Gender Differences in Cardiovascular Responses to Postural and Cutaneous Cold Stress Among Healthy Young Adults Residing in Nigeria

***Fabunmi OA,[1] Olaniyan TA,[2] Olatunji LA[3]**

ABSTRACT
Temperature and postural stress are known to affect cardiovascular indices such as heart rate and blood pressure. However, males and females may respond differently during pathological states. Of importance is the magnitude of this variation amongst otherwise healthy young individuals across various regions globally. The cold pressor test (CPT) can be used clinically to evaluate autonomic and left ventricular function. It is also used to assess neural control of the cardiovascular system by observing the pressor response during the immersion of one hand in cold water. This study examined the gender differences in cardiovascular responses to cold pressor test and postural stress among young healthy adult Nigerians (20 males and 20 females). Systolic blood pressure (SBP), diastolic blood pressure (DBP) and Heart rate (HR) were measured and recorded before and after either postural change or CPT. The results of this study showed significant gender differences in measured cardiovascular indices response following postural change and CPT. Female DBP and HR responses (difference between pre- and post- measurements) to postural change were significantly higher than males. Thus, females tend to elicit higher autonomic responses to postural change especially in HR (sympathetic tachycardia) and DBP (a function of peripheral resistance) than males.

Keywords: Postural, Cold, Stress, Hemodynamics, Adult, Nigerian

INTRODUCTION

The cold pressor test (CPT) is a method that was first reported by Hines and Brown,[1] to evaluate how neural control affects the cardiovascular system by immersing a hand in cold water and observing the pressor response. It is a method used as a standard test for depiction of sympathetic role and is used to foretell the concomitant risk of hypertension in normotensive persons.[2] It has become a symptomatic test for autonomic related diseases like hypertension and other cardiovascular disorders.

The purpose of the CPT is to evaluate the sympathetic function of the cardiovascular system. CPT was reported to accelerate α-adrenergic response with vasoconstriction and an enhanced total peripheral resistance.[3] A previous study demonstrated that subjects with more than 15 mmHg variations in Systolic or Diastolic Blood Pressure response were classified as being excessively reactive to CPT.[4]

Department of Physiology,[1] College of Medicine, Ekiti State University, P.M.B. 5355, Ado- Ekiti 36001, Nigeria.
School of Public Health and Family Medicine,[2] University of Cape Town, Cape Town, 7925, South Africa
Cardiovascular Research Laboratory,[3] Department of Physiology, College of Health Sciences, University of Ilorin, P.M.B.1515, Ilorin 240001, Nigeria.

*Corresponding author: fabunmioyesanmi@gmail.com; oyesanmi.fabunmi@eksu.edu.ng.

Autonomic nervous system controls various visceral activities of the body including blood pressure and heart rate and it is regulated by many factors like orthostatic stress, cold shower, body posture etc.[5,6] The pumping action of the heart comes with a major dynamic change which often result in an increased peripheral arterial resistance due to pressor response. However, increased cardiac output (CO) occurs due to increased heart rate (HR) and increased pulmonary arterial pressure.[1]

Furthermore, changes in blood pressure occur in moderation among healthy cohorts from time-to-time. Factors like postural change can have an influence. More so, individuals changing from a recumbent to upright posture will experience a moderate and measurable change in hemodynamics primarily due to delayed movement of fluid from the lower extremities due to gravity.[2]

In a previous study by Convertino, orthostatic intolerance was observed to be prominent among female cohorts when compared with their male counterparts which contradict another study by Frey and Porth.[7,8] Gender can affect sympathetic response to postural changewhile under different physiological stressors.[9,10] More so, the influence of gender differences on arterial pressure is due to the effect of hormone action on β-adrenergic receptors shutting down the α-adrenergic vasoconstriction among female cohorts.[11]

In another study, orthostatic intolerance was significant among young female adults when compared with their male counterparts and was accompanied with high increase in HR during a cardiovascular challenge.[12] Venous return and cardiac output also reduced significantly among the young female adults.[12] However, studies on the mechanisms responsible for gender difference remain inconclusive.

