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RESEARCH ARTICLE

Effect of a neck compression collar on cardiorespiratory and cerebrovascular function in postural orthostatic tachycardia syndrome (POTS)

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Nardone M, Guzman J, Harvey PJ, Floras JS, Edgell H. Effect of a neck compression collar on cardiorespiratory and cerebrovascular function in postural orthostatic tachycardia syndrome (POTS). *J Appl Physiol* 128: 907–913, 2020. First published March 12, 2020; doi: 10.1152/japplphysiol.00040.2020.—Postural orthostatic tachycardia syndrome (POTS) is accompanied by reduced brain blood flow, autonomic dysfunction, and orthostatic intolerance. We hypothesized that wearing a neck compression collar would attenuate orthostatic symptoms, increase brain blood flow, and influence autonomic reflexes. Ten participants with POTS (9 women, age: 36 ± 10) underwent two trials of supine rest, paced deep breathing (6 breaths/min), Valsalva maneuver (40 mmHg for 15 s), and 70° upright tilt. For one trial, participants wore a neck compression device (Q30 Innovations). Blood pressure, heart rate (HR), brain blood flow velocity, stroke volume, respiratory rate, and end-tidal gases were continuously measured. The Vanderbilt Orthostatic Symptom Score was compiled at the end of tilt. The use of the collar reduced the orthostatic symptom score of participants with POTS during upright tilt (26.9 ± 12.5 to 18.7 ± 13.1, $P = 0.04$). Collar compression in the supine condition reduced the low-frequency domain of HR variability (60 ± 18 to 51 ± 23 normalized units, $P = 0.04$) and increased the change in HR (15 ± 5 to 17 ± 6 bpm, $P = 0.02$) and E:I ratio (1.2 ± 0.1 to 1.3 ± 0.1, $P = 0.01$) during paced deep breathing. Throughout tilt, wearing the collar reduced respiratory rate (baseline: 13 ± 3 to 12 ± 4 breath/min; tilt: 18 ± 5 to 15 ± 5 breath/min; main effect of collar $P = 0.048$), end-tidal oxygen (baseline: 115 ± 5 to 112 ± 5 mmHg; tilt: 122 ± 10 to 118 ± 11 mmHg; main effect of collar $P = 0.026$). In participants with POTS, wearing the Q-collar reduced orthostatic symptoms, increased the HR response to deep breathing, and decreased resting ventilation.

NEW & NOTEWORTHY We found that using a neck compression collar alleviated orthostatic symptoms in upright posture in participants with postural orthostatic tachycardia syndrome (POTS). This could be due to compression of the baroreceptors and subsequent changes in autonomic function. Indeed, we observed increased heart rate responsiveness to paced deep breathing and reductions of respiratory rate and end-tidal O_2 (suggesting reduced ventilation). Further, wearing the collar reduced mean blood velocity in the brain during Valsalva perhaps due to higher brain blood volume.

heart rate variability; paced deep breathing; upright tilt; Valsalva maneuver

INTRODUCTION

Participants with postural orthostatic tachycardia syndrome (POTS), a condition defined by an exaggerated heart rate response during orthostasis (>120 bpm during upright tilt or an increase of 30 bpm within 10 min of upright tilt) (7, 23), suffer from chronic orthostatic intolerance leading to reduced quality of life (2). Though the mechanisms driving the exaggerated heart rate responses in POTS are unclear (14), several studies have highlighted abnormal autonomic control (6, 9, 11, 16, 24). For instance, participants with POTS demonstrate enhanced sympathetic activity during orthostasis (9, 11), potentially due to augmented baroreflex (6, 16) and chemoreflex activity (24, 25).

Several pharmacological and nonpharmacological strategies have been suggested for the treatment and management of POTS (10, 14) The current study investigated a novel nonpharmacological strategy, the application of mild lower neck compression. Neck compression via use of a Q-collar has been used to reduce brain damage in athletes exposed to head impacts (17–19) and acutely increase brain blood flow in healthy participants (8). Indeed, we recently found compression of the jugular vein and carotid artery in men and women, and found that in women, wearing the collar increased resting middle cerebral artery flow velocity (12). Whether neck compression can increase brain blood flow in POTS at rest or during orthostasis is currently unknown.

The purpose of this study was to test the effect of mild neck compression in participants with POTS to determine if wearing a collar would influence brain blood flow velocity, autonomic function, and cardiorespiratory responses during paced deep breathing, Valsalva maneuver, and 5 min of 70° upright tilt. We hypothesized that wearing a compression collar would increase brain blood flow and alleviate symptoms associated with orthostatic intolerance.

