ENABLING POST TRAUMATIC STRESS DISORDER (PTSD) HYPERAROUSAL MONITORING THROUGH INVESTIGATION OF HEART RATE PATTERNS AND MACHINE LEARNING

A Dissertation

by

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DOCTOR OF PHILOSOPHY

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ABSTRACT

PTSD is a psychiatric condition experienced by individuals after exposure to a traumatic event such as war. PTSD is a major public health concern in the United States since it is among one of the most prevalent mental disorders. Over 6% of the U.S. population suffer from this condition at any given time. PTSD has serious consequences including (but not limited to) depression and anxiety which will lead to avoidance, intrusive thoughts and hyperarousal. Hyperarousal symptoms include hypervigilance, feelings of irritability, and an exaggerated startle response following a startling event.

PTSD mostly has been assessed using subjective methods such as surveys and questionnaires. Although these methods are promising for PTSD diagnosis, they lack the capability of detecting the onset of symptoms (e.g., hyperarousal). Capturing hyperarousal events is specifically crucial because individuals may experience the most intense moments of their lives during these events when they are not with their clinicians. Therefore, there is a vital need to monitor hyperarousal events and provide timely feedback for individuals.

In this research I tried to address this gap by 1. statistically understanding hyperarousal events, 2. detecting them using machine learning algorithms, and 3. creating an actual tool that individuals who have PTSD can use to monitor their events. To do so, I used heart rate since heart rate is the main physiological indicator of PTSD. In chapter 2, I created a framework that can be used to analyze heart rate in response to PTSD. In chapter 3 I used the framework to investigate specific heart rate patterns

associated with hyperarousal events. In chapter 4, I used these patterns along with a few other heart rate and body acceleration features to develop a machine learning algorithm that can detect hyperarousal events in real time. Finally, in chapter 5, I validated the developed algorithm in naturalistic settings to investigate the real world application of such algorithms. Altogether, this research presents a tool that can predict hyperarousal events in real time and has real-world validity.

DEDICATION

I dedicate this dissertation to the closest person to my heart, my beloved sister, Simin, who has always been a constant source of guidance and support in my life. Simin, you are my best friend, my ally, my critic, and my biggest fan. I could not have done this without you, and I owe every success I have in my life to you. Thank you for being the best sister, I love you more than anything in the world combined.

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Contributors

This work was supervised by a dissertation committee consisting of committee chair and co-chair, Dr. Farzan Sasangohar and Dr. Anthony McDonald, committee members Dr. Thomas Ferris of the Department of Industrial and Systems Engineering and Dr. Darrell Worthy of the Department of Psychology. All other work conducted for the dissertation was completed by the student under the advisement of Dr. Farzan Sasangohar of the Department of Industrial and Systems Engineering.

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1. CHAPTER 1 INTRODUCTION

1.1. Overview

Post-Traumatic Stress Disorder (PTSD) is a psychiatric condition associated with stress and anxiety that affects over 24 million people in the United States [1]. Veterans who return from war zones are particularly prone to PTSD due to their combat exposure. Recent estimates suggest that 17% of military veterans are affected by PTSD [2]. Other reports documented as much as 20% prevalence among the returning veterans from the current conflicts in Afghanistan and Iraq [3]. The total costs for providing medical care for returning veterans of Iraq and Afghanistan from 2011-2020 (excluding disability) were estimated to be around $40-54 billion in inflation adjusted 2010 dollars [4]. It is expected that such medical costs will peak 30-40 years after a major conflict. For Iraq/Afghanistan veterans cost of care will peak around 2035. The increase in costs were attributed to new conflicts and the increase in comorbid conditions resulting from PTSD, traumatic brain injury (TBI) and polytrauma [4].

PTSD is characterized by a traumatic event and at least one month of re-experiencing that traumatic event [5]. The Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5) [5] further classifies re-experiencing symptoms into intrusive recollections, recurrent dreams, and flashbacks. Avoidance and hyperarousal are other main symptoms of PTSD. Avoidance symptoms include avoiding activities or cognitions associated with the traumatic event, decreased interest in daily life and an overall feeling of detachment from one's surroundings. Hyperarousal symptoms include hypervigilance or feelings of being constantly on guard, feelings of irritability, and an

exaggerated startle response following a startling event. Other symptoms include anxiety, insomnia, fatigue, anger, and aggression [6].

There are several methods to diagnose PTSD. The gold standard and most common approach for detecting and measuring the severity of PTSD symptoms is clinician-administered assessments. Such assessments include the Clinician-Administered PTSD scale [7], [8] and the Structured Clinical Interview for DSM-5, PTSD module [8], [9]. Another approach to diagnose PTSD is to use self-reported measures. The Impact of Event Scale-Revised [10]; PTSD Checklist (PCL)-Civilian Version [11]; Trauma Screening Questionnaire [12] and the Self-Rating Inventory for Posttraumatic Stress Disorder [13] have shown a 90% or higher level of diagnostic accuracy compared to the self-reported DSM-5 PTSD detection instruments for civilian trauma populations. The main criteria used to measure diagnostic efficiency of such instruments are sensitivity, positive predictive power, negative predictive power and overall efficiency for the test [8], [12]. Although subjective measures are helpful, they have a few limitations [7], [11]. Despite commonality of self-reported measures to diagnose and monitor PTSD, such methods suffer from several important limitations. For example, self-report techniques might be subject to emotional numbing and dissociation [14], which may negatively affect the compliance rates to follow a therapeutic regimen, self-management, as well as quality and reliability of self-administered assessments. While clinician-administered instruments may partly address this limitation, the effectiveness of diagnosis and treatments might depend on the frequency of administration. Moreover, PTSD subjective measures fail to capture

isolated and mild cases, and most importantly are not capable of detecting hyperarousal events.

It is apparent that without objective methods for effective continuous monitoring of PTSD symptoms, it will be challenging to improve care due to uncertainty associated with between-session self-management. In line with the World Health Organization agenda to "Monitor the health situation and assess health trends," there is a vital need to develop remote and continuous monitoring capabilities that facilitate data-driven care and support self-management [15]. An outcome-based research and real-time epidemiology for tracking veterans' progress through their healthcare journey can guide therapies and preventive strategies and reduce the gap between treatments received in clinician sessions at one end and self-care at the other end, however, such research remains a gap. Early intervention and treatment may also reduce suicidal thoughts and avoid alcohol or tobacco abuse and may save costs arising from secondary complications associated with alcohol or tobacco such as alcoholic liver disease or a pulmonary complication [4].

Psychophysiology might improve PTSD care and self-management by providing objective tools for tracking and assessing PTSD symptoms. Psychophysiology involves the non-invasive recording of biological processes [16]. Commonly used physiological measures to assess PTSD are: (1) heart rate (cardiac activity); (2) heart rate variability (3) Galvanic Skin Conductance (GSC); (4) Systolic Blood Pressure (SBP), and (5) Diastolic Blood Pressure (DBP) [16]. It has been shown that changes in these measures correlate with PTSD symptom severity such as a PTSD hyperarousal [16]. Such

physiological measures may help distinguish between patients that respond well to PTSD treatments and non-responders to such treatments [17] and can provide additional information regarding PTSD's pathophysiology [16].

A meta-analysis of psychophysiological variables related to PTSD conducted by Pole et al. (2007) [16] shows that studies have used four overarching conditions in laboratory environments to assess PTSD symptoms: (1) resting baseline; (2) exposure to startling sounds; (3) exposure to standardized trauma cues; and (4) exposure to idiographic trauma cues [16]. The changes in measures that are found to be reliably related to PTSD are: (1) higher resting heart rate; (2) larger heart rate responses to standardized trauma cues; and (3) for idiographic cues, facial muscle Electromyography (EMG) and heart rate responses. It should be noted that facial muscle EMG might be difficult to assess in the field discretely without people noticing. Other related changes in measures include elevations in GSC, SBP, and DBP. Diastolic blood pressure is more strongly associated with PTSD than systolic blood pressure [18]. Eye blink rate and GSC for startling sounds, increased GSC for standardized trauma cues and increased GSC and DBP for idiographic trauma cues.

Among these variables, heart rate shows promise for its application in PTSD monitoring, given the prevalence of wearable and non-intrusive heart rate sensors and preliminary evidence suggesting its reactivity to PTSD symptoms, heart rate can be considered as a reliable indicator of PTSD [19]. For example, in a recent meta-analysis, Morris et al. [18] found that increased heart rate measured after trauma exposure is associated with higher PTSD symptoms. This study indicates that heart rate changes is

strongly associated with hyperarousal and re-collection symptoms for PTSD ([18], [20]) and heart rate reactivity may normalize after successful treatment [18], [21]–[23]. Although it is known that PTSD symptoms impact heart rate, the documented evidence is limited to correlational analyses and specific heart rate mechanisms or patterns associated with hyperarousal events remain unknown. In addition, heart rate is influenced by other factors such as medication, pain, underlying medical conditions [24] as well as activity and such potentially confounding variables need to be considered for a robust assessment of construct validity of using heart rate to monitor PTSD symptoms.

It seems that developing effective heart-rate-based PTSD monitoring methods that work based on objective and measurable data, is contingent on investigating how heart rate responds to PTSD hyperarousal events. Such knowledge can then be used to monitor such unique responses. In response to this potential, the objectives of my dissertation are to answer following questions:

- What are the unique heart rate cues, patterns, and identifiers in response to PTSD hyper-arousal episodes?
- Can a machine learning algorithm detect heart rate patterns associated with PTSD hyperarousal events?
- How can we operationalize the developed algorithm as a smartwatch-based detection tool?

This dissertation addresses these questions in different phases as detailed below (Figure 1). As this dissertation is a collection of published/submitted articles, following elaborates on different chapters of this dissertation.

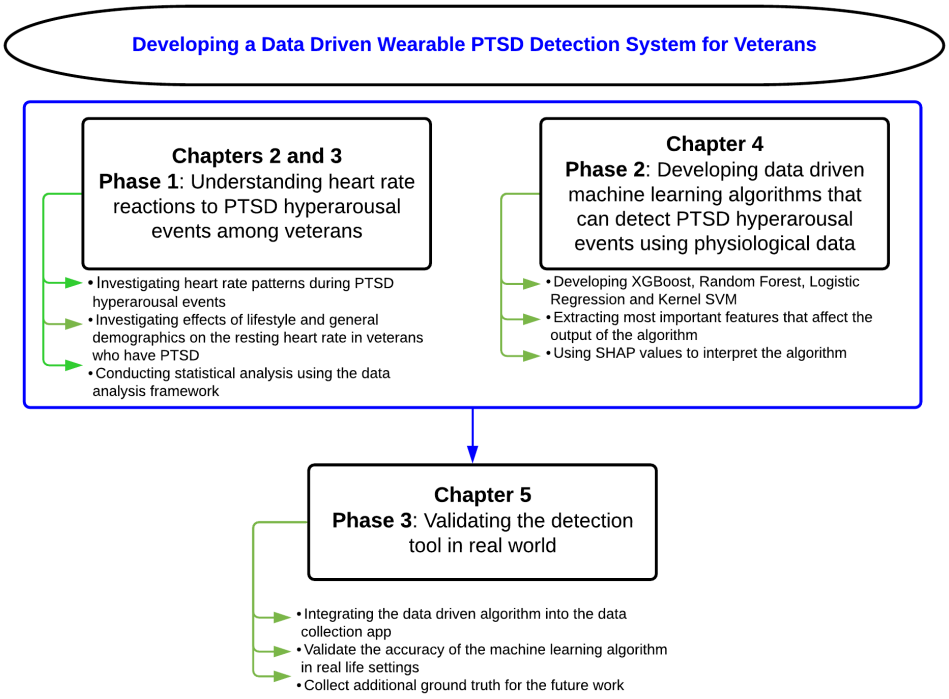

Figure 1.1. Dissertation roadmap

- Chapter 1: Introduction chapter or current chapter helps readers understand the objective and organization of this dissertation as well as background information about PTSD symptoms, their relationship with heart rate and provides a road map for this dissertation.

- Chapter 2 (Article 1): This chapter elaborates on findings from a comprehensive literature review about understanding physiological indicators of PTSD.

Using Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) framework [25], 54 articles were chosen to be included in this review. Several research gaps were identified from the literature review looking into the objective assessment of PTSD: the research is lacking in the area of naturalistic studies to assess the importance of heart rate measures while examining PTSD hyperarousal. Characterization of PTSD hyperarousal events from heart rate data seems to be a research gap. It is worth looking into two aspects of heart rate as a risk factor, resting heart rates in people who have PTSD, and heart rate patterns during hyperarousal events. A more acute characterization of PTSD symptoms can be implemented using continuous monitoring of instantaneous heart rate to improve prediction and detection of PTSD symptoms to create awareness towards PTSD symptoms, particularly hyperarousal. These gaps are important because an important aspect missing from PTSD care system today is how to deal with PTSD symptoms when patients are on their own or with their families. Not being able to deal with symptoms further isolates PTSD patients, as they know their reactions to PTSD symptoms might be harmful to others in the vicinity as well as themselves. As an overview of research gaps, there is a general lack of understanding of PTSD triggers and lack of continuous monitoring of PTSD patients to characterize the symptoms based on psychophysiological parameters.

- Chapter 3 (Article 2): This chapter provides answers to the first question of the dissertation that whether heart rate provides unique cues, patterns and identifiers for PTSD hyperarousal episodes in the population of veterans suffering from polytrauma. It will provide a comprehensive understanding of heart rate responses to

PTSD especially during hyperarousal events. This chapter contributes to the body of knowledge by providing a comprehensive understanding of the correlations between heart rate baseline and demographic information, medications, and medical history in people who have PTSD. Moreover, this chapter determines significant risk factors associated with the accelerations and decelerations in heart rate, and elaborates on specific heart rate statistical features when hyperarousal events happen. The specific characteristics of heart rate identified in this chapter in correlation with PTSD could be investigated for detection of PTSD symptoms using a wearable sensor that can be monitored discretely.

- Chapter 4 (Article 3): This chapter presents answers to the second research question in this dissertation. Several machine learning algorithms are developed that can detect PTSD hyperarousal events in real time. Based on the best performance in terms of accuracy, sensitivity, and specificity, one algorithm is chosen for further analysis.

- Chapter 5 (Article 4): This chapter addresses the last research question of this dissertation on whether the algorithm developed in chapter 4 can detect hyperarousal events in real world, naturalistic settings, and with actual people who have PTSD. To address this question, the machine learning algorithm is integrated in the data collection tool and then it is validated in the real world. In this chapter I specifically looked at the

accuracy of the detection tool, perceived accuracy, participants' trust in the device, and participants interactions with the device.

- Chapter 6: This chapter represents the conclusion of this dissertation. It summarizes the key findings, contribution to the body of literature, limitations, and future work. This is the first major section of your document.

1.2. References

[1] R. B. Goldstein et al., "The epidemiology of DSM-5 posttraumatic stress disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III," Social psychiatry and psychiatric epidemiology, vol. 51, no. 8, pp. 1137–1148, 2016.

[2] E. A. Stefanovics, M. N. Potenza, and R. H. Pietrzak, "PTSD and obesity in US military veterans: Prevalence, health burden, and suicidality.," Psychiatry research, vol. 291, p. 113242, 2020.

[3] R. Ramchand, T. L. Schell, B. R. Karney, K. C. Osilla, R. M. Burns, and L. B. Caldarone, "Disparate prevalence estimates of PTSD among service members who served in Iraq and Afghanistan: possible explanations," Journal of Traumatic Stress: Official Publication of The International Society for Traumatic Stress Studies, vol. 23, no. 1, pp. 59–68, 2010.

[4] J. Geiling, J. M. Rosen, and R. D. Edwards, “Medical costs of war in 2035: long-term care challenges for veterans of Iraq and Afghanistan,” Military medicine, vol. 177, no. 11, pp. 1235–1244, 2012.

[5] American Psychiatric Association, Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub, 2013.

[6] K. F. Carlson et al., “Prevalence, assessment, and treatment of mild traumatic brain injury and posttraumatic stress disorder: a systematic review of the evidence,” The Journal of head trauma rehabilitation, vol. 26, no. 2, pp. 103–115, 2011.

[7] D. D. Blake et al., “The development of a clinician-administered PTSD scale,” Journal of traumatic stress, vol. 8, no. 1, pp. 75–90, 1995.

[8] N. Del Vecchio, A. R. Elwy, E. Smith, K. A. Bottonari, and S. V. Eisen, “Enhancing self-report assessment of PTSD: Development of an item bank,” Journal of traumatic stress, vol. 24, no. 2, pp. 191–199, 2011.

[9] M. B. First and M. Gibbon, “The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II).,” 2004.

[10] C. R. Marmar, T. J. Metzler, and C. Otte, The peritraumatic dissociative experiences questionnaire. The Guilford Press, 2004.

[11] F. W. Weathers, B. T. Litz, T. M. Keane, P. A. Palmieri, B. P. Marx, and P. P. Schnurr, “The ptsd checklist for dsm-5 (pcl-5),” Scale available from the National Center for PTSD at www. ptsd. va. gov, vol. 10, 2013.

[12] C. R. Brewin, “Systematic review of screening instruments for adults at risk of PTSD,” Journal of Traumatic Stress: Official Publication of The International Society for Traumatic Stress Studies, vol. 18, no. 1, pp. 53–62, 2005.

[13] J. E. Hovens, H. M. Van der Ploeg, I. Bramsen, M. T. A. Klaarenbeek, J. N. Schreuder, and V. V. Rivero, “The development of the self-rating inventory for posttraumatic stress disorder,” Acta Psychiatrica Scandinavica, vol. 90, no. 3, pp. 172–183, 1994.

[14] N. C. Feeny, L. A. Zoellner, L. A. Fitzgibbons, and E. B. Foa, “Exploring the roles of emotional numbing, depression, and dissociation in PTSD,” Journal of traumatic stress, vol. 13, no. 3, pp. 489–498, 2000.

[15] “WHO | World Health Organization,” WHO. https://www.who.int/workforcealliance/members_partners/member_list/who/en/ (accessed Aug. 04, 2021).

[16] N. Pole, “The psychophysiology of posttraumatic stress disorder: a meta-analysis.,” Psychological bulletin, vol. 133, no. 5, p. 725, 2007.

[17] P. J. Colvonen et al., “Pretreatment biomarkers predicting PTSD psychotherapy outcomes: a systematic review,” Neuroscience & Biobehavioral Reviews, vol. 75, pp. 140–156, 2017.

[18] M. C. Morris, N. Hellman, J. L. Abelson, and U. Rao, “Cortisol, heart rate, and blood pressure as early markers of PTSD risk: A systematic review and meta-analysis,” Clinical psychology review, vol. 49, pp. 79–91, 2016.

[19] M. Sadeghi, F. Sasangohar, and A. D. McDonald, “Toward a taxonomy for analyzing the heart rate as a physiological indicator of posttraumatic stress disorder: systematic review and development of a framework,” JMIR Mental Health, vol. 7, no. 7, p. e16654, 2020.

[20] M. E. Costanzo et al., “Psychophysiological response to virtual reality and subthreshold posttraumatic stress disorder symptoms in recently deployed military,” Psychosomatic Medicine, vol. 76, no. 9, pp. 670–677, 2014.

[21] T. M. Keane and D. G. Kaloupek, “Imaginal flooding in the treatment of a posttraumatic stress disorder.,” Journal of Consulting and Clinical Psychology, vol. 50, no. 1, p. 138, 1982.

[22] R. K. Pitman et al., “Psychophysiologic assessment of posttraumatic stress disorder in breast cancer patients,” Psychosomatics, vol. 42, no. 2, pp. 133–140, 2001.

[23] N. Pole and P. Bloomberg-Fretter, “Using control mastery therapy to treat major depression and posttraumatic stress disorder,” Clinical Case Studies, vol. 5, no. 1, pp. 53–70, 2006.

[24] N. R. Nugent, N. C. Christopher, and D. L. Delahanty, “Emergency medical service and in-hospital vital signs as predictors of subsequent PTSD symptom severity in pediatric injury patients,” Journal of Child Psychology and Psychiatry, vol. 47, no. 9, pp. 919–926, 2006.

[25] D. Moher, A. Liberati, J. Tetzlaff, D. G. Altman, and P. Group, "Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement," PLoS med, vol. 6, no. 7, p. e1000097, 2009.

2. CHAPTER 2 (ARTICLE 1) BACKGROUND AND LITERATURE REVIEW[1]

Overview

Post Traumatic Stress Disorder (PTSD) is a prevalent psychiatric condition that is associated with symptoms such as hyperarousal and overreactions. Treatments for PTSD are limited to medications and in-session therapies. Assessing heart responses to PTSD has shown promise in detecting and understanding the onset of symptoms. To extract statistical and mathematical approaches that researchers can use to analyze heart rate data to understand PTSD. A scoping literature review was conducted to extract heart rate models. Five databases including Medline OVID, Medline EBSCO, CINAHL EBSCO, Embase Ovid, and Google Scholar were searched. Non-English studies, as well as the studies that did not analyze human data, were excluded. 54 articles that met the inclusion criteria were included in this review. We identified four categories of models: descriptive time-independent output, descriptive/time-dependent output, predictive/time-independent output, and predictive/time-dependent output. Descriptive/time-independent output models include Analysis of Variance (ANOVA) and first-order exponential; descriptive time-dependent output includes classical time series analysis and mixed regression. Predictive time-independent output models include machine learning methods and analyzing heart rate-based fluctuation-dissipation theory. Finally, predictive time-dependent output includes time variant method and nonlinear dynamic

[1] Reprinted with permission from "Towards a taxonomy for analyzing heart rate as a physiological indicator of Posttraumatic Stress Disorder: systematic review and development of a framework" by Mahnoosh Sadeghi, Farzan Sasangohar, Anthony D McDonald, 2020, JMIR Mental Health 7(7), e16654. (See Appendix A for the copyright permission)

modeling. All of the identified modeling categories have relevance for PTSD, although modeling selection is dependent on the specific goals of the study. Descriptive models are well-founded for inference about PTSD. However, there is a need for additional studies in this area that explore a broader set of predictive models, and other factors (e.g., activity level) that have not been analyzed with descriptive models.

2.1. Introduction

Post-Traumatic Stress Disorder (PTSD) is a psychiatric condition that develops as a result of experiencing injury, severe psychological shocks, and other trauma [1]. Individuals with PTSD suffer from the recall of traumatic experience and often develop depression, anxiety, emotional instabilities, and suicidal thoughts [2]. Recent reports suggest that individuals with PTSD are about 5 times more likely to commit suicide than individuals without PTSD [3]. Approximately 10% of American women and 4% of men experience PTSD in their lifetime [4]. PTSD is an endemic disorder among veterans as well—affecting between 17% to 24% of veterans from recent conflicts [5].

While an alarming number of individuals are afflicted with PTSD, there are significant barriers to care delivery [6,7]. These barriers include shortage of qualified clinicians and understaffed mental health clinics, geographical constraints to access mental health facilities, financial obstacles, and cultural factors such as the social stigma and limited capabilities in objective diagnosis (currently limited to self-reported measures such as the PTSD Checklist [PCL-5]) [8]. Studies have shown that self-management and factors such as positivity directly affect PTSD symptoms and ease in dealing with them [9]. Mobile health apps (mHealth) have shown promise to facilitate

self-management (e.g., education, mindfulness, and self-assessment) and have the potential to facilitate direct communication between people who have PTSD and their health care providers [10]. mHealth apps deployed on wearable devices (e.g., smartwatches) that are equipped with an array of physiological sensors (e.g., heart rate) may also enable remote continuous monitoring of signs and symptoms of PTSD. Indeed, recent efforts have shown promising application of watch-based heart rate sensors to detect the onsets of PTSD hyperarousal events [11].

Despite the recent work, the extent of knowledge on the physiological reactions to PTSD and, in particular, Heart Rate (HR) is limited and work is needed to better understand changes to HR associated with PTSD. Few models (e.g., Analysis of Variance, regression analysis) have been developed to relate changes in heart activity to disorder states. In particular, given the opportunity to collect HR data non-intrusively, it is important to use appropriate mathematical and statistical methods to ensure the accumulation of convergent knowledge in this field and to characterize and understand heart rate in terms of PTSD. In this article, we document the findings from a review of the current literature on measures and models used in various domains to analyze HR data. In addition to summarizing and synthesizing the HR analysis methods, we provide an evaluation of methods for applications relevant to PTSD detection and diagnosis.

2.2. Methods

2.2.1. Search Strategy

A scoping review was conducted using the strategies outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology

[12]. The scoping review approach was selected because it is effective for knowledge evaluation and gap identification [13]. The review spanned five main databases: (1) Medline OVID, (2) Medline EBSCO, (3) CINAHL EBSCO, (4) Embase Ovid and (5) Google Scholar. Search terms included: “heart*”, “pulse*”, “Heart Rate*”, “model*”, “heart beat*”, and “analysis*”. All studies published in or after the year 2000 were included. This search was supplemented by secondary search of cited articles in the results. The search was completed on January 15th, 2020.

2.2.2. Study Selection, Inclusion, and Exclusion Criteria

Abstracts were reviewed for relevance and articles that did not discuss heart rate related measures in detail and did not provide/use quantitative methods for analysis were excluded. Other exclusion criteria were non-English articles and articles that assessed non-heart-based physiology measures such as skin conductance and blood pressure. Further, studies that did not analyze human physiology were excluded. The inclusion criteria were all articles that discussed human heart rate analysis. Our initial search yielded 1,905 results. After removing duplicate articles and checking for eligibility using Rayyan (a web application for assisting literature reviews), 270 articles were further reviewed. Out of the 270, 138 were exclusively about non-heart-based measures reactions, 67 did not focus on human physiology, and 11 had duplicated content. 54 articles from the search were included in this review based on their relevance to the topic.

Further, the bibliography of references in each research paper was investigated thoroughly (backward search) to identify pertinent articles, and then Google Scholar

searches (forward search) were conducted to find the full text. Figure 1 shows the PRISMA flow chart for the article selection process.

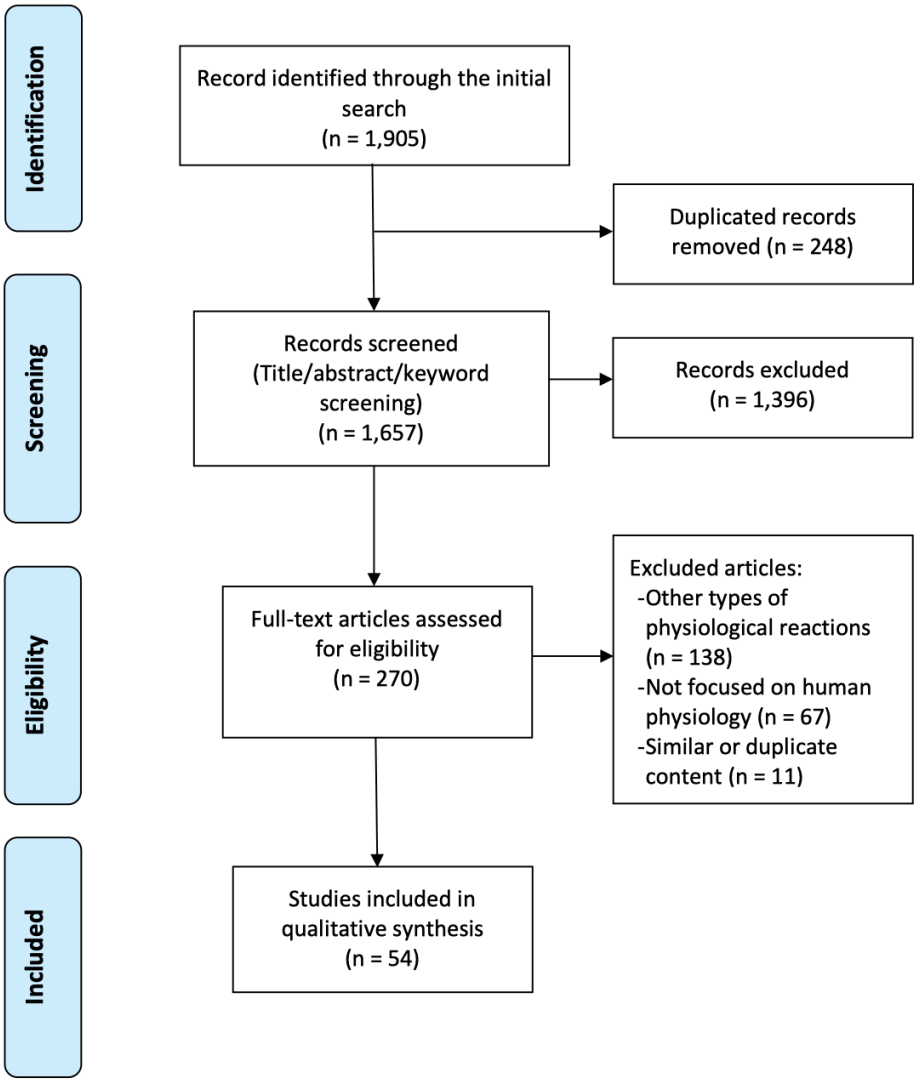

Figure 2.1. PRISMA flow chart for the literature review. Reprinted with permission from [136]

2.3. Results and Discussion

We listed the articles identified by the search process into two categories based on our synthesis: studies of the effects of PTSD on heart physiology and quantitative

modeling techniques for heart data. We further partitioned studies of PTSD effects into two types: (1) studies that investigate the effect of PTSD on heart rate variability and (2) studies that explore the effect of PTSD on heart rate. The literature on models can be further classified by the model's focus on describing versus predicting data, and the model output. These categories and sub-divisions are discussed in the following sections.

2.3.1. Effects of PTSD on Heart Rate Variability

Heart rate variability (HRV) measures variations in heartbeats and is related to the electrical activity of the heart [14]. Common frequency domain analysis metrics for HRV include: High Frequency (HF), Low Frequency (LF), the ratio of LF to HF (LF/HF), Coherence Score (COH), the Root Mean Square of Successive Differences between normal heart beats (RMSSD), and the Standard Deviation of the interbeat interval of Normal sinus beats (SDNN) [15–18]. LF and HF are frequency bands of HRV that tend to correlate with parasympathetic nervous system activity. LF is the frequency activity in the range of 0.04–0.15Hz and HF is the activity in the range of 0.15–0.4Hz. The quantified relative intensity of these measures is referred to as power [1] and such power is obtained by applying power spectral and frequency domain analyses [19].