Orthostatic hypertension occurs due to increase in arterial blood pressure during postural changes. Itis a physiological phenomenon that is underappreciated and understudied clinically.[13] The underlying pathophysiology is not clear but has been linked to the activation of sympathetic trunk of the nervous system.[13] Thus, the aim of this study was to investigate the role of gender difference in cardiovascular responses to cold pressor test and postural

MATERIALS AND METHODS

Subjects and protocol

To avoid the effect of confounding variables such as age, height, or fitness, a total of 40 healthy (20 males: 20 females) subjects were selected randomly. The exclusion criteria for the study included: a history of vasovagal syncope, vertigo, and vestibular disturbance and excluding cardiovascular, respiratory, and neurological diseases, use of oral contraceptives or any long-term medication, or presence of a medical condition using a questionnaire.[14] Subjects were instructed not to engage in any rigorous exercise or stressful activity 48 hours before testing, including abstinence from caffeine consumption, frequent smoking, and other alternative stimulants 24 hours before testing. The experiment was conducted following the Declaration of Helsinki, and was approved by the local Ethics Committee of the University of Ilorin Teaching Hospita (UITH).[15] Subjects gave their written informed consent to participate in the study. Prior to giving consent, all potential subjects were familiarized with the test protocol and informed of their right to withdraw at any time. Additionally, individuals received a full comprehensive medical examination.

Measurements

All the experiments were carried out in the Physiology laboratory at an ambient room temperature of 25-28 degree Celsius. Digital body weight scale was used to record the weight of the subjects. Charder HM210D Digital Stadiometer was used to measure the height. Onwon Waterproof Multi-function Electronic Sports Stopwatch Timer Water Resistant was used to monitor the time of cold pressor test and postural changes. A pan of ice and water was prepared and maintained at 4°C using a digital thermometer to check any temperature change.

Experimental protocol

The subjects were allowed a 10-minute rest in a supine position, after which the baseline blood pressure and heart rate were measured in the upper left arm using a standard digital sphygmomanometer. After 5 minutes of quiet rest, the subjects stood up immediately, and both the blood pressure and heart rate measurement were obtained. For the CPT, Hines and Brown method was used - the left hand of the subject was immersed to just above the wrist in cold water at 4 degree Celsius for 2 minutes, and both the heart rate and the blood pressure were recorded after immersion. This was done while the subjects were comfortably seated in an upright position. In the last ten seconds of the immersion, blood pressure and heart rate measurements were obtained. The readings were recorded, and the subjects were allowed to rest for recovery. The maximal changes in SBP and DBP from resting values during cold stimulus were defined as systolic response and diastolic response respectively. Subjects whose Systolic/Diastolic response exceeded 15mm Hg were defined as Systolic /Diastolic hyperreactors.[4]

Statistical analysis

All statistical analyses were performed using SPSS v. 20.0, (SPSS, Chicago, IL). All values recorded in this study are in mean ± SD (Standard Deviation). Statistical analysis and comparisons were made using the student independent T-test with subjects grouped by gender. Differences were considered significant when $p < 0.05$.

RESULTS

Physical characteristics of subjects in the population study

The descriptive data for both groups are summarized in table 1. This table showed that females demonstrated a higher significant difference in hip circumference when compared with males. Furthermore, waist-to-hip ratio in females was significantly lower when compared with males. However, all other anthropometric data were similar statistically without significant difference.

Clinical hemodynamic variables

Our study showed that females demonstrated significant higher systolic blood pressure (SBP) in upright position when compared to males (Table 2).

More so, females also demonstrated significant higher diastolic blood pressure (DBP) in supine and upright position when compared with males. However, rate of change in DBP during postural adjustment was also significantly higher in females when compared to males as shown in table 3.

In addition, females also demonstrated significant higher Heart rate (HR) in the upright position when compared with male subjects as shown in table 2. However, the rate of change in heart rate was significantly higher in females compared with males (Table 3).

Furthermore, at baseline during the commencement of CPT, females had significantly higher HR when compared with males (Table 4). Also, during CPT, HR was significantly higher in females when compared with males (Table 4). The rate of change of the cardiovascular responses during CPT was not significantly different among cohorts (Table 5).

Table 1: Physical characteristics males and females in the study population.