METHODS

Participant Selection

This study adhered to the ethical principles of the Declaration of Helsinki and was approved by the Research Ethics Board at York University (e2018–104). All participants gave written informed consent. Ten participants (men, $n = 1$; women, $n = 9$; Table 1) who were clinically diagnosed with any subtype of POTS, and were under routine care of a physician, were recruited for this study. On the day of testing, patients were asked to refrain from caffeine, exercise, and

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Table 1. *Participant description*

	Participants, $n = 10$
Men, *n*	1
Age, yr	40 ± 10
Height, cm	165 ± 6
Weight, kg	65 ± 10
BMI, mg/m^2	24 ± 4
Resting SBP, mmHg	119 ± 17
Resting DBP, mmHg	79 ± 10
Resting HR, bpm	77 ± 14
Medications, *n*	
Vitamin/mineral supplements	5
CBD/THC	4
Corticosteroid	4
Infusion (IgG, plasma, saline)	2
Antihistamine	2
Proton pump inhibitor	2
α1-agonist	2
β-blocker	1
Anticholinesterase inhibitor	1
Blood thinner	1
Monoclonal antibodies	1
Antidepressant	1
Oral contraceptives	1
Opioids	1
Antibiotic	1

BMI, body mass index; CBD, cannabinoid; DBP:, diastolic blood pressure; HR, heart rate; IgG, immunoglobulin; SBP, systolic blood pressure; THC, tetrahydrocannabinoid.

cardiovascular medications [cannabinoid/tetrahydrocannabinol (CBD/THC), corticosteroids, α1-agonists, β-blockers, anticholinesterase inhibitors, blood thinners, and monoclonal antibodies; infusions were conducted at least 4 days before laboratory testing]. Habitual smokers were excluded. Because of symptom severity, one patient was unable to suspend cardiovascular medications. Patients did not fast, but were asked to refrain from consuming fatty foods (e.g., deep fried foods) the morning of testing. Day of menstrual cycle was not controlled (2 women had hormonal intrauterine devices, 2 women were taking oral contraceptives, and 2 women self-described as perimenopausal).

Experimental Protocol

In a randomized crossover design, participants completed four autonomic tests both with and without the Q-collar (Q30 Innovations, Westport), in the following order: *1*) 5-min supine rest to determine heart rate variability and cardiovagal baroreflex sensitivity, *2*) paced deep breathing to determine respiratory sinus arrhythmia, *3*) Valsalva maneuver as an index of sympathetic activity, and *4*) upright tilt to determine orthostatic responses. Tests were timed ~5 min apart to allow variables to return to baseline. Further, trials (collar vs. no collar) were randomized and separated by at least 10 min to minimize any order effects. All participants completed both trials. Metronome-guided paced deep breathing was performed at 6 breaths/min for 90 s, maintaining 5-s inhalation and 5-s exhalation. One minute before the Valsalva maneuver, participants were tilted to 20° to prevent a flat-top response (26). The Valsalva maneuver was performed by forcefully exhaling into a tube attached to a pressure gauge for 15 s, aiming to maintain a pressure of 40 mmHg. Lastly, following 5 min of supine rest, participants were tilted to 70° for 5 min. The protocol mandated termination of the tilt test if systolic blood pressure (SBP) dropped below 70 mmHg, or at the request of the participant. However, such events did not arise.

Q-Collar

The Q-collar is a commercially available compression collar (Q30 Innovations, Westport) ~2-cm wide with an opening at the front of the neck to accommodate the trachea. The collar lies low on the neck to allow full range of motion. For the present protocol, it was fitted according to manufacturer recommendations.

Cardiopulmonary Measurements

Hemodynamics. Heart rate (HR) was measured using a single lead electrocardiogram (ECG). Blood pressure (BP) was measured using beat-to-beat finger photoplethysmography (NexFin, WR Testworks, Maplewood), which was calibrated to a manual BP measure (BPTru Medical Devices, Canada). Stroke volume (SV) and subsequently calculated cardiac output (Q) and total peripheral resistance (TPR) were collected using the Modelflow algorithm of Nexfin. Brain blood flow was estimated using a transcranial Doppler (TCD; Multigon Industries Inc., Yonkers, NY) which measured middle cerebral artery (MCA) velocity by placing a 2-MHz TCD probe on the right side of the head in the temporal window, held in place by an adjustable headband. Cerebrovascular resistance index (CVRi) during the Valsalva maneuver was calculated as mean arterial pressure/mean MCA velocity. Resistance index (RI) was calculated as (systolic MCA velocity− diastolic MCA velocity)/systolic MCA velocity.

