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The association of resting state heart rate variability and 24-hour blood pressure variability in spinal cord injury

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ABSTRACT

Patients with high cervical complete spinal cord injuries (tetraplegia) sustain damage to the autonomic neural pathways that influence cardiovascular functioning and produce variability in the heart rate (HR) and blood pressure (BP). In non-injured individuals, an inverse relationship exists between resting autonomic control of the heart (as evidenced by HR variability (HRV)) and BP variability (BPV). This study examined the relationship between HRV, BP and BPV in individuals with tetraplegic ($n = 10$) and paraplegic ($n = 10$) spinal cord injuries, and a group of healthy controls ($n = 14$). Resting HRV at baseline and 24-hour ambulatory BP measurements were collected from electrocardiogram measures of each participant. HRV was quantified using time- and frequency-domain measures. The standard deviation of the BP measurements was used as an index of BPV. Multivariate analyses of variance were performed to examine group differences for laboratory-based and 24-h dependent variables. The MANOVAs for HRV parameters ($\lambda_{(14,50)} = .352$, $p = .010$, $\eta^2 = .407$) and for BP indices and HR ($\lambda_{(16,48)} = .318$, $p = .013$, $\eta^2 = .436$) were significant. Furthermore, in line with existing evidence, we found that vagally mediated HRV was inversely related to BPV in healthy controls. However, this relationship did not hold for the tetraplegia group ($\rho < |.42|$), and mixed results were found for the paraplegia group (e.g., $\rho < |.29|$ for time domain HRV, $\rho > |.65|$ for low-frequency power). These results support the conclusion that the damage to the spinal sympathetic pathways to the heart found in people with tetraplegia causes a significant disruption in baroreflex control of BP.

1. Introduction

Epidemiological studies have suggested that a greater risk of hypertension and cardiovascular disease (CVD) are present for people with spinal cord injury (SCI), especially for those with complete tetraplegic injuries [1]. Many traditional risk factors for cardiovascular problems, such as increased body weight and higher blood pressure (BP), do not explain the greater risk for cardiovascular difficulty experienced in tetraplegic SCI [1,2]. Therefore, a more detailed exploration of the cardiovascular consequences of SCI is needed.

The autonomic nervous system, which is involved in the regulation of respiration, heart rate (HR), BP, and other vegetative functions, is often damaged in SCI. Because of this damage, people with complete tetraplegia suffer from disorders of cardiovascular regulation, such as orthostatic hypotension and autonomic dysreflexia [3]. Autonomic control of the cardiovascular system has been examined noninvasively with the use of techniques that quantify beat-to-beat changes in HR and BP. The use of these techniques has revealed differences in the character of autonomic cardiovascular modulation that have helped to elucidate the mechanisms for increased risk of CVD and hypertension in SCI. The present study was an extension of these investigations, designed to examine the interplay between autonomic influences on HR and BP in individuals with complete tetraplegia. Specifically, the present study was designed to investigate the relationship of resting heart rate variability (HRV) as measured in the laboratory to 24-hour ambulatory BP variability (BPV) in individuals with tetraplegia, who have intact

Abbreviations: CVD, cardiovascular disease; SCI, spinal cord injury; BP, higher blood pressure; HR, heart rate; HRV, heart rate variability; BPV, BP variability; HF, high frequency; LF, low frequency; pNN50, the percentage of pairs of successive R–R intervals that differ by more than 50 ms; MSD, the mean standardized difference of adjacent RR intervals; IBI, inter-beat-interval; SBP, mean systolic BP; DBP, mean diastolic BP; MAP, mean arterial BP; HOUSTON, University of Houston Non-Exercise Questionnaire; VO_2max, maximal oxygen uptake.

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parasympathetic vagal inputs to the heart but interrupted central control of sympathetic activity.

The high frequency (HF) power band of the HRV time series is defined as the sum of the variance that occurs between 0.15–0.50 Hz. This band represents very rapid, beat-to-beat changes in HR that reflect respiratory-gated parasympathetic outflow [4]. Thus, HF power is consistently used in the literature as an index of vagal cardiac modulation [4,5].

Low frequency (LF) power reflects slower changes in HR (0.03–0.15 Hz). This component has been the subject of much debate in the literature. While some have claimed that LF power expressed in normalized units is an index of the relative contribution of sympathetic activity to HRV, contradictory evidence exists. For example, beta-adrenergic blockade does not always reduce LF power [4]. Thus, most researchers have concluded that LF power reflects a combination of sympathetic and parasympathetic influences [4,5]. Other data indicate that LF power indexes short-term baroreceptor-mediated changes in BP control [4,6]. Thus, a secondary goal of the present research is to examine the relationship between LF power and 24 hour BPV, which is thought to reflect baroreceptor mediated BPV [7].