The reviewed articles found that PTSD causes sustained changes in Autonomic Nervous System (ANS) (part of the nervous system that is responsible for regulating automated functions in the body such as heart activity) [20]. The ANS consists of Parasympathetic Nervous System (PNS)—which regulates blood pressure and breathing rate during rest, and the Sympathetic Nervous System (SNS)—which adjusts blood

pressure and heart rate during activity. Heart activity is representative of the performance of these systems [21]. Various effects of PTSD on ANS have also been documented. Higher heart rate levels indicate lower heart rate variability and are linked to increased rates of mental stress and physical activity [22,23]. PTSD as a particular type of anxiety disorder also disturbs HR and HRV. Heart rate variability has been studied widely in the literature to assess PTSD (e.g., [18,24–26]). Evidence suggest that individuals with PTSD have lower resting HRV than individuals without PTSD when other factors (age, gender, and health level) are controlled [27]. According to Nagpal et al.'s [1] metareview, HF, a measure for the parasympathetic activity of ANS, is significantly lower in individuals with PTSD than individuals without PTSD (~0.6ms2). However, LF which assesses both sympathetic and parasympathetic activity of the ANS is slightly reduced in individuals with PTSD (~0.2 ms2). This results in a significant increase in LF/HF individuals with PTSD [1,28–30].

RMSSD and SDNN are time domain measures of HRV. SDNN is an index for SNS activity [24]. SDNN is decreased in individuals with PTSD compared to healthy individuals (~6.7ms) showing an increase in sympathetic activity [1,31]. In addition, decreased levels of RMSSD was observed among individuals with PTSD (~7.5ms) that suggests lower vagal activity in this population [1,31].

Although HRV analysis is common among studies of anxiety [32], some factors need to be considered when HRV measures are used. First, studies show that HRV is dependent upon heart rate and cannot be analyzed independently to represent the ANS activity [32,33]. In addition, prior research has linked high HRV to pathological

conditions related to heart deficiencies [32]. For instance, diseases such as atrial fibrillation increase HRV and HR, and are associated with higher mortality rates [34]. Hence, higher rates of HRV do not always indicate abnormal mental state. Ideally, measurements should take into account patient's comorbidities such as heart deficiencies in addition to subjective (e.g., self-reported scales) and objective (e.g., HRV, ECG) methods [35]. Gender, health , age, and heart rate also affect HRV, and they need to be considered as covariates when HRV measures are used [24]. Aging decreases HRV time domain features such as SDNN [36,37]. HRV time domain features increase by improved health conditions [38,39]. LF and SDNN are also lower in females than in males; however, HF parameter of HRV is greater in women than in men [40]. Higher heart rate levels are also associated with decreased HRV [41], because when the heart beats faster, beat to beat intervals are smaller. Other factors such as climate, job satisfaction, lifestyle, and medications can also affect HRV and should be considered as an influential factor when HRV is analyzed [42].

2.3.2. Effect of PTSD on Heart Rate

Heart Rate (HR) is the count of heartbeats per 60 seconds. Normal heart rate differs among individuals based on age and gender, health level, and respiratory activity [43]. Both HR and HRV are modulated by ANS [44]. As the SNS activates, PNS activity decays; therefore HR increases and HRV decreases [45]. As a result, there is an inverse relationship between HR and HRV [33].

PTSD can affect heart rate (HR) in two modalities: resting, and fluctuation tone [1,46–48]. Studies suggest that resting heart rate can be between 5 to 6.6 beats higher in individuals with PTSD than individuals without PTSD depending on the type of population (e.g., veteran, civilian) [49–51]. For example, resting HR is roughly 5 beats per minute higher in civilians with PTSD than civilians with no PTSD, and this number increases to 6.6 beats per minute difference in the veterans population [51,52]. In the non-resting state, evidence suggests that heart rate increases in the exposure of PTSD stressors [1].

Another heart rate measure that has been investigated in terms of PTSD is heart rate fluctuations (changes in heart rate levels) in the presence of stimuli [53]. There are conflicting findings on the comparison of this measure between individuals with and without PTSD. While the study by [54] show that heart rate changes are higher in people with PTSD than people without PTSD, [55] claims the opposite.

Heart rate models

Based on our synthesis of the existing literature, we categorized mathematical models of heart rate into descriptive and predictive models, both of which could provide insight relevant to understanding the psychophysiological responses to PTSD. Descriptive methods can be used to describe and make inferences about a dataset, while predictive ones can be applied to forecast trends and patterns in the data. Predictive and descriptive models can be further characterized by their type of output—time-independent or time-dependent (Figure 2). Time-dependent outputs use time as one of the descriptive variables to analyze the dependent variable(s) or output(s). Time-

independent output, however, does not depend on time and does not change over time. While the models reviewed below are summarized and synthesized for relevance to PTSD-related analysis, these methods are not limited to PTSD and anxiety disorder domains.

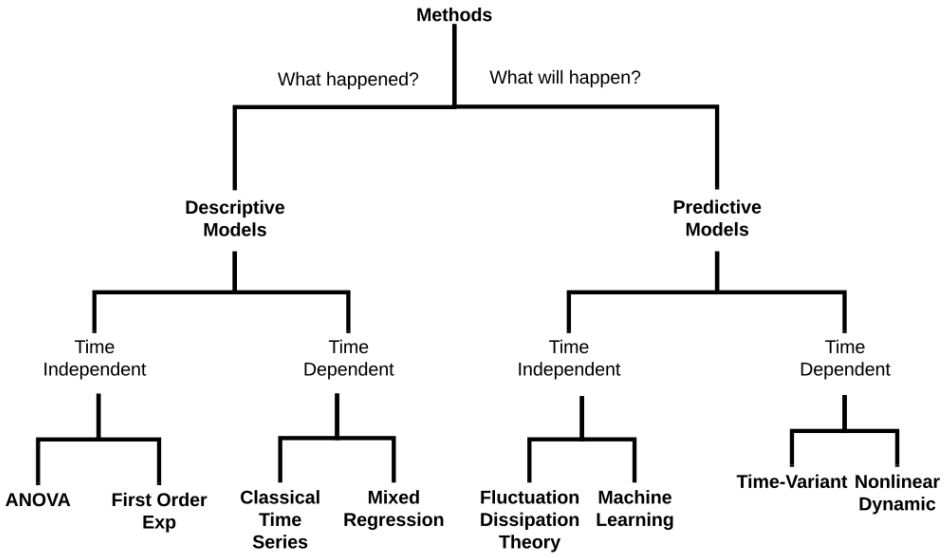

Figure 2.2. Taxonomy of heart rate analysis methods. Reprinted with permission from [136]

2.3.3. Descriptive Models

2.3.3.1. Time-independent output

Analysis of Variance (ANOVA)

Linear regression, and in particular ANOVA, is a statistical model used for analysis of HR in several articles (Table 1). ANOVA can be used to compare HR trends, and group means in experimental studies [56,57]. Studies used ANOVA to account for the effectiveness of treatments in individuals with PTSD as measured by HR [58]. Some

studies chose ANOVA as their method of analysis to show that resting heart rate is higher in individuals with PTSD than individuals without PTSD [57]. For example, the study by Gelpin et al. [59] compared the resting HR in individuals pre- and post-treatment to measure the success of therapy sessions. Buckley et al. [52] used ANOVA to compare resting HR in PTSD patients with that of healthy controls, finding that PTSD patients, in general, have significantly higher resting HR levels (~6 beats per minute difference). While using ANOVA for the analysis of time-independent HR data, it is limited in several respects. ANOVA has strong assumptions and is ill-suited to model-dependent measures with strong temporal correlations. For instance, independency of observations is one of the main assumptions of ANOVA; however, consecutive heart rate real time-based data is a highly correlative type of data. Thus ANOVA should not be used to make time-based HR predictions [60].

2.3.3.2. First-order exponential model

A first-order exponential model provides a function with a sustained growth or decay rate [61]. In terms of heart rate analysis, first order exponential models have been used to generate a nonlinear regression model for HR based on Heart Rate

Recovery (HRR) [62]. Heart Rate Recovery (HRR) is an indicator of vagal reactivation and SNS deactivation [63].

Bartels-Ferreira et al. [63] used first order exponential method to measure postexercise time-independent HRR based on heart rate decay curves. Recovering from the onset of PTSD symptoms is associated with activation of vagal tone and withdrawal of SNS activity, both of which are correlated with HRR [64]. While this method shows

promise in assessment of heart rate fluctuations associated with PTSD, the reviewed literature (Table 1) examined ANS in the context of physical acitivity and HR decay after activity was curve fitted by a first order exponential function ([63]). In this case the goodness of fit was moderate (R2~0.65), which warrants additional research. Another limitation associated with this method is that the exponential functions show erroneous patterns for very small (30-second) and very large (600-second) time windows [61]. For instance, Bartels-Ferreira et al. [63] found that the least goodness of fit was for the smallest time window which was 30 seconds (r^2=0.42). Conversely, when the length of the window of time is a moderate number (~360 seconds) a relatively better goodness of fit was obtained (~0.69). This shows that HRR curve fitted by first order exponential models performs better (higher R2) when windows of times are neither too big nor too small. Table 1 shows a summary of articles that studied descriptive models with time-independent output. In this table, domain is the field of the study. Independent variables are factors that are controlled by researchers, and dependent variable are dependent on them. “Independent Variables” are used to describe/classify dependent variable.

Table 2.1. Results studies that used descriptive models with time-independent output. Reprinted with permission from [136]

Method	Authors	Domain	Independent Variables	Dependent Variable
ANOVA				
	Shalev et al. (1998) [57]	PTSD	Gender, age, heart rate, trauma history, event security	HR
	Strath et al. (2000) [65]	Physical Activity	Heart rate, Oxygen intake, age, fitness	HR
	Romero-Ugalde et al. (2017) [66]	Physical Activity	Accelerometer, energy expenditure, heart rate	HR
	Khoueiry et al. (2012) [67]	Medical	Heart rate, hospitalization duration, age	HR
	Tonhajzerova et al. (2012) [68]	Physiology	Resting HR, Major depressive disorder	HR
First order exponential				
	Bartels et al. (2015) [63]	Physical activity	Heart rate peak, resting heart rate, heart rate recovery	HR Variation

2.3.3.3. Time-dependent output

Classical time series analysis

Classical time series analysis is a common statistical method that can analyze time-dependent data trends by looking into linear relationships. Classical time series analysis is also a promising method for analyzing HR and HR fluctuations since these measures are time-based [69,70].

Peng et al. [70] applied time series analysis to look into longterm correlation within heart rate data and its relation to heart diseases such as cogestive heart failure. Using this method, the authors showed that there is some independency between beat to beat HR fluctuations in healthy people that does not exist in cardiovascular disease patients. The findings further suggest that classical time series analysis is a promising direction for PTSD hyperarousal analysis because similar HR changes have been

documented in PTSD patients compared to healthy people in the presence of stimuli [71].

Beyond the analogous use case, classical time series has several benefits compared to ANOVA. Since the model explicitly considers autocorrelation, it does not require the assumption of independence of observations [72]. The models also have predictive capability and are well validated for illustrating trends and forecasting [73]. However, one drawback of this method is the stationary assumption (constant mean value of the series), which is not always reasonable in HR data (e.g., when data is collected before and during exercise).

Mixed regression model

Mixed regression analysis has been used in the literature to evaluate physiological responses to energy expenditure [74]. This type of modeling can be applied with correlated observations. Thus, it is beneficial for psychophysiology analyses that need to account for individual similarities in responses that make these reponses correlated [60]. Multiple regression typically proceeds in a stepwise process with a focus on identifying two main effects: the population-fixed effect and the random effect. The population effect explains similarities in the dataset (for instance HR), while random effect represents the differences among observations (the error term). For instance, Gee et al. [75] used respiration as a random effect to estimate heart rate and ultimately predict episodes of bradycardia in infants. Using mixed regression method and accounting for respiration as a covariate in this case has increased accuracy of the measured heart rate by 11%.

The ability of mixed regression models to account for individual differences makes them an advantageous choice for modeling PTSD. Several studies have identified significant individual differences in people with PTSD [1,57,76,77]. Specifically, HR and heart rate variability levels are significantly affected by individual differences such as age, general health, and gender [24].

This type of modeling might produce similar results to ANOVA in many cases. However, in comparison with ANOVA, mixed regression models are more effective for datasets with missing values and multiple random effects [78]. This is important since in real world and naturalistic studies, datasets with high rates of missing values are common and can be challenging to deal with [79]. For comparison of time-dependent output methods, see Table 2.

Table 2.2. Results from studies that used descriptive models with time-dependent output. Reprinted with permission from [136]

Method	Authors	Domain	Independent Variables	Dependent Variable
Classical time series				
	Chen et al. (2016) [69]	Healthcare (patient data)	HR, resting heart rate	Heartbeat
	Kazmi et al. (2016) [33]	Physiology	HR, HRV, time	Heart rate
	Zakeri et al. (2012) [80]	Physical activity	Heart rate, energy expenditure, accelerometer, age	Energy expenditure
	Peng et al. (1995) [70]	Medical	Heart rate, heartbeat, time	Heart rate
Mixed regression				
	Gee et al. (2017) [75]	Biomedical	Heart rate, heartbeat, respiration, time	Heart rate
	Bonomi et al. (2015) [81]	Physical activity	Heart rate, energy expenditure, photoplethysmographi, accelerometer	Heart rate
	Xu et al. (2015) [82]	Physical activity	Heart rate, energy expenditure, different training paradigms, age, height, weight	Energy expenditure

2.3.4. Predictive Models

2.3.4.1. Time-independent output

Machine learning methods

Machine learning methods refer a set of training and predictive algorithms that use data to learn complex trends assoicated with labels (e.g., symptom presence) in a dataset. Machine learning analysis is a multiple step process consisting of dividing a dataset into training and testing data (or leveraging re-sampling techniques such as cross-validation), developing a model from the training data, and evaluating the model on the testing data. This approach is advantageous relative to approaches that use all of the data for training a model (e.g., ANOVA) and approximate metrics to evaluate generalizability (e.g., Adjusted R^2). Furthermore, the ability of machine learning algorithms to identify complex patterns in datasets make them a promising approach for analyzing physiological data that is often noisy[cite the review paper on HRV etc. for stress].

The success of applying machine learning methods depends on the data used to train and evaluate the algorithm. Machine learning algoriths typically require large training sets—several thousand observations—and they implicitly assume that the data and assoicated labels are of equal quality. In cases where the data is noisy or labels are unreliable, machine learning training algorithms may fail to converge to a generalizable solution. Further, if the training data examples are biased (e.g., non-representative population samples) the machine learning algorithms trained on the data may also be similarly biased. It is often difficult to identify these issues through standard training and

testing processes of machine learning algorithms, thus machine learning analyses should be accompanied by descriptive analyses to obtain better understanding of the data and potential errors or bias [83].

Most of the reviewed studies used heart rate variability along with machine learning algorithms to predict the stress level in individuals [84–86]. Machine learning studies evaluating HR primarily have focused on energy expenditure[87,88]. One exception is McDonald et al. [11] who evaluated several machine learning algorithms—neural networks, decision trees, support vector machines, convolutional neural networks, and random forests—to predict the onset of PTSD symptoms for the veteran population. This study used heart rate data with 1HZ frequency (1 observation per second) as the input of these algorithms. While the raw 1Hz data was used to train the neural network-based models, additional feature generation and selection was performed before training the decision tree, support vector machine, and random forest algorithms. This feature generation identified linear trends, Fouier Transforms, and change quantiles as relevant features for PTSD symptom onset detection. Among all machine learning methods, support vector machines and random forest algorithms performed best (i.e., had the highest area under the Receiver Operating Characteristic (ROC) curve: 0.67). While machine learning shows promise for inferential analysis of HR data for PTSD research, explaining the purpose of machine learning componenets may be difficult, and often predictive results have limited rational explanation [89].

Fluctuation-dissipation theory

Fluctuation-dissipation Theory (FDT) is a common approach in thermodynamics that is used to predict system behavior by breaking the system responses into small forces [90]. This theorem that follows thermodynamic rules can model heart rate response after stress moments.

Chen et al. [91] used FDT to predict patients' HR reactions to pre- and post-spontaneous breathing trial treatment. They used this method to divide the system (in this case, treatment process) into different phases, including pre-treatment, mid-treatment, and post-treatment. After breaking the entire treatment process to these small phases, each phase was modeled separately. The reactions to treatments in each phase were modeled with HRR measures. All models were then combined to make the final comprehensive model. Chen et al. [91] found that thermodynamic rules can also model HR response after stress moments. This is because of the similar effect of stress and spontanous breathing trials on organs (common clinical procedure used to assess ventilation performance of patients). These researchers suggest dividing the system into pre and post stress moments, modeling each phase and finally assembling a model for final prediction. They further suggest that the HRR extracted from this type of modeling can be used to personalize care as HR can be remotely monitored through noninvasive hospital devices.

In terms of mathematical concepts, this type of modeling has a powerful predictive capability by grouping individuals and therefore minimizing error rate [91]. This approach requires significantly less data than other methods such as time-variant modeling of heart rate. Hence, it enables researchers to include more variables in their

model. Moreover, Chen et al. [91] claim that while models that use Gaussian functions have around 65% error rate to predict patients' response to spontaneous breathing trial, implementing FDT decreases this error rate by over 10%. Therefore, this approach provides more accurate results than methods that use Gaussian function such as some machine learning algorithms (e.g., ANFIS). A potential reason for this could be that by using FDT the system is broken down into smaller pieces where each part has its own specific and defining features. However, in ANFIS the system was considered as a whole, and a set of features was defined for the entire system overlooking dissimilarities within the system. Also, unlike most of the statistical approaches that make assumptions about the data, this method is assumption-free and is considered more robust to assumptions (e.g., normality of residuals, independency of measurements). Despite its promising application to anaylsis of HR and the lack of restrictive assumptions, FDT is computationally intense. This means that the model needs a high levels of proficiency in understanding mathematics and statistics behind FDT. Esepcially in comparison to approaches such as ANOVA, classical time series and mixed regression using this approach requires higher levels of domain knowledge. For example studies in machine learning and FDT methods, see Table 3.

Table 2.3. Results from example studies that used predictive models with time-independent output. Reprinted with permission from [136]

Method	Authors	Domain	Independent Variables	Dependent Variable
Machine learning				
	Kolus et al. (2016) [87]	Biomedical (Energy expenditure)	Heart rate, oxygen consumption, work rate	Work Rate
	McDonald et al. (2019) [11]	PTSD	Heart rate, subjective stress moments	Stress moment
	Healey et al. (2005) [86]	Driving	Heart rate, HRV, skin conductance, muscle activity, Muscle tension, breathing rate	To detect stress
	Kolus et al. (2016) [88]	Physical activity	Heart rate, Max heart rate, oxygen consumption, body type, work rate	Work rate
	Zhang et al. (2012) [92]	Physical activity	Heart rate, body attitude information, body movement	HR

Table 2.3. Continued.

Method	Authors	Domain	Independent Variables	Dependent Variable
Fluctuation-dissipation Theory				
	Chen et al. (2013) [91]	Healthcare	Hear rate recovery, blood pressure, instantaneous heart rate	HR

2.3.4.2. Time-dependent output

Time-variant modeling

Time-variant modeling is a mathemathical approach used to analyze time-dependent datasets, and provides time-dependent output. Time-variant models of HR can generate heart rate recovery measures in real time. Some studies suggest that measuring heart rate recovery in real time can especially help assess arousals and arousability in different individuals in response to mental stressors [93]. This shows promise for PTSD research given its potential to enable the comparison between the effect of internal stimuli (stressors generated through memory) to external stimuli (stressors generated from the environment) on PTSD patients' arousability.

Although time-variant modeling has been replicated in the literature and has showed promise in analyzing heart rate data [33,94], it is computationally intense. The process of solving the equations within the model includes defining multiplex matrices for each variable, which is time- and space-consuming. Moreover, time-variant modeling

requires large datasets of high frequency (e.g., 100 Hz) HR data which is often not feasible for real-time data collection instruments such as wearable devices which record continuous data for large windows of time (e.g., more than 30 minutes).

Nonlinear dynamic modeling

Nonlinear dynamic modeling of HR consists of depicting HR as the output of a non-linear dynamic system [95].

Nonlinear dynamic modeling of HR can be a promising method to assess arousal patterns by measuring SNS activity [96]. Hence, this approach may be useful for analyzing PTSD hyperarousal patterns since they are associated with SNS activity. Despite the advantages of this model, it requires high-frequency HR data (e.g., 100 Hz) or even instantaneous HR [96]. Instantaneous HR is an HR measure derived from HRV, which is different from raw HR measured by wearable devices. Instantaneous HR can be extracted from multiplying RR intervals by the number 60 and needs to be measured with high frequency (>250HZ), whereas smart watches collect heart rate data with much lower frequency (<5HZ) [96].

This model accounts for the natural nonlinearity and time-dependent features of heart rate data. Also, the learnability and predictability of this method can help detect the onset of symptoms in PTSD patients. A limitation of this method to characterize PTSD aspects is the assumption of invertibility [97]. This assumption indicates that all the variable matrices used in equations are required to be invertible. In many cases, and mainly in non-laboratory settings, this assumption cannot be met [97]. Moreover, these methods are relatively slow and more intense computationally compared to other

methods like machine learning (for both training and testing the model) because they involve solving multiple complex mathematical equations [66]. For examples of predictive models with time-dependent output, see Table 4.

Table 2.4. Results from studies that used predictive models with time-dependent output. Reprinted with permission from [136]

Method	Authors	Domain	Independent Variables	Dependent Variable
Time-variant				
	Lefever et al. (2014) [94]	Sports science - biomedical	Heart rate, participants' input power, road gradient,	HR Variation
	Olufsen et al. (2013) [98]	Biology, Healthcare	Heart rate, resting heart rate, blood pressure	Heart rate regulations
Nonlinear-dynamic				
	Chen et al. (2016) [69]	Healthcare (Patient data)	Resting HR, ABP (Arterial Blood Pressure), heart rate, heart rate variability	Heart Beat
	Kazmi et al. (2016) [33]	Biophysics	Human normal sinus rhythm (NSR), human Congestive heart rate failure (CHF)	HRV (they look at the correlation)

2.3.5. Descriptive Framework Based on the Summary of Findings

We categorized methods used to analyze heart rate data in to two categories: descriptive and predictive. In the context of PTSD, descriptive models may be used to characterize PTSD triggers and the factors that affect their occurrence, whereas predictive models may be useful to predict PTSD onset to facilitate timely intervention. The extracted models provide methods of evaluating, describing, comparing, interpreting and understanding patterns in the HR data. However, interpreting the data in a meaningful way depends on the specific objectives of the study. The data at hand can be analyzed with one or multiple of the reviewed models based on the goal of the study and the assumptions of models. Each model corresponds to the distinct type of output and different interpretation of the data with different assumptions. Based on the process of data collection, number of observations, and variables in the data, researchers might choose one or a combination of models provided. Table 5 provides a framework for choosing a model based on the limitations, assumptions, and features of each model and the data at hand. Further, table 5 represents the articles that used a specific method.

Table 2.5. Descriptive framework for the HR-related analysis methods extracted from the literature. Reprinted with permission from [136]

Model	Assumptions	Features	Limitations	Cases
Descriptive, time-independent output				
Analysis of Variance (ANOVA)	• Normal distribution of residuals • Constant variance of populations • Independence and identically distributed observations	• Capable of comparing groups and looking at trends • Computationally simple	• Restrictive assumptions • Type 1 error • Just applicable to linear analysis	[65], [66], [67], [47], [57],[52],[58] ,[59], [53],[68],[54] ,[99], [100],[101],[1 02]
A first-order exponential model	• Continuous observations • Observations should be identical (e.g., no age, gender difference) • Environmental effects are constant	• Easy to apply and learn • Gives higher weights to recent observations	• Not repeated in studies • Higher error rates than classical time series and mixed regression • Does not show trends • Not accurate for very small and very large windows of time	[63]

Table 2.5. Continued

Model	Assumptions	Features	Limitations	Cases
Descriptive, time-dependent output				
Classical time series analysis	• Stationary observations (constant mean values of series)	• Advantageous for analyzing time-based trends • Does not require independence of data points • Used in the literature to analyze cardiovascular disease • Includes linear and nonlinear analysis	• Requires stationary datasets	[69], [33], [80], [70]
Mixed regression model	• Normality of residuals distribution	• Accounts for differences between individuals (e.g., age, gender), • Can be used for analyzing repeated measures • Can be applied to non-normal data	• Cannot be used for nonlinear models	[75], [81], [82], [66], [103], [80], [50], [67], [104], [105],[106],[107]

Table 2.5. Continued

Model	Assumptions	Features	Limitations	Cases
Machine learning methods	• Limited dependencies of the observations (each machine learning algorithm has its assumptions that need to be checked)	• Proactive algorithm (can be used for action-reaction type of datasets) • Powerful predictive method • Rapid analysis prediction, and processing, • Simplifies time-intensive computations	• Can over fit-under fit data • Cannot be applied to datasets with highly dependent variables • The process has little rational explanation	[88], [87], [11], [92], [86],[108],[109],[110]
Fluctuation-dissipation theory	• Equilibrium system (the system and observations are not changing)	• Powerful predictive capability, • Does not have restrictive assumptions such as normality of residuals • Significantly less data needed compared to general data fitting approach	• Computationally intense • Time-consuming	[91], [70], [111]

Table 2.5. Continued

Model	Assumptions	Features	Limitations	Cases
Predictive, time-dependent output				
Time-variant modeling	• Requires big datasets with high-frequency data points (more than 60 HZ)	• Can be used to describe data as well as forecasting the future	• Computationally intense • Slow process	[33], [112], [94], [113], [98], [114], [96], [115], [116],[93]
Nonlinear dynamic modeling	• Invertible matrices	• Very accurate • Replicated multiple times in studies	• Computationally intense • Slow process • Requires invertible matrices that is not always feasible in naturalistic settings	[66], [33], [113], [117], [98], [96], [112], [118], [116], [104], [119], [120], [121]
Model	Assumptions	Features	Limitations	Cases
Descriptive, time-independent output				
Analysis of Variance (ANOVA)	• Normal distribution of residuals • Constant variance of populations • Independence and identically distributed observations	• Capable of comparing groups and looking at trends • Computationally simple	• Restrictive assumptions • Type 1 error • Just applicable to linear analysis	[65], [66], [67], [47], [57], [52], [58], [59], [53],[68],[54],[99],[100],[101],[102]

Table 2.5. Continued

Model	Assumptions	Features	Limitations	Cases
A first-order exponential model	• Continuous observations • Observations should be identical (e.g., no age, gender difference) • Environmental effects are constant	• Easy to apply and learn • Gives higher weights to recent observations	• Not repeated in studies • Higher error rates than classical time series and mixed regression • Does not show trends • Not accurate for very small and very large windows of time	[63]
Descriptive, time-dependent output				
Classical time series analysis	• Stationary observations (constant mean values of series)	• Advantageous for analyzing time-based trends • Does not require independence of data points • Used in the literature to analyze cardiovascular disease • Includes linear and nonlinear analysis	• Requires stationary datasets	[69], [33], [80], [70]

Table 2.5. Continued

Model	Assumptions	Features	Limitations	Cases
Mixed regression model	• Normality of residuals distribution	• Accounts for differences between individuals (e.g., age, gender), • Can be used for analyzing repeated measures • Can be applied to non-normal data	• Cannot be used for nonlinear models	[75], [81], [82], [66], [103], [80],[50], [67], [104], [105], [106], [107]
Predictive, time-independent output				
Machine learning methods	• Limited dependencies of the observations (each machine learning algorithm has its assumptions that need to be checked)	• Proactive algorithm (can be used for action-reaction type of datasets) • Powerful predictive method • Rapid analysis prediction, and processing, • Simplifies time-intensive computations	• Can over fit-under fit data • Cannot be applied to datasets with highly dependent variables • The process has little rational explanation	[88], [87], [11], [92], [86], [108], [109], [110]

Table 2.5. Continued

Model	Assumptions	Features	Limitations	Cases
Fluctuation-dissipation theory	• Equilibrium system (the system and observations are not changing)	• Powerful predictive capability, • Does not have restrictive assumptions such as normality of residuals • Significantly less data needed compared to general data fitting approach	• Computationally intense • Time-consuming	[91], [70], [111]
Predictive, time-dependent output				
Time-variant modeling	• Requires big datasets with high-frequency data points (more than 60 HZ)	• Can be used to describe data as well as forecasting the future	• Computationally intense • Slow process	[33], [112], [94], [113], [98], [114], [96], [115], [116], [93]

2.3.6. Fit Assessment

Fit assessment can be conducted to examine the efficiency of each method in modeling a specific dataset. Fit assessment is especially promising for comparing different methods if they are applied to the same dataset. However, considering the wide range of applicable fit indices, researchers might struggle comparing them. In the category of descriptive models, R^2 and adjusted R^2 are the main indices of fit

assessment. R^2 indicates the degree of variation in the dependent variable caused by the independent variable(s). Adjusted R^2 is a revised version of R^2 that accounts for the number of independent variables in a model [122]. Generally, adjusted R^2 is more promising than R^2 as it is more robust to overfitting [122]. In the prediction methods category, a variety of measures other than R^2 and adjusted R^2 were used to assess quality of fit. Some of these measures include sensitivity, specificity, accuracy, and Area Under the Receiver Operating Characteristics Curve (AUC)-ROC. Sensitivity is the number of true positives divided by the total number of observations and specificity is the number of true negatives divided by the total number of observations [123]. Accuracy is the number of true predictions divided by total number of predictions. Error rate is 1 minus accuracy or the number of wrong detections divided by the total number of observations [124]. Finally, AUC-ROC is a curve that plots true positive rate (Y axis) vs false positive rate (X axis) to measure the performance of the model. It is important to bear in mind that fit indices are data dependent; therefore, comparisons are best made by fitting multiple models to the same dataset.

In statistical analysis of data in the PTSD domain, fit assessments have been used to show the efficiency of results. For instance, McDonald et al. [11] used ROC curves along with accuracy to show that random forest works better than other machine learning methods to predict hyperarousal moments in people with PTSD. Shalev et al. [125] used sensitivity and specificity to predict development of PTSD based on their instant responses to trauma. Bartels et al. [63] applied adjusted R^2 to assess the goodness of fit

for their proposed exponential model. Examples of fit adjustments are summarized in Table 6.

Table 2.6. Examples of fit assessment for different methods used in studies. Reprinted with permission from [136]

Study	Method	Variables	Fit measure
Strath et al. (2000) [65]	ANOVA	Heart rate, oxygen intake, age, fitness	R^2=0.87
Zakeri et al. (2012) [80]	Classical time series	Heart rate, energy expenditure, accelerometer, age	R^2=0.84
McDonald et al. (2019) [11]	Machine learning	Heart rate, subjective stress moments	AUC (area under receiver operating characteristics curve) = 0.67
Healey et al. (2005) [86]	Machine learning	Heart rate, HRV, skin conductance, muscle activity, muscle tension, breathing rate	Accuracy=97%
Chen et al. (2013) [91]	Fluctuation dissipation theory	Hear rate recovery, blood pressure, instantaneous heart rate	Error rate= 25%
Chen et al. (2016) [66]	Nonlinear dynamic	Resting HR, ABP (Arterial Blood Pressure), heart rate, heart rate variability	Sensitivity: 0.941 Predictability: 0.988

2.3.7. Methodological Considerations for Heart Rate Assessments

The models identified in this review represent several promising directions for future exploration, but they also illustrate a hidden complexity in the use of HR data as model input. HR is impacted by individual charactristics including age, sex, health, resting HR, respiration, and lifestyle [24]. Maximum HR typically decreases with age. Females have higher HR levels than men [126]. Athletes have lower HRs levels than sedentary people [127]. Resting HR is lower in more active people, and lower resting heart rates result in lower HR levels [128]. Since the respiratory system affects heart activity, studies suggest that incorporating respiration as a factor in HR models improves HR estimation significantly [78]. Lifestyle such as smoking habits affect heart rate as well; people who smoke have higher heart rate than non-smokers [129].

