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EFFECTS OF RESPIRATORY TRAINING ON HEART RATE VARIABILITY AND BAROREFLEX SENSITIVITY IN INDIVIDUALS WITH CHRONIC SPINAL CORD INJURY

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Abstract

Objective—To evaluate the effects of pressure threshold respiratory training (RT) on heart rate variability and baroreflex sensitivity in persons with chronic spinal cord injury (SCI).

Design—Before-after intervention case-controlled clinical study.

Setting—SCI research center and outpatient rehabilitation unit.

Participants—Persons with chronic SCI ranging from C_2 to T_{11} that participated in RT (n=24) and untrained chronic SCI controls ranging from C_2 to T_9 (n=20).

Intervention—A total of 21 ± 2 of RT sessions performed 5 days a week during a four-week period using a combination of pressure threshold inspiratory and expiratory devices.

Main Outcome Measures—Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and beat-to-beat arterial blood pressure (BP) and heart rate (HR) changes during 5-second long maximum expiratory pressure maneuver (5s MEP) and sit-up orthostatic stress test acquired before and after the RT program.

Results—In contrast to the untrained controls, individuals in RT group experienced significantly increased FVC and FEV_1 (both $p < .01$) in association with improved quality of sleep, cough, and speech. Sympathetically (phase II) and parasympathetically (phase IV) mediated baroreflex sensitivity both significantly ($p < .05$) increased during 5s MEP. During orthostatic stress test, improved autonomic control over HR was associated with significantly increased sympathetic and parasympathetic modulation (low- and high-frequency change, $p < .01$ and $p < .05$, respectively).

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Conclusion—The results indicate that inspiratory-expiratory pressure threshold RT is a promising technique to positively impact both respiratory and cardiovascular dysregulation observed in persons with chronic SCI.

Keywords

Autonomic nervous system; Blood pressure; Breathing exercises; Hypotension; Rehabilitation; Respiration; Spinal cord injuries

INTRODUCTION

It is estimated that the number of people living with spinal cord injury (SCI) in the U.S ranges from 243,000 to 347,000[1] and while life expectancy for individuals with SCI is lower than general population, survival of patients with SCI has improved. However, medical complication rates greatly increase with the advancing age of persons with SCI[2]. Due to injury to the motor and autonomic nervous systems and accelerated aging mechanisms associated with immobility, persons with SCI are more likely to die from pneumonia, heart attacks, stroke, and other cardiopulmonary complications compared with their age-matched, non-injured counterparts[3–8]. Vascular and respiratory adaptations can occur as soon as 6 weeks after injury[9]. Chronic SCI can result in maladaptive blood pressure regulation and respiratory deficits leading to hypotension, bradycardia, dyspnea, and impaired cough that together may predict the development of cardiovascular disease[7, 10–14]. Higher SCI levels with more complete neurological lesions demonstrate greater cardiovascular and pulmonary functional deficits; however, even incomplete SCI lesions as low as L_4 should be considered as risk factors for cardiopulmonary disability as they still exhibit deficits from functional impairment due to accelerated aging, lifestyle factors, and decreased mobility[7, 15–17].

As stated above, co-presentation of cardiovascular and pulmonary diseases in SCI is common and could be, in part, due to the interdependence of the cardiovascular and pulmonary systems. Physiologically, these systems are closely linked: arterial blood pressure (BP) oscillates with breathing and engages the baroreceptors[18–20] while chemoreceptors and pulmonary mechanoreceptors participate in heart rate (HR) and vasomotor tone regulation in response to arterial blood gas content and inspiratory volume changes[18, 21]. The chemoreflexes exert profound influences not only on breathing, but also on cardiovascular function. Moreover, baroreflex-chemoreflex interactions may have relevance to disease states in which baroreflex function is impaired, such as SCI[22].

There is clinical evidence that this relationship still exists post-SCI: it is demonstrated that morbidity and mortality rates are significantly decreased when cardiovascular and pulmonary deficits are addressed together during the acute treatment of SCI[23, 24]. In the chronic phase, individuals with greater pulmonary function outcomes demonstrate higher resting BP values[25]. Despite this evidence, cardiovascular and pulmonary dysfunction testing and treatment in SCI are targeted independently: interventions that demonstrate increased pulmonary function outcomes are not tested for resulting changes in cardiovascular regulation[26–32]. Recently, we reported that orthostatic hypotension and respiratory dysfunction can be ameliorated in persons with chronic SCI after respiratory

motor training[33]. However, much of the cardiovascular therapy currently available to persons with SCI is limited to management of unstable BP with little evidence of long-term changes in BP regulation[34–36]. There is therefore a gap in therapies available to persons with SCI to ameliorate cardiovascular dysregulation and subsequently decrease the risk of future cardiovascular events. Respiratory Training (RT) is commonly used in persons with SCI to increase cough capacity and respiratory capacity and improve performance[27, 30–32, 37, 38]. It is thus a logical intervention to test the theory of cardiovascular and pulmonary system interdependence effect in the treatment of chronic SCI subjects to prevent long term complications secondary to cardiovascular events. Therefore, we hypothesized that RT improves cardiovascular response to respiratory and cardiovascular challenges due to improved reflex activity.

