HEART RATE VARIABILITY AS A BIOMARKER FOR WORKING MEMORY PERFORMANCE AND FATIGUE PERCEPTION

An Undergraduate Research Scholars Thesis

by

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RESEARCH COMPLIANCE CERTIFICATION

Research activities involving the use of human subjects, vertebrate animals, and/or biohazards must be reviewed and approved by the appropriate Texas A&M University regulatory research committee (i.e., IRB, IACUC, IBC) before the activity can commence. This requirement applies to activities conducted at Texas A&M and to activities conducted at non-Texas A&M facilities or institutions. In both cases, students are responsible for working with the relevant Texas A&M research compliance program to ensure and document that all Texas A&M compliance obligations are met before the study begins.

I, Yixin Zhang, certify that all research compliance requirements related to this Undergraduate Research Scholars thesis have been addressed with my Research Faculty Advisor prior to the collection of any data used in this final thesis submission.

This project required approval from the Texas A&M University Research Compliance & Biosafety office.

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ABSTRACT

Heart Rate Variability as a Biomarker for Working Memory Performance and Fatigue Perception

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Fatigue is a debilitating condition especially in the emergency response (ER) domain where long work hours and sustained cognitive demands impede job performance. Typical solutions such as pharmacological aids (e.g., caffeine or other stimulants), or user-interface alterations (e.g., multimodal feedback) do not address the root of the problem. This is partly because fatigue is a complex, non-linear phenomenon influenced by lifelong subjective experiences and neurophysiological responses. Personalized and task-specific modes of intervention, beyond pharmacological aids, could improve work conditions and the outcome for all stakeholders.

Heart rate variability (HRV) is a commonly used non-invasive diagnostic index of cardiac autonomous regulation. Previous studies have discovered strong links between cardiac processes and a variety of prefrontal neural responses, as well as pointing to HRV as an indicator of cognitive performance level and working memory (WM). The electrocardiogram (ECG) is a commonly used non-invasive diagnostic tool; and ECG data have been used in a variety of medical research, such as biometric human identification and sleep staging.

We take data from a fatigue experiment done by our group that investigated the use of transcranial direct current stimulation (tDCS) – a non-invasive brain stimulation technique on mitigating fatigue and improving individual working memory (WM) performance. The study used a repeated measure, counterbalanced Latin square design where participants were randomly grouped under control, sham or anodal conditions. Subjective responses, WM performance, and HRV data were recorded. We hypothesize that: (1) individuals with higher resting-state HRV will exhibit better performance and report lower levels of perceived fatigue; and (2) changes in HRV during tasks will be associated with concurrent, positively related changes in performance and (or) negatively related changes in fatigue perception.

This study intends to unveil the relationship between HRV, WM performance, and fatigue perceptions. We will investigate the relevance of resting-state and time-on-task changes in HRV on reflecting fatigue perceptions and task performance during the WM exercise. Ultimately, we aim to provide a fieldable and unobtrusive measurement of fatigue for emergency responders using HRV that will contribute to personalized fatigue countermeasures.

ACKNOWLEDGEMENTS

Contributors

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Thanks also go to my friends and colleagues and the department faculty and staff for making my time at Texas A&M University a great experience.

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The data used for Heart Rate Variability as a Biomarker for Working Memory Performance and Fatigue Perception were provided by Rohith Karthikeyan. The analyses depicted in Heart Rate Variability as a Biomarker for Working Memory Performance and Fatigue Perception were conducted by Yixin Zhang and were unpublished.

All other work conducted for the thesis was completed by the student independently.

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NOMENCLATURE

ER	emergency response
tDCS	transcranial direct current stimulation
DLPFC	left dorsolateral prefrontal cortex
WM	working memory
HRV	heart rate variability
POMS	Profile of Mood States
KSS	Karolinska Sleepiness Scale
HR	Heart rate
IBI	Interbeat interval
ECG	Electrocardiogram

1. INTRODUCTION

Fatigue is defined as a lack of sufficient energy to power physical and (or) cognitive work [1]. In the real world, injuries and accidents associated with fatigue are estimated to cost employers over 100 billion dollars annually in the United States [2], [3]. To reduce the risks, certain measures are necessary to assess the individual's "fitness for duty" [4]. And especially in the emergency response (ER) sector, as emergency responders work long hours under high pressure where cognitive fatigue can significantly limit job performance, resulting in increased danger to workers and the public [5]. Therefore, tests should be delivered on a daily basis to protect public safety from fatigue-induced errors [6]. In the cases of emergency responders, non-pathological fatigue experienced by healthy individuals usually continues for a short period and can be reduced by rest or sleep [1], [7]. Several measurements of fatigue commonly used by researchers or the general public include questionnaires (e.g., health assessments [8], [9], quality of life [10], and the Fatigue Assessment Scale (FAS) [11]) and performance-based measures (e.g., muscle fatigue [12] and task simulations [8], [13]).

Heart rate variability (HRV) illustrates the change in the time interval between successive heartbeats [14]. The central autonomic network (CAN) integrates parasympathetic signals from the brain to the heart via the vagus nerve [15]. HRV is considered an index of the parasympathetic nervous system [14], [16] due to the known association between cardiac vagal activity and the activation of the prefrontal cortex [17]. The interbeat interval (IBI) – the time between successive R-peaks—was detected using electrocardiogram (ECG) or photoplethysmography (PPG) sensors. The normal-to-normal (NN) intervals measure the interval between normalized R-peaks and are summarized into more specific HRV features [18]. The time domain of HRV consists of SDNN, RMSSD, and pNN50. SDNN is the standard deviation of the NN intervals that represents the cyclic components contributing to HRV [19]. RMSSD (root mean square of successive differences) and pNN50 (percentage of successive NN intervals larger than 50ms) both reflect vagal heart rate control. Frequency domain of HRV consists of VLF, LF, HF, and LF/HF ratio. VLF represents the very low frequency ranging between 0.0033 to 0.04 Hz and is often related to thermal and hormone control [20]. LF (low frequency; 0.04 – 0.15 Hz), HF (0.15 – 0.4 Hz), and LF/HF ratio are all used to target vagal activity which was the primary interest of this study.

Working memory (WM) provides the brain the ability to temporarily store and process information [21]. Experiments on WM found significant association between WM capacity and the ability to multitask, focused, and make less errors [22].

Previous research revealed the association between HRV and emotion regulation and cognitive performance, such that high HRV is associated with better emotional adaptation to environmental stimuli [23] and better executive cognitive performance (e.g., faster and more accurate) [24], [17]. Research work has also linked HRV with fatigue and found that fatigue is associated with changes in certain HRV features (LF, HF, and LF/HF ratio, more specifically) [25]. This study intended to further investigate the association between HRV and fatigue. Six HRV features related to vagal and sympathetic activity (i.e., SDNN, RMSSD, pNN50, LF, HF, and LF/HF ratio) and mean heart rate (HR) were used in the analysis.

The measurement of fatigue in this study was separate into two parts— WM task performance (i.e., sensitivity, specificity, and accuracy) and self-reported subjective responses (fatigue, effort, and discomfort), to ensure accurate capture of fatigue. We hypothesized that (1) individuals with higher resting-state HRV would show better WM performance and report lower levels of perceived fatigue; and (2) changes in HRV during tasks would positively associate with concurrent changes in performance and (or) negatively relate to concurrent changes in fatigue perception.

This study was an extension of our attempt to provide a closed-loop solution to counterbalance fatigue using non-invasive neuromodulation [26]. Traditional ways like caffeine or other stimulants do not address the root of the problem due to the complex nature of fatigue. Transcranial direct current stimulation (tDCS) is a non-invasive neurostimulation technology that has been shown to improve working memory and serve as an effective countermeasure to cognitive fatigue [27]. We intended to implement tDCS as a novel solution to offset fatigue and improve WM performance that can be tailored to specific individuals or tasks. This study used HRV, performance and subjective data from these experiments. We envision the use of HRV will provide a fieldable, noninvasive and unobtrusive mode of predicting performance decline and fatigue perception that can serve as an indicator in the closed-loop solution detailed above.

