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Orthostatic Stress Induced Changes in Heart Rate Variability, Pulse Transit Time and QRS Duration

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Abstract

Studies have shown the application of non-invasive cardiovascular parameters like heart rate variability (HRV), pulse transit time (PTT) and QRS duration. However no information is available about effects of orthostatic stress on these parameters. Our objective was to study the changes in HRV, PTT and QRS duration caused by orthostatic stress. Electrocardiogram (ECG) and photoplethysmogram (PPG) data was collected from 22 subjects in supine and upright positions. Comparison of parameters in supine and upright positions revealed that every parameter was effected by orthostatic stress. High frequency power of HRV showed the largest response (75%), while QRS duration had the smallest response of (7%). We found that gender played a significant role in PTT, R-R interval and QRS duration values, with male subjects showing higher values of all three parameters. Subject height also played a distinguishing role, with taller subjects showing higher values of R-R interval and PTT. The results allow us to better understand the interaction between various parameters and how they reflect the hemodynamic changes caused by orthostatic stress.

Keywords: Pulse transit time; Heart rate variability; QRS duration; Orthostatic stress

Introduction

Cardiovascular disease (CVD) is the leading cause of death in United States [1]. Various parameters can provide useful insight into the health of cardiovascular system. Heart rate variability (HRV) can be used to determine the level of stress during daily activity [2]. QRS complex width has been shown to predict risk of sudden cardiac death and increased mortality in patients with congestive heart failure [3].

Pulse transit time (PTT) can provide information about arterial stiffness [4], and pulse transit time variability (PTTV) can be used as a marker of blood pressure variability (BPV) [5]. Both arterial tone and BPV are risk factors for CVD [6,7]. Previous studies had looked at these parameters independently and there is no information about their interaction. Our objective is to study the changes in HRV, QRS duration and PTT by orthostatic stress. We are going to study the effect of orthostatic stress and interaction of these parameters using data collected from a subject population. We will also investigative population characteristics based changed in these parameters.

Background

It has been established that heart rate variability (HRV) can be used to assess autonomic nervous system function, studies have shown that pulse transit time variability (PTTV) can be used to detect blood pressure variability (BPV) [8]. QRS complex width measures duration of ventricular activation and increased QRS duration is a predictor of sudden cardiac death [9]. Previous studies have looked at these parameters independently but their interaction has not been studied. By combining HRV, PTTV and QRS duration this study proposes to investigate interaction among these parameters. HRV is linked to PTTV through variation in blood pressure as demonstrated in Figure 1.

HRV variability can be used as a measure of autonomic nervous system activity [10]. While parasympathetic activity mostly affects heart rate, sympathetic activity has more systemic effects. Sympathetic system activity affects heart rate, heart contractility along with vascular tone [11,12]. Changes in heart rate and contractility affect cardiac output. Variation in cardiac output combined with changes in vascular tone cause variation in blood pressure. Changes in blood pressure affect the velocity of pressure

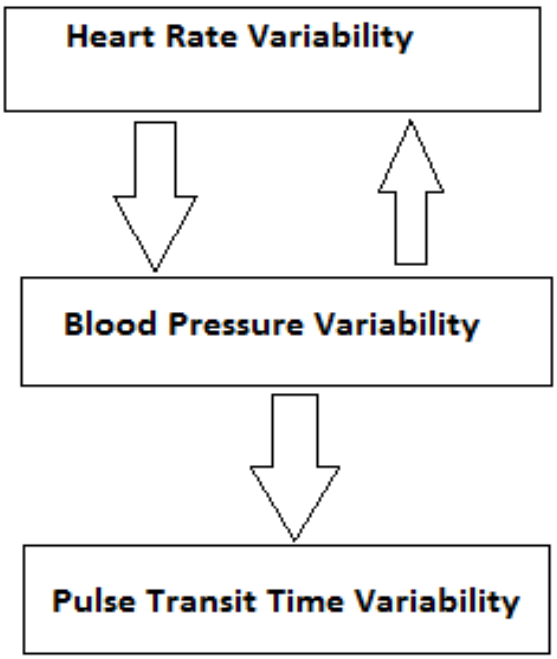

Figure 1: Link between heart rate variability (HRV) and pulse transit time variability (PTTV). Change in heart rate effects blood pressure and change in blood pressure effects heart rate through baroreceptor feedback. Variation in blood pressures is reflected as PTTV.