Physical Characteristics	**Male (n = 20)**	**Female (n = 20)**	***p-value***
Age (years)	21.55 ± 2.68	20.35 ± 1.03	0.069
Waist Circumference (cm)	76.02 ± 12.7	76.16 ± 1.03	0.961
Hip Circumference (cm)	90.75 ± 12.5	100.9 ± 15.9	0.031
Weight (kg)	62.00 ± 17.1	64.70 ± 19.9	0.648
Height (m)	1.675 ± 0.84	1.622 ± 0.58	0.812
Waist-to-Hip Ratio	0.836 ± 0.00	0.715 ± 0.04	0.000
Body Mass Index (BMI) (kg/m^2)	21.81 ± 4.65	24.52 ± 7.24	0.167

Values are means ± SD for 40 cohorts.
p-value < 0.05 denotes significant difference between males and females

Table 2: Hemodynamic Responses during Postural Changes

Variables	**Male (no = 20)**	**Females (no = 20)**	***p-value***
Supine SBP, mmHg	119.40 ± 2.82	118.75 ± 3.89	0.549
Upright SBP, mmHg	125.80 ± 2.82	129.55 ± 3.67	0.001*
Supine DBP, mmHg	78.20 ± 3.09	81.05 ± 5.72	0.057*
Upright DBP, mmHg	81.10 ± 7.20	90.35 ± 5.19	0.000*
Supine HR, beats/min	71.75 ± 1.34	73.80 ± 4.92	0.080
Upright HR, beats/min	78.00 ± 8.50	87.70 ± 4.83	0.000*

Values are means ± SD for 40 cohorts. SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.
**P-value < 0.05*

Table 3: Rate of Change of Hemodynamic Responses to Postural Change

Variables	Male (n = 20)	Female (n = 20)	P-value
? SBP, mmHg	6.40 ± 4.74	10.80 ± 9.84	0.080
? DBP, mmHg	2.90 ± 8.27	9.30 ± 6.39	0.009*
? HR, beats/min	6.25 ± 8.14	13.90 ± 7.20	0.003*

Values are means ± SD for 40 cohorts. *P-value < 0.05*

Table 4: Hemodynamic Responses during Cold Pressor Test (CPT)

Variables	Male (no = 20)	Females (no = 20)	*p-value*
Baseline SBP, mmHg	116.05 ± 10.5	114.95 ± 12.6	0.765
SBP (CPT), mmHg	131.95 ± 15.7	132.72 ± 14.2	0.871
Baseline DBP, mmHg	73.95 ± 8.18	76.00 ± 8.77	0.449
DBP (CPT), mmHg	84.95 ± 10.3	83.15 ± 12.7	0.625
Baseline HR, beats/min	72.50 ± 9.39	78.75 ± 10.2	0.050*
HR (CPT), beats/min	75.35 ± 10.8	83.55 ± 9.30	0.014*

Values are means ± SD for 40 cohorts. CPT, cold pressor test; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.
**P-value < 0.05*

Table 5: Rate of Change in Hemodynamic Responses to Cold Pressor Test (CPT)

Variables	Male (n = 20)	Female (n = 20)	P-value
? SBP, mmHg	15.90 ± 14.4	17.80 ± 10.9	0.641
? DBP, mmHg	11.00 ± 9.75	7.15 ± 11.20	0.254
? HR, beats/min	2.85 ± 11.0	4.80 ± 11.7	0.591

Values are means ± SD for 40 cohorts. *P-value < 0.05.*

DISCUSSION

In this study we observed cardiovascular parameters during postural stress and cold pressor test (CPT) intervention in healthy Nigerians. Most of the cardiovascular parameters tested were significantly altered. Our findings corroborate with a previous study where it was shown that there was a significant difference across gender with regards to hemodynamic changes, heart rate variability and sympathetic response during postural stress.[9] It is also in consistent with a study that demonstrated significant increased change in diastolic blood pressure and heart rate among female cohorts when compared with male counterpart during postural stress with a slight increase in magnitude.[9]

Most of the observed hemodynamic changes and sympathetic responses are due to the influence of gravity. Host response mechanisms are activated to regulate the observed temporary changes. The most prominent amongst these responses is the baroreflex configuration.[16] This configuration is made of receptors on the carotid artery found in the neck and the thorax. These receptors act swiftly to detect any hemodynamic changes and then activate increased sympathetic responses while decreasing parasympathetic responses and adjusting hormonal effect.