2. METHODS

2.1 Experiment Design and Methodology

2.1.1 Participants

Fifty-four participants were recruited for this study with 32 participants completing the experiment and 30 participants with full data to be used for analysis (15 female; median age = 26 $\in$ [18, 34] years). During the eligibility check, participants were subject to a list of exclusion criteria [28] including past neurological disorders, over the counter medication, and caffeine habits. All participants were right-handed. All reported to be neurotypical without treatments for neuropsychiatric or brain-related disorders, or adverse history to tDCS. Regarding the participants' physical status at the moment of the experiment, 91% (N = 29) reported getting at least 6 hours of sleep in the days preceding each experiment session and 0 participant indicated a state of "severe exhaustion" due to lack of sleep; 59% reported taking 4000 – 8000 steps each day; participants reported a median score of 7 on a 10-point scale (0 = "absolutely no motivation", 10 = "extremely motivated") regarding their motivation to participate in the study.

Study procedures followed an infection control plan and the Ethics Code of the American Psychological Association and were approved by the Texas A&M University's Institutional Review Board (IRB2019-1591DCR). Participants provided written informed consent before the start of the experiment and were reimbursed for the completion of the study.

2.1.2 Design

The experiment followed a repeated measure, counterbalanced *Latin* square design [29]. The participant returned on separate days to complete a WM exercise under three distinct conditions – control, sham or anodal tDCS. Participants were grouped into three sex-balanced cohorts with designated treatment conditions based on the Latin square.

2.1.3 Working memory task

Participants were subjected to a 60 minute long visuospatial two-back WM task while sitting in front of a computer monitor and providing responses using a keyboard. As depicted in Figure 2.1, participants tracked the position of a circle on a 3x3 grid: when the circle's position matched its position from two steps prior, the participants were asked to press the spacebar on the keyboard as quickly as they could. Before starting the first session, participants were introduced to the task and allowed to practice for a minimum of five minutes under a training mode in which textual feedback were provided on their response time and correctness (RED = incorrect, GREEN = correct). This feedback was withheld during the actual experiment. Each session began with a series of subjective questions where the participants indicated their willingness to proceed the experiment. The interface recorded every keypress with a timestamp, allowing experimenters to retrieve response correctness (hit, miss, or false) and response time (in ms) that were later summarize into performance metrics for analysis.

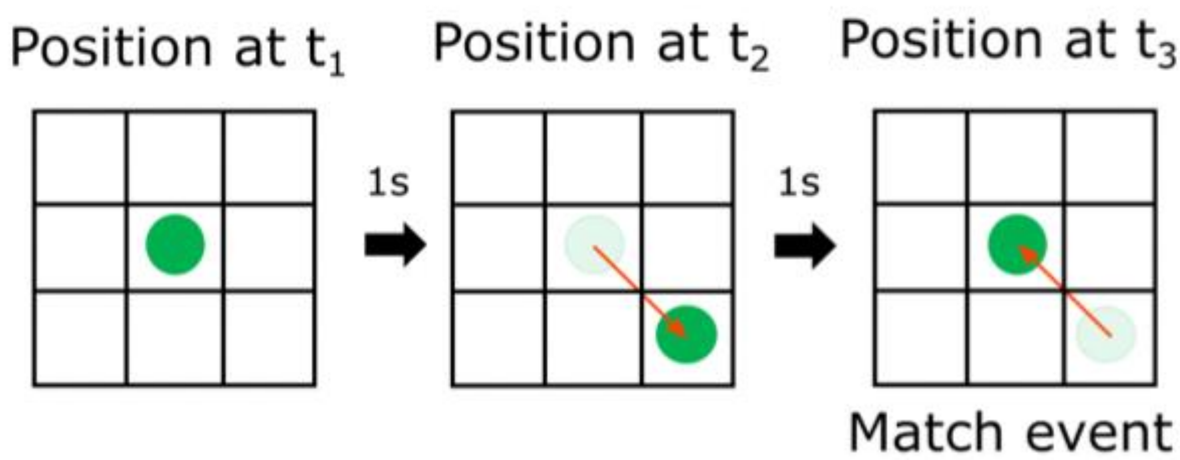

Figure 2.1: Two-back schematic. Image copyright permission released by R. Karthikeyan.

2.1.4 Study workflow

As shown in Figure 2.2, prior to the start of the experiment, the participants filled out an informed consent form followed by a background questionnaire and two subjective questionnaires on their mood (Profile of Mood States; POMS [30]) and sleepiness (Karolinska Sleepiness Scare; KSS [31]) levels. The sessions were approximately 60 minutes each and were dived into 12 blocks of WM tasks. Between each block, participants were given around 10 seconds to provide responses, as quickly as possible, to a series of subjective questions regarding their levels of fatigue, effort, and perceived discomfort (details described in 2.4.2.1). Participants were not informed of the precise duration of each block or experiment session. For sham and anodal sessions, tDCS intervention were administered at the start of the fifth block (approximately 20 minutes from the start of the session) outside of the participant's field of view. Participants were blinded to the sham or anodal conditions but were aware of the control sessions due to the absence of stimulation instruments.

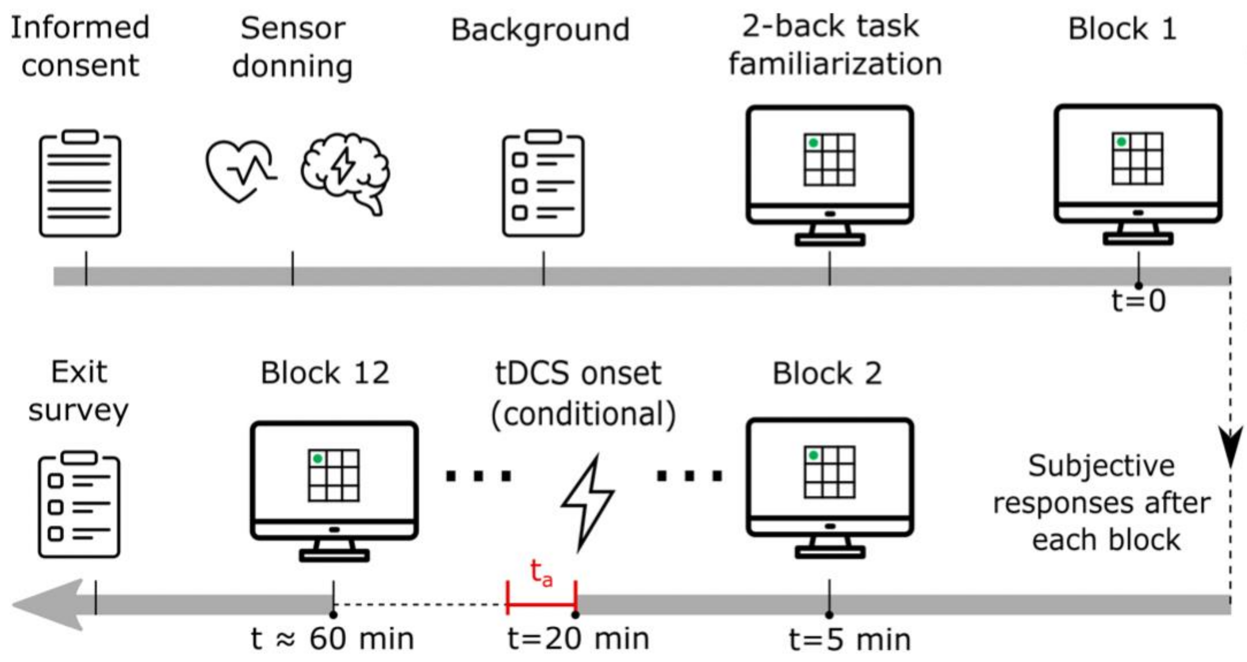

Figure 2.2: Experiment workflow. Image copyright permission released by R. Karthikeyan.

2.2 Transcranial Direct Current Stimulation

Stimulation was administered via a 1x1 tDCS device (Soterix Medical, NY, USA) on the left DLPFC (according to the 10-10 EEG system, anode electrode was located at F3, and reference electrode was located at FP2). Only the sham and anodal groups were instrumented with tDCS. The current intensity was set to 1mA, and the current density was 0.028 A/m2 (area = 5x7 cm^2). The stimulation onset time was the same for both sham and anodal conditions at the start of the fifth WM task block. Under anodal tDCS, the stimulation duration was 10 minutes; and under sham condition, the stimulation ramped up to the set point and immediately ramped down to zero, lasting approximately 20 seconds. Stimulation onset time and conditions were withheld from participants.

2.3 Heart rate variability

Cardiac electrical activity was obtained from a chest-worn electrocardiogram (ECG) probe and amplifier interface at 128 Hz (Actiheart4, CamNTeck, Inc., UK). The electrode was positioned at the base of the participants' sternum and over the left pectoralis minor muscle. Raw ECG signal was filtered for motion artifacts [32] and corrected for ectopics with polynomial interpolation [33]. A peak detection algorithm was used to isolate the R peaks of the ECG signal and the inter-beat-interval (IBI) was derived from the processed peak signals [34]. Epoch for peak analysis was 5 minutes.