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pulse traveling from the heart to a periphery, resulting in a strong association between blood pressure variability (BPV) and PTTV [13]. Figure 2 shows various factors linking HRV with PTTV.

At rest major component of HRV is caused by respiration related changes in heart rate known as respiratory sinus arrhythmia (RSA). Movement of the thoracic cavity during respiration also results BPV, which in turn causes PTTV. Thus respiration causes both HRV and PTTV, resulting in a coupling of HF power of HRV and PTTV [14]. Some studies have concluded that PTTV can be used to detect changes in systolic blood pressure [5,15] while others have indicated that PTTV is not a sufficient marker of BPV [16]. Studies looking at PTTV during exercise have also reported mixed results, some have reported that PTTV is a good indicator of BPV during exercise [17] while others have reported that PTTV and BPV are not directly related during exercise [18]. One conclusion we can draw from these results is that PTT is not a simple parameter that can be used as surrogate marker of another parameter such as BPV or arterial tone. PTT is a complex parameter and is a representation of interaction of many parameter, this complexity has also been observed by previous studies [18,19].

We are going to study the changes in PTT, R-R interval and QRS duration with postural change from supine to upright. Previous study investigating localized postural change of limb concluded that PTT is able to reflect the local circulatory response [20]. Since postural change from supine to upright effects blood pressure, heart rate and pulse pressure [21] studying R-R interval, PTT and QRS duration after postural change can provide insight into responsiveness of cardiovascular and autonomic system to orthostatic stress.

Objectives

The objective of this paper is to investigate the interaction between HRV, PTTV and QRS duration with orthostatic stress. ECG and PPG data will be collected in supine and upright position. This work will contribute to a future goal of establishing criteria that can be used to qualify normal and abnormal relationship between HRV, PTTV and QRS duration to quantify the impact of stress on deregulating autonomic cardiac control. ECG and PPG data will be collected from healthy volunteers and this data will then be analyzed to calculate various parameters for each subject.

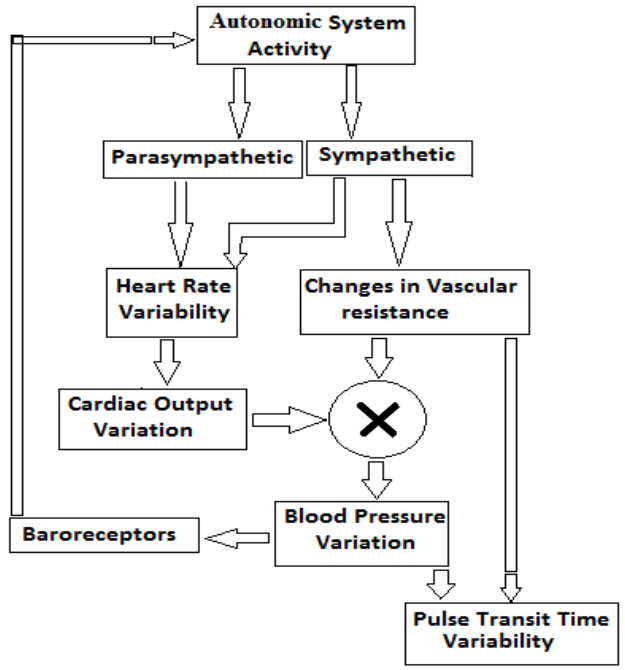

Figure 2: Heart Rate Variability (HRV) and Pulse Transit Time Variability (PTTV). A breakdown of various factors that affect HRV and PTTV. Autonomic system uses baroreceptor to regulate blood pressures, in order to maintain the desired blood pressure the autonomic system varies cardiac output and vascular tone.

Methods

Institutional Review Board (IRB) approval was obtained before the start of study. Twenty two healthy volunteers were included in the study. Each volunteer was screened over phone. Any volunteer taking medication for cardiovascular or pulmonary disorder was excluded from the study. Screened volunteers were assigned a date and time window for data collection.

