ORIGINAL ARTICLE

Cardiovascular and autonomic responses to passive arm or leg movement in men and women

Bahareh Fouladi[1] · Hitesh Joshi[1] · Heather Edgell[1,2]

Abstract

Purpose Women display an attenuated mechanoreflex during leg movement; however, sex differences in the response to arm movement are unknown.

Methods Men ($n = 12$) and women ($n = 10$) performed passive arm or leg movement where either the right elbow or right knee was passively flexed/extended for 3 min at 30 times/min. Mean arterial pressure (MAP), cardiac output index (Qi), and heart rate (HR) were continuously measured and 1-min averages along with peak values were obtained. Heart rate variability was measured at baseline and throughout 3 min of passive movement.

Results Men had a greater average HR ($P = 0.006$) and Qi ($P = 0.05$) responses to passive limb movement compared to women. Men also had a greater ($P = 0.02$) and faster ($P = 0.04$) peak Qi response compared to women. During arm movement, men exhibited a greater change of average MAP compared to both women ($P = 0.002$) and leg movement ($P = 0.05$). Movement of either limb in both sexes decreased low-frequency power (LF; $P = 0.04$), decreased low-frequency to high-frequency ratio (LF/HF; $P = 0.03$), and increased high-frequency power (HF; $P = 0.01$) of heart rate variability. Women had lower pulse wave velocity ($P = 0.02$), higher root mean square of the successive differences (RMSSD; $P = 0.04$), lower LF power ($P = 0.04$), higher HF power ($P = 0.03$), and higher cardiovagal baroreceptor sensitivity ($P = 0.003$) compared to men at all time points.

Conclusions We have found sex- and limb-dependent responses where men exhibit higher blood pressure in response to passive arm movement compared to women and compared to leg movement.

Keywords Cardiac output · Blood pressure · Heart rate · Heart rate variability · Sex differences · Mechanoreflex

Abbreviations

ANOVA	Analysis of variance
cBRS	Cardiovagal baroreceptor sensitivity
CPM	Continuous passive motion
ECG	Electrocardiogram
EMG	Electromyography
CO_2	Carbon dioxide
HF	High-frequency spectrum
HR	Heart rate
HRV	Heart rate variability
LF	Low-frequency spectrum
LF/HF	Ratio of low frequency to high frequency
MAP	Mean arterial pressure
nu	Normalized units
O_2	Oxygen
PWV	Pulse wave velocity
Q	Cardiac output
Qi	Cardiac output index
RMSDD	Root mean square of successive differences
SDNN	Standard deviation of NN intervals

✉ Heather Edgell
edgell@yorku.ca

1 School of Kinesiology and Health Sciences, York University, 355 Bethune College, 4700 Keele St, Toronto, ON M3J 1P3, Canada

2 Muscle Health Research Centre, York University, Toronto, ON, Canada

Introduction

During exercise both the metaboreflex and the mechanoreflex are activated via group III/IV afferent nerves in the skeletal muscle contributing to the exercise pressor reflex (Hayes et al. 2005; Kaufman and Hayes 2002), and

women are known to have attenuated metaboreflex function compared to men (Jarvis et al. 2011). Ives et al. determined that the mechanoreflex was attenuated in women (Ives et al. 2013); however, they only investigated passive movement of the knee, not the elbow. Passive movement of the knee increased femoral blood flow in both men and women, yet cardiac output increased to a greater degree in men (Ives et al. 2013). Similarly, passive leg cycling has been shown to elicit a greater change in heart rate variability in men compared to women (Shi et al. 2016) implying a greater effect of limb movement on autonomic control in men. These sex differences could be due to variance in muscle mass. Indeed, Vianna et al. concluded that mechanoreflex activation in men is dependent on the number of limbs involved and, therefore, muscle mass (Vianna et al. 2010); however, they found similar changes in R–R interval when comparing the passive movement of one arm versus two arms (Vianna et al. 2010). Further, the increase in response when the legs were also moved was not augmented to a degree which would be expected if only muscle mass was important. Therefore, we suggest that while the mechanoreflex may depend on muscle mass to a certain degree, a limb-dependent mechanoreflex response may also exist. Indeed, in men, upper body resistance exercise elicits a greater increase of sympathetic activity with a greater decrease of parasympathetic activity compared to lower body resistance exercise (Machado-Vidotti et al. 2014), and upper body cycling exercise elicits a greater increase of blood pressure compared to lower body cycling (Calbet et al. 2015).