METHODS

This study was approved by the Institutional Review Board for Human Research. Forty-four persons with SCI were recruited from Frazier Rehabilitation and Neuroscience institute in Louisville, KY, according to the following inclusion criteria: at least 18 years of age; chronic (a minimum of 6 months since SCI), non-progressive SCI; no ventilatory dependence; respiratory functional deficit defined as a decrease in predicted FVC and FEV_1 values at least 10%; no tobacco or drug use; and no cardiovascular or respiratory diseases unrelated to SCI.

Clinical assessment

Twenty-four individuals participated in the RT protocol, while 20 physically (age, sex, height, and weight) matched participants were in the control group. The International Standards for the Neurological Classification of Spinal Cord Injury (ISNCSCI) were used to determine the neurological level and clinical severity of the spinal cord lesion according to the American Spinal Injury Association Impairment Scale (AIS)[39]. Twenty-seven participants were classified as having motor-complete (AIS-A or AIS-B) SCI and 17 participants were diagnosed with motor-incomplete (AIS-C or AIS-D) SCI, with a neurological range from C_2 to T_{11} (Table 1).

Study Protocol

Data collection occurred between 2011 and 2014. FVC and FEV_1, baroreflex sensitivity (BS), and HR variability (HRV) values were assessed at baseline (called the “Pre-Test” time point) in all participants. Individuals in the RT group then participated in 20, 45-minute sessions of training using a threshold positive expiratory pressure device and inspiratory muscle trainer (Respironics Inc., Cedar Grove, NJ) assembled together using a three-way valve system (Airlife 001504, Allegiance Healthcare Corp., McGaw Park, IL) with flanged mouthpiece[29, 38]. Participants were trained on-site with a team member tracking progression and monitoring the training load. Each participant received 20 training sessions. No participants dropped out during the study. Training load was increased regularly so participants were training at 60% of their maximum inspiratory and expiratory airway pressure generation by the last week. Besides experimental procedures, all participants maintained their normal routine as active participants in the community fitness gym. After

four weeks of training for the RT group, and four to six weeks for the control group, participants were assessed again at the “Post-Test” time point.

Data acquisition

A Finometer MIDI (Finapres Medical System B.A., Netherlands) and finger plethysmograph synchronized with FMS 3-lead ECG device recorded continuous arterial BP waveform and HR. Brachial BP measurements were acquired to calibrate BP values obtained from the finger cuff (GE’s Dinamap Patient Monitor, Boston, MA)[40]. Data were converted from analog to digital signals using a Powerlab 16/35 system, recorded by LabChart 7 (AD Instruments, Denver, CO). Hemodynamic variables were acquired at 1000 Hz and calculated in Labchart; BS outcomes (see below) were analyzed in R[41], while HRV was analyzed using Matlab software (The MathWorks, Natick, MA)[42].

Baroreflex Sensitivity

Participants were assessed in a seated position, without the aid of compression garments or abdominal binders[43, 44]. To assess BS, participants blew with maximal effort into a mouthpiece for the duration of an audible, 5s tone (5s MEP)[45]. Each event was attempted three times, with at least 30s rest in between events to allow BP values to return to baseline. The increased intrathoracic pressure decreases venous return during the maneuver, eliciting a reflex tachycardia (similar to early phase II of the Valsalva maneuver), while the systolic blood pressure (SBP) overshoot following the maneuver elicits a reflex bradycardia (similar to phase IV of the Valsalva). For phases II and IV of the 5s MEP, SBP values were plotted against the following R-R interval (RRI) using a linear regression analysis with a Pearson correlation coefficient. The slope of each phase is reported in ms/mmHg, which quantifies the change in RRI for every 1 mmHg increase or decrease of SBP[46–48]. Acceptable attempts were those between 5 and 7s in duration[49, 50] with a Pearson correlation coefficient > .80[47, 51, 52]; BS outcomes were excluded if the maneuver did not meet 27 cmH_2O[45], or if they triggered spasms, autonomic dysreflexia, or coughs. The phases analyzed began with three consecutively increasing or decreasing RRIs[47, 52]; the mean of all acceptable attempts was used for statistical analysis.

Orthostatic Stress Test

The orthostatic stress test was performed in the morning, between 9:00 and 10:30AM, in a dimly lit, temperature controlled room (22°C). Participants were asked to eat a light breakfast (i.e., little to no sugar or fat), to refrain from caffeine for 12 hours prior to the experiment, and to empty their bladder prior to arrival. Participants were recumbent upon a Hausted Manual Gurney Chair (GF Health Products, Atlanta, GA) for 15 minutes and then passively moved to a sitting position for an additional 15 minutes. The participant was instructed to refrain from non-essential movement or speech for the duration of the study. The test was terminated if the participant experienced autonomic dysreflexia, uncontrolled orthostatic hypotension that would lead to syncope, or if the participant felt too uncomfortable to continue.