Each participant began experiment with five minutes of baseline HRV data collection, during which they were asked to sit still with their eyes closed. To match performance and subjective data, HRV data during the tasks were down sampled into 12 five-minute blocks corresponding to the 12 blocks of WM tasks. Seven representative feature statistics were used for subsequent analysis – three in the time domain (SDNN, RMSSD, and pNN50; see Table 1), three in the frequency domain (LF, HF, and LF/HF; see Table 1) [19], and mean HR. The measures were min – max normalized across all three sessions before statistical analysis.

Table 1. Heart Rate Variability Indices

Variable	Description
SDNN (ms)	Standard Deviation of all NN Intervals
RMSSD (ms)	Root mean square of successive differences
pNN50 (%)	Percentage of successive normal sinus RR intervals differ by more than 50 ms
LF power (ms^2)	Absolute power of the low-frequency (LF) band (0.04–0.15 Hz)

HF (ms^2)	Absolute power of the high-frequency (HF) band (0.15–0.4 Hz)
LF/HF (%)	Low frequencies/high frequencies ratio
Mean HR (bpm)	Mean heart rate

2.4 Performance and Subjective Ratings

2.4.1 Working memory performance

As listed in Table 2, key-press recordings from WM tasks were summarized into three ratings – accuracy, specificity, and sensitivity to assess task performance. The data were grouped into 12 blocks with each 5-minute WM session as one block.

Table 2. Visuospatial two-back task performance metrics

Performance measure	Description
Accuracy	*(TP+TN)/(P+N)*
Sensitivity	*(TP)/(P)*
Specificity	*(TN)/(N)*

Note: TP = True Positives; P = all Positive or response selection events; TN = True Negatives; N = all Negative or response inhibition events.

2.4.2 Subjective responses

2.4.2.1 Inter-block Subjective Responses

Participants were subjected to three subjective questions related to their levels of fatigue, effort, and discomfort during the approximately 10s of transition interval after each experiment blocks (12 total). All questions were based on a 1 to 10 rating scale with 1 being “low or minimal” and a score of 10 indicating “extreme or unbearable.”

2.4.2.2 Pre- and Post-experiment Surveys

Due to high amount of data loss (approximately 30%), pre- and post- experiment surveys data were not used in this analysis. Before (PRE) and after (POST) each experiment session, participants were also asked to complete the POMS and KSS surveys. The POMS survey used in data collection was the bridged version, consisting of 39 questions across 6 emotive categories – tension-anxiety, depression-rejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment [30]. All questions were rated on a 5-point scale with 0 being “not at all” and 4 being “extremely.” The scores of each question were summed across all participants to generate a factor score to use to generate a composite mood disturbance score. The KSS scores were on a 10-point scale with 1 being “Extremely Alert” and 10 meaning “Extremely sleepy, can’t keep awake.”

2.5 Statistical analysis

To assess the association between HRV, WM performance, and subjective perception, the analysis was separated into three parts – (1) baseline HRV vs. mean (i.e., mean of the 12 blocks) performance and subjective ratings for each participant, (2) baseline HRV vs. throughout (i.e., 12 blocks separately) performance and subjective ratings, and (3) throughout HRV vs. throughout performance and subjective ratings. Seven parameters (SDNN, RMSSD, pNN50, LF, HF, LF/HF, and mean HR) from HRV data, three parameters (accuracy, specificity, and sensitivity) from performance data, and three parameters (fatigue, effort, and discomfort) were used in the analysis.

2.5.1 Baseline HRV vs. Mean Performance and Subjective Ratings

Baseline HRV data and mean performance and subjective ratings for each participant were not normally distributed. Therefore, Spearman’s rank correlation coefficient was performed on each pair of baseline HRV feature and performance and subjective rating (e.g., baseline SDNN vs mean accuracy for each participant). One participant with outlying baseline HRV was excluded from Spearman's rank correlation coefficient analysis.

2.5.2 Baseline HRV vs. Throughout Performance and Subjective Ratings

We performed median split on each HRV features, with each feature resulting in 15 participants with high HRV and 15 participants with low HRV. Paired sample t-tests were used to compare the differences between high HRV and low HRV groups for each of the performance and subjective ratings.

2.5.3 Throughout HRV vs. Throughout Performance and Subjective Ratings

HRV data and performance and subjective ratings for each of the 12 blocks were not normally distributed. Therefore, Spearman's rank correlation coefficient was implemented to assess the significance of correlation between each pair of HRV features and performance and subjective ratings (e.g., mean SDNN for each block vs mean accuracy for each block).

3. RESULTS

3.1 Baseline HRV vs. Mean Performance and Subjective Ratings

3.1.1 Performance

3.1.1.1 Sensitivity

We used Spearman's rank correlation coefficient to examine the association between HRV and performance sensitivity on each participant. Figure 3.1 depicts significant negative correlations in PNN50 (p = 0.042, r = -.38), RMSSD (p = 0.043, r = -.38), and LF Power (p= 0.004, r = -.52) with sensitivity, such that higher PNN50, RMSSD, and LF Power were associated with lower levels of overall performance sensitivity. Mean HR was also found to be positively correlated with sensitivity (p = 0.038, r = 0.39), such that higher mean HR was associated with higher levels of overall performance sensitivity.

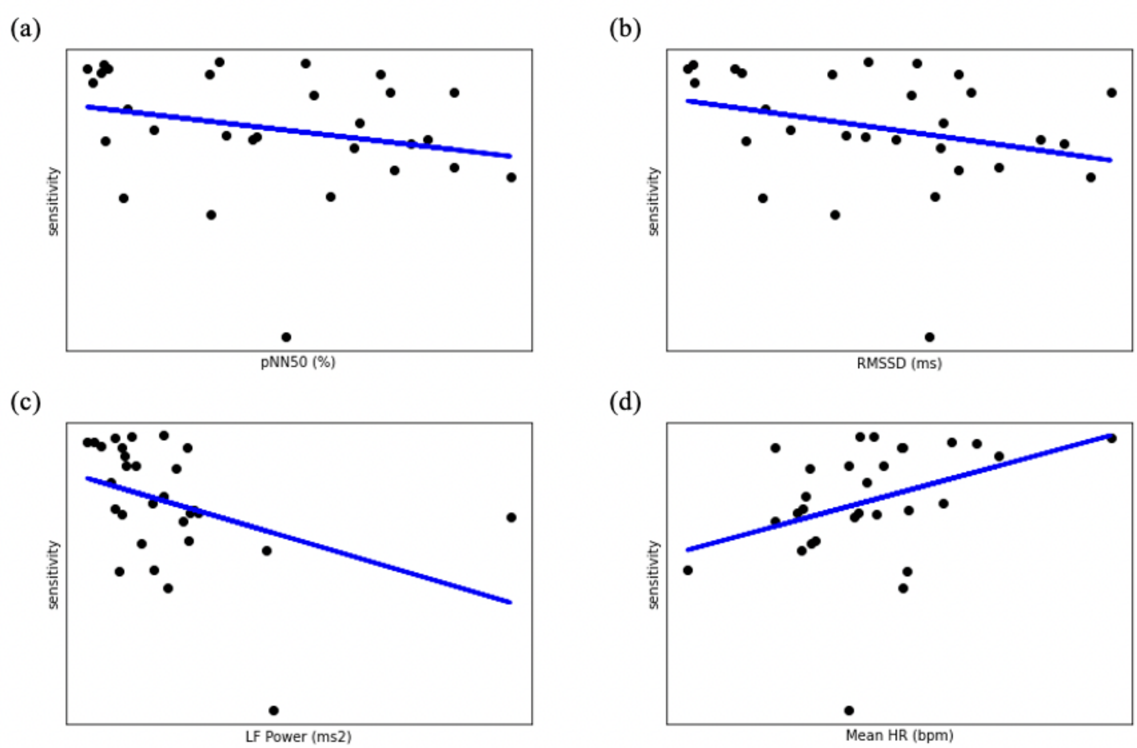

Figure 3.1 Scatterplot of (a) Sensitivity vs. PNN50, (b) Sensitivity vs. RMSSD, (c) Sensitivity vs. LF Power, and (d) Sensitivity vs. Mean HR.

