Original Article

The Influence of Autonomic Nervous System during Resting State on the Peripheral Pulse Wave Velocity in Young Adult Males

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Abstract

Background: The association between the activity of autonomic nervous systems (ANS) and pulse wave velocity (PWV) was commonly deduced after adjusting for confounding factors. The relationship between the ANS and PWV was either maintained, but attenuated, or no longer statistically connected after controlling for confounding variables. Research in young healthy individuals showed that the ANS does not control aortic stiffness (indexed by PWV) in a pressure-independent manner. Therefore, the role of the ANS in controlling PWV is debatable. **Objectives:** The objective of this study was to examine the possibility that ANS directly affects PWV independent of blood pressure (BP) and heart rate (HR). **Subjects and Methods:** Thirty-four healthy male volunteers (19 years old) were recruited. Stable brachial systolic BP (SBP)/diastolic BP (DBP) and HR were measured in semi-supine position after a 15-min rest. During the last 5 min, fingertip digital pulse wave (DPW) and lead II electrocardiogram (ECG) signals were recorded. The pulse transit time, and consequently PWV, was calculated by measuring the duration between the ECG R wave climax and a reference point on the DPW in the same cardiac cycle. The ANS activity was assessed by calculating the HR variability (HRV) indices obtained from the ECG record of 5-min R-R intervals (RRIs). **Results:** HRV indices low-frequency (LF)/high-frequency (HF) (LF band power measured in the 0.04–0.15 Hz)/the HF band power measured in the 0.15–0.4 Hz band) and SD2/SD1 ratios (SD1 and SD2 represent the dispersion along the minor and major axis of the fitted ellipse of the Poincaré plot) (sympathovagal balance) were significantly and positively correlated with PWV. In addition, the standard deviation of RRI, or normal-to-normal "NN" (SDNN) interval, after excluding ectopic beats, the square root of the mean squared differences of successive NN intervals (RMSSD) were significantly and negatively correlated with the PWV. No correlation was obtained between PWV and HR, SBP, or DBP. **Conclusion:** Peripheral PWV during rest or inactivity is affected directly by the sympathovagal balance independent of BP.

Keywords: Autonomic nervous system, heart rate variability, pulse wave velocity

Introduction

Pulse wave velocity (PWV) is recognized as a surrogate marker of vascular injury and an indicator of arterial stiffness and independently predicts cardiovascular morbidity and mortality.[1] PWV was found to increase proportionally to the number of abnormal autonomic function tests, as determined by Ewing's protocol for cardiovascular reflexes.[2] This result indicates the link between PWV and autonomic nervous systems (ANS). It also suggests that arterial stiffness and cardiac autonomic dysfunction have a pathophysiological basis and that the maintenance of the elastic characteristics of arteries relies critically on ANS health.[3]

An alternative autonomic function test for assessing ANS integrity is heart rate variability (HRV) measurement.[4] HRV is a noninvasive, useful, and reproducible indicator of ANS health. The HRV is the difference in time between two successive heartbeats. Accordingly, HRV reflects the balance between the sympathetic and parasympathetic influences on the intrinsic rhythm of the sinoatrial node.[4]

The link between the ANS activity and PWV was, in many cases, inferred after adjusting (by multivariate logistic regression analyses) the confounding factors such as age, systolic blood pressure (SBP), diastolic blood pressure (DBP), peripheral and central mean blood pressure, heart rate (HR),

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gender, body mass index (BMI), smoking, psychological stress, diabetes, and inflammation.[2,5-9] The associated link between the ANS and PWV was maintained, although attenuated, in some studies after adjusting the confounding factors[2,5] or was no longer significantly associated with each other in other studies.[6,10] In addition, a study in young, healthy individuals revealed that the ANS regulates aortic stiffness (and thus, central PWV) in a pressure-dependent manner.[7] Therefore, the importance of the ANS in regulating arterial stiffness is contentious.

The goal of the current study is to confirm or exclude the possibility that the ANS directly affects PWV independent of blood pressure (BP) and HR. This goal is achieved by finding the possible correlation between the ANS activity (determined by HRV) and the peripheral PWV during rest or inactivity with minimum possible intervention of the confounding factors (age, gender, BP, and HR).