Spectral power of RR interval was calculated during the last 10 minutes of the passively seated position. Each interval was linearly detrended, and spectral power was estimated

using Welch's averaged periodogram method (500-point windows with 50% overlapping segments). Mean spectral power was calculated for low-frequency (LF, 0.04 - 0.15 Hz) and high-frequency (HF, 0.15 - 0.4 Hz) regions using trapezoidal integration over the specified frequency range[53–55]. The first 5 minutes of the passively seated position were excluded because the rapid position change often triggered spasms that altered BP and heart rate. During orthostatic stress, like in a passively seated position, the LF RRI oscillation primarily reflects sympathetic control over the heart, while HF oscillation principally reflects vagally-mediated oscillations coupled to respiration[55–58]. Respiration frequency obtained from respiratory belts was checked to make sure it fell within the HF range.

Statistical Analysis

Data were analyzed in R (R Foundation for Statistical Computing, Vienna, Austria) and represented as mean ± standard deviation (SD); significance was set to $\alpha = .05$. The presence of multiple covariates in the data and normally distributed residuals made the linear regression an appropriate test for significance[59]. To compare pre- to post-test outcomes, change scores were calculated for each participant by subtracting their post-test score from their pre-test score. This new measure was used as the dependent variable in all regression models; change score of the control group was the reference to which RT was compared. To control some of the variability between participants, level of injury (cervical or thoracic) and/or AIS impairment (A, B or C/D) were covariates in models (Table 2).

RESULTS

There were no significant between-group differences in any measured variable prior to onset of RT. Pulmonary function outcomes increased significantly in the RT group compared to controls: FVC increased from 76 ± 13% to 82 ± 13% ($p < .01$), and FEV_1 increased from 68 ± 15% to 76 ± 15% ($p < .01$).

We found significant BS increases in the trained group in response to maximal, acute expiratory effort that were not seen in the control group. After training, heart rate changes in response to oscillations in systolic BP improved (Figure 1). Slope of the 5s MEP (Figure 2; Table 2) during phase II increased from 2 ± 2 to 3 ± 2 ms/mmHg ($p = .01$), while phase IV slope increased from 5 ± 2 to 7 ± 3 ms/mmHg ($p < .01$), demonstrating increased sympathetic (phase II) and parasympathetic (phase IV) control over the heart. These responses occurred without any significant differences to SBP during the maneuver (lowest SBP pre to post RT: 68 ± 18 mmHg to 71 ± 13 mmHg; peak SBP pre to post RT: 132 ± 39 mmHg to 126 ± 31 mmHg). There was also no correlation between phase II and phase IV gains in the RT group. There was a significant relationship between level of injury and phase IV in one of the models (Table 2), which could reflect the greater gains demonstrated by the cervical group compared to thoracic. There was no significant relationship between severity of injury and gains after RT (Table 2), demonstrating AIS impairment did not detectably affect gains post training.

After training, the drop in sitting DBP was ameliorated (Δ pre: −14/−5 ± 26/16 mmHg; Δ post: −4/0 ± 14/9 mmHg) and there was an improved cardiac and hemodynamic response during the orthostatic stress test (Figure 3) for a number of participants, but the changes

were not significant (p = .061). HRV increased in the RT group in both the LF and HF bands in the last 5 minutes of the sitting position (Figure 4): LF power increased from 284 ± 490 to 432 ± 592, (p < .01), and HF power increased from 169 ± 311 ms^2 to 333 ± 343 ms^2 (p < .05). There were neither significant changes in primary contributing frequency of the LF (pre and post: 0.08 ± 0.02 Hz) and HF (pre and post: 0.25 ± 0.05 Hz) bands when comparing the RT group to the control, nor were there changes to respiration frequency, demonstrating the increased power results from greater oscillation within the same frequency. There were no significant relationships between severity of injury and HRV (Table 2), reflecting gains exhibited by all participants in the training group.

DISCUSSION

Our study found that a four-week RT protocol utilizing inspiratory and expiratory training can lead to significant increases in pulmonary function outcomes, BS, and HRV as well as better cardiovascular response during orthostatic stress test indicating RT has the ability to influence and improve both respiratory and cardiac autonomic function which ameliorates cardiovascular stress response in persons with chronic SCI.

Percent-predicted values of FVC and FEV_1 increased significantly after RT (Table 2). Reduction of these values are attributed to neuromuscular weakness[60–62] which can lead to pulmonary infections[63, 64] and increase mortality risk by three percent with each percentage decrease in function[4]. It is therefore possible that RT can reduce the risk of developing SCI-induced pulmonary disease by improving the ability to overcome airway obstruction and increasing respiratory endurance. Indeed, participants reported improved cough capacity, respiration, and speech, and overall improved quality of life after RT. Our data also suggest improvements in pulmonary function outcomes are not limited to cervical injuries. Participants with thoracic lesions also demonstrated improvements after RT with no significant relationship between level and severity of injury and functional gains. Previously, other researchers have found factors like smoking[62], duration of injury[17], weight and health status[7] contribute significantly to pulmonary dysfunction, exacerbating functional impairment from SCI. This could help explain why there was no significant relationship between functional improvement and level or severity of injury: there is impairment in addition to what can be attributed to SCI that can be targeted with RT. We are not the first to find improvements to pulmonary function in persons with SCI following respiratory exercises[26, 28–32], but we are the first to investigate the effects of RT on lower thoracic injuries which could lead to significant clinical benefits including improvement in endurance, lung capacity, ability to tolerate activities during transfers, exercising, and improvement in quality of life. Thus, our data suggest RT has the potential to improve pulmonary function even in persons with incomplete or low-level SCI.