Beyond these general characteristics, it is important to consider the type of physical activity in the analysis. Physical activity significantly affects HR [130], where high-intensity activities such as running and cycling affect HR differently from low intense activities such as sitting and lying down [99]. Concerns regarding activity were common in the reviewed studies, particularly in energy expenditure domain [131]. Green et al. [131] suggest that body acceleration is a reliable indicator of physical activity and should be included in all analyses as a covariate or constraint. While activity is directly related to energy expenditure outcomes, it is also relevant for studies investigating stress. While some of the reviewed studies on stress included body acceleration in their analysis [100], many neglected this factor [46,132].

2.3.8. Heart Rate Assessments in Anxiety Domains

Heart rate data has been widely investigated in the domain of physical activity and energy expenditure. Although there are some differences between the effects of mental stress on HR and the effects of physical activity on HR, there are many similarities that make these domains connected. Physical activity affects SNS performance in the short term and PNS performance in the long term [133]. As a result, heart rate elevates during physical activities (due to SNS activation), and resting heart rate is lower in athletes who have higher rates of physical activity (because of PNS performance) [133].

Similarly, in terms of mental stress, while acute stress or immediate response to stressors activates SNS, chronic stress increases the vagal and parasympathetic activity [134]. These similarities enable researchers in mental stress domains to employ models and pathways that are extracted in physical activity domains. For instance, one main measure that is used broadly to examine energy expenditure is heart rate recovery (HRR). This measure is an accepted indicator of SNS deactivations and PNS activation. Recovering from acute stress and arousability is also associated with withdrawal of SNS and activation of PNS. As a result, HRR can be a proper measure to be considered in studies that examine acute stress.

2.3.9. Limitations

This scoping review attempted to include all articles that analyzed heart rate; however, it is still likely that some were overlooked. Further, the authors categorized the heart rate models based on their own synthesis of literature and relevance to PTSD.

These models can be listed and categorized in a variety of ways such as deterministic vs. stochastic.

Another limitation in this review is that while the identified models have been applied across various domains (e.g., energy expenditure, general stress prediction), to our knowledge only two papers [11,57] directly applied these methods to data from patients diagnosed with PTSD. In particular, only one study [11] used a predictive approach in the PTSD domain. Other studies were primarily limited to linear descriptive statistics such as the t-test or ANOVA [60,65–67]. These methods are valid for making inferences about PTSD and comparing its effects on HR among different groups. However, there is a need for additional studies in this area that explore a broader set of predictive models and other factors (e.g., activity level) that have not been analyzed with descriptive models.

Beyond the specific application of these models to PTSD, there are several more general challenges. The reviewed research often proceeded independently with few links between the various studies. This diversity makes comparison across studies difficult. Studies have used different datasets with different variables based on individual goals. Further, the reviewed work often focused on testing one specific model rather than a broad comparison. Often critical details, such as the model and parameter selection process, were not reported in the articles. Another critical detail often not addressed in the reviewed studies was the mismatch between the model requirements and the sampling rates, which may result in conditions such as overfitting [135].

Collectively these limits suggest a need for substantial additional work in modeling the relationship between HR and PTSD. Future studies should consider comparisons between several models, analyze or explicitly discuss decisions made throughout the modeling process, and comprehensively document their HR data collection. As future studies are conducted that enact these criteria, the utility of the modeling approaches identified here will become clearer, and the path to more effective PTSD treatments will become more attainable.

2.4. Conclusions

The goals of this review were to identify and characterize quantitative heart rate models for relevant applications in PTSD. One of the gaps in this area is the absence of a framework that researchers can use before, during, and after their data collection to choose a method to analyze heart rate data. In this regard, we developed a descriptive framework that can be used to determine the method to apply to heart rate data in order to achieve more efficient results. We identified four broad categories of methods: descriptive time-independent output, descriptive time-dependent output, predictive time-independent output, and predictive time-dependent output. Descriptive time-independent output models include ANOVA and first-order exponential while descriptive time-dependent output includes classical time series analysis and mixed regression. Predictive time-independent output includes machine learning methods and analyzing heart rate-based fluctuation-dissipation theory. Finally, predictive time-independent output includes time variant method and nonlinear dynamic modeling.

All of the identified modeling categories have relevance for PTSD, although modeling selection is highly dependent on the specific goals of the modeler. For instance, one might use ANOVA to look at the differences in resting heart rate in individuals with PTSD vs without PTSD [54].

2.5. References

[1]. Nagpal M, Gleichauf K, Ginsberg J. Meta-analysis of heart rate variability as a psychophysiological indicator of posttraumatic stress disorder. J Trauma Treat 2013;3(2167–1222):1000182.

[2]. Spivak B, Segal M, Mester R, Weizman A. Lateral preference in post-traumatic stress disorder. Psychol Med 1998;28(1):229–232.

[3]. LeBouthillier DM, McMillan KA, Thibodeau MA, Asmundson GJ. Types and number of traumas associated with suicidal ideation and suicide attempts in PTSD: Findings from a US nationally representative sample. J Trauma Stress 2015;28(3):183–190.

[4]. Resnick HS, Kilpatrick DG, Dansky BS, Saunders BE, Best CL. Prevalence of civilian trauma and posttraumatic stress disorder in a representative national sample of women. J Consult Clin Psychol 1993;61(6):984.

[5]. Richardson LK, Frueh BC, Acierno R. Prevalence estimates of combat-related post-traumatic stress disorder: critical review. Aust N Z J Psychiatry 2010;44(1):4–19.

[6]. Moon J, Smith A, Sasangohar F, Benzer JK, Kum H. A Descriptive Model of the Current PTSD Care System: Identifying Opportunities for Improvement. Proc Int Symp Hum Factors Ergon Health Care 2017;6(1):251–251.

[7]. Reisman M. PTSD treatment for veterans: What's working, what's new, and what's next. Pharm Ther 2016;41(10):623.

[8]. Rodriguez-Paras C, Tippey K, Brown E, Sasangohar F, Creech S, Kum H-C, Lawley M, Benzer JK. Posttraumatic stress disorder and mobile health: App investigation and scoping literature review. JMIR MHealth UHealth 2017;5(10).

[9]. Khusid MA, Vythilingam M. The emerging role of mindfulness meditation as effective self-management strategy, part 1: clinical implications for depression, post-traumatic stress disorder, and anxiety. Mil Med 2016;181(9):961–968.

[10]. Galea S, Basham K, Culpepper L, Davidson J, Foa E, Kizer K, Koenen K, Leslie D, McCormick R, Milad M. Treatment for posttraumatic stress disorder in military and veteran populations: Initial assessment. Washington, DC: National Academies Press; 2012.

[11]. McDonald AD, Sasangohar F, Jatav A, Rao AH. Continuous Monitoring and Detection of Post-Traumatic Stress Disorder (PTSD) Triggers Among Veterans: A Supervised Machine Learning Approach. IISE Trans Healthc Syst Eng 2019 Jul 3;9(3):201–211.

[12]. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009;151(4):264–269.

[13]. Tricco AC, Lillie E, Zarin W, O'Brien K, Colquhoun H, Kastner M, Levac D, Ng C, Sharpe JP, Wilson K. A scoping review on the conduct and reporting of scoping reviews. BMC Med Res Methodol 2016;16(1):15.

[14]. Acharya UR, Joseph KP, Kannathal N, Lim CM, Suri JS. Heart rate variability: a review. Med Biol Eng Comput 2006;44(12):1031–1051.

[15]. Cohen H, Benjamin J, Geva AB, Matar MA, Kaplan Z, Kotler M. Autonomic dysregulation in panic disorder and in post-traumatic stress disorder: application of power spectrum analysis of heart rate variability at rest and in response to recollection of trauma or panic attacks. Psychiatry Res 2000;96(1):1–13.

[16]. Ginsberg JP, Ayers E, Burriss L, Powell DA. Discriminative delay Pavlovian eyeblink conditioning in veterans with and without posttraumatic stress disorder. J Anxiety Disord 2008;22(5):809–823.

[17]. Ginzburg K, Ein-Dor T, Solomon Z. Comorbidity of posttraumatic stress disorder, anxiety and depression: a 20-year longitudinal study of war veterans. J Affect Disord 2010;123(1–3):249–257.

[18]. Tan G, Dao TK, Farmer L, Sutherland RJ, Gevirtz R. Heart rate variability (HRV) and posttraumatic stress disorder (PTSD): a pilot study. Appl Psychophysiol Biofeedback 2011;36(1):27–35.

[19]. Kamath MV, Fallen EL. Power spectral analysis of heart rate variability: a noninvasive signature of cardiac autonomic function. Crit Rev Biomed Eng 1993;21(3):245–311.

[20]. Prins A, Kaloupek DG, Keane TM. Psychophysiological evidence for autonomic arousal and startle in traumatized adult populations. 1995.

[21]. Hynynen ESA, Uusitalo A, Konttinen N, Rusko H. Heart rate variability during night sleep and after awakening in overtrained athletes. Med Sci Sports Exerc 2006;38(2):313–317.

[22]. Buchheit M, Simon C, Charloux A, Doutreleau S, Piquard F, Brandenberger G. Relationship between very high physical activity energy expenditure, heart rate variability and self-estimate of health status in middle-aged individuals. Int J Sports Med 2006;27(9):697–701.

[23]. Weber CS, Thayer JF, Rudat M, Sharma AM, Perschel FH, Buchholz K, Deter HC. Salt-sensitive men show reduced heart rate variability, lower norepinephrine and enhanced cortisol during mental stress. J Hum Hypertens 2008;22(6):423.

[24]. Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. Front Public Health 2017;5:258.

[25]. Wahbeh H, Oken BS. Peak high-frequency HRV and peak alpha frequency higher in PTSD. Appl Psychophysiol Biofeedback 2013;38(1):57–69.

[26]. Pyne JM, Constans JI, Wiederhold MD, Gibson DP, Kimbrell T, Kramer TL, Pitcock JA, Han X, Williams DK, Chartrand D. Heart rate variability: Pre-deployment predictor of post-deployment PTSD symptoms. Biol Psychol 2016;121:91–98.

[27]. Gillie BL, Thayer JF. Individual differences in resting heart rate variability and cognitive control in posttraumatic stress disorder. Front Psychol 2014;5:758.

[28]. Mellman TA, Pigeon WR, Nowell PD, Nolan B. Relationships between REM sleep findings and PTSD symptoms during the early aftermath of trauma. J Trauma Stress 2007;20(5):893–901.

[29]. Lee SM, Han H, Jang K-I, Huh S, Huh HJ, Joo J-Y, Chae J-H. Heart rate variability associated with posttraumatic stress disorder in victims' families of sewol ferry disaster. Psychiatry Res 2018;259:277–282.

[30]. Minassian A, Maihofer AX, Baker DG, Nievergelt CM, Geyer MA, Risbrough VB. Association of predeployment heart rate variability with risk of postdeployment posttraumatic stress disorder in active-duty marines. JAMA Psychiatry 2015;72(10):979–986.

[31]. Park JE, Lee JY, Kang S-H, Choi JH, Kim TY, So HS, Yoon I-Y. Heart rate variability of chronic posttraumatic stress disorder in the Korean veterans. Psychiatry Res 2017;255:72–77.

[32]. Monfredi O, Lyashkov AE, Johnsen A-B, Inada S, Schneider H, Wang R, Nirmalan M, Wisloff U, Maltsev VA, Lakatta EG. Biophysical characterization of the underappreciated and important relationship between heart rate variability and heart rate. Hypertension 2014;64(6):1334–1343.

[33]. Kazmi SZH, Zhang H, Aziz W, Monfredi O, Abbas SA, Shah SA, Kazmi SSH, Butt WH. Inverse correlation between heart rate variability and heart rate demonstrated by linear and nonlinear analysis. PloS One 2016;11(6):e0157557.

[34]. Stein PK, Domitrovich PP, Hui N, Rautaharju P, Gottdiener J. Sometimes higher heart rate variability is not better heart rate variability: results of graphical and nonlinear analyses. J Cardiovasc Electrophysiol 2005;16(9):954–959.

[35]. How to measure mental health [Internet]. Cent Urban Des Ment Health. [cited 2019 Nov 19]. Available from: https://www.urbandesignmentalhealth.com/how-to-measure-mental-health.html

[36]. Bonnemeier H, Wiegand UK, Brandes A, Kluge N, Katus HA, Richardt G, Potratz J. Circadian profile of cardiac autonomic nervous modulation in healthy subjects: differing effects of aging and gender on heart rate variability. J Cardiovasc Electrophysiol 2003;14(8):791–799.

[37]. Almeida-Santos MA, Barreto-Filho JA, Oliveira JLM, Reis FP, da Cunha Oliveira CC, Sousa ACS. Aging, heart rate variability and patterns of autonomic regulation of the heart. Arch Gerontol Geriatr 2016;63:1–8.

[38]. Agelink MW, Boz C, Ullrich H, Andrich J. Relationship between major depression and heart rate variability.: Clinical consequences and implications for antidepressive treatment. Psychiatry Res 2002;113(1–2):139–149.

[39]. Liao D, Cai J, Brancati FL, Folsom A, Barnes RW, Tyroler HA, Heiss G. Association of vagal tone with serum insulin, glucose, and diabetes mellitus—The ARIC Study. Diabetes Res Clin Pract 1995;30(3):211–221.

[40]. Koenig J, Thayer JF. Sex differences in healthy human heart rate variability: a meta-analysis. Neurosci Biobehav Rev 2016;64:288–310.

[41]. Zhang D, Shen X, Qi X. Resting heart rate and all-cause and cardiovascular mortality in the general population: a meta-analysis. Cmaj 2016;188(3):E53–E63.

[42]. Sammito S, Böckelmann I. Factors influencing heart rate variability. Int Cardiovasc Forum J 2016.

[43]. Umetani K, Singer DH, McCraty R, Atkinson M. Twenty-four hour time domain heart rate variability and heart rate: relations to age and gender over nine decades. J Am Coll Cardiol 1998;31(3):593–601.

[44]. Kandel ER, Schwartz JH, Jessell TM, Biochemistry D of, Jessell MBT, Siegelbaum S, Hudspeth AJ. Principles of neural science. McGraw-hill New York; 2000.

[45]. Mathias CJ, Bannister R. Autonomic failure: a textbook of clinical disorders of the autonomic nervous system. OUP Oxford; 2013.

[46]. Shalev AY, Sahar T, Freedman S, Peri T, Glick N, Brandes D, Orr SP, Pitman RK. A prospective study of heart rate response following trauma and the subsequent development of posttraumatic stress disorder. Arch Gen Psychiatry 1998;55(6):553–559.

[47]. Pole N, Cumberbatch E, Taylor WM, Metzler TJ, Marmar CR, Neylan TC. Comparisons between high and low peritraumatic dissociators in cardiovascular and emotional activity while remembering trauma. J Trauma Dissociation 2006;6(4):51–67.

[48]. Bryant RA, Creamer M, O'Donnell M, Silove D, McFarlane AC. A multisite study of initial respiration rate and heart rate as predictors of posttraumatic stress disorder. J Clin Psychiatry 2008;69(11):1694–1701.

[49]. Beckham JC, Feldman ME, Barefoot JC, Fairbank JA, Helms MJ, Haney TL, Hertzberg MA, Moore SD, Davidson JR. Ambulatory cardiovascular activity in Vietnam combat veterans with and without posttraumatic stress disorder. J Consult Clin Psychol 2000;68(2):269.

[50]. Kannel WB, Kannel C, Paffenbarger Jr RS, Cupples LA. Heart rate and cardiovascular mortality: the Framingham Study. Am Heart J 1987;113(6):1489–1494.

[51]. Woodward SH, Arsenault NJ, Voelker K, Nguyen T, Lynch J, Skultety K, Mozer E, Leskin GA, Sheikh JI. Autonomic activation during sleep in posttraumatic stress disorder and panic: a mattress actigraphic study. Biol Psychiatry 2009;66(1):41–46.

[52]. Buckley TC, Holohan D, Greif JL, Bedard M, Suvak M. Twenty-four-hour ambulatory assessment of heart rate and blood pressure in chronic PTSD and non-PTSD veterans. J Trauma Stress 2004;17(2):163–171.

[53]. Orr SP, Pitman RK, Lasko NB, Herz LR. Psychophysiological assessment of posttraumatic stress disorder imagery in World War II and Korean combat veterans. J Abnorm Psychol 1993;102(1):152.

[54]. Roy MJ, Costanzo ME, Jovanovic T, Leaman S, Taylor P, Norrholm SD, Rizzo AA. Heart rate response to fear conditioning and virtual reality in subthreshold PTSD. Annu Rev Cybertherapy Telemed 2013;191:115–119.

[55]. Halligan SL, Michael T, Wilhelm FH, Clark DM, Ehlers A. Reduced heart rate responding to trauma reliving in trauma survivors with PTSD: Correlates and consequences. J Trauma Stress 2006;19(5):721–734.

[56]. Tabachnick BG, Fidell LS. Experimental designs using ANOVA. Thomson/Brooks/Cole; 2007.

[57]. Shalev AY, Freedman S, Peri T, Brandes D, Sahar T, Orr SP, Pitman RK. Prospective study of posttraumatic stress disorder and depression following trauma. Am J Psychiatry 1998;155(5):630–637.

[58]. Foa EB, Rothbaum BO, Riggs DS, Murdock TB. Treatment of posttraumatic stress disorder in rape victims: a comparison between cognitive-behavioral procedures and counseling. J Consult Clin Psychol 1991;59(5):715.

[59]. Gelpin E, Bonne O, Peri T, Brandes D, Shalev AY. Treatment of recent trauma survivors with benzodiazepines: a prospective study. J Clin Psychiatry 1996;57(9):390–394.

[60]. Cacioppo JT, Tassinary LG, Berntson G. Handbook of psychophysiology. Cambridge University Press; 2007.

[61]. Hardy GH. Properties of Logarithmico-Exponential Functions. Proc Lond Math Soc 1912;2(1):54–90.

[62]. Marquardt DW. An algorithm for least-squares estimation of nonlinear parameters. J Soc Ind Appl Math 1963;11(2):431–441.

[63]. Bartels-Ferreira R, de Sousa ÉD, Trevizani GA, Silva LP, Nakamura FY, Forjaz CL, Lima JRP, Peçanha T. Can a first-order exponential decay model fit heart rate recovery after resistance exercise? Clin Physiol Funct Imaging 2015;35(2):98–103.

[64]. Lipov E. Post traumatic stress disorder (PTSD) as an over activation of sympathetic nervous system: an alternative view. J Trauma Treat 2013;3(181):2167–1222.

[65]. Strath SJ, Swartz AM, Bassett JD, O'Brien WL, King GA, Ainsworth BE. Evaluation of heart rate as a method for assessing moderate intensity physical activity. Med Sci Sports Exerc 2000;32(9 Suppl):S465–70.

[66]. Romero-Ugalde HM, Garnotel M, Doron M, Jallon P, Charpentier G, Franc S, Huneker E, Simon C, Bonnet S. An original piecewise model for computing energy expenditure from accelerometer and heart rate signals. Physiol Meas 2017;38(8):1599.

[67]. Khoueiry Z, Roubille C, Nagot N, Lattuca B, Piot C, Leclercq F, Delseny D, Busseuil D, Gervasoni R, Davy J-M. Could heart rate play a role in pericardial inflammation? Med Hypotheses 2012;79(4):512–515.

[68]. Tonhajzerova I, Ondrejka I, Chladekova L, Farsky I, Visnovcova Z, Calkovska A, Jurko A, Javorka M. Heart rate time irreversibility is impaired in adolescent major depression. Prog Neuropsychopharmacol Biol Psychiatry 2012;39(1):212–217.

[69]. Chen H, Erol Y, Shen E, Russell S. Probabilistic model-based approach for heart beat detection. Physiol Meas 2016;37(9):1404.

[70]. Peng C-K, Havlin S, Stanley HE, Goldberger AL. Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. Chaos Interdiscip J Nonlinear Sci 1995;5(1):82–87.

[71]. Cohen H, Kotler M, Matar MA, Kaplan Z, Loewenthal U, Miodownik H, Cassuto Y. Analysis of heart rate variability in posttraumatic stress disorder patients in response to a trauma-related reminder. Biol Psychiatry 1998;44(10):1054–1059.

[72]. Kantz H, Schreiber T. Nonlinear time series analysis. Cambridge University Press; 2004.

[73]. Montgomery DC, Johnson LA, Gardiner JS. Forecasting and time series analysis. McGraw-Hill New York.; 1990.

[74]. Galwey NW. Introduction to mixed modelling: beyond regression and analysis of variance. John Wiley & Sons; 2014.

[75]. Gee AH, Barbieri R, Paydarfar D, Indic P. Improving heart rate estimation in preterm infants with bivariate point process analysis of heart rate and respiration. Eng Med Biol Soc EMBC 2016 IEEE 38th Annu Int Conf Of IEEE; 2016. p. 920–923.

[76]. Boscarino JA. A prospective study of PTSD and early-age heart disease mortality among Vietnam veterans: implications for surveillance and prevention. Psychosom Med 2008;70(6):668.

[77]. Kassam-Adams N, Garcia-España JF, Fein JA, Winston FK. Heart rate and posttraumatic stress in injured children. Arch Gen Psychiatry 2005;62(3):335–340.

[78]. Darlington RB. Regression and linear models. McGraw-Hill New York; 1990.

[79]. Greenacre M. Correspondence analysis in practice. Chapman and Hall/CRC; 2017.

[80]. Zakeri IF, Adolph AL, Puyau MR, Vohra FA, Butte NF. Cross-Sectional Time Series and Multivariate Adaptive Regression Splines Models Using Accelerometry and Heart Rate Predict Energy Expenditure of Preschoolers1–3. J Nutr 2012;143(1):114–122.

[81]. Bonomi AG, Goldenberg S, Papini G, Kraal J, Stut W, Sartor F, Kemps H. Predicting energy expenditure from photo-plethysmographic measurements of heart rate under beta blocker therapy: Data driven personalization strategies based on mixed models. Eng Med Biol Soc EMBC 2015 37th Annu Int Conf IEEE IEEE; 2015. p. 7642–7646.

[82]. Xu Z, Zong C, Jafari R. Constructing energy expenditure regression model using heart rate with reduced training time. Eng Med Biol Soc EMBC 2015 37th Annu Int Conf IEEE IEEE; 2015. p. 6566–6569.

[83]. James G, Witten D, Hastie T, Tibshirani R. An introduction to statistical learning. Springer; 2013.

[84]. Sano A, Picard RW. Stress recognition using wearable sensors and mobile phones. 2013 Hum Assoc Conf Affect Comput Intell Interact IEEE; 2013. p. 671–676.

[85]. Thayer JF, \AAhs F, Fredrikson M, Sollers III JJ, Wager TD. A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker of stress and health. Neurosci Biobehav Rev 2012;36(2):747–756.

[86]. Healey J, Picard RW. Detecting stress during real-world driving tasks using physiological sensors. IEEE Trans Intell Transp Syst 2005;6(2):156–166.

[87]. Kolus A, Dubé P-A, Imbeau D, Labib R, Dubeau D. Estimating oxygen consumption from heart rate using adaptive neuro-fuzzy inference system and analytical approaches. Appl Ergon 2014;45(6):1475–1483.

[88]. Kolus A, Imbeau D, Dubé P-A, Dubeau D. Classifying work rate from heart rate measurements using an adaptive neuro-fuzzy inference system. Appl Ergon 2016;54:158–168.

[89]. Michie D, Spiegelhalter DJ, Taylor CC. Machine learning. Neural Stat Classif 1994;13.

[90]. Kubo R. The fluctuation-dissipation theorem. Rep Prog Phys 1966;29(1):255.

[91]. Chen M, Niestemski LR, Prevost R, McRae M, Cholleti S, Najarro G, Buchman TG, Deem MW. Prediction of heart rate response to conclusion of the spontaneous breathing trial by fluctuation dissipation theory. Phys Biol 2013;10(1):016006.

[92]. Zhang Y, Chen W, Su SW, Celler B. Nonlinear modelling and control for heart rate response to exercise. Int J Bioinforma Res Appl 2012;8(5–6):397–416.

[93]. Roger D, Jamieson J. Individual differences in delayed heart-rate recovery following stress: The role of extraversion, neuroticism and emotional control. Personal Individ Differ 1988;9(4):721–726.

[94]. Lefever J, Berckmans D, Aerts J-M. Time-variant modelling of heart rate responses to exercise intensity during road cycling. Eur J Sport Sci 2014;14(sup1):S406–S412.

[95]. Haber R, Unbehauen H. Structure identification of nonlinear dynamic systems—a survey on input/output approaches. Automatica 1990;26(4):651–677.

[96]. Valenza G, Lanata A, Scilingo EP. The role of nonlinear dynamics in affective valence and arousal recognition. IEEE Trans Affect Comput 2012;3(2):237–249.

[97]. Langford J, Salakhutdinov R, Zhang T. Learning nonlinear dynamic models. Proc 26th Annu Int Conf Mach Learn ACM; 2009. p. 593–600.

[98]. Olufsen MS, Ottesen JT. A practical approach to parameter estimation applied to model predicting heart rate regulation. J Math Biol 2013;67(1):39–68.

[99]. Boulay MR, Simoneau J-A, Lortie G, Bouchard C. Monitoring high-intensity endurance exercise with heart rate and thresholds. Med Sci Sports Exerc 1997;29(1):125–132.

[100]. Vrijkotte TG, Van Doornen LJ, De Geus EJ. Effects of work stress on ambulatory blood pressure, heart rate, and heart rate variability. Hypertension 2000;35(4):880–886.

[101]. Feng J, Huang Z, Zhou C, Ye X. Study of continuous blood pressure estimation based on pulse transit time, heart rate and photoplethysmography-derived hemodynamic covariates. Australas Phys Eng Sci Med Springer; 2018;41(2):403–413.

[102]. Champéroux P, Fesler P, Judé S, Richard S, Le Guennec J-Y, Thireau J. High-frequency autonomic modulation: a new model for analysis of autonomic cardiac control. Br J Pharmacol Wiley Online Library; 2018;175(15):3131–3143.

[103]. Diderichsen PM, Cox E, Martin SW, Cleton A, Ribbing J. Predicted heart rate effect of inhaled PF-00610355, a long acting β-adrenoceptor agonist, in volunteers and patients with chronic obstructive pulmonary disease. Br J Clin Pharmacol 2013;76(5):752–762.

[104]. Hoyer D, Nowack S, Bauer S, Tetschke F, Rudolph A, Wallwitz U, Jaenicke F, Heinicke E, Götz T, Huonker R. Fetal development of complex autonomic control evaluated from multiscale heart rate patterns. Am J Physiol-Regul Integr Comp Physiol 2012;304(5):R383–R392.

[105]. Alrefaie MT, Summerskill S, Jackon TW. In a heart beat: Using driver's physiological changes to determine the quality of a takeover in highly automated vehicles. Accid Anal Prev Elsevier; 2019;131:180–190.

[106]. Oliveira MJ, Marcoa R, Moutinho J, Oliveira P, Ladeira I, Lima R, Guimarães M. Reference equations for the 6-minute walk distance in healthy Portuguese subjects 18–70 years old. Pulmonology Elsevier; 2019;25(2):83–89.

[107]. Sartipy U, Savarese G, Dahlström U, Fu M, Lund LH. Association of heart rate with mortality in sinus rhythm and atrial fibrillation in heart failure with preserved ejection fraction. Eur J Heart Fail Wiley Online Library; 2019;21(4):471–479.

[108]. Ni J, Muhlstein L, McAuley J. Modeling Heart Rate and Activity Data for Personalized Fitness Recommendation. World Wide Web Conf 2019. p. 1343–1353.

[109]. Signorini MG, Pini N, Malovini A, Bellazzi R, Magenes G. Integrating machine learning techniques and physiology based heart rate features for antepartum fetal monitoring. Comput Methods Programs Biomed Elsevier; 2020;185:105015.

[110]. Chaudhuri T, Soh YC, Li H, Xie L. Machine learning driven personal comfort prediction by wearable sensing of pulse rate and skin temperature. Build Environ Elsevier; 2020;170:106615.

[111]. Lu Y, Burykin A, Deem MW, Buchman TG. Predicting clinical physiology: a Markov chain model of heart rate recovery after spontaneous breathing trials in mechanically ventilated patients. J Crit Care 2009;24(3):347–361.

[112]. Valenza G, Citi L, Barbieri R. Estimation of instantaneous complex dynamics through lyapunov exponents: a study on heartbeat dynamics. PloS One 2014;9(8):e105622.

[113]. Ferrer E, Helm JL. Dynamical systems modeling of physiological coregulation in dyadic interactions. Int J Psychophysiol 2013;88(3):296–308.

[114]. Valenza G, Lanata A, Scilingo EP. Oscillations of heart rate and respiration synchronize during affective visual stimulation. IEEE Trans Inf Technol Biomed 2012;16(4):683–690.

[115]. Zazula D. Optimization of heartbeat detection based on clustering and multimethod approach. Eng Med Biol Soc EMBC 2012 Annu Int Conf IEEE IEEE; 2012. p. 5–8.

[116]. Echeverría JC, Álvarez-Ramírez J, Pena MA, Rodríguez E, Gaitán MJ, González-Camarena R. Fractal and nonlinear changes in the long-term baseline fluctuations of fetal heart rate. Med Eng Phys 2012;34(4):466–471.

[117]. Park Y-S, Ryu K-Y, Shim S-S, Hoh J-K, Park M-I. Comparison of fetal heart rate patterns using nonlinear dynamics in breech versus cephalic presentation at term. Early Hum Dev 2013;89(2):101–106.

[118]. Scalzi S, Tomei P, Verrelli CM. Nonlinear control techniques for the heart rate regulation in treadmill exercises. IEEE Trans Biomed Eng 2012;59(3):599–603.

[119]. Cheng TM, Savkin AV, Celler BG, Su SW, Wang L. Nonlinear modeling and control of human heart rate response during exercise with various work load intensities. IEEE Trans Biomed Eng 2008;55(11):2499–2508.

[120]. Mazzoleni MJ, Battaglini CL, Martin KJ, Coffman EM, Mann BP. Modeling and predicting heart rate dynamics across a broad range of transient exercise intensities during cycling. Sports Eng 2016;19(2):117–127.

[121]. Zakynthinaki MS. Modelling heart rate kinetics. PloS One 2015;10(4):e0118263.

[122]. Gelman A, Hill J. Data analysis using regression and multilevel/hierarchical models. Cambridge university press; 2006.