Subjects and Methods

From 1st-year medical students, 35 healthy male volunteers (19 years old) were selected. They had no medical conditions and were not taking any drugs, and neither did their parents have diabetes or hypertension. Using a medical history questionnaire, this was evaluated. Each volunteer was issued a detailed clarification of the study before obtaining their written informed permission. The Mustansiriyah University, College of Medicine, Department of Physiology's Ethical Committee approved all operations and protocols. The research followed the guidelines of the Helsinki Declaration. Other anthropometric measurements, including gender, were recorded.

Experimental setup

After 10 min of full rest, the right brachial SBP, DBP, and HR were recorded in a semi-supine position. An automatic sphygmomanometer (Rossmax Swiss GmbH, Switzerland) was used to test the patient's BP and HR repeatedly until stable readings were attained. A piezoelectric finger pulse transducer captured the fingertip digital pulse wave (DPW) data for 5 min, and three surface electrodes collected lead II electrocardiogram (ECG) signals. Power Lab's converter and LabChart Pro software (version 7.2) transformed and digitally recorded data on the computer for the offline analysis (AD Instruments Pty Ltd, New South Wales, Australia).

Measurement of heart rate variability

The R-R intervals (RRIs) from the ECG recording were examined carefully for abnormal beats and artifacts. Abnormal ectopic beats or artifacts affect HRV analysis by compromising the validity of the parameters if not removed. They were removed manually by careful visual examination of all RRI across the 5-min recording to ensure the normal distribution of the data by detecting the outlier RRI. After removing abnormal beats, the residual data were stored in a comma Separated Values (CSV), comma delimited) as an "Excel" format and were then exported to and processed by the free version of Kubios HRV Standard software (version 3.4.1, The Biomedical Signal and Medical Imaging Analysis Group, Department of Applied Physics, University of Kuopio, Finland) without application of filters. This software calculated the time and frequency domain measures of HRV. The default settings were used to calculate the time domain (SDANN, RMSSD, and SD2/SD1) and frequency domain (low-frequency [LF]/high-frequency [HF] ratio) indices of HRV.SDNN is SD of average normal sinus R–R intervals for all 5-min segments.[11] RMSSDis a square root from the sum of squared differences of sequential NN pairs (normal RR intervals) expressed in milliseconds (ms)" ==> Change to "RMSSD is root mean square of successive RR interval differences expressed (ms). Typically, greater HRV values on time-domain measures, such as RMSSD and SDNN, are regarded as higher vagal tone. The time-domain HRV parameters, however, measure ANS activity but cannot distinguish between changes in HRV brought on by a decrease in vagal tone or an increase in sympathetic tone.[12] LF is the low-frequency band power (0.04–0.15 Hz) and reflects the sympathetic nervous activity (although it might be a mixture of sympathetic and parasympathetic activity).[11] HF is the high-frequency band power (0.15–0.4 Hz) and reflects the parasympathetic regulation.[11] LF/HF is an index of vagosympathetic interaction.[11] The Poincaré plot has two basic descriptors: SD1 in ms (which is the standard deviation perpendicular to the line of identity) and SD2 in ms (which is the standard deviation along the line of identity), while SD2/SD1 is the ratio of SD2 to SD1.[11] SD1 has been correlated with HF power (parasympathetic activity), while SD2 has been correlated mainly with sympathetic activity.[13] The SD2/SD1 ratio is used to measure autonomic balance (vagosympathetic equilibrium). Therefore, SD2/SD1 is correlated with the LF/HF ratio.[14]

Pulse wave velocity measurement

The duration between the climax of the ECG "R" wave and a predetermined reference point on the DPW was the basis

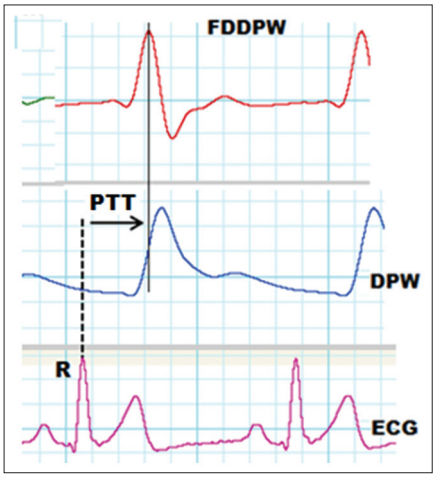

Figure 1: A representative drawing to demonstrate the methods used for the measurement of pulse transit time. DPW: Digital pulse wave, ECG: Electrocardiograph, FDDPW: First derivative of digital pulse wave, PTT: Pulse transit time

for measuring the pulse transit time (PTT), which method is described in detail elsewhere [Figure 1].[15] PTT consisted of an average of around 30–40 cardiac cycles for each 30-s interval. PWV is calculated as PTT (seconds)/D (meter), where "D" is the length of the artery between the heart and the middle finger of the left hand.[16]

