

Journal of Visualized Experiments

Calculating Heart Rate Variability from ECG Data from Youth with Cerebral Palsy during Active Video Game Sessions

--Manuscript Draft--

Article Type:	Methods Article - JoVE Produced Video
Manuscript Number:	JoVE59230R2
Full Title:	Calculating Heart Rate Variability from ECG Data from Youth with Cerebral Palsy during Active Video Game Sessions
Keywords:	Heart Rate Variability; Cerebral Palsy; Active Video Gaming; Bioharness; MATLAB; ECG; physical therapy
Corresponding Author:	Patricia A Shewokis, PhD Drexel University College of Nursing and Health Professions Philadelphia, Pennsylvania UNITED STATES
Corresponding Author's Institution:	Drexel University College of Nursing and Health Professions
Corresponding Author E-Mail:	shewokis.drexel@gmail.com
Order of Authors:	Corey Landis Margaret E O'Neil, PT PhD Andrew Finnegan Patricia A Shewokis, PhD
Additional Information:	
Question	Response
Please indicate whether this article will be Standard Access or Open Access.	Standard Access (US\$2,400)
Please indicate the city, state/province, and country where this article will be filmed . Please do not use abbreviations.	Philadelphia, PA USA

TITLE:

Calculating Heart Rate Variability from ECG Data from Youth with Cerebral Palsy during Active Video Game Sessions

AUTHORS & AFFILIATIONS:

Corey Landis¹, Margaret E. O'Neil^{2,3}, Andrew Finnegan^{2,3}, Patricia A. Shewokis^{1,3,4}

¹School of Biomedical Engineering, Science and Health Systems, Drexel University, Philadelphia, PA

²Department of Physical Therapy and Rehabilitation Sciences, Drexel University, Philadelphia, PA

³College of Nursing and Health Professions, Drexel University, Philadelphia, PA

⁴Department of Nutrition Sciences, Drexel University, Philadelphia, PA

E-MAIL ADDRESSES:

Corey Landis (corey.landis222@gmail.com)

Margaret E. O'Neil (meo23@drexel.edu)

Andrew Finnegan (agf49@drexel.edu)

Patricia A. Shewokis (pas38@drexel.edu)

CORRESPONDING AUTHOR:

Dr. Patricia A. Shewokis

pas38@drexel.edu

KEYWORDS:

Heart Rate Variability, Cerebral Palsy, Active Video Gaming, Electrocardiogram, Physical Therapy, Aerobic Performance

SUMMARY:

This protocol describes a method for calculating Heart Rate Variability (HRV) from electrocardiogram (ECG) waveforms. Waveforms from continuous heart rate (HR) recordings during active video game (AVG) sessions were used to measure the aerobic performance of youth with cerebral palsy (CP).

ABSTRACT:

The aim of this study was to generate a method for calculating heart rate variability (HRV) from electrocardiogram (ECG) waveforms. The waveforms were recorded by a HR monitor that participants (youth with cerebral palsy (CP)) wore during active video game (AVG) sessions. The AVG sessions were designed to promote physical activity and fitness (aerobic performance) in participants. The goal was to evaluate the feasibility of AVGs as a physical therapy (PT) intervention strategy. The maximum HR (mHR) was determined for each participant and the Target Heart Rate Zone (THRZ) was calculated for each of three exercise phases in the 20 min AVG session: (warm-up at 40-60% mHR, conditioning at 60-80% mHR, and cool down at 40-60% mHR). Each participant played three 20 min games during the AVG session. All games were

played while sitting on a bench because many youth with CP cannot stand for extended periods of time. Each game condition differed with participants using hand icons only, hand and feet icons together or feet icons only to collect objects. The objective of the game (called KOLLECT) is to collect objects to gain points and avoid hazards to not lose points. Hazards were used in the warm-up and cool down phases only to promote slower, controlled movement to maintain HR in the target heart rate zone (THRZ). There were no hazards in the conditioning phase to promote higher levels and more intense physical activity. Analytic methods were used to generate HRV (selected time-domain and frequency-domain measures) from ECG data to examine aerobic workload. Recent applications of HRV indicate that short-term measurements (5 min bouts) are appropriate and that HRV biofeedback may help improve symptoms and the quality of life in a variety of health conditions. Although HR is a well-accepted clinical measure to examine aerobic performance and intensity in PT interventions, HRV may provide information of the autonomic system functions, recovery and adaptation during AVG sessions.

INTRODUCTION:

Cerebral palsy (CP) is the most common physical disability of childhood¹. CP is caused by a neurologic insult to the developing brain and is associated with motor impairments such as muscle weakness, spasticity, deconditioning, and decreased motor control and balance^{2,3}. CP is a non-progressive condition but with age, children become less physically active and more sedentary compared to their peers with typical development (TD) mostly because of the increased demands of growth on their compromised neuromuscular and musculoskeletal systems⁴.

Youth with CP usually receive physical therapy (PT) services to improve functional mobility and promote physical activity and fitness (e.g. aerobic and muscular endurance)². Oftentimes, there is limited access to PT services and community resources to achieve and sustain these PT goals^{5,6}. Active video games (AVGs) may be a feasible strategy in activity-based PT interventions in clinic, home or community settings^{7,8}. Commercial AVGs have limited flexibility to adapt game play and meet the specific needs and PT goals for youth with CP⁹. However, customized AVGs provide flexible gaming parameters to challenge youth with CP while promoting physical activity and fitness¹⁰.

Our team has developed a customized AVG (called KOLLECT) to examine youth exercise responses (e.g., physical activity and aerobic fitness). The game uses a motion sensor to track youth motion during game play. The goal of the game is to 'collect' as many objects as possible for a high score and to avoid the hazards to avoid losing points. Objects may be collected with hand and/or feet icons as determined by the therapist in the flexible game parameters.

Designing activity-based PT interventions that dose physical activity intensity to promote aerobic fitness is critical for youth with CP¹¹. Custom AVGs may be an effective strategy to dose intensity and engage youth in physical activity to promote fitness¹⁰. Heart rate (HR) monitors are often used in clinical PT practice to determine aerobic performance and activity intensity. Therefore, HR monitors will help determine feasibility of AVGs in dosing physical activity intensity to promote aerobic fitness⁹. ECG data generated from a HR monitor can be used to

calculate heart rate variability (HRV). Analytic methods were used to generate HRV from ECG data to examine aerobic workload. Recent applications of HRV indicate that short-term measurements (5 min bouts) are appropriate and that HRV biofeedback may help improve symptoms and the quality of life in a variety of health conditions^{32,33,34}. The application of short-term HRV measures is an appropriate means of assessing cardiovascular function during AVG sessions. Given that HRV is derived from the R-R interval of an ECG, we used selected time-domain and frequency-domain measures. Time-domain measure of HRV quantify the amount of variability in the interbeat intervals which represents the time between successive heartbeats. We used the AVNN (average NN interval), RMSSD (root mean square of successive differences), SDNN (standard deviation of NN interval), NN50 (number of NN intervals >50 ms) and PNN50 (percentage of NN intervals). Frequency domain measures estimate the distribution of absolute or relative power into possibly four frequency bands, we specifically addressed on two bands, low frequency (LF) power and high frequency (HF) power along with the LF/HF ratio. Although HR is a well-accepted clinical measure, HRV may be useful because it provides information about autonomic system function, recovery, adaptation, and provides an estimate of aerobic workload during an AVG session²⁸.

The purpose of this study was to examine the feasibility of using AVG strategies to promote physical activity and fitness. A second purpose was to present the AVG data collection protocol and the methodology to calculate HRV from ECG data obtained via a HR monitor. These measures and this protocol may prove relevant to clinicians to monitor and dose PT intervention sessions.

PROTOCOL:

Institutional Review Board approval was obtained. All youth provided written assent and parents provided consent prior to participation.

1. AVG data collection sessions

1.1. The AVG game session

1.1.1. In this study, have youth with CP participate in an AVG session which is comprised of three 20 min games. See **Table 5** for Youth Demographics. It was expected that a total of 30 games would be played; however, 29 games were completed because one subject only played 2 games in his AVG session.

1.1.2. Have the subjects wear a HR monitor throughout the session to record HR and ECG responses.

1.1.3. In the AVG session, have youth play each AVG while seated on a bench with feet flat on the floor and knees and hips flexed to 90 degrees (90/90 sitting) for postural support and stability.

1.1.4. Use the following three gaming conditions for collection objects: 1) hand icons only; 2) feet icons only; and 3) both hand and feet icons. Use a counterbalanced order between subjects. Choose these three conditions to determine which is more effective in promoting physical activity and fitness and not too demanding to cause early, undue fatigue.

NOTE: Each game was designed using the phases of exercise prescription: warm-up, conditioning and cool-down. [Please see **Table 1**]. Additionally, there was a rest phase before game play began to document baseline HR and a recovery phase after game play to document time to return to baseline HR.

1.1.5. Allow subjects a rest period between games for HR to return to baseline level.

1.2. Calculating HRV from ECG Data

1.2.1. Organize data into 5 min time intervals to ensure comparable data for each phase. Therefore, there were 6 phases defined for these calculations: 1) Rest; 2) Warm-up; 3) Conditioning 1 (first 5 min); 4) Conditioning 2 (second 5 min); 5) Cool-Down (5 min) and 6) Recovery. Dividing the conditioning phase into two 5 min phases allows examination of subject aerobic performance in shorter intervals to account for fatigue due to deconditioning ¹² (**Table 4**).

1.2.2. To properly calculate HRV measures for each segment of a subject's session, perform R-peak detection on the raw ECG signal^{12,13}. Use the raw signal to avoid manipulations that could skew the data.

