Analyzing Heart Rate as a Physiological Indicator of Post-Traumatic Stress Disorder: A Scoping Literature Review

The relationship between PTSD and Heart Rate (HR) has been widely studied since assessing HR can be a promising way to characterize and detect the episodes of outbreak in PTSD sufferers. However, most of the studies are limited to simple math-stat tools in terms of their statistical analysis. In this regard, this paper has reviewed 34 articles discussing HR statistical modeling. We extracted eight main approaches that researchers can use to analyze and interpret their HR data. Further, these approaches have been categorized into descriptive and predictive methods. A platform and a decision tree is introduced for heart rate data analysis for the future studies.

INTRODUCTION

Post-Traumatic Stress Disorder (PTSD) is a psychiatric condition that develops when people experience a shocking event in their life and have difficulties recovering from it (Nagpal, Gleichauf, & Ginsberg, 2013). Patients who suffer from PTSD often develop depression, anxiety, emotional instabilities, and heart disorders. Roughly 10% of women, 4% of men in the United States experience PTSD in their lives (Resnick, Kilpatrick, Dansky, Saunders, & Best, 1993). Additionally, PTSD is an endemic disorder among veterans affecting between 17% to 24% of veterans from recent conflicts (Richardson, Frueh, & Acierno, 2010).

While an alarming number of individuals suffer from PTSD, treatments for this disorder are limited to in-session therapies (Moon, Smith, Sasangohar, Benzer, & Kum, 2017). Clinicians are understaffed, and treatment avenues are not sufficient especially when PTSD patients are struggling with the onset of symptoms outside of their clinicians' office (Rodriguez-Paras et al., 2017).

Mobile health apps (mHealth) may help resolve this issue (Galea et al., 2012). mHealth apps deployed on wearable devices (e.g., smartwatches) enable patients to continuously have access to their physiological state. Clinicians can also use these apps to collect physiological data and continuously monitor patients by assessing their reactions between therapy sessions (Rodriguez-Paras et al., 2017).

The success of physiology-based mHealth apps depends on their ability to model the relationship between physiological conditions and disease states. Heart-based measures are often used for this purpose because it is feasible to passively collect HR data from current smartwatch technology. HR is representatives of the performance of the Autonomic Nervous System (ANS) (Hynynen, Uusitalo, Konttinen, & Rusko, 2006). The ANS consists of parasympathetic (PNS) and sympathetic (SNS) systems, which regulate blood pressure and breathing rate during rest, and accelerate HR and regulate blood pressure during activity, respectively (Kandel et al., 2000). PTSD and its episodes of outbreak are also associaed with sustained changes in ANS (Prins, Kaloupek, & Keane, 1995). Therefore, HR as a physiological indicator of ANS can be used for assessing PTSD symptoms in patients when they are not in their therapy sessions (Khanade & Sasangohar, 2017).

The other main physiology measure of heart that can be analyzied to examine PTSD is heart rate variability (Cohen et al., 2000). Heart rate variability has been analyzed in a variety of studies in domains such as energy expenditure and mental stress disorders. More than 17,000 articles were published about heart rate variability analysis methods by the year 2014 (Monfredi et al., 2014). However, heart rate variability currently has limited application in consumer applications because it is not collected in most aftermarket smartwatches. Heart rate may be a promising alternative, but studies of heart rate modeling in PTSD are limited.

Investigating HR and the associated quantitative models may be a promising future direction for mHealth applications that can provide better PTSD care between therapy sessions. The goals of this article are to review mathematical and statistical models used to analyze heart rate data in the anxiety and physical activity domains, identify opportunities for these models in the PTSD domain, and highlight research gaps in the current models.

METHOD

The review spanned five databases: (1) Medline OVID, (2) Medline Ebsco, (3) CINAHL Ebsco, (4) Embase Ovid and (5) Google Scholar. The initial search was carried out on March 12, 2018; all studies published in or after the year 2000 were included. The search terms included: "heart*", "pulse*", "Heart Rate*", "model*", "heart beat*", and "analysis*". Abstracts were reviewed for relevance and articles that met inclusion/exclusion criteria were reviewed manually. Non-English articles, as well as the articles that exclusively had studied other physiological reactions, such as skin conductance and blood pressure, were excluded. The inclusion criteria was all the papers that discussed heart rate analysis approaches. The searches identified 261 articles, of which 34 were included in this review. The 34 articles were selected based on their similarity and comparability to the scope of the research question.