In contrast to a previous studies, male cohorts demonstrated high cardiovascular responses to postural stress when compared with females with low shift in fluid volume shift.[7,10] However, the reason for this disparity is linked to a high shift in body fluid volume from the thoracic region during postural change among female cohorts. Whether these variations could be as a result of racial background is unknown.

More so, the higher cardiovascular response observed in females when compared to their male counterparts is due to high sympathetic nerve activity in females. Therefore, it is plausible to link the difference between the males and females' cardiovascular responses to various stressors to the rate at which sensory afferent fibers become sensitive or in central integration and altered reflex input signals. Sensory signal leads to sympathetic activation and responses during change in posture associated with head-up-tilt and they are initiated in the cardiac chambers, aortic and carotid structures, and vestibular receptors.[9] Moreover, detection of alterations in venous return, which exert control over specific sympathetic nerve activity, takes place in afferent neurons residing in the cardiac chambers and pulmonary structures.[17]

Our study also demonstrated a reflex increase in heart rate during postural changes in females when compared with males which is in consistent with previous studies.[7,18] The tilt-induced heart rate response demonstrated by the female cohorts is due to a high vagal cardiac control at rest and high parasympathetic withdrawal during postural changes.[7,18] Studies have shown that oxytocin as a component of the mammalian body has a capacity to influence the response to various stressors among humans.[19] Acute stressors can release oxytocin in both sexes which can influence the activation of sympathetic nervous system.[20] Oxytocin release differs widely among individuals and the release can be linked to social and racial history of cohorts.[21] This further support the gender difference observed in this study.

Furthermore, there was no significant difference in cardiovascular responses during CPT even though alterations occurred in the hemodynamic parameters observed in our study. Pain intolerance was more pronounced in females when compared with male cohorts which is unclear. However, gender responses in this study may be linked to several factors such as hormonal changes, pain threshold mechanism, psychogenic, environmental and other genetic factors. Studies have shown pain sensation during hand immersion in cold water below 4^0C among cohorts where females were more intolerable and this supports our findings.[22]

Pain sensation can promote increase in blood pressure in hyperreactors due to increased heart rate rather than increased contractility of the heart suggesting that parasympathetic deactivation may promote exaggerated cardiovascular responses in hyperreactors.[22] One of the probable factors for this variation is linked to hormonal factors. However, Estrogen or Oxytocin in females has vascular protective benefit especially in young females.[23,24] One of the limitations of this study was that we do not know each of the female cohort's phases of menstruation. In addition, we had a limited sample size.

In conclusion, our study suggest that women are more susceptible to postural or orthostatic stress when compared to their male counterparts. Further research could focus on the role of sex hormones in women's pain perception in relation to social experiences, reward and motivation.

SOURCE OF FUNDING: None declared

CONFLICT OF INTEREST

The authors declare no financial or other conflicts of interests in the design and interpretation of study results.

ACKNOWLEDGEMENT

The authors thank the participants for their time and profound co-operation.

REFERENCES

1. Hines EA, Brown GE. The cold pressor test for measuring the reactivity of the blood pressure: data concerning 571 normal and hypertensive subjects. *Am Heart J.* 1936;11: 1-9.
2. Madanmohan UK, Bhavanani BA, Krishnamurthy N, Pal GK. Modulation of cold pressor-induced stress by shavasan in normal adult volunteers. *Indian J Physiol Pharmacol* 2002;46:307-12.
3. Pickering TG, Gerin W. Area review blood pressure reactivity: cardiovascular reactivity in the laboratory and the role of behavioral factors in hypertension: a critical review. *Ann. Behav. Med.* 1990;12:3-16.
4. Kasagi F, Akahoshi M, Shimaoka K. Relation between cold pressor test

and development of hypertension based on 28-year follow-up. *Hypertension* 1995; 25:71-6.