In a separate study, Vianna et al. (2008) investigated isolated passive arm movement (sex not reported) and similarly found that R–R interval decreased providing more evidence that movement of the arm alone has the potential to affect autonomic cardiovascular control. Further, Llwyd et al. (2017) investigated 1 min of passive arm movement in an older mixed sex group of participants and found a small increase of mean arterial pressure. Similarly, Burns et al. found an increase of limb blood flow during passive movement of either the elbow or knee in a mixed sex group; however, they only observed an increase of mean arterial pressure with knee movement (Burns et al. 2016). These studies clearly indicate that the mechanoreflex is active during either knee or elbow movement; however, they did not investigate sex differences and only tested for up to 1 min of movement even though clinical rehabilitation techniques involving passive limb movement often last for longer periods (Ter Woerds et al. 2006). While studies of passive movement of the leg for 3 min have been conducted previously [and have found no effect on hemodynamics (Ives et al. 2013)], there are no studies that have investigated passive arm movement for this duration despite the potential importance for clinical rehabilitation techniques.

We hypothesized that (1) both sexes would exhibit limb-dependent autonomic and cardiovascular responses to passive movement, (2) limb-dependent hemodynamic responses would be present during acute movement (1 min) but not during longer duration movement (3 min), and (3) men would have enhanced responses to passive movement of either limb compared to women.

Materials and methods

Participant description

Young healthy participants with no history of cardiovascular or respiratory disease were recruited to this study (12 men; 10 women). Men were 22.8 ± 0.9 years old with a body mass index of 24.3 ± 1.1 kg/cm^2. Women were 21.8 ± 0.5 years old with a body mass index of 20.7 ± 0.7 kg/cm^2. Women were not taking oral contraceptives and were tested from day 2 to 5 of the menstrual cycle when estrogen and progesterone levels are low. Participants were asked to refrain from eating fatty food, drinking coffee, drinking alcohol, and engaging in physical exercise for a minimum of 12 h prior to assessment. Informed consent was obtained from all individual participants included in the study, and the study was approved by the Office of Research Ethics at York University in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Hemodynamic measurements

Heart rate (HR) was determined using the R–R interval of a standard electrocardiogram. Beat-to-beat blood pressure and cardiac output (Q) were determined using a non-invasive blood pressure device (Finometer Pro, Finapres Medical Systems, Amsterdam, Netherlands). Resting blood pressure was calibrated with a standard manual blood pressure measurement, and Q was normalized to body surface area for cardiac output index (Qi, Dubois and Dubois formula). Total peripheral resistance index was calculated as mean arterial pressure divided by Qi.

Respiratory measurements

End-tidal CO_2 and O_2 were sampled using a nasal cannula connected to gas analyzers (Vacumed, Ventura, USA). Respiratory rate was determined from the breath-to-breath peaks in end-tidal CO_2.

Heart rate variability and cardiovagal baroreceptor sensitivity

Heart rate variability (HRV) provides an indicator of the autonomic control of heart rate (Pomeranz et al. 1985; Malik

et al. 1996), and was determined using 3 min of data before and during passive limb movement. The Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology have suggested that segments of data used for heart rate variability analysis should be 2 min or longer to adequately assess both low- and high-frequency components (Malik et al. 1996). Spectral analysis was conducted using the HRV Module of LabChart Pro 8.0 software (ADInstruments, Colorado, USA). A Hann (cosine-bell) data window was used with a window overlap of 50%. Fast Fourier transform size was 1024. The low-frequency spectrum (LF) was defined as 0.04–0.15 Hz and the high-frequency spectrum (HF) was defined as 0.15–0.45 Hz. Any ectopic heart beats were removed prior to analysis. Cardiovagal baroreceptor sensitivity (cBRS; lag 0 data) was calculated using the sequence method (Bertinieri et al. 1988; Blaber et al. 1995) using uninterrupted blood pressure and ECG recordings for 3 min at baseline and 3 min of limb movement. Segments of data where both R–R interval and systolic blood pressure increased or decreased for at least three sequential heart beats were plotted, and the overall slope of these segments was determined to be cBRS. Only those recordings with greater than ten averaged segments were used.