[123]. Harrington P. Machine learning in action. Manning Publications Co.; 2012.

[124]. D'Agostino RB. Goodness-of-fit-techniques. CRC press; 1986.

[125]. Shalev AY, Peri T, Canetti L, Schreiber S. Predictors of PTSD in injured trauma survivors: a prospective study. Am J Psychiatry 1996;153(2):219–225.

[126]. Magder SA. The ups and downs of heart rate. Crit Care Med 2012;40(1):239–245.

[127]. Lester M, Sheffield LT, Trammell P, Reeves TJ. The effect of age and athletic training on the maximal heart rate during muscular exercise. Am Heart J 1968;76(3):370–376.

[128]. Sacknoff DM, Gleim GW, Stachenfeld N, Coplan NL. Effect of athletic training on heart rate variability. Am Heart J 1994;127(5):1275–1278.

[129]. Felber Dietrich D, Schwartz J, Schindler C, Gaspoz J-M, Barthélémy J-C, Tschopp J-M, Roche F, von Eckardstein A, Brändli O, Leuenberger P. Effects of passive smoking on heart rate variability, heart rate and blood pressure: an observational study. Int J Epidemiol 2007;36(4):834–840.

[130]. Freedson PS, Miller K. Objective monitoring of physical activity using motion sensors and heart rate. Res Q Exerc Sport 2000;71(sup2):21–29.

[131]. Green JA, Halsey LG, Wilson RP, Frappell PB. Estimating energy expenditure of animals using the accelerometry technique: activity, inactivity and comparison with the heart-rate technique. J Exp Biol 2009;212(4):471–482.

[132]. Taelman J, Vandeput S, Spaepen A, Van Huffel S. Influence of mental stress on heart rate and heart rate variability. 4th Eur Conf Int Fed Med Biol Eng Springer; 2009. p. 1366–1369.

[133]. Pagani M, Somers V, Furlan R, Dell'Orto S, Conway J, Baselli G, Cerutti S, Sleight P, Malliani A. Changes in autonomic regulation induced by physical training in mild hypertension. Hypertension 1988;12(6):600–610.

[134]. McCarty R, Horwatt K, Konarska M. Chronic stress and sympathetic-adrenal medullary responsiveness. Soc Sci Med 1988;26(3):333–341.

[135]. Chen H-S, Simpson DG, Ying Z. Infill asymptotics for a stochastic process model with measurement error. Stat Sin 2000;141–156.

[136]. Sadeghi M, Sasangohar F, McDonald AD. Toward a Taxonomy for Analyzing the Heart Rate as a Physiological Indicator of Posttraumatic Stress Disorder: Systematic Review and Development of a Framework. JMIR Mental Health. 2020;7(7):e16654.

3. CHAPTER 3 (ARTICLE 2) INVESTIGATING HEART RATE REACTIONS[2]

Overview

We collected naturalistic heart rate data from veterans diagnosed with Post-Traumatic Stress Disorder (PTSD) to investigate the effects of various factors on heart rate. Veterans were recruited during five cycling events in 2017 and 2018 to record resting and activity-related heart rate data using a wrist-worn device. The device also logged self-reported PTSD hyperarousal events. Regression analyses were performed on demographic and behavioral covariates including gender, exercise, antidepressants, smoking habits, sleep habits, average heart rate during reported hyperarousal events, age, glucocorticoids consumption and alcohol consumption. Heart rate patterns during self-reported PTSD hyperarousal events were analyzed using Auto Regressive Integrated Moving Average (ARIMA). Heart rate data were also compared to an open-access non-PTSD representative case. Of 99 veterans with PTSD, 91 participants reported at least 1 hyperarousal event, with a total of 1,023 events; demographic information was complete for 38 participants who formed the subset for regression analyses. The results show that factors including smoking, sleeping, gender, and medication significantly affect resting heart rate. Moreover, unique heart rate patterns associated with PTSD symptoms in terms of stationarity, autocorrelation, and fluctuation characteristics were identified. Our findings show distinguishable heart rate patterns and characteristics during PTSD

[2] Reprinted with permission from "Understanding heart rate reactions to pot-traumatic stress disorder (PTSD) among veterans: a naturalistic study" by Mahnoosh Sadeghi, Farzan Sasangohar, Anthony D McDonald, Sudeep Hegde, 2021, Human Factors, 00187208211034024. (See Appendix B for the copyright permission)

hyperarousal events. These findings show promise for future work to detect the onset of PTSD symptoms.

3.1. Introduction

Post-traumatic Stress Disorder (PTSD) is a psychiatric disorder affecting approximately 11% of the United States population and 24.5% of combat veterans [1]. PTSD is characterized by at least one month of re-experiencing a traumatic event followed by avoidance symptoms and hyperarousal events [2]. Avoidance symptoms include, decreased interest in daily life, and an overall feeling of detachment from one's surroundings. Hyperarousal symptoms include hypervigilance, feelings of irritability, and an exaggerated startle response following a traumatic event. Other symptoms include anxiety, insomnia, fatigue, anger, and aggression [3]. The secondary and tertiary comorbidities of PTSD are depression, substance abuse, smoking, heart disease, obesity, diabetes, chronic fatigue, and increased dementia [4].

PTSD is typically diagnosed and monitored using subjective self-report tools, such as the Davidson Trauma Scale (DTS; [5]), PTSD-Checklist 5 (PCL-5; [6]) or questionnaire-based interviews, such as the Clinician Administered PTSD Scale (CAPS; [6]). However, objective means for assessment of PTSD symptoms are largely absent. Given the known limitations of subjective and self-reported measures, there is a timely need to investigate objective methods for monitoring PTSD symptoms. The rapid growth of physiological monitoring methods and mobile health (mHealth) applications provide an opportunity for the application of human factors and ergonomics to the design of user-centered PTSD monitoring technologies. However, the foundational knowledge of

psychophysiological characteristics of PTSD reactions required for continuous monitoring and detection of PTSD symptoms, is limited [7].

PTSD is correlated with several physiological measures including heart rate variability, blood pressure, respiratory rate, skin conductance, and of particular interest in this study, heart rate ([8], [9]). It is known that individuals who develop PTSD after a traumatic incident, such as a motor vehicle crash, have higher resting heart rate than those without PTSD [10]. Shalev et al. (1998) [11] found that compared to healthy adults, individuals with PTSD had elevated heart rate immediately after a traumatic incident and one week after, though the effects dissipated after one month. More recent studies have found that elevated heart rate post-trauma and heart rate at the time of hospital admission are predictors of PTSD even four months after the incident [12]. Among veterans, those with PTSD have consistently higher heart rate than veterans with comparable combat experience who do not suffer from PTSD [13]. The findings on heart rate have been replicated in laboratory studies. Blanchard et al. (1986) [14] induced hyperarousal among combat veterans using triggers such as combat noises, and measured physiological reactions including heart rate reactivity to such stimuli. Rizzo et al. (2017) [15] used virtual reality to simulate combat scenarios to assess the relationship between PTSD symptoms and physiological variables. Both studies found strong positive correlation between heart rate and hyperarousal among veterans diagnosed with PTSD. However, these studies were mostly correlational and did not describe or model the heart rate patterns associated with PTSD.

A major limitation of the aforementioned work is the gap in naturalistic investigation of physiological reactions to PTSD symptoms. Given the sporadic nature of hyperarousal incidents and ethical issues related to inducing trauma in the lab setting, investigating PTSD in patients' natural work-life environment seems necessary. However, there are only a few documented naturalistic attempts ([10], [16], [17]). Buckley et al. (2004) [10] used heart rate monitors placed on occlusion cuffs worn by participants on their non-dominant hand at the level of the heart. Heart rate was measured every 20 minutes during waking hours and every 120 minutes during sleeping hours. Their findings suggest that participants diagnosed with PTSD have a higher resting heart rate than those without PTSD. Green et al. (2016) [16] used ECG sensors to measure heart rate changes in participants over a 24-hour period. They found elevated heart rate for PTSD patients at higher distress levels compared to baseline. McDonald et al. (2019) [17] used a smart watch-based application to record heart rate and activity as well as self-reported PTSD hyperarousal events. The data were used to develop a machine learning algorithm for detection of the onset of PTSD symptoms. Post-hoc analysis of that algorithm showed that the algorithm associated increases in heart rate with PTSD symptom onset.

Despite the considerable evidence suggesting a positive correlation between heart rate and PTSD hyperarousal events, objective clinical assessment of PTSD and detection of its onset requires a deeper understanding of the nature of the change in heart rate. While the relationship between heart rate rhythms (patterns) and various cardiovascular diseases have been studied [18], to our knowledge such relationship is an important

research gap for PTSD. Addressing this gap will advance the knowledge of psychophysiological properties of PTSD. The aim of the current research is to address the gap in knowledge about descriptive and mathematical modeling of heart rate patterns during PTSD hyperarousal events. In this paper, we document our findings from a naturalistic study that investigated heart rate profiles associated with PTSD hyperarousal events, as well as the relationship between heart rate and demographic and behavioral factors among a large sample of veterans with PTSD. We first present our evaluation of the general characteristics of heart rate among participating veterans diagnosed with PTSD. We then discuss the relationship between factors such as age and gender; lifestyle factors such as sleeping habits, exercise routines, alcohol consumption; and medications such as antidepressants with resting heart rate. Finally, we document our descriptive and statistical evaluation of heart rate time-dependent data during PTSD hyperarousal events. A sample of heart rate data of healthy subjects as a representative composite is used to illustrate differences. The results presented in this paper provide critical insight into heart rate co-variates and patterns in individuals with PTSD which can be used to improve and personalize the design of mHealth applications, and improve the treatment of PTSD.

3.2. Method

Naturalistic data collection was conducted during Project Hero's United Healthcare Ride 2 Recovery (R2R) events to evaluate the heart rate patterns associated with PTSD. Project Hero is a non-profit organization committed to helping veterans and first responders diagnosed with PTSD by coordinating recreational events such as group

biking as part of a social therapy effort. During each event, veterans rode bicycles in groups between key destinations for an average duration of three to seven days. The activity involved an average of eight hours biking each day with the remaining time for resting, relaxing, and social events. The research team joined a total of five events in 2017 and 2018—in California, Washington DC, Minneapolis, Texas, and Nevada—and recruited participants from each event. The study was approved by the Institutional Review Board (IRB) at Texas A&M University (IRB2017-0210D).

3.2.1. Participants

A voluntary response sample of 99 Project Hero R2R riders (from a population of about 500 eligible participants) were recruited to participate in the study across the five events. All 99 participants consented to complete the study. Cardiac data were collected from all 99 participants and were used for analysis of heart rate patterns. However, due to the voluntary nature of participation, strict anonymity protocols, and the sensitivities involved in studying mental health, completion of demographics information was unsupervised and opportunities to follow up with participants were limited. Consequently, association between demographics data and cardiac data was only possible for 38 out of 99 participants. Thus, regression analyses accounting for demographics included only those 38 participants. To investigate the representativeness of this subset, their cardiac data (mean and standard deviation of count of reported hyperarousal events) (M = 9.78, SD = 10.67) was compared to participants with incomplete demographic data (n=61) (M = 10.48, SD = 11.12) and the results showed no significant differences; $t(4) = 0.15$, $p = 0.9$. The mean age of all participants (n=99) was

45.5 years (SD = 10, Range = 22-75). The mean age of participants with complete demographic data (n=38) was 46 years old (SD = 11, Range = 27-74). Out of 99 participants, 82 were male and 17 were female. In terms of race and ethnicity, 44 people were White, 15 were Black/African American, 26 people were Hispanic/Latino, four were American Indian or Alaska Native, one was Native Hawaiian, one was Asian, and eight reported their ethnicity as Other. Out of the 38 participants used for the regression analysis, 25 were male and 13 were female, 18 were White, 9 were Black/ African, 8 were Hispanic/Latino and 3 reported their ethnicity as Other. In addition, participants were asked about current usage of antidepressants (Yes/No) and anxiolytics (drugs used to treat anxiety-based disorder symptoms; Yes/No), smoking habits (Currently Smoking/Non-smoker), current alcohol consumption (Yes/No), and sleep quality (0-6 hours per night/More than 6 hours per night), exercise (Yes/No), alcohol consumption, and glucocorticoids usage (Yes/No).

3.2.2. Procedure

Project Hero provided their events' attendees with information about the study and invited them to participate during the event registration. Participants who agreed to participate were asked to complete informed consent and were then provided with an Apple Watch Series 2, 3, and 4 (for studies in Texas and California) or an Android smartwatch (MOTO 360 Gen 1 and Gen 2 [Motorola Inc], for the remainder of locations) equipped with a data collection application. The participants were then trained to operate the smartwatch application. Participants were instructed to wear the watch at all times unless they were swimming, bathing, or charging the watch.

The data collection app was developed by the research team and served several purposes including providing a summary of heart rate activity (beats per minute [bpm]) of the user as well as mindfulness features. It also included a function which allowed the user to report PTSD hyperarousal events by tapping their finger anywhere on the watch face twice in quick succession (i.e., a double tap) which created a time-stamped self-reported event. The smartwatches were equipped with accelerometers and gyroscopic sensors which allow kinematic data, including linear and angular acceleration, to be captured. The app ran continuously in the background and used the smartwatch's sensors to measure heart rate and accelerometer data. Participants could interact with the application throughout the course of the event. Four sets of data were collected using smartwatches in all five events: 1) real-time heart rate data (1 Hz), 2) reported hyperarousal events based on double taps recorded by the watch, 3) real-time angular accelerator data (1 Hz), and 4) real-time linear accelerator data (1 Hz). Overall, about 25% of heart rate data is considered missing. While many reasons contributed to non-sampling, including issues with the devices, defective sensors, and improper fit, the exit interviews revealed that the majority of the missing data is due to the time required to charge the devices. As shown in Figure 1, most participants confirmed that they charged their devices at night before going to bed.

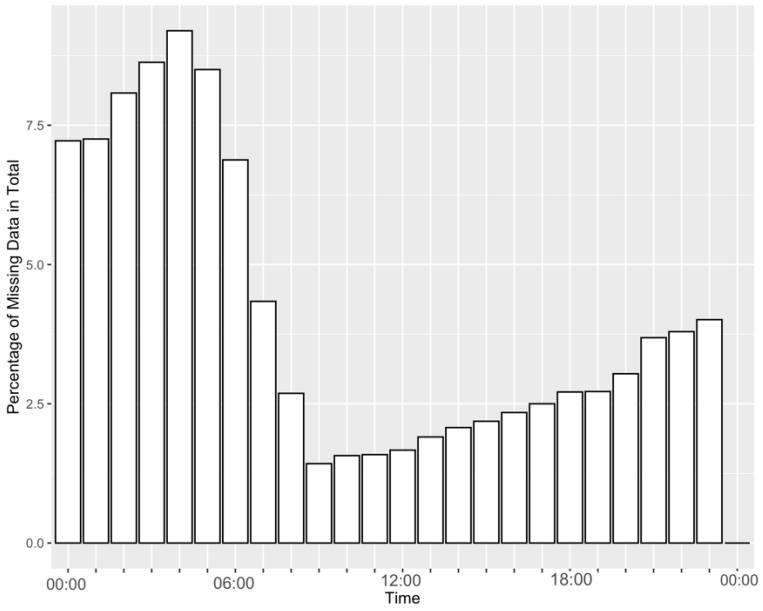

Figure 3.1. Percentage of missing cardiac data (on average) by hour of the day. Reprinted with permission from [51]

3.2.3. Analysis

Activity classification: Since the data collection occurred during events that included physical activities, the accelerometer data were used to classify periods involving physical activity (e.g., riding bicycle or exercising) compared to resting by processing the linear acceleration data with the validated algorithm developed by Ravi et al. (2005) [19]. This algorithm; which is a combination of Decision Trees, Naïve Bayes, and K nearest neighbors; uses the single triaxial accelerometer data to classify resting states (standing) and activities including running and walking with over 84% accuracy. We used this algorithm to differentiate between periods involving activity and those without to calculate the resting heart rate.

Resting heart rate: For both Apple Watch and Android devices we developed a method similar to Venkatraman & Yuen (2015) [20] to calculate resting heart rate based on activity levels. In this method, resting heart rate is obtained by taking the average heart rate during the moments that individuals are considered to be least active physically based on Ravi et al.'s (2005) [19] algorithm.

Correlation and regression analysis: Data from the 38 participants who provided a complete dataset including demographic data, heart rate data, acceleration data, and reported stress moments was used to conduct a Pearson correlation analysis [21]. A linear regression model was built to investigate if resting heart rate was affected by gender, exercise, antidepressants, smoking habits, sleep habits, average heart rate during reported hyperarousal events, age, glucocorticoids consumption or alcohol consumption. Assumptions of normality, multicollinearity and homoscedasticity were checked according to Weisberg's (2005) [22] guidelines. In addition, given the potential variability in self-reports due to emotional numbness ([23], [24]), leverage analysis was conducted to identify influential observations [25].

Time series analysis of heart rate: To investigate heart rate patterns and statistical characteristics of heart rate data during the self-reported hyperarousal events, windows of heart rate data including 600 seconds of observations (100 seconds before the first recorded trigger and 500 seconds after the recorded trigger) were extracted for all 99 participants and a time-series analysis was conducted. The heart data were analyzed using Autoregressive Integrated Moving Average (ARIMA) models which are widely used for forecasting time-series data [26] with applications in medical domains

due to their utility in enabling descriptive and predictive analyses on non-stationary time-series [27]. An important advantage of using ARIMA relative to non-temporal analysis methods like ANOVA is that it explicitly models time-dependent measures [28]. The fitted ARIMA models were used to assess the stationarity, fluctuation, and autocorrelation of the data.

Stationarity—an index of the consistency of the mean and variance of a time-series—was assessed with the Dickey-Fuller test [29] to investigate irregularities (non-stationarity) in heart rate rhythms. Previous research indicates that healthy subjects' heart rate data include long stationary stretches under various conditions including resting and activity [30]. The Dickey-Fuller test was conducted on each window of heart rate and the average test is reported in the results section. Autocorrelation—a statistical feature representing the correlation of a time-series with itself as a function of delay—was used to investigate the repeating heart rate patterns. The autocorrelation test was conducted on each window of heart rate data and the average autocorrelation values was plotted for comparison. Detrended Fluctuation Analysis (DFA)—a statistical method that has been used for analyzing changes in heart rate data ([31], [32]) —has shown promise to understand irregularities in time series data with stochastic features that show long-term correlation [33]. DFA assesses self-affinity of time series data which indicates data variation and changes within a time window. DFA also evaluates the turbulence (i.e., irregular changes) in the data. DFA was applied to each window of heart rate data and DFA values were calculated and averaged over all windows of PTSD hyperarousal events. To make meaningful comparisons with fixed baselines and describe hyperarousal

events, ARIMA was used to illustrate the differences between heart rate during a PTSD hyperarousal event and heart rate data for a sample of healthy individuals with neither mental nor pathological disorder. The data were obtained from the MIT-BIH (Beth Israel Hospital) Arrhythmia database [34], and PhysioNet ([32], [35]) open-access community resources on clinical and physiological data.

All data analyses were conducted using RStudio 3.5.1, and Python 3.7.4. The ggplot2 package in R was used to develop visualizations [36]. The nonlinear T-series package was used for fluctuation analysis [37].

3.3. Results

In this section, we first describe the overall characteristics of the heart rate data for the sample of veterans with PTSD followed by our findings related to statistical characteristics of heart rate time-series during PTSD hyperarousal events. Finally, we illustrate the differences between the identified heart rate profiles and a representative heart rate profile of a healthy subject.

3.3.1. Characteristics of Heart Rate and Hyperarousal Events

PTSD hyperarousal events and heart rate: Ninety-one (91) of the 99 participants reported at least 1 hyperarousal event, and a total of 1,023 events were reported (M = 10.23 per participant, SD = 11, Median = 5; Figure 2 [left]). For events that occurred heart rate ranged from 57-191 bpm (M = 93.98, SD = 21.32). However, when participants were riding bikes, their heart rate during self-reported hyperarousal was between 71-164.5 bpm (M = 105.75, SD = 21.66), and when they were not riding, their heart rate ranged from 57-192 (M = 91.2, SD = 20.61). As shown in the density function

of heart rate in Figure 2 (right), most reported heart rates during hyperarousal events peaked between 80-90 bpm (Median = 89 bpm).

Resting heart rate: Our findings show that resting heart rates for PTSD patients ranged from 61-120 bpm (*M* = 81.99, *SD*= 10.07) with a median of 80.46 bpm.

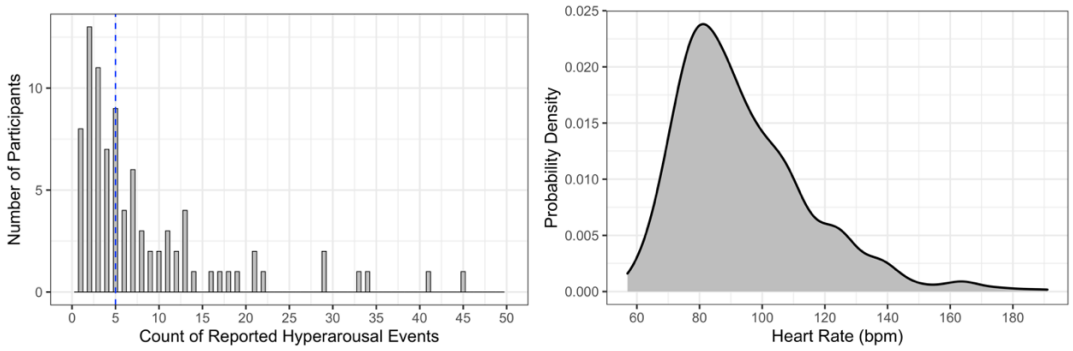

Figure 3.2. Reported stress moments frequency numbers (left); the dashed vertical line represents the median; estimated distribution function of recorded heart rate during PTSD hyperarousal events (right). Reprinted with permission from [51]

Figure 3 (left) shows the frequency of reported hyperarousal events by time of the day. Fewer than 5% of events were reported between midnight and 6 am. However, most participants reported using that period to charge their devices (as illustrated in Figure 1). Figure 3 (right) shows heart rate values at the time of the self-reported event vs time of the day.

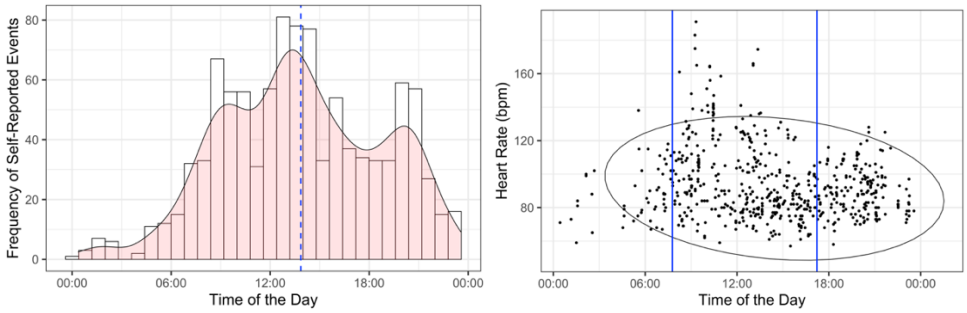

Figure 3.3. Frequency of stress moments reported by time of the day (left); the dashed vertical line shows the mean value for time of reported events; heart rate scatter plot with confidence ellipse (right); the vertical blue lines show riders' riding time intervals (9am – 5pm approximately). Reprinted with permission from [51]

Hyperarousal events and activity: Figure 4 shows the number of reported hyperarousal events by activity classification (based on the Ravi et al.'s 2005 [19] classification). The figure illustrates that the majority of stress events (87%) occurred when participants were resting.

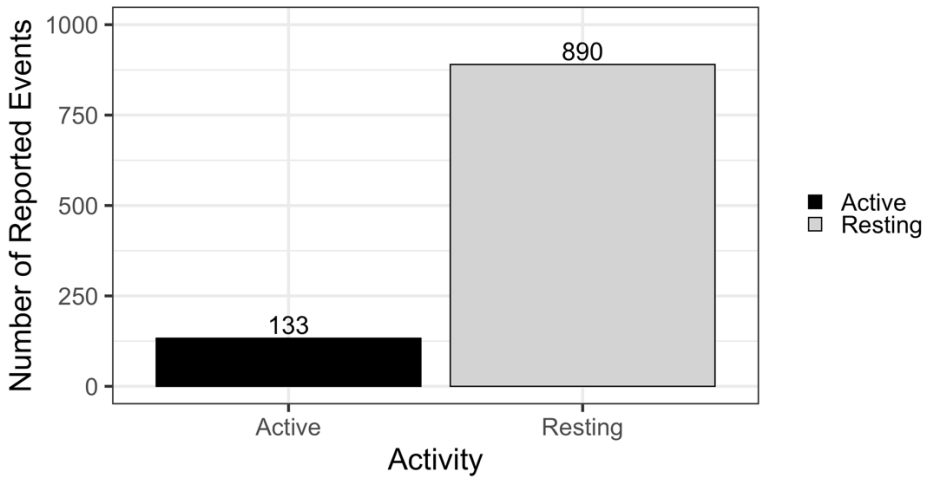

Figure 3.4. Number of PTSD triggers during active or resting phases (N_{Active} = 133, $N_{Resting}$ = 890). Reprinted with permission from [51]

3.3.2. Effects of Medications, Sleep, Age, Gender, Smoking, and Alcohol Consumption on Resting Heart Rate

It is well-documented that resting heart rate has a strong correlation with cardiovascular risk, and in general elevated resting heart rate is a reliable indicator of clinical events [38]. However, the relationships between resting heart rate, demographics, and other lifestyle and health variables such as sleep, medication, smoking, and alcohol consumption in patient populations with PTSD have not been well-documented. Understanding these relationships is critical to developing human-centered mHealth applications that are robust to individual differences.

Correlation analysis: Resting heart rate and average heart rate during reported PTSD hyperarousal events were significantly correlated (r (36) = 0.58, $p < .001$). Smoking (r (36) = 0.44, $p = 0.005$), antidepressant use (r (36) = 0.38, $p = 0.019$), age (r (36) = -0.34, $p = 0.038$), and sleep (r (36) = -0.37, $p = 0.046$) were also significantly correlated with heart rate.

Linear regression: The multiple linear regression was calculated to predict resting heart rate based on gender, anti-depressants, anxiolytics, smoking habits, sleeping habits, average heart rate during PTSD hyperarousal events, age, glucocorticoids, exercise, and alcohol consumption (Table 1). A significant regression equation was found ($F(10,27) = 6.635$, $p < 0.001$), with an adjusted R^2 of 0.61. Participants' predicted resting heart rate is equal to 61.04 - 3.656 (GENDER) + 10.394 (ANTIDEPRESSANTS) – 3.312 (ANXIOLYTICS) + 9.158 (SMOKING) – 2.919 (SLEEPING) + 0.374 (AVERAGE HEART RATE) – 0.001 (AGE) – 1.236

(GLUCOCORTICOIDS) – 1.560 (EXERCISE) + 0. 430 (ALCOHOL CONSUMPTION), where gender is coded as 0 = Male, 1 = Female, antidepressants were coded as 0 = not taking antidepressants, 1 = taking antidepressants, smoking was coded as 0 = not smoking, 1 = smoking, sleeping was coded as 0 = less than 6 hours of reported sleep per day, 1 = more than 6 hours of reported sleep per day, average heart rate during PTSD hyperarousal events are measured in beats per minute, age was measured in years, glucocorticoids was coded as 0 = not taking glucocorticoids medicine, 1= taking glucocorticoids medicine, exercise was coded as 0 = not exercising regularly, 1 = exercising regularly, and alcohol consumption was coded as 0 = not consuming alcohol, 1 = consuming alcohol. Participants' resting heart rate increased by about 3.7 bpm for females compared to their male counterparts. Resting heart rate also increased by about 10.4 bpm for participants who used antidepressants compared to those who did not use antidepressants. Participants' resting heart rate who used anxiolytics decreased by 3.3 bpm compared to those who did not use anxiolytics. Smokers' resting heart rate was 9.1 bpm higher than non-smokers resting heart rate. Participants who had more than 6 hours of sleep per day had about 2.9 bpm lower resting heart rate compared to participants who had fewer sleep hours. The resting heart rate was 0.4 bpm higher for each 1 bpm increase in the average heart rate during hyperarousal events. For each 1 year increase in age, the resting heart rate decreased by 0.001 bpm. Participants who took glucocorticoids medicine had on average 1.2 bpm lower resting heart rate than those who did not take glucocorticoids. The ones who exercised regularly had 1.5 bpm lower resting heart rate on average than the ones who did not exercise on

regular basis. Finally, participants who consumed alcohol had roughly 0.4 bpm higher resting heart rate than those who did not consume alcohol. However, from these variables only gender, antidepressants, smoking, sleeping, and average HR were significant predictors of resting heart rate (Table 1).

Table 3.1. Results of the Full Model Analysis (Overall model R^2 adjusted = 0.61). Reprinted with permission from [51]

Variable	B	E	t	p	β
Gender	-3.6563	2.3825	-1.535	0.0131	-0.1772
Antidepressants	10.3944	2.6684	3.895	0.0005	0.4514
Anxiolytics	-3.3119	2.6146	-1.267	0.216	-0.1692
Smoking	9.1576	3.7607	2.435	0.0217	0.2871
Sleeping	-2.9185	1.6326	-1.788	0.0443	-0.2204
Average HR during hyperarousal events	0.3740	0.0961	3.891	0.0005	0.485
Age	-0.0014	0.1126	-0.013	0.9897	0.0016
Glucocorticoids	-1.2355	2.4662	0.501	0.6204	-0.0608
Exercise	-1.5602	3.4020	0.459	0.6501	-0.0538
Alcohol consumption	0.4301	2.2901	0.188	0.8524	0.0204

3.3.3. Heart Rate Profiles During PTSD Hyperarousal Events

Heart rate rhythm: A healthy window of heart rate data in resting position is steady with normal sinus rhythms [39]. Such healthy rhythm is characterized using sinusoidal waves with no significant deviations between successive waves [40].

However, our finding suggests that when individuals experience PTSD hyperarousal, their heart rate rhythm is irregular and sporadic. More specifically, in most cases heart rate continues to accelerate immediately after the perceived (self-reported) PTSD hyperarousal event for an average of 21 bpm for 107 seconds on average with clear deceleration after about 81 seconds on average (up to 200 seconds for some participants) for an average of 26 bpm which may suggest the recovery from the event. However, we observed a large variability in such abnormal rhythms with no uniform gradient in heart rate arousal or recovery in PTSD windows. Figure 5 shows a sample 10-minute window of heart rate data for a healthy individual compared to heart rate data during a PTSD hyperarousal event in our study.

