the normalized augmentation index (AIx75) in DS Subject 1 (**Figure 3**). CTRL Subject 3's AIx and AIx75 increased more following the resistance training compared to the other CTRL Subjects.

Previous research shows following upright tilt, individuals without DS have a significant increase in HR and systolic blood pressure (Novak P., 2011). Autonomic function and response to stimuli are altered and improved following long-term aerobic training. An increase in baroreflex sensitivity is seen, as well as improvements in heart rate variability (La Rovere M.T., et al., 2002, Zhang B., et al., 2003). Specifically an increase in high frequency power is seen with a decrease in low frequency power (Collier S.R., et al., 2009). Previous studies have shown BRS declines and HRV does not change significantly with resistance training in individuals without DS (Collier S.R., et al., 2009). The control subjects in this study had similar responses to RE that support the aforementioned research.

Altered parasympathetic regulation of heart rate is accompanied by a blunted initial heart rate response to upright tilt. Recent data indicate that subjects with DS exhibit reduced parasympathetic withdrawal during static handgrip exercise, suggesting the sluggish heart rate observed in the subjects with DS may be explained by this occurrence. **Figure 6** shows HF prior to tilt and during tilt of all subjects' pre and post intervention. The DS Subjects initial values are lower than the controls and their responses to tilt are blunted, which suggests they have reduced vagal tone at rest and a reduced parasympathetic withdrawal during tilt. The DS Subjects LF values are also slightly divergent from the control subjects (**Figure 5**). Their LF values prior to tilt are lower than individuals without DS, but during tilt their LF follow similar trends to the controls. DS Subjects LF/HF were slightly elevated in comparison to the control subjects, which may indicate they have increased sympathetic innervation at rest.

A major limitation to the present study is only having a sample size of 3 per group (n=6). A larger subject pool will allow for statistical analysis of the data collected. Another potential limitation could be the inability to match groups by age since the incidence of cardiovascular disease increases with age.

In conclusion, our data showed that individuals with Down syndrome exhibit divergent responses to resistance training compared to individuals without DS. These responses indicate the need for further investigations into the autonomic and vascular changes following RE in individuals with DS.

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