Global Journal of Psychology Research: New Trends and Issues

Volume 11, Issue 2, (2021) 70-80

www.gjpr.eu

Stress-induced cardiovascular responses to cold pressure test in healthy young subjects

Valeri Nikolov[a*], Trakia University, Medical Faculty, 11 Armeiska str., Stara Zagora 6000, Bulgaria vtsnikolov@gmail.com https://orcid.org/0000-0002-3242-9245
Miroslava Petkova[b], Trakia University, Medical Faculty, 11 Armeiska str., Stara Zagora 6000, Bulgaria petkovaa@hotmail.com https://orcid.org/0000-0002-4242-9070
Emil Nikolov[c], Sofia University, Faculty of Medicine, Address, Sofia 1000, Bulgaria. e.vnikolov@outlook.com https://orcid.org/0000-0002-0086-4445 https://doi.org/10.18844/gjpr.v11i2.4777

Suggested Citation:
Nikolov V., Petkova M., & Nikolov E. (2021). Stress-induced cardiovascular responses to cold pressure test in healthy young subjects. *Global Journal of Psychology Research: New Trends and Issues*. *11*(2), 70-80. https://doi.org/10.18844/gjpr.v11i2.4777

Received from May 8.2021; revised from July 18,2021; accepted from September 17,2021.
Selection and peer review under responsibility of Prof. Dr. Tulay Bozkurt, Istanbul Kultur University, Turkey.

Abstract
Sleep quality and stress have been linked to a number of diseases such as cardiovascular problems ,the aim of the study is to investigate the various effects of CPT on cardiovascular responses in healthy young subjects. The sample consisted of 56 healthy individuals aged between 21 and 26 years. The Cardiovascular responses to CPT were recorded by using the applanation tonometry. Data collection tools included the Medical Outcomes Study Sleep Scale and the State-Trait Anxiety Inventory. According to the results, Hyperreactors showed a significantly higher increase in sleep disturbances and anxiety when compared to the normoreaktors. The CPT used to diagnose cardiovascular reactivity in young individuals and the assessment of perceived stress can help identify candidates for a future risk of hypertonic disease.

Keywords: Applanation tonometry; blood pressure; cold pressor; cardiovascular reactivity; stress

* ADDRESS OF CORRESPONCE: Valeri Nikolov[a], Trakia University, Medical Faculty, 11 Armeiska str., Stara Zagora 6000, Bulgaria
Email: vtsnikolov@gmail.com *

1. Introduction

More than 80 years ago Hines & Brown (1936) suggested that vascular hyperreactivity, manifested by cold pressor test was a potential predictor of hypertension (Wood, Sheps, Elveback, & Schirger, 1984). Menkes et al, (1989) note that cardiovascular reactivity to stress has been hypothesized to be a marker for subsequent neurogenic hypertension. Many investigators indicate that the intensity of cold and pain stress is involved in the blood pressure response to cold pressor test (Moriyama & Ifuku, 2010; Kregel, Seals, & Callister, 1992). The typical cardiovascular cold pressor effect consists of systolic and/or diastolic BP raise by 10-20 mmHg combined with increased heart rate (Simoes et al., 2013). The pressor response is characterized by an increased cardiac output in the initial period (0-30s) (Yamamoto et al, 1992), followed by an increased sympathetic muscle tone (30-120 s). Although there is a fair fluctuation of the results for the heart rate, most authors describe a similar cardiovascular response (Willemsen et al., 1998; Ring et al., 2000). The interpretation of the CP effect is widely researched but most studies reach the conclusion that it involves primary neurogenic reflexes with triggering activity of the peripheral autonomic structures, leading to activation of the spinal cord, thalamus, sensory cortex, and autonomic nervous system (Lovallo, 1975).