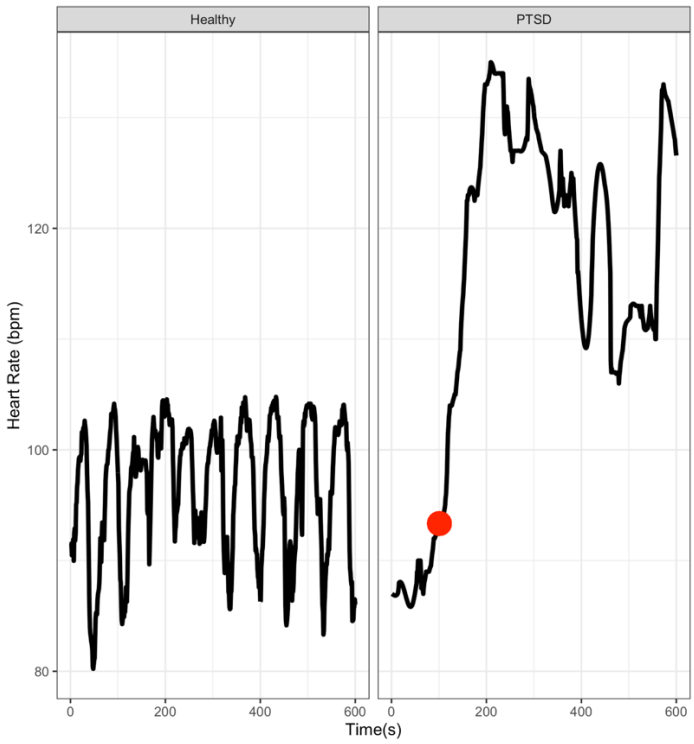

Figure 3.5. Heart rate patterns in a healthy subject (left) compared to a PTSD trigger (right). The red circle represents the self-reported event. Reprinted with permission from [51]

Stationarity. The results from the Dickey-Fuller stationarity test [29] suggest that heart rate during onset of PTSD symptoms are highly non-stationary (Dickey-Fuller = -1.137 p = 0.92 for PTSD windows, where the null hypothesis was that the time series data is not stationary). Furthermore, a visual inspection of the stationarity graphs suggests that while both healthy windows and PTSD windows of heart rate data are non-stationary, windows of heart rate data with PTSD events have higher fluctuation rates compared to healthy counterparts. This observation was later validated using Detrended Fluctuation Analysis (DFA; see below).

Autocorrelation. Figure 6 shows the autocorrelation function for 11 healthy heart rate windows and aggregated PTSD trigger windows. As shown in the figure, for healthy windows of heart rate, the direction of the correlation changes faster (from positive to negative); however, for PTSD hyperarousal windows of heart rate, the correlation coefficient is positive for a longer period of time. For instance, in Figure 6, the direction of correlation changes multiple times before a lag of 100 seconds in healthy windows of heart rate data, but this direction does not change for PTSD windows of heart rate data. Also, this correlation is 0 for PTSD windows of time when participants reported an event (lag 100) meaning that heart rate behaves in a more chaotic manner close to the reported event.

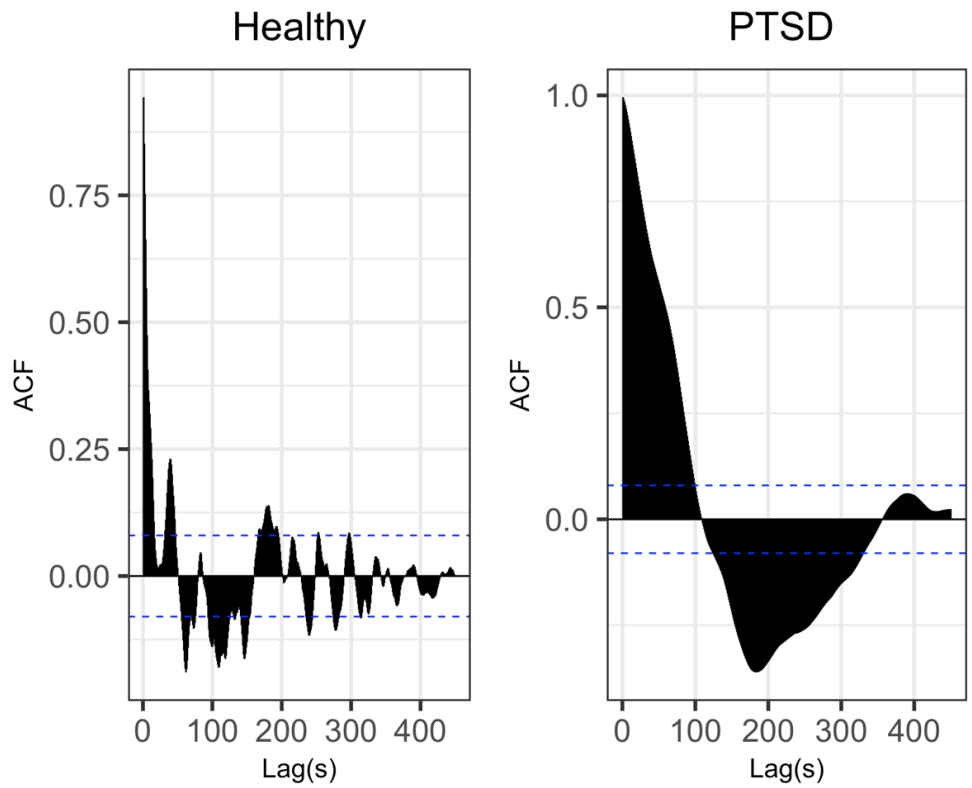

Figure 3.6. Autocorrelation graphs for healthy windows of heart rate (left) and PTSD windows of heart rate (right). Reprinted with permission from [51]

Detrended Fluctuation Analysis (DFA): Figure 7 shows DFA profiles plotted in R for samples of 600 seconds of 11 healthy windows and samples of 600 seconds of PTSD hyperarousal windows. As shown in Figure 7, the DFA function values measured in the PTSD hyperarousal windows are much higher compared to the corresponding values in the healthy window especially for longer time windows (>200 seconds).

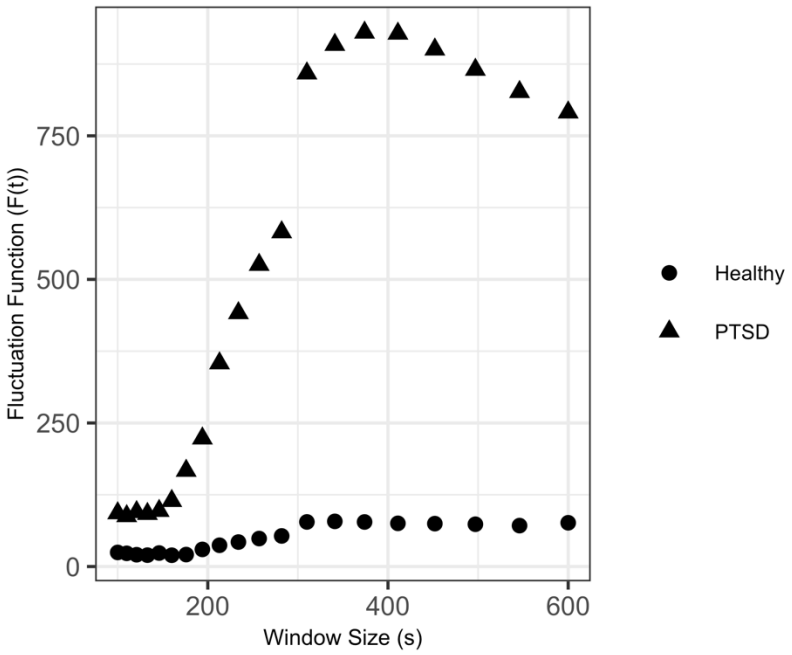

Figure 3.7. DFA graph for healthy windows of heart rate and PTSD hyperarousal windows of heart rate. Reprinted with permission from [51]

3.4. Discussion

The goal of this study was to investigate the effects of various factors on heart rate in veterans who are diagnosed with PTSD, as well as to model and describe heart rate patterns during PTSD hyperarousal events. To our knowledge, this is the first study to report on self-reported hyperarousal events as well as the characteristics of heart rate (other than correlations) during onset of PTSD symptoms in longitudinal and naturalistic settings. Our results showed that all 99 veterans who participated in this study experienced at least one PTSD hyperarousal event every three days with some experiencing an alarming rate of such events (up to 45 events over 6 days).

Although most participants reported not wearing the device between midnight and 6am, about 5% of hyperarousal events were reported during this timeframe which may suggest a significant underestimation of occurrence during sleep. This may support findings by others (e.g., [41]) who found poor sleep quality and reduced sleep duration and efficiency among PTSD patients. Another interesting finding was related to the occurrence of PTSD during the riding activities compared to resting. Our findings suggest that frequency of hyperarousal events is almost 7 times higher during resting periods compared to periods involving physical activity. This may support Oppizzi and Umberger's (2018) [42] review that showed a reduction of PTSD symptoms when engaged in physical activity especially for those who are resistant to therapy. This finding also has significance for the design of PTSD monitoring technologies—our findings suggest the need to optimize designs for detection and interaction during rest periods. However, more work is needed to investigate individual characteristics that result in differences in outcomes related to physical activity as well as different types and duration of activity.

Our results also showed that demographic factors such as smoking and use of medications such as anti-depressants may increase resting heart rate in veterans who suffer from PTSD. In addition, females had higher resting heart rate compared to males and those who reported more hours of sleep per night had significantly lower resting heart rate. While we are not aware of any comparative studies for the veteran population, these findings are partly in line with previous research that shows similar effects of gender [43], smoking [44] and anti-depressants [45] on resting heart rate in the civilian

population. Although all these parameters have known effects on the resting heart rate of healthy individuals, to our knowledge this is the first study that documents these effects in PTSD patients. Given the emergence of heart-rate-based PTSD symptom detection technologies (e.g., [17]), our findings suggest that machine learning algorithms that do not account for changes in heart rate attributable to gender, smoking, medication use, and sleep behavior, may introduce unintended biases. The effect of these biases should be investigated in future work.

While the application of ARIMA to investigate heart rate patterns is not novel, our findings show promise for the development of descriptive models of PTSD hyperarousal based on identification of unique heart rate markers. In particular, our findings suggest that heart rate patterns during PTSD hyperarousal events exhibit unique non-stationary and high fluctuation characteristics compared to healthy heart rate patterns. We believe this novel application of ARIMA with the preliminary evidence of efficacy presented here is an important contribution to the literature on psychophysiology of PTSD and an important first step in describing the heart rate response to PTSD hyperarousal events. While more work is needed to verify the identified heart rate patterns, this preliminary evidence shows potential heart-rate sensor-based tools for detection of PTSD symptoms. Such detection may play a vital role in supporting just-in-time self-management, digital therapeutics and coaching technologies.

When autocorrelation analysis was used to compare heart rate during PTSD hyperarousal events and within healthy windows of heart rate, significant differences in periodicity was observed. This result and the pattern observed is similar to the findings

from Peng et al. (1995) [32] that show dependency in heart rate data of healthy people that does not exist in the heart rate data of people who have cardiovascular disease. Given the evidence suggesting the higher risk of heart attacks and other cardiovascular diseases for PTSD patients ([46], [47], [48]), our findings may support such link between PTSD and higher rates of heart diseases.

The results from the DFA analysis suggest that the heart rate fluctuates widely during a perceived PTSD hyperarousal event. Given known associations between high fluctuation in heart rate and cardiac autonomic dysfunction in individuals [49], our results may suggest a potential link between PTSD and higher rates of cardiovascular diseases. However, further investigation is needed to validate this assumption.

This study had several notable limitations that may affect the generalizability of findings. While naturalistic testing enjoys a high level of external validity, the self-reported data collected is prone to subjectivity and individual differences. In particular, participants might have over- or under-reported events, or some hyperarousal events may have been inadvertently reported (e.g., tapping twice on the interface when a single tap was intended). Another issue related to collecting data in naturalistic settings was the high number of missing values especially during the first three HERO events. In general, Apple Watches proved to be more reliable and provided a more complete dataset compared to Moto 360 devices. This is in line with El-Amrawy and Nounou (2015) [50] who also suggest a near-perfect accuracy of Apple Watch's heart rate sensor (92.8%) compared to Moto 360s when the two were compared to professional clinical pulse oximeters. Smartwatches provided a discreet and non-intrusive platform for soliciting

self-reported events. However, future work may use other wearable sensors with higher sampling rate and accuracy, including chest straps. Another important limitation of this study was that the cardiac data related to PTSD hyperarousal events was collected during group events that involved extended physical activity (which was associated with considerably lower reporting of hyperarousal events) and may not generalize to all contexts. Future work may replicate this study for patients who are not involved in physical activities and/or who are in a home environment. Finally, we did not investigate differences between smartwatch heart rate and accelerometer sensors used in different studies. Therefore, the findings need to be interpreted as a preliminary case study, and future work is needed to evaluate the resulting patterns while comparing different devices.

3.5. Conclusion

PTSD is a prevalent condition among returning combat veterans and is negatively affecting their quality of life. Despite efforts and advances in therapeutics methods and medications used to treat this condition, self-management is challenging and remains largely unsupported. In an effort to investigate objective methods for detection of PTSD symptoms, a naturalistic study was conducted to investigate the impact of hyperarousal events on heart rate patterns. Our findings show distinguishable heart rate patterns and characteristics during PTSD hyperarousal events. While our understanding of psychophysiology of PTSD is still at its infancy, understanding the dynamics of this prevalent condition and its effect on physiology is critical to develop

therapeutic tools that fit human needs and may set the stage for advanced real-time detection of onsets and digital therapeutics.

3.6. References

[1] M. Spottswood, D. S. Davydow, and H. Huang, "The prevalence of posttraumatic stress disorder in primary care: a systematic review," *Harvard review of psychiatry*, vol. 25, no. 4, p. 159, 2017.

[2] American Psychiatric Association, *Diagnostic and statistical manual of mental disorders (DSM-5®)*. American Psychiatric Pub, 2013.

[3] A. A. Gravely, A. Cutting, S. Nugent, J. Grill, K. Carlson, and M. Spoont, "Validity of PTSD diagnoses in VA administrative data: comparison of VA administrative PTSD diagnoses to self-reported PTSD Checklist scores," *Journal of rehabilitation research and development*, vol. 48, no. 1, pp. 21–30, 2011.

[4] J. Geiling, J. M. Rosen, and R. D. Edwards, "Medical costs of war in 2035: long-term care challenges for veterans of Iraq and Afghanistan," *Military medicine*, vol. 177, no. 11, pp. 1235–1244, 2012.

[5] J. R. Davidson, "Davidson trauma scale (DTS)," 1996.

[6] F. W. Weathers, B. T. Litz, T. M. Keane, P. A. Palmieri, B. P. Marx, and P. P. Schnurr, "The ptsd checklist for dsm-5 (pcl-5)," *Scale available from the National Center for PTSD at www. ptsd. va. gov*, vol. 10, 2013.

[7] C. Rodriguez-Paras *et al.*, "Posttraumatic stress disorder and mobile health: App investigation and scoping literature review," *JMIR mHealth and uHealth*, vol. 5, no. 10, p. e156, 2017.

[8] P. R. Zoladz and D. M. Diamond, “Current status on behavioral and biological markers of PTSD: a search for clarity in a conflicting literature,” *Neuroscience & Biobehavioral Reviews*, vol. 37, no. 5, pp. 860–895, 2013.

[9] R. K. Pitman *et al.*, “Psychophysiologic assessment of posttraumatic stress disorder in breast cancer patients,” *Psychosomatics*, vol. 42, no. 2, pp. 133–140, 2001.

[10] T. C. Buckley, D. Holohan, J. L. Greif, M. Bedard, and M. Suvak, “Twenty-four-hour ambulatory assessment of heart rate and blood pressure in chronic PTSD and non-PTSD veterans,” *Journal of Traumatic Stress*, vol. 17, no. 2, pp. 163–171, 2004.

[11] A. Y. Shalev *et al.*, “A prospective study of heart rate response following trauma and the subsequent development of posttraumatic stress disorder,” *Archives of general psychiatry*, vol. 55, no. 6, pp. 553–559, 1998.

[12] M. C. Morris, N. Hellman, J. L. Abelson, and U. Rao, “Cortisol, heart rate, and blood pressure as early markers of PTSD risk: A systematic review and meta-analysis,” *Clinical psychology review*, vol. 49, pp. 79–91, 2016.

[13] E. B. Blanchard, “Elevated basal levels of cardiovascular responses in Vietnam veterans with PTSD: a health problem in the making?,” *Journal of Anxiety Disorders*, vol. 4, no. 3, pp. 233–237, 1990.

[14] E. B. Blanchard, L. C. Kolb, R. J. Gerardi, P. Ryan, and T. P. Pallmeyer, “Cardiac response to relevant stimuli as an adjunctive tool for diagnosing post-traumatic

stress disorder in Vietnam veterans," *Behavior Therapy*, vol. 17, no. 5, pp. 592–606, 1986.

[15] A. Rizzo *et al.*, "Virtual reality applications for the assessment and treatment of PTSD," in *Handbook of military psychology*, Springer, 2017, pp. 453–471.

[16] K. T. Green *et al.*, "Exploring the relationship between posttraumatic stress disorder symptoms and momentary heart rate variability," *Journal of psychosomatic research*, vol. 82, pp. 31–34, 2016.

[17] A. D. McDonald, F. Sasangohar, A. Jatav, and A. H. Rao, "Continuous monitoring and detection of post-traumatic stress disorder (PTSD) triggers among veterans: a supervised machine learning approach," *IISE Transactions on Healthcare Systems Engineering*, vol. 9, no. 3, pp. 201–211, 2019.

[18] P. Lechat *et al.*, "Heart rate and cardiac rhythm relationships with bisoprolol benefit in chronic heart failure in CIBIS II Trial," *Circulation*, vol. 103, no. 10, pp. 1428–1433, 2001.

[19] N. Ravi, N. Dandekar, P. Mysore, and M. L. Littman, "Activity recognition from accelerometer data," in *Aaai*, 2005, vol. 5, no. 2005, pp. 1541–1546.

[20] Venkatraman, 8,998,815

[21] J. Benesty, J. Chen, Y. Huang, and I. Cohen, "Pearson correlation coefficient," in *Noise reduction in speech processing*, Springer, 2009, pp. 1–4.

[22] S. Weisberg, *Applied linear regression*, vol. 528. John Wiley & Sons, 2005.

[23] T. B. Kashdan, J. D. Elhai, and B. C. Frueh, “Anhedonia, emotional numbing, and symptom overreporting in male veterans with PTSD,” *Personality and Individual Differences*, vol. 43, no. 4, pp. 725–735, 2007.

[24] M. T. Tull and L. Roemer, “Alternative explanations of emotional numbing of posttraumatic stress disorder: An examination of hyperarousal and experiential avoidance,” *Journal of Psychopathology and Behavioral Assessment*, vol. 25, no. 3, pp. 147–154, 2003.

[25] S. Chatterjee and A. S. Hadi, “Influential observations, high leverage points, and outliers in linear regression,” *Statistical science*, pp. 379–393, 1986.

[26] G. E. Box, G. M. Jenkins, G. C. Reinsel, and G. M. Ljung, “Time series analysis: forecasting and control John Wiley & Sons,” *Hoboken, NJ*, 2008.

[27] A. E. Gelfand and P. Vounatsou, “Proper multivariate conditional autoregressive models for spatial data analysis,” *Biostatistics*, vol. 4, no. 1, pp. 11–15, 2003.

[28] M. Sadeghi, F. Sasangohar, and A. D. McDonald, “Toward a taxonomy for analyzing the heart rate as a physiological indicator of posttraumatic stress disorder: systematic review and development of a framework,” *JMIR Mental Health*, vol. 7, no. 7, p. e16654, 2020.

[29] D. A. Dickey and W. A. Fuller, “Likelihood ratio statistics for autoregressive time series with a unit root,” *Econometrica: journal of the Econometric Society*, pp. 1057–1072, 1981.

[30] E. J. Weber, P. C. Molenaar, and M. W. Van der Molen, “A nonstationarity test for the spectral analysis of physiological time series with an application to respiratory sinus arrhythmia,” *Psychophysiology*, vol. 29, no. 1, pp. 55–62, 1992.

[31] M. Sadeghi, F. Sasangohar, and A. McDonald, “Analyzing Heart Rate as a Physiological Indicator of Post-Traumatic Stress Disorder: A Scoping Literature Review,” in *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*, 2019, vol. 63, no. 1, pp. 1936–1936.

[32] C.-K. Peng, S. Havlin, H. E. Stanley, and A. L. Goldberger, “Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series,” *Chaos: an interdisciplinary journal of nonlinear science*, vol. 5, no. 1, pp. 82–87, 1995.

[33] J. W. Kantelhardt, S. A. Zschiegner, E. Koscielny-Bunde, S. Havlin, A. Bunde, and H. E. Stanley, “Multifractal detrended fluctuation analysis of nonstationary time series,” *Physica A: Statistical Mechanics and its Applications*, vol. 316, no. 1–4, pp. 87–114, 2002.

[34] G. B. Moody and R. G. Mark, “The impact of the MIT-BIH arrhythmia database,” *IEEE Engineering in Medicine and Biology Magazine*, vol. 20, no. 3, pp. 45–50, 2001.

[35] A. L. Goldberger *et al.*, “PhysioBank, PhysioToolkit, and PhysioNet: components of a new research resource for complex physiologic signals,” *circulation*, vol. 101, no. 23, pp. e215–e220, 2000.

[36] H. Wickham, “ggplot2,” *Wiley Interdisciplinary Reviews: Computational Statistics*, vol. 3, no. 2, pp. 180–185, 2011.

[37] C. A. Garcia and G. Sawitzki, “nonlinearTseries: nonlinear time series analysis,” *R package version 0.2*, vol. 3, 2015.

[38] J. M. Arnold, D. H. Fitchett, J. G. Howlett, E. M. Lonn, and J.-C. Tardif, “Resting heart rate: a modifiable prognostic indicator of cardiovascular risk and outcomes?,” *Canadian Journal of Cardiology*, vol. 24, pp. 3A-15A, 2008.

[39] W. H. Sauer and B. Olchansky, “Normal sinus rhythm and sinus arrhythmia,” *UpToDate in Medicine, Rose BD (Ed), UpToDate in Medicine, Wellesley*, vol. 2014, 2010.

[40] M. Gertsch, “The Normal ECG and its (Normal) variants,” in *The ECG*, Springer, 2004, pp. 19–43.

[41] M. van Wyk, K. G. Thomas, M. Solms, and G. Lipinska, “Prominence of hyperarousal symptoms explains variability of sleep disruption in posttraumatic stress disorder.,” *Psychological Trauma: Theory, Research, Practice, and Policy*, vol. 8, no. 6, p. 688, 2016.

[42] L. M. Oppizzi and R. Umberger, “The effect of physical activity on PTSD,” *Issues in mental health nursing*, vol. 39, no. 2, pp. 179–187, 2018.

[43] J. A. Larsen and A. H. Kadish, “Effects of gender on cardiac arrhythmias,” *Journal of cardiovascular electrophysiology*, vol. 9, no. 6, pp. 655–664, 1998.

[44] A. Linneberg *et al.*, “Effect of smoking on blood pressure and resting heart rate: a Mendelian randomization meta-analysis in the CARTA consortium,” *Circulation: Cardiovascular Genetics*, vol. 8, no. 6, pp. 832–841, 2015.

[45] A. H. Kemp *et al.*, “Effects of depression, anxiety, comorbidity, and antidepressants on resting-state heart rate and its variability: an ELSA-Brasil cohort baseline study,” *American Journal of Psychiatry*, vol. 171, no. 12, pp. 1328–1334, 2014.

[46] S. S. Coughlin, “Post-traumatic stress disorder and cardiovascular disease,” *The open cardiovascular medicine journal*, vol. 5, p. 164, 2011.

[47] D. Edmondson, I. M. Kronish, J. A. Shaffer, L. Falzon, and M. M. Burg, “Posttraumatic stress disorder and risk for coronary heart disease: a meta-analytic review,” *American heart journal*, vol. 166, no. 5, pp. 806–814, 2013.

[48] H. Spindler and S. S. Pedersen, “Posttraumatic stress disorder in the wake of heart disease: prevalence, risk factors, and future research directions,” *Psychosomatic medicine*, vol. 67, no. 5, pp. 715–723, 2005.

[49] J.-Y. Chiang *et al.*, “Detrended fluctuation analysis of heart rate dynamics is an important prognostic factor in patients with end-stage renal disease receiving peritoneal dialysis,” *PloS one*, vol. 11, no. 2, p. e0147282, 2016.

[50] F. El-Amrawy and M. I. Nounou, “Are currently available wearable devices for activity tracking and heart rate monitoring accurate, precise, and medically beneficial?,” *Healthcare informatics research*, vol. 21, no. 4, pp. 315–320, 2015.

[51] Sadeghi M, Sasangohar F, McDonald AD, Hegde S. Understanding heart rate reactions to post-traumatic stress disorder (PTSD) among veterans: a naturalistic study. Human factors. 2021 Jul 22:00187208211034024.

4. CHAPTER 4 (ARTICLE 3) MACHINE LEARNING ALGORITHM[3]

Overview

Treatment for PTSD typically consists of a combination of in-session therapy and medication. However; patients often experience their most severe PTSD symptoms outside of therapy sessions. Mobile health applications may address this gap, but their effectiveness is limited by the current gap in continuous monitoring and detection capabilities enabling timely intervention. The goal of this article is to develop a novel physiological and activity-based machine learning algorithm to detect PTSD symptom onset. Physiological data including heart rate and body acceleration as well as self-reported hyperarousal events were collected using a tool developed for commercial off-the-shelf wearable devices from 99 United States veterans diagnosed with PTSD over several days. The data were used to develop four machine learning algorithms: Random Forest, Support Vector Machine, Logistic Regression and XGBoost. The XGBoost model had the best performance in detecting onset of PTSD symptoms with over 83% accuracy and an AUC of 0.70. Post-hoc SHapley Additive exPlanations (SHAP) additive explanation analysis showed that algorithm predictions were correlated with average heart rate, minimum heart rate and average body acceleration. Findings show promise in detecting onset of PTSD symptoms which could be the basis for developing remote and continuous monitoring systems for PTSD. Such systems may address a vital gap in just-

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in-time interventions for PTSD self-management outside of scheduled clinical appointments.

4.1. Introduction

Over 70% of the U.S. population will experience a traumatic event in their lifetime of whom 20% will subsequently develop Post-Traumatic Stress Disorder (PTSD). PTSD is a psychiatric condition experienced by individuals after exposure to life-threatening events, such as physical assault, sexual abuse, and combat exposure [1]. PTSD symptomology includes avoidance, hyperarousal, and reexperiencing trauma through dreams and recollections [1]. Avoidance symptoms include circumventing activities or thoughts associated with the traumatic event, decreased interest in daily life, and an overall feeling of detachment from one's surroundings. Hyperarousal symptoms include hypervigilance, feelings of irritability, and an exaggerated response following a startling event. Other symptoms of PTSD include anxiety, insomnia, fatigue, anger, and aggression [2].

Combat veterans are particularly prone to PTSD, with recent estimates of prevalence as high as 24% [3]. Veterans with PTSD are also at a greater risk of suicide [4], and suicidal thoughts [5]—an average of 20 veterans per day commit suicide, with a majority of cases linked to PTSD [6]. Beyond personal costs, PTSD has an enormous societal cost associated with healthcare service utilization. The costs of caring for war veterans usually peaks 30-40 years following a major conflict. For example, for Iraq/Afghanistan conflicts, it is estimated that costs of veterans' care will peak around 2035 [7]. This increased healthcare use is estimated to cost the United States over $60

billion each year. The costs are also expected to increase due to secondary and tertiary comorbidities including depression, substance abuse, smoking, heart disease, obesity, diabetes, chronic fatigue, and increased dementia [7].

PTSD is typically managed by a combination of therapeutic and pharmaceutical treatments, although many cases go undiagnosed or untreated potentially due to mental illness stigma and care shortages [8]. Therapeutic methods include eye movement desensitization and reprocessing; exposure therapy; cognitive therapy; cognitive restructuring therapy; cognitive processing therapy; stress inoculation therapy as part of stress management therapy [9]; and the trauma-focused cognitive behavioral therapy [10]. While these methods are effective [11], [12], there are several barriers to care access including geographical, financial, and cultural constraints, and limited care delivery resources [13], [14]. In addition, most intense symptoms of PTSD are often experienced outside clinical environments and in-between therapeutic sessions [15]. Therefore, there is a critical need for tools and methods for real-time monitoring and detection of PTSD signs and symptoms, as well as mechanisms to support self-management of such symptoms. Recent advances in wearable physiological sensors and mobile health (mHealth) technologies may provide a viable alternative to address this need.

Prior work has shown that PTSD is correlated with several physiological measures including heart rate, heart rate variability, blood pressure, respiratory rate and skin conductance [16]. Among these, heart rate has shown promise as a reliable correlate of PTSD [17]. [18] used the Autoregressive Integrated Moving Average (ARIMA)

analysis to model veterans' heart rate patterns during PTSD hyperarousal events. Their results indicated strong correlation between heart rate characteristics such as autocorrelation and fluctuation and hyperarousal events. Recent efforts have utilized supervised machine learning tools to detect perceived stress using heart rate, other physiological metrics, and self-reported measures with reported accuracies ranging between 67%-92% [19]–[23], however, to our knowledge, only one study [19] used machine learning algorithms to predict the onset of PTSD symptoms among veterans based on heart rate data.

In their study, [19] investigated self-reported periods of hyperarousal to extract heart rate time-dependent features and developed five machine learning algorithms: a Conventional Neural Network, Neural Network, Support Vector Machine (SVM), Random Forest, and Decision Tree. Among these methods, the SVM showed the highest accuracy (over 70%). While this study provided preliminary evidence supporting the efficacy of using heart rate to detect hyperarousal events, using heart data alone may be subject to significant noise associated with movement or physical activity [24], [25]. In line with previous research (e.g. [21], [22], [26]). [19] suggested that body acceleration data might improve the accuracy of machine learning algorithms and enable algorithms to distinguish between heart rate fluctuations due to physical activity and heart rate fluctuations due to mental stress. Therefore, the objective of this article is to expand [19] study to machine learning algorithms that uses body acceleration and heart rate data to predict PTSD hyperarousal events in veterans. In addition, in an effort to improve the

interpretation of the algorithm, we further analyze the developed model to investigate significant factors contributing to model's detection output.

4.2. Method

Four machine learning algorithms were trained using self-reported data collected naturalistically from veterans to predict PTSD hyperarousal events: Random Forest, XGBoost, Logistic Regression and non-linear SVM.

4.2.1. Participants

Participants were recruited from Project Hero's United Healthcare Ride 2 Recovery (R2R) challenges. Project Hero is a non-profit organization dedicated to help veterans and first responders diagnosed with PTSD. In each challenge, veterans rode for an average of 7 days between key destinations in California, Washington DC, Minneapolis, Texas, and Nevada. Each day of the challenge involved approximately 8 hours of biking with the remaining time for resting and socializing. The research team joined a total of 5 rides in 2017, 2018 and 2019.