We found significant increases to BS in the RT group, in both phase II and phase IV of the 5s MEP maneuver (Figure 2). The 5s MEP engages both sides of the baroreceptor reflex arc: the drop in BP during phase II increases HR via available sympathetic engagement and vagal withdrawal, while the BP overshoot during phase IV increases vagal activity (Figure 3)[47, 51, 65, 66]. We now report significant increases to BS post-RT without changes to the absolute peak and trough SBP values between timepoints; as such, the changes in BS are not

attributable to a change in the phase relationship between SBP and RRI and instead demonstrate a more effective baroreceptor response for the same change in SBP during the maneuver. This could potentially be a reversal of the vessel stiffening common in SCI, as changes in intrathoracic pressure during training affect BP, or it could result from more effective use of available sympathetic and parasympathetic efferents. The clinical implications of this findings lead us to believe that deconditioning of the baroreflex induced by SCI can be reversed by RT, which may serve as a protective measure to maintain respiratory-cardiovascular health.

There were also significant increases in HF power during the last 5 minutes of orthostatic stress in our RT group (Figure 4). Increased power spectral density of HRV without changes to the primary contributing frequency results from increased oscillation of RRI, demonstrating an increased ability of vagal pulmonary reflexes to match RRI to inspiration[67, 68]. While it is true that respiration increases during orthostatic stress[69, 70], we did not find any increases in respiratory rate from pre- to post-RT. We therefore speculate the increased HF power is the result of increased cardiovagal reflex activity which lead to increased oscillation of RRI from a better match of HR to inspiration.

Oscillation of RR interval in the LF band is attributed to sympathetic nervous system activity, possibly modulation of HR via the activity of the baroreceptor reflex loop[71–74]. We detected significant increases in sympathetic control of HR during the last 5 minutes of the seated position (Figure 4), which happened to be the time period containing the lowest BP values overall. Indeed, the last 5 minutes of the seated position was the period when orthostatic hypotension alleviated in our previously published study[33]. The theory that LF frequencies result only from baroreceptor activity would also align with our findings, as sympathetic recruitment by the baroreceptors increases sigmoidally as SBP drops[75], which could explain why significant increases in LF power occurred during the last 5 minutes of the seated position: the lowest BP values would cause the greatest firing by the baroreceptors. This could also be subsequent to changes in respiration, as greater pulmonary function would lead to greater oscillations in BP which would increasingly activate the baroreceptors. Thus, we speculate increased sympathetic tone post-RT is related to increased baroreceptor activity, but further analysis is required. Irrespective of the mechanism it is evident that, following RT, sympathetic control of the heart via reflex-mediated oscillation increases in response to orthostatic stress. Impaired HRV has been associated with increased mortality and a greater risk of cardiac events in several populations[76, 77]. Improved autonomically mediated cardiovascular responses during cardiovascular stress reported herein indicate RT in patients with chronic SCI may help ameliorate long-term cardiovascular risks.

Finally, we did not see significant changes to SBP or DBP values during the sitting position in this group, perhaps because few participants demonstrated orthostatic hypotension prior to training, but several participants demonstrated an improved cardiovascular response to orthostatic stress after RT (Figure 3) which could positively impact cardiovascular fitness in chronic SCI as well as improvement in quality of life; this combined with a p-value of .061 leads us to speculate changes to absolute blood pressure values would be significant with a larger sample size.

We have thus demonstrated a therapy that targets and improves pulmonary function outcomes can ultimately lead to improved cardiac-autonomic responses to rapid changes in SBP. Moreover, these changes can be seen irrespective of injury level and completeness: except for phase IV of the 5s MEP (Table 2, Cervical vs. Thoracic), there was no outcome in which a particular group experienced greater gains than another. This is a novel and exciting finding, particularly in a population with significant increase in mortality from cardiovascular and pulmonary diseases when compared with their non-injured counterparts[3–7]. In addition to the accelerated aging of these organ systems, impaired BS on its own is a risk factor for development of cardiovascular disease because of poorly regulated BP[78–80]. Thus, RT not only has the potential to improve the pulmonary function and cardiovascular regulation in persons with SCI, it could potentially impact long-term outcomes in SCI by potentially reducing the risk of cardiovascular disease in patients with chronic SCI.

In addition to being a potentially effective therapy with benefits to cardiopulmonary function, this training has the added advantage of being easily administered: participants require an inexpensive training device and a nose clip. Training sessions can take place in their own chairs and might be at home instead of at a facility that would require a commute and clinician to administer the therapy. We also found significant changes with only 20, 45-minute sessions of RT, which means participants could see improved regulation as little as a month.

Limitations

The study was limited by group heterogeneity and available sample size due to the challenge to form demographically and clinically homogeneous randomly formed groups from a highly diverse but limited SCI population, particularly with respect to the factors related to level/severity and duration of injury. In addition, true quality of life changes were not investigated statistically.