RESULTS

Heart rate models

Mathematical models can be categorized into two major subsets: descriptive models and predictive models. Descriptive models address the question "what is happening and why is it happening?" while predictive models address questions such as "what will happen and why it will happen?" (Rosenbröijer, 2014). Both types of questions and their associated models are relevant to PTSD. For example, 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 and intervene. Beyond the predictive and descriptive dimension, models can be characterized by their type of output—discrete or continuous. The output of discrete models is time invariant, whereas the output in continuous models is time-based. Again, both types of models are relevant for PTSD characterization, as researchers may be interested in discrete states (e.g., stress moments) or continuous output (e.g., changes in heart rate during a stress moment). The applicability of descriptive and predictive models and discrete and continuous predictions suggests that they are valid categories to characterize the studies discussed in this review. Figure 1 represents a decision tree for choosing a model among the methods.

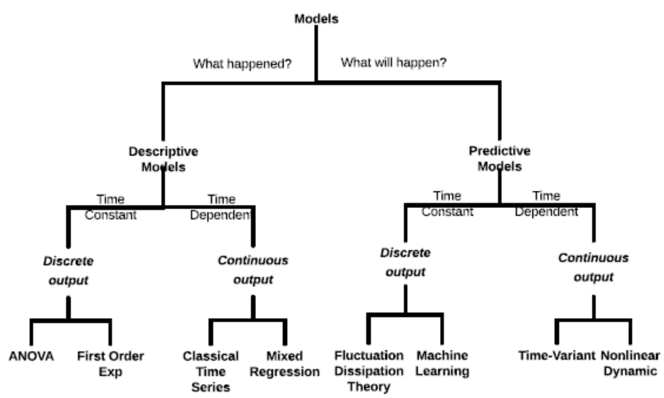

Figure 1: Decision tree for choosing models

Descriptive Models

1- Discrete output

***Analysis of Variance (ANOVA)*:** Linear regression, and in particular ANOVA, was a common statistical method used in several articles (e.g., Bremner et al., 1997). ANOVA can be used to compare trends, and group means in experimental studies (Tabachnick & Fidell, 2007). Several studies used ANOVA to account for the effectiveness of treatments in PTSD patients as measured by HR (e.g., Foa, Rothbaum, Riggs, & Murdock, 1991). For example, the study by Gelpin et al. (1996) compared the resting HR in individuals pre- and post-treatment to measure the success of that treatment. Buckley, Holohan, Greif, Bedard, & Suvak (2004) used ANOVA to compare resting HR in PTSD sufferrers with healthy controls, finding that PTSD sufferrers, in general, have higher resting HR levels (Buckley, Holohan, Greif, Bedard, & Suvak, 2004). While studies have found success with the use of ANOVA for inference in PTSD, it is limited in several respects. ANOVA has strong assumptions and is ill-suited to model dependent measures with strong temporal correlations. Thus it should not be used to make time-based HR predictions (Cacioppo et al., 2007).

***First-order exponential model*:** A first order exponential model provides a function with a sustained growth or decay rate. In terms of heart rate anaysis, first order exponential models generate a nonlinear regression model for HR based on heart rate recovery (Marquardt, 1963). Heart Rate Recovery (HRR) is an indicator of vagal reactivation and SNS deactivation (Bartels-Ferreira et al., 2015). Although in the reviewed studies this approach was used to examine ANS in terms of physical activity, the model can be used to assess PTSD. Specifically, recovering from the onset of PTSD symptoms is associated with activation of vagal tone and withdrawal of SNS nervous system, both of which are correlated with HRR (Lipov, 2013). However, the HR and HRR correlations observed in the reivewed studies (e.g., Bartels-Ferreira et al., 2015) were moderate, which suggests a need for significant additional research.

1- Continuous output

***Classical time series analysis*:** Classical time series analysis is a common statistical method that can analyze time-dependant data trends. Classical time series analysis is also a promising method for analyzing HR and HR fluctuations since these measures are time-based (H. Chen, Erol, Shen, & Russell, 2016; Peng, Havlin, Stanley, & Goldberger, 1995). Peng et al. (1995) showed that there are some independency between beat to beat HR fluctuations in healthy people that does not exist in cardiovascular disease patients. The findings of Peng et al. (1995) 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 (Cohen et al., 1998).