Data from 99 veteran participants (82 male; 17 female) were used in this study. Participants' age ranged from 22 to 75 years old (M = 45.5, SD = 10). Majority of participants reported Veterans Affairs disability rating of over 90% related to PTSD. Table 1 summarizes other relevant demographics.

Table 4.1. Participants' demographics, the numbers show the number of veterans per each group

Gender		Ethnicity		Branch		VA Disability Rating	
Female	82	American Indian or Alaska Native	4	Air Force	5	40%	2
Male	17	Asian	1	Army	68	50%	4
		Black/African American	15	Navy	2	70%	5
		Hispanic/Latino	26	Marine Corpse	4	80%	6
		Native Hawaiian	1	NA	6	≥ 90%	74
		White	44				
		Other	8				

4.2.2. Data Collection

The data collection application (app) for smart wearable devices utilized in [19]. [19] was used. Participants were asked to wear smart watches (MOTO 360 Gen 1 or Gen 2, Apple Watch series 3 or 4) with the app installed on them. The app ran continuously in the background and connected to participants' phones for the purpose of data transfer. The app had the ability to continuously and remotely collect physiological data including heart rate and acceleration from participants at the frequency of 1 Hz. The app included functionality which allowed the user to report a hyperarousal event (symptomatic of PTSD) through a simple 'double tap' anywhere on the watch face which created a time-

stamped self-reported event. These events were used for training the machine learning algorithm.

4.2.3. Data Preprocessing

All data analysis including data preprocessing and machine learning were conducted in Python 3.8.2 and R 3.6.2. The data preprocessing included four main steps: (1) imputation, (2) windowing and labeling, (3) dividing the data into training and testing, and (4) resampling the training dataset.

Data Imputation

Kalman filter imputation was used to impute missing acceleration and heart rate data. Kalman filter imputation is an established method for time-series data imputation [27], especially for heart rate data [28]. To determine the cut off range, we calculated the average Mean Square Error (MSE) of the imputed data and corresponding actual values. A cut off range of 15 MSE for estimating the randomly dropped values is suggested by [28]. Based on Kalman filter imputation analysis, we chose 5 as the maximum imputation range because it was the greatest value among a set of successive values to have the highest MSE less than 15 [19].

Windowing and labeling

To investigate the patterns of hyperarousal events, the data was divided into 60-second sliding windows with 30 seconds overlap, chosen based on prior work [20] to predict stress severity based on physiological reactions. Each window was assigned a label based on the presence or absence of reported hyperarousal events. If a hyperarousal event occurred anywhere in the window, it was labeled as hyperarousal event; otherwise,

it was labeled as non-hyperarousal event. All windows with over 80% missing values were dropped from the dataset. The final dataset included 530 and 13,554 instances of hyperarousal and non-hyperarousal events, respectively.

4.2.4. Training, Testing, and Upsampling

To validate the algorithm, the data was separated into training (70%) and testing (30%) sets. Table 1 shows the initial dataset classifications. One of the challenges of training the algorithm to detect PTSD hyperarousal events was the imbalanced dataset—96.2% of the windows were labeled non-hyperarousal events. To address this issue, we upsampled the training data. Upsampling was selected because it decreases the information lost in the quantification process, thereby reducing the noise and increasing the resolution of the results [29], [30]. Based on a sensitivity analysis comparing different resampling ratio including 1-1, 2-1, 3-1, 3-2, and 4-3, a ratio of 4 (non-hyperarousal events) to 3 (hyperarousal events) windows was used for upsampling (Table 4.2).

Table 4.2. Training and testing datasets after and before resampling

	Label	Training set	Test set
Training and testing datasets before resampling	Non-hyperarousal events	9486	4068
	Hyperarousal events	372	158
Training and testing datasets after resampling	Non-hyperarousal events	9486	4068
	Hyperarousal events	7114	158

4.2.5. Feature Generation and Selection

Heart rate data

Previous research has shown that that time domain features of heart rate are strongly correlated with PTSD [31]. We extracted time domain features of heart rate including maximum heart rate (bpm), minimum heart rate (bpm), heart rate standard deviation (bpm), heart rate range (max-min) (bpm), and average heart rate (bpm) from each window of time to use for PTSD hyperarousal prediction. Key features were extracted based on recommendations from a review article by [32]on detecting psychological stress using bio signals [32].

Acceleration data

Research on stress prediction have used scalars of body acceleration to estimate body activity and to remove noise from the data [21], [23], [33], [34]. [33] used time domain and frequency domain features of acceleration to predict stress in participants in real work environments. [21] used body acceleration to classify activity and extracted time domain features of body acceleration such as average and standard deviation to feed machine learning algorithms.

In line with these approaches, we calculated the vector of body acceleration for each moment using the following widely used formula.

$$Body\ acceleration = \sqrt{{a_x}^2 + {a_y}^2 + {a_z}^2}$$

Where a_x is the body acceleration in X direction, $a_y$is body acceleration in Y direction, and a_z is body acceleration in Z direction.

Further, based on previous research (e.g., [21], [33]), time domain features of body acceleration including average body acceleration (m/s^2), maximum body acceleration (m/s^2), minimum body acceleration (m/s^2), and range of body acceleration (m/s^2) were extracted to feed machine learning algorithms.

4.2.6. Model Assessment

We then generated a confusion matrix to assess the performance of each model. Model comparisons were conducted with a 5x2 cross validation test following the recommendations in [35] to minimize the type 1 error. This method uses *p* values and t statistics to compare the algorithms. The null hypothesis indicates that there is no significant difference between the algorithms in terms of performance (average accuracy) where the alternative hypothesis shows that one algorithm is more accurate than the others. Algorithms were further assessed with the Area Under the receiver operating characteristic (ROC) Curve (AUC).

4.2.7. Feature Importance and Model Interpretation

The complexity of black box machine learning models and the need to make these models explainable necessitate an evaluation of the influence of algorithm's features on algorithm predictions. In this study, we used Shapley Additive exPlanations (SHAP) to address this. SHAP uses game theoretic concepts to allocate values to features in a model based on their importance in prediction [36]. SHAP values indicate how much each feature contributes to the prediction of the machine learning algorithm. SHAP value summary plots generate a feature importance list along with the distribution of each feature and shows how each value affects the output of the model. This method

is computationally efficient, consistence with human intuition, and interpretable for explaining class differences [37]. Using SHAP values to interpret machine learning algorithms has several advantages over using more traditional methods such as dependency plots [37]. For example, dependence plots do not usually show features' distributions, which may lead to misinterpreting regions with significant missing data. Conversely, SHAP plots show feature distributions. SHAP values also indicate how much a feature affects the output of the prediction by considering interaction effects, whereas partial dependence plots do not account for interactions between features.

4.3. Results

4.3.1. Model Performance and Comparison

Figure 1 shows the ROC curves for each algorithm along with the AUC values. As shown in the plots, XGBoost had the highest AUC (0.70). Random Forest, Logistic Regression, and non-linear Kernel SVM had AUC of 0.63, 0.62, and 0.61, respectively. Table 3 shows confusion matrices for developed algorithms at three probability cutoffs. The first confusion matrix prioritizes hyperarousal detection, the second confusion matrix balances the true positives and false positives rate, and the third matrix prioritizes minimizing false positive rates. The pairwise 5*2 cross validation test results showed that XGBoost significantly outperformed the Random Forest ($t = -13.25$, $p < 0.001$), SVM ($t = -13.02$, $p < 0.001$), and Logistic Regression ($t = -11.97$, $p < 0.001$). Based on the results from this table, XGBoost showed the best performance in detecting PTSD hyperarousal events.

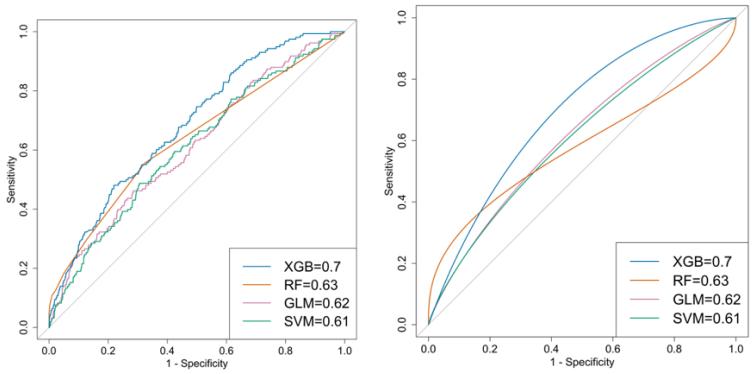

Figure 4.1. AUC-ROC empirical (left) and smooth (right) curves for algorithm

Table 4.3. Confusion matrices for all models at different probability cut offs.

Design Performance	Algorithm	TP	FN	FP	TN	TPR	FPR
Prioritize hyperarousal detection (TPR=1)	XGB	158	0	821	47	1	0.94
	RF	58	0	853	05	1	0.95
	GLM	58	0	4066	2	1	0.99
	SVM	58	0	4065	3	1	0.99
Balanced priorities (TPR=0.5)	XGB	79	79	1064	3004	0.5	0.26
	RF	88	70	1322	2746	0.55	0.33
	GLM	79	79	1467	2601	0.5	0.36
	SVM	79	79	1401	2667	0.5	0.34
Prioritize false positive minimization (FPR=0.1)	XGB	46	112	420	3648	0.29	0.1
	RF	29	129	205	3863	0.18	0.1
	GLM	38	120	410	3658	0.24	0.1
	SVM	30	128	409	3659	0.19	0.1

4.3.2. Model Interpretation

Figure 2 shows the SHAP summary plot for the XGBoost model. In this figure, the Y-axis shows the feature as well as the mean SHAP values ordered from top to bottom, the color shows the significance of the feature's value in predicting the output, and the X-axis indicates how the feature affects the output of the model (whether that feature with that specific value is contributing to experiencing a hyperarousal event or not). The X axis further indicates log-odds of perceiving a PTSD hyperarousal event. According to the SHAP analysis, the most important body acceleration features are average body acceleration (linaccmean) and minimum body acceleration (linaccmin). The most important heart rate time-domain features for predicting PTSD hyperarousal events are minimum heart rate and heart rate standard deviation.

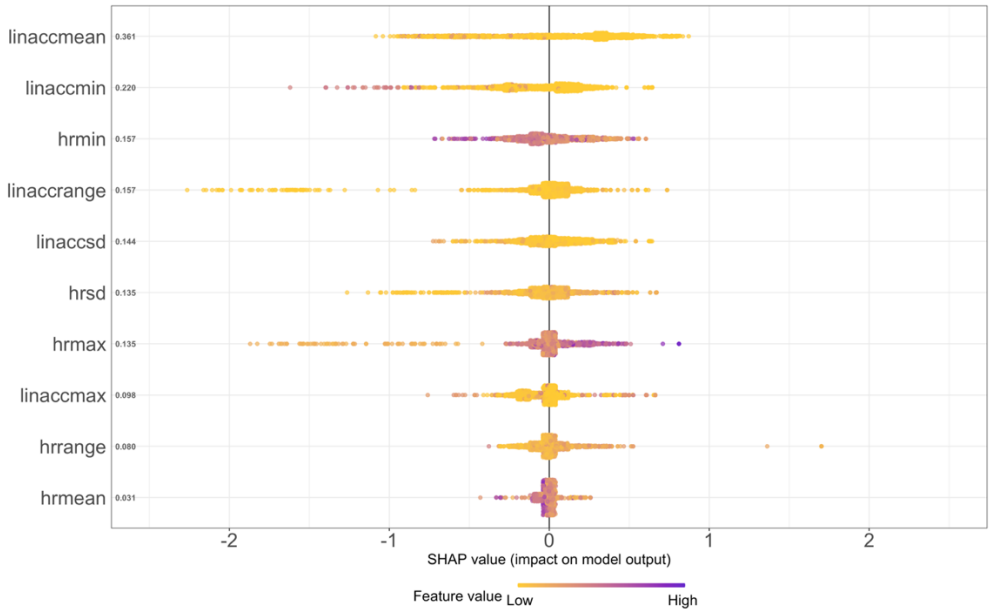

Figure 4.2. SHAP summary plot, Y axis shows each of the variables, and X axis shows log odds of perceiving a hyperarousal event.

SHAP dependence plots show contribution of a specific feature to a model based on the feature's distribution. In this plot each point shows an observation from the dataset, the X-axis line shows the value of the feature in that row, and the Y-axis shows the SHAP value for that feature that indicates the effect of that feature with that specific value on the prediction. The unit of X-axis is the same as the unit of the feature (for instance for heart rate measures it is beats per minute), and the unit of the Y-axis is log-odds of perceiving a PTSD hyperarousal event. In Figure 3, we provided SHAP dependence plots for the two most important acceleration and heart rate features.

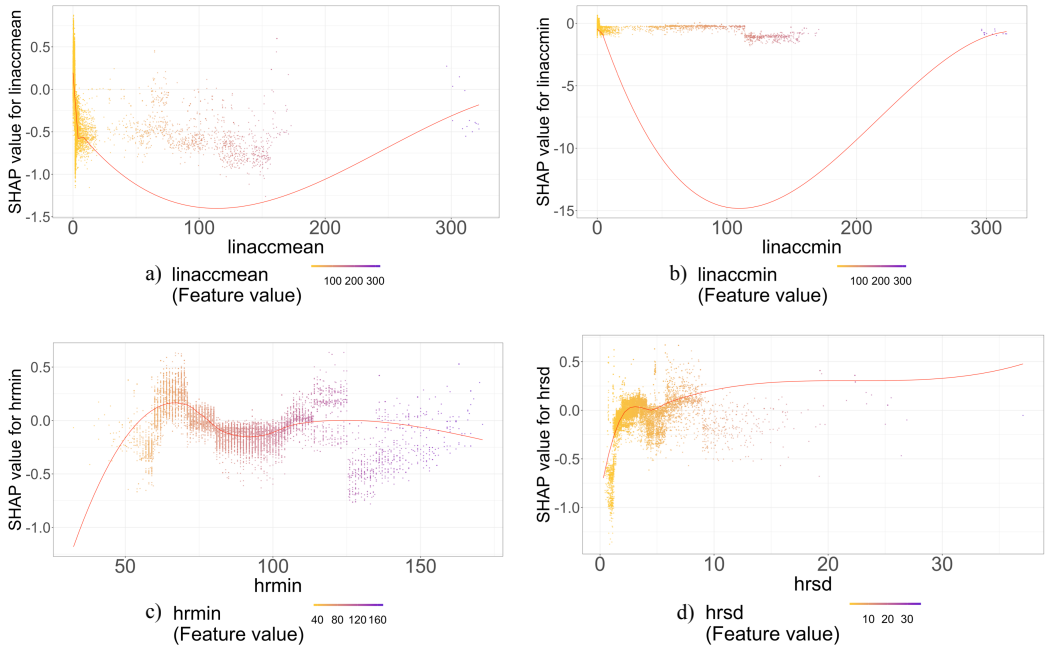

Figure 4.3. SHAP dependence plots, a) SHAP plot for average body acceleration (m/s^2), b) SHAP plot for minimum body acceleration (m/s^2), c) SHAP plot for minimum heart rate (bpm), and d) SHAP plot for heart rate standard deviation (bpm)

Figure 4 shows that hyperarousal events are more likely to be observed with higher minimum heart rate values over the window. When the minimum heart rate is over 140 the risk of perceiving hyperarousal events increases. Also, as the average body acceleration and minimum body acceleration increase, the odds of the detecting PTSD hyperarousal events decrease. Finally, higher heart rate standard deviation, i.e. higher heart rate fluctuation, increases the risk of hyperarousal events.

4.4. Discussion

This study developed, evaluated, and explicated machine learning algorithms to predict PTSD hyperarousal events among veterans using smartwatch based naturalistic heart rate and accelerometer data. The ground truth was subjectively-reported PTSD hyperarousal events. After preprocessing the data, we trained four different algorithms including Random Forest, SVM, Logistic Regression and XGBoost. Among the developed algorithms, the XGBoost was the most robust algorithm which yielded an AUC of 0.70 and over 81% accuracy. We sorted the most important features in the prediction process. The top three body acceleration features included average body acceleration, minimum body acceleration and range of body acceleration. The top three heart rate time domain features were minimum heart rate, standard deviation of heart rate and maximum heart rate. The initial analysis from the SHAP summary plot and SHAP dependence plots show that heart rate and body acceleration features have nonlinear relationships with PTSD episodes. A deeper look into SHAP plots indicate that as the body acceleration increases, indicating more activity from the participant, the algorithm is less likely to predict a PTSD hyperarousal events. This result is consistent

with prior studies demonstrating a significant relationship between increased physical activity and a reduction in PTSD hyperarousal events [38]–[40].

The SHAP dependence plot for the average heart rate data corroborates that when the heart rate is between 60-70 bpm, PTSD hyperarousal events are more likely to happen cf. [41]. The SHAP summary plot indicates that heart rate standard deviation was one of the most important features contributing to the odds that the algorithm will predict PTSD hyperarousal event manifestation. In particular, our findings suggest that as the heart rate standard deviation increases, i.e., as heart rate fluctuates more and in higher ranges, the odds of detecting a PTSD hyperarousal event increases. This result supports the findings from [18] and [42] who showed that during PTSD hyperarousal events, participants experience increased heart rate acceleration and fluctuation.

The results documented in this paper show an improvement in the machine learning algorithm performance compared to the findings from [19]. While there were differences in data processing methods used in this study, the current findings may suggest that the addition of acceleration data as well as using XGBoost algorithms to train the machine learning model may result in a considerable increase in the PTSD hyperarousal detection accuracy (81% in this study compared to 70 % in [19]). Results are in line with previous work on stress detection indicating that adding acceleration data decreases the noise in the data by differentiating heart rate changes due to physical activity versus fluctuations due to stress [23].

Several limitations of this study should be addressed in future work. First, stress and PTSD hyperarousal events are highly idiosyncratic. A stimulus that triggers one

individual may or may not trigger someone else. Because of the subjective and sustained characteristics of stress, defining the start, end, duration, and intensity of a hyperarousal event is an uncertain task [43]. As a result, it is significantly complex and difficult to define and measure a ground truth for stress. Hyperarousal events might have been over- or under-reported due to the subjectivity of the perceived events. Individual differences such as gender, age, lifestyle and other factors can affect PTSD hyperarousal events; therefore, personalizing machine learning algorithms might boost their performance. Another issue in this study was the high number of missing values due to the naturalistic nature of the study. Lastly, although machine learning algorithms work in theory, external validation of these algorithms are necessary to proof the applicability of these algorithms in the real world settings. Further laboratory and naturalistic studies are needed to complete and verify the accuracy of this study.

This article provides preliminary evidence of efficacy for data-driven real-time PTSD hyperarousal detection tools that can be used beyond clinic walls to remotely and continiously monitor veterans suffering from PTSD. In addition to the promise shown by the machine learning algorithm, in this article we utilized analytical techniques to which identifies most important features contributing to such detection, hence, improving the interpretation of the outcomes and moving towards explainable ML tools for PTSD monitoring. Although other machine learning algorithms exist to detect stress, to the best of our knowledge, the algorithm documented in this paper is one of very few algorithms that is specific to PTSD. The work is in progress to validate this algorithm in real world using smart watches and smart phones.

4.5. References

[1] American Psychiatric Association, *Diagnostic and statistical manual of mental disorders (DSM-5®)*. American Psychiatric Pub, 2013.

[2] K. F. Carlson *et al.*, "Prevalence, assessment, and treatment of mild traumatic brain injury and posttraumatic stress disorder: a systematic review of the evidence," *J. Head Trauma Rehabil.*, vol. 26, no. 2, pp. 103–115, 2011.

[3] M. Spottswood, D. S. Davydow, and H. Huang, "The prevalence of posttraumatic stress disorder in primary care: a systematic review," *Harv. Rev. Psychiatry*, vol. 25, no. 4, p. 159, 2017.

[4] C. A. Brake, S. M. Rojas, C. L. Badour, C. E. Dutton, and M. T. Feldner, "Self-disgust as a potential mechanism underlying the association between PTSD and suicide risk," *J. Anxiety Disord.*, vol. 47, pp. 1–9, 2017.

[5] J. M. McKinney, J. K. Hirsch, and P. C. Britton, "PTSD symptoms and suicide risk in veterans: Serial indirect effects via depression and anger," *J. Affect. Disord.*, vol. 214, pp. 100–107, 2017.

[6] U.S. Department of Veteran Affairs, "National Veteran Suicide Prevention Annual Report," p. 32, 2019.

[7] J. Geiling, J. M. Rosen, and R. D. Edwards, "Medical costs of war in 2035: long-term care challenges for veterans of Iraq and Afghanistan," *Mil. Med.*, vol. 177, no. 11, pp. 1235–1244, 2012.

[8] D. Mittal, K. L. Drummond, D. Blevins, G. Curran, P. Corrigan, and G. Sullivan, “Stigma associated with PTSD: Perceptions of treatment seeking combat veterans.,” *Psychiatr. Rehabil. J.*, vol. 36, no. 2, p. 86, 2013.

[9] Department of Veterans Affairs, “VA/DoD CLINICAL PRACTICE GUIDELINE FOR MANAGEMENT OF POST-TRAUMATIC STRESS,” 2019, [Online]. Available: https://www.healthquality.va.gov/guidelines/MH/ptsd/cpg_PTSD-full-201011612.PDF

[10] J. F. Haagen, G. E. Smid, J. W. Knipscheer, and R. J. Kleber, “The efficacy of recommended treatments for veterans with PTSD: A metaregression analysis,” *Clin. Psychol. Rev.*, vol. 40, pp. 184–194, 2015.

[11] E. B. Foa and B. O. Rothbaum, Treating the trauma of rape: Cognitive-behavioral therapy for PTSD. Guilford Press, 2001.

[12] S. A. Rauch, A. Eftekhari, and J. I. Ruzek, “Review of exposure therapy: a gold standard for PTSD treatment,” *J. Rehabil. Res. Dev.*, vol. 49, no. 5, pp. 679–688, 2012.

[13] E. Kazlauskas, “Challenges for providing health care in traumatized populations: barriers for PTSD treatments and the need for new developments,” *Glob. Health Action*, vol. 10, no. 1, p. 1322399, 2017, doi: 10.1080/16549716.2017.1322399.

[14] C. Rodriguez-Paras *et al.*, “Posttraumatic stress disorder and mobile health: App investigation and scoping literature review,” *JMIR MHealth UHealth*, vol. 5, no. 10, p. e156, 2017.

[15] J. Moon, A. Smith, F. Sasangohar, J. K. Benzer, and H.-C. Kum, "A descriptive model of the current PTSD care system: Identifying opportunities for improvement," in *Proceedings of the International Symposium on Human Factors and Ergonomics in Health Care*, 2017, vol. 6, no. 1, pp. 251–251.

[16] P. R. Zoladz and D. M. Diamond, "Current status on behavioral and biological markers of PTSD: a search for clarity in a conflicting literature," *Neurosci. Biobehav. Rev.*, vol. 37, no. 5, pp. 860–895, 2013.

[17] R. K. Pitman *et al.*, "Psychophysiologic assessment of posttraumatic stress disorder in breast cancer patients," *Psychosomatics*, vol. 42, no. 2, pp. 133–140, 2001.

[18] M. Sadeghi, F. Sasangohar, and A. D. McDonald, "Toward a taxonomy for analyzing the heart rate as a physiological indicator of posttraumatic stress disorder: systematic review and development of a framework," *JMIR Ment. Health*, vol. 7, no. 7, p. e16654, 2020.

[19] A. D. McDonald, F. Sasangohar, A. Jatav, and A. H. Rao, "Continuous monitoring and detection of post-traumatic stress disorder (PTSD) triggers among veterans: a supervised machine learning approach," *IISE Trans. Healthc. Syst. Eng.*, vol. 9, no. 3, pp. 201–211, 2019.

[20] D. McDuff, S. Gontarek, and R. Picard, "Remote measurement of cognitive stress via heart rate variability," in *2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2014, pp. 2957–2960.

[21] A. Sano *et al.*, “Recognizing academic performance, sleep quality, stress level, and mental health using personality traits, wearable sensors and mobile phones,” in *2015 IEEE 12th International Conference on Wearable and Implantable Body Sensor Networks (BSN)*, 2015, pp. 1–6.

[22] A. Sano and R. W. Picard, “Stress recognition using wearable sensors and mobile phones,” in *2013 Humaine Association Conference on Affective Computing and Intelligent Interaction*, 2013, pp. 671–676.

[23] E. Smets, W. De Raedt, and C. Van Hoof, “Into the wild: the challenges of physiological stress detection in laboratory and ambulatory settings,” *IEEE J. Biomed. Health Inform.*, vol. 23, no. 2, pp. 463–473, 2018.

[24] G. Comtois, Y. Mendelson, and P. Ramuka, “A comparative evaluation of adaptive noise cancellation algorithms for minimizing motion artifacts in a forehead-mounted wearable pulse oximeter,” in *2007 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2007, pp. 1528–1531.

[25] T. Matsumura *et al.*, “Device for measuring real-time energy expenditure by heart rate and acceleration for diabetic patients,” in *2009 IEEE 35th Annual Northeast Bioengineering Conference*, 2009, pp. 1–2.

[26] M. Gjoreski, H. Gjoreski, M. Luštrek, and M. Gams, “Continuous stress detection using a wrist device: in laboratory and real life,” in *proceedings of the 2016 ACM international joint conference on pervasive and ubiquitous computing: Adjunct*, 2016, pp. 1185–1193.

[27] G. Welch and G. Bishop, “An introduction to the Kalman filter,” 1995.

[28] Q. Gui, Z. Jin, and W. Xu, “Exploring missing data prediction in medical monitoring: A performance analysis approach,” in *2014 IEEE Signal Processing in Medicine and Biology Symposium (SPMB)*, 2014, pp. 1–6.

[29] B. Beferull-Lozano and A. Ortega, “Coding techniques for oversampled steerable transforms,” in *Conference Record of the Thirty-Third Asilomar Conference on Signals, Systems, and Computers (Cat. No. CH37020)*, 1999, vol. 2, pp. 1198–1202.

[30] R. W. Stewart and E. Pfann, “Oversampling and sigma-delta strategies for data conversion,” *Electron. Commun. Eng. J.*, vol. 10, no. 1, pp. 37–47, 1998.

[31] M. Nagpal, K. Gleichauf, and J. Ginsberg, “Meta-analysis of heart rate variability as a psychophysiological indicator of posttraumatic stress disorder,” *J. Trauma Treat.*, vol. 3, no. 182, pp. 2167–1222, 2013.

[32] G. Giannakakis, D. Grigoriadis, K. Giannakaki, O. Simantiraki, A. Roniotis, and M. Tsiknakis, “Review on psychological stress detection using biosignals,” *IEEE Trans. Affect. Comput.*, 2019.

[33] E. Garcia-Ceja, V. Osmani, and O. Mayora, “Automatic stress detection in working environments from smartphones’ accelerometer data: a first step,” *IEEE J. Biomed. Health Inform.*, vol. 20, no. 4, pp. 1053–1060, 2015.

[34] M. Porumb, S. Stranges, A. Pescapè, and L. Pecchia, “Precision medicine and artificial intelligence: A pilot study on deep learning for hypoglycemic events detection based on ECG,” *Sci. Rep.*, vol. 10, no. 1, pp. 1–16, 2020.

[35] T. G. Dietterich, “Approximate statistical tests for comparing supervised classification learning algorithms,” *Neural Comput.*, vol. 10, no. 7, pp. 1895–1923, 1998.

[36] S. M. Lundberg and S.-I. Lee, “A unified approach to interpreting model predictions,” in *Advances in neural information processing systems*, 2017, pp. 4765–4774.

[37] C. Molnar, *Interpretable Machine Learning*. Lulu.com, 2020.

[38] G. J. Asmundson, M. G. Fetzner, L. B. DeBoer, M. B. Powers, M. W. Otto, and J. A. Smits, “Let’s get physical: a contemporary review of the anxiolytic effects of exercise for anxiety and its disorders,” *Depress. Anxiety*, vol. 30, no. 4, pp. 362–373, 2013.

[39] M. G. Fetzner and G. J. Asmundson, “Aerobic exercise reduces symptoms of posttraumatic stress disorder: A randomized controlled trial,” *Cogn. Behav. Ther.*, vol. 44, no. 4, pp. 301–313, 2015.

[40] L. M. Oppizzi and R. Umberger, “The effect of physical activity on PTSD,” *Issues Ment. Health Nurs.*, vol. 39, no. 2, pp. 179–187, 2018.

[41] S. H. Woodward, M. M. Murburg, and D. L. Bliwise, “PTSD-related hyperarousal assessed during sleep,” *Physiol. Behav.*, vol. 70, no. 1–2, pp. 197–203, 2000.

[42] K. Elsesser, G. Sartory, and A. Tackenberg, “Attention, heart rate, and startle response during exposure to trauma-relevant pictures: a comparison of recent

trauma victims and patients with posttraumatic stress disorder.," *J. Abnorm. Psychol.*, vol. 113, no. 2, p. 289, 2004.

[43] M. Gjoreski, M. Luštrek, M. Gams, and H. Gjoreski, "Monitoring stress with a wrist device using context," *J. Biomed. Inform.*, vol. 73, pp. 159–170, 2017.

5. CHAPTER 5 (ARTICLE 4) NATURALISTIC VALIDATION[4]

5.1. Introduction

Post-Traumatic Stress Disorder (PTSD) is a psychiatric condition experienced by individuals after exposure to life-threatening events such as combat exposure, physical assault, and sexual abuse [1]. PTSD is becoming a major public health concern and one of the most prevalent mental health disorders in the United States. According to previous research, over 70% of the U.S. population will experience a traumatic event in their lifetime, and 20% of those affected will go on to develop PTSD, which translates into more than 13 million Americans suffering from this condition at any given time [2]. PTSD is even more common among combat veterans [3] with a recent study suggesting over 24% prevalence [4].

Post-Traumatic Stress Disorder (PTSD) is a psychiatric condition experienced by individuals after exposure to life-threatening events such as combat exposure, physical assault, and sexual abuse (Kessler et al., 2005). PTSD is a major public health concern and one of the most prevalent mental health disorders in the United States; over 70% of the U.S. population will experience a traumatic event in their lifetime, and 20% of those affected will go on to develop PTSD, which translates into more than 13 million Americans suffering from this condition at any given time (Sidran Institute, 2018).

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Also submitted to arXiv.

PTSD is even more common among combat veterans (Kilpatrick et al., 2013) with a recent study suggesting over 24% prevalence (Stefanovics et al., 2020).

PTSD leads to a significant increase in the utilization of healthcare services, especially among combat veterans. The cost of caring for combat veterans usually peaks 30-40 years after a major conflict. For the Iraq/Afghanistan conflicts, it is estimated that cost of veterans' care will peak around 2035 at an estimated $60 billion each year (Geiling et al., 2012). The costs are also expected to increase due to comorbidities including depression, substance abuse, smoking, heart disease, obesity, diabetes, chronic fatigue, and increased dementia.