CONCLUSION

Chronic SCI patients have a very high risk of acute admissions and increased mortality due to complications from cardiovascular and respiratory diseases. The lack of effective therapies to manage cardiovascular and respiratory deficits negatively affects the life span of persons with chronic SCI. Our findings indicate that inspiratory-expiratory pressure threshold RT is a promising technique to positively impact both respiratory and cardiovascular dysregulation observed in persons with chronic SCI.

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List of abbreviations

5s	MEP maximum expiratory pressure generation maneuver, sustained for 5s
AIS	american spinal injury assessment impairment scale
BP	blood pressure
BS	baroreflex sensitivity
FEV_1	Forced Expiratory Volume in 1 second
FVC	Forced Vital Capacity
HF	high-frequency
HR	heart rate
HRV	heart rate variability
LF	low-frequency
RRI	R-R interval
RT	respiratory training
SBP	systolic blood pressure
SCI	spinal cord injury

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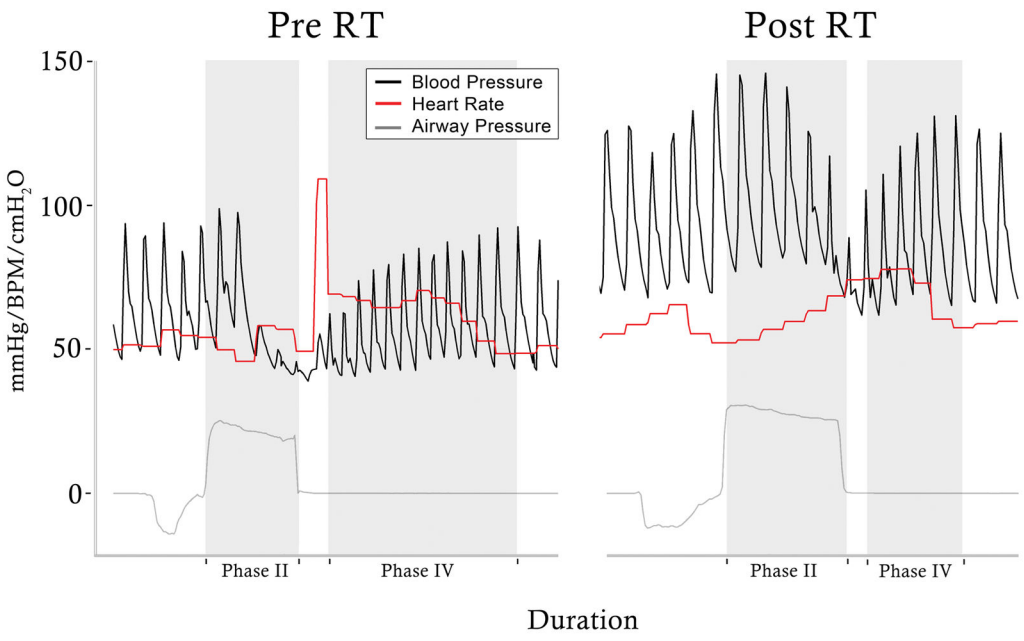

Figure 1.

Recording of the maximum expiratory pressure (5s MEP) pre- and post- respiratory training (RT) program. Sample recording of arterial blood pressure (black), heart rate (red) and airway pressure (gray) during 5s MEP from male with C6, AIS B spinal cord injury. The relationship between heart rate and systolic blood pressure oscillations improved after respiratory training, during (Phase II: 1.4 ms/mmHg to 3.4 ms/mmHg) and after (Phase IV: 6.8 ms/mmHg to 9.6 ms/mmHg) the maneuver.

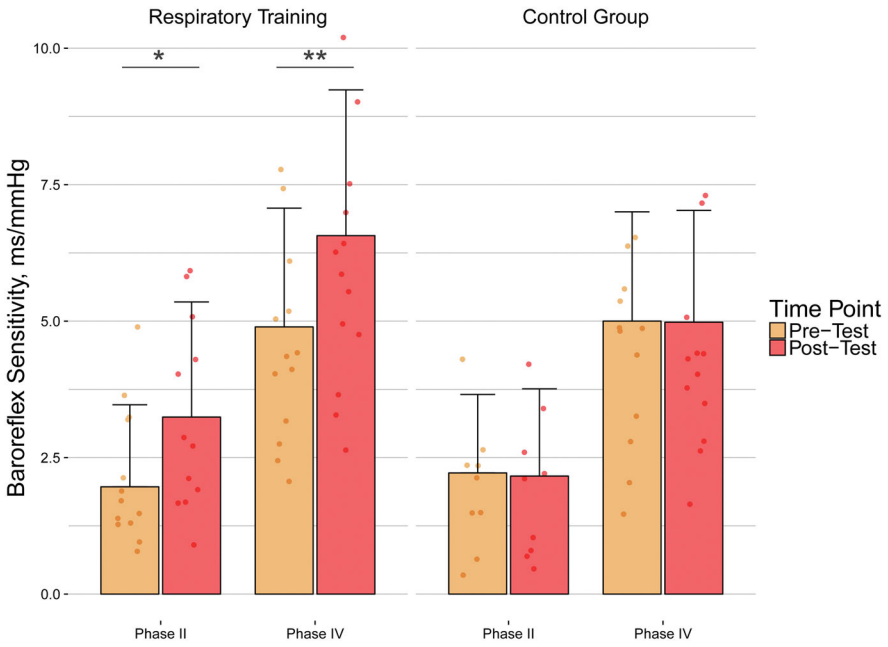

Figure 2.