Beyond the analagous use case, classical time series has several benefits compared to ANOVA. Since the model explicitly considers autocorrelation, it does not require the independence of observations (Kantz & Schreiber, 2004). The models also have predictive capability and are well validated for illustrating trends and forecasting (Montgomery, Johnson, & Gardiner, 1990). However, one drawback of these methods is the assumption of stationary (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 linear regression analysis has been used in the literature to evaluate physiological responses to energy expenditure (Bonomi et al., 2015). This type of modeling can be applied with correlated observations (e.g., individuals similarities). Thus, it is beneficial for psychophysiology analyses that need to account for individual differences in responses (Cacioppo, Tassinary, & Berntson, 2007). 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 data set (for instance HR), while random effect represents the differences among observations (the error term).

The ability of mixed regression models to account for individual differences make them an advantageous choice for modeling PTSD. Several studies have identified significant individual differences in PTSD sufferers (Nagpal et al., 2013). Specifically, HR and heart rate variability levels are significantly affected by individual differences such as age, general health, and gender (Shaffer & Ginsberg, 2017).

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 multipe random effects (Darlington, 1990).

Predictive Models

1- Discrete output

Machine learning methods: Deep learning and machine learning methods are popular approaches that are commonly used in recent research for prediction and forecasting (B.-J. Chen & Chang, 2004). Typically, in machine learning analysis, researchers divide their data set into testing and training data (or leverage techniques such as cross validation). After developing a statistical model by using training data, they validate their approach with the testing dataset. 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).

Most of the reviewed studies used heart rate variability along with machine learning algorithms to predict the stress level in individuals (e.g., Sano & Picard, 2013). Machine learning studies evaluating HR primarily have focesd on energy expenditure. One exception is McDonald et al. (2019) who evaluated several machine learning algorithms—neural networks, decision trees, support vector machines and random forests—to predict the onset of PTSD symptoms in PTSD sufferers. Among all machine learning methods, support vector machines, and random forest algorithms performed best. The results of the reviewed studies suggest that machine learning analysis is a promising direction for future PTSD analysis, however they are limited in their inference capability. Machine learning methods are like black boxes where often predictive results have little rational explanation (Michie, Spiegelhalter, & Taylor, 1994).

Fluctuation-dissipation theory

Fluctuation-dissipation theory is a common approach in thermodynamics that is used to predict system behavior by breaking the system responses into small forces (Kubo, 1966). M. Chen et al. (2013) used fluctuation-dissipation theory to predict patients' HR reactions to pre and post- spontaneous breathing trial treatment. The reactions were modeled with HRR measures . M. Chen et al. (2013) found that thermodynamic rules can model HR response after stress moments. They further suggest that the HRR extracted from this type of modeling can be used to personalize critical care as HR can be remotely monitored through noninvasive wearable devices. This can be very helpful for between-session therapies in PTSD sufferers, particularly for predicting reactions after an arousal event. Despite its promising application, and the lack of restrictive assumptions, fluctuation-dissipation theory is computationally intense and time-consuming during equation computation.

2- Continuous output

Time-variant modeling: Time-variant modeling models HR based on its time-dependent feature. This type of modeling 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 (Roger & Jamieson, 1988). Again, this type of computation will be beneficial for PTSD given that it may be adapted to compare 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 can be accurate and has been replicated in the literature (e.g., Kazmi et al., 2016; Lefever et al., 2014), 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 on wearable devices.

Nonlinear dynamic modeling: Nonlinear dynamic modeling of HR consists of depicting HR as a set of nonlinear, time dependent mathematical equations (Haber & Unbehauen, 1990). Nonlinear dynamic modeling of HR can be a promising method to assess arousal patterns by measuring SNS outflow (Valenza, Lanata, & Scilingo, 2012). Hence, this approach may be useful for analyzing PTSD hyperarousal patterns. Despite the advantages of this model, it requires high frequency HR data (e.g., 100 Hz) or even instantaneous HR (e.g., Valenza et al., 2012). Instantaneous HR is a HR measure derived from HRV, which is often different from directly measured HR on smartwatches. Instantaneous HR can be extracted from multiplying RR intervals by the number 60 (Valenza et al., 2012).