1.1. Hypotheses

First, group differences on resting HRV measures were expected to replicate prior results. That is, healthy controls were expected to show the most vagally mediated HRV as indexed by the percentage of pairs of successive R-R intervals that differ by more than 50 ms (pNN50), the mean standardized difference of adjacent RR intervals (MSD), HF power, and normalized HF power. The tetraplegia group was expected to show the least vagally mediated HRV because of compensatory decreases in vagal activity that occur in response to sympathetic isolation [8]. The HRV of the paraplegia group was expected to fall between the other two groups, because people with paraplegia sustain some sympathetic disruption to the lower body. Consistent with previous literature, the LF power component was expected to be greatly reduced in the tetraplegia group, and moderately reduced in the paraplegia group as compared to healthy controls. Normalized LF power was expected to follow the same pattern across groups as LF power. The LF/HF ratio, used as an index of sympathovagal balance, was expected to be greatest in the noninjured group because they were expected to show the greatest values for LF power. The mean inter-beat-interval (IBI) was not expected to differ significantly between groups because individuals with SCI have shown normal values for IBI in the past [9].

Second, consistent with previous literature, mean 24-hour BP (mean systolic BP (SBP), mean diastolic BP (DBP), and mean arterial BP (MAP)) were expected to be lowest in the tetraplegia group because of low sympathetic tone. Persons with paraplegia were expected to show lower BP than healthy controls but higher BP than participants with tetraplegia because of partial sympathetic deregulation. As with mean IBI, mean HR was not expected to differ between groups.

Thirdly, individuals with tetraplegia were expected to show the largest BPV (standard deviation, in SBP, DBP and MAP) because they have impaired baroreflex control of BP. Because BP control is somewhat impaired in paraplegia, these individuals were expected to show more BPV than healthy controls.

Fourthly, both time domain measures in this study (pNN50 and MSD) reflect cardiac vagal activity. In accordance with Ashley et al. [10], these measures were expected to be negatively correlated with BPV in healthy controls. Because of the significant disruption of baroreflex control of BP, individuals with tetraplegia were expected to show a greatly attenuated relationship between vagally mediated HRV and BPV. The relationship between vagal HRV and BPV was predicted to be less negative in the paraplegia group than in healthy controls, because of partial disruption in baroreflex control. HF power and normalized HF power were expected to follow the pattern described above for pNN50 and MSD because they also reflect cardiac vagal activity.

Finally, the relationship between LF power and BPV has not been investigated in SCI. Because of the multiple autonomic influences on LF power, it was difficult to predict the nature of this relationship. In healthy controls, normalized LF power and the LF/HF ratio were expected to be positively correlated with BPV. As normalized LF power and LF/HF increase, autonomic control of the heart becomes more sympathetic and less vagal in character. Decreased vagal cardiac modulation and increased BPV are both associated with cardiovascular morbidity and mortality, so these indices were expected to covary positively in individuals without SCI.

2. Materials and methods

2.1. Participants

Twenty-seven individuals with chronic neurologically complete spinal cord injuries were recruited from a midwestern rehabilitation hospital. Seven individuals originally recruited for the SCI groups were excluded from the analyses. One individual refused to complete the ambulatory blood pressure monitoring portion of the protocol. Three more individuals were excluded because the blood pressure monitor failed to record an adequate sample of the twenty-four hour monitoring period (these participants each had less than ten blood pressure measurements available for analysis). Two participants had to be excluded because their injuries were later determined incomplete, and one individual was unable to complete the study protocol due to equipment failure.

Ten individuals (two women) with high cervical spinal cord injuries (C8 or above) were included in the tetraplegia group, and ten individuals (three women) with thoracic spinal cord injuries below T5 made up the paraplegia group. The tetraplegia and paraplegia groups were also combined into a single group labeled “injured” for certain statistical analyses in order to compare the larger sample of individuals with SCI to a group of healthy controls. Fourteen graduate students (seven women) were used as a healthy control group. The Institutional Review Board of the University of Missouri approved the study.

The mean ages of the groups were not significantly different (controls: ($M = 27.79$ years, $SD = 5.95$), injured: ($M = 33.00$, $SD = 8.42$), paraplegia: ($M = 33.90$, $SD = 9.11$), tetraplegia: ($M = 32.10$, $SD = 8.05$)). The healthy controls included one African-American participant and one Asian participant, the paraplegia group contained one African-American, and one Hispanic and one African-American were in the tetraplegia group. All other participants were Caucasian.

2.2. Apparatus and questionnaires

Continuous HR data was recorded using disposable Ag-AgCl electrodes with the AMS ambulatory EKG monitor (Vrije Universiteit, Amsterdam, The Netherlands). Ambulatory BP measurements were recorded using the Accutracker BP monitor (Suntech Medical Instruments, Raleigh, North Carolina).

To estimate fitness levels for participants in the noninjured group, the University of Houston Non-Exercise Questionnaire (HOUSTON) was used [11]. This questionnaire was developed as part of an effort to easily estimate maximal oxygen uptake (VO_2max), the standard index of aerobic fitness, without using an actual exercise test. The researchers found a multiple correlation of $R^2 = 0.78$ when gender, age, self-reported exercise levels, and body mass index (BMI) were used to predict actual VO_2max scores.

Because it describes activities that are largely impossible for individuals in wheelchairs, the Houston Non-Exercise Questionnaire was not used in its original form for this population. Instead, participants were asked to describe their exercise activities in detail. These activities were rated by the experimenter for frequency and aerobic intensity using the HOUSTON anchors. Because this modified version of the HOUSTON has not been examined for reliability and validity, it can only serve as a rough measure of participants' fitness levels. Additionally,