Baroreflex sensitivity (BS) during phases II and IV of the maximum expiratory pressure (5s MEP) maneuver. Note that there were significant increases in BS values during phase II and phase IV of 5s MEP in the respiratory training (RT) group (n=14; *p < .05; **p < .01) compared to controls (n=11), demonstrating an increased relationship between heart rate and systolic blood pressure oscillations after RT.

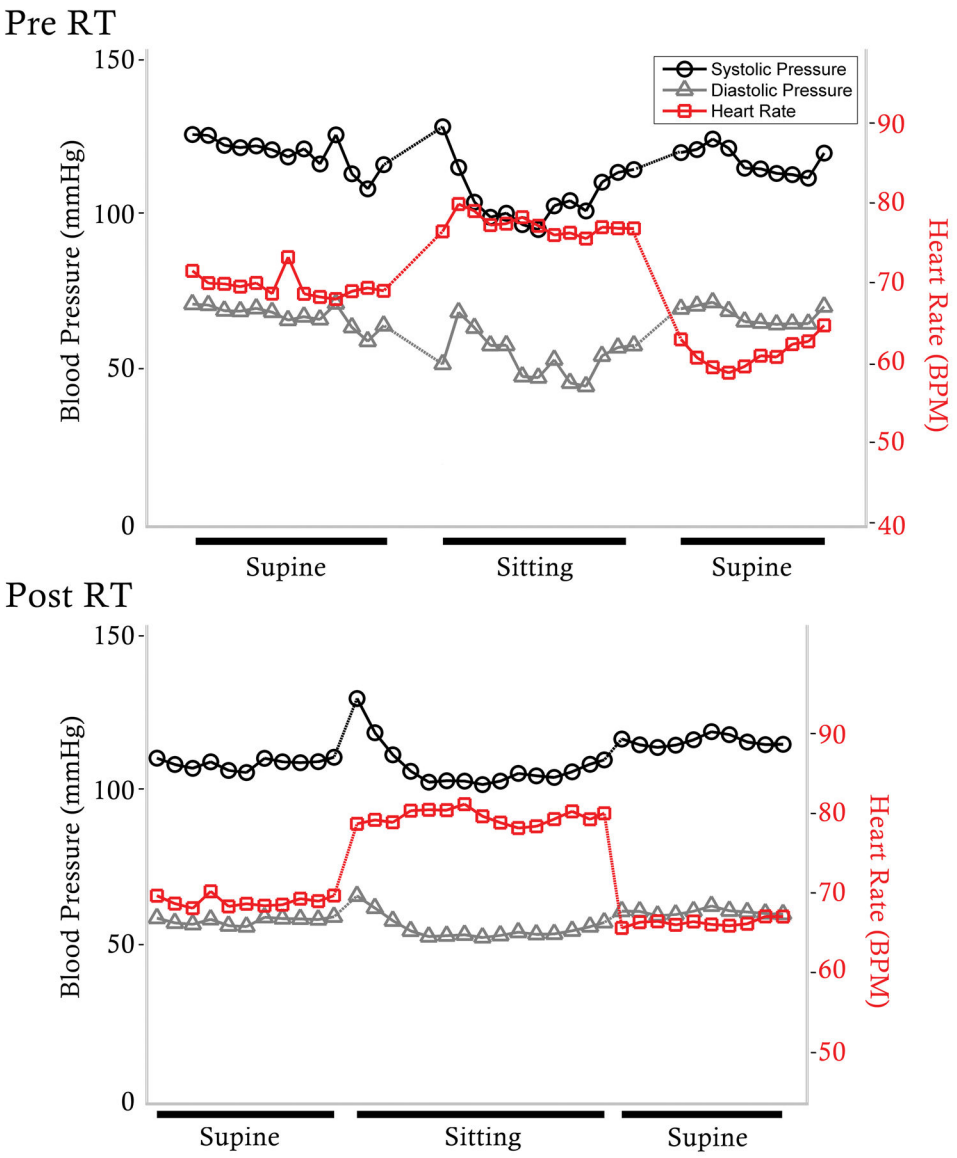

Figure 3.

Blood pressure (BP) and heart rate (HR) during orthostatic stress test before (Pre) and after (Post) respiratory training (RT) program. Example from female with C4, AIS A SCI of one-minute means of systolic blood pressure (black), diastolic blood pressure (gray), and heart rate (red) during orthostatic stress test. Before (top) respiratory training, the participant demonstrated a poorly regulated response to orthostatic stress, while after (bottom) respiratory training, the hemodynamic and cardiac responses improved.