Cardiovascular reactivity, especially blood pressure (BP), changes during the cold pressor test (CPT) depending on various factors. The pressor response by CPT is induced by enhanced sympathetic nerve activity and by increased cardiac output during the initial period (Yamamoto, Iwase, & Mano, 1992; Ifuku, 2015). Undoubtedly, psychological stress is one of the most important factors (Sanchez-Gonzalez, May, Brown, Koutnik, & Fincham, 2013; Cuevas, Williams, & Albert, 2017). Participants experience the CPT as painful and demonstrate increased levels of perceived stress and arousal during and imedaiately after the experiment, which demonstrates changes on the subjective level as well (al'Absi et al., 2002; Zoladz et al., 2014).

Stress is regarded to be an adaptive reaction to an adverse stimulus or situation. The stress response is a multi-level, complex shift in the organism's physiological and psychological functioning (Del Giudice, 2010). The physiological stress response allocates bodily resources to facilitate quick, evasive actions at the expense of more long term, regenerative functions. Acute stress involves an endocrinal response (de Kloet, 2003) and activation of the sympathetic nervous system (Ulrich-Lai,2009), and influences somatic motor behavior and psychological adjustments.

Sleep duration and sleep complaints can have predictive power relative to cardiometabolic health outcomes (Grandner, Jackson, Pak & Gehrman, 2011). The most of authors consider that pulse wave velocity (PWV) is the precidest way to evaluate, non-invasively, arterial stiffness. As authors concludes high PWV values are associated with increased arterial stiffness and increased risk for cardiovascular disease (Doupis, Papanas, Cohen, McFarlan & Horton, 2016). However, the subjective sleep duration variably associated with arterial stiffness, differing from studies, and the evidence of the relationship between sleep duration and cardiovascular risks for women was weaker and less conclusive than men (Aziz, et al., 2017).

1.1.Purpose of study

Sleep adequacy and quality are important issues in the process of maintaining optimal health and well-being (Mullan, 2014). Stress and sleep are in significant correlation. Many psychological and social factors as emotional stress, anxiety, depressive mood, financial hardship, smoking, alcohol consumption affect the sleep. (Nunes da Silva, Martins, Waquim, & Lopes, 2012). Sleep quality has been linked to a number of diseases such as cardiovascular problems. (Kashani, Eliasson, & Vernalis, 2012). The relationship between sleep duration and sleep quality with arterial stiffness is also shown (Tsai, Wu, Yang, Huang & Chang, 2014). Pulse wave velocity (PWV) is now scientifically proven to be the most accurate way to assess non-invasive arterial stiffness. (Doupis, et al., 2016). The aim of the study is to investigate the various stress related effects of CPT on cardiovascular responses in healthy young subjects.

2. Methods and Materials

2.1. Participants and procedure

Fifty-six healthy individuals aged between 21 and 26 years have been investigated. Participants had been non-smokers for at least 6 months prior to the investigation. The participants were non-hypertensive individuals (exclusion criteria for this group were: BP >140/90 mmHg). People, taking antihypertensive medications or other medications known to affect blood pressure (e.g., β-blockers, thyroid, hormones, or steroids) were excluded from the study. Participants with known cardiac conditions (e.g., heart failure, coronary artery disease, myocardial infarction), known vascular conditions (e.g., peripheral vascular diseases), and those who were currently taking medications for a psychiatric disorder (e.g., schizophrenia or major depressive disorder) that may affect psychological measures were also excluded. The study was conducted in Stara Zagora during the period: February - June 2019. Before the CPT, participants completed a questionnaire, containing information on socio-demographic data and psychological scales. Before entering the study, all participants provided written informed consent conducted according to the principles of the declaration of Helsinki (World Medical Association, 2001).