Statistics

All the results were expressed using the mean and standard deviation (SD). The correlations between variables were calculated by "Excel" program running under the "Windows" operating system. The outlier data (abnormal beats and artifacts) were specified and removed using Rosner's Extreme Studentized Deviate test for multiple outliers at a $P < 0.05$ (available online: https://contchart.com/outliers.aspx).

Results

The characteristics of the participants in the present study are shown in Table 1. Only 9 volunteers (26%) out of 34 were overweight/obese and had a BMI ≥25 (kg/m^2). The SBP ranged between 101 and 135 mmHg and the DBP recorded in the present ranged between 60 and 89 mmHg. The minimum and the maximum beat-to-beat HR were 63 and 113 beats/min. PWV ranged between 3.1 and 3.8 m/s.

HRV indices LF/HF and SD2/SD1 ratio were highly significant and positively correlated with PWV [Figure 2]. In addition, Table 2 shows that the other HRV indices that marked the ANS activity (SDNN and RMSSD) were significantly and negatively correlated with the PWV. Among HRV indices, only RMSSD is correlated significantly with SBP and has no correlation with DBP. No correlation was obtained between PWV and SBP or DBP.

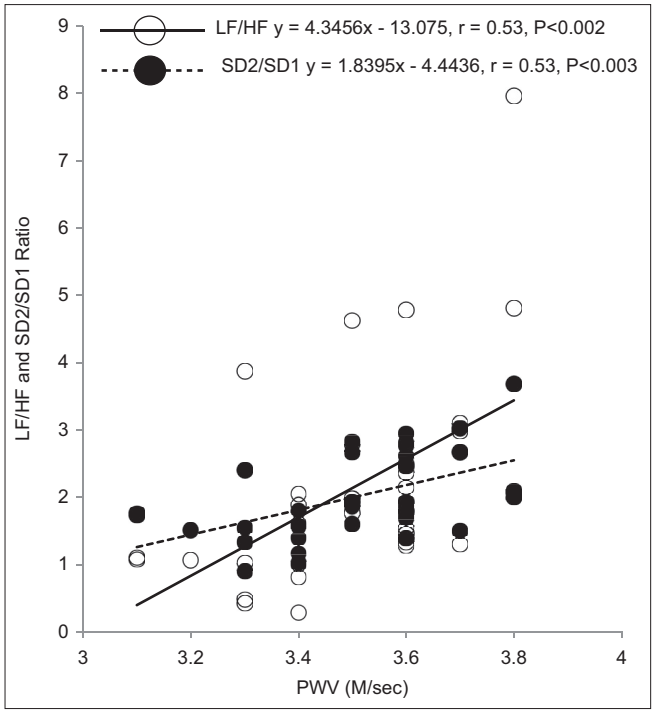

Figure 2: Correlation of pulse wave velocity with low-frequency/high-frequency and D2/D1 heart rate variability indices (n = 35). LF: Low-frequency, HF: High-frequency

Discussion

One unresolved notion is whether the activity of the sympathetic nervous system (SNS) *per se* during rest or inactivity contributes to determining arterial stiffness independent of changes in BP and HR. The established BP and HR dependence of central PWV measurements is a crucial factor for experimentally examining putative mechanisms causing arterial stiffness because both of them are strongly associated positively with central PWV.[7] Fixing the age (19 years old) of the volunteers and their gender (males) were essential to restrict the effects of these two confounding factors on the measurement of PWV. More important is the finding that the BP did not significantly affect the PWV under the present experimental conditions, probably because the PWV

Table 1: General characteristics of the recruited participants after 10 min of rest in semi-supine position (n=35)