Respiratory rate and end-tidal gases. A nasal cannula connected to gas analyzers (Vacumed, Ventura, CA) was utilized to measure continuous end-tidal O_2 and CO_2. Respiratory rate was subsequently determined using the breath-to-breath peaks in end-tidal CO_2.

Autonomic function. Heart rate variability (HRV; LabChart Pro 8.0, ADInstruments, Colorado Springs, CO) was determined from the ECG recording over 5 min of supine rest (i.e., test 1 listed above). A Hann (cosine-bell) data window was used with a window overlap of 50%. Fast Fourier transform size was 1,024. The low-frequency spectrum (LF) was 0.04–0.15 Hz, and the high frequency (HF) spectrum was 0.15–0.45 Hz). Spontaneous cardiovagal baroreceptor sensitivity was determined as previously described (4, 5), during the same time points as HRV analyses.

Carotid and jugular cross-sectional area. By using a linear array high-resolution (9L-RS; 3–10 MHz) ultrasound transducer, the carotid artery and the jugular vein were imaged in the transverse plane, on the cranial side of the Q-collar, using B-mode ultrasound (Vivid i, GE Healthcare Systems, Mississauga, Canada). Imaging was conducted after all other testing was conducted. In the seated position, short video loops of the carotid artery and jugular vein were collected following 3 s of deep inhalation and 3 s of deep exhalation, both separated by 30 s of normal breathing. To ensure the same anatomical location, images were first collected while wearing the collar, and landmarks were noted for imaging during the subsequent removal of the collar. Carotid artery and jugular vein cross-sectional area were quantified at diastole using the EchoPAC ultrasound software (GE Healthcare, Mississauga, Canada). Inhalation and exhalation values were averaged for presentation.

Orthostatic symptoms. To quantify symptom severity, the Vanderbilt Orthostatic Symptom Score was compiled during the last minute of upright tilt (21). Participants scored the severity of symptoms on a scale of 0–10 with 0 indicating the absence of the particular symptom, and 10 indicating maximal intensity of the symptom. Symptoms included the following: mental clouding, blurred vision, shortness of breath, rapid heartbeat, tremulousness, chest discomfort, headache, lightheadedness, and nausea. Category scores were summed to determine the Vanderbilt Orthostatic Symptom Score.

Data and Statistical Analysis

All signals were obtained using a Powerlab data acquisition device (1,000 Hz) and LabChart Pro software (ADInstruments, Colorado Springs, CO). During deep breathing trials, the maximal and minimal HR achieved during each respiratory cycle were identified for the last six respiratory cycles and were averaged to obtain the average maximal HR and average minimal HR. The change score was subsequently calculated as the difference between the average maximal HR

Table 2. *Resting heart rate variability and cardiovagal baroreceptor sensitivity*

Variables	No Collar Baseline	Collar Baseline	*P* Value
SDNN, ms	41.5 ± 17.8	41.0 ± 14.4	0.87
RMSSD, ms	31.4 ± 18.9	34.5 ± 15.8	0.42
pRR50, %	14.2 ± 17.1	17.1 ± 15.7	0.42
Total power, ms^2	1,743 ± 1,250	1,660 ± 1,101	0.75
VLF, ms^2	659 ± 625	563 ± 343	0.52
VLF, %	36 ± 14	37 ± 14	0.91
LF, ms^2	596 ± 432	539 ± 438	0.60
LF, %	37 ± 12	32 ± 16	0.33
LF, nu	60 ± 18	51 ± 23	0.04*
HF, ms^2	480 ± 457	551 ± 556	0.45
HF, %	26 ± 14	30 ± 15	0.17
HF, nu	40 ± 17	48 ± 22	0.08
LF/HF	2.2 ± 2.0	2.7 ± 4.8	0.61
cBRS slope	25.4 ± 19.1	26.2 ± 18.7	0.64

Values are means ± SD. cBRS: cardiovagal baroreflex sensitivity; HF, high-frequency domain; LF, low-frequency domain; pRR50, number of successive RR intervals that differ by >50 ms divided by the total number of all RR intervals; SDNN, standard deviation of the RR intervals; RMSSD, square root of the mean of the sum of squared differences of successive RR intervals; nu, normalized units. *Main effect of tilt.