After introduction to the study and collection of demographic data (age, gender, education, marital status, and occupation), smoking status and body weight, all the individuals were subjected to instrumental measurement of the condition of the arterial walls using applanation tonometry and blood pressure measurement. These operations were done by a qualified physician, with the help of a few medical students. To reduce the effect of the circadian cycle the participants were assessed at approximately the same time during the morning (Papaioannou et al., 2013). The instrumental measurements were performed on an empty stomach after instructions to refrain from any beverages of caffeine, ethanol and smoking at least 12 hours prior to the estimates. The measurement of arterial blood pressure (BP) was preceded by a record of medical history and family history. A self-assessment questionnaire, measuring anxiety and sleep disturbances and conducted by a qualified psychologist, was handed out to the subjects after that.

2.1.1. CPT

All the participants underwent the cold pressor test according to Hines & Brown (1936). The right hand was immersed up to the wrist in ice-chilled water (4° ± 0.5°C) for 2 min.

Immediately before and after the period of ice-water immersion, the cardiovascular responses (BP, heart rate, aortic pulse wave velocity) to CPT were recorded by using the applanation tonometry. The difference between peak and basal blood pressures determined the level of vascular reactivity. Subjects were then classified according to their response to the cold pressor test. Subjects who responded to the cold pressor test with an increase in blood pressure of at least 25 mm Hg systolic or 20 mm Hg diastolic were designated as hyprreactors; subjects with an increase less than that were designated as normoreactors. (Wood et al, 1984, Menkes et al, 1989).

2.1.2. Applanation tonometry

Arterial stiffness was evaluated with the tonometric method (PulsePen, DiaTecne, Milan, Italy) (Salvi et al., 2004). This method provides estimates of pulse wave velocity (PWV) and in which central systolic blood pressure (SBPcentr), central pulse pressure (PPcentr) and pulse pressure amplification (PPAmp) can be calculated.

The PWV measurements in duplicate were performed using a SphygmoCor apparatus (SphygmoCor system, AtCor Medical, Sydney, Australia) after a 10-min rest (supine position) (Laurent et al., 2006; Townsend, et al., 2015). To reduce the effect of the circadian cycle the participants were assessed at approximately the same time during the morning (Papaioannou et al., 2013). Measurements were performed on an empty stomach after instructions to refrain from any beverages of caffeine, ethanol and smoking at least 12 hours prior to the estimates. The measurement of arterial blood pressure (BP) was preceded by a record of medical history and family history. PWV was registered between the carotid and femoral artery in the supine position. The SphygmoCor probe over the carotid and femoral artery was used for non-invasive pulse measurements. Simultaneously was performed ECG record (Qureshi, Blaha, Nasir & Al-Mallah, 2013). The values of the distance from the carotid to femoral artery, measured directly between artery location and the supra-sternal notch were entered into the SphygmoCor software database. PWV was automatically calculated using AtCor software.

2.2. Data collection instrument

The research made use of Psychological questionnaires in the collection of data.

2.2.1. Medical Outcomes Study Sleep Scale – MOS-SS (Stewart, & Ware, 1992)

Medical Outcomes Study Sleep Scale includes 12 items assessing sleep disturbance, sleep adequacy, somnolence, quantity of sleep, snoring, and awakening with shortness of breath or with a headache. A sleep problem indexes grouping items from each of the former domains.

2.2.2. The State-Trait Anxiety Inventory

Anxiety was measured by the Spielberger State-Trait Anxiety Inventory (STAI). The 40 item 4-point Likert scale was developed to measure anxiety in adults. The first subscale measures state anxiety, and the second subscales measures trait anxiety (Spielberger, Gorsuch, Lushene, Vagg & Jacobs, 1983). Total scores obtained from the subscales range from 20 to 80 with higher scores indicating greater anxiety. In this study, the internal consistency of the STAI was very good; Cronbach's α was .89 for state anxiety and .87 for trait anxiety).

2.3. Statistical analyses

Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM SPSS Corp.) was used for study statistical analyses. The significance was evaluated at the level of $p < 0.05$. Stratified percentages were used for descriptive statistics. Pearson correlation analysis was used to assess the relationship between study variables. An independent T-test was calculated to examine whether the groups of normoreactors and hyperreactors differs by systolic blood pressure (SBP), diastolic blood pressure (DBP), state anxiety and sleep disturbances and arterial stiffness. To examine the internal consistency and test-retest reliability of the used scales, Cronbach's alpha was examined.

