Appendix:
Letter of Support #1: Jeremy Gunn, The Knowles Family Director of Men's Soccer at Stanford University

Jeremy Gunn
The Knowles Family Director of Men's Soccer
Stanford University
May 30th 2023

Subject: Support for NeuroBeat - A Device for Concussion Detection

Hello,

I hope this letter finds you in good health and high spirits. I am writing to express my utmost support for the remarkable innovation brought forth by NeuroBeat Inc., specifically their groundbreaking device for detecting concussions using heart rate variability as a biomarker.

As the head coach of the Stanford Men's Soccer Program, I am concerned about the well-being and safety of my players. Concussions are an unfortunate but common occurrence in contact sports such as soccer. According to research conducted by the American Academy of Pediatrics, soccer ranks among the top five sports for the highest concussion rates among male and female high school athletes in the United States. A study published in the British Journal of Sports Medicine found that approximately 22% of male and 27% of female soccer players had reported experiencing at least one concussion during their soccer careers.

However, the traditional methods of concussion detection often fall short, relying heavily on visible symptoms or subjective assessments. Players often choose not to disclose their symptoms for longer time on the field, making it difficult to address these issues in a timely and safe manner. This is why I find NeuroBeat's device to be a game-changer in the field of sports safety.

NeuroBeat's device, which monitors heart rate variability, offers an objective and reliable means of detecting concussions. By analyzing the subtle changes in heart rate patterns, the device can provide valuable insights into potential brain injuries. This early detection mechanism holds immense promise for preventing further harm and enabling prompt medical intervention.I firmly believe that integrating NeuroBeat's device into our soccer program will greatly enhance the safety measures we have in place. The real-time monitoring of heart rate variability during matches and training sessions will allow us to identify potential concussions more accurately and efficiently. This will contribute to the overall well-being of our players and foster a safer playing environment.

In conclusion, I wholeheartedly support NeuroBeat and its device for concussion detection based on heart rate variability. Should you require any additional information or have any queries, please do not hesitate to reach out to me at jgunn@stanford.edu .

Yours sincerely,

Jeremy Gunn
The Knowles Family Director of Men’s Soccer
Stanford University

Letter of Support #2: Brian White, Associate Athletic Trainer of Men’s Soccer at Stanford University

Brian White
Associate Athletic Trainer
Stanford Men’s Soccer
May 31st 2023

Subject: Letter of Support for Neurobeat

Hello,

I hope this letter finds you well. I am writing to express my strong support for Neurobeat Inc. and their innovative device designed to detect concussions based on heart rate variability. As the athletic trainer of Stanford Men’s Soccer Program, I understand the necessity of timely and accurate concussion diagnosis in my players. Soccer is a sport with one of the highest rates of concussions, so this device will play an important role in detecting these occurrences.

The current methods of concussion detection often rely on self-reporting by athletes and a series of subjective tests that often lack accuracy. It can be challenging to evaluate the occurrence of a concussion in the heat of competition. Therefore, the introduction of Neurobeat's device holds promise for how we address concussions in soccer.

The ability of Neurobeat's device to monitor heart rate variability and provide objective data for concussion detection holds great potential. By analyzing the subtle changes in heart rate patterns, the device offers an early indication of potential brain injuries, enabling prompt medical intervention and minimizing the risk of further harm. This objective and data-driven approach will significantly aid our ability to identify concussions in wrestlers, ensuring their well-being and facilitating appropriate treatment during both games and practices.

Furthermore, the impact of Neurobeat's device extends beyond our soccer program. It can benefit the wider soccer community, both at the amateur and professional levels. In conclusion, I support Neurobeat and its device for concussion detection based on heart rate variability.

Should you require any additional information or have any questions, please reach out to me at bwhite23@stanford.edu .

Yours sincerely,

Brian White
Associate Athletic Trainer
Stanford Men’s Soccer

Letter of Support #3: Tyler Eischens, Member of the Men's Wrestling Team at Stanford University

Tyler Eischens
Member of Stanford Wrestling
Stanford University
May 30th 2023

Subject: Supporting NeuroBeat, A Concussion Detection Tool

Hello,

As a wrestler who has personally experienced the devastating effects of a concussion, I want to express my unwavering support for the innovation brought forth by NeuroBeat Inc. and their device for detecting concussions using heart rate variability as a biomarker.

Being a wrestler, I understand the inherent risks associated with head injuries. Concussions are unfortunately common in our sport, and the consequences can be severe. Being forced to sit out of the sport I have built my entire life around for over a month because I received a second blow to the head after not being diagnosed with a concussion the week prior was devastating. Beyond having to sit out at practice and miss competitions I spent months training for, I fell behind in my schoolwork and became isolated from my social life to prioritize my recovery. Had I received a diagnosis immediately and without the subjectivity of my trainer, I could have been back on the mat within two weeks rather than six.