3.1.1.2 Specificity

As depicted in Figure 3.2, Spearman's rank correlation coefficient indicated significant negative correlation between LF Power and specificity (p = 0.005, r = -.50), such that higher LF power was associated with lower levels of overall performance specificity. Significant positive correlation was also found between mean HR and specificity (p = 0.039, r = .39), such that higher mean HR was associated with higher levels of overall performance specificity.

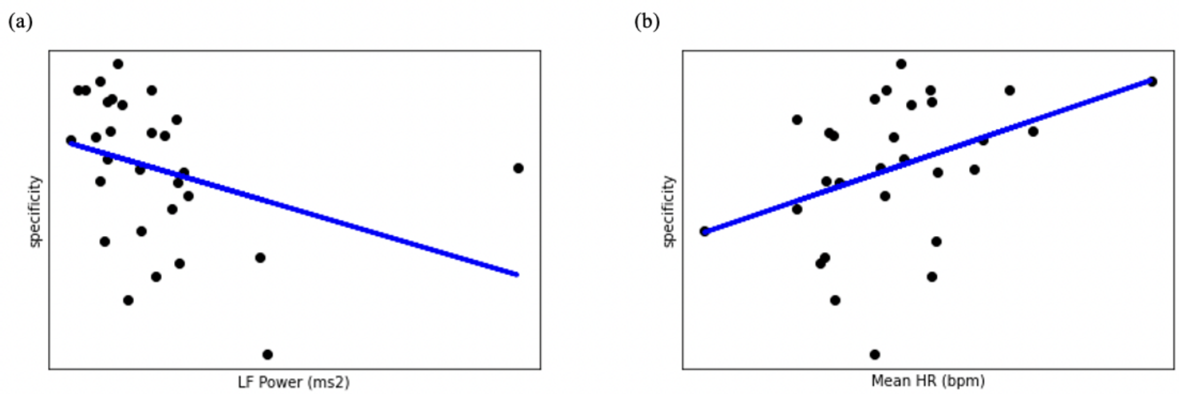

Figure 3.2 Scatterplot of (a) Specificity vs. LF Power and (b) Specificity vs. mean HR.

3.1.1.3 Accuracy

As depicted in Figure 3.3, Spearman's rank correlation coefficient indicated significant negative correlation between LF Power and accuracy (p = 0.004, r = -.52), such that higher LF power was associated with lower levels of overall performance specificity. Significant positive correlation was also found between mean HR and specificity (p = 0.029, r = .41), such that higher mean HR was associated with higher levels of overall performance specificity.

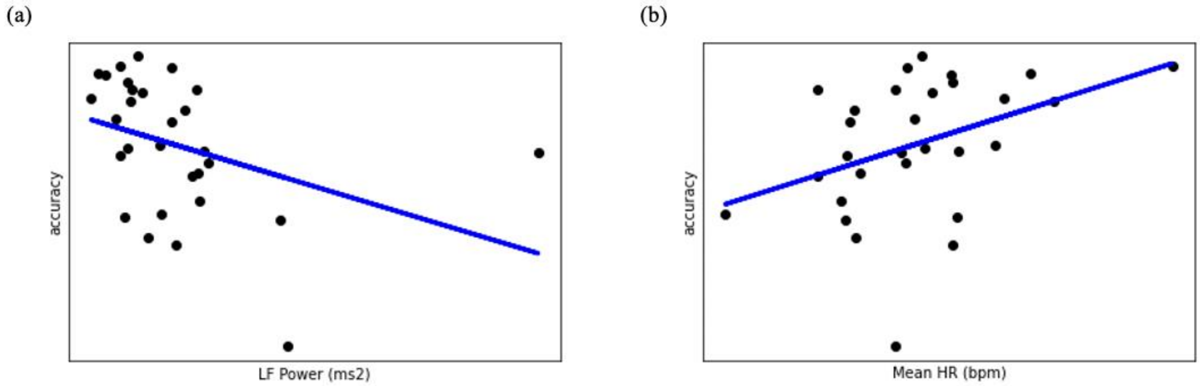

Figure 3.3 (a) Scatterplot of Accuracy vs. LF Power and (b) Accuracy vs. Mean HR.

3.1.2 Subjective

3.1.2.1 Fatigue

No significant correlation was found between HRV and fatigue perception.

3.1.2.2 Effort

As depicted in Figure 3.4, Spearman's rank correlation coefficient indicated significant negative correlation between HF and effort perception ($p = 0.027$, $r = -.41$), such that higher HF was associated with lower levels of overall effort perception. Significant positive correlation between LF/HF ratio and effort perception ($p = 0.026$, $r = .41$) was found, such that higher LF/HF ratio was associated with higher levels of overall effort perception.

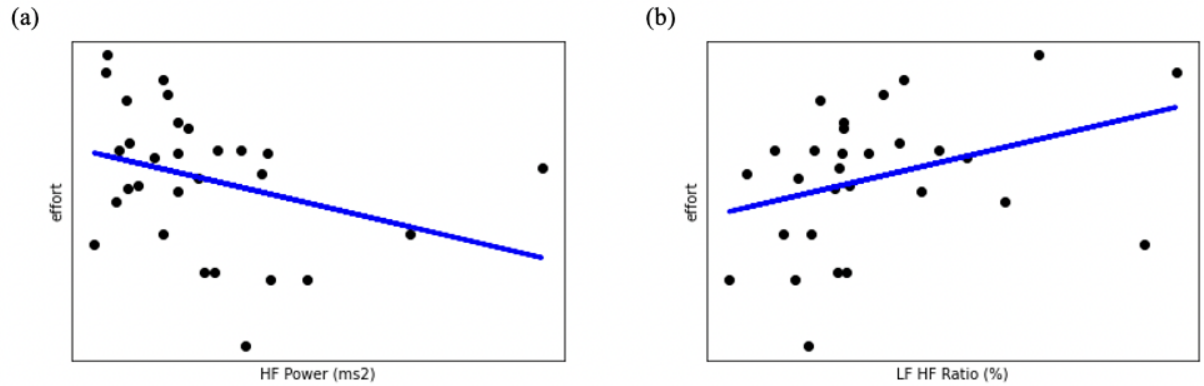

Figure 3.4 (a) Scatterplot of Effort vs. HF Power and (b) Effort vs. LF/HF Ratio.

3.1.2.3 Discomfort

As depicted in Figure 3.5, Spearman's rank correlation coefficient indicated significant negative correlation between mean HR and discomfort perception (p = 0.044, r = -.38), such that higher mean HR was associated with lower levels of overall discomfort perception.

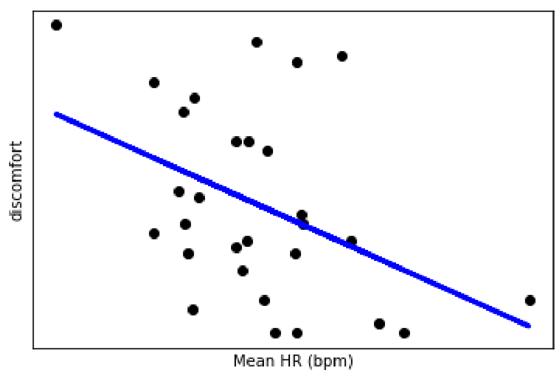

Figure 3.5 Scatterplot of Effort vs. Mean HR.

3.2 Baseline HRV vs. Throughout Performance and Subjective Ratings

3.2.1 Performance

3.2.1.1 Sensitivity

Median split and pair sample t-tests were used to outline the throughout performance sensitivity differences between groups with high HRV and low HRV. As depicted in Figure 3.6, significance was found between high and low groups of SDNN ($t(14) = 3.10$, $p = .010$), PNN50 ($t(14) = 6.01$, $p < .001$), RMSSD ($t(14) = 6.01$, $p < .001$), LF power ($t(14) = 10.12$, $p < .001$), , HF power($t(14) = 7.60$, $p < .001$), and LF/HF ratio ($t(14) = 7.41$, $p < .001$), such that groups with high baseline SDNN, PNN50, RMSSD, LF, HF, and LF/HF ratio showed higher levels of performance sensitivity throughout the WM tasks. Significance was also found between high and low groups of mean HR ($t(14) = -10.91$, $p < .001$), such that the group with high baseline mean HR showed lower levels of performance sensitivity throughout the WM tasks.