3. Results and discussion

Vascular reactivity to the CPT is measured by the difference between peak and basal blood pressure. Subjects are classified according to their response to the cold pressor test. Individuals with an increase in blood pressure of at least 25 mmHg systolic or 20 mmHg diastolic are classified as hyper-reactors whereas the normoreactors are subjects with an increase less than that (Wood et al, 1984, Menkes et al, 1989).

In the present study the individuals who had showed difference in systolic BP more than 22 mm of Hg and difference in diastolic BP more than 18 mm of Hg after the CPT were defined as hyperreactors (Table 1.).

Table 1

Comparison on values of BP in normoreactors and hyperreactors

Values (mm Hg)	**Mean±SD**		***t* value**	***P* value**
	Normoreactors	**Hyperreactors**		
SBP_1	113,33±6,12	119,23±8,64	3,18	0,01
DBP_1	77,15±7,44	79,26±11,76	2,45	0,01
SBP_2	125,14±10,16	146,65±8,83	9,54	<0,001
DBP_2	86,09±8,14	99,38±6.26	4,32	0,01
Difference of SBP	13,35±2,23	25,83±7,19	6,24	<0,001
Difference of DBP	8,92±4,38	21,13±6,78	10,38	<0,001

SBP_1: Initial systolic blood pressure, DBP_1: Initial blood pressure after immersion blood pressure,
SBP_2: Systolic blood pressure after immersion, DBP_2: Diastolic blood pressure after immersion SD: Standard deviation

For the present study, the distribution between the two groups (normoreactors and hyperreactors) was 67.9% (n = 38) normoreactors, respectively, to 32.1% (n = 18) hyperreactors (Table 2). Previous studies of children and young people share similar data. Hines and Brown (1936) established 10% hyperreactors in children (7-17 years), Moriyama & Ifuku (2007) - 29% and 35.3% - Ifuku (2015) in young people (18-24).

Table 2

Percentage of normoreactors and hyperreactors among the studied subjects

Groups	Number of individuals	%
Normoreactors	38	67,9
Hyperreactors	18	18

After the deviation from the standard values, which we observed in hyperreactors, we established larger increases of the heart rate. In both normoreactors and hyperreactors, the heart rate (HR) during cold stress increased significantly (Table 3.). Similar results have been found by other authors (Ifuku, 2015). The results of the stroke volume did not differ with respect to the two groups.

Table 3

Comparison on values of heart rate (beats/min) in normoreactors and hyperreactors

Groups	HR_1	HR_2
Normoreactors	64,7±9,2	66,6±7,8*
Hyperreactors	67.2±8.5	78.7±10.4**

Data are mean±SD. HR_1: Initial heart rate, HR_2: Heart rate after immersion.
**, * Significantly different: $P<0.01$, $P<0.05$, respectively.

In terms of arterial stiffness, the aortic PWV increase during cold-water immersion is greater in hyperreactors than in normoreactors. This response to PWV in hyperreactors may be due to a greater increase in arterial stiffness caused by increased BP, which is manifested at increased heart rate (Moriyama & Ifuku, 2007; Laurent et al., 2003).

Menkes and coauthors found a significant independent association between blood pressure reactivity to the CPT and incidence of subsequent hypertension (Menkes et al., 1989). 2 other prospective studies achieved similar results. Subjects classified as hyper-reactors to the CPT at either of the two time periods were found to be at a 3,7-fold risk of hypertension, according to Wood et al who followed 47% of a study cohort of 300 school students for 45 years. Barnett and associates found a 10% (4/40) incidence of hypertension among hyper-reactors at the first time of the experiment, but no hypertension among normoreactors.