Data collection

Photoplethysmograth (PPG) and electrocardiograph (ECG) data was recorded for all subjects. ECG data was obtained using standard 3 lead cable. PPG data was collected using fingertip pulse oximeter sensor placed on the index finger of right hand. ECG waveform was sampled at 500 Hz and PPG waveforms was sampled at 125 Hz. Each subject was allowed to lay down in a quiet room and allowed to get familiar with the equipment before data collection. Five minutes of data was collected in supine position then subjects were asked to stand up and were allowed time to get comfortable in upright position. Five more minutes of data was collected in upright position.

Data analysis

A python based algorithm was designed to detect R waves in ECG waveform and the associated PAP wave in PPG waveform. The algorithm has been described in earlier chapter. Time and frequency domain analyses were performed on various calculated parameters.

Time domain analysis: In time domain mean and standard deviation calculations were performed. These calculations were performed for each subject in supine and upright position. R-R interval mean (RRm), R-R interval standard deviation (R-Rstd), pulse transit time mean (PTTm) and pulse transit time standard deviation (PTTstd) were calculated in time domain analysis.

Frequency domain analysis: In frequency domain low frequency (LF) and high frequency (HF) of R-R intervals was used as a measure of HRV. Frequency domain analysis of HRV provided information about strength of different frequency components causing HRV. Frequency domain analysis of R-R intervals was performed using Fourier transformation. Fourier transformation is a mathematical transformation that converts a signal from time to frequency domain. Power of frequency components in the range of 0.04 Hz to 0.14 Hz were added to computer LF power, while power of frequency components in the range of 0.15 Hz to 0.4 Hz were added to computer HF power. High frequency (HF) component of the HRV indicates vagal tone while LF power of HRV is associated with a combination of sympathetic and parasympathetic system activities [22]. Frequency analysis of R-R interval was performed using Kubios HRV tool [23].

Correlation: Time series of R-R interval and PTT were correlated to determine relationship between R-R interval and PTT for each subject. Correlation coefficients for each subject were averaged to determine mean value for population. Both R-R interval and PTT time series showed high and low frequency variations but visual inspection of R-R and PTT plots revealed a correlation of low frequency variation.

Figure 3 shows one instance of such low frequency correlation in PTT and R-R intervals. Mean value was subtracted from both R-R intervals and PTT values in order to plot both waveforms on the same scale in Figure 3.

In order to investigate the correlation of low frequency variation, a high frequency filter was implemented. A moving average filter with was implemented to remove high frequency components as shown in Figure 4. Moving average filter removes high frequency components from a waveform. Cut off frequency of moving average filter is half the width of the filter, as filter width is increased high frequency components are further reduced.

Results

Sample population characteristics

Data was collected from 22 subjects. Subjects were college students mostly in mid-twenties. A mix of male and female subjects was selected. Sample population characteristic's is shown in Table 1.

Calculated parameters

HRV, PTTV and QRS duration parameters were calculated for all subjects. The calculations were made in both supine and upright positions. Results for entire sample population are shown in Table 2.

Paired T-test

Paired T test was performed to determine the significance of position based change in parameters. Results of the test indicate that there was a significant change in RRm, PTTm, QRS duration, HF. However LF, RRstd and PTTstd didn't show a significant change. Results of Paired T test are shown in Table 2.

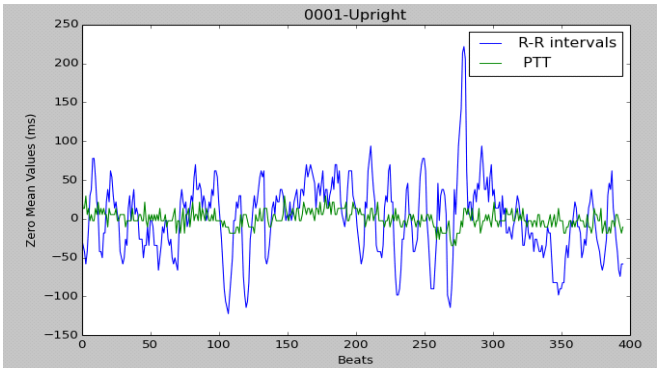

Figure 3: Zero mean (mean subtracted) time series of PTT and R-R interval taken from subject 0001 in upright position. Low frequency variation is visually corrected in both waveforms.