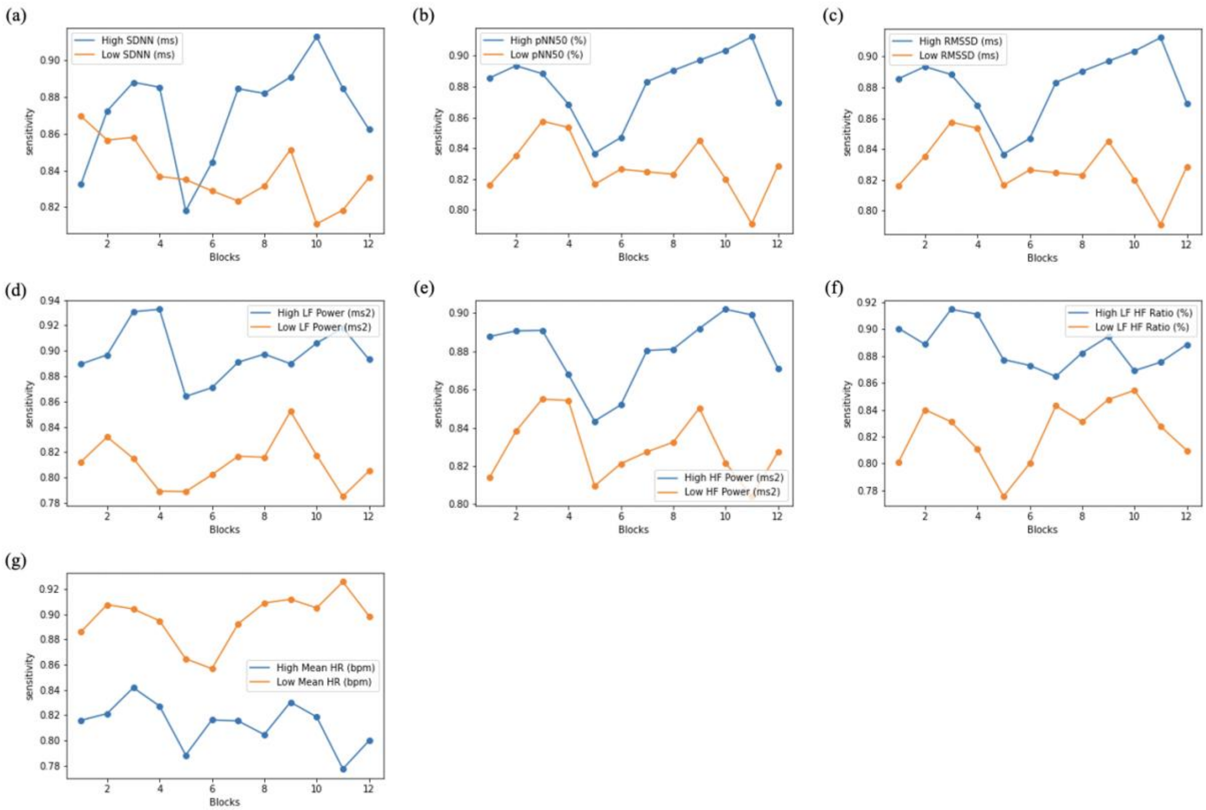

Figure 3.6 Line plots for sensitivity in groups of high vs low (a) SDNN, (b) pNN50, (c) RMSSD, (d) LF Power, (e) HF Power, (f) LF/HF Ratio, and (g) mean HR.

3.2.1.2 Specificity

Median split and pair sample t-tests were used to outline the throughout performance specificity differences between groups with high HRV and low HRV. As depicted in Figure 3.7, significance was found between high and low groups of SDNN ($t(14) = 2.31$, $p = .041$), PNN50 ($t(14) = 6.32$, $p < .001$), RMSSD ($t(14) = 6.32$, $p < .001$), LF Power ($t(14) = 8.98$, $p < .001$), HF Power($t(14) = 6.44$, $p < .001$), and LF/HF ratio ($t(14) = 4.71$, $p < .001$), such that groups with high baseline SDNN, PNN50, RMSSD, LF, HF, and LF/HF ratio showed higher levels of performance specificity throughout the WM tasks. Significance was also found between high and low groups of mean HR ($t(14) = -8.93$, $p < .001$), such that the group with high baseline mean HR showed lower levels of performance specificity throughout the WM tasks.

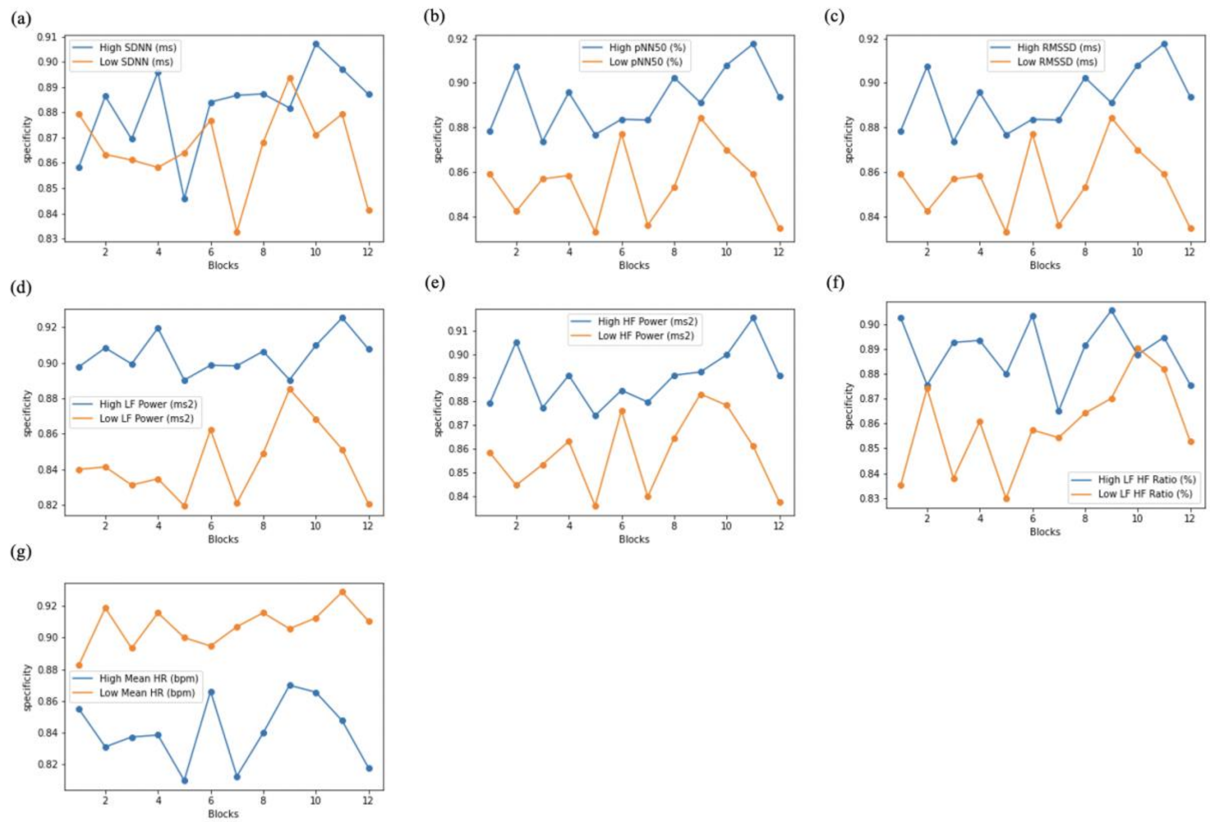

Figure 3.7 Line plots for specificity in groups of high vs low (a) SDNN, (b) pNN50, (c) RMSSD, (d) LF Power, (e) HF Power, (f) LF/HF Ratio, and (g) mean HR.

3.2.1.3 Accuracy

Median split and pair sample t-tests were used to outline the throughout performance accuracy differences between groups with high HRV and low HRV. As depicted in Figure 3.8, significance was found between high and low groups of SDNN ($t(14) = 2.90$, $p = .014$), PNN50 ($t(14) = 7.47$, $p < .001$), RMSSD ($t(14) = 7.47$, $p < .001$), LF Power ($t(14) = 10.25$, $p < .001$), , HF Power($t(14) = 8.82$, $p < .001$), and LF/HF ratio ($t(14) = 5.85$, $p < .001$), such that groups with high baseline SDNN, PNN50, RMSSD, LF, HF, and LF/HF ratio showed higher levels of performance specificity throughout the WM tasks. Significance was also found between high and low groups of mean HR ($t(14) = -10.96$, $p < .001$), such that the group with high baseline mean HR showed lower levels of performance accuracy throughout the WM tasks.