and the average minimal HR, and the expiratory:inspiratory ratio (E:I ratio) was calculated as the average maximal HR relative to the average minimal HR. The Valsalva maneuver was analyzed as previously described (1). In brief, the lowest mean arterial pressure (MAP) and mean MCA velocity during the 15-s strain phase were used to identify the *phase 2 minimal*, and the highest MAP and mean MCA velocity toward the end of exhalation were used to identify the *phase 2 maximal*. SBP, diastolic BP (DBP), MAP, maximal MCA velocity, minimal MCA velocity, and mean MCA velocity were then identified during baseline, *phase 2 minimal*, and *phase 2 maximal*. During tilt trials, 1-min averages of hemodynamics, respiratory rate, and end-tidal gases were calculated during the last minute of supine baseline and during the second last minute of upright tilt (i.e., 4th minute), due to the completion of the Vanderbilt Orthostatic Symptom Score during the last minute of tilt.

Deep breathing measures, carotid and jugular cross-sectional areas, and autonomic measures were compared between collar trials by using a paired samples *t* test. Blood pressures and MCA velocities were compared at baseline, during *phase 2 minimum*, and *phase 2 maximum* between collar trials by using a two-by-three repeated measures ANOVA. Hemodynamics and MCA velocities at rest and during tilt were also compared between collar trials by using a two-by-two repeated measures ANOVA. The Vanderbilt Orthostatic Symptom Score was compared between trials by using a paired samples *t* test, and individual questions were compared using the Wilcoxon signed-rank test. Chronological comparisons between trials were done with a one-way repeated measures ANOVA by using resting data before each set of deep breathing, Valsalva, or tilt.

Statistical analyses were performed using IBM SPSS Statistics 23 (Armonk). Data are presented as means ± SD. Significance was defined as $P < 0.05$.

Table 3. *Heart rate responses to paced deep breathing*

Variables	No Collar Trials	Collar Trials	*P* Value
Average maximum HR, bpm	80.7 ± 9.7	80.2 ± 12.9	0.80
Average minimum HR, bpm	65.7 ± 9.5	63.3 ± 10.0	0.11
Change in HR, bpm	15.0 ± 5.1	16.9 ± 6.4	0.02*
E:I ratio	1.2 ± 0.1	1.3 ± 0.1	0.01*

Values are means ± SD. HR is heart rate. E:I ratio is the ratio of HR during exhalation and inhalation. *Significant difference ($P < 0.05$).

RESULTS

Wearing the Q-collar resulted in a reduction of carotid artery cross-sectional area from 0.41 ± 0.23 cm^2 to 0.33 ± 0.18 cm^2 ($P = 0.047$) and an increase of jugular cross-sectional area from 0.08 ± 0.04 cm^2 to 0.40 ± 0.33 cm^2 ($P = 0.01$). During supine rest, heart rate variability and cardiovagal baroreflex

