EC ORTHOPAEDICS
Research Article

Heart Rate Variability: A Possible Biomarker to Detect Head Injury Severity

Janet S Dufek* and Warren Forbes

Department of Kinesiology and Nutrition Sciences, School of Integrated Health Sciences, University of Nevada, Las Vegas, Las Vegas, NV, USA

***Corresponding Author:** Janet S Dufek, Office of Faculty Affairs, University of Nevada, Las Vegas, Las Vegas, NV, USA.

Received: November 23, 2020; **Published:** January 28, 2021

Abstract

Objective: The objective of this study was to examine the relationship between the temporal variation in heart beats termed heart rate variability (HRV) and magnitude of head impact severity.

Background: Traumatic brain injuries (TBIs) account for over 56,000 deaths annually in the United States. Following injury, considerable attention is taken to assess the severity of damage to the brain. Current evaluation techniques are not only costly but may also impose the risk of exposure to high levels of radiation. Thus, development of a less invasive and lower-cost TBI diagnostic technique would address this health care concern. Given the known relationship between autonomic nervous system (ANS) control and cardiac function, we hypothesized any disruption in ANS control due to TBI may be reflected in heart rate response. Thus, HRV may serve as a key biomarker to assess TBI severity.

Materials and Methods: After granting institutionally approved consent, nine healthy male volunteers with no history of lower extremity injury were instrumented with a heart rate monitor and a forehead mounted accelerometer. Five minutes of quiet sitting (rest) was completed during which time heart rate was monitored. This was followed by continuous performance of landing off of a 45 cm platform onto a hard tile floor under two conditions: 1) soft landings, and 2) stiff landings. A five-minute rest period was interjected between landing conditions and following stiff landings. During landing, heart rate and head acceleration were continuously monitored. Dependent variables included maximum head acceleration (HA), standard deviation of R-R intervals (RRsd), and the root mean square of R-R intervals (RMSsd) in the time domain and high and low frequency power in the frequency domain. Repeated measures analysis of variance ($\alpha = 0.05$) was used to assess differences among conditions. Correlations between HA and the indices of HRV were also computed. Results: RRsd for both soft and stiff landings was significantly less than resting conditions ($p=0.007$ and $p=0.001$ respectively). A significant correlation was identified between HAstiff and RMSsd ($r=-0.664$, $p = 0.026$).

Conclusion: HRV was shown to be a potentially effective, non-invasive biomarker to quantify head impact severity.

Keywords: *Concussion; Falls; Head Acceleration; Landing*

Introduction

Traumatic brain injury (TBI) is a significant contributor to deaths in the United States with 56,000 TBI-related fatalities occurring in 2014 [1-2]. As well, TBIs accounted for over 2.8 million emergency room visits in the same time period [1-2], further taxing health care infrastructure and contributing to rising health care costs. Four events are typically associated with the occurrence of TBI. These include: 1) contact of the head with external objects such as equipment, 2) loss of balance resulting in a fall, 3) motor vehicle accidents, and 4) violent acts such as those experienced during assaults [3]. Since these contributors occur over a plethora of situations or environments, large segments of the population may be vulnerable to TBI. Such populations include those at the extreme ranges of the lifespan (youth and elderly) due to the excessively high fall rate they experience [1-2]. Children (0 - 4 years), adolescents (15 - 19 years), and adults 65 years of age and older are the most likely groups to experience TBI resulting from a fall. [3]. A wider age-range of the population is affected if one considers sport-related TBIs exclusively, as this environment accounts for an additional 4 million annual concussive events [4]. These data demonstrate that the incidence of TBI is prevalent across the lifespan.

The mechanisms for TBI includes a combination of high linear and angular accelerations of the head. Excessive linear acceleration of the head is typically the result of the head coming in direct contact with a stationary or moving object. Angular acceleration occurs as a result of head motion relative to motion of ancillary body parts (*e.g.*, whiplash) [5]. Since the brain and skull are not a rigidly linked anatomical system, the angular motion results in the impact force being transmitted first to the skull and then to the brain. Given the material properties of these biological structures, their unique moments of inertia, and the differential rates of rotation of the skull and brain, the combination of effects can result in TBI [6]. Another mechanism of TBI is the coup-countercoup response [7]. A coup injury, typically caused by blunt impact, occurs on the brain under the point of impact. A countercoup injury is the result of the brain contacting the skull opposite the point of impact. Excessive angular accelerations of the head can result in a coup-countercoup injury where the brain is literally shaking in the head, resulting in bruising of the brain.

There currently exist several neuroimaging techniques to assess injury severity following a blow or jolt to the head. These include magnetic resonance imaging (MRI) and computerized tomography (CT). Such diagnostic tools can expose the individual to high levels of radiation. The National Cancer Institute has cautioned against excessive use of CT as a diagnostic tool for children, due to this population's vulnerability to long term deleterious radiation exposure effects [8]. Additionally, new techniques are being developed including diffusor tensor imaging and magnetic resonance spectroscopy. The latter are not without shortcomings including both high cost and the inability to detect incidence of less severe TBI cases [9]. Thus, there may be an increasing need for non-invasive, non-carcinogenic, and inexpensive TBI diagnostic and screening techniques.