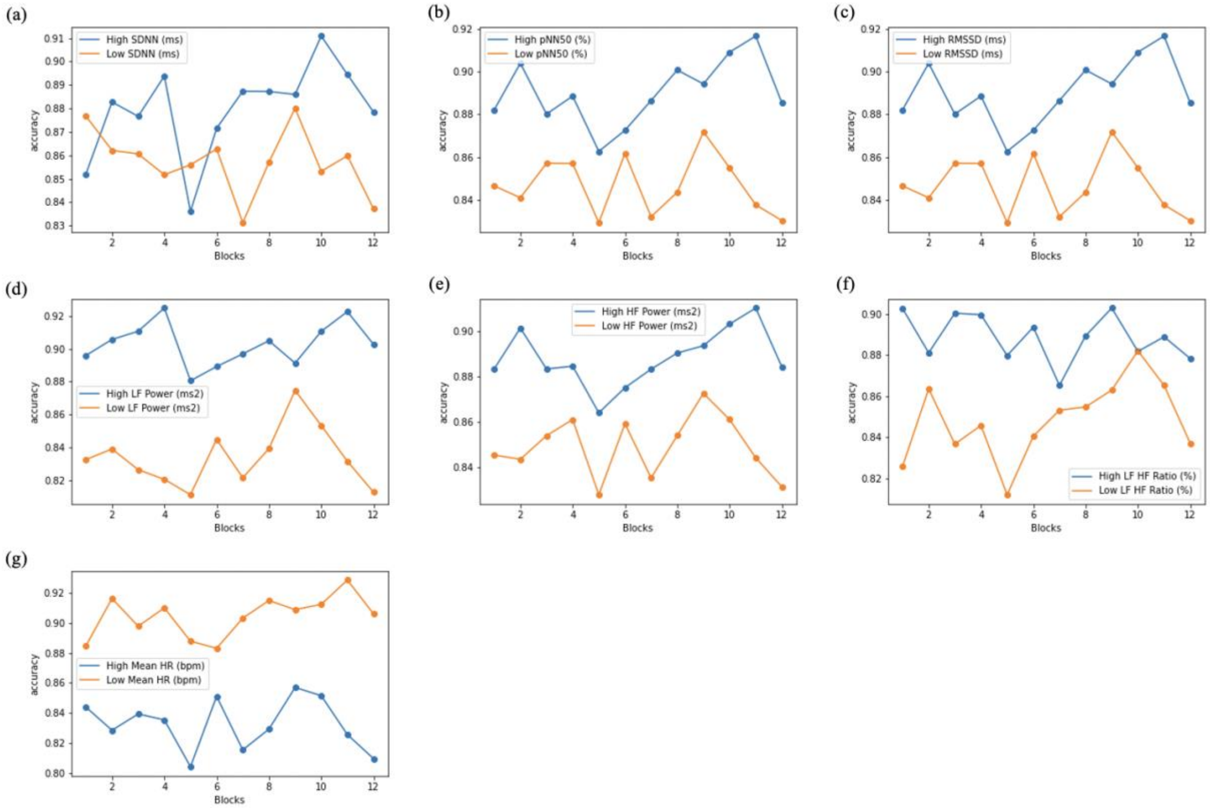

Figure 3.8 Line plots for accuracy in groups of high vs low (a) SDNN, (b) pNN50, (c) RMSSD, (d) LF Power, (e) HF Power, (f) LF/HF Ratio, and (g) mean HR.

3.2.2 Subjective

3.2.2.1 Fatigue

Median split and pair sample t-tests were used to outline the throughout fatigue perception differences between groups with high HRV and low HRV. As depicted in Figure 3.8, significance was found between high and low groups of LF ($t(14) = -3.85$, $p = 0.002$), HF ($t(14) = 2.45$, $p = 0.032$), and LF/HF ratio ($t(14) = -13.65$, $p < 0.001$), such that groups with high baseline HF showed higher levels of fatigue perception, while groups with high LF and LF/HF ratio showed lower levels of fatigue perception throughout the WM tasks.

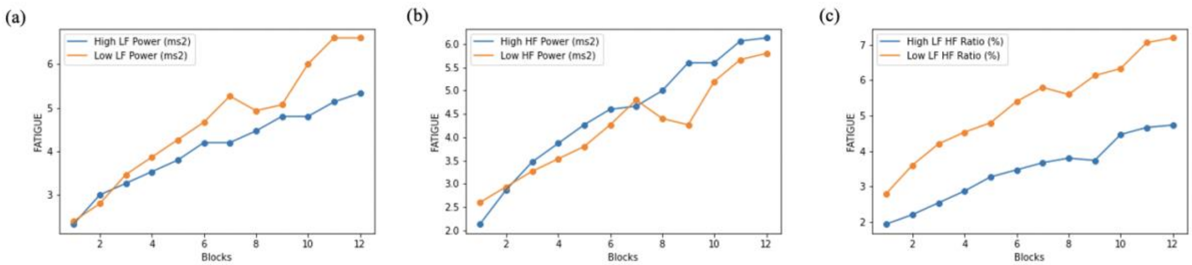

Figure 3.9 Line plots for fatigue in groups of high vs low (a) LF Power, (b) HF Power, and (c) LF/HF ratio.

3.2.2.2 Effort

Median split and pair sample t-tests were used to outline the throughout effort perception differences between groups with high HRV and low HRV. As depicted in Figure 3.10, significance was found between high and low groups of PNN50 ($t(14) = 9.72$, $p < 0.001$), RMSSD ($t(14) = 9.72$, $p < 0.001$), LF ($t(14) = 3.53$, $p = 0.005$), HF ($t(14) = 11.08$, $p < 0.001$), and LF/HF ratio ($t(14) = -15.40$, $p < 0.001$), such that groups with high baseline PNN50, RMSSD, LF, and HF showed higher levels of effort perception, while groups with high LF/HF ratio showed lower levels of effort perception throughout the WM tasks. Significance was also found between high and low groups of mean HR ($t(14) = -12.14$, $p < .001$), such that the group with high baseline mean HR showed lower levels of effort perception throughout the WM tasks.

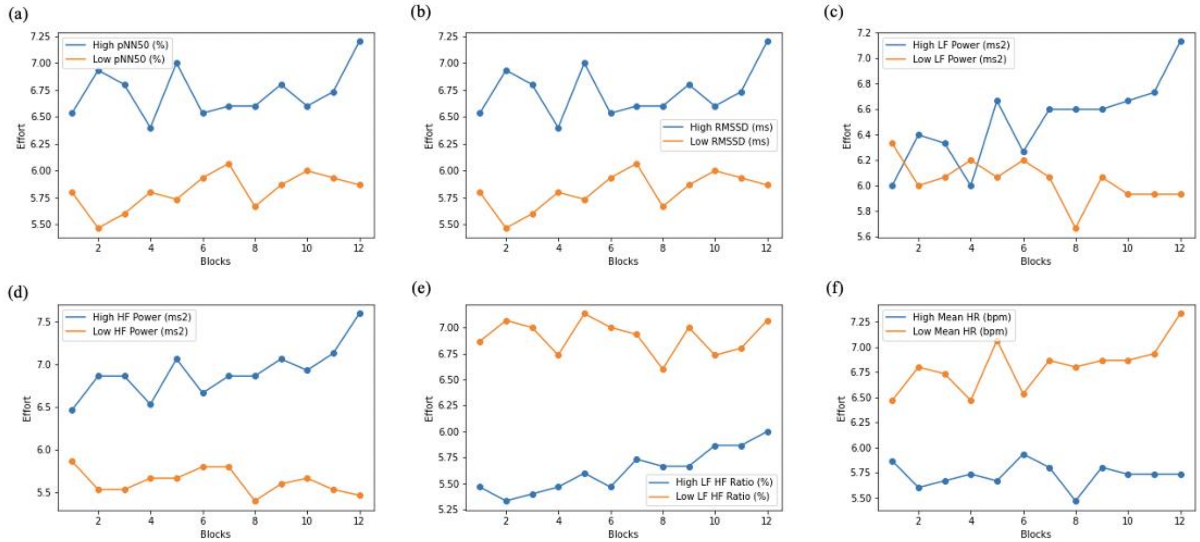

Figure 3.10 Line plots for effort in groups of high vs low (a) pNN50, (b) RMSSD, (c) LF Power, (d) HF Power, (e) LF/HF ratio, and (f) mean HR.