Pulse wave velocity

Pulse wave velocity (PWV) was determined using the foot-to-foot method (Laurent et al. 2006) using pulse waveforms from the finger (Finometer) and from a piezo-electric pulse transducer placed on the toe (ADInstruments, USA). Finger-toe PWV has been shown to be highly correlated to carotid-radial PWV in young adults (Edgell et al. 2016). Averages of 20 beats at baseline and during the 3rd min of passive limb movement were used. PWV was calculated as change in time between the initiation of each waveform divided by change in distance between measurement sites. While PWV measurements are typically used to measure arterial stiffness, acute elevations of sympathetic activity have been shown to increase PWV in young healthy participants (Nardone et al. 2018). Therefore, PWV is being used as a hypothesized index of sympathetic activity.

Experimental protocol

Participants lay supine for at least 20 min prior to starting the protocol. A blood pressure cuff was placed distal to either the right knee or right elbow and inflated to 160 mmHg 1 min prior to starting passive limb movement to prevent fluid shifts during movement. While a buildup of lactate was expected from occlusion, we did not expect an influence from the metaboreflex during supine passive movement (Venturelli et al. 2017a). After at least 5 min of baseline measurement, either the lower leg or the forearm was passively flexed to 90° and extended to 180° at a pace of 0.5 Hz. While many studies have used a pace of 1 Hz per minute (Ives et al. 2013; Venturelli et al. 2017a, b), Kruse et al. (2018) have recently found that movement at 0.5 Hz also elicits a hemodynamic response albeit attenuated compared to 1 Hz. Participants were reminded throughout the protocol not to assist with the movement. There was at least 5 min of rest between trials, and the trials (arm and leg movement) were randomized.

Data and statistical analysis

All signals were collected using PowerLab data acquisition and LabChart software (ADInstruments, Colorado, USA). Thirty-second averages were obtained prior to limb movement, from 30 to 60 s of limb movement ("one minute" time point in figure), and from 2.5 to 3 min of limb movement ("three minute" time point in figure). Changes were calculated as the 1- or 3-min time point minus the baseline average. To determine peak values for Table 2, beat-by-beat analysis was conducted.

Three-way ANOVAs were conducted for hemodynamic responses, respiratory responses, pulse wave velocity, and heart rate variability with time, limb and sex as factors. Two-way repeated measures ANOVAs were used for resting data with sex and trial as factors, and were also used on the time to peak response with sex and limb as factors. Where main or interaction effects were found Tukey post hoc tests were used. All statistical tests were performed with Sigmaplot 13.0 software (Sigmaplot 13.0, Systat Software, Inc., San Jose, USA). Significance was set at $P \leq 0.05$. Data are presented as mean ± standard error.

Results

There were no sex differences with regard to resting mean arterial pressure ($P = 0.20$), heart rate ($P = 0.93$), cardiac output index ($P = 0.18$), total peripheral resistance index ($P = 0.07$), pulse wave velocity ($P = 0.42$), respiratory rate ($P = 0.73$), end-tidal CO_2 ($P = 0.11$), or end-tidal O_2 ($P = 0.77$) prior to movement of either limb. There were no differences between trials for the resting values of mean arterial pressure ($P = 0.96$), heart rate ($P = 0.80$), cardiac output index ($P = 0.68$), total peripheral resistance index ($P = 0.99$), respiratory rate ($P = 0.45$), end-tidal CO_2 ($P = 0.11$) or end-tidal O_2 ($P = 0.13$). However, resting pulse wave velocity was lower throughout the arm movement trial compared to the leg movement trial ($P = 0.05$; Table 1).