1.2.3. To process the data, obtain the start times of each recording session and convert from 'datetime' variables (MM/DD/YYYY HH:MM:SS.SS) to seconds. None of the sessions occurred across two days which allowed the MM/DD/YYYY portion to be ignored during these calculations. Acquire the start time of the game of interest from the timing table to locate each game session within the electrocardiogram (ECG) file; this time was converted to seconds after it had been extracted from the timing file. The timing file contained start times for each phase of the game as well as the end of the recovery period (**Table 2**).

1.2.4. Calculate the rest period as the 5 min prior to the game start and the Recovery Phase as the 5 min after the end of the Cooldown Phase. Once these times were obtained, obtain the location (S) of the game phase of interest within the ECG file through the following equation:

$$S = \text{round}\left(\frac{(\text{Phase}(h)*3600)+(\text{Phase}(mi))*60+\text{Phase}(s)-\text{Start}}{1/\text{Frequency}}\right) \quad (1)$$

where Phase is set to either Rest, Warmup, Conditioning 1, Conditioning 2, Cooldown, or Recovery; the time was divided by 1/Frequency to account for the ECG sample rate. The HR monitor had a sampling rate of 250 Hz and therefore contained a measure every 4 ms.

1.2.4.1. Change this number by altering the sampling rate with the first prompt from the *Peak_Detection.m* program to account for the use of alternate recording devices. Choose which 5 min segment to work with while running the peak detection program. This was done via a prompt to the user. Set the end time to 5 min after the start time and take the frequency of the recording device into consideration.

1.2.5. Once the 5 min section had been chosen, calculate a threshold for peak-detection based upon the average and standard deviation of the waveform.

1.2.5.1. Set the threshold as $\min H = \bar{x} + (0.5 * \sigma)$ but this can be increased in the program if the data are uniform to reduce false-positive detection from T peaks which are higher than their corresponding R peaks. Examples of these false positives can be seen in **Figure 1**.

1.2.5.2. Along with a minimum height for the R peak, assign a minimum distance between peaks to minimize the detection of incorrect peaks around the desired R. Set this value to 75 which corresponded to 0.3 s between peaks or 200 beats per min (bpm) (this value changes with frequency). The value of 200 bpm is higher than any HR achieved by the subjects in this study and can be changed based on the population being studied.

1.2.6. Once the threshold was calculated, let the program run through the waveform and attempt to discern all the R's for RR interval and HRV calculations. Generate a preliminary plot so that the user could review it for irregularities such as those shown in **Figure 1** or **Figure 2**.

1.2.6.1. Correct these irregularities manually by editing the Detection variable which contains the microvolt (μV) reading of the peak in column 1 and the location in the current game session (s/0.004) in the second column. In most cases the proper R peaks can easily be found by zooming into the problem location as seen in **Figure 1**. Many data sessions are fairly uniform as shown in **Figure 3** and will therefore only require a few corrections. Some cases, however are fairly messy and require more time to review and obtain proper R locations.

1.2.6.2. If the fluctuations in the waveform make it excessively difficult to properly locate a peak, ignore small segments ~1-2 s and attribute to ectopic beats which are not used in HRV calculations¹².

1.2.7. After the R's have been located, run the *HRV_Measures* program. Calculate RR intervals first as they are the basis of the HRV measures used in this study¹².

1.2.7.1. Obtain a matrix of intervals and ignore any interval greater than 1.5 s (40 bpm) as it was due to the aforementioned ectopic beats being removed from the calculations. Save these RR intervals for further calculations and verification of data. Use these intervals to calculate the Root Mean Square of the Successive Differences (RMSSD) with the following equation:

$$\text{RMSSD} = \sqrt{\frac{1}{N-1} \left(\sum_{i=1}^{N-1} ((R-R)_{i+1} - (R-R)_i)^2 \right)} \quad (2)$$

Where N = Number of RR Intervals $(R-R)_i$ = Interval between neighboring QRS Peaks $(R-R)_{i+1}$ = Interval between subsequent set of peaks

1.2.8. Choose this variable as it has been shown to be efficacious on intervals ranging from 1 min to 24 h in length^{13,14,15,16,17} and can therefore be used to assess these 5 min intervals in the game phases. Along with RMSSD, obtain the Standard Deviation of NN intervals to measure changes in HR throughout the phase^{14,16,18}.

1.2.9. Use the RR intervals to calculate NN50, the number of intervals that differ from the previous interval by more than 50 ms¹² which has also been used on intervals ranging from one min to 24 h^{16,17,19,20,21}.

1.2.9.1. Calculate the NN50 variable via a simple count function that checked whether or not the difference between consecutive RR interval lengths was greater than 50 ms. Once NN50 was obtained in this manner, divide by the total number of intervals to calculate pNN50 which is the percentage of intervals that differ by more than 50 ms. This calculation allowed the measured data to be compared across subjects, games, and even sessions of varying lengths as it is a unit-less variable^{13,14,16,17}.

1.2.10. Calculate mean RR interval length for each phase and subject as a separate HRV measure^{16,17,19,22,23,24}. Use this measure to calculate Average HR by dividing the mean RR interval by 60 s. Both of these measures are easily comparable across game sessions to observe the trend of the subject's activity^{16,17,19,22,23,24}.

1.2.11. Once these measures were calculated, calculate the Low Frequency and High Frequency Power Spectral Density (PSD) for both the raw ECG of the 5-min interval and the RR interval matrix by obtaining PSD from Fast-Fourier transforms^{13,14,17,19,25}. All these data were then stored in a table, an example of which is shown in **Table 4**.

2. Acquire ECG Data from the Patient

2.1. Prepare the HR monitor chest strap and Bluetooth module for application to the subject.

2.1.1. Ensure that the Bluetooth module has been fully charged (3 h) using the charge cradle.

2.1.2. Plug the module into the data computer via the charge cradle and open the config tool. Enter a name for logging purposes.

2.1.3. Select the HR device, click the **Time** tab and select **Set Date/Time** to sync the module to the correct time and date. The device can now be removed from the charge cradle.

2.1.4. Moisten the conductive areas (beige) on the HR monitor chest strap by placing a hand in water and rubbing the conductive areas.

2.1.5. Place the HR monitor Bluetooth module into the chest strap with the conductive surfaces of the module lined up with those of the chest strap: it will click into place.

2.1.6. Press and hold the button on the module until the lights flash. The module is now on and recording.

2.1.7. Apply the HR monitor chest strap (with Bluetooth module) to the player with the module aligned with the left mid-axillary line and the strap just under the pectoral muscles. Once properly positioned, tighten the device so that it will not move during the session but is not uncomfortable for the player.

2.2. Acquire a signal and view the live feed.

2.2.1. Plug the connector into the USB port of computer that will be used to view the data.

2.2.2. Open the **Live View** program and enter **Setup Mode** by clicking the icon with the wrench and screwdriver.

2.2.3. Choose a player from the list if appropriate or add a new subject with the **New** button in the bottom left corner of the screen.

2.2.4. Enter Subject information as desired for identification purposes (name, age, gender, height, weight).

2.2.5. Click on the **Hardware** tab and select the current subject.

2.2.6. Click **Assign** in the bottom of the tab and select the current device (listed as 01 if no other devices are present). Then click assign in the pop-up box.

2.2.7. Click on the **Team** tab. Highlight the subject and then click the right arrow button to place the player on **Team A**.

2.2.8. Click on the **Deployment** tab and then move the newly created team to the first tab.

2.2.9. Open the **Live Mode** tab by clicking the blue **Wi-Fi** symbol in the top left corner.

2.2.10. Use the **Live Mode** tab to monitor HR, respiratory rate, and posture of the subject in real time.

NOTE: Signal strength, battery power, and confidence of the measures can also be viewed.

2.2.11. Record accurate timing (MM/DD/YYYY HH:MM:SS) of the start and end of each session and phase for processing.

2.3. Download the ECG Data from the HR monitor.

2.3.1. Remove the strap from the player at the end of the session and remove the Bluetooth Module from the chest strap.

2.3.2. Place the module in the charge cradle and plug it into a computer with the software program installed.

2.3.3. Open the log.

2.3.4. Select the device from the dropdown menu. All sessions currently on the device are displayed with dates and times.

2.3.5. Uncheck the box that says **Use Default Save Location** and chose a new save location.

2.3.6. Click **Save**. A progress bar will then appear. Saving may take up to an hour depending on the length of the session.

2.3.7. Rename the date, once it has been saved.

3. Data Analysis and Calculation of Heart Rate Variability Measures

3.1. Prepare files for processing.

3.1.1. Name ECG files as 'KOLLECT_Subject#_AVG4' (e.g., KOLLECT_01_AVG4.csv').

3.1.2. Generate a timing table in comma separated variable (.csv) format to draw timing data from during data processing. See **Table 1** for an example of the correct format.

3.1.3. Import the Date-time data from the .csv file and right click on the name of the newly created variable and change it to '*Timing.mat*'.

3.2. Preliminary R peak detection.

3.2.1. Open and run ***Peak_Detection.m***.

3.2.2. Enter the frequency of ECG recording device when prompted by the program.

3.2.3. Enter the player number for the data to be analyzed when prompted.

NOTE: Some players did not complete active video game 4 (AVG4) and therefore only players 1-10 are used for this study. Other numbers will provide an error message.

3.2.4. Enter the number of the game to be analyzed (1, 2, or 3) when prompted.

3.2.5. Enter the phase to be analyzed (Rest, Warmup (WU), Conditioning (Con), Rest, or Recovery).

3.2.5.1. Enter an offset in minutes if desired, or enter **0** for no offset.

3.2.6. Select the magnifying tool and select an area of the plot that is output to create a window with a width of approximately 2000 (s/0.004) and a height that will show the full waveform as shown in **Figure 3**. Zoom in or out if the window is not easily inspected visually.