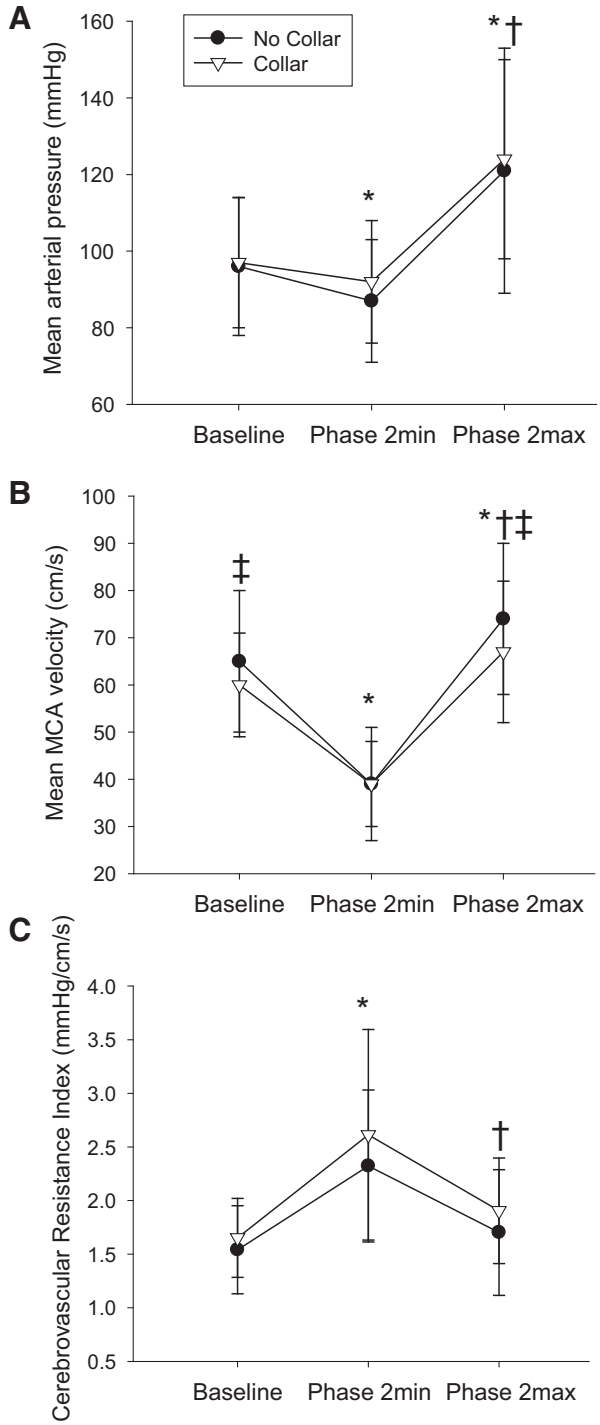

Fig. 1. Mean arterial pressure (*A*), mean velocity through the middle cerebral artery (MCA) (*B*), and cerebrovascular resistance index (*C*) at baseline, *phase 2 minimum*, and *phase 2 maximum* of the Valsalva maneuver. *Significant difference from baseline; †significant difference from *phase 2 minimum*; ‡significant effect of the collar at that timepoint.

Table 4. *Hemodynamic and cerebrovascular responses to upright tilt*

Variables	No Collar Trials		Collar Trials		Main Effects		Interaction
	Pre-Tilt	Tilt	Pre-Tilt	Tilt	Collar	Tilt	
Hemodynamics Data							
Heart rate, bpm	72 ± 12	91 ± 20	71 ± 12	90 ± 20	0.49	<0.01*	0.49
Systolic BP, mmHg	129 ± 24	124 ± 22	130 ± 27	128 ± 23	0.41	0.07	0.14
Diastolic BP, mmHg	84 ± 16	84 ± 13	84 ± 14	86 ± 13	0.67	0.57	0.09
Mean BP, mmHg	100 ± 20	97 ± 17	101 ± 19	100 ± 17	0.20	0.23	0.13
SV, mL	83.8 ± 11.6	65.0 ± 12.5	85.9 ± 12.1	66.9 ± 12.8	0.07	<0.01*	0.91
Q, L/min	6.07 ± 1.02	5.80 ± 1.03	6.09 ± 1.15	5.92 ± 1.29	0.64	0.10	0.50
TPR, mmHg/L/min	17.0 ± 4.2	17.3 ± 4.5	17.0 ± 4.2	17.6 ± 5.0	0.70	0.38	0.65
TCD Data, $n = 7$							
Max Velocity, cm/s	93 ± 18	85 ± 21	96 ± 15	88 ± 17	0.63	<0.01*	0.19
min velocity, cm/s	40 ± 16	35 ± 20	40 ± 15	37 ± 17	0.70	0.053	0.35
Mean velocity, cm/s	61 ± 17	53 ± 21	62 ± 15	56 ± 18	0.61	<0.01*	0.24
Mean BP_{MCA}, mmHg	106 ± 20	86 ± 19	101 ± 19	84 ± 18	0.12	<0.01*	0.38
CVRi, mmHg/cm/s	1.9 ± 0.7	2.2 ± 2.0	1.8 ± 0.6	1.9 ± 1.2	0.32	0.56	0.41
RI	0.60 ± 0.12	0.63 ± 0.21	0.60 ± 0.11	0.61 ± 0.16	0.48	0.60	0.41

Values are means ± SD. BP, blood pressure; CVRi, cerebrovascular resistance index; mean BP_{MCA}, blood pressure at the level of the middle cerebral artery; RI, resistance index; SV, stroke volume; Q, cardiac output; TCD, transcranial Doppler; TPR, total peripheral resistance. *Main effect of tilt.

sensitivity were largely unchanged when wearing the collar; however, the low-frequency domain was significantly lower when wearing the collar (Table 2). There was no change in maximum or minimum HR when participants were wearing the collar during the paced deep breathing trial, yet the change in HR and the E:I ratio were significantly higher when wearing the collar (Table 3).