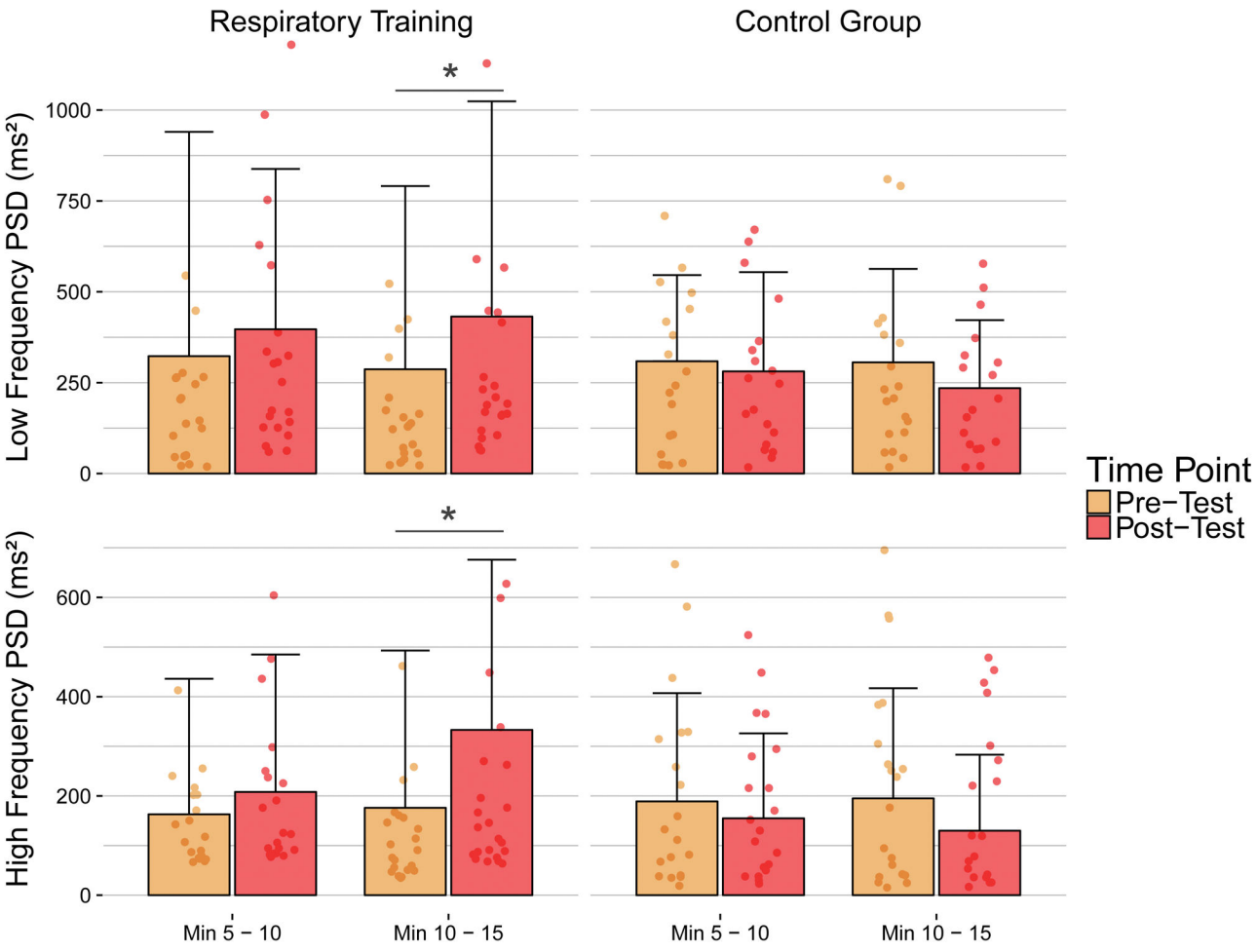

Figure 4.

Heart rate (HR) variability during orthostatic stress test. Sitting power spectral density (ms^2) from the Respiratory Training (RT) (n=24) and Control (n=20) groups during minutes 5–10 and 10–15 in the low and high frequency (LF and HF, respectively) bands. There was a significant increase in LF and HF power in the last 5 minutes of the sitting position in the RT group.

Table 1

Demographic Summary of Participants

ID		Age	Sex	Height (in)	Weight (lbs)	LOI	AIS	Months Since Injury
RMT Group	A58	40	M	70	230	C3	A	22
	A38 +	37	F	69	130	C4	A	248
	A65 *	29	M	68	180	C4	A	10
	B18 *	56	M	72	155	C3	B	29
	B06 +	42	F	67	123	C4	B	70
	B11	25	M	70	185	C4	B	98
	B16 +	60	M	71	220	C4	B	31
	B19	40	M	74	177	C6	B	6
	C33 *	59	M	69	145	C2	C	532
	C27	58	M	70	190	C4	C	47
	C30 +	19	F	67	94	C4	C	12
	C34	20	M	76	140	C4	C	53
	C26	33	M	72	165	C6	C	4
	C38	42	M	70	245	C2	D	156
	B17	59	M	75	217	C4	D	15
	C18 +	31	M	71	214	C4	D	36
	A46 +	47	F	62	192	T6	A	43
	A66	48	M	72	170	T6	A	65
	A75 +	49	M	73	188	T9	A	84
	A55	35	M	68	165	T11	A	50
	C16 +	35	M	72	185	T1	C	70
	C28	29	M	70	160	T5	C	56
	C24	40	F	68	125	T11	C	110
	C39	45	F	68	135	T11	C	21
Mean ± SD		**40 (12)**	**NA**	**70 (3)**	**173 (37)**	**NA**	**NA**	**76 (109)**
Control Group	A33 +	58	M	74	232	C3	A	20
	A38 +	39	F	69	113	C4	A	237