3.2.7. Visually inspect the graph to evaluate if the peaks detected are correctly labeled. See **Figure 1** for example of incorrectly detected and missed peaks caused by irregular ECG data (**Figure 2**).

3.3. Peak Correction

3.3.1. Correct the incorrectly detected or missing peaks by locating the **Detection** variable and double clicking in the workspace.

3.3.2. Utilize the **Data Cursor** tool on the plot of the ECG waveform to obtain the x and y coordinates of the incorrect peak; X (time*frequency) is the first column in **Detection.mat** and Y (Voltage) is the second column (**Figure 3**).

3.3.2.1. Right click the text box that appears and click **Select Cursor Update Function**.

3.3.2.2. Select **TooltipUpdate.m** from the folder containing the files used for this analysis. This will allow the tooltip to display more exact values.

3.3.3. If the point is a false positive, remove it from the array by clicking on its row in the **Detection.mat** variable and pressing **Control** and the **Minus** key. An example of false positive detection can be seen in **Figure 3**.

3.3.4. Edit incorrectly marked peaks that are adjacent to unmarked peaks, as shown by the two T peaks marked as R in **Figure 1**, by changing their values to match that of the unmarked peak.

3.3.5. Obtain the value of the missed peak can be obtained with the **Data Cursor** tool.

3.3.6. Add additional rows to **Detection.mat** using control and the plus key for peaks missed due to low voltage levels.

3.3.7. Enter the values in numerical order to avoid negative values during the calculation process (i.e., add the peak located at 11000 between the peaks at 10908 and 11167) (**Figure 5**).

3.3.8. Ensure that values are entered correctly before continuing through the full session as numbers are occasionally clipped off when entered.

3.3.9. Repeat step 2.3 until all peaks have been checked and/or corrected.

NOTE: Some files have limited variability in waveform amplitude and are quicker to check, as seen in **Figure 4** while others are more variable and may require closer zoom to accurately locate peaks during visual inspection.

3.4. Obtain HRV measure calculations.

3.4.1. Save the original plot generated from *Peak_Detection.m* for later reference.

3.4.2. Run *HRV_Measures.m* to generate the correctly labeled plot. A sample of corrected data is shown in **Figure 6**.

3.4.2.1. Change the plot title by using **Insert | Title** on the plot window and changing it to the desired title.

3.4.2.2. Check the window for output, the program will notify the user of the location incorrectly entered data if any exists.

3.4.3. Save the variable named interval.

3.4.4. Open the variable entitled HRV from the **Workspace** window to view Mean RR (ms), Average HR (bpm), RMSSD (ms), SDNN (ms), NN50 (count), pNN50 (%), low frequency (LF)/ high frequency (HF) (ECG), LF/HF RR, Low Frequency Power RR, and High Frequency Power (RR)). Save the h values of these variable to a table such as the one shown in **Table 4**.

3.5. Repeat Sections 3.2 – 3.4 for all other segments, sessions, and subjects that need analysis.

REPRESENTATIVE RESULTS:

This method provides data for use in analyzing the effect that a newly developed method has on the subject's Heart Rate Variability (HRV). It does this by locating the R portion of the QRS waveform of a subject's ECG data, as shown in **Figure 6**, and by calculating various HRV values from it. If the HR monitor is making proper contact with the subject, the data will be uniform, substantially reducing the need for corrections (as seen in **Figure 4**).

Thresholds should be set to handle messy and irregular data as depicted in **Figure 1** and **Figure**

2. If the data are sufficiently variable due to momentary changes in the HR monitor skin contact, the initial analysis may incorrectly label peaks as shown in **Figure 3**. This error can be rectified by manually correcting values or entering extra data points as explained in Section 3 of the protocol. Altering the threshold levels and minimum time between peaks can also help to clean up the detection values and produce an adjusted plot like **Figure 6** from **Figure 5**.

Once the data have been obtained and analyzed for discrepancies, they can be used to calculate HRV values for statistical analysis. The analysis of ECG data can be used to quantify observations made during sessions for evaluation purposes.

Figure 1. Representative graph of continuous HR (y-axis) in μV across time (x-axis in s) for subject one game 3 during the warmup session representing ‘messy’ data. Messy data: In this section R peaks are smaller than the T portion of the waveform. This can cause issues with peak detection.

Figure 2. An example of some electrocardiogram (ECG) irregular waveform patterns. Irregular Waveform Patterns: Changes in contact with the subject due to movement can cause voltage variations reducing uniformity of the waveform.

Figure 3. An example of an electrocardiogram (ECG) output with an incorrectly labeled peak HR Incorrectly Labeled Peak. Near the top of the figure a spike in voltage causes part of the waveform to be detected as matching the R pattern. It can also cause nearby R patterns to be ignored due to proximity such as the one highlighted at (9924, 2074).

Figure 4. Representative graph of continuous HR (y-axis) in μV across time (x-axis in s) clean electrocardiogram (ECG) waveform. Clean Waveform: An example of a section of uniform ECG data with a relatively even waveform and voltage level.

Figure 5. Representative graph of continuous HR (y-axis) in μV across time (x-axis in s) of a raw electrocardiogram (ECG) prior to cleaning. Data Prior to Cleaning: A 30 sec segment of ECG data from Subject 01 Game 3 during the conditioning phase is shown. Some peaks have been missed and some are incorrectly labeled due to high voltage variability.

Figure 6. Representative graph of continuous HR (y-axis) in μV across time (x-axis in s) of a raw electrocardiogram (ECG) after cleaning. Data Post cleaning: The same 30 sec of ECG data from Subject 01 Game 3 after it has been properly labeled as described in Section 3 of the protocol.

Table 1. Active video game (AVG) game phases. KEY: Target heart rate (THR); NA (Not applicable).

Table 2. Timing File KEY: AVG = Active video game

Table 3. Heart Rate Variability (HRV) Data for Subject 03 Game 01

Table 4. Descriptive Statistics of Heart Rate Variability Measures for Various Phases of Exercise for Each Game

Table 5. Patient demographics

DISCUSSION:

Ten youth with CP participated in this study (mean + SD) [age (yrs) = 15.53 ± 3.57 ; height (cm) 154.8 ± 12.6 ; weight (kg) 50.69 ± 11.1 ; body mass index (BMI) 50.46 ± 29.2 ; mHR 9 bpm) = 186.8 ± 12.4]. Please see **Table 5** for patient demographics.

There are some considerations for use of HR monitors and the associated measures of HR and HRV which relate to modifications and troubleshooting. Two issues that are apparent, regardless of the technology employed to acquire the data are: 1) motion artifacts and 2) ectopic beats. The problems that arise from motion artifacts and ectopic beats are typically addressed through post-processing activities subsequent to the acquisition of the RR interval^{12,13,18,22,26}. Troubleshooting post-processing manipulations require consideration of the temporal fluctuations in HR which highlight respiratory sinus arrhythmias as well as calculation of the normalized HRV values so differentiations can be made between physiologically and mathematically mediated changes in HRV^{13,27,29}.

Limitations in HRV measurements were initially identified with the application of spectral analysis techniques (i.e., frequency domain measures)^{13,27,29}. There are physiological considerations which include the respiratory sinus arrhythmias, cardiovascular drift, hydration status and environmental factors (e.g., temperature, heat, cold, altitude) that are associated with day-to-day variations in HR^{27,29}. Mathematical considerations involve time domain measures (e.g., SDNN, r-MSSD, pNN-50 index) as well as the recent inclusion of non-linear dynamic analysis techniques^{13,27,29}. To correctly interpret the various HRV measures we need to consider whether the body is in a state of rest or stress. Typically we expect parasympathetic influences when the body is rested which increased variability in the responses and results in higher HRV while during stress we expect sympathetic influences which reduce variability and have lower HRV measures. The limitations in HRV measurements can influence the accuracy autonomic balance hypothesis is associated with the LF/HF ratio. This hypothesis assumes that the sympathetic nervous system and parasympathetic nervous system are in competition to regulate SA node firing. The authors note tha the LF/HR ratio needs to be interpreted with caution while noting the context of obtaining information as well as reviewing the LF and HF values. Concerning the application of LF/HF ratio to AVG games in short-term episodes of HR measurements and HRV, a high LF/HF ratio may indicate higher sympathetic activity that may be observed when meeting a challenge that requires effort and increases the sympathetic nervous system activation³⁵.

It is important to use optimal measures to determine aerobic performance and capacity in youth with CP to examine appropriate intervention dosing and effectiveness^{6,11}. Clinical standards of care most often include measuring HR to determine intervention dosing

(intensity)^{6,11}. However the inherent variability in HR measures make it difficult to determine actual workload in aerobic training^{12,13,22,27}. Therefore, this methodology of calculating HRV from ECG data from a HR monitor provides a more accurate measure to assess intervention outcomes^{27,28}. Also, the HRV measures provide new information on the autonomic nervous system responses, adaptation and recovery during the AVG exercise^{12,13,29,34,35}. We posit that application of HRV measures during short duration exercise may provide information on the improvement of the physiological systems based on work by Kerppers and colleagues with a short duration³².

Noted here are the important applications we have made relative to the existing applications of HR monitoring and HRV measures during exercise performance. This methodology allows the user to extract RR intervals and HRV measures from ECG waveforms during gaming physical activities in youth with CP. The method is currently tailored towards AVG sessions in a specific game but could easily be adapted to other protocols and ECG devices for future experiments. In cases where the data are uniform and the ECG recording device is well fitted to the subject, this protocol will allow for quick data processing with minimal input from the user. However, in the case of non-uniform data with large variances in signal amplitude the protocol will require user input to correctly label missed peaks and to remove false positives from the data set. In the future this method may be improved with a more robust detection method to reduce user aid for peak detection and correction (e.g., non-linear dynamic analysis techniques²⁹).