In a contact sport like wrestling, head collisions are incredibly common and often leave you feeling a little bit "off." Because of this only the most severe head injuries are taken seriously and even then, there are plenty of concussions that go undetected for days. The current methods of concussion detection are unreliable. This leaves athletes like myself vulnerable to undetected concussions and the subsequent risks they pose. Because of this, I believe that NeuroBeat's device is vital for the health of athletes like me throughout sports.

I believe that integrating NeuroBeat's device into wrestling programs and competitions will improve the way we protect student athletes. This will not only safeguard the well-being of wrestlers but also create a safer environment for our sport to thrive. I express my support for NeuroBeat to detect concussions based on heart rate variability. As a wrestler who understands the importance of early intervention and athlete safety, I believe NeuroBeat holds the potential to improve concussion diagnosis.

Best,
Tyler Eischens
tyeisch@stanford.edu

Appendix:

Supplementary Table 1: Stakeholder interviews.

Stakeholder	Sample Size	Interview Highlights
Collegiate Athletes	3	• Reservations about the reliability of SCAT5, given that it relies on subjective assessments • Difficult to communicate symptoms in high-pressure situations, especially in context of a team sport • Experienced symptoms like dizziness/difficulty in focusing but did not deliver symptoms because of pressure
College Athletic Coaches	2	• Often difficult because players fake their baseline to be able to increase play time • Athletes hide symptoms and under-report severity of symptoms
College Athletics Team Clinicians	2	• Does not compare in accuracy to actual neurological assessments • Not very effective in diagnosing concussions, as it is prone to bing manipulated

Supplementary Report 1: Experimental protocol used to collect data (N=30) from athletes simulating non-TBI ANS perturbations.

SR 1.1: Testing pipeline workflow.

Workflow Steps	Detailed Steps
Subject Selection	1. Select 30 healthy and physically active individuals between the ages of 18 and 22 years. 2. Ensure that all participants have no history of cardiovascular or respiratory diseases and are not taking any medications that may affect their HRV.
Baseline Rest Measurements	1. Prior to the exercise session, record each participant's resting HRV using the FrontierX ECG monitoring band for a period of 10 minutes. Have them sit in a chair. Give them the opportunity to color or just sit and converse. 2. Make sure they do not have any other diseases or injuries and are not taking any medications that may affect their HRV.
Exercise Session	1. Warm up: jog a lap around the field 2. Have individual put on the band around their chest and connect it to a phone or computer device 3. Go to the workout tab and set it to run, press start. The band should buzz when the workout starts 4. Have the runner walk to starting line and start the running when the timer hits 1 minute 5. Have the individual hold a phone on the runs to maintain constant connection to the band. 6. The exercise session will consist of 5 sets of 50 meter sprints, they will sprint 50 meters out, and jog 50 meters back. Starting each sprint on the minute. 7. Record each participant's HRV using the FrontierX ECG monitoring band for the exercise period
Post-Exercise Measurements	1. Immediately after the exercise session, they have the rest of the minute to walk to the chair where they will sit for the remainder of the 10 minutes 2. The time will start at minute 6 on the clock and end at minute 16. 3. Record each participant's HRV using the FrontierX ECG monitoring band and have them sit in a chair. 4. Offer them a coloring book or soothing music to listen to or just talk to them
Data Analysis	1. Analyze the HRV data using appropriate software. 2. Export ECG strip from frontier app to google drive 3. Compare the HRV values during and after the exercise session to the baseline HRV values. 4. Analyze the relationship between HRV and perceived exertion. 5. Run through our algorithm 6. Record the percent accuracy our algorithm calculates
Ethics	1. Obtain informed consent from all participants. 2. Ensure the study complies with all relevant ethical guidelines. 3. Guarantee that participant data is kept confidential and secure.

SR 1.2: Location & materials needed for testing.

Practical Needs	Detailed Purchases/Locations
Location	Euland Soccer Field

Materials	Frontier X bands Fatal vision goggles

SR 1.3: Tests conducted for ANS perturbations.

