Heart Rate Variability Is Associated with Motor Outcome 3-Months after Stroke

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Objectives: The primary objective of this paper was to determine whether heart rate variability (HRV) acquired upon admission to inpatient rehabilitation is associated with motor outcome 3 months after stroke. The secondary objective of this paper was to determine whether HRV shows a strong association with the motor outcome 3 months after stroke in individuals with severe initial motor impairments. *Methods:* We recruited 13 patients with acute stroke from an acute inpatient rehabilitation hospital. A Holter monitor was placed upon admission and Fugl-Meyer Upper Extremity and Lower Extremity Subscales were used to assess the movement of the affected upper and lower extremities 3 months after admission. The standard deviation of R-R intervals was used to quantify HRV. *Results:* A Spearman rank correlation revealed a strong positive and significant correlation between HRV upon admission and movement of the affected upper extremity ($r = .70$, $P = .01$) and affected lower extremity ($r = .60$, $P = .03$) at 3 months. For patients with severe initial motor impairments, HRV showed a strong positive association with the movement of the affected upper ($r = .61$, $P = .04$) and lower ($r = .70$, $P = .04$) extremities at 3 months. *Conclusion:* HRV is strongly associated with motor outcome after stroke and provides a promising marker to explore the mechanisms associated with motor recovery after stroke. **Key Words:** Heart rate variability—cerebrovascular disease—rehabilitation—motor.

Introduction

Among the 795,000 individuals who sustain a stroke annually in the United States, almost 85% exhibit motor impairments in 1 limb immediately after stroke.[1] These motor impairments are associated with a significant loss of long-term independence.[2,3] For example, motor impairments in the affected upper extremity and lower extremity not only limit individuals from independently performing daily tasks such as dressing or bathing but also restrict the ability to return to work or prestroke roles. This loss of independence is costly, with the cost of rehabilitation projected to be 1.29 billion dollars by 2050.[4] Thus, there is a major public health need to minimize long-term dependency after stroke and to reduce associated personal and societal costs. Accurate predictors of the future motor outcome will allow clinicians to establish realistic and attainable rehabilitation goals, provide targeted interventions to enhance long-term independence, and reduce the length of inpatient stay and the cost of stroke rehabilitation. Although initial motor impairment is the best predictor to date,[5,6] it is still difficult to predict the long-term motor outcome in majority of individuals with severe motor impairments after stroke.[7] An exploration of the physiological mechanisms associated with the motor outcome may further elucidate our

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understanding of the prediction of long-term motor outcome after stroke.

Heart rate variability (HRV), or the temporal variations between consecutive heartbeats, is one such physiological parameter, which may be associated with the future motor outcome after stroke. The cortical regions that control motor function also modulate vagus nerve activity,[8] a cranial nerve that controls the autonomic functions of the heart. Vagal activity can be quantified using many analyses of HRV, such as the standard deviation (SD) between the consecutive heartbeats (SDNN).[9] Fluctuations in HRV mediated by the vagal activity may be influenced by central or peripheral nervous system disorders.[10] Furthermore, HRV has been studied to investigate the physiological changes and prognostic factors associated with many pathological conditions including stroke.[10] When stroke damages the cortical pathways controlling the upper and lower extremities, concurrent reduction in vagal activity control reduces HRV.[11] Thus, HRV is a plausible proxy marker for the integrity of cortical pathways related to the motor impairments of the affected upper and lower extremities, and stroke survivors with high HRV generally require less assistance to complete daily tasks.[12]

There are few specific data about the degree to which HRV measured shortly after stroke is related to the future motor outcome. The primary aim of this paper was to determine whether HRV acquired upon admission to inpatient rehabilitation is associated with motor outcome 3 months after stroke. We hypothesized that individuals with higher HRV at acute inpatient rehabilitation admission would exhibit greater movement in the affected upper and lower extremities after 3 months. The secondary aim of this paper was to determine whether HRV shows a stronger association with the motor outcome 3 months after stroke in individuals with severe initial motor impairments.

Methods

We recruited a convenience sample of 13 patients with acute stroke with a mean age of 61 years (SD = 12) from an acute inpatient rehabilitation hospital. Participants were included if they (1) were between the ages of 18 and 90 years of age; (2) had experienced a single episode of stroke, which was confirmed with magnetic resonance imaging scans; (3) had unilateral motor weakness characterized by 3 or less on Medical Research Council Score of major muscle groups of upper and lower extremities to include patients with lesions to corticospinal pathways; and (4) were able to follow 2-step commands. We included patients taking antihypertensives (e.g., β-blockers) because these drugs only have modest effects upon HRV.[13,14] We excluded patients who had a history of atrial fibrillation or other nonsinus arrhythmias, and used pacemakers because it is difficult to accurately measure and interpret HRV in these patients.[9] We also excluded patients with cerebellar lesions who typically do not exhibit unilateral motor weakness. Table 1 shows the demographic and clinical characteristics of the participants.

Procedures

Eligible participants provided written informed consent approved by the University of Pittsburgh Institutional Review Board. After careful skin preparation, an H12+ Mortara Holter monitor (Mortara Instrument, Milwaukee, WI) was placed for 24 hours on eligible participants to measure HRV within 3 days of acute inpatient rehabilitation admission. All lead placements were checked routinely through coordinated efforts with nursing and rehabilitation staff to avoid poor or missing data. A trained and experienced evaluator unaware of the HRV results of the patients used Fugl-Meyer Upper Extremity Subscale (FMUE)[15] and Fugl-Meyer Lower Extremity Subscale (FMLE)[15] to assess the movement of the affected upper extremity and lower extremity, respectively, 3 months after admission to the acute inpatient rehabilitation hospital. FMUE and FMLE are reliable and valid ordinal scales widely used to asses the movement of the affected upper and lower extremities after stroke.[16,17] The total FMUE score ranges from 0 to 66, and the FMLE score ranges from 0 to 34, with higher scores indicating better movement of the affected upper and lower extremities.[15] Based upon the admission criteria of acute inpatient rehabilitation admission, all participants were medically able to participate in rehabilitation for at least 3 hours per day.

Data Analysis

Data Preprocessing

All electrocardiogram (ECG) streams were sampled at 1000 Hz. An expert technician manually annotated all the ECG streams to clean artifacts using H-Scribe 5.11 (Mortara Instrument). The raw continuous ECG streams were then preprocessed using Super ECG (Mortara Instrument) to eliminate (without interpolation) premature, missing, or ectopic beats resulting in a data file with a columnar matrix of R-R intervals over 24 hours. We eliminated the R-R intervals that fall outside 5% and 95% of the distribution using a customized MATLAB code (MathWorks, Inc., Natick, MA) to remove additional artifacts.

HRV Analysis

SDNN was calculated as a measure of HRV using a customized MATLAB code. SDNN is the SD of the R-R intervals over 24 hours in milliseconds.[9]

Statistical Analysis

To address the primary aim, we performed 2 Spearman correlations between SDNN and 3-month FMUE