When comparing the peak hemodynamic response to baseline, all participants increased heart rate, cardiac output index, and mean arterial pressure in response to movement

of either limb ($P < 0.001$). Women and men had similar peak heart rate and mean arterial pressure responses to movement ($P > 0.05$); however, men had a greater cardiac output index response ($P = 0.02$). There were no differences in peak responses between the limbs ($P > 0.05$). The time to the peak response was similar between women and men for heart rate and mean arterial pressure ($P > 0.05$), yet the peak cardiac output index response was faster in men ($P = 0.04$; Table 2).

Compared to women, men had a greater average heart rate response to limb movement ($P = 0.01$); however, there was no difference in the response between limbs ($P = 1.00$) nor the change over time ($P = 0.21$; Fig. 1a). There was a significant interaction between sex and limb for the average mean arterial pressure response to limb movement ($P = 0.05$). Men had a greater increase of average mean arterial pressure during arm movement compared to leg movement ($P = 0.05$), and during arm movement men had a greater response compared to women ($P = 0.002$; Fig. 1b). Similar to the heart rate response, compared to women, men had a greater average cardiac output index

response to limb movement ($P = 0.05$); however, there was no difference in the response between limbs ($P = 0.78$) nor the change over time ($P = 0.16$; Fig. 1c). Men had a significantly greater increase of pulse wave velocity compared to women during limb movement ($P = 0.02$), and both sexes had a greater increase of pulse wave velocity during arm movement compared to leg movement ($P = 0.03$). There was no effect of time on the response of pulse wave velocity during limb movement ($P = 0.88$; Fig. 1d). There were no effects of sex ($P = 0.38$), limb ($P = 0.52$), or time ($P = 0.16$) on total peripheral resistance index (data not shown). There were no main effects of sex, limb, or movement on end-tidal CO_2, end-tidal O_2, or respiratory rate ($P > 0.05$; Table 3).

There were no heart rate variability indicators which displayed a significant main effect of limb ($P > 0.05$). Women displayed a higher RMSSD ($P = 0.04$), lower LF (nu) ($P = 0.04$), higher HF (ms^2) ($P = 0.03$), and higher cBRS ($P = 0.003$) compared to men. In both sexes, limb movement resulted in a reduction of LF (ms^2) ($P = 0.04$), an increase

Table 1 Resting hemodynamic and respiratory data

	Arm trial		Leg trial	
	Men	Women	Men	Women
Mean arterial pressure (mmHg)	107 ± 4	108 ± 7	108 ± 3	107 ± 5
Heart rate (bpm)	61 ± 2	62 ± 3	61 ± 2	61 ± 3
Cardiac output index (L/min/m^2)	2.9 ± 0.2	2.5 ± 0.2	2.8 ± 0.2	2.5 ± 0.2
Total peripheral resistance index (mmHg/L/min/m^2)	29 ± 3	34 ± 1	29 ± 2	34 ± 1
Respiratory rate (breaths/min)	19 ± 1	19 ± 1	20 ± 1	19 ± 1
End-tidal CO_2 (mmHg)	41 ± 1	37 ± 2	40 ± 1	37 ± 2
End-tidal O_2 (mmHg)	117 ± 2	118 ± 2	119 ± 2	120 ± 1
Pulse wave velocity (cm/s)	7.2 ± 0.3	6.7 ± 0.4	7.6 ± 0.5^a	7.1 ± 0.4^a

[a]Significant main effect of trial

Table 2 Peak hemodynamic response to passive limb movement and time to peak

	Heart rate (bpm)			Cardiac output index (L/min/m^2)			Mean arterial pressure (mmHg)		
	Baseline	Peak response	Time of peak (s)	Baseline	Peak response	Time of peak (s)	Baseline	Peak response	Time of peak (s)
Men									
Arm movement	61 ± 2	74 ± 3^a	74 ± 19	2.8 ± 0.2	3.5 ± 0.2^a	98 ± 18	77 ± 3	96 ± 5^a	119 ± 14
Leg movement	61 ± 2	76 ± 2^a	83 ± 16	2.8 ± 0.1	3.5 ± 0.2^a	84 ± 16	78 ± 3	91 ± 3^a	113 ± 12
Women									
Arm movement	62 ± 3	77 ± 4^a	118 ± 16	2.5 ± 0.2	3.2 ± 0.2^{ab}	135 ± 10^b	86 ± 6	96 ± 7^a	101 ± 14
Leg movement	61 ± 3	75 ± 3^a	101 ± 22	2.5 ± 0.2	3.1 ± 0.2^{ab}	122 ± 17^b	84 ± 5	98 ± 5^a	84 ± 18