Major symptoms of PTSD include avoidance, hyperarousal, and reexperiencing the trauma (American Psychiatric Association, 2015). Avoidance symptoms include avoiding activities or cognitions associated with the traumatic event, decreased interest in daily life, and an overall feeling of detachment from one's surroundings. Hyperarousal symptoms include hypervigilance, feelings of irritability, and an exaggerated startle response following a startling event. Other symptoms include anxiety, insomnia, fatigue, anger, and aggression (Carlson et al., 2011). The Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2015) further divides re-experiencing symptoms into intrusive recollections, recurrent dreams, and flashbacks.

Traditionally, PTSD has been diagnosed using self-reported tools, such as surveys and health questionnaires (e.g., PTSD Checklist for DSM-5 or PCL-5) (American Psychiatric Association, 2013). However, self-reported measures fail to capture isolated and mild cases, and most importantly are not suitable for monitoring or

detecting the onset of symptoms (e.g., hyperarousal). Monitoring PTSD hyperarousal events is particularly important because patients may experience intense and severe hyperarousal episodes outside a clinical facility or therapy session. In addition, a major barrier in providing PTSD care is the uncertainty associated with self-management and adherence to therapeutics or medication routines (Rodrigues-Paras et al., 2017). Therefore, there is a vital need to develop effective monitoring systems that provide real-time PTSD hyperarousal detection capability and facilitate data-driven care.

Prior work has shown that several physiological measures including heart rate, heart rate variability, blood pressure, respiratory rate and skin conductance may be correlated with PTSD symptoms (Zoladz & Diamond, 2013). Among these variables, heart rate has shown promise as a reliable PTSD correlate (McDonald et al., 2019; Sadeghi, Sasangohar, & McDonald, 2020; Sadeghi et al., 2019)f and a few studies (Galatzer-Levy et al., 2014, 2017; Saxe et al., 2017) have focused on understanding specific relationships between heart rate and PTSD . However, to our knowledge, only one study has focused on investigating heart rate patterns associated with hyperarousal events (Sadeghi, Sasangohar, Hegde, et al., 2020, 2021; Sadeghi, Sasangohar, McDonald, et al., 2021). That study found that heart rate shows specific patterns during hyperarousal events in terms of fluctuation, stationarity and autocorrelation that is distinct from a typical healthy heart rate pattern in the resting position. Similarly, studies (Galatzer-Levy et al., 2014; Leightley et al., 2019; Liu & Salinas, 2017) have attempted to detect or predict early indicators of PTSD using machine learning algorithms. These studies mostly focused on predicting chances of developing PTSD after a traumatic

event. For instance, in one study (Galatzer-Levy et al., 2014) researchers tried to forecast chronic PTSD in individuals based on their early symptoms within 10 days of a traumatic incident. However, all of these studies focused on forecasting and predicting PTSD, and only two studies (McDonald et al., 2019; Sadeghi, McDonald, et al., 2021) focused on PTSD hyperarousal detection based on time and frequency domain features of heart rate and built a machine learning tool for real-time detection of such symptoms.

5.2. Methods

To evaluate the efficacy of heart-rate-based machine learning tools to monitor PTSD and assess the perceived accuracy of one such tool, the PTSD hyperarousal detection tool developed by Sadeghi et al. (2021) was integrated in an application designed for iOS smartphones and smartwatches. In what follows, we summarize the machine learning tool, the integration process, and details of a home study conducted for naturalistic validation of the tool.

5.2.1. Machine Learning Algorithm

The machine learning tool documented in Sadeghi et al. (2021) used the XGBoost algorithm to detect irregular heart rate patterns associated with hyperarousal events (see Sadeghi et al., 2021 for more details). This algorithm was trained based self-reported hyperarousal events of 99 combat veterans who were diagnosed with PTSD. The algorithm had an overall accuracy of 85% on a held aside test set. In addition to heart rate features reported in (Sadeghi, Sasangohar, & McDonald, 2020; Sadeghi et al., 2019), this algorithm used body acceleration to reduce noise in the classification and

distinguish between heart rate elevations related to stress and heart rate elevations related to physical activity.

5.2.2. Integration into a Wearable Device

The XGBoost algorithm was integrated in an iOS application (app) for iPhones and iWatches which was previously designed and developed by the Applied Cognitive Ergonomics Lab (ACE-lab) at Texas A&M University (Rao & Sasangohar, 2021). The app was designed exclusively for PTSD self-management. To integrate the machine learning algorithm into the app, we used CoreMLtools function, a framework used for integrating machine learning predictive tools into iOS devices (Marques, 2020; Sahin, 2021), from CoreML package in Python which allows deployment of trained machine learning models on iOS devices. The advantage of CoreML compared to similar frameworks such as TensorFlowlite is its ability to optimize memory usage, and conserve battery life (Tran, 2019).

The pretrained algorithm integrated in the app could identify irregular patterns in heart rate associated with PTSD hyperarousal events based on real time data collected through iWatch sensors (e.g., heart rate and accelerometer). Upon detection of a hyperarousal event, the tool triggered a notification on the watch interface that asked the user if they perceived any hyperarousal events (Figure 1, top). The users were asked to respond “Yes” or “No” to confirm whether they felt a hyperarousal event or not. The app also had the functionality of self-reporting hyperarousal events by tapping on a specific icon (bell-shaped icon) on the watch face and then confirming that the event happened (Figure 1, bottom). Users could also check their heart rate in real-time by tapping on the

heart-shaped icon on the watch interface. Users had to have the application running on their watch at all times, and the app had to be continuously on the watch face to be able to send notifications and collect their data. The app could not be used simultaneously with other activity tracking applications.

Figure 5.1. Illustration of the detection and self-reporting interfaces on iWatch

5.2.3. Study Process

Participants

Twelve participants were recruited from the Texas A&M University students, staff and faculty population to participate in the study through campus bulk mail. The mean age of all participants was 28 years old (SD = 11.37, range = 18-57). Out of 12 participants, 10 were female and 2 were male. Participants were required to be clinically-diagnosed with PTSD, be over 18 years old, and already own an iPhone (6S or newer) and an Apple iWatch (2nd Gen or newer). Participants were provided with a demographic questionnaire, consent forms, and an Anxiety and Depression Association of America (ADAA) form (cf. American Psychiatric Association, 2015; *Screening for Posttraumatic Stress Disorder (PTSD) | Anxiety and Depression Association of America, ADAA*, n.d.)

to prescreen their PTSD diagnosis. In the demographic questionnaire, participants answered questions about their age, gender and PTSD diagnosis. The study was approved by the International Review Board at Texas A&M University (IRB2020-0955DCR).

Procedure

Virtual orientation in one-on-one sessions were scheduled with each participant separately. During sessions participants were given instructions on how to install the app on their phone and their watch. Further, participants were instructed on how to interact with the app and the pop-up notifications. Participants were asked to wear the watch continuously for 21 days (between December 20th 2020 – January 25th 2021) and respond to notifications except for when they wanted to charge their devices. They were asked to self-report any instances of hyperarousal. We also emailed participants detailed information about the app installation process and its functionalities. Participants were provided with a list of local licensed therapists to contact in case of an emergency.

Data collection

For each participant, we collected data including detected events, participants' responses to symptom detection events (Yes or No), self-reported symptom onset, continuous heart rate data and body acceleration data in three axes: X, Y, and Z. To facilitate and enable data monitoring, we synced the developed the app with Amazon Web Services (AWS). The app stored and uploaded the collected data automatically on AWS at the end of each day of data collection when the user's phone was connected to

Wi-Fi. We checked the data on daily basis for each participant to ensure that they are using the app and the detection tool consistently.

5.2.4. Quantitative Analysis

Perceived precision was measured by calculating the ratio of correctly detected events (as reported by the user) or true positives to the total number of automated detected events. The equation for perceived accuracy is:

Perceived precision = Number of True Positives / (Number of True Positives+ Number of False Positives)

Where number of true positives is when the tool detected an event and the user responded “Yes” to the notification, and false positive is when the tool detected an event and the user responded “No” to the notification. To investigate time-series trends in the perceived precision , a MannKendall trend test was applied to evaluate the monotonic vs. significant increasing/decreasing trends in the time-series data. For this analysis, we used the Kendall library version 2.2 in RStudio version 3.5.1.

5.2.5. Interviews and Qualitative Analysis

At the end of study, we conducted exit interviews with each participant. The interviews were semi-structured with a focus on user’s experience with the detection tool. The participants were asked questions about the accuracy of the tool, their willingness to use this tool, their trust in the detection capability, any issues or barriers related to interaction with the tool, and their expectations from the tool for monitoring of PTSD symptoms. All interviews were virtual through Zoom and were recorded. Additionally, notes were taken during each interview and were later checked with the

recorded videos for accuracy. We first transcribed the recordings. We then found a number of themes in the transcriptions and categorized that we will discuss in the results section. Table 1 shows the list of questions used in the interviews.

Table 5.1. List of exit interview questions

How was your overall experience with the app and the detection tool?
Overall, do you think the tool can accurately detect hyperarousal events?
Do you trust the hyperarousal detection capability of the tool? Why/why not?
How many notifications a day did you receive on average?
What percentage of these notifications do you think were false alarms?
Do you find this level of false alarm to be acceptable?
My data shows you responded (either said yes or no) to notifications X percent of the time. Can you describe why you didn't respond to some alerts? [Probe: were you engaged in any sort of activity? What were some of these common activities?]
Can you describe what you feel during a hyperarousal event? what happens to you physiologically? Are there any effects on your heart rate?
Let's discuss the alert message itself. What type of message do you expect to see on the alert when the tool detects a hyperarousal moment?
What would you expect from a tool (for example a mobile app or smartwatch app) to do for you when it detects a hyperarousal event?
Overall, was it helpful to be reminded of your hyperarousal events?
Would you use this detection tool on a daily basis? What are some of the barriers in using this tool continuously?

5.3. Results

5.3.1. Quantitative Results

During 21 days of the data collection 1244 (M = 114.33, SD = 94.68) hyperarousal events were detected and 128 (M = 10.67, SD = 10.86) were reported. Out of the 1244 detected events, users responded "Yes" 788 (M = 65.66, SD = 74.02) times to the pop-up notifications indicating a true positive event, and 456 (M = 38.01, SD = 38.55) times participants reported "No" indicating a false alarm. Figure 2 shows the true positives, false positives, and self-reported events for each participant.

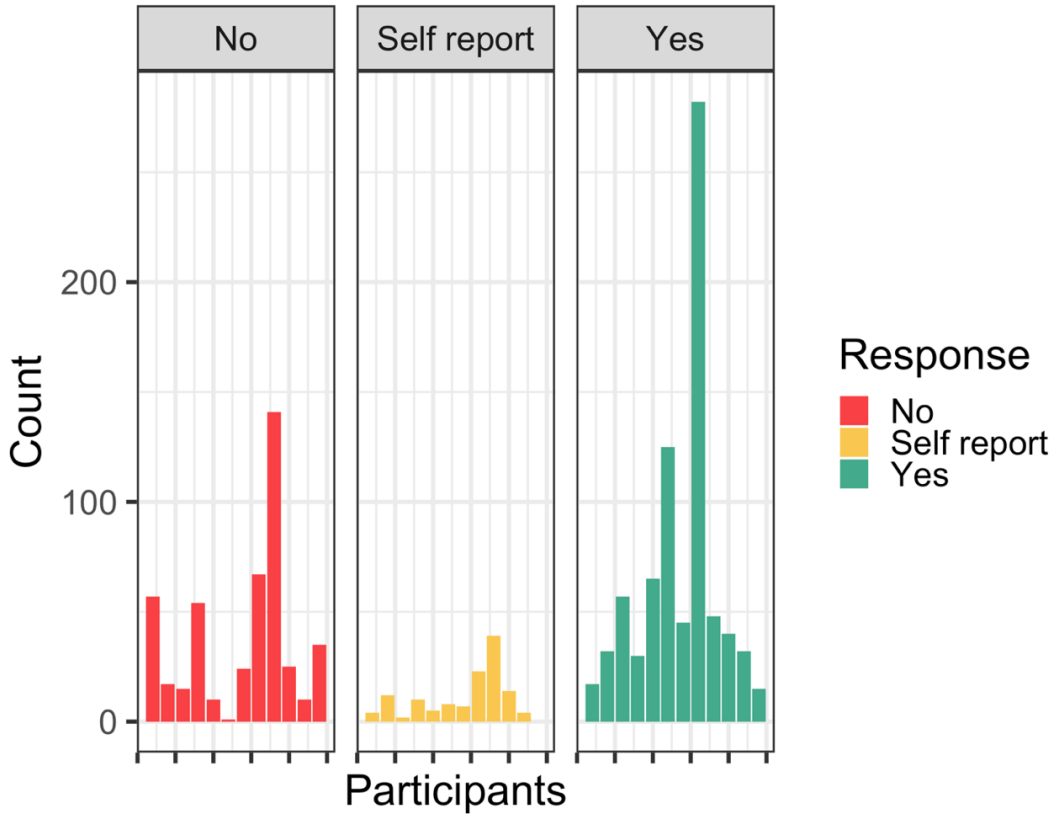

Figure 5.2. Count of Yes, No, and Self-Reported events for each participant.

Based on the analysis, the median perceived accuracy for all participants was 65.27% (*SD* = 25.9%) ranging from 22.9% to 99.1%. Figure 3 shows the perceived accuracy for each participant and the probability density of perceived accuracy for all participants.

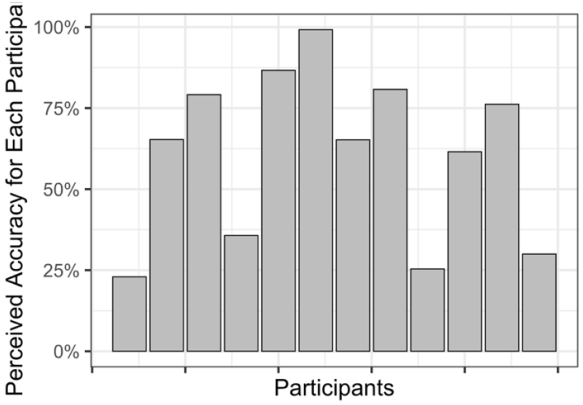

Figure 5.3. Perceived accuracy for each participant

Further, we investigated heart rate during recorded events. Our findings show that heart rate averaged over a 20 second window (10 seconds before and 10 seconds after the detected events) ranged from 60-182 (*M* = 82.04, *SD* = 21.49) with a median of 76. Figure 4 shows the probability distribution for heart rate during hyperarousal events.

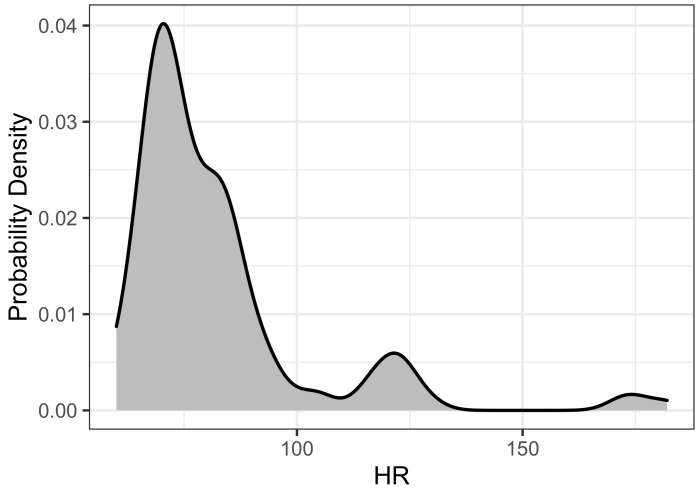

Figure 5.4. Heart rate distributions during detected events

Trend analysis

To investigate perceived precision trends, we conducted Mann-Kendall trend analysis on daily perceived precision. The results showed a significant increasing trend for the perceived precision for 11 out of 12 participants (tau = 0.735, $p < .001$). The only exception was a participant who had over 95% perceived precision and their perceived precision did not alter and was uniform throughout the study. We did not observe the same trend for the number of true positives or the number of false positives. Figure 5 shows average perceived precision trend for all participant during 21 days of the study.

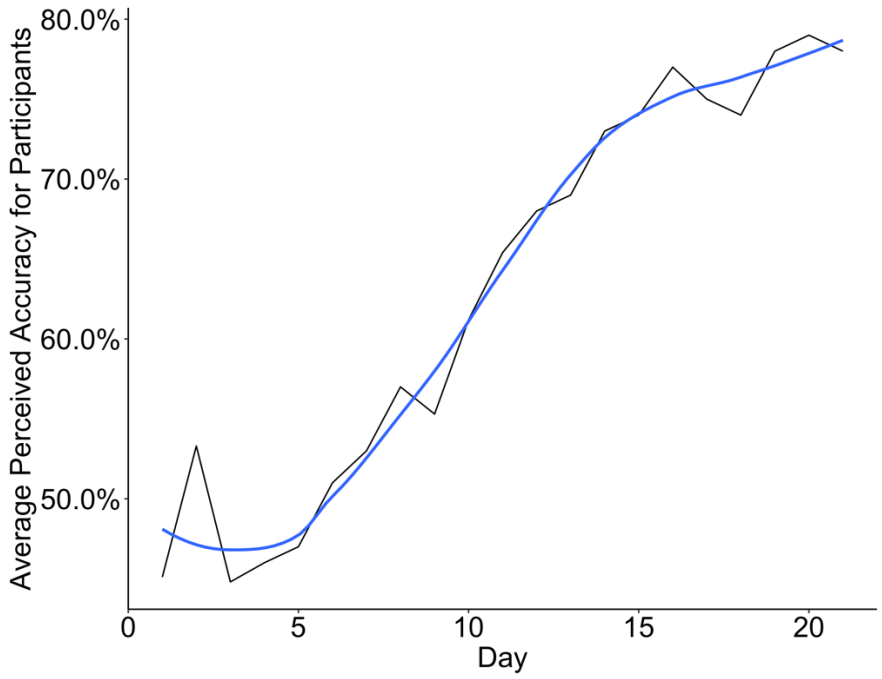

Figure 5.5. Average perceived accuracy trend for all participant during 21 days of the study.

5.3.2. Qualitative Results

During exit interviews participants were asked questions about their experience with the tool including their trust in the detection capability, their willingness to use the tool, their expectations from the tool, and main issues with the tool.

Overall experience

All participants (12/12) mentioned that they had a positive experience with the detection tool and the app. Participants further commented that the app was easy to use and intuitive.

"*It was pretty good. It was simple to use, didn't have any problem with it. I enjoyed being able to go back and look back at my data."* - Participant 9.

The majority of participants (10/12) mentioned that it was helpful for them to be aware and mindful of their hyperarousal events.

"*I liked that it kind of pinged me to try to think about it. It was right most of the times. It provides another opportunity for you to stop and reflect, but again, depending on how deeply in the therapy that person is or how aware that person is, the app can do so much. The rest of it is on the use to sit and think about it.*" Participant 2.

"*I thought that it was helpful, especially one of the things that I'm working on in therapy right now is actually gauging my stress and anxiety level and how to cope appropriately, so I thought that it was definitely helpful*" Participant 9.

"*Yes, I think it was helpful in the fact that it made me more aware of what was going on, and I was able to recognize it, be aware of the moment, and bring myself back down, or maybe even figure out what was causing stress and what not*." Participant 10.

However, 2 participants explained that being reminded of hyperarousal events has a negative reinforcement effect.

"*I think it made me hypersensitive of it, so I would notice it more usually than I would.*" Participant 1.

"*For me because the way I experience PTSD is to shut down, I think it would be helpful maybe to just receive a report at the end of the day that says hey these are all the times today that we noticed hyperarousal instead of being notified in the moment where it might amplify it more than it should*" Participant 3.

Perceived precision

Most participants (11/12) mentioned that the tool could accurately detect their hyperarousal events. These participants reported that they trust the tool's detection capability for hyperarousal events.

"*Yes definitely! I am personally grounded in my routines, just one day my girlfriend and I were getting dinner. She forced me to try something new and the app immediately asked if I was [hyperaroused]*." Participant 7.

"*I think it's relatively trustworthy, there were a couple of times that it detected that weren't accurate but other than that it was incredibly consistent*." Participant 9.

In particular, participants perception of percentage of false alarms ranged from 0-50% with an average of 18.58%. This number is roughly 16% lower than the reported false alarm rates from the self-reports (34.73%) (i.e., percentage of No responses to the detection notification). Three participants (3/12) reported that they did not receive any false alarms, one of whom had an objective perceived precision of almost 100% (i.e., responded YES to all detection notification). Despite such perception, the data from these three participants showed up to 10% reported false alarms. All participants (12/12) found the frequency of false alarms to be acceptable. Participants commented that notifications were easy to respond to and not interruptive.

"*I would say like it was just a quick Yes or No, it was not interruptive because it was so quick, and I just had to look at my watch to say Yes or No*" Participant 11.

"*Yeah, it is acceptable. I think that with any stress detection tool there is going to be certain levels of inaccuracy that you have to understand and account for. This was a low-enough number*." Participant 9.

Some participants (3/12) mentioned that the app sometimes falsely notified them when they were engaging to an activity; while others mentioned that they received false alarms when they were in relaxed position.

"*I think most of the times it was when I was sitting down, and I was like probably in a conversation with somebody, or I was trying to figure out a work project, or just thinking about my day. I don't think that I was doing any sort of active thing*" Participant 7.

"*I was usually engaged in an activity doing something like cleaning out the garage, you know, that was moving around. And most of the other times was frustration with work*." Participant 8.

However, one participant mentioned difficulties in assessing the accuracy of detected events due to issues related to lack of self-awareness.

"*I don't know! It requires the person to be self-aware enough to know that they are stressed. I have to sit in and check with myself to see if I am having a hyperarousal moment*." Participant 2.

Interaction with notifications

Overall, 3.57% of detection notifications did not receive a response. Over 50% of the participants (7/12) mentioned that they missed notifications because of their surrounding situation such as discreetness or the time that they received notifications.

"*It's just very hard to respond to something like that, and also just when people are around, sometimes it's just you don't want them to see, you know, because people ask questions about it*" Participant 5.

"*A lot of these notifications came at night, and I was not sure, so I dismissed them*" Participant 2.

Expectations for notifications

Over 50% of the participants (7/12) indicated that they liked the visual notification and the vibration. Participants explained that the notification message was clear, the vibration was sensible, and it was easy to respond to notification.

"*I like how it was Yes or No, just didn't have to think about it that much, it was just simple. I like the vibration because like when my watch detected something I could sense it. I also prefer vibration to -sound and other things because other things stress me out more*." Participant 4.

"*I liked the message and can't think about a way that I would change it. I like the vibration more I think than something like a sound. Because other people can hear the sound. I had a friend in town and I told him about this app, and it got to the point that when I did have the sound on then he knew that I was stressed and I did not want anybody else to know. And the sound can sometimes be triggering*" Participant 6.

A few participants (4/12) commented that they did not like that the notification message stayed on their watch face since it was noticeable by others.

"*I liked the vibration, but I didn't like how the alert stayed on the screen, just because everybody could see it.*" Participant 1.

A few participants (4/12) elaborated that the vibration was not strong enough and they missed notifications because of that.

" *I think during the day the amount of vibration is fine, but during the night if you want to catch somebody sleeping it needs to be stronger.*" Participant 2.

"*I think the vibration could have been a little stronger. I am a very active person and I use my hands a lot at work, so I think sometimes the motion outweighs the vibration*" Participant 6.

"*It was a pretty low vibration sensation and so if I had been like in class or something like that, it probably would have been a lot harder to pick up on. I'd like to get a second notification shortly after if there is no response to the initial."* Participant 9.

Expectations for post-detection interaction

Most participants (10/12) expected the tool to support users develop coping skills post-detection. Among the coping skills, breathing exercises (8/12), and meditation such as focusing exercises (5/12) were mentioned by some.

"*I think telling me to breathe would be good or maybe a message that says you are OK right now, or some type of encouraging message that will bring you back to reality.*" Participant 3.

However, a few participants (2/12) mentioned that improving self-awareness through using the detection tool is sufficient for them and the scope of the tool should be limited to awareness rather than being directed to coping activities.

"*For me it was just enough to acknowledge and like actively press something that said Yes I am feeling the stressful moment instead of just like trying to keep it in, for me that was enough*." Participant 2.

"*I don't really expect it to do anything. I think it brings the awareness to myself you know that its detecting something. I'll be able to bring myself back down*" Participant 10.

Acceptance and barriers to adopt

All participants (12/12) mentioned that they would use the tool on a daily basis with a few adjustments. The main issue that prevented most participants from using the app continuously was the battery life. Continuous monitoring of physiological data through watch sensors affects the battery life significantly. Most participants (10/12) commented on this issue and explained that they had to charge their watch more frequently (e.g., 1 to 2 times a day compared to once every 48 hours).

"*I really would use it. I liked monitoring my heart rate and I liked it really pointing out the event, cause then I could sit there and almost predict them and then be able to deal with them from there."* Participant 12.

"*Yeah, I would like to use the app on a daily basis. I guess the only thing is that it takes up a lot of battery power when I'm wearing it. That was the main issue like having to charge it every night."* Participant 4.

"*I would definitely use it, I think it would be helpful. The downside was the battery life. It would be nice if it did not drain the battery so you could wear it for a longer period of time*." Participant 8.

5.4. Discussion

This work describes a novel mixed-methods analysis for naturalistic validation of a machine learning algorithm to detect PTSD hyperarousal events. While PTSD treatments and psychophysiological assessments in the laboratory setting have been well documented, there is a need for additional research to bridge the gap in continuous monitoring of PTSD symptoms to improve self-management and inform therapeutic care. Although naturalistic studies have been conducted to develop machine learning tools to detect PTSD hyperarousal events (e.g., McDonald et al., 2019), to our knowledge, this study is the first to evaluate the perceived precision of real-time PTSD hyperarousal detection in naturalistic settings.

Our findings suggest that the average perceived precision of the detected events was about 65%, indicating that majority of participants agreed with the automated real-time detection of an irregular heart rate pattern associated with PTSD hyperarousal. The range of the perceived precision showed substantial between participants' variability in perception of accuracy (Range: 23%-99%) with false alarm rates as high as 77%. However, our qualitative suggest that false alarms were tolerated well and accepted by the users.

These findings highlight the importance of naturalistic evaluation and validation of machine learning tools. While common approaches in machine learning accuracy

measurements and performance evaluation may provide initial evidence of objective efficacy, in applications involving interactions with humans, subjective perceptions may be exhibit misalignment with empirical evidence. This misalignment has been shown in various comparisons of objective and subjective evidence (Chellappa et al., 2018; Kosmadopoulos et al., 2017). In particular, in our study, we noticed a significant disparity between the theoretical precision for the developed machine learning algorithm and the users' perceived precision (70% vs. 65% for the algorithm used in this study, respectively). Therefore, sole reliance on theoretically-driven performance metrics without accounting for users' perception of accuracy may result in negative impacts on sustainable usage and acceptance of machine-learning-based tools.

Another interesting finding was that perceived precision increased over time for majority of participants. Given the known correlation between perceived precision of automation and trust (Findley, 2015; Merritt, 2011), this finding may suggest that while users may have initially distrusted the tool, longitudinal exposure to true positives increased and calibrated their trust in the tool's capability in detecting hyperarousal events. Such initial mistrust of automation has been shown in other research (Fowler, 2021; Tenhundfeld et al., 2019). This is also supported by findings from the exit interviews. Several participants elaborated on the process of trust-building over time. For example, participant 12 explained that: *"the first week I was denying notifications because I didn't think they were stressful enough to be considered stressful events, and then I realize all of them probably were stressful events, but I think I mentally have a threshold of what is considered a hyperarousal event. In that thought, I*

don't think there were any real false positives". This important finding highlights the importance of conducting naturalistic validation studies longitudinally. While we did not notice a decline in trust or usage over time, future work may use longer study durations to understand users' behavior over an extended period. Future improvements in personalized and reinforcement learning (i.e., adjusting the detection based on participants' responses) may also improve the calibration in trust and needs to be examined.

The results provided preliminary evidence that the tool detected hyperarousal events, albeit with a high false alarm rate. However, overall, the tool was received well, and most participants found it helpful in increasing self-awareness and being mindful of hyperarousal events. This is in line with previous research indicating that stress awareness facilitates and improves stress management (Morris et al., 2010). However, a few participants elaborated on the negative reinforcement of the detection tool's notifications to trigger further stress. It is well documented that alarms and notifications may result in a startle effect or further stress (Taylor et al., 1996). Additionally, false alarms might trigger panic attacks and put the body in a fight-or-flight episode which may exacerbate anxiety and stress (Fowles, 2019). While this study focused on subjective validation and perceived precision of detection, more work is warranted to investigate user-centered design of notifications and alerts and other interactive features to identify and mitigate stress-inducing design factors and improve users' experience. In addition, while majority of participants in this study valued real-time notifications, a few

preferred on-demand access to such information. This may suggest the importance of personalized notification settings to tailor interventions to variety of users.

There are several limitations that impose constrains on the generalizability of the findings reported in this work. First, the sample size was small, limiting the ability to conduct inferential statistics. We tried to partly address this limitation by conducting a longitudinal study over 21 days. However, more work is needed to confirm our findings with a larger sample size. Second, we did not account for the PTSD severity or other co-morbidities. Third, the analysis of perceived precision assumes a collectively-exhaustive account of all perceived hyperarousal events. While we emphasized the importance of self-reporting to our participants, events may have been under-reported. Finally, while this study addresses an important gap in naturalistic evaluation of machine-learning-based tools for detecting PTSD hyperarousal events (and broadly stated "stress"), there are several limitations and barriers associated with conducting a home study using wearables. For example, real-time monitoring required significant computational power which had significant impact on the smartwatch battery life. This barrier resulted in but also potential impact on participants' self-reporting behavior and overall impressions of the tool. More work is warranted to optimize the machine learning tools for computational efficiency and improve the integration into wearables technologies.

5.5. Conclusion

Non-intrusive monitoring tools for PTSD hyperarousal events to improve self-management and self-awareness is a timely need and a general gap in research. This paper contributes to the body of literature by providing preliminary evidence of efficacy

for one such tool while highlighting the importance of naturalistic evaluation of machine-learning-based detection tools accounting for users' perceptions and interactions. Future work in utilizing user-centered design methods and just-in-time evaluation techniques will help improving the design of effective PTSD continuous monitoring and self-management tools that address an important gap in current PTSD care models and is expected to have a positive impact on quality of life and PTSD health outcomes.

5.6. References

[1] R. C. Kessler, P. Berglund, O. Demler, R. Jin, K. R. Merikangas, and E. E. Walters, "Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication," *Arch. Gen. Psychiatry*, vol. 62, no. 6, pp. 593–602, 2005.