During the Valsalva maneuver, mean arterial pressure decreased below baseline during *phase 2 minimum* and increased above baseline during *phase 2 maximum* (Fig. 1*A*). Similarly, the mean MCA velocity decreased below baseline at *phase 2 minimum* and increased above baseline at *phase 2 maximum* during the Valsalva maneuver. Wearing the collar decreased mean MCA velocity at baseline and *phase 2 maximum* (Fig. 1*B*), which was driven by decreases in diastolic MCA velocity at these timepoints (data not shown). CVRi increased during *phase 2 minimum* of the Valsalva maneuver and decreased back to baseline at *phase 2 maximum* (Fig. 1*C*). There was a strong trend for RI to be higher while wearing the collar throughout the Valsalva maneuver (no collar trials: baseline: 0.54 ± 0.08; *phase* 2 *minimum*: 0.59 ± 0.14; *phase 2 maximum*: 0.40 ± 0.05; collar trials: baseline: 0.58 ± 0.07; *phase 2 minimum*: 0.61 ± 0.13; *phase 2 maximum*: 0.45 ± 0.05; $P = 0.06$).

Upright tilt elicited an increase of HR, a decrease of SV, a decrease of systolic MCA velocity, and a decrease of mean MCA velocity (Table 4). There were no significant effects of tilt on blood pressure, Q, TPR, diastolic MCA velocity, or cerebrovascular resistance indices, and there were no significant effects of wearing the collar on any hemodynamic or cerebrovascular variable (Table 4). Importantly, when the collar was worn, several orthostatic symptoms (blurred vision, tremulousness, lightheadedness) were attenuated, and the Vanderbilt Symptom Score, overall, was reduced significantly (Table 5). Upright tilt resulted in an increase of respiratory rate and end-tidal oxygen while wearing the collar reduced both measurements (Fig. 2, *A* and *B*). Upright tilt also decreased end-tidal CO_2, yet there was no significant effect of wearing the collar (Fig. 2*C*).

When investigating for chronological order effects between trials (i.e., baseline differences), there were no significant effects on any variable ($P > 0.05$) except for resting MAP, which was lower before performing any trials compared with before the last two trials ($P < 0.05$).

DISCUSSION

The effect of neck compression in participants with POTS was previously unknown. In the current study, we found that wearing the neck compression collar *1*) increased jugular vein and decreased carotid artery cross-sectional area, *2*) increased the change in HR and E:I ratio during paced deep breathing, *3*) decreased resting low-frequency heart rate variability, *4*) decreased end-tidal O_2 and respiratory rate at baseline and tilt, and *5*) decreased the Vanderbilt Orthostatic Symptom Score.

Mechanical stimulation of the carotid sinus can modulate baroreflex activity, since the application of neck pressure or suction has been shown activate and suppress sympathetic activity, respectively (20, 22). The effect of mechanical compression of the carotid sinus on baroreflex function in participants with POTS is currently unknown, which is important considering their elevated baroreflex mediated sympathetic activity (6, 16) and the potential interactions with the chemoreflex (25). In health, we recently found an increased systolic pressure response to the Valsalva maneuver when wearing the collar, possibly implying greater baroreflex activity (12); however, in the current study, the collar did not alter the pressor

Table 5. *Responses to the Vanderbilt Orthostatic Symptom Score questionnaire*

Variables	No Collar Trials	Collar Trials	*P* Value
Mental clouding	2.4 ± 1.8	1.7 ± 2.0	0.22
Blurred vision	2.7 ± 2.2	1.1 ± 1.1	0.03*
Shortness of breath	2.6 ± 2.3	2.2 ± 1.9	0.41
Rapid heart rate	3.2 ± 2.1	2.9 ± 2.9	0.67
Tremulousness	2.8 ± 3.1	1.7 ± 2.9	0.04*
Chest discomfort	2.6 ± 2.1	1.4 ± 2.0	0.051
Headache	3.6 ± 2.9	3.3 ± 2.9	0.44
Lightheadedness	5.0 ± 2.9	3.5 ± 3.3	0.03*
Nausea	2.0 ± 2.4	1.1 ± 1.7	0.29
Total	26.9 ± 12.5	18.7 ± 13.1	0.04*

Values are means ± SD. *Significant difference ($P < 0.05$).