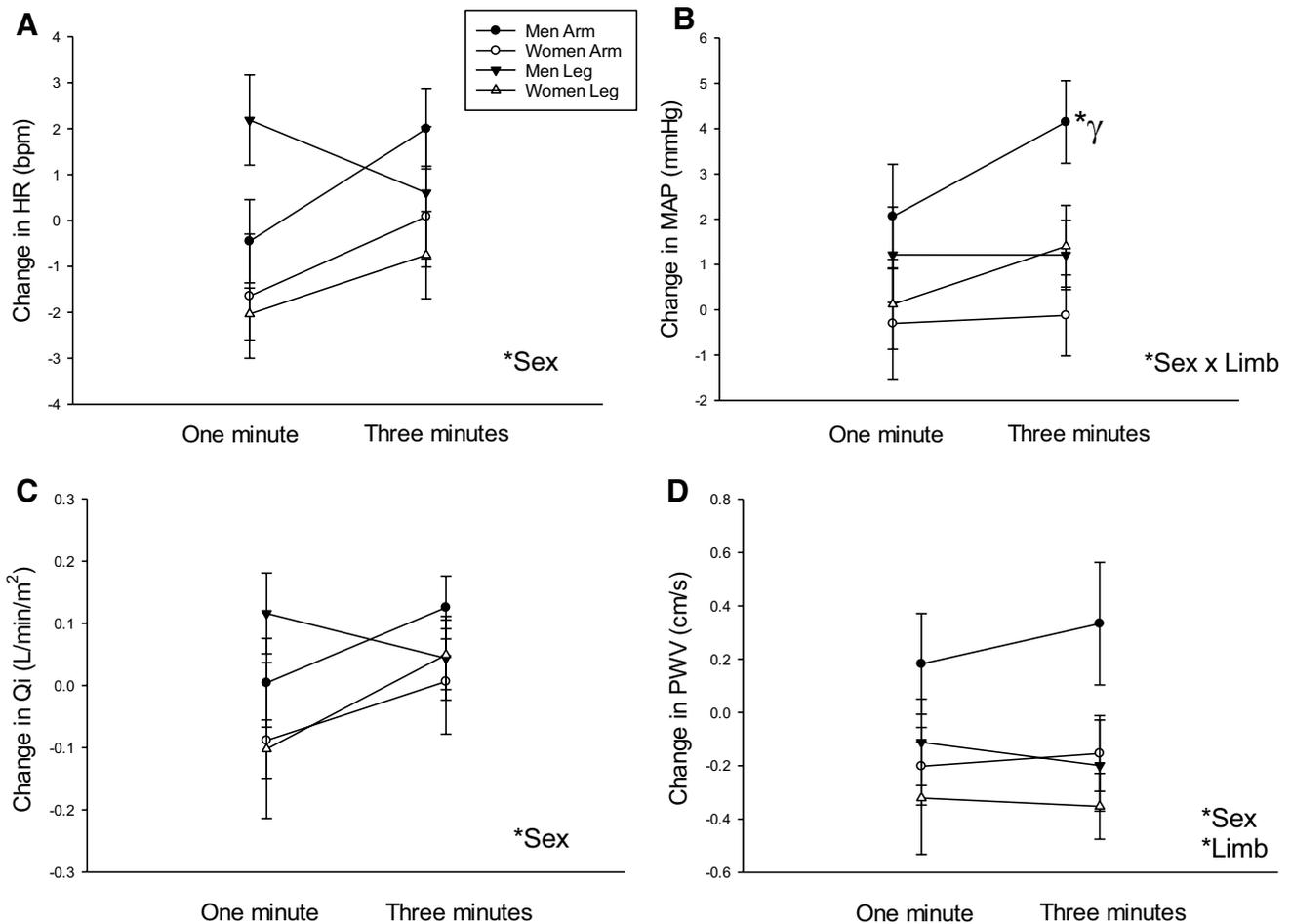[a]Significant difference from baseline

[b]Sex difference

Fig. 1 Changes in average heart rate (HR), mean arterial pressure (MAP), cardiac output index (Qi), and pulse wave velocity (PWV) during passive arm movement. Men are indicated with black symbols, women are indicated with white symbols. The arm movement trial is indicated with circles, the leg movement trial is indicated with triangles. *Men have a greater arm response compared to leg response; γMen have a greater arm response compared to women. Main and interaction effects are noted at the bottom right