One possible diagnostic and screening measurement technique may be assessment of the variation in time between heart beats, termed heart rate variability (HRV). The relationship between reduced HRV and cardiovascular disease has been documented [10]. Regulation of heart rhythm is controlled by the sinoatrial node of the heart It is in turn modulated by the sympathetic and parasympathetic branches of the autonomic nervous system (ANS). The brain directly regulates the ANS, thus drawing a possible link between brain function and regulation of heart rhythm. Slight changes in nervous system inputs result in variations in heart rate. Spectral analysis of HRV has been shown to be related to Glasgow coma scale results, a tool commonly used to assess head injury. As well, frequency analysis of HRV has been suggested to be related to brain damage severity and head impact severity [11-12]. Given this shown relationship and the purported neurophysiological ties between the ANS and cardiac regulation, our research team sought to explore the use of a direct biological measurement (HRV) to determine head impact severity. The purpose of the study was to examine the relationship between HRV and linear head acceleration. The magnitude of head acceleration was used as a measure of head impact severity and potential of brain injury (TBI).

Methods

Nine apparently healthy male volunteers (175.9 ± 2.4 cm, 75.1 ± 7.3 kg, 25.3 ± 2.4 yrs), with no history of lower extremity injury in the last six months granted institutionally approved written consent to participate. A Polar heart rate monitor (model RS800cx; Polar Electro, Kempele, Finland), was set to R-R interval mode and was secured to the chest. Heart rate data were transmitted to a wireless receiver which was secured to the participant's wrist. Sampling frequency was set to 1,000 Hz thereby providing signal resolution in the time domain of 1 ms for each R–R period. A uniaxial accelerometer (PCB Piezotronics Inc. 52456; Depaw, NY) was secured to a plastic headpiece and was tightly secured to the forehead. Bioware data acquisition software (Kistler 4.0; Amherst, NY; 1000 Hz) was used to measure head vertical acceleration (HA) values from the accelerometer.

The experimental protocol consisted of a period of quiet sitting followed by performance of bouts of continuous landing. An initial seated resting heart rate measurement was recorded over five min. Participants were then instructed to continuously step onto a 45 cm platform, step off the platform, and come to rest (land) on the floor with maximum knee joint flexion (soft landing). Participants repeated this process for five min during which time both heart rate and head acceleration were measured continuously. Next, a second five min seated resting heart rate measurement was recorded followed by five min of continuous 45 cm step-off landings, this time minimizing the amount of knee joint flexion upon landing (stiff landing). A final five min resting heart rate measurement was obtained. Data were extracted over the five min samples using Polar Pro Trainer 5 software (Polar Electro, Kempele, Finland) was used to extract data across the five min samples. Each R-R interval file was analyzed using Kubios HRV Analysis Software 2.0 (Biomedical Signal and Medical Imaging Analysis Group, Kuopio, Finland).

Three-time domain dependent variables were examined during landing. These included maximum head acceleration (HA), the standard deviation of R-wave to R-wave intervals (RRsd) and the root mean square (RMSsd) of R-wave to R-wave intervals. Two frequency domain dependent variables were also extracted. These included low frequency power (LF; range: 0.04-0.15 Hz) and high frequency power (HF; range: >0.15 - 0.40 Hz). Repeated measures ANOVAs ($\alpha = 0.05$) were used to evaluate all dependent variables. Huynh-Feldt corrections were applied as necessary. Pearson product moment correlations between HA and the evaluated indices of HRV were also computed. All statistical comparisons were conducted using SPSS version 22 statistical software (IBM; Armonk, NY).

Results

There was a significant difference ($p = 0.001$) observed between HA_{soft} (3.05 ± 1.11 g's) and HA_{stiff} (7.61 ± 2.73 g's) thus confirming that participants did distinguish performance between landing conditions, producing uniquely soft and stiff landings as instructed. There were no significant differences among resting conditions for RRsd (70.9 ± 15.3, 74.8 ± 10.0, 72.6 ± 13.3 ms, for pre-, mid- and final rest, respectively) or similarly for RMSsd (44.2 ± 16.1, 37.2 ± 17.5, 31.4 ± 10.4 ms, respectively). A significant RRsd ANOVA result ($F_{(1,8)} = 2.056$, $p=0.001$, $\eta^2=.836$) was followed up with *post hoc* contrasts using Sidak adjustments. RRsd for both the soft (37.6 ± 9.2 ms) and stiff (32.4 ± 8.1 ms) landing conditions were significantly less ($p = 0.007$ and $p = 0.001$, respectively) than any of the resting conditions. RRsd between landing conditions was not significantly different, although it did decrease for the stiff landing condition (Figure 1). A similar trend was observed for RMSsd with the source of the significant ANOVA ($F_{(1,8)} = 25.24$; $p < 0.001$; $\eta^2 = .759$) between both the soft (10.5 ± 5.6 ms) and stiff (9.5 ± 5.0 ms) landings compared to the three resting conditions (44.2 ± 16.1, 37.2 ± 17.5, and 31.4 ± 10.5 ms, respectively).