Throughout execution of the protocol, it is essential that the following critical steps are performed. It is important to ensure a high level of signal confidence throughout data collection sessions to reduce the processing and peak correction time required. This can be improved by ensuring that the ECG recording device is making proper contact with the subject prior to each session. It is also important to keep the conductive contacts moist during the sessions which can be done by rewetting the recorder prior to each session. As well, after the data are collected, post-processing activities need to address the methodological considerations with time domain measures, frequency domain measures, non-linear dynamic analyses as well as calculating normalized HRV values to distinguish between physiologically derived and mathematically mediated changes in HRV^{12,13,29}.

Considerations for future work include application of HRV measurements for children and adults involved in physically challenging activities of different intensities and body positions^{6,7,8,9,10,17,23,26,29}, cognitively challenging games and mental workload^{24,25,26,27}, virtual and simulation type experiences, assessment of overtraining^{23,31}, quality of sleep assessments^{13,26,27,31}, chronic fatigue, physical exhaustion and combat readiness³¹ as well as the vagal connection between HR and the brain regarding prosocial behavior³⁰.

ACKNOWLEDGMENTS:

The authors thank the participants and their families for their time and effort expended for participation in the study. As well, the authors acknowledge Dr. Yichuan Liu and Dr. Hasan Ayaz for their assistance with the timing calculation of the HR monitoring and Dr. Paul Diefenbach for development of the KOLLECT Active Video Gaming software. Funding for this work was

provided by Coulter Foundation Grants #00006143 (O'Neil; Diefenbach, Pls) and #00008819 (O'Neil; Diefenbach, Pls).

DISCLOSURES:

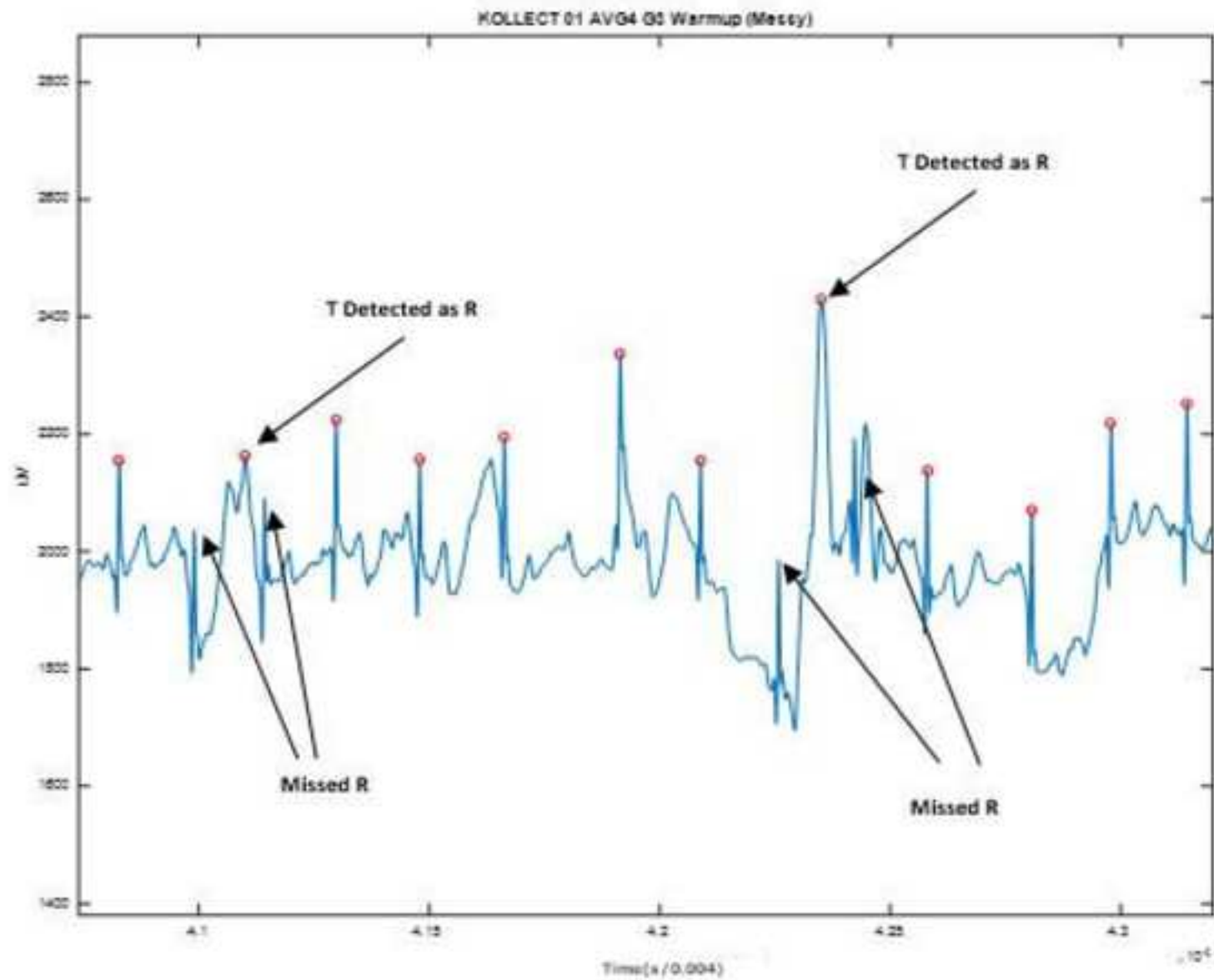
At this time, the authors (CL and PAS) have nothing to disclose. Dr. O'Neil is a co-founder of enAbleGames, LLC and Kollect is one of the games offered by this web-based company. enAbleGames is in game development phase and is not a public company at this time (www.enAbleGames.com).