Table 3 Changes in average respiratory rate and end-tidal gases during passive movement

	Arm trial				Leg trial			
	Men		Women		Men		Women	
	1 min	3 min	1 min	3 min	1 min	3 min	1 min	3 min
Respiratory rate (breaths/min)	$+0.5 \pm 1.1$	$+0.2 \pm 1.2$	$+0.2 \pm 1.5$	$+1.1 \pm 1.2$	$+0.7 \pm 0.6$	$+0.3 \pm 1.0$	$+1.4 \pm 1.4$	-0.4 ± 1.6
End-tidal CO_2 (mmHg)	$+0.2 \pm 0.2$	$+0.1 \pm 0.3$	-0.03 ± 0.25	-0.1 ± 0.4	$+0.02 \pm 0.3$	-1.3 ± 1.2	$+0.04 \pm 0.2$	-0.2 ± 0.2
End-tidal O_2 (mmHg)	$\pm 0.4 \pm 1.0$	$+1.3 \pm 1.2$	$+0.4 \pm 1.0$	$+2.2 \pm 1.4$	$+1.1 \pm 0.9$	$+2.8 \pm 1.8$	$+0.3 \pm 1.1$	$+1.8 \pm 0.7$

of HF (nu) ($P = 0.01$), and a reduction of LF/HF ($P = 0.03$) (Table 4).

Discussion

We have shown that (1) when investigating the peak response to passive limb movement, men and women have increases of heart rate, cardiac output index, and mean arterial pressure compared to baseline; however, the

Table 4 Heart rate variability during passive limb movement in men and women

	Men				Women				Significance
	Baseline	Arm movement	Baseline	Leg movement	Baseline	Arm movement	Baseline	Leg movement	
SDNN (ms)	70.6 ± 7.3	58.2 ± 7.1	80.6 ± 4.9	64.9 ± 6.9	71.1 ± 7.9	69.4 ± 7.6	73.5 ± 9.8	69.3 ± 11.3	–
RMSSD (ms)	66.4 ± 7.9	62.1 ± 7.9	72.2 ± 5.9	58.2 ± 8.3	77.5 ± 11.5	80.5 ± 12.4	82.0 ± 13.5	75.9 ± 12.9	Sex ($P = 0.04$)
Total power (ms^2)	4904 ± 1180	3495 ± 782	6285 ± 809	3774 ± 805	6073 ± 1388	5558 ± 1254	6350 ± 2046	5336 ± 1449	–
LF (ms^2)	1213 ± 204	885 ± 254	1637 ± 264	977 ± 307	1488 ± 378	1196 ± 240	2058 ± 728	1162 ± 451	Time ($P = 0.04$)
LF (nu)	44.6 ± 3.6	33.3 ± 3.9	45.3 ± 4.2	38.8 ± 4.4	31.5 ± 6.1	36.2 ± 4.3	38.7 ± 5.1	28.8 ± 5.1	Sex ($P = 0.04$)
HF (ms^2)	1967 ± 655	1733 ± 495	1973 ± 382	1343 ± 350	2966 ± 924	2807 ± 1009	3174 ± 1193	2567 ± 847	Sex ($P = 0.03$)
HF (nu)	54.2 ± 3.5	64.6 ± 3.6	52.2 ± 3.2	57.7 ± 3.5	57.8 ± 5.4	60.3 ± 4.2	55.4 ± 4.2	67.7 ± 4.9	Time ($P = 0.01$)
LF/HF	0.91 ± 0.13	0.58 ± 0.11	0.96 ± 0.15	0.75 ± 0.11	0.79 ± 0.19	0.67 ± 0.13	0.81 ± 0.20	0.53 ± 0.20	Time ($P = 0.03$)
cBRS (ms/mmHg)	27.8 ± 5.0	28.0 ± 4.4	29.8 ± 6.6	23.4 ± 3.2	34.2 ± 3.8	39.2 ± 5.6	40.3 ± 5.7	39.9 ± 4.2	Sex ($P = 0.003$)