	Mean±SD
Age (years)	20±0
BMI (kg/m^2)	24.1±5.2
SBP (mmHg)	120.1±7.7
DBP (mmHg)	76.2±7.1
MBP (mmHg)	90.8±6.3
HR (beat/min)	76.4±6.7
PWV (m/s)	3.5±0.2
LF/HF ratio	2.1±1.6
SDNN (ms)	39.9±19.8
RMSSD (ms)	39.3±24.4
SD2/SD1	2.0±0.6

SD: Standard deviation, LF: Low frequency, HF: High frequency, SDNN: SD of average normal sinus R–R intervals for all 5-min segments, RMSSD: Root mean square of successive RR interval differences expressed (ms), SD1 and SD2: Poincaré plot index SD1 and SD2 in normalized units, BMI: Body mass index, BP: Blood pressure, SBP: Systolic BP, DBP: Diastolic BP, MBP: Mean BP, HR: Heart rate, PWV: Pulse wave velocity

Table 2: Linear correlation between heart rate variability indices, pulse wave velocity, and systolic and diastolic blood pressure (n=35)

HRV indices	PWV (m/s) (r, P)	SBP (mmHg) (r, P)	DBP (mmHg) (r, P)
SDNN (ms)	−0.50, <0.003	NS	NS
RMSSD (ms)	−0.34, 0.05	−0.34, <0.05	NS
HR (beat/min)	NS	NS	NS
PWV (m/s)		NS	NS

SD: Standard deviation, SDNN: SD of average normal sinus R–R intervals for all 5-min segments, RMSSD: Root mean square of successive RR interval differences expressed (ms), r: Correlation coefficient, BP: Blood pressure, SBP: Systolic BP, HR: Heart rate, DBP: Diastolic BP, PWV: Pulse wave velocity, HRV: HR variability, NS: Nonsignificant

was measured in the peripheral muscular conduit artery (brachial and ulnar arteries in heart–finger PWV) rather than central elastic arteries (aorta, carotid, and femoral arteries). At comparable age and number of volunteers, heart–finger PWV was increased upon sympathetic stimulation by a mental arithmetic task or a mirror tracing task,[17] and the change in arterial stiffness was related to BP and HR. These results are expected because sympathetic overactivity increases vascular tone (mainly vasoconstriction of small resistance muscular arteries). However, these results of the latter authors do not contradict the present findings obtained during rest or inactivity, i.e. without SNS stimulation. Central PWVs, such as brachial–ankle and carotid–femoral PWVs, were found to be correlated with SBP and DBP.[2,18,19] The lack of such a correlation between BP and peripheral PWV in the current study may be related to the difference in the arterial pathway, in which PWV was measured. This possibility is more likely, as reported by others,[19] which showed that such a correlation was abolished when the heart–brachial PWV (peripheral pathway) is used instead of the central pathway. The result parallels the result of using the cardiac–finger pathway in the current research. This is also confirmed by the finding that the heart–finger PWV value reported in the present research is comparable to those reported through the heart–brachial pathway.[19] Moreover, reduced brachial artery distensibility (increase in stiffness) with sympathetic activation was shown to occur independent of changes in arterial pressure, HR, and diameter.[20]

Most of the studies focused on examining the effect of ANS activity on the measurement of PWV in the central (core) arteries (carotid, aorta, and femoral arteries). The present research provides substantial evidence that ANS activity (as identified by HRV indices) during rest or homeostasis also determines PWV. These evidences are expressed by strong positive associations between PWV and high sympathetic activity (marked by an increase in SD2/SD1 ratio and LF/HF ratio) and negative associations between PWV and parasympathetic activity (marked by SDNN and RMSSD). In agreement with the current data, patients with anxiety disorders showed strong negative connections between the brachial artery PWV and the RRI HF power.[21]

Conclusion

The influence of ANS and the sympathovagal balance on the peripheral PWV is direct, and it is a BP-and HR-independent effect.

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Conflicts of interest

There are no conflicts of interest.

