

# “Ask Your Heart What it Doth Know”: 100+ Heart Rate Variability-Based Biomarkers of Mental and Physical Health Identified in a Large Cohort of Trauma Survivors

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## Introduction

- The majority of individuals experience a traumatic event in their lifetime, and a portion of these experience Adverse Posttraumatic Neuropsychiatric Sequelae (APNS) such as pain, posttraumatic stress disorder, and depression.
- Personal health monitors, such as assessment of heart rate variability (HRV), are becoming ubiquitous. Short-term HRV variables highlight complex interactions, including between the autonomic nervous system, respiratory rate, and baroreceptors.
- This analysis aims to identify and validate associations between such HRV biomarkers and ten self-report symptom domains in trauma survivors.
- There is increasing interest in determining whether caregivers and patients can leverage such monitors to help assess mental and physical health, and response to treatment.

**Table 1. Demographic information**

	Overall (N=2,626)
<b>Age in Year (Mean, SD)</b>	<b>35.7 (13.1)</b>
<b>Female (n, %)</b>	1631 (62.1%)
<b>Race (n, %)</b>	
Hispanic	300 (11.4%)
Non-Hispanic White	884 (33.7%)
Non-Hispanic Black	1330 (50.6%)
Non-Hispanic Other	101 (3.8%)
<b>Education Status (n, %)</b>	
High school or less	998 (38.0%)
Some college	1080 (41.1%)
College or more	549 (20.9%)
<b>Trauma Type (n, %)</b>	
Motor Vehicle Collision	1979 (75.4%)
Physical Assault	246 (9.4%)
Sexual Assault	16 (0.6%)
Other	385 (14.6%)

**Table 2. Latent constructs indicator variable questions from follow-up surveys**

Latent Constructs	Timepoints (Days) (first 6 months)	Timeframe; Symptoms Assessed
<b>Pain</b>	1,9, 21,31,43,53,67, 77,105,147,196	24 hrs; worst pain, average pain
<b>Depressive Symptoms</b>	5,19,29,39,51,61, 75,91,133,175	24 hrs; down on yourself, no good, or worthless, sad, depressed or empty, trouble experiencing positive feelings
<b>Sleep Disturbance</b>	3,15,25,35,47,57, 71,81,119,161	Last few nights; trouble falling asleep, trouble staying asleep all night, waking up too early
<b>Nightmares</b>	3,15,25,35,47,57, 71,81,119,161	Last few nights; nightmares or bad dreams about the event, nightmares or bad dreams about other things, panic attacks during the night
<b>Anxiety</b>	5,19,29,39,51,61, 75,91,133,175	24 hrs; severe anxiety or panic, very nervous, worried or anxious
<b>Hyperarousal</b>	5,19,29,39,51,61, 75,91,133,175	24 hrs; “superalert” or watchful, or on guard, jumpy or easily startled
<b>Avoidance</b>	4,17,27,37,49,59, 73,83,126,168	24 hrs; avoid memories, thoughts, or feelings related to the event, avoid external reminders of the event
<b>Re-experiencing</b>	4,17,27,37,49,59, 73,83,126,168	24 hrs; repeated, disturbing, and unwanted memories of the event, very upset and strong physical reactions when something reminded you of the event
<b>Somatic Symptoms</b>	2,11,23,33,45,55,69, 79,112,154,203	24 hrs; headaches, dizziness, nausea
<b>Mental Fatigue</b>	2,11,23,33,45,55,69, 79,112,154,203	24 hrs; fatigue, trouble concentrating, taking longer to think

## Methods

- This analysis leveraged data from an ongoing longitudinal study (the AURORA study) evaluating adverse symptom development among individuals presenting to the emergency department (ED) after traumatic stress exposure (most commonly MVC).
- The AURORA Study began participant recruitment in September 2017. Wrist wearables (Verily Study Watch) were worn by 2,626 individuals recruited from the emergency department after a traumatic event (75% MVC) for six months.
- Participants also completed brief serial smartphone-based surveys (Table 1) assessing ten symptom domains: pain, depressive, somatic, anxiety, avoidance, re-experiencing, and hyperarousal symptoms, as well as sleep disturbance, nightmares, and concentration difficulty/mental fatigue (each assessed every 2 weeks on average).
- HRV features were extracted from wrist wearable photoplethysmography (PPG) data. Bivariate linear mixed models were used to derive (FDR ≤ 0.05) and validate (Bonferroni ≤ 0.05) HRV features associated with each of these ten self-report domains.
- Between-participant health differences at a point in time (“trait differences”) and changes in health status of an individual over time (“state differences”) were assessed.