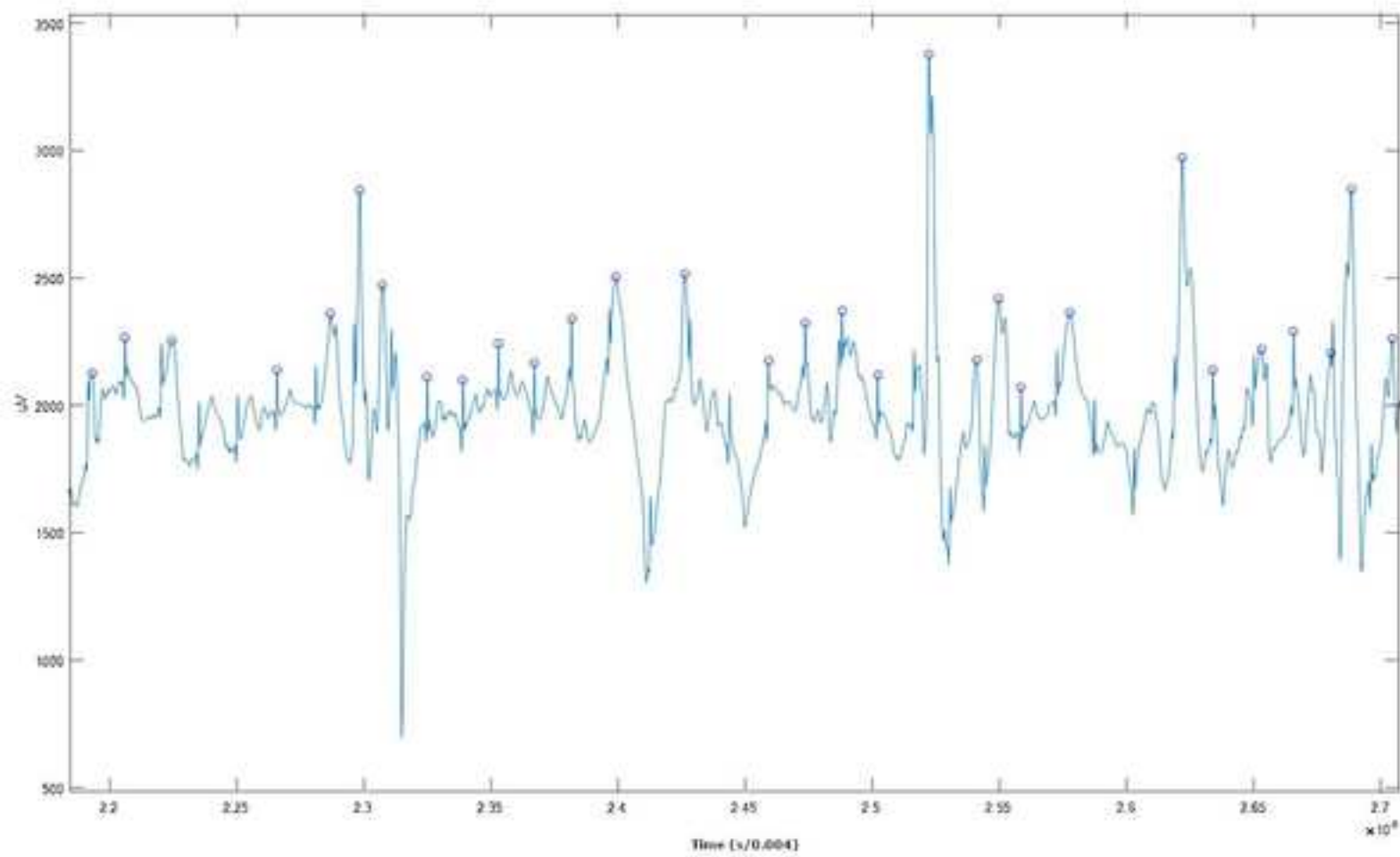
REFERENCES

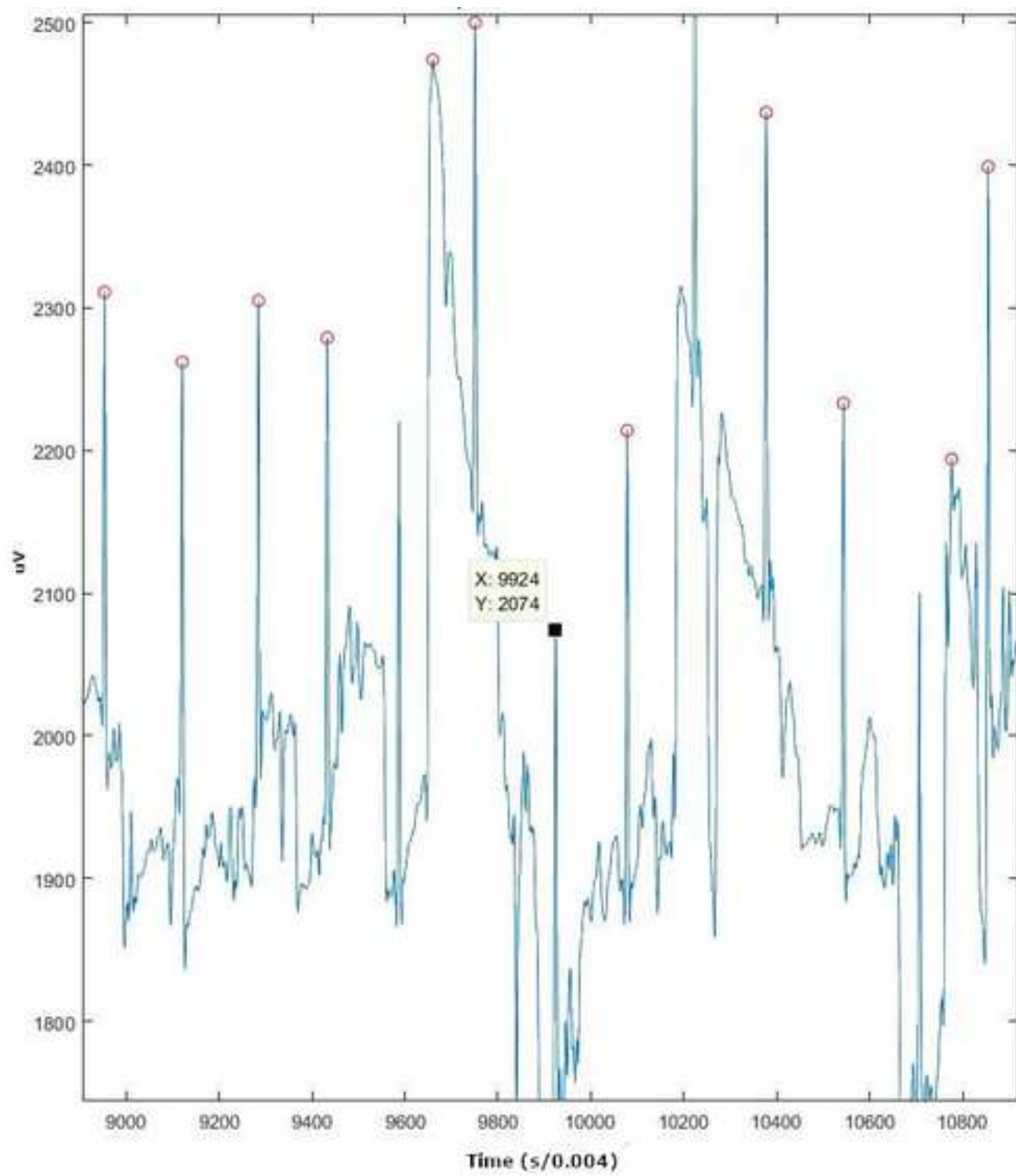
1. Winter, S., Autry, A., Boyle, C., Yeargin-Allsopp, M. Trends in the prevalence of cerebral palsy in a population-based study. *Pediatrics*. **110** (6), 1220-1225 (2002).
2. Fowler, E. et al. Promotion of physical fitness and prevention of secondary conditions for children with cerebral palsy: Section on Pediatrics Research Summit Proceedings. *Physical Therapy*. **87** (11), 1495-1510, DOI: 10.2522/ptj.20060116 (2007).
3. Rosenbaum, P., Paneth, N., Leviton, A., Goldstein, M., Bax, M. A report: The definition and classification of cerebral palsy: April 2006. *Developmental Medicine & Child Neurology*. **49** (s109), 8-14, DOI: 10.1111/j.1469.8749.2007.5b12610.x (2007).
4. Hanna, S. et al. Stability and decline in gross motor function among children and youth with cerebral palsy aged 2 to 21 years. *Developmental Medicine & Child Neurology*. **51**(4):295-302, DOI:10/1111/j.1469-8749.2008.03196.x (2009).
5. Rimmer, J., Rowland, J. Health promotion for people with disabilities: Implications for empowering the person and promoting disability-friendly environments. *American Journal of Lifestyle Medicine*. **2**(5), 409-420, DOI: 10.1177/1559827608317397 (2008).
6. Feehan K. et al. Factors influencing physical activity in children and youth with special health care needs: A pilot study. *International Journal of Pediatrics*. Article ID 583249. DOI:10.1155/2012/583249 (2012).
7. Fehlings, D., Switzer, L., Findlay, B., Knights, S. Interactive computer play as motor therapy for individuals with cerebral palsy. *Seminars in Pediatric Neurology*. **20** (2), 127-138 DOI:10.1016/j.spen.2013.06.003 (2013).
8. Sandlund, M., Dock, K., Hager, C., Waterworth, E. Motion interactive video games in home training for children with cerebral palsy: parents' perceptions. *Disability & Rehabilitation*. **34** (11), 925-933, DOI: 10.3109/09638288.2011.626489 (2012).
9. Howcroft, J. et al. Active video game play in children with cerebral palsy: Potential for physical activity promotion and rehabilitation therapies. *Archives of Physical Medicine and Rehabilitation*. **93** (8), 1448-1456, DOI: 10.1016/j.apmr.2012.02.033 (2012).
10. Bilde, P., Kliim-Due, M., Rasmussen, B., Petersen, L., Petersen, T., Nielsen, J. Individualized, home-based interactive training of cerebral palsy children delivered through the Internet. *BMC Neurology*. **11**, 32, DOI: 10.118/1471-2377-11-32 (2011).
11. Kolobe, T. et al. Research Summitt III proceedings on dosing in children with an injured brain or cerebral palsy. *Physical Therapy*. **94** (7), 907-920, DOI: 10.2522/ptj.20130024 (2014).
12. Schipke, J., Pelzer, M., Arnold, G. Effect of respiration rate on short-term heart rate variability. *Journal of Clinical and Basic Cardiology* **2** (1), 92-95, DOI:10.1161/01.CIR.93.5.1043 (1999).