Test # & Title	Test Description
1: Baseline (exercise) and make sure they are well rested (ask how much sleep they got)	Perform the exercise session. This will serve as a baseline for comparison with the other tests.
2: Spin	Perform the same exercise session as before, but after the last sprint and before the sit down, have them spin in a circle with their head down 10 times after the last sprint.
3: Sleep (removed)	Have athletes sleep less than 5 hours the night before, perform the same exercise session as before.
4: Quiz	Perform the same exercise session as before, but before the running Inform them about a quiz they will have to take after the sprints. Memorize 10 words: vase, tiger, camera, book, ice Cream, cushion, spade, piano, hat, orange. After the last sprint once they sit down, have them repeat out the words they remember from the list of 10. Have them repeat them in backwards order. Have them repeat them in alphabetical order.
5: Fatal Vision	Perform the same exercise session as before. After the last sprint once the athlete has sat down in the chair have them wear the fatal vision goggles for the remainder of the time.
Other Considerations	**We will provide water and snacks for the athlete to drink as they sit in the chair.** **Each test should take a total of 15-20 minutes, from warm up and exercise session to post exercise measurements** **Total time for experimentation will be 85-90 minutes per individual** (if they perform all tests)

Supplementary Report 2: Data processing/data analysis methods & technicalities
SR 2.1: Pre-processing detailed methods.

We used ECG data from multiple Physionet databases, including the CHARIS database with TBI patients, and the CEBSDB database/Healthy RR Intervals database with healthy patients. Each of these datasets have slightly different information and file types, so we developed a method to standardize these datasets to a unilateral format.

1) First we had to remove the noise from ECG readings. We did this by setting threshold values of where we expected the ECG signal to be, and removed the chunks that fell outside of these thresholds.
2) Next we set cut-off values and chose the points with the highest signal values that were part of the R-wave:

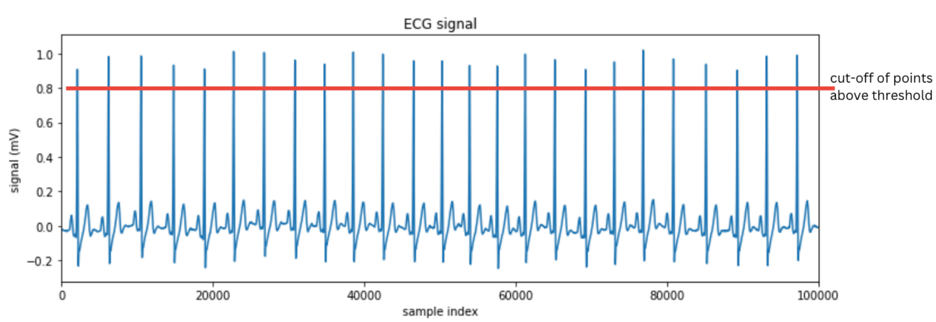


__Figure 2.1.1:__ This is a subsection of an ECG reading. The largest peaks are the R-Waves that we wanted to measure intervals between. We would set a cut-off threshold to keep only the data points from the peaks.

3) Then we calculated intervals between each of the points. Plotting these values on a histogram, we could see which intervals were from points next to each other, and which were from R-R intervals. Though the interval calculated was not exact, the error was less than a millisecond, and we determined this would be satisfactory for our model

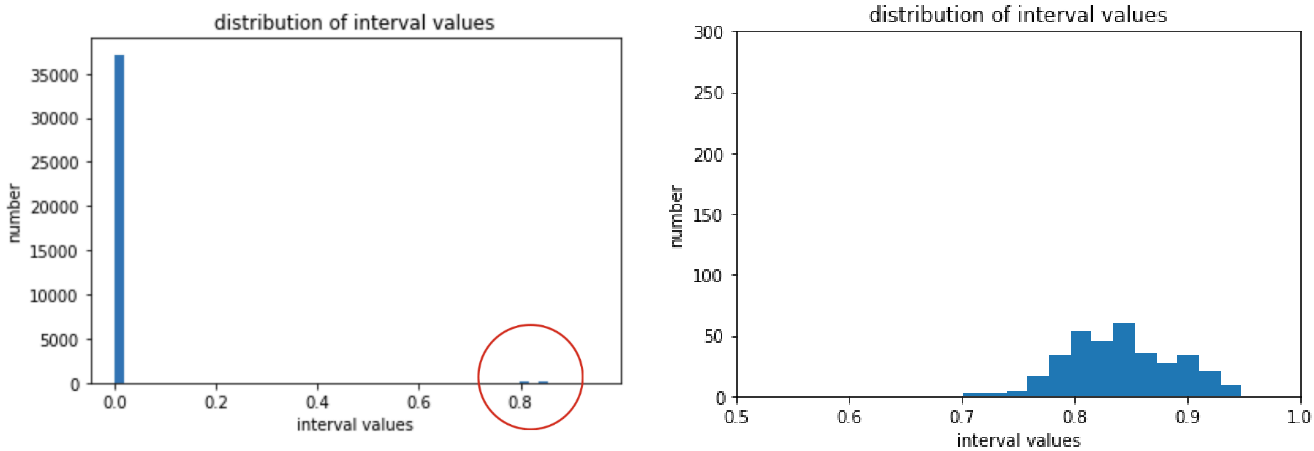


Figure 2.2.2: *On the left is the distribution of all the intervals measured from the top 2.5% kept after the cut-offs. The points circled in Red are the intervals to be kept. On the right figure is a zoomed in perspective of the points in the circled area.*