## Results

- Eighty-five trait biomarkers (Table 2) distinguished variation in symptom domains between individuals at a point in time, pain(29), somatic(14), anxiety(14), avoidance(11), re-experiencing(11), hyperarousal(6), and mental fatigue(6) symptoms.
- Forty-nine state biomarkers (Table 3) identified changes in mental or physical health over time, including pain(2), somatic(10), avoidance(3), re-experiencing(17), and hyperarousal(5) symptoms.
- State HRV variables predict recovery with sensitivities ranging 0.47-0.72, specificities 0.29-0.48.

**Table 3. State Biomarkers that Identify Within-Person Changes in Specific Symptoms. Red indicates positive correlation. Blue indicates negative correlation.**

Biomarker	Pain	Somatic Symptoms	Mental Fatigue	Depressive	Anxiety	Hyperarousal	Avoidance	Re-experiencing	Sleep	Nightmares
Approximate Entropy (daily max)								Red		
Average signal-quality-index(daily min)		Blue						Blue		
Average signal-quality-index (daily max)	Red	Red						Red		
Average signal-quality-index (daily variance)	Red	Red						Red		
Deceleration capacity (daily min)							Blue			
Deceleration capacity (daily max)						Red				
Deceleration capacity (# of daily obs >median)						Red				
Ratio of low and high frequency power (daily min)									Blue	
Ratio of low and high frequency power (# of daily obs >median)		Red								Red
Interquartile range (daily min)								Blue		
Interquartile range (daily max)							Red			
Interquartile range (# of daily obs >median)						Red				
Kurtosis (1 <sup>st</sup> quartile)								Blue		
Kurtosis (daily max)		Red						Red		
Kurtosis (# of daily obs >median)			Red					Red		
Mean (daily max)								Red		
Skewness (daily min)								Blue		
Skewness (daily max)								Red		
Skewness (# of daily obs >median)		Red						Red		Red
Root mean square difference (daily min)								Blue		
Root mean square difference (daily max)		Red	Red					Red	Red	Red
Root mean square difference (# of daily obs >median)		Red				Red		Red	Red	Red
Ratio of SD1 SD2 (daily min)								Blue		
Standard deviation (daily max)		Red						Red		
Standard deviation (# of daily obs >median)								Red		

## Conclusions

- Heart rate variability-based biomarkers of mental and physical health show promise in helping individuals and health care providers monitor health status and response to treatment.

**Table 4. Trait Biomarkers that Identify Between-Person Changes in Specific Symptoms. Red indicates positive correlation. Blue indicates negative correlation.**

Biomarker	Pain	Somatic Symptom	Mental Fatigue	Depressive	Anxiety	Hyperarousal	Avoidance	Re-experiencing	Sleep	Nightmares
Approximate Entropy (daily min)	Red									
Approximate Entropy (daily 1 <sup>st</sup> quartile)	Red									
Approximate Entropy (daily mean)	Red							Red		
Approximate Entropy (daily variance)	Blue									
Average signal-quality-index (daily 1 <sup>st</sup> quartile)	Blue									
Average signal-quality-index (daily mean)	Blue									
Average signal-quality-index (daily max)	Blue							Blue		
Deceleration capacity (daily 1 <sup>st</sup> quartile)	Blue									
Deceleration capacity (daily mean)	Blue									
Deceleration capacity (daily max)	Blue									
Deceleration capacity (# of daily obs >median)	Blue									
Ratio of low and high frequency power (daily 1 <sup>st</sup> quartile)	Blue									
Ratio of low and high frequency power (daily mean)	Blue									
Ratio of low and high frequency power (daily max)	Blue									
Ratio of low and high frequency power (daily variance)	Blue									
Ratio of low and high frequency power (# of daily obs >median)	Blue									Blue
Interquartile range (daily 1 <sup>st</sup> quartile)	Blue									
Interquartile range (daily mean)	Blue								Blue	
Interquartile range (daily max)	Blue									
Interquartile range (daily variance)	Blue									
Kurtosis (daily mean)	Red									Red
Mean_q1 (daily 1 <sup>st</sup> quartile)	Blue									
Mean (daily mean)	Blue									
Mean (daily max)	Blue									
Mean (daily variance)	Blue									
Skewness (daily min)	Blue									
Skewness (# of daily obs >median)	Blue									Blue
Root mean square difference (# of daily obs >median)	Blue									Blue
Ratio of SD1 SD2 (daily min)	Red	Red						Red	Red	Red
Ratio of SD1 SD2 (daily 1 <sup>st</sup> quartile)	Red	Red						Red	Red	Red
Ratio of SD1 SD2 (daily mean)	Red	Red						Red	Red	Red
Ratio of SD1 SD2 (daily max)	Red	Red						Red	Red	Red
Ratio of SD1 SD2 (# of daily obs >median)	Blue	Blue						Blue	Blue	Blue
Standard deviation (daily mean)	Blue									
Standard deviation (daily max)	Blue									
Standard deviation (daily variance)	Blue									
Standard deviation (# of daily obs >median)	Blue									

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