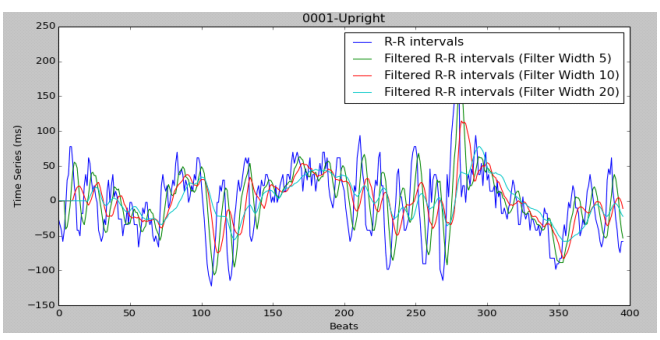

Figure 4: R-R intervals from subject 0001 in upright position filtered using a moving average filter. Effects of various filter widths are shown.

Characteristic	Mean (STD)
Number of Subjects	22
Age (years)	26 (7.5)
Male (%)	50
Height (inches)	67.5 (4)
Weight (lbs.)	163 (26)

Table 1: Population Characteristic's.

Parameters	Supine Position Mean (STD)	Upright Position Mean (STD)	Supine to Upright Change in mean	Percentage change (%)	Paired T Test P value
RRm (ms)	930 (173)	744 (135)	-186	20	<0.01
RRstd (ms)	65 (30)	58 (27)	-7	10	>0.1
PTTm (ms)	605 (23)	573 (14)	-32	5	<0.01
PTTstd (ms)	13 (6)	12 (5)	-1	7	>0.1
QRS duration (ms)	91 (10)	85 (8)	-6	6	<0.01
HF (ms2)	1380 (1628)	335 (441)	-1025	74	<0.01
LF (ms2)	1816(2020)	1829(1777)	13	0.7	>0.05

Table 2: Calculated Parameters, Change with Position and Paired T Test.

Results based on population characteristics

Subjects were grouped together using various population characteristics such as gender, age, height and weight. Population median values of age, height and weight were used to determine the grouping criteria. Results from gender based grouping are shown in Table 3. Female subjects had high heart rate, lower PTT value and smaller QRS duration. Results from age based grouping are shown in Table 4. Population median age was 23 years. Grouping criteria was based on age above or below 23 years. Results show that younger subjects had lower heart rate, lower PTT value and lower QRS duration.

Results from height based grouping are shown in Table 5. Population median height was 66.5 inches. Grouping criteria was based on height above or below 66.5 inches. Results show that taller subjects had lower heart rate, higher PTT value and larger QRS duration.

Results from weight based grouping are shown in Table 6. Population median weight was 155 pounds. Grouping criteria was based on weight above or below 155 pounds. Results show that heavier subjects had lower heart rate, higher PTT value and larger QRS duration.

Correlation

Filtered and unfiltered R-R interval and PTT waveforms were correlated to determine correlation coefficient for each subject. The correlation coefficients for each subject were averaged to determine correlation coefficients of entire population. Correlation coefficients for unfiltered and filtered waveforms are shown in Table 7.

Discussion

Results showed a significant decrease in mean values of all parameters.

Decrease in mean values

The decrease in RRm during upright position is expected since the body compensates for increased gravitation pull in upright position by increasing heart rate to maintain blood pressure. Decrease in PTTm

Parameter	Male Supine Mean Value	Female Supine Mean Value	Male Upright Mean Value	Female Upright Mean Value
RRm (ms)	1000	854	786	700
PPTm (ms)	597	583	575	562
QRS duration (ms)	96	91	93	87

Table 3: Gender Based Values.

Parameter	Above Median Age Supine	Below Median Age Supine	Above Median Age Upright	Below Median Age Upright
RRm (ms)	969	867	768	705
PPTm (ms)	598	588	571	565
QRS duration (ms)	95	91	91	87

Table 4: Age Based Values, where Median Age=23 years.