Other prospective studies have not found a significant association between cardiovascular cold pressor reactivity and subsequent hypertension. For example, an 18-year follow-up study of a cohort of aviators, a group that is healthy and physically fit, with expected lower overall heart rate and blood pressure (Harlan, 1964). A possible explanation as to why it didn't find a significant correlation was that by the end of the 18-year follow up the mean age of the group was 41 years, an age considered to be too early for the development of hypertension. The prevalence of hypertension dramatically increases with age. Thus, an assumption is made that the assessment of the end point should not be made until the targeted population reaches a mean age of 45-50 years. That is when a precise and comprehensive conclusion can be made.

Significant variations in sleep disturbance were ddistinguishedd during the analysis of sleep problems between hyperreactors and normoreators, although the rest of the factors also tended to have higher values among the hyperreactors (Table 4.). The results were similar during the anxiety tests amongst the subjects.

Table 4
Comparing levels of sleep problems between normoreactors and hyperreactors

Groups	Number	Sleep disturbance	Somnolence	Sleep adequacy	Snoring	Sleep quantity
Normoreactors	38	4,76	7.12	2,73	2.54	6.17
Hyperreactors	18	10,30	8.53	3,67	3.15	7,97
T		-8.14	-1.82	-0.97	-1.42	1.86
Sig		0.0001	0.52	0.43	0.08	0,06

Discussion

The levels of anxiety in hyperreactors are higher in comparison to the normoractors. These elevated levels of anxiety and sleep disturbances in hyperreactors lead us to believe that they are at the root of their increased cardiovascular reactivity, due mainly to changes in heart rate, most likely due to increased sympathetic activation, which is confirmed by the opinion of other authors (Moriyama & Ifuku, 2007; Laurent et al., 2003; Grassi et al., 1998).

The increase in BP during immersion in cold water is a specific response to the cardiac function of the cold pressor test in hyperreactors and depends on heart rate rather than cardiac contractility, and these findings suggest that the increased activity of the sympathetic lobe of the autonomic nerve has led to increased HR (Laurent et al., 2003). In this study, this is established against the background of increased levels of psychological stress provoked by sleep disorders and increased anxiety in hyperreactors. These results also confirm the opinion of Grassi et al. (1998) that HR differences as a reflection of differences in sympathetic tone, particularly when differences in sympathetic tone are inferred from HR changes between different subjects rather than within the same subject.

4. Conclusions and Recommendations

A possible explanation liking psychological factors (for example anxiety) to CVD and cardiovascular mortality is cardiovascular reactivity. The increase in BP during immersion in cold water is a specific response to the cardiac function of the cold pressor test in hyperreactors and suggests an increased activity of the sympathetic lobe of the autonomic nervous system. Higher levels of stress (measured as state anxiety) in healthy young people, identified as hyperreactors in this study shows elevated sympathetic activity and are a signal of their increased cardiovascular reactivity during the CPT. CPT can be useful for diagnosing cardiovascular reactivity in young individuals and evaluating anxiety and sleep quality can help identify candidates for a future risk of hypertension.

The mechanisms connecting anxiety and sleep problems with cardiovascular diseases are complex and are yet to be fully understood. However, most studies fail to clarify why episodic cardiovascular hyperresponsiveness is related to risk for hypertension. It might be, in fact, one of the mechanisms underlying essential hypertension, should it represent a central defect in the autonomic nervous system, or indicate changes in arterial compliance. All measures explained in this study would facilitate the involvement of the individuals with clinical or sub-clinical symptoms of anxiety and sleep problems in experimental studies and would further help in a more precise assessment of the cardiovascular risk amongst them.

Acknowledgements

This study was supported by Grant 8/2018 from the Medical Faculty, Trakia University, Stara Zagora, Bulgaria.