3.2.2.3 Discomfort

Median split and pair sample t-tests were used to outline the throughout discomfort perception differences between groups with high HRV and low HRV. As depicted in Figure 3.11, significance was found between high and low groups of SDNN ($t(14) = -10.14$, $p < 0.001$), PNN50 ($t(14) = -2.42$, $p = 0.034$), RMSSD ($t(14) = -2.42$, $p = 0.034$), LF ($t(14) = -6.82$, $p < 0.001$), and LF/HF ratio ($t(14) = -8.74$, $p < 0.001$), such that groups with high baseline SDNN, PNN50, RMSSD, LF, and LF/HF ratio showed lower levels of discomfort perception throughout the WM tasks. Significance was also found between high and low groups of mean HR ($t(14) = 8.14$, $p < .001$), such that the group with high baseline mean HR showed higher levels of effort perception throughout the WM tasks.

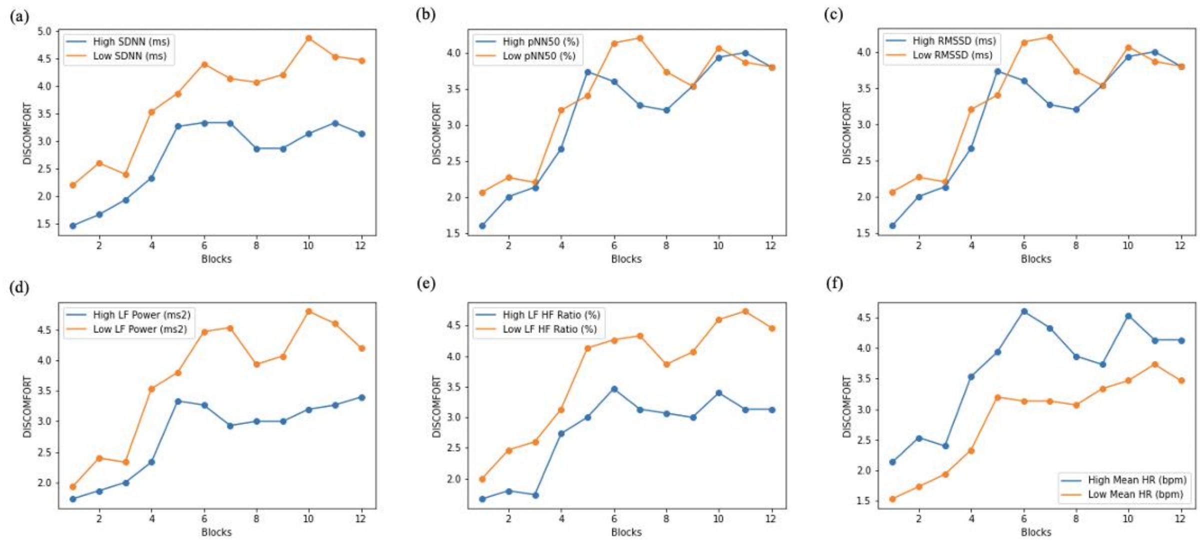

Figure 3.11 Line plots for discomfort in groups of high vs low (a) SDNN, (b) pNN50, (c) RMSSD, (d) LF Power, (e) LF/HF ratio, and (f) mean HR.

3.3 Throughout HRV vs. Throughout Performance and Subjective Ratings

3.3.1 Performance

3.3.1.1 Sensitivity

No significant correlation was found between HRV and performance sensitivity throughout the WM tasks.

3.3.1.2 Specificity

No significant correlation was found between HRV and performance specificity throughout the WM tasks.

3.3.1.3 Accuracy

No significant correlation was found between HRV and performance accuracy throughout the WM tasks.

3.3.2 Subjective

3.3.2.1 Fatigue

As depicted in Figure 3.12, Spearman's rank correlation coefficient indicated significant positive correlations in SDNN ($p = .002$, $r = .79$), PNN50 ($p < .001$, $r = .87$), RMSSD ($p = .007$, $r = .73$), and LF Power ($p = 0.048$, $r = .58$) with fatigue, such that higher SDNN, PNN50, RMSSD, and LF Power were associated with higher levels of fatigue perception throughout the WM tasks. Significant positive correlation was also found between mean HR and fatigue ($p < 0.001$, $r = -.88$), such that higher mean HR was associated with lower levels of fatigue perception throughout the WM tasks.

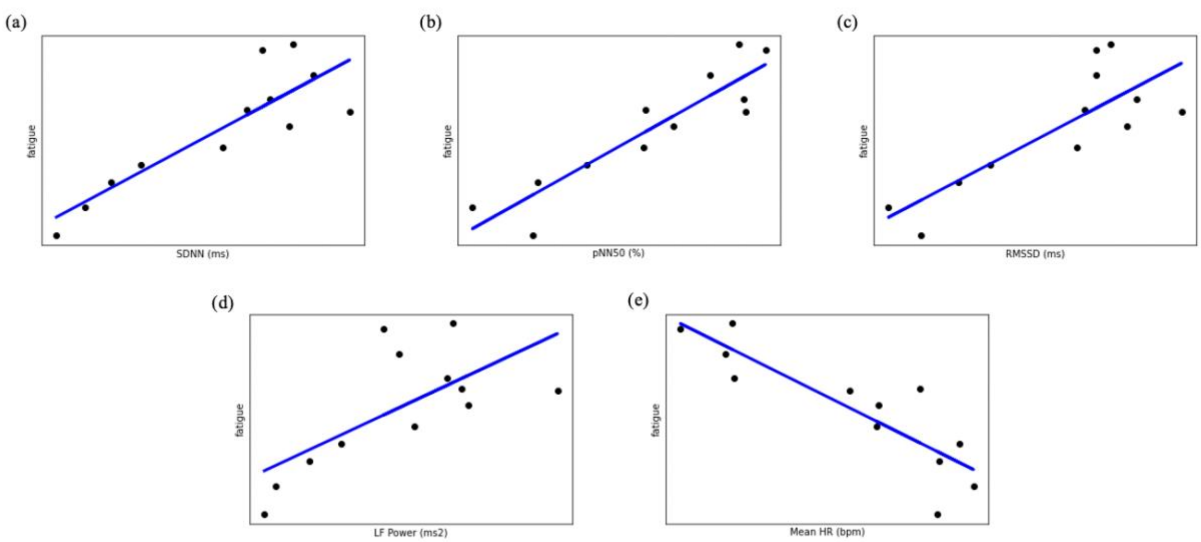

Figure 3.12 (a) Fatigue vs SDNN, (b) Fatigue vs pNN50, (c) Fatigue vs RMSSD, (d) Fatigue vs LF Power, and (e) Fatigue vs Mean HR.

3.3.2.2 Effort

As depicted in Figure 3.13, Spearman's rank correlation coefficient indicated significant positive correlations in mean HR ($p = 0.039$, $r = -.60$) with fatigue, such that higher mean HR was associated with lower levels of fatigue perception throughout the WM tasks.

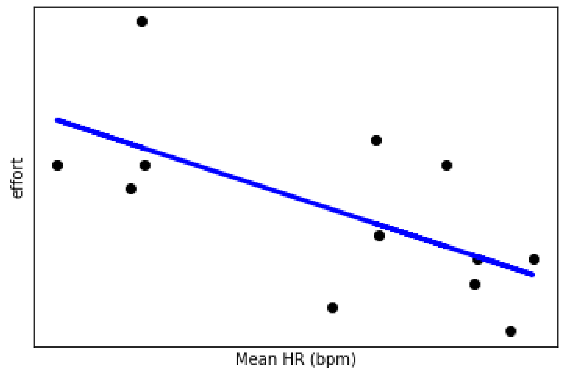

Figure 3.13 Effort vs Mean HR.

3.3.2.3 Discomfort

As depicted in Figure 3.14, Spearman's rank correlation coefficient indicated significant positive correlations in SDNN (p = .008, r = .72), pNN50 (p = .013, r = .69), and RMSSD (p = .044, r = .59) with discomfort, such that higher SDNN, pNN50, and RMSSD were associated with higher levels of discomfort perception throughout the WM tasks. Significant positive correlation was also found between mean HR and fatigue (p = 0.002, r = -.79), such that higher mean HR was associated with lower levels of discomfort perception throughout the WM tasks.