Parameter	Above Median Height Supine	Below Median Height Supine	Above Median Height Upright	Below Median Height Upright
RRm (ms)	1004	850	748	738
PPTm (ms)	608	579	577	560
QRS duration (ms)	93	94	90	89

Table 5: Height Based values, where Median Height=66.5 inches.

Parameter	Above Median Weight Supine	Below Median Weight Supine	Above Median Weight Upright	Below Median Weight Upright
RRm (ms)	1006	848	776	709
PPTm (ms)	604	583	575	562
QRS duration (ms)	98	89	93	86

Table 6: Weight Based values, where Median Weight=155 pounds.

R-R and PTT Waveforms	Mean population correlation coefficient in supine position	Mean population correlation coefficient in upright position
Unfiltered	0.05	0.06
Filtered with filter width=10	0.36	0.27
Filtered with filter width=20	0.38	0.3
Filtered with filter width=30	0.40	0.37
Filtered with filter width=40	0.42	0.38
Filtered with filter width=50	0.42	0.38

Table 7: Mean correlation coefficient for entire population.

can be caused two factors, change in pre-ejection period (PEP) or change in pulse wave velocity. PEP is time taken by the heart to eject blood after R wave. R wave corresponds to the electrical activity of ventricle depolarization but there is a mechanical delay between ventricle depolarization and ejection of blood into the aorta. PEP in healthy adults is approximately 100 ms [24]. PEP remains fairly constant across a wide range of heart rates [25] shows the PEP values in healthy subjects (Table 8).

If PEP remains constant then the second factor is change in pulse wave velocity (PWV). As pulse wave moves through the arteries the PWV varies depending on the cross sectional area and elasticity of the artery as calculated by Bramwell-Hill equation [26].

$$\text{Pulse Wave Velocity} = \pm\sqrt{1/(\rho.DC)}$$

$$DC = (\Delta A/A)/\Delta P$$

Where ρ is the blood density (1000 kg/m^3), A is the cross section area of artery during diastole, ΔA is the change in cross section area from diastole to systole and ΔP is the change in pressure from diastole to systole. We know that blood pressure increases in upright position [21]. This increase in blood pressure would result in greater pulse wave velocity and reduction in PTT. Other studies have also linked reduction in PTT to increased blood pressure [19].

Decrease in QRS duration during upright position can be a result of increased sympathetic system activity. Previous studies have reported a reduction in QRS duration with increase in sympathetic tone [27]. Since decrease in QRS duration is accompanied by increase in heart rate and blood pressure, decrease in QRS duration can be associated with increased cardiac output (CO). Results show that there was an increase in HR and reduction of PTT in upright position, both of them indicate that systolic blood pressure is increased. Increase in blood pressure can be accomplished by two factors, cardiac output and systemic vascular resistance. Cardiac output in turn depends on heart rate and stroke volume as shown in Figure 5. Stroke volume can be increased by increasing contractility of the ventricles. Since increased contractility reduces the signal transduction pathways in ventricles [28] it causes reduction in QRS duration as seen in the population.

Frequency domain

HF power decreased for every subject in upright position, this indicates an increase in sympathetic activity or decrease in parasympathetic activity in upright position. Sympathetic activity can override the effects of parasympathetic activity as demonstrated by a study [29]. The effects of sympathetic activity on HF component can also be seen by reduced HF power during physical activity [30]. This means that increase in sympathetic activity might or might not be accompanied by a decrease in parasympathetic activity. LF component didn't show a significant change in upright position. Since LF component is composed of both sympathetic and parasympathetic activity, we can assume that increase in low frequency sympathetic activity might have been balanced by a decrease in low frequency parasympathetic activity.

Standard deviation values

While a significant change was observed in mean values of all parameters, there was no significant change in standard deviation

Condition	PEP (ms)
Sleep	105
Sitting	97
Mild Physical activity	97

Table 8: PEP Values [24].