ID	Age	Sex	Height (in)	Weight (lbs)	LOI	AIS	Months Since Injury
B21 *	30	M	73	165	C4	B	64
B22	51	M	70	180	C4	B	37
B28 +	39	M	68	163	C6	B	113
C14 +	47	M	76	130	C3	C	10
D35 +	60	M	71	220	C2	D	35
A35 +	55	M	73	200	T3	A	377
A36 +	56	M	68	210	T3	A	341
A57	27	F	73	165	T4	A	45
A69	26	M	73	140	T4	A	27
A39 +	36	M	70	175	T5	A	185
A53	30	M	70	141	T5	A	23
A73 +	28	M	67	180	T6	A	58
A74 +	56	M	69	240	T9	A	418
B20 +	28	M	65	128	T2	B	53
C44	40	M	71	173	T4	B	24
C37	20	F	60	190	T2	C	77
C36	23	M	74	157	T6	C	9
C45	22	M	70	260	T2	D	6
Mean ± SD	**39 (12)**	**NA**	**70 (4)**	**177 (36)**	**NA**	**NA**	**128 (146)**

Participants that could not perform the 5s MEP are marked with (*) if spasms prohibited analysis, or (+) if participants entered study prior to addition of the 5s MEP to the research protocol.

Table 2

Summary of Pulmonary Function Testing (PFT) values obtained from the Pre-Test and Post-Test timepoints

RMT Group	FVC (% predicted)		FEV_1 (% predicted)	
	Pre-Test	Post-Test	Pre-Test	Post-Test
C33 (C2C)	78	88	70	80
D38 (C2D)	85	99	87	92
A58 (C3A)	65	60	53	50
B18 (C3B)	65	67	39	56
A38 (C4A)	63	53	66	49
A65 (C4A)	63	58	30	32
B06 (C4B)	46	57	38	40
B11 (C4B)	57	66	41	47
B16 (C4B)	86	85	75	75
B17 (C4B)	70	74	58	68
C27 (C4C)	64	57	41	40
C30 (C4C)	41	69	45	46
C34 (C4C)	37	40	29	28
C18 (C4D)	77	67	74	66
B19 (C6B)	70	81	66	77
C26 (C6C)	60	76	67	76
C16 (T1C)	59	73	52	64
C28 (T5C)	82	85	74	78

RMT Group	FVC (% predicted)		FEV_1 (% predicted)	
	Pre-Test	Post-Test	Pre-Test	Post-Test
A46 (T6A)	96	93	73	77
A66 (T6A)	78	80	70	76
A75 (T9A)	82	80	75	74
C24 (T11C)	100	95	81	83
C25 (T11C)	94	94	90	92
C39 (T11C)	98	99	87	82
Mean ± SD	**76 (13)**	**82 (13)** **	**68 (15)**	**76 (15)** **
Control Group	**FVC (% predicted)**		**FEV_1 (% predicted)**	
	Pre-Test	**Post-Test**	**Pre-Test**	**Post-Test**
Mean ± SD	**77 (27)**	**73 (25)**	**67 (24)**	**68 (24)**

Results are reported as Mean (SD);

* $p < .05$,

** $p < .01$

Table 3

Multivariate Linear Regression Models of RT Outcomes Compared to Control.

	RT vs Control+	Cervical vs Thoracic+	AIS A vs AIS CD+	AIS B vs AIS CD+	Adjusted R^2
FVC (%)	10 (3) **	0 (7)	3 (1)	0 (4)	0.49
FEV_1 (%)	8 (2) **	0 (6)	2 (1)	0 (3)	0.54
BS (ms/mmHg) During 5s MEP					
Phase II	1.24 (0.4) *	0.33 (0.4)	1.09 (0.5)	0.13 (0.6)	0.45
Phase IV	1.47 (0.5) **	1.47 (0.5) **	−0.17 (0.4)	0.55 (0.7)	0.57
Power Spectral Density					
Low Frequency R-R Interval					
Minutes 5–10	122 (113)	−173 (116)	20 (128)	157 (155)	0.17
Minutes 10–15	206 (73) **	−56 (76)	62 (82)	389 (102)	0.46
High Frequency R-R Interval					
Minutes 5–10	80 (57)	27 (51)	−21 (68)	62 (79)	0.08
Minutes 10–15	114 (50) *	−17 (51)	−14 (55)	106 (70)	0.23

Reference factor for independent variables are marked with (+). Results are reported as beta coefficient (standard error);

* $p < .05$,

** $p < .01$. RT: respiratory training; FVC: forced vital capacity; FEV_1: forced expiratory volume in one second;

BS: baroreflex sensitivity; MEP: maximum expiratory pressure generation.