Table 1: Reviewed articles categorize based on each model

Method	Articles
Analysis of Variance (ANOVA)	Strath et al. (2000), Xu et al. (2015), Romero-Ugalde et al. (2017), Khoueiry et al. (2012), Tonhajzerova et al. (2012), Hoyer et al. (2012), Shalev et al
First-Order Exponential	Bartels-Ferreira et al. (2015)
Classical time series analysis	Chen et al. (2016), Kazmi et al. (2016), Zakeri et al. (2012), Peng et al. (1995)
Mixed regression	Gee et al. (2017), Bonomi et al. (2015), Xu et al. (2015), Romero-Ugalde et al. (2017), Diderichsen et al. (2013), Zakeri et al. (2012), Khoueiry et al. (2012), Hoyer et al. (2012)
Machine learning	Kolus et al. (2016), Kolus et al. (2014), McDonald et al. (2019), Zhang et al. (2012),
Fluctuation-dissipation theory	Chen et al. (2013), Peng et al. (2009), Lu et al. (2009)
Time-Variant modeling	Kazmi et al. (2016), Valenza et al. (2014), Lefever et al. (2014), Ferrer et al. (2013), Ferrer et al. (2013), Olufsen et al. (2013), Valenza et al. (2012a), Valenza et al. (2012b), Zazula et al. (2012), Echeverría et al. (2012)
Nonlinear dynamic modeling	Chen et al. (2016), Kazmi et al. (2016), Ferrer et al. (2013), Park et al. (2013), Olufsen et al. (2013), Valenza et al. (2012a), Valenza et al. (2012b), Zazula et al. (2012), Scalzi et al. (2012), Echeverría et al. (2012), Hoyer et al. (2012), Cheng et al. (2008), Mazolleni et al. (2016), Zakynthinaki (2015)

Methodolical 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 age, sex, health, resting HR and respiration (Shaffer & Ginsberg, 2017). Maximum HR typically decreases with age. Females have higher HR levels than men (Magder, 2012). Athletes have lower HRs levels than sedentary people (Lester, Sheffield, Trammell, & Reeves, 1968). Resting HR is lower in more active people, and lower resting heart rates result in lower HR levels (Sacknoff, Gleim, Stachenfeld, & Coplan, 1994). Since the respiratory system affects heart activity, studies suggest that incorporating respiration as a factor in HR models improves HR estimation significantly (Gee, Barbieri, Paydarfar, & Indic, 2016).

Beyond these general characteristics, it is important to consider the type of physical activity in the analysis. Physical activity significantly affects HR and HR elevations (Freedson & Miller, 2000). Further, high-intensity activities such as running and cycling affect HR differently from low intense activities such as sitting and laying down (Boulay, Simoneau, Lortie, & Bouchard, 1997). Concerns regarding activity were common in the reviewed studies, particularly in energy expenditure domain (Green, Halsey, Wilson, & Frappell, 2009). Green et al. (2009) 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 (e.g., Vrijkotte, Van Doornen, & De Geus, 2000), many neglected this factor (e.g., Shalev, Sahar, et al., 1998; Taelman, Vandeput, Spaepen, & Van Huffel, 2009).

DISCUSSION

The goals of this review were to identify and characterize quantiative heart rate models for relevant applications in PTSD. We identified four broad categories of models: descriptive discrete output,descriptive continuous output, predictive discrete output, and predictive continuous output. All of the identified modelling categories have relevance for PTSD, although modeling selection is highly dependent on the specific goals of the modeller. While the identified models have been applied across various domains (e.g., energy expenditure, general stress prediction), few approaches were directly applied to data from PTSD sufferers. Exceptions to this included: Shalev et al. (1998), McDonald et al. (2019). Of these studies, the analysis of McDonald et al. 2019 was the only predictive approach. Further the other studies were primarily limited to linear descriptive statistics such as the t-test or ANOVA (Cacioppo et al., 2007). 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 excluded from the articles. For example, in the study by Kolus, Imbeau, Dubé, & Dubeau (2016), the authors used backward variable selection method and did not discuss the rationale for this choice. Another critical detail often not addressed in the reviewed studies. Mismatches between the model requirements and the sampling rates may result in conditions such as overfitting (H.-S. Chen, Simpson, & Ying, 2000).

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, analzye 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.

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