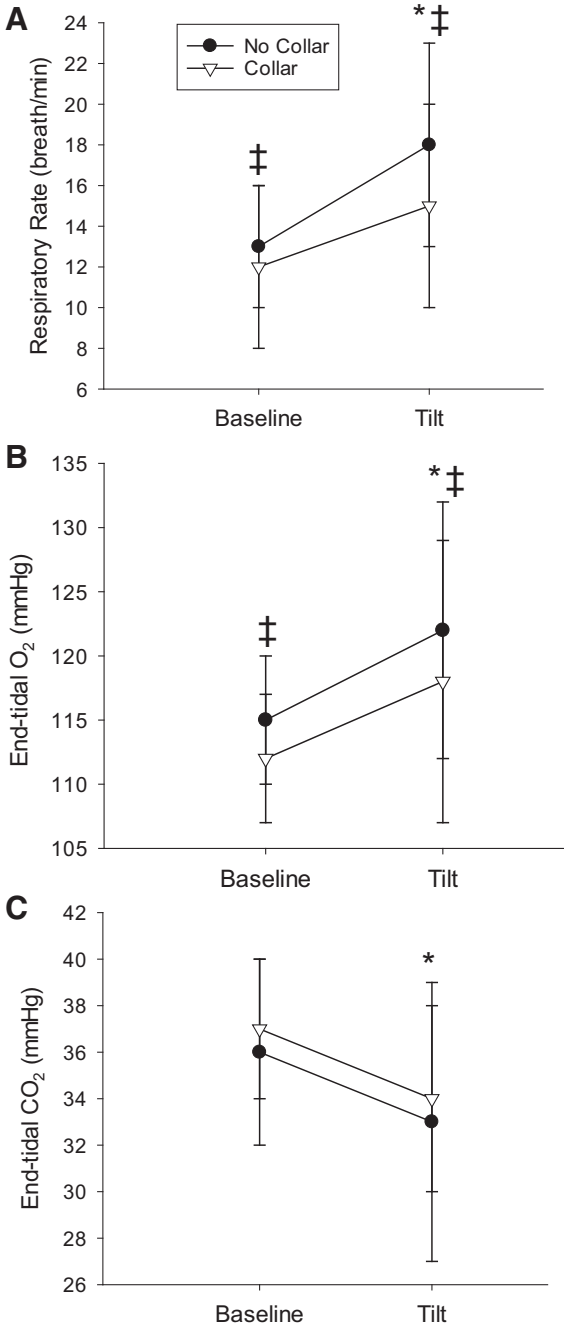

Fig. 2. Respiratory rate (*A*), end-tidal O_2 (*B*), and end-tidal CO_2 (*C*) responses to upright tilt. *Significant difference from baseline; ‡significant effect of wearing the collar.

responses to the Valsalva maneuver in POTS, perhaps due to their already elevated activity/sensitivity.

Taneja et al. (25) found that the peripheral chemoreflex was enhanced in POTS compared with controls and sensitized in the upright posture (i.e., when the baroreceptors were unloaded), whereas the central chemoreflex was lower in POTS and suppressed in the upright posture. Further, Stewart et al. (24) suggested that orthostatic hyperventilation plays an important pathological role in some people with POTS, which may, in part, be mediated by abnormal chemoreflex activity. Interestingly, in the present study, respiratory rate and end-tidal O_2 were decreased after application of the collar, suggesting that compression of baroreceptors in the carotid body may have suppressed overall chemoreflex activation and therefore hyperventilation. Alternatively, the enhanced HR response that we observed during paced deep breathing while wearing the collar and the lower resting low-frequency component of heart rate variability could also indicate a baroreceptor-mediated sensitization of the pulmonary stretch receptors, which would also be expected to decrease respiratory rate via the Hering–Breuer inflation reflex. Lastly, although there was no difference in end-tidal CO_2 while wearing the collar, this could have been due to the presumed decrease of venous return from the brain. Perhaps a longer duration study would have detected higher ventilatory CO_2.

We observed that the compression collar increased jugular vein cross-sectional area. Previous work compressing the jugular vein observed increases in cerebral blood volume (13), suggesting that jugular vein compression in the current study also elevated cerebral blood volume. During baseline and *phase 2 maximum* of the Valsalva maneuver, wearing the collar decreased MCA mean and diastolic velocity. Increased cerebral blood volume likely played an important role in mediating this response. Cerebrovascular autoregulatory mechanisms could have increased cerebrovascular resistance due to the increase in cerebral blood volume, in an attempt to preserve cerebrovascular flow (27, 28). In support of this, there was a trend toward an increase in RI throughout the Valsalva maneuver with the use of the collar. In healthy women, we previously observed higher resting MCA velocity and an attenuated increase of MCA velocity during the end of Valsalva while wearing the collar (12), which was not observed in POTS. Participants with POTS have impaired autoregulation (15), which could be contributing to impaired cerebrovascular responses.