References

al'Absi, M., Petersen, K. L., & Wittmers, L. E. (2002). Adrenocortical and hemodynamic predictors of pain perception in men and women. Pain, 96(1-2), 197–204. https://doi.org/10.1016/s0304-3959(01)00447-x

Aziz, M., Ali, S. S., Das, S., Younus, A., Malik, R., Latif, M. A., ... & Elizondo, J. V. (2017). Association of subjective and objective sleep duration as well as sleep quality with non-invasive markers of sub-clinical cardiovascular disease (CVD): a systematic review. *Journal of atherosclerosis and thrombosis*, *24*(3), 208-226. https://doi.org/10.5551/jat.36194

Cuevas, A. G., Williams, D. R., & Albert, M. A. (2017). Psychosocial Factors and Hypertension: A Review of the Literature. *Cardiology clinics*, *35*(2), 223–230. https://doi.org/10.1016/j.ccl.2016.12.004

de Kloet ER Hormones , brain and stress. Endocr Regul. 2003;37(2):51-68

Del Giudice, M., Ellis, B. J., & Shirtcliff, E. A. (2011). The Adaptive Calibration Model of stress responsivity. Neuroscience and Biobehavioral Reviews, 35(7), 1562-1592. https://doi.org/10.1016/j.neubiorev.2010.11.007

Doupis, J., Papanas, N., Cohen, A., McFarlan, L., & Horton, E. (2016). Pulse wave analysis by applanation tonometry for the measurement of arterial stiffness. *The open cardiovascular medicine journal*, *10*, 188. https://doi.org/10.2174/1874192401610010188 .

Grandner, M. A., Jackson, N. J., Pak, V. M., & Gehrman, P. R. (2012). Sleep disturbance is associated with cardiovascular and metabolic disorders. *Journal of sleep research*, 21(4), 427-433. https://doi.org/10.1111/j.1365-2869.2011.00990.x .

Grassi, G., Vailati, S., Bertinieri, G., Seravalle, G., Stella, M. L., Dell'Oro, R., & Mancia, G. (1998). Heart rate as marker of sympathetic activity. *Journal of hypertension*, 16(11), 1635-1639. https://journals.lww.com/jhypertension/fulltext/1998/16110/heart_rate_as_marker_of_sympathetic_activity.10.aspx

Harlan Jr, W. R., Osborne, R. K., & Graybiel, A. (1964). Prognostic value of the cold pressor test and the basal blood pressure: Based on an eighteen-year follow-up study. *The American journal of cardiology*, *13*(5), 683-687. https://www.sciencedirect.com/science/article/pii/000291496490205X

Hines Jr, E. A., & Brown, G. E. (1936). The cold pressor test for measuring the reactibility of the blood pressure: data concerning 571 normal and hypertensive subjects. *American heart journal*, *11*(1), 1-9. https://www.sciencedirect.com/science/article/pii/S0002870336903708

Ifuku, H., Moriyama, K., Arai, K., & Shiraishi-Hichiwa, Y. (2007). Regulation of cardiac function during a cold pressor test in athletes and untrained subjects. *European journal of applied physiology*, *101*(1), 75-79. https://doi.org/10.1007/s.00421-007-0475-y

Ifuku, H. (2015). Cardiovascular responses of blood pressure hyperreactors to the cold pressor test and exercise. *The Journal of Physical Fitness and Sports Medicine*, *4*(4), 331-335. https://doi.org/10.7600/j.pfsm.4.331

Kashani, M., Eliasson, A., & Vernalis, M. (2012). Perceived stress correlates with disturbed sleep: a link connecting stress and cardiovascular disease. *Stress*, *15*(1), 45-51. https://doi.org/10.3109/10253890.2011.578266

Kregel, K. C., Seals, D. R., & Callister, R. O. B. I. N. (1992). Sympathetic nervous system activity during skin cooling in humans: relationship to stimulus intensity and pain sensation. *The Journal of physiology*, *454*(1), 359-371. https://doi.org/10.1113/jphysiol.1992.sp019268