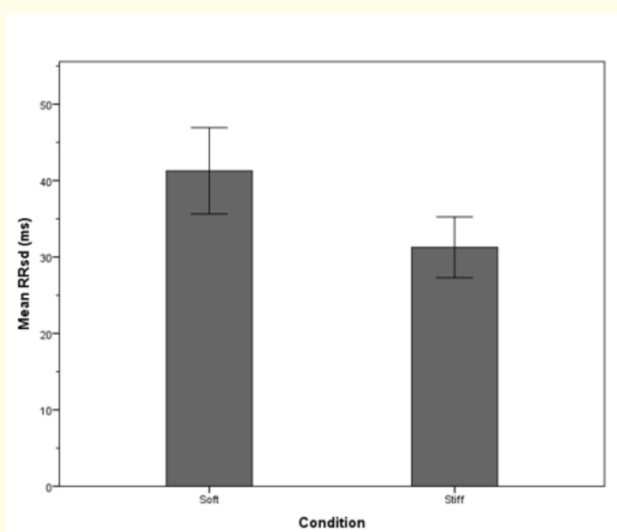

Figure 1: *Mean and Standard Deviation Values for RRsd Between Landing Conditions.*

In the frequency domain, no significant differences were observed among LF or HF measures (Figure 2). Correlations between HA and HRV measures ranged from ±0.162-0.664 with a significant relationship demonstrated between HA_{stiff} and RMSsd ($r = -0.664$, $p = 0.026$).

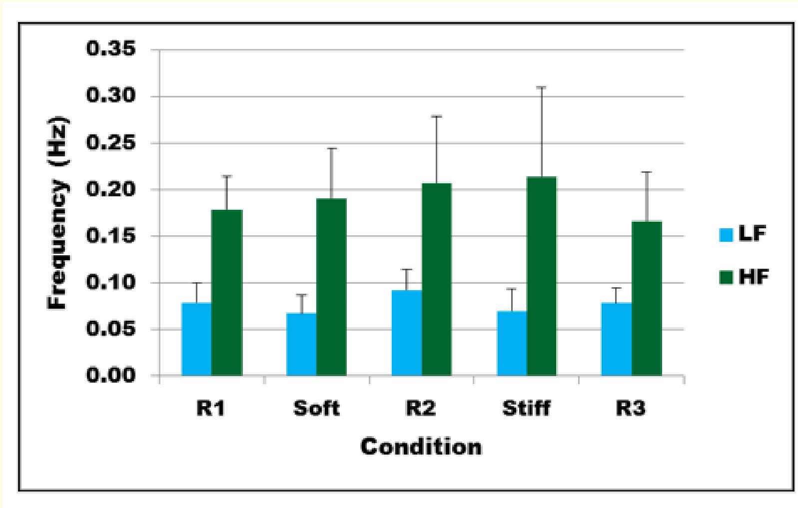

Figure 2: *Mean and Standard Deviation Values for Frequency Domain (LF and HF) Analysis Across All Conditions.*

Discussion

HRV is posited to mirror the control of the cardiovascular system. In the time domain, one measure of HRV (RMSsd) significantly decreased with increased HA as simulated by knee joint stiffness during landing. This suggests that increased HRV is influenced by increased HA. While not significantly different, RRsd did decrease for the stiff landing condition, demonstrating a similar trend to RMSsd. No differences were observed in HRV across all rest conditions, suggesting that the rest period was appropriate to allow participants to adequately recover following activity.

The parasympathetic nervous system serves to "slow the system down" and is associated with a resting state. It is primary controlled by high frequency signals. The sympathetic nervous system controls the "flight response" and is a combination of high and low frequency signals, with a dominance of low frequency signal components. Our data supported these relationships relative to frequency domain outcomes (Figure 2). This is consistent with observations reported by Purkayasta., *et al.* [13] who stated that the sympathetic nervous system response has been associated with neurodegeneration following occurrences of mild TBI. Surprising, a similar outcome to Purkayasta., *et al.* [13] was not observed at the group level between the soft and stiff landing conditions in the current investigation. This may have been due to the specific protocol we used which simulated head impact via landing technique versus evaluating individuals who had actually experienced TBI. The lack of observed differences in the frequency domain between landing conditions may also be explained by instrumentation. Nunan., *et al.* [14] suggested there may be lesser agreement between LF and HF measures obtained from the Polar monitor versus 12-lead electrocardiogram measurement. Increased variability in HF for the stiff landing condition (Figure 2), might also have influenced this outcome. It should also be noted that the study was limited by a small and fairly homogenous sample of participants.

Conclusion

Results suggest the potential application of HRV as a viable, quantifiable, non-invasive biomarker for detection of head impact severity. Time domain differences observed for RMSsd and a trend for a reduction in RRsd for conditions with greater HA as produced with lesser knee joint flexion support this statement. Future research should consider head and neck rotational components relative to HRV across a wider range of impact activities, such as hopping versus landing. In addition, it may be insightful to examine the relationships between LF and HF signal responses.

Acknowledgement

The authors would like to acknowledge the assistance of A. Prado on selected aspects of this project.

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Volume 12 Issue 2 February 2021