LF low frequency, *HF* high frequency, *cBRS* cardiovagal baroreceptor sensitivity, *SDNN* standard deviation of the R–R interval, *RMSSD* root mean square of the successive differences

increase of cardiac output index is smaller and delayed in women, (2) men and women have similar increases in the high-frequency component of heart rate variability, with no change in cardiovagal baroreceptor sensitivity during passive limb movement, (3) men and women have similar reductions of the low-frequency component of heart rate variability (and LF/HF ratio) during passive limb movement, (4) compared to women, men have a greater heart rate, cardiac output index, and pulse wave velocity response to passive limb movement, and (5) men increase mean arterial pressure in response to passive arm movement to a greater degree than their response to leg movement and their response to arm movement is greater than the response of women.

During passive limb movement both sexes displayed reduced LF power, reduced LF/HF ratio, and increased HF power. These results suggest either a relative reduction of sympathetic control (Malik et al. 1996) or a reduction of baroreceptor function (Goldstein et al. 2011), and a relative increase of parasympathetic control of heart rate (Malik et al. 1996). The concurrent finding that there was no change in cardiovagal baroreceptor sensitivity during passive limb movement supports the hypothesis that the lower LF indicates a reduction of sympathetic control. In men, these results echo those of Shi et al. (2016) who found lower LF power and higher HF power during continuous passive cycling (at 5–10 cycles/min); however, in women they did not observe a significant reduction of LF power or an increase of HF power (yet they did observe a reduction of LF/HF) (Shi et al. 2016). These differences could stem

from the use of dual-leg passive cycling (i.e., more muscle mass) at a slower rate of flexion/extension compared to the current study. Supportive of our findings, Doherty et al. recently found a reduction of leg muscle sympathetic activity and a reduction of sympathetic baroreceptor sensitivity with 1–2 min of single-leg passive leg cycling (50 revolutions/min) in a mixed sex group (Doherty et al. 2018). Ives et al. have suggested that during passive leg movement an impaired baroreflex does not likely play a role in the reduced cardiac output response in women (Ives et al. 2013) further suggesting that our observed reduction of LF is likely a reduction of sympathetic output. Ives et al. also found that men and women had similar hyperemic responses to passive leg movement (despite smaller body size in women) suggesting that the hyperemic response is driven by the increase of cardiac output in men, but local vasodilatory responses in women (Ives et al. 2013). This is supported by our hemodynamic data (greater average and peak cardiac output in men). The greater increase of HR and cardiac output in men is likely not a result of direct autonomic nervous control since autonomic control of HR during movement was similar to that observed in women. We suggest that the greater HR and cardiac output in men could be due to changes in hormonal factors such as a rise in circulating epinephrine. Indeed, Matsukawa et al. (2001) found that muscle stretch of cat hindlimbs resulted in an increase of circulating epinephrine (sex of animals not described) (Matsukawa et al. 2001).

Little is known about the autonomic and hemodynamic responses to passive arm movement in men and women. Our findings suggest that as with passive leg movement, during

passive arm movement there is a relative reduction of sympathetic control of HR (i.e., lower LF/HF) and an increase of parasympathetic control of HR (i.e., higher HF power) in both men and women. Pulse wave velocity was higher during arm movement compared to leg movement, and there was no change in cardiovagal baroreceptor sensitivity during movement. This increase in pulse wave velocity is likely driven by the greater increase of mean arterial pressure during arm movement in men. This augmented response of blood pressure to arm movement in men further suggests that passive arm movement may be eliciting sexually dimorphic vasoactive hormonal responses.