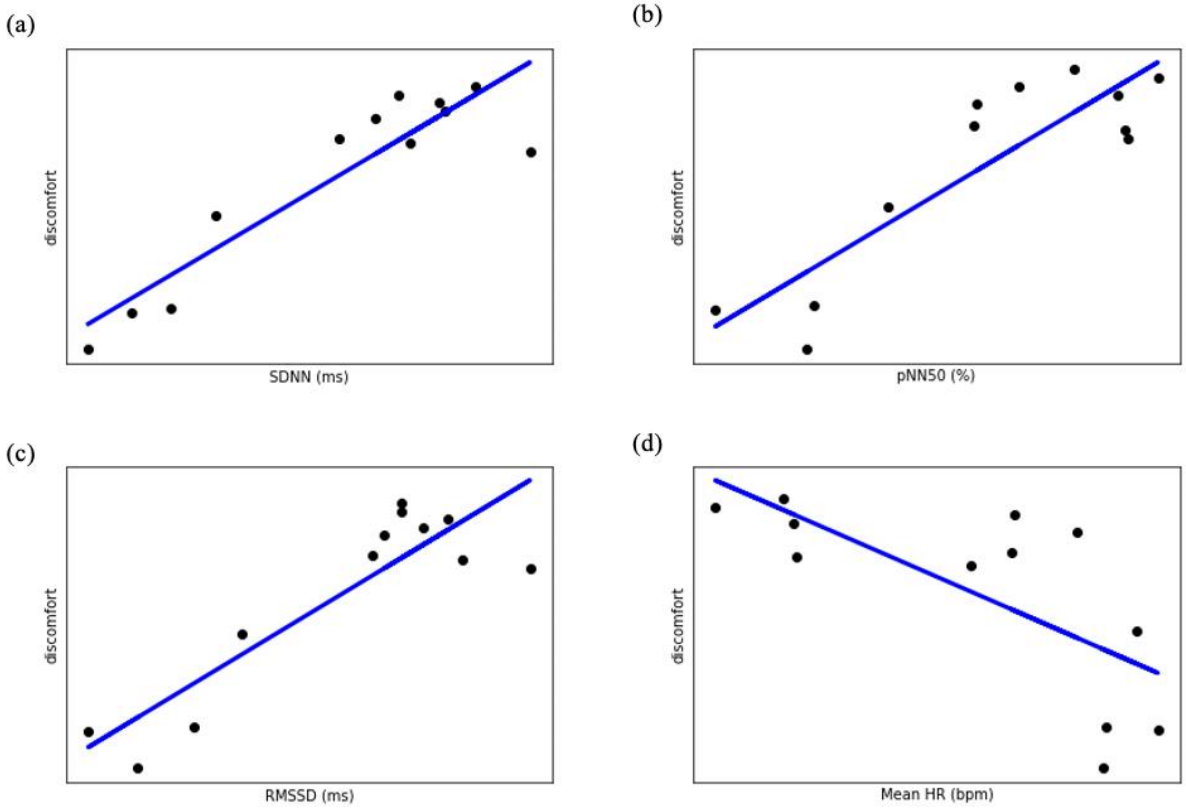

Figure 3.14 (a) Discomfort vs SDNN, (b) Discomfort vs pNN50, (c) Discomfort vs RMSSD, and (d) Discomfort vs Mean HR.

4. CONCLUSION

The present study examined the correlation between HRV and performance and subjective responses during a fatiguing visuospatial WM exercise. We hypothesized that higher baseline HRV would associate with overall larger WM capacity and less perceptions of fatigue when engaging in cognitively demanding tasks over an extended period of time. We also hypothesized that the HRV measures throughout the WM exercise were positively correlated with the coincident WM performance levels and were negatively correlated with the coincident fatigue perceptions. These hypotheses were made because fatigue was found to be associated with increased levels of autonomic nervous system sympathetic activity [35], [36]. WM task requires active short-term storage, processing, and manipulation of information which relies on inhibitory neuro processes [37], [38]. The neurovisceral integration model suggests that such inhibitory processes are mediated by the prefrontal cortex that is linked with the heart via the vagus nerves [17], [39]. Moreover, higher resting HRV is associated with effective functioning of prefrontal-subcortical inhibitory circuits [40], [17] while lower resting HRV is associated with hypoactive prefrontal regulation that leads to maladaptive cognitive and emotional self-regulation [39]. Previous research demonstrated that fatigue is associated with increased LF, LF/HF ratio, and heart rate [25]. Similar findings from a study targeting chronic fatigue adolescents also revealed increased LF and decreased HF during mild orthostatic stress [41], [42]. We employed the visuospatial two-back test to exert demands of both WM and sustained attention on participants over a prolonged period of time [43]. Performance, subjective and physiological responses were recorded and analyzed for three different perspectives: baseline

HRV vs. mean performance and subjective ratings, baseline HRV vs. throughout performance and subjective ratings, and throughout HRV vs. throughout performance and subjective ratings.

The baseline HRV vs. mean performance and subjective ratings analysis implemented Spearman's rank correlation coefficient and yielded several significances. However, the correlation coefficients were small (all |r|s < .52), suggesting weak correlation despite statistical significance.

The baseline HRV vs. throughout performance and subjective ratings analysis provided a less rigorous but clearer view at the relationship between baseline HRV and performance using median split. Regarding performance, high SDNN, PNN50, RMSSD, LF power, HF power, and LF/HF ratio were all found significantly associating with higher levels of performance sensitivity, specificity and accuracy throughout the tasks. This finding agreed with our hypothesis that posited a positive correlation between HRV and WM performance. High mean HR was found significantly associating with lower levels of performance sensitivity, specificity and accuracy throughout the tasks, also agreeing with results from prior research [25]. Groups with high LF and LF/HF ratio showed lower levels of fatigue perception and groups with high HF showed higher levels of fatigue perception throughout the tasks. Groups with high PNN50, RMSSD, LF and HF showed higher levels of effort perception and groups with high LF/HF ratio and mean HR showed lower levels of effort perception throughout the tasks. Groups with high SDNN, PNN50, RMSSD, LF power, and LF/HF ratio showed lower levels of discomfort perception throughout the WM tasks and groups with high mean HR showed higher levels of discomfort perception throughout the tasks. Results regarding fatigue and discomfort perception aligned with our hypothesis that higher HRV correlates with lower fatigue related subjective perceptions. The positive correlation between HF power and fatigue perception matched previous finding of fatigue associating with decreased normalized HF [25]. One reason behind effort perception being positively correlated with HRV may be the nature of the visuospatial two-back task used in this study: the task induced fatigue by protractedness, instead of difficulty, which lead participants to perceive less demanded effort.

Spearman's rank correlation coefficient was implemented on examining the association between throughout HRV vs. throughout performance and subjective ratings. No significance was found between HRV and performance throughout the 12 blocks of the task. Higher levels of SDNN, PNN50, and RMSSD were associated with higher levels of both fatigue and discomfort perception and higher levels of LF power was associated with higher levels of fatigue perception throughout the WM task. Higher level of mean HR was associated with lower levels of all three subjective metrics. The correlation coefficients were relatively large, suggesting strong positive correlation between HRV and fatigue and discomfort perception throughout the task. These findings on subjective perception were opposite to our hypothesis that HRV throughout the tasks would negatively correlate with subjective perceptions. Previously published analysis on the same data revealed significant increase in discomfort and fatigue measures over time throughout the task and significant increase in RMSSD and LF during the first 10 minutes and last 15 minutes [26]. This perceived increase in HRV at the beginning and end of the task can be explained by the sense of novelty at the beginning and self-reported anticipation bias when participants estimated the end of the task and regained alertness [26]. Analysis on other HRV features other than RMSSD and LF would be considered as a next step to confirm the increase in HRV over time.

Future analysis should consider excluding the first and last few blocks due to sense of novelty and reported anticipation bias. Second, we would also extend the analysis to the anodal condition (i.e., with tDCS delivered 20 minutes into the WM task), though the electric current could increase discomfort during the stimulation period. Third, we are currently performing phase II of the data collection with several modifications including a between subject design, separate participant orientation, prolonged WM task (10-minute blocks for two hours), enhanced stimulation delivery, addition of functional near infrared spectroscopy (fNIRS), improved subjective ratings (motivation, fatigue, effort, and mental demand). Comparison between HRV and fNIRS data would bring out a more accurate relationship between HRV and the mental state of participants.

Cognitive fatigue has a significant impact on executive functions during ER operations. Our research presented a possibility of using HRV devices to predict time-on-task WM performance and perceived fatigue level in real time and eventually contribute to the closed-loop framework of fatigue detection and intervention which proper modes of intervention (e.g., tDCS) are delivered to offset fatigue before fatigue onset and (or) performance decline.

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