Laurent, P., Albaladejo, P., Blacher, J., Rudnichi, A., Smulyan, H., & Safar, M. E. (2003). Heart rate and pulse pressure amplification in hypertensive subjects. *American journal of hypertension*, *16*(5), 363-370. https://doi.org/10.1016/S0895-7061(03)00063-3

Laurent, S., Cockcroft, J., Van Bortel, L., Boutouyrie, P., Giannattasio, C., Hayoz, D., ... & Struijker-Boudier, H. (2006). Expert consensus document on arterial stiffness: methodological issues and clinical applications. *European heart journal*, *27*(21), 2588-2605. https://doi.org/10.1093/eurheartj/ehl254

Lovallo W. T. (1975) The cold pressor test and autonomic function: a review and integration. *Psychophysiology*. May;12(3):268-282. DOI: 10.1111/j.1469-8986.1975.tb01289.x.

Menkes, M. S., Matthews, K. A., Krantz, D. S., Lundberg, U., Mead, L. A., Qaqish, B., ... & Pearson, T. A. (1989). Cardiovascular reactivity to the cold pressor test as a predictor of hypertension. *Hypertension*, *14*(5), 524-530. https://doi.org/10.1161/01.HYP.14.5.524

Moriyama, K., & Ifuku, H. (2010). Increased cardiovascular reactivity to the cold pressor test is not associated with increased reactivity to isometric handgrip exercise. *European journal of applied physiology*, *108*(4), 837-843. https://doi.org/10.1007/s00421-009-1299-8

Moriyama, K., & Ifuku, H. (2007). Assessment of cardiac contractility during a cold pressor test by using (dP/dt)/P of carotid artery pulses. *European journal of applied physiology*, *100*(2), 185-191. https://doi.org/10.1007/s00421-007-0415-x

Mullan BA (2014) Sleep, stress and health: a commentary. Stress Health 30: 433-435. https://doi.org/10.1002/s.mi.2605

Nunes da Silva, J. M., Martins Costa, A. C., Waquim Machado,W., & Lopes Xavier, C. (2012). Avaliação da qualidade de sono em idosos não institucionalizados. ConScientiae Saúde, 11(1), 29-36. https://doi.org/10.5585/c.onssaude.v11n1.2940

Papaioannou, D., Brazier, J., & Paisley, S. (2013). Systematic searching and selection of health state utility values from the literature. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research, 16(4), 686–695. https://doi.org/10.1016/j.jval.2013.02.017

Papaioannou, T. G., Karatzis, E. N., Papamichael, C. M., Karatzi, K. N., Zakopoulos, N. A., Lekakis, J. P., ... & Stefanadis, C. (2006). Circadian variation of arterial pressure wave reflections. *American journal of hypertension*, *19*(3), 259-263. https://doi.org/10.1016/j.amjhyper .

Qureshi, G., Brown, R., Salciccioli, L., Qureshi, M., Rizvi, S., Farhan, S., & Lazar, J. (2007). Relationship between aortic atherosclerosis and non-invasive measures of arterial stiffness. *Atherosclerosis*, *195*(2), e190-e194. https://doi.org/10.1016/j.atherosclerosis.2007.06.021

Qureshi, W., Blaha, M. J., Nasir, K., & Al-Mallah, M. H. (2013). Gender differences in coronary plaque composition and burden detected in symptomatic patients referred for coronary computed tomographic angiography. The international journal of cardiovascular imaging, 29(2), 463–469. https://doi.org/10.1007/s.10554-012-0098-1n

Ring, C., Harrison, L. K., Winzer, A., Carroll, D., Drayson, M., & Kendall, M. (2000). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic, cold pressor, and exercise: Effects of alpha-adrenergic blockade. Psychophysiology, 37(5), 634-643. https://www.cambridge.org/core/services/aop-cambridge-core/content/view/S0048577200991030