[2] Sidran Institute, "Post Traumatic Stress Disorder Fact Sheet," 2018. Accessed: Sep. 24, 2020. [Online]. Available: https://www.sidran.org/wp-content/uploads/2018/11/Post-Traumatic-Stress-Disorder-Fact-Sheet-.pdf

[3] D. G. Kilpatrick, H. S. Resnick, M. E. Milanak, M. W. Miller, K. M. Keyes, and M. J. Friedman, "National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria," *J. Trauma. Stress*, vol. 26, no. 5, pp. 537–547, 2013.

[4] E. A. Stefanovics, M. N. Potenza, and R. H. Pietrzak, “PTSD and obesity in US military veterans: Prevalence, health burden, and suicidality.,” *Psychiatry Res.*, vol. 291, p. 113242, 2020.

[5] J. Geiling, J. M. Rosen, and R. D. Edwards, “Medical costs of war in 2035: long-term care challenges for veterans of Iraq and Afghanistan,” *Mil. Med.*, vol. 177, no. 11, pp. 1235–1244, 2012.

[6] American Psychiatric Association, *Depressive Disorders: DSM-5® Selections*. American Psychiatric Pub, 2015.

[7] K. F. Carlson *et al.*, “Prevalence, assessment, and treatment of mild traumatic brain injury and posttraumatic stress disorder: a systematic review of the evidence,” *J. Head Trauma Rehabil.*, vol. 26, no. 2, pp. 103–115, 2011.

[8] American Psychiatric Association, *Diagnostic and statistical manual of mental disorders (DSM-5®)*. American Psychiatric Pub, 2013.

[9] P. R. Zoladz and D. M. Diamond, “Current status on behavioral and biological markers of PTSD: a search for clarity in a conflicting literature,” *Neurosci. Biobehav. Rev.*, vol. 37, no. 5, pp. 860–895, 2013.

[10] A. D. McDonald, F. Sasangohar, A. Jatav, and A. H. Rao, “Continuous monitoring and detection of post-traumatic stress disorder (PTSD) triggers among veterans: a supervised machine learning approach,” *IISE Trans. Healthc. Syst. Eng.*, vol. 9, no. 3, pp. 201–211, 2019.

[11] M. Sadeghi, F. Sasangohar, and A. D. McDonald, “Toward a taxonomy for analyzing the heart rate as a physiological indicator of posttraumatic stress disorder:

systematic review and development of a framework," *JMIR Ment. Health*, vol. 7, no. 7, p. e16654, 2020.

[12] M. Sadeghi, F. Sasangohar, and A. McDonald, "Analyzing Heart Rate as a Physiological Indicator of Post-Traumatic Stress Disorder: A Scoping Literature Review," in *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*, 2019, vol. 63, no. 1, pp. 1936–1936.

[13] I. R. Galatzer-Levy, K.-I. Karstoft, A. Statnikov, and A. Y. Shalev, "Quantitative forecasting of PTSD from early trauma responses: A machine learning application," *J. Psychiatr. Res.*, vol. 59, pp. 68–76, 2014.

[14] I. R. Galatzer-Levy, S. Ma, A. Statnikov, R. Yehuda, and A. Y. Shalev, "Utilization of machine learning for prediction of post-traumatic stress: a re-examination of cortisol in the prediction and pathways to non-remitting PTSD," *Transl. Psychiatry*, vol. 7, no. 3, pp. e1070–e1070, 2017.

[15] G. N. Saxe, S. Ma, J. Ren, and C. Aliferis, "Machine learning methods to predict child posttraumatic stress: a proof of concept study," *BMC Psychiatry*, vol. 17, no. 1, pp. 1–13, 2017.

[16] M. Sadeghi, F. Sasangohar, S. Hegde, and A. McDonald, "Understanding Heart Rate Reactions to Posttraumatic Stress Disorder (PTSD) Among Veterans," in *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*, 2020, vol. 64, no. 1, pp. 780–780.

[17] M. Sadeghi, F. Sasangohar, S. Hegde, and A. McDonald, "Investigating Heart Rate Patterns During Hyperarousal Events Among Veterans Who Have

Posttraumatic Stress Disorder (PTSD),” in *Proceedings of the International Symposium on Human Factors and Ergonomics in Health Care*, 2021, vol. 10, no. 1, pp. 91–91.

[18] M. Sadeghi, F. Sasangohar, A. D. McDonald, and S. Hegde, “Understanding Heart Rate Reactions to Post-Traumatic Stress Disorder (PTSD) Among Veterans: A Naturalistic Study,” *Hum. Factors*, p. 00187208211034024, 2021.

[19] D. Leightley, V. Williamson, J. Darby, and N. T. Fear, “Identifying probable post-traumatic stress disorder: applying supervised machine learning to data from a UK military cohort,” *J Ment Health*, vol. 28, no. 1, pp. 34–41, 2019.

[20] N. T. Liu and J. Salinas, “Machine learning for predicting outcomes in trauma,” *Shock Inj. Inflamm. Sepsis Lab. Clin. Approaches*, vol. 48, no. 5, pp. 504–510, 2017.

[21] M. Sadeghi, A. D. McDonald, and F. Sasangohar, “Posttraumatic Stress Disorder Hyperarousal Event Detection Using Smartwatch Physiological and Activity Data,” *ArXiv Prepr. ArXiv210914743*, 2021.

[22] K. Zahed, F. Sasangohar, R. Mehta, M. Erraguntla, and K. Qaraqe, “Diabetes Management Experience and the State of Hypoglycemia: National Online Survey Study,” *JMIR Diabetes*, vol. 5, no. 2, p. e17890, 2020.

[23] M. J. Fowler, “Assessing the Development of Operator Trust in Automation,” PhD Thesis, 2021.

[24] A. H. Rao and F. Sasangohar, “Designing for Veterans,” in *The Patient Factor*, CRC Press, 2021, pp. 107–124.

[25] O. Marques, “Machine Learning with Core ML,” in *Image Processing and Computer Vision in iOS*, Springer, 2020, pp. 29–40.

[26] Ö. Sahin, “Introduction to Apple ML Tools,” in *Develop Intelligent iOS Apps with Swift*, Springer, 2021, pp. 17–39.

[27] X. T. Tran, “Applying computer vision for detection of diseases in plants,” PhD Thesis, Iowa State University, 2019.

[28] “Screening for Posttraumatic Stress Disorder (PTSD) | Anxiety and Depression Association of America, ADAA.” https://adaa.org/screening-posttraumatic-stress-disorder-ptsd (accessed Jul. 28, 2021).

[29] S. L. Chellappa, C. J. Morris, and F. A. Scheer, “Daily circadian misalignment impairs human cognitive performance task-dependently,” *Sci. Rep.*, vol. 8, no. 1, pp. 1–11, 2018.

[30] A. Kosmadopoulos *et al.*, “The efficacy of objective and subjective predictors of driving performance during sleep restriction and circadian misalignment,” *Accid. Anal. Prev.*, vol. 99, pp. 445–451, 2017.

[31] N. L. Tenhundfeld, E. J. de Visser, K. S. Haring, A. J. Ries, V. S. Finomore, and C. C. Tossell, “Calibrating trust in automation through familiarity with the autoparking feature of a Tesla Model X,” *J. Cogn. Eng. Decis. Mak.*, vol. 13, no. 4, pp. 279–294, 2019.

[32] M. E. Morris *et al.*, “Mobile therapy: case study evaluations of a cell phone application for emotional self-awareness,” *J. Med. Internet Res.*, vol. 12, no. 2, p. e10, 2010.

[33] S. Taylor, S. Woody, W. J. Koch, P. D. McLean, and K. W. Anderson, "Suffocation false alarms and efficacy of cognitive behavioral therapy for panic disorder," *Behav. Ther.*, vol. 27, no. 1, pp. 115–126, 1996.

[34] D. C. Fowles, "Motivational approach to anxiety disorders," in *Anxiety: Recent developments in cognitive, psychophysiological, and health research*, Taylor & Francis, 2019, pp. 181–192.

6. CHAPTER 6 CONCLUSION

6.1. Summary of Key Findings

This chapter elaborates on key findings of this dissertation, its contributions to the body of knowledge, limitations of this work, and future work in related research agendas. In this dissertation, I documented a series of studies aimed at understanding heart rate reactions to PTSD. In particular, three research questions were addressed: 1- Does heart rate show unique patterns during PTSD hyperarousal events? 2- Can these patterns be used to develop an algorithm that can detect hyperarousal events in real time? and 3- How can the developed algorithm be operationalized as a smartwatch-based detection tool?

To answer question 1, first, a comprehensive review of literature was conducted to investigate the previous research on the relationship between heart rate and PTSD as well as methods to analyze heart rate. In chapter 2, I documented a new framework that contains various types of descriptive and predictive analysis methods to analyze heart rate. Findings from this literature review were published in an article titled "Toward a Taxonomy for Analyzing the Heart Rate as a Physiological Indicator of Posttraumatic Stress Disorder: Systematic Review and Development of a Framework" in *JMIR Mental Health* [1]. The framework also informed my analyses to identify unique patterns in heart rate during hyperarousal events. In particular, I collected data from over 100 combat veterans who were diagnosed with PTSD in a series of naturalistic studies using momentary self-reports enabled by a mobile platform (detailed in chapter 3). Next, I used ARIMA; a classical time series analysis method; to compare heart rate patterns

during 1034 hyperarousal events with heart rate patterns from 11 healthy participants. The results indicated that heart rate has unique measurable statistical characteristics during hyperarousal events. More specifically, ARIMA analysis showed that during hyperarousal events, heart rate is more nonstationary with higher fluctuations rates and higher autocorrelation compared to healthy heart rates, suggesting that there are some statistical dependencies between consecutive heart rate measures during hyperarousal events that do not exist in healthy resting heart rates.

One of the interesting findings of this study was that most hyperarousal events happened when the heart rate was in a healthy range (75-85 bpm) which may suggest that threshold-based analysis of heart rate, commonly used in stress detection, may fall short in hyperarousal detection which requires advanced pattern-based analysis methods. Further, to understand the effects of lifestyle and demographic on the resting heart rate I conducted mixed regression analysis. The results indicated that smoking, sleeping habits, antidepressants use, anxiolytics use, and gender affect resting heart rate in people who have PTSD. For instance, I found out that using antidepressants and smoking increase the heart rate by 10 bpm and 9 bpm respectively [2], [3]. This finding is in line with findings from These findings (documented in chapter 3) are disseminated in an article titled “Understanding heart rate reactions to post-traumatic stress disorder (PTSD) among veterans: a naturalistic study” in *Human Factors* [4].

To address the second research question, I used the ground truth collected in the aforementioned naturalistic studies to develop an XGBoost machine learning model that utilized some of the features found in pattern recognition analysis (e.g., heart rate

fluctuations or standard deviation) as well as time domain features of heart rate, and time domain features of body acceleration. The accuracy of this detection tool in theory was 84%. Further in this chapter, I interpreted these major contributors to machine learning results using SHAP values. The results showed that the average body acceleration and heart rate standard deviation are the most important features to detect hyperarousal events. Details on the developed XGBoost algorithm and how each of the features contribute to the prediction are provided in chapter 4 and the resulting article titled "x" is under review in PlosOne.

To address the third research question, I used the algorithm documented in chapter 4 to create a mobile health application for PTSD hyperarousal monitoring. I deployed the machine learning algorithm on an iOS application and validated the perceived accuracy of this tool's detection accuracy by conducting a longitudinal home study with 12 participants diagnosed with PTSD. The results showed over 65% of detected hyperarousal events were perceived as accurate. The results further indicated an increasing level of trust in the device throughout the study as users interacted more with the detection tool. All participants found the device helpful and mentioned that they could trust the device for detecting their hyperarousal events. The findings from this study are detailed in Chapter 5 of this dissertation and in preparation for submission to Human Factors in Health Care Journal.

6.2. Dissertation Contributions

This dissertation advances the body of knowledge in psychophysiology by providing several contributions and motivating for further research.

The first contribution of this dissertation is the in-depth statistical analysis of heart rate patterns during PTSD hyperarousal events. While comprehensive work has been done to investigate heart rate variability reactions to PTSD [5]–[8], there is limited knowledge on how heart rate reacts to PTSD. Investigating heart rate reactions to PTSD is specifically important due to the practicality of using heart rate measures for real-world applications including availability of and non-intrusiveness of heart rate sensors. Currently, while most wearable devices are able to measure heart rate with high accuracy, there are very few off-the-shelf wearables that can gauge heart rate variability. Even the wearables that commercially claim to do so (e.g., Apple iWatch, Fitbit) are subjected to several restrictions including limited accuracy, limited time windows (e.g., iWatch can capture HRV for just 30 seconds), and limited frequency of capturing heart rate variability [9], [10]. Considering these limitations in terms of collecting heart rate variability data, my research adds to the body of knowledge by analyzing heart rate instead of HRV.

Second, while previous research has investigated heart rate changes in relation to PTSD [1], [11], [12], describing and modeling heart rate patterns during PTSD hyperarousal events is novel and a major contribution to the body of knowledge on PTSD psychophysiology. Specifically, a unique contribution of this dissertation (detailed in chapter 3) is using the ARIMA method to probe specific patterns in heart rate during hyperarousal events. The evidence presented in this dissertation documenting unique statistical characteristics of heart rate patterns in PTSD patients in terms of autocorrelation and fluctuation is novel, and although preliminary, may provide

foundational knowledge to advance the understanding of psychophysiology of PTSD. More specifically, the results from autocorrelation analysis suggested that there are some dependencies in the heart rate during hyperarousal events that do not exist in the healthy heart rates. The results from detrended fluctuation analysis showed higher fluctuation rates in heart rate during hyperarousal events compared to the heart rate of healthy subjects. Previous work has shown that higher heart rate fluctuations is associated with hyperactivity of the sympathetic nervous system and therefore clinical manifestation of cardiovascular diseases [13], [14]. Moreover, the results showed strong connections between lifestyle and resting heart rate. Resting heart rate is an indicator of health level and cardiovascular risk in individuals [15]. While previous work has shown correlations between the resting heart rate and demographics such as gender and use of medication in healthy individuals [16]–[19], the findings documented in this dissertation is the only evidence connecting such demographics to PTSD among veterans. In particular, my research suggests that antidepressants, smoking, and sleep deprivation might have effects on the health of veterans who have PTSD by elevating their resting heart rate significantly.

Third, this research contributes to the body of knowledge naturalistic evaluation of PTSD hyperarousal events. Collecting data in such settings leads to results with higher external validity and generalizability. Most research on objective assessment of PTSD has been conducted in controlled lab settings by inducing external stimuli, e.g., [20]–[22]; however; a majority of PTSD stimuli are internally generated [23]. Failing to capture hyperarousal events related to internal stimuli might affect the validity,

precision, and generalizability of the results. My research addresses this limitation by collecting longitudinal data in real life settings.

Fourth, although several studies have looked into detecting mental stress using machine learning algorithms and physiological indicators e.g., [24]–[26], only one study by McDonald et al. (2019) [27] has investigated PTSD hyperarousal detection using machine learning algorithms. I enhanced and expanded the findings from McDonald et al.'s study by adjusting several important factors. First, I added data collected from two additional field studies to the analysis. Second, I used time domain features of heart rate instead of frequency domain features for better application (e.g., integration in iOS applications) and interpretation [28]. Additionally, I added body acceleration features to the developed machine learning algorithm to account for both the noise in the data and differentiation between heart rate changes due to PTSD hyperarousal and heart rate fluctuations due to activity. I used upsampling for data preprocessing analysis instead of downsampling to address another limitation mentioned in McDonald et al. These changes increased the accuracy of the developed algorithm by 10% (from 70% to 80%). I then interpreted the algorithm using SHAP values to investigate the contribution of each of the factors. In line with the results from chapter 3, SHAP analysis in chapter 4 showed that heart rate standard deviation or fluctuation is one of the critical characteristics of heart rate that needs be considered closely when probing hyperarousal events. Both chapters 3 and 4 further suggested that heart rate demonstrates non-linear behavior with explicit patterns during hyperarousal events.

Last, this research contributes to the body of knowledge on practical PTSD monitoring by developing a machine-learning-enabled mobile health application that can detect hyperarousal events in real-time. While there are a few apps that help coping with PTSD (e.g., PTSD Coach), to my knowledge this is the first tool that can detect PTSD hyperarousal events in real time non-invasively and continuously. Being able detect these events in real life might have a promising impact on the direction of treating PTSD. This chapter further highlights the need for naturalistic validation of machine learning tools to account for human interaction and perception.

6.3. Limitations and Future Work

Several limitations might affect the generalizability of the results and need to be addressed in future work. First and foremost, the hyperarousal events used in this work are self-reported and subjected to individual biases. Participants might have over- or under-reported the events they perceived. For instance, there was a participant who reported 10 hyperarousal events within a 5 minutes time frame. Although I attempted to address this limitation by implementing a comprehensive data preprocessing and imputation procedure, future work might minimize this limitation by conducting controlled lab studies along with naturalistic field studies to understand and address such biases.

There were also a few limitations associated with the data collection method. Naturalistic data collection approach led to a high number of missing values in datasets. Almost 25% of the data was missing in the datasets. I tried to address this issue by applying a variety of imputation methods such as Kalman imputation to the data to

estimate the missing values; however, data imputation might have added additional biases to the results [29]. Future work should use more advanced heart rate and accelerometer sensors with higher sampling frequency and better accuracy to minimize the number of missing values in data collection processes. Moreover, naturalistic data collection (detailed in chapters 3 and 4) happened during Project Hero R2R challenges that involved intensive activity including roughly eight hours of bike riding per day. The study needs to be replicated in the future work by collecting data in other environments with low-intensity activity or during normal daily life activities.

Further, I did not account for individual differences in pattern recognition analysis and the developed XGBoost algorithm. Every PTSD patient has a specific and individualized set of triggers and stimuli [30]. Heart rate measures are also affected by individuals' characteristics. Therefore, future work should account for these differences and add between-subject variability to the analysis. Another future direction of this research is developing customized machine learning algorithms to boost detection accuracy. By performing active learning methods and interactively adjusting the algorithm based on the user's input, each user can have a specific detection algorithm that works based on their own hyperarousal patterns. Using these active learning methods might eventually decrease number of false alarms, increase count of correctly detected events, and finally improve perceived accuracy.

Furthermore, my research found connections between PTSD and increased cardiovascular disease through pattern analysis. Future work should attempt to clarify

these connections and look toward preventive strategies to minimize risks of cardiovascular diseases as a comorbidity of PTSD.

Finally, while the validation study (detailed in chapter 5) showed promise, the small sample size was small (12 participants). Future work should include larger sample sizes to verify these results and shed more light on practicality and sustainability of using continuous PTSD monitoring tools as well as the perceived accuracy over longer periods.

While this research contributed to and informed the design of PTSD hyperarousal detection technologies, more work is warranted to evaluate how such detections can lead to effective therapeutics or self-management capabilities. For example, the developed machine learning algorithm has over 80% of theoretical accuracy and 65% of perceived accuracy. During the interviews of the detection tool study, a majority of participants requested for receiving coping skills upon correct detection of a hyperarousal event. As for the future directions, researchers should add coping skills such as breathing exercises to the developed detection tool to expedite recovery from hyperarousal events. Addressing the limitations through this proposed future work will eventually help recovering from PTSD, decrease public expenditure on mental health, and finally promotes mental health of the society.

6.4. References

[1] M. Sadeghi, F. Sasangohar, and A. D. McDonald, “Toward a taxonomy for analyzing the heart rate as a physiological indicator of posttraumatic stress disorder:

systematic review and development of a framework," *JMIR Mental Health*, vol. 7, no. 7, p. e16654, 2020.

[2] A. Linneberg *et al.*, "Effect of smoking on blood pressure and resting heart rate: a Mendelian randomization meta-analysis in the CARTA consortium," *Circulation: Cardiovascular Genetics*, vol. 8, no. 6, pp. 832–841, 2015.

[3] A. H. Kemp *et al.*, "Effects of depression, anxiety, comorbidity, and antidepressants on resting-state heart rate and its variability: an ELSA-Brasil cohort baseline study," *American Journal of Psychiatry*, vol. 171, no. 12, pp. 1328–1334, 2014.

[4] M. Sadeghi, F. Sasangohar, A. D. McDonald, and S. Hegde, "Understanding Heart Rate Reactions to Post-Traumatic Stress Disorder (PTSD) Among Veterans: A Naturalistic Study," *Human Factors*, p. 00187208211034024, 2021.

[5] J. M. Pyne *et al.*, "Heart rate variability and cognitive bias feedback interventions to prevent Post-deployment PTSD: results from a randomized controlled trial," *Military medicine*, vol. 184, no. 1–2, pp. e124–e132, 2019.

[6] D. Rabellino *et al.*, "Neural correlates of heart rate variability in PTSD during sub-and supraliminal processing of trauma-related cues," *Human Brain Mapping*, vol. 38, no. 10, pp. 4898–4907, 2017.

[7] S. J. Ridout *et al.*, "Heart rate variability responses to a standardized virtual reality exposure in Veterans with PTSD," *Current Treatment Options in Psychiatry*, vol. 4, no. 3, pp. 271–280, 2017.

[8] G. J. van Boxtel *et al.*, "Heart rate variability, sleep, and the early detection of post-traumatic stress disorder," in *Sleep and combat-related post traumatic stress disorder*, Springer, 2018, pp. 253–263.

[9] M. Altini, "On Heart Rate Variability and the Apple Watch," *Medium*, Jun. 07, 2020. https://medium.com/@altini_marco/on-heart-rate-variability-and-the-apple-watch-24f50e8e7bc0 (accessed Sep. 10, 2021).

[10] D. Hernando, S. Roca, J. Sancho, Á. Alesanco, and R. Bailón, "Validation of the apple watch for heart rate variability measurements during relax and mental stress in healthy subjects," *Sensors*, vol. 18, no. 8, p. 2619, 2018.

[11] T. C. Buckley, D. Holohan, J. L. Greif, M. Bedard, and M. Suvak, "Twenty-four-hour ambulatory assessment of heart rate and blood pressure in chronic PTSD and non-PTSD veterans," *Journal of Traumatic Stress*, vol. 17, no. 2, pp. 163–171, 2004.

[12] P. J. Colvonen *et al.*, "Pretreatment biomarkers predicting PTSD psychotherapy outcomes: a systematic review," *Neuroscience & Biobehavioral Reviews*, vol. 75, pp. 140–156, 2017.

[13] J.-Y. Chiang *et al.*, "Detrended fluctuation analysis of heart rate dynamics is an important prognostic factor in patients with end-stage renal disease receiving peritoneal dialysis," *PloS one*, vol. 11, no. 2, p. e0147282, 2016.

[14] U. S. Bedi and R. Arora, "Cardiovascular manifestations of posttraumatic stress disorder.," *Journal of the National Medical Association*, vol. 99, no. 6, p. 642, 2007.

[15] J. M. Arnold, D. H. Fitchett, J. G. Howlett, E. M. Lonn, and J.-C. Tardif, "Resting heart rate: a modifiable prognostic indicator of cardiovascular risk and outcomes?," *Canadian Journal of Cardiology*, vol. 24, pp. 3A-15A, 2008.

[16] A. Linneberg *et al.*, "Effect of smoking on blood pressure and resting heart rate: a Mendelian randomization meta-analysis in the CARTA consortium," *Circulation: Cardiovascular Genetics*, vol. 8, no. 6, pp. 832–841, 2015.

[17] J. A. Larsen and A. H. Kadish, "Effects of gender on cardiac arrhythmias," *Journal of cardiovascular electrophysiology*, vol. 9, no. 6, pp. 655–664, 1998.

[18] M. van Wyk, K. G. Thomas, M. Solms, and G. Lipinska, "Prominence of hyperarousal symptoms explains variability of sleep disruption in posttraumatic stress disorder.," *Psychological Trauma: Theory, Research, Practice, and Policy*, vol. 8, no. 6, p. 688, 2016.

[19] A. H. Kemp *et al.*, "Effects of depression, anxiety, comorbidity, and antidepressants on resting-state heart rate and its variability: an ELSA-Brasil cohort baseline study," *American Journal of Psychiatry*, vol. 171, no. 12, pp. 1328–1334, 2014.

[20] H. Adenauer, C. Catani, J. Keil, H. Aichinger, and F. Neuner, "Is freezing an adaptive reaction to threat? Evidence from heart rate reactivity to emotional pictures in victims of war and torture," *Psychophysiology*, vol. 47, no. 2, pp. 315–322, 2010.

[21] K. Elsesser, G. Sartory, and A. Tackenberg, "Attention, heart rate, and startle response during exposure to trauma-relevant pictures: a comparison of recent

trauma victims and patients with posttraumatic stress disorder.," *Journal of abnormal psychology*, vol. 113, no. 2, p. 289, 2004.

[22] K. Elsesser, G. Sartory, and A. Tackenberg, "Initial symptoms and reactions to trauma-related stimuli and the development of posttraumatic stress disorder," *Depression and Anxiety*, vol. 21, no. 2, pp. 61–70, 2005.

[23] G. Buswell, Z. Haime, B. Lloyd-Evans, and J. Billings, "A systematic review of PTSD to the experience of psychosis: prevalence and associated factors," *BMC psychiatry*, vol. 21, no. 1, pp. 1–13, 2021.

[24] D. McDuff, S. Gontarek, and R. Picard, "Remote measurement of cognitive stress via heart rate variability," in *2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2014, pp. 2957–2960.

[25] A. Sano and R. W. Picard, "Stress recognition using wearable sensors and mobile phones," in *2013 Humaine Association Conference on Affective Computing and Intelligent Interaction*, 2013, pp. 671–676.

[26] R. W. Picard, E. Vyzas, and J. Healey, "Toward machine emotional intelligence: Analysis of affective physiological state," *IEEE transactions on pattern analysis and machine intelligence*, vol. 23, no. 10, pp. 1175–1191, 2001.

[27] A. D. McDonald, F. Sasangohar, A. Jatav, and A. H. Rao, "Continuous monitoring and detection of post-traumatic stress disorder (PTSD) triggers among veterans: a supervised machine learning approach," *IISE Transactions on Healthcare Systems Engineering*, vol. 9, no. 3, pp. 201–211, 2019.

[28] F. Shaffer and J. P. Ginsberg, “An overview of heart rate variability metrics and norms,” *Frontiers in public health*, vol. 5, p. 258, 2017.

[29] N. Mittag, “Imputations: Benefits, risks and a method for missing data,” *Unpublished Manuscript*, 2013.

[30] E. Shvil, H. L. Rusch, G. M. Sullivan, and Y. Neria, “Neural, psychophysiological, and behavioral markers of fear processing in PTSD: a review of the literature,” *Current psychiatry reports*, vol. 15, no. 5, p. 358, 2013.

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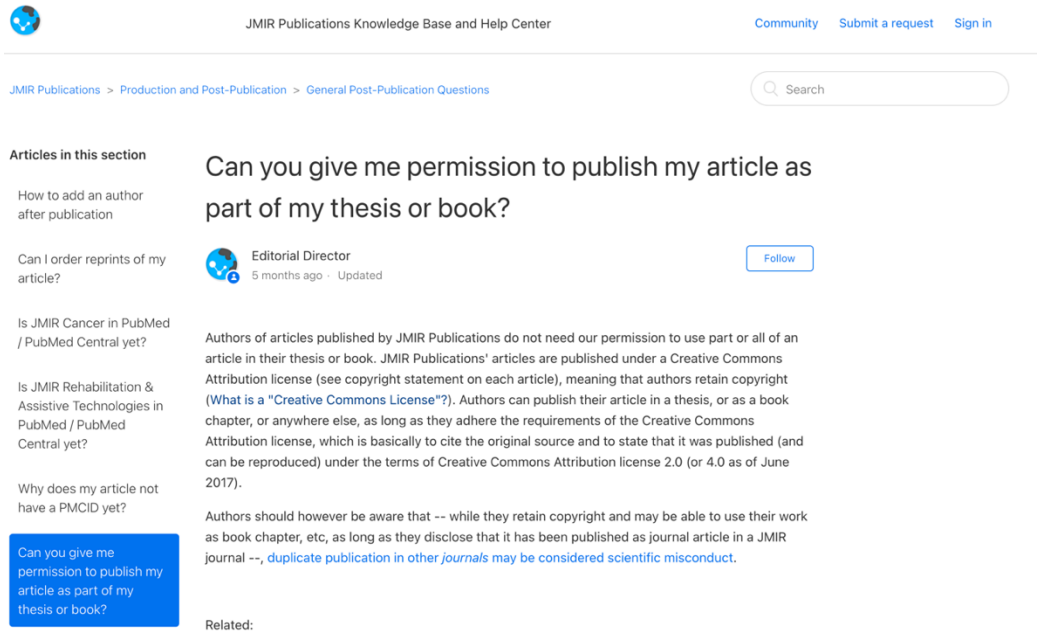

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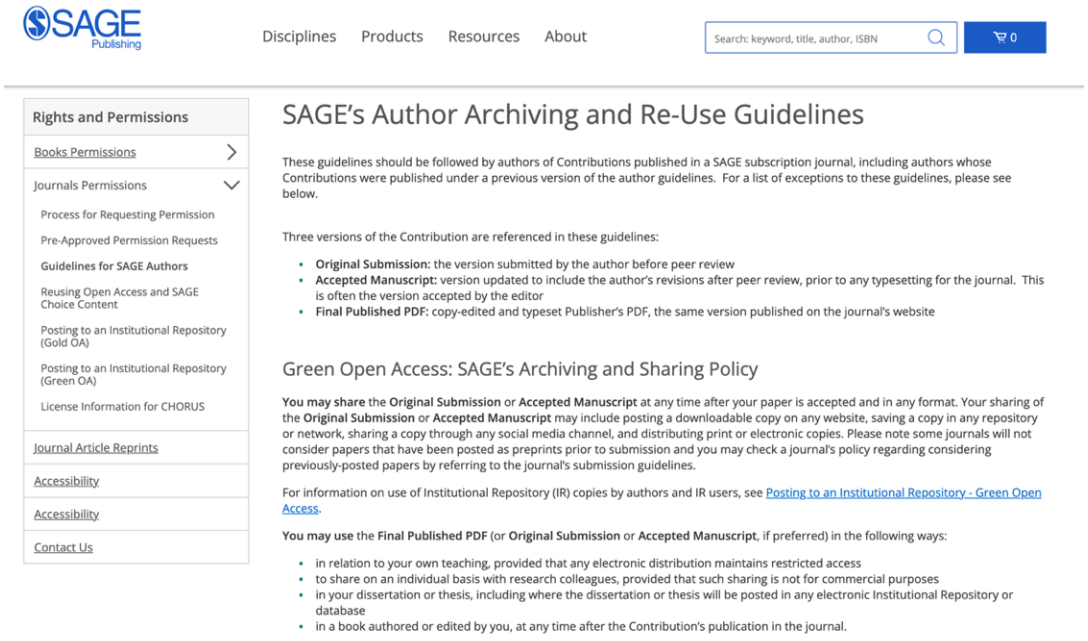

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Thank you so much, Dr. DeLucia, really appreciate your help.

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