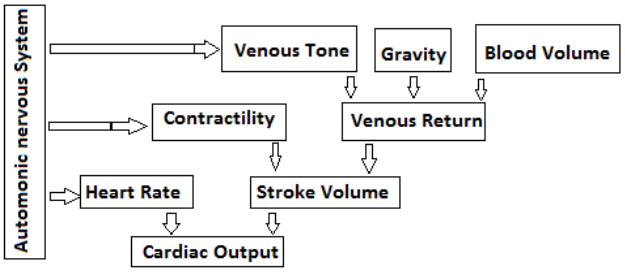

Figure 5: Factors Affecting Cardiac Output. Autonomic nervous system compensates for the additional force of gravity by increasing heart rate, heart contractility and venous tone. These changes result in greater cardiac output and help maintain blood pressure.

values. Even though frequency analysis indicated a decrease in HF component, standard deviation didn't show a significant decrease. Since standard deviation is a measure of total variability in time domain we can assume that factors causing variability in R-R interval and PTT continued to affect both parameters after postural change.

Population characteristics based changes

Female subjects showed lower R-R interval values and higher PTT, QRS duration values in both supine and upright positions. Results from weight, height and age based grouping showed same results. Since female population was younger, lighter and shorter than male population, it is hard to decouple the effects of gender from age, weight and height. Looking at results from all population groups we can see that higher R-R interval, corresponds to higher PTT. Height based grouping showed biggest difference in PTT. Since PTT dependents on distance between heart and index finger, bigger subject height results in bigger PTT value. Weight based grouping showed the biggest difference in QRS duration, heavier subjects had larger QRS duration then lighter subjects. This observation has not been previously reported in literature, but it could be the result of size of heart. Lighter subjects could have smaller sized hearts resulted in smaller QRS duration. The most surprising results came from age based grouping, older subjects showed higher PTT value. This results contradicts a recent study [31] that showed that PTT decreased with age. The contradiction might be due to our population characteristics, our population was a mix of males and females while earlier study only looked at male subjects. Results from age based grouping suggest that a general statement cannot be made that PTT decreased with age for a homogenous population.

Correlation

Results from Table 7 show that unfiltered R-R interval and PTT have no correlation. This result contradicts with finding from a study of R-R interval and PTT during paced breathing that reported a correlation coefficient value of 0.69 for a population of 15 subjects. We only observed some correlation between R-R interval and PTT waveforms when they were filtered to remove high frequency variation. Overall some correlation was observed (r=+0.4) when both waveforms were filtered using sliding average filter of width 30. Our results indicate that only low frequency changes in R-R interval and PTT are related to each other. We also found that low frequency correlation varied among subjects. Some subjects showed high correlation while showed no correlation. Correlation for entire population decreased in upright. We conclude that R-R intervals show some correlation with PTT but this correlation only exists for low frequency variation.

Position based changes

Orthostatic stress induced change in PTT was much smaller the R-R interval. This can be explained by studying the factors that cause change in PTT. PTT is mainly effected by blood pressure variation. Effects of postural change are much smaller in blood pressure than heart rate. A study in large population found the mean change in systolic blood pressure (SBP) to be 10.8 mmHg in response to postural change [32]. Normal (SBP) is 120 mmHg a change of 10.8 mmHg means 9% change. The study also found that postural related changes in diastolic blood pressure (DBP) changes are 4% higher than change in SBP. PTT is affected by change in pressure gradient (i.e. SBP – DBP). A 9% increase in SBP minus 4% increase in DBP will change the pressure gradient by 5%. According to our model this should result in ~5% change in PTT. Looking at results from Table 2, there is a 5% decrease in PTT in supine position.

Summary

We studied the interaction of HRV, PTT and QRS duration in the presence of orthostatic stress. We found that all parameters decreased in supine position. High frequency power of HRV showed the largest response (75%), while QRS duration had the smallest response of (7%). We found moderate relation between R-R interval and PTT (r 0.42), but this relationship was only present in low frequency variation of both parameters. We also observed a reduction in R-R interval and PTT relationship (r 0.38) in supine position. We found that gender played a significant role in PTT, R-R interval and QRS duration values, with male subjects showing higher values of all three parameters. Subject height also played a distinguishing role, with taller subjects showing higher values of R-R interval and PTT. Data presented in this study can contribute to a future goal of establishing criteria that can be used to qualify normal and abnormal relationship between HRV, PTT and QRS duration and to quantify the impact of stress on deregulating autonomic cardiac control.

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