References

1. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: A systematic review and meta-analysis. J Am Coll Cardiol 2010;55:1318-27.
2. Wu N, Cai X, Ye K, Li Y, He M, Zhao W, *et al.* Association between brachial-ankle pulse wave velocity and cardiac autonomic neuropathy in type 2 diabetes. Diabetol Metab Syndr 2014;6:82.
3. Meyer C, Milat F, McGrath BP, Cameron J, Kotsopoulos D, Teede HJ. Vascular dysfunction and autonomic neuropathy in type 2 diabetes. Diabet Med 2004;21:746-51.
4. Bereksi-Reguig MA, Bereksi-Reguig F, Ali AN. A new system for measurement of the pulse transit time, the pulse wave velocity and its analysis. J Mech Med Biol 2017;17:1750010.
5. Chorepsima S, Eleftheriadou I, Tentolouris A, Moyssakis I, Protogerou A, Kokkinos A, *et al.* Pulse wave velocity and cardiac autonomic function in type 2 diabetes mellitus. BMC Endocr Disord 2017;17:27.
6. Chandra P, Sands RL, Gillespie BW, Levin NW, Kotanko P, Kiser M, *et al.* Relationship between heart rate variability and pulse wave velocity and their association with patient outcomes in chronic kidney disease. Clin Nephrol 2014;81:9-19.
7. Mäki-Petäjä KM, Barrett SM, Evans SV, Cheriyan J, McEniery CM, Wilkinson IB. The role of the autonomic nervous system in the regulation of aortic stiffness. Hypertension 2016;68:1290-7.
8. Logan JG, Barksdale DJ, Carlson J, Carlson BW, Rowsey PJ. Psychological stress and arterial stiffness in Korean Americans. J Psychosom Res 2012;73:53-8.
9. Jaiswal M, Urbina EM, Wadwa RP, Talton JW, D'Agostino RB Jr., Hamman RF, *et al.* Reduced heart rate variability is associated with increased arterial stiffness in youth with type 1 diabetes: The SEARCH CVD study. Diabetes Care 2013;36:2351-8.
10. Ahn JH, Kong M. The relationship among pulse wave velocity, ankle-brachial pressure index and heart rate variability in adult males. Korean J Fam Med 2011;32:406-11.
11. Baevsky RM, Chernikova AG. Heart rate variability analysis: Physiological foundations and main methods. Cardiometry 2017;10:66-76.
12. Plaza-Florido A, Alcantara JM, Migueles JH, Amaro-Gahete FJ, Acosta FM, Mora-Gonzalez J, *et al.* Inter- and intra-researcher reproducibility of heart rate variability parameters in three human cohorts. Sci Rep 2020;10:11399.
13. Humeau-Heurtier A, Gospodinova E, Domuschiev I, Dey N. Ashour A. Nonlinear analysis of heart rate variability in type 2 diabetic patients. Fractal Geom Nonlinear Anal Med Biol 2016;2:134-9.
14. Guzik P, Piskorski J, Krauze T, Schneider R, Wesseling KH, Wykretowicz A, *et al.* Correlations between the Poincaré plot and conventional heart rate variability parameters assessed during paced breathing. J Physiol Sci 2007;57:63-71.
15. Adnan SK, Neda FS, Al-Gailani BT. Vascular stiffness in cold pressor test hyper-reactors. Pol J Med Phys Eng 2023;29:151-4.
16. Gesche H, Grosskurth D, Küchler G, Patzak A. Continuous blood pressure measurement by using the pulse transit time: Comparison to a cuff-based method. Eur J Appl Physiol 2012;112:309-15.
17. Matsumura K, Noguchi I, Rolfe P, Yamakoshi T, Matsuoka Y. Differential effect of two mental stress tasks on arterial stiffness. Jpn Psychol Res 2019;61:249-61.
18. Cicek Y, Durakoglugil ME, Kocaman SA, Guveli H, Cetin M, Erdogan T, *et al.* Increased pulse wave velocity in patients with panic disorder: Independent vascular influence of panic disorder on arterial stiffness. J Psychosom Res 2012;73:145-8.
19. Arakeri S, Patil SG. Relationship between adiposity, blood pressure, cardiac autonomic function and arterial stiffness in young healthy individuals. J Cardiovasc Dis Res 2018;9:76-81.
20. Salzer DA, Medeiros PJ, Craen R, Shoemaker JK. Neurogenic-nitric oxide interactions affecting brachial artery mechanics in humans: Roles of vessel distensibility versus diameter. Am J Physiol Regul Integr Comp Physiol 2008;295:R1181-7.
21. Yeragani VK, Tancer M, Seema KP, Josyula K, Desai N. Increased pulse-wave velocity in patients with anxiety: Implications for autonomic dysfunction. J Psychosom Res 2006;61:25-31.