Importantly, the application of the collar reduced orthostatic symptoms such as blurred vision, tremulousness, and lightheadedness. We postulate that the accumulation of blood volume in the brain containing higher concentrations of CO_2 could be causing vasodilation of cerebral vessels, thus increasing brain blood flow and reducing orthostatic symptoms. We further suggest that studies involving regional blood flow throughout the brain are important. For example, we speculate that increased blood flow in the posterior regions of the brain could be responsible for the improvements observed, as therein lie the cerebellum and occipital lobes, which are responsible for vision and motor control. Venous outflow could be redirected to the posterior brain to flow through the vertebral veins rather than the partially occluded jugular veins. The use of bilateral transcranial Doppler to concurrently investigate anterior and posterior cerebral blood flow velocity, and/or the use of functional magnetic resonance imaging throughout the brain, is recommended.

Limitations

We observed changes in the respiratory rate and end-tidal O_2 at rest and during orthostasis, potentially suggesting that the use of the collar modulated pulmonary stretch receptor or chemoreflex activity. However, tidal volume and therefore minute ventilation were not measured. Further, we did not have direct evidence that brain blood flow or volume were changed

while wearing the collar as we were relying on the indirect method of transcranial Doppler to determine blood velocity. This was partially due to the inability to acquire longitudinal images of the jugular vein and carotid artery due to the physical impediment of wearing the collar. Importantly, this study was not placebo controlled and had a limited sample size in which the women were tested at random times during their menstrual cycle without controlling for hormonal contraceptive usage.

Many of our physiological measurements that were small yet significantly different may not have clinical significance nor be responsible for the changes observed in orthostatic symptoms. However, a recent study of healthy individuals in Ontario, Canada, has found that the relationship between the heart rate response to deep breathing (6 breaths/min) and age has a slope of −0.25 bpm/yr (3). Therefore, the changes seen while wearing the collar imply an improvement equivalent to ~8 yr of aging. Further, some variability in measurements and improvements may be dependent on the subtype(s) of POTS within each participant (i.e., hyperadrenergic, immune, hyperventilation, neurogenic, hypovolemic). Future studies need to discriminate between subtypes to minimize variability and to determine the effectiveness of neck compression in each subtype of patient.

Measurements of cerebral near-infrared spectroscopy and direct measurements of ventilation via a pneumotach in a greater number of participants where sex hormone concentrations are measured/controlled in women would have been ideal. Further, our current investigation of cardiorespiratory function during deep breathing, Valsalva maneuver, and tilt required participants to wear the collar for only ~1 h. The benefits and safety of the use of the neck compression collar during longer durations is unknown and should be investigated, particularly during activities of daily living.

Conclusions

Our findings suggest that in participants with POTS wearing a neck compression collar alters respiratory autonomic reflexes, perhaps through unloading of carotid baroreceptors. During paced deep breathing there was increased HR responsiveness and throughout the upright tilt protocol there were reductions of respiratory rate and end-tidal O_2, suggesting lower ventilation. Importantly, we observed a reduction of orthostatic symptoms during tilt. Lastly, wearing the collar decreases mean blood velocity in the MCA during the Valsalva maneuver, likely due to increased resistance from higher brain blood volume. We hypothesize that the external neck pressure is unloading the carotid body and thus sensitizing the pulmonary stretch reflex and/or reducing chemoreflex activity, and we further hypothesize that the increased brain blood volume, which is impeded at the jugular vein due to partial occlusion from the collar, will have a higher than normal level of CO_2, leading to greater cerebral microvascular flow and therefore reduced orthostatic symptoms.

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GRANTS

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DISCLOSURES

The Q-collars were provided by Q30 Innovations. No other conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

M.N. and H.E. conceived and designed research; M.N. and H.E. performed experiments; M.N. analyzed data; M.N., J.G., P.J.H., J.S.F., and H.E. interpreted results of experiments; H.E. prepared figures; H.E. drafted manuscript; M.N., J.G., P.J.H., J.S.F., and H.E. edited and revised manuscript; M.N., J.G., P.J.H., J.S.F., and H.E. approved final version of manuscript.

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