4) After narrowing down the data points to the top 2.5% signal values, we calculated the distances between each value. The points next to each other (around 0.0) had small distances and were removed. The distances around 0.8 were the real R-R intervals

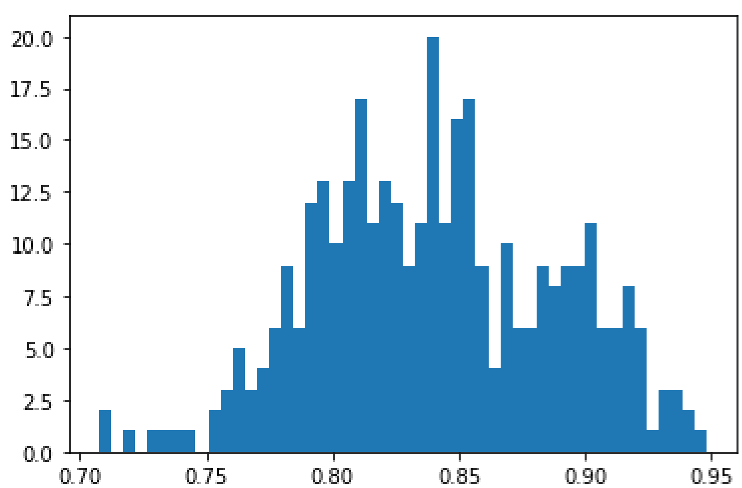


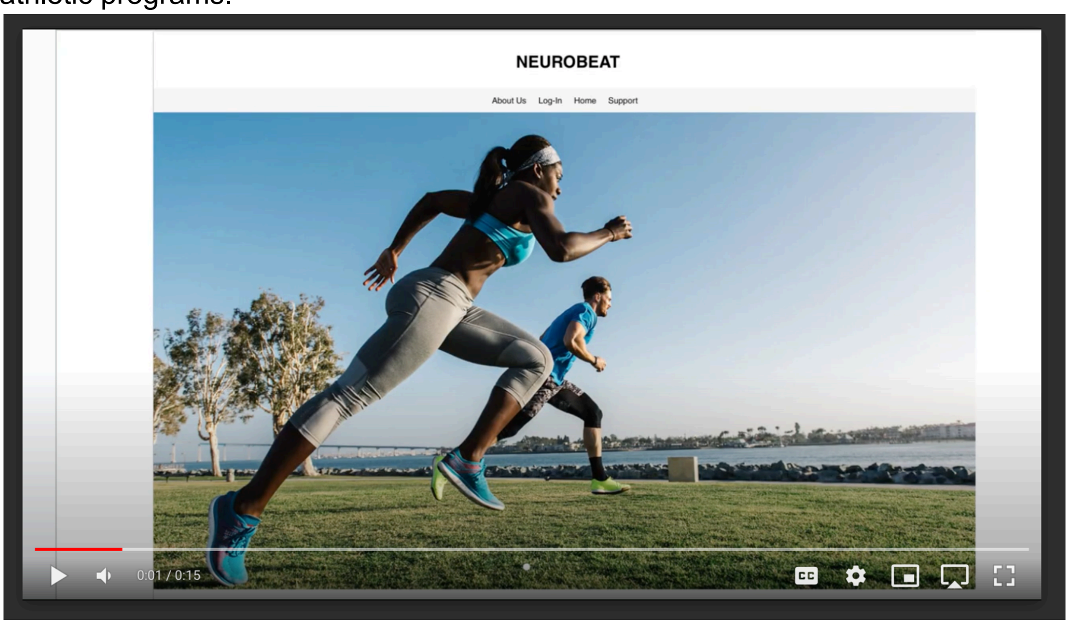
Figure 2.1.3: *H*istogram of the data points after removing the intervals below the cut-off.

SR 2.2: Feature selection detailed methods.
We chose several features to calculate from the R-R interval data in our first run: Range, IQR, Variance, Standard Deviation, and Coefficient of Variance. We calculated these values and put them in a table in a CSV file. The concussed data was given a value of 1 and healthy data was 0. For our second trial, we are adding patient age, gender, average heart rate, and mean HRV

as features. We selected the identified features because they present the most salient ones related to affecting the heart rate variability of individuals.

Supplementary Link 1: [Video of Experimental Protocol]
Link presents a video detailing the various tests that we ran for our data collection process including exercise, baseline/fatal vision, and spin tests.

Supplementary Link 2: [Mock-up of App Interface]
Link presents a preliminary app interface that will be used when dispersing our software to the athletic programs.



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