5. Richerson GB. The Autonomic Nervous System. Boron WF, Boulpaep EL, editors. Medical Physiology. 1st ed. Philadelphia: *Saunders* 2003; 379.
6. Mishra N, Mahajan KK. Cardio-vascular response to orthostatic stress following cold challenge. *Biomed Res* 1995; 6:103-07.
7. Convertino VA. Gender differences in autonomic functions associated with blood pressure regulation. *Am J Physiol* 1998;275:R1909-20.
8. Frey MAB, Porth CM. Sex differences in response to orthostatic and other stresses. *Circulatory Response to the Upright Posture*, edited by Smith JJ. Boca Raton, FL: *CRC*, 1990:141-67.
9. Shoemaker JK, Hogeman CS, Khan M, Kimmerly DS, Sinoway L. Gender affects sympathetic and hemodynamic response to postural stress. *Am J Physiol Heart Circ Physiol*. 2001;281:H2028-35.
10. Patel K, Rössler A, Lackner H.K, Trozic I., Laing C, Lorr D *et al*. Hinghofer-Szalkay H., Goswami N. Effect of postural changes on cardiovascular parameters across gender. *Medicine* 2016;95:28
11. Hart EC, Charkoudian N, Wallin BG, Curry TB, Eisenach J, Joyner MJ. Sex and ageing differences in resting arterial pressure regulation: the role of the β-adrenergic receptors. *J Physiol.* 2011;589:5285-97.
12. Harm DL, Jennings RT, Meck JV, Powell MR, Putcha L, Sams CP *et al*. Invited review: gender issues related to spaceflight: a NASA perspective. *J Appl Phys* 2001;91:2374-83.
13. Fessel J, Robertson D. Orthostatic hypertension: when pressor reflexes overcompensate. *Nat Clin Pract Nephrol*. 2006;2:424-31.
14. Foley P, Kirschbaum C. Human hypothalamus-pituitary-adrenal axis responses to acute psychosocial stress in laboratory settings. *Neurosci Biobehav Rev*. 2010;35:91-6.
15. World Medical Association. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. *Bulletin of the World Health Organization*. 2001;79:373-4.
16. Izzo JL Jr, Taylor AA. The sympathetic nervous system and baroreflexes in hypertension and hypotension. *Curr Hypertens Rep.* 1999;1:254-63
17. Luzier AB, Nawarskas JJ, Anonuevo J, Wilson MF,Kazierad DJ. The effects of gender on adrenergic receptor responsiveness. *J Clin Pharmacol* 1998;38:618-24.
18. Barnett SR, Morin RJ, Kiely DK, Gagnon M, Azhar G,Knight EL *et al*. Effects of age and gender on autonomic control of blood pressure dynamics. *Hypertension* 1999;33: 1195-200.
19. Pournajafi-Nazarloo H, Kenkel W, Mohsenpour SR, Sanzenbacher L, Saadat H, Partoo L. *et al*. Exposure to chronic isolation modulates receptors mRNAs for oxytocin and vasopressin in the hypothalamus and heart. *Peptides* 2013;43:20-6.
20. Neumann ID, Landgraf R. Balance of brain oxytocin and vasopressin: implications for anxiety, depression and social behaviors. *Trends Neurosci* 2012;35:649-59.
21. Bartz JA, Zaki J, Bolger N, Ochsner KN. Social effects of oxytocin in humans: context and person matter. *Trends Cogn. Sci* 2011*;*15:301-9.
22. Moriyama K, Ifuku H. Assessment of cardiac contractility during a cold pressor test by using (dP/dt)/P of carotid artery pulses. *Eur J Appl Physiol*. 2007;100:185-91.
23. Vaccarino V, Badimon L, Corti R, de Wit C, Dorobantu M, Hall A *et al*. Ischaemic heart disease in women: are there sex differences in pathophysiology and risk factors?: Position Paper from the Working Group on Coronary Pathophysiology and Microcirculation of the European Society of Cardiology. *Cardiovasc Res* 2011;90:9-17.
24. Olatunji LA, Soladoye AO. Effects of chronic administration of vitamin E on haemodynamic responses to postural stress or cold pressor test in apparently healthy young men. *Niger Postgrad Med J*. 2008;15:225-8.