Salvi, P., Lio, G., Labat, C., Ricci, E., Pannier, B., & Benetos, A. (2004). Validation of a new non-invasive portable tonometer for determining arterial pressure wave and pulse wave velocity: the PulsePen device. Journal of hypertension, 22(12), 2285–2293. https://doi.org/10.1097/00004872-200412000-00010 b

Sanchez-Gonzalez, M. A., May, R. W., Brown, P. C., Koutnik, A. P., & Fincham, F. D. (2013). Depressive symptoms contribute to increased wave reflection during cold pressor test in young adult men. *American journal of hypertension*, *26*(6), 778-783. https://doi.org/10.1093/a.jh/hpt012

Simoes, G. M., Campagnaro, B. P., Tonini, C. L., Meyrelles, S. S., Kuniyoshi, F. H., & Vasquez, E. C. (2013). Hemodynamic reactivity to laboratory stressors in healthy subjects: influence of gender and family history of cardiovascular diseases. International journal of medical sciences, 10(7), 848–856. https://doi.org/10.7150/i.jms.5967

Spielberger, C. D., Gorsuch, R. L., Lushene, R. E., Vagg, R., & Jacobs, G. A. (1983). State-trait anxiety inventory. Self-evaluation questionnaire (form Y). Manual for the State-Trait Anxiety Inventory. Palo Alto, CA.

Stewart, A. L., & Ware, J. E. (1992). *Measuring functioning and well-being: the medical outcomes study approach*. Duke University Press. https://pesquisa.bvsalud.org/portal/resource/pt/biblio-1076541

Tsai, T. C., Wu, J. S., Yang, Y. C., Huang, Y. H., Lu, F. H., & Chang, C. J. (2014). Long sleep duration associated with a higher risk of increased arterial stiffness in males. *Sleep*, *37*(8), 1315-1320. https://doi.org/10.5665/s.leep.3920

Townsend, R. R., Wilkinson, I. B., Schiffrin, E. L., Avolio, A. P., Chirinos, J. A., Cockcroft, J. R., ... & Najjar, S. S. (2015). Recommendations for improving and standardizing vascular research on arterial stiffness: a scientific statement from the American Heart Association.

Hypertension, *66*(3), 698-722. https://doi.org/10.1161/H.YP.0000000000000033

Ulrich-Lai, Y. M., & Herman, J. P. (2009). Neural regulation of endocrine and autonomic stress responses. Nature reviews. Neuroscience, 10(6), 397–409. https://doi.org/10.1038/n.rn2647

Willemsen, G., Ring, C., Carroll, D., Evans, P., Clow, A., & Hucklebridge, F. (1998). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic and cold pressor. Psychophysiology, 35(3), 252-259. https://onlinelibrary.wiley.com/doi/abs/10.1111/1469-8986.3530252

Wood, D. L., Sheps, S. G., Elveback, L. R., & Schirger, A. (1984). Cold pressor test as a predictor of hypertension. *Hypertension*, *6*(3), 301-306. https://www.ahajournals.org/doi/abs/10.1161/01.HYP.6.3.301

World Medical Association. (2001). World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. *Bulletin of the World Health Organization*, *79*(4), 373. https://www.ncbi.nlm.nih.gov/pmc/articles/pmc2566407/

Yamamoto, K., Iwase, S., & Mano, T. (1992). Responses of muscle sympathetic nerve activity and cardiac output to the cold pressor test. *The Japanese journal of physiology*, *42*(2), 239-252. https://doi.org/10.2170/j.jphysiol.42.239

Zoladz, P. R., Cadle, C. E., Dailey, A. M., Fiely, M. K., Peters, D. M., Nagle, H. E., Mosley, B. E., Scharf, A. R., Brown, C. M., Duffy, T. J., Earley, M. B., Rorabaugh, B. R., & Payment, K. E. (2017). Blunted cortisol response to acute pre-learning stress prevents misinformation effect in a forced confabulation paradigm. Hormones and behavior, 93, 1–8. https://doi.org/10.1016/j.yhbeh.2017.04.003