Passive limb movement can be used as a rehabilitation technique in both men and women with spinal cord injury to prevent contractures and increase blood flow (Harvey 2016; Venturelli et al. 2014). This increase in blood flow to a moving limb is often the rationale for using passive limb movement in rehabilitation of spinal cord injury patients. Ter Woerds et al. found that supine passive leg movement does not actually change blood flow or blood pressure in male spinal cord injury patients during 10 min of movement or for 10 min after completion of movement (Ter Woerds et al. 2006). However, shorter bouts of passive movement have been shown to be beneficial for increased blood flow. McDaniel et al. (2010) found increased cardiac output and femoral blood flow for 45 s after the onset of passive leg movement in healthy men (McDaniel et al. 2010). Further, Burns et al. (2018) have subsequently found that in spinal cord injury patients multiple 1-min bouts of passive leg movement (with a 1-min period of rest between bouts) results in a steady increase of blood flow in each movement session (Burns et al. 2018). These previous studies suggest that passive leg movement may be beneficial for spinal cord injury patients; however, sex differences have not yet been investigated. Female patients may exhibit a greater increase of limb blood flow during passive movement due to local vasodilatory factors. More studies are needed investigating passive limb movement in women with spinal cord injury.

Continuous passive motion (CPM) protocols can also be used after a stroke or joint surgery to increase blood flow and improve disability (Harvey et al. 2010; O'Driscoll and Giori 2000; Denis et al. 2006; Lynch et al. 2005; Ver et al. 2016). While passive limb movement will indeed increase blood flow to the respective joint (knee or elbow) within 1 min of movement (Burns et al. 2016), our results show that blood pressure will increase in men during 3 min of arm movement. Since stroke patients often have concurrent hypertension and spinal cord injury patients can suffer from autonomic dysreflexia [i.e., a sudden onset of hypertension (Sharif and Hou 2017)], we suggest caution in these populations and frequent blood pressure measurements during CPM of the arm in men. However, we also suggest that future studies should investigate arm movement in male patients with orthostatic intolerance as a potential intervention to increase blood pressure during upright posture.

Limitations

Neither physical activity levels and/or maximal oxygen consumption were measured, nor was muscle mass or limb volume. These measurements would have given indications of muscle size and overall fitness which may have made our results more robust. However, the purpose of this study was to investigate the potential for limb-specific mechanoreflex responses rather than the role of muscle mass. We also did not measure surface muscle electrical activity (EMG) which would have supported our claim that participants did not actively use their muscles during limb movement. However, we expect that we would have seen greater increases of heart rate during limb movement in the case of voluntary muscle activity.

It has recently been found that ventilation increases during the first 30 s of passive leg movement in a mixed sex group (Silva et al. 2018; Hotta et al. 2007) and greater ventilation and respiratory rate are known to influence heart rate variability by reducing LF power in men (DeBeck et al. 2010). We did not measure tidal volume or ventilation in this study; however, we did measure respiratory rate and end-tidal gases. Since we did not observe any changes in these variables due to passive limb movement, we are assuming that ventilation did not change over the course of passive limb movement in this study. Future studies should investigate changes in tidal volume and ventilation on longer duration mechanoreflex activation in men and women.

Heart rate variability measurements should be determined in resting data rather than periods where perturbations in heart rate are to be expected, particularly when comparing groups with different heart rate responses such as in the current study. While heart rate variability is often used in situations where heart rate is expected to change (e.g., exercise, hypoxia, hypercapnia), alternative analysis options such as the integral pulse frequency model (Bailon et al. 2011) should be used in future studies to be confident in our results.

Conclusions

We have provided evidence that during passive movement of either the arm or the leg men and women have similar increases of parasympathetic control and similar reductions of sympathetic control. We have also found that in response to movement of either limb men have a greater hemodynamic response compared to women. Importantly, we have provided evidence that men have a greater blood pressure response to passive arm movement compared to

passive leg movement and compared to women indicating a limb-specific mechanoreflex in men. These results should be considered when using passive or continuous passive motion protocols during rehabilitation in clinical populations.

Author contributions BF and HE contributed to the conception and design of the work. BF, HJ, and HE contributed to the acquisition, analysis and interpretation of the data and drafting of the work/revising it critically for important intellectual content. All authors read and approved the final version of the manuscript.

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