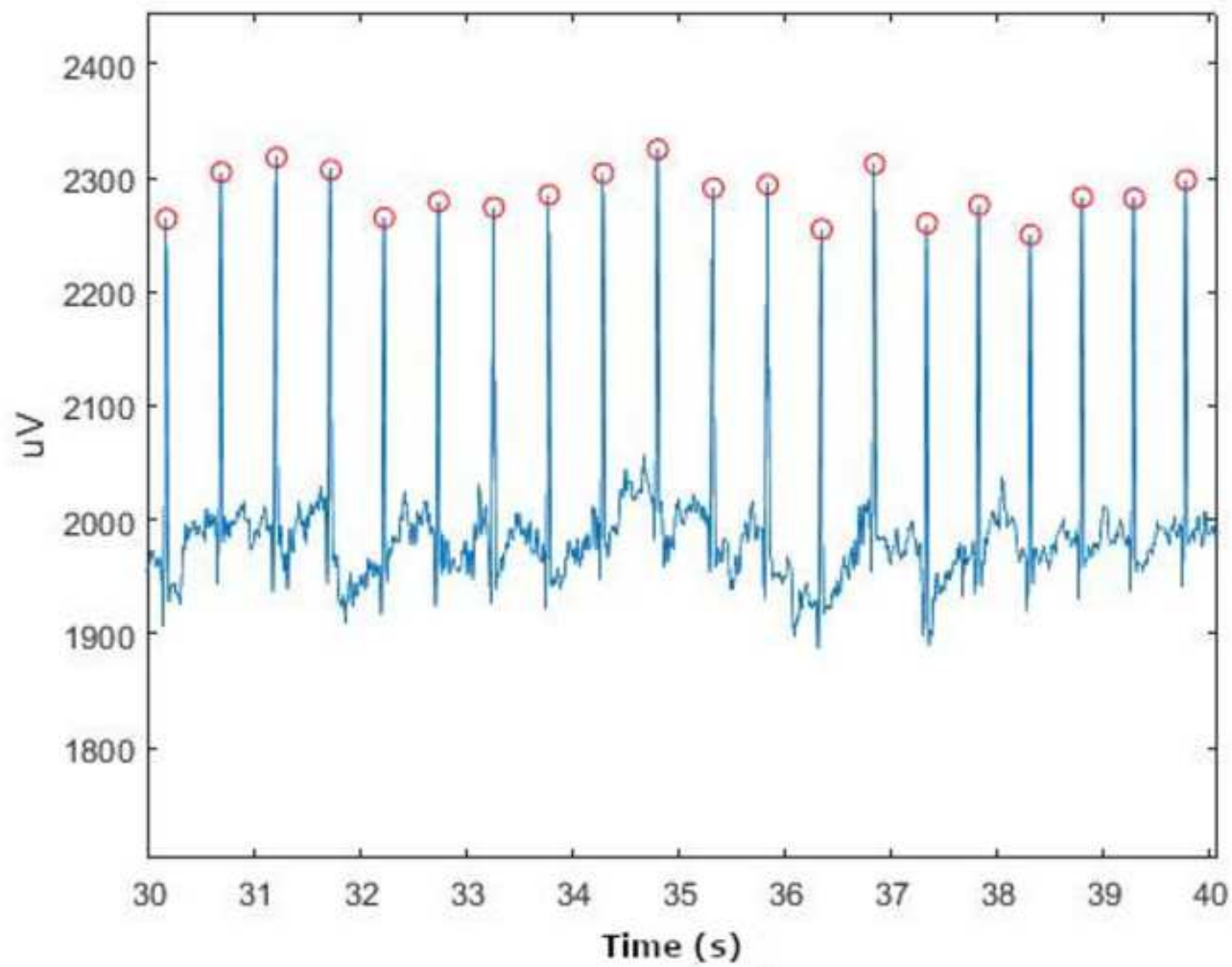
13. Ernst, G. Heart rate variability. *Heart Rate Variability*, 1–336, DOI:10.1007/978-1-4471-4309-3 (2014).
14. Francis, J. et al. Association between symptoms of depression and anxiety with heart rate variability in patients with implantable cardioverter defibrillators. *Psychosomatic Medicine* **71** (8), 821–827, DOI:10.1097/PSY.0b01 (2009).
15. Mendes, R. et al. Is applying the same exercise-based inpatient program to normal and reduced left ventricular function patients the best strategy after coronary surgery? A focus on autonomic cardiac response. *Disability and Rehabilitation: An International, Multidisciplinary Journal* **36** (2), 155–162, DOI:10.3109/09638288.2013.782362 (2014).
16. Muralikrishnan, K., Balakrishnan, B., Balasubramanian, K., Visnegarawla, F. Measurement of the effect of Isha Yoga on cardiac autonomic nervous system using short-term heart rate variability. *Journal of Ayurveda and Integrative Medicine* **33** (2), 279–283, DOI:10.4103/0975 (2012).
17. Yadav, R.K., Gupta, R., Deepak, K.K. A pilot study on short term heart rate variability & its correlation with disease activity in Indian patients with rheumatoid arthritis. *Indian Journal of Medical Research* **136** (4), 593–598 (2012).
18. Thuraisingham, R. A. Preprocessing RR interval time series for heart rate variability analysis and estimates of standard deviation of RR intervals. *Computer Methods and Programs in Biomedicine* **83** (1), 78–82, DOI:10.1016/j.cmpb.2006.05.002 (2006).
19. Alamili, M., Rosenberg, J., Gögenur, I. Day-night variation in heart rate variability changes induced by endotoxaemia in healthy volunteers. *Acta Anaesthesiologica Scandinavica* **59** (4), 457–464, DOI:10.1111/aas.12472 (2015).
20. Pal, G. et al. Preference for salt contributes to sympathovagal imbalance in the genesis of prehypertension. *European Journal of Clinical Nutrition* **67** (6), 586–91, DOI:10.1038/ejcn.2013.64 (2013).
21. Telles, S., Raghavendra, B. R., Naveen, K. V., Manjunath, N. K., Kumar, S. Subramanya, P. Changes in autonomic variables following two meditative states described in yoga texts. *Journal of Alternative and Complementary Medicine* **19** (1), 35–42, DOI:10.1089/acm.2011.0282 (2013).
22. Kičmerová, D. Methods for Detection and Classification in ECG Analysis. Doctoral thesis. Department of Biomedical Engineering. BRNO University of Technology. Czech Republic. (2009)
23. Murai, K., Hayashi, Y. Evaluation of mental workload for ship handling using physiological indices. *2009 Second International Conference on Emerging Trends in Engineering & Technology* (October), 604–608, DOI:10.1109/ICETET.2009.91 (2009).
24. Taelman, J., Vandeput, S., Spaepen, A., Van Huffel, S. Influence of mental stress on heart rate and heart rate variability. *Heart* **29** (1), 1366–1369, DOI:10.1007/978-3-540-89208-3_324 (2009).
25. Durantin, G., Gagnon, J.-F., Tremblay, S., Dehais, F. Using near infrared spectroscopy and heart rate variability to detect mental overload. *Behavioural Brain Research* **259**, 16–23, DOI:10.1016/j.bbr.2013.10.042 (2014).
26. Buchheit, M. Monitoring training status with HR measures: Do all roads lead to Rome? *Frontiers in Physiology* **5**, DOI: 10.3389/fphys.2014.00073 (2014).
27. Achten, J., Jeukendrup, A. Heart rate monitoring: Applications and limitations. *Sports Medicine* **33**(8), 517-538. DOI: 10.2165/00007256-200333070-00004 (2012).

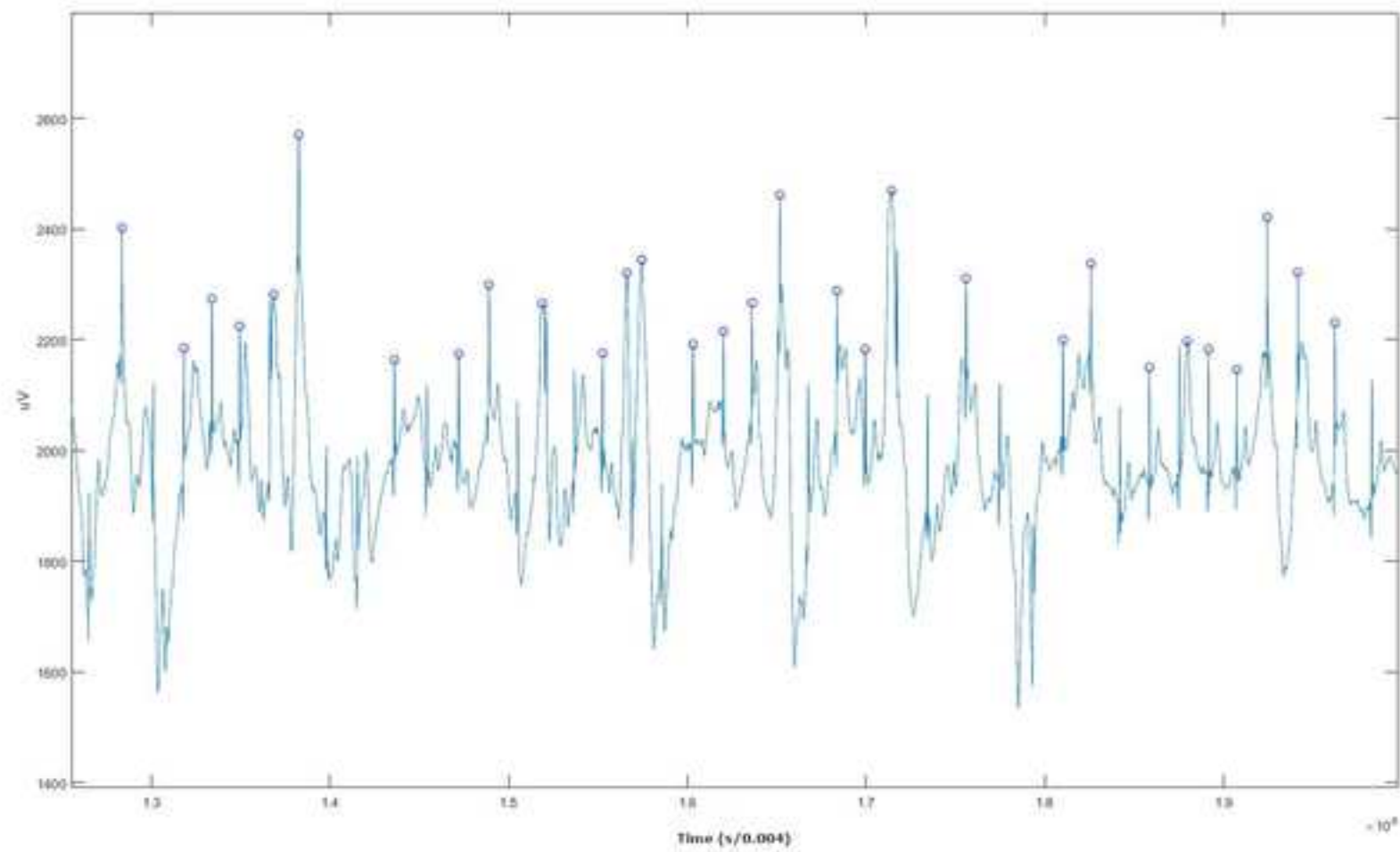
28. Amichai, T., Katz-Leurer, M. Heart rate variability with cerebral palsy: Review of literature and meta-analysis. *NeuroRehabilitation* **35**, 113-122. DOI: 10.3233/NRE-141097 (2014).
29. Billman, G, Haikuri H., Sacha, J., Trimmel, K. An introduction to heart rate variability: Methodological considerations and clinical applications. *Frontiers in Physiology* **6**, DOI: 10.3389/fphys.2015.00055 (2015).
30. Beffara, B., Bret, A., Vermeulen, N., Mermillod, M. Resting high frequency heart rate variability selectively predicts cooperative behavior. *Physiology & Behavior* **164**,417-428. DOI: 10.1016/j.physbeh.2016.06.011 (2016).
31. Fogt, D., Cooper, P., Freeman, C., Kalns, J., Cooke, W. Heart rate variability to assess combat readiness. *Military Medicine*, **174**, 491-495. DOI: 107205/MILMED-0-02-6808 (2009).
32. Kerppers, I.L., Arisawa, E. A. L., Oliveira, L.V.F., Sampaio, L.M.M., Oliverira, C. S. Heart rate variability in individual with cerebral palsy. *Archives of Medical Science*,**5**, 45-50. (2009).
33. Giggins, O.M., Persson, U. M., Caulfield, B. Biofeedback in Rehabilitation. *Journal of Neuroengineering and Rehabilitation* **10**, DOI: doi.org/10.1186/1743-0003-10-60 (2013).
34. Shaffer, F., Ginsberg, J.P. An overview of heart rate variability metrics and norms. *Frontiers in Public Health* **5**, 258. DOI: 10.3389/fpubh.2017.00258 (2017).
35. Shaffer, F., McCarty, R., Zeir, C.L. A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. *Frontiers in Psychology* **5**, 1040. DOI: 10.3389/fpsyg.2014.01040 (2014).











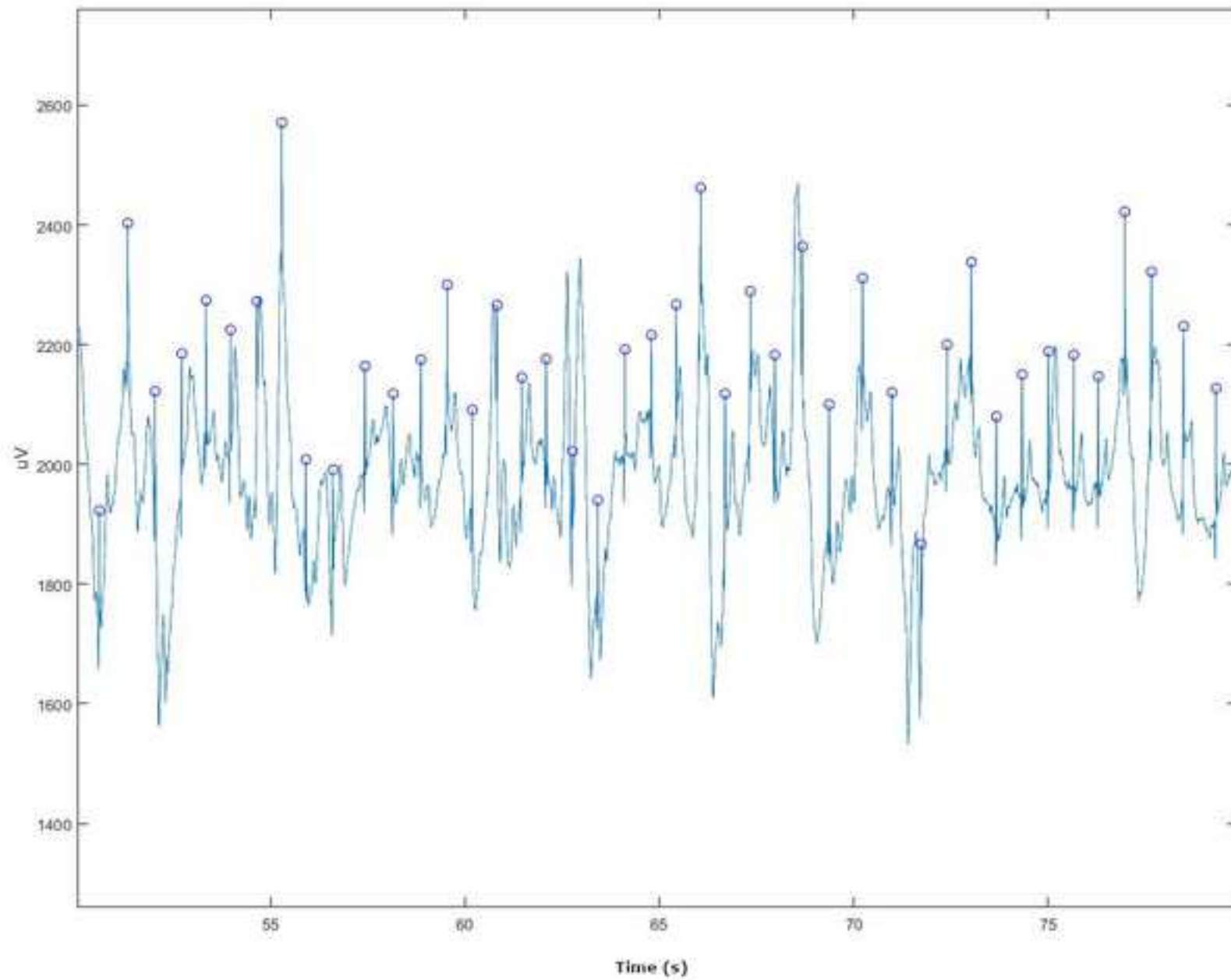


Table 1. Active Video Game (AVG) Game Phases			
Phase	Time	THR Zone	Game Features
Resting	5 min	Baseline rest	NA
Warm-up	5 min	40-60% mHR	4 objects + 4 hazards; slower speed
Conditioning	10 min	60-80% mHR	8 objects + 0 hazards; faster speed
Cool-down	5 min	40-60% mHR	4 objects + 4 hazards; slower speed
Recovery	5 min	Baseline rest	NA

KEY: THR = Target Heart Rate; NA = Not applicable

Table 2. Timing File					
Subject	AVG	Game	Warmup Start (MM/DD/YYYY) (HH:MM:SS)	Conditioning Start (MM/DD/YYYY) (HH:MM:SS)	Cooldown Start (MM/DD/YYYY) (HH:MM:SS)
1	4	1	11/25/2015	11/25/2015	11/25/2015
1	4	1	16:33:53	16:39:03	16:49:04
1	4	2	11/25/2015	11/25/2015	11/25/2015
1	4	2	17:27:47	17:32:57	17:43:01
1	4	3	11/25/2015	11/25/2015	11/25/2015
1	4	3	18:25:22	18:30:33	18:40:35
2	4	1	4/10/2016	4/10/2016	4/10/2016
2	4	1	11:59:19	12:04:29	12:14:36
2	4	2	4/10/2016	4/10/2016	4/10/2016
2	4	2	12:40:25	12:45:37	12:55:44
2	4	3	4/10/2016	4/10/2016	4/10/2016
2	4	3	13:19:57	13:25:02	13:35:04
3	4	1	11/18/2015	11/18/2015	11/18/2015
3	4	1	17:08:10	17:13:20	17:23:21
3	4	2	11/18/2015	11/18/2015	11/18/2015
3	4	2	17:59:46	18:04:48	18:14:54
3	4	3	11/18/2015	11/18/2015	11/18/2015
3	4	3	18:42:03	18:47:03	18:57:04

Recovery Start

(MM/DD/YYYY)

(HH:MM:SS)

11/25/2015

16:54:09

11/25/2015

17:48:03

11/25/2015

18:45:38

4/10/2016

12:19:50

4/10/2016

13:00:53

4/10/2016

13:40:11

11/18/2015

17:28:28

11/18/2015

18:19:55

11/18/2015

19:02:02

Table 3. Heart Rate Variability (HRV) Data for Subject

ID_AVG_Game	AVNN (s)	Avg HR (bpm)	RMSSD (ms)
03_AVG4_G1_Rest	719.875	83.347	29.827
03_AVG4_G1_WU	656.373	91.411	26.52
03_AVG4_G1_Con 1 -5	557.772	107.57	20.651
03_AVG4_G1_Con 6 10	532.483	112.679	27.771
03_AVG4_G1_Con 2 - 7	538.546	111.41	20.389
03_AVG4_G1_Con 3 - 8	530.761	113.045	27.756
03_AVG4_G1_Cool	597.019	100.499	31.806
03_AVG4_G1_Recovery	665.511	90.156	42.136

AVNN = Average NN Interval; Avg HR = Average heart Rate; RMSSD = Root Mean Square Standard Deviation of NN Interval; NN50 = Number of NN Intervals > 50 ms; pNN50 = Percentage of NN Intervals > 50 ms; LF = Low Frequency Power; HF = High Frequency Power; LF/HF = Low Frequency - High Frequency Ratio; ms = milliseconds; ECG = Electrocardiogram - which contains the QRS complex; RR = Root Mean Square of the QRS complex of the ECG wave and RR is the interval between successive R peaks.

st 03 Game 1

SDNN (ms)	NN50	pNN50 (%)	LF / HF (ECG)	LF / HF (RR)	LFP (RR)	HFP (RR)
55.604	35	8.393	1.328	0.602	0.123	0.204
50.372	28	5.932	1.288	0.675	0.125	0.185
43.932	4	0.743	1.187	0.76	0.119	0.157
33.481	9	1.599	1.244	0.809	0.118	0.146
34.351	6	1.077	1.198	0.819	0.118	0.144
34.26	8	1.413	1.192	0.826	0.118	0.143
41.96	16	3.181	1.281	0.712	0.120	0.169
70.698	57	12.639	1.301	0.636	0.122	0.191

quare of Successive Differences; SDNN -
 = % of NN intervals > 50 ms; LF = Low
 quency Ratio. bpm = beats per minute; ms
 where R is a point associated with a peak
 points;

Table 4. Descriptive Statistics of Heart Rate Variability Measures For Various Phases of Exercise For Each Game.																															
Phase	Game	AVNN (ms)			Avg HR (bpm)			RMSSD (ms)			SDNN (ms)			NN50			pNN50 (%)			LF / HF (ECG)			LF / HF (RR)			LFP (RR)			HFP (RR)		
		1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3			
Rest	Mean	607.434	625.109	634.144	100.596	97.603	95.766	34.979	45.690	49.561	47.398	54.741	59.588	43.767	52.917	54.722	10.238	12.484	12.610	1.278	1.218	1.230	0.727	0.702	0.684	0.120	0.120	0.120	0.169	0.175	0.179
	SD	86.463	84.159	70.268	13.205	12.423	10.722	24.675	38.826	42.259	21.967	28.994	30.265	59.214	67.607	57.603	15.816	17.896	14.587	0.058	0.132	0.141	0.102	0.094	0.084	0.002	0.002	0.002	0.026	0.025	0.022
Warmup	Mean	621.654	633.038	643.475	97.712	95.902	93.763	33.804	47.644	47.183	44.847	51.613	55.802	44.100	51.600	56.556	10.215	12.075	12.741	1.291	1.258	1.248	0.703	0.688	0.670	0.121	0.121	0.121	0.174	0.178	0.182
	SD	75.744	74.569	49.095	11.024	10.663	7.684	23.801	33.747	30.034	19.018	22.047	20.463	65.927	71.878	58.117	17.022	18.468	13.719	0.032	0.074	0.074	0.075	0.074	0.055	0.003	0.002	0.001	0.022	0.022	0.015
Conditioning Min 1-5	Mean	566.554	588.718	601.407	107.323	103.272	100.399	28.267	45.965	58.614	37.877	49.725	57.239	33.300	40.900	40.111	7.544	9.364	8.841	1.248	1.155	1.194	0.782	0.746	0.715	0.119	0.119	0.119	0.155	0.163	0.169
	SD	74.474	76.127	50.550	12.114	11.771	8.517	23.173	33.815	70.239	14.644	20.961	42.810	64.476	70.205	50.126	16.237	18.270	12.043	0.064	0.166	0.185	0.101	0.091	0.074	0.002	0.002	0.001	0.024	0.023	0.017
Conditioning Min 6-10	Mean	543.665	571.824	582.587	111.855	106.760	103.622	26.957	53.558	48.786	32.410	48.941	50.082	22.800	40.100	31.222	5.066	9.501	6.457	1.238	1.153	1.174	0.824	0.780	0.737	0.118	0.119	0.119	0.146	0.155	0.163
	SD	72.344	86.899	47.705	12.574	13.582	8.728	23.513	73.722	46.815	17.348	42.468	33.215	48.691	75.552	41.236	11.799	20.383	8.795	0.080	0.170	0.220	0.111	0.114	0.077	0.002	0.001	0.002	0.025	0.026	0.018
Cooldown	Mean	591.029	609.573	615.464	102.845	99.638	98.282	34.369	36.347	44.513	41.925	44.110	50.601	38.000	41.900	41.444	8.653	9.673	8.978	1.296	1.192	1.196	0.739	0.711	0.701	0.120	0.120	0.120	0.164	0.171	0.173
	SD	76.179	72.048	57.180	11.587	11.465	9.676	30.433	23.829	42.068	18.842	17.672	28.022	61.898	68.714	54.599	16.052	17.307	12.365	0.060	0.155	0.153	0.087	0.087	0.081	0.002	0.002	0.001	0.023	0.022	0.020
Recovery	Mean	654.850	654.928	657.790	92.740	92.260	92.585	41.925	42.968	44.174	62.665	67.747	73.881	54.700	60.000	70.222	13.320	13.717	16.571	1.302	1.267	1.293	0.660	0.657	0.666	0.121	0.121	0.121	0.185	0.186	0.186
	SD	81.424	57.397	80.696	10.101	8.224	12.805	26.715	23.642	26.685	24.959	35.258	26.305	60.764	59.279	64.569	17.950	14.047	16.706	0.031	0.077	0.053	0.057	0.053	0.115	0.001	0.001	0.002	0.019	0.016	0.027

AVNN = Average NN Interval; Avg HR = Average heart Rate; RMSSD = Root Mean Square of Successive Differences; SDNN - Standard Deviation of NN Interval; NN50 = Number of NN Intervals > 50 ms; pNN50 = % of NN intervals > 50 ms; LF = Low Frequency Power; HF = High Frequency Power; LF/HF = Low Frequency - High Frequency Ratio
bpm = beats per minute; ms = milliseconds; ECG = Electrocardiogram - which contains the QRS complex; RR = where R is a point associated with a peak of the QRS complex of the ECG wave and RR is the intrval between successive R points;

Table 5. Patient					
ID	Age (years)	Gender	GMFCS Level	Clinical Diagnosis	Movement Disorder
1	15.83	boy	2	diplegia	dystonia
2	12.17	boy	3	diplegia	spasticity
3	16.50	boy	2	left hemiplegia	spasticity
4	16.08	boy	3	diplegia	spasticity
5	17.67	girl	2	left hemiplegia	spasticity
6	15.92	girl	2	left hemiplegia	spasticity
7	20.08	girl	2	right hemiplegia	spasticity
8	20.17	girl	3	left hemiplegia	spasticity
9	11.58	boy	2	left hemiplegia	spasticity
10	9.25	boy	3	diplegia	spasticity

KEY: GMFCS= Gross Motor Function Classification System

Ant Demographics

Dominant Side	Height (cm)	Weight (kg)	BMI (kg/m2)	BMI percentile
right	161.20	47.60	18.32	17.00
left	141.17	49.20	24.70	95.00
right	165.80	50.50	18.40	13.00
right	154.30	57.00	23.90	83.00
right	161.20	60.30	22.86	71.00
right	146.40	40.80	19.00	30.00
left	154.60	64.00	26.80	85.00
right	166.10	61.20	22.20	42.00
right	168.10	49.70	17.60	51.00
right	135.00	29.80	16.00	43.00

; **BMI**= Body Mass Index

Name of Material/ Equipment	Company	Catalog Number
BioHarness Bluetooth Module (Electronics sensor)	Zephyr	9800.0189
BioHarness Chest Strap	Zephyr	9600.0189, 9600.0190
BioHarness Charge Cradle & USB Cable	Zephyr	9600.0257
BioHarness Echo Gateway	Zephyr	9600.0254
MATLAB R2016a	Mathworks	1.7.0_.60

Comments/Description

Detects Heart Rate, Respiration Rate, Posture, and Skin Temperature.

Sizes Small XS-M, Large M-XL

Used to Transfer Data from the Module to a Computer for Analysis.

Allows for Realtime Viewing of Subject's Heart Rate.

Used for All Programming.



1 Alewife Center #200
Cambridge, MA 02140
tel. 617.945.9051
www.jove.com

ARTICLE AND VIDEO LICENSE AGREEMENT

Title of Article:

Calculating Heart Rate Variability from ECG Data from Youth with Cerebral Palsy during Active Video Game Sessions

Author(s):

Corey Landis, Andrew Finnegan, Margaret E. O'Neil, Patricia A. Shewokis

Item 1 (check one box): The Author elects to have the Materials be made available (as described at <http://www.jove.com/author>) via: ☒ Standard Access ☐ Open Access

Item 2 (check one box):

- ☒ The Author is NOT a United States government employee.
- ☐ The Author is a United States government employee and the Materials were prepared in the course of his or her duties as a United States government employee.
- ☐ The Author is a United States government employee but the Materials were NOT prepared in the course of his or her duties as a United States government employee.

ARTICLE AND VIDEO LICENSE AGREEMENT

1. Defined Terms. As used in this Article and Video License Agreement, the following terms shall have the following meanings: "**Agreement**" means this Article and Video License Agreement; "**Article**" means the article specified on the last page of this Agreement, including any associated materials such as texts, figures, tables, artwork, abstracts, or summaries contained therein; "**Author**" means the author who is a signatory to this Agreement; "**Collective Work**" means a work, such as a periodical issue, anthology or encyclopedia, in which the Materials in their entirety in unmodified form, along with a number of other contributions, constituting separate and independent works in themselves, are assembled into a collective whole; "**CRC License**" means the Creative Commons Attribution-Non Commercial-No Derivs 3.0 Unported Agreement, the terms and conditions of which can be found at: <http://creativecommons.org/licenses/by-nc-nd/3.0/legalcode>; "**Derivative Work**" means a work based upon the Materials or upon the Materials and other pre-existing works, such as a translation, musical arrangement, dramatization, fictionalization, motion picture version, sound recording, art reproduction, abridgment, condensation, or any other form in which the Materials may be recast, transformed, or adapted; "**Institution**" means the institution, listed on the last page of this Agreement, by which the Author was employed at the time of the creation of the Materials; "**JoVE**" means MyJoVE Corporation, a Massachusetts corporation and the publisher of *The Journal of Visualized Experiments*; "**Materials**" means the Article and / or the Video; "**Parties**" means the Author and JoVE; "**Video**" means any video(s) made by the Author, alone or in conjunction with any other parties, or by JoVE or its affiliates or agents, individually or in collaboration with the Author or any other parties, incorporating all or any portion of the Article, and in which the Author may or may not appear.

2. Background. The Author, who is the author of the Article, in order to ensure the dissemination and protection of the Article, desires to have the JoVE publish the Article and create and transmit videos based on the Article. In furtherance of such goals, the Parties desire to memorialize in this Agreement the respective rights of each Party in and to the Article and the Video.

3. Grant of Rights in Article. In consideration of JoVE agreeing to publish the Article, the Author hereby grants to JoVE, subject to **Sections 4 and 7** below, the exclusive, royalty-free, perpetual (for the full term of copyright in the Article, including any extensions thereto) license (a) to publish, reproduce, distribute, display and store the Article in all forms, formats and media whether now known or hereafter developed (including without limitation in print, digital and electronic form) throughout the world, (b) to translate the Article into other languages, create adaptations, summaries or extracts of the Article or other Derivative Works (including, without limitation, the Video) or Collective Works based on all or any portion of the Article and exercise all of the rights set forth in (a) above in such translations, adaptations, summaries, extracts, Derivative Works or Collective Works and (c) to license others to do any or all of the above. The foregoing rights may be exercised in all media and formats, whether now known or hereafter devised, and include the right to make such modifications as are technically necessary to exercise the rights in other media and formats. If the "Open Access" box has been checked in **Item 1** above, JoVE and the Author hereby grant to the public all such rights in the Article as provided in, but subject to all limitations and requirements set forth in, the CRC License.

ARTICLE AND VIDEO LICENSE AGREEMENT

4. Retention of Rights in Article. Notwithstanding the exclusive license granted to JoVE in **Section 3** above, the Author shall, with respect to the Article, retain the non-exclusive right to use all or part of the Article for the non-commercial purpose of giving lectures, presentations or teaching classes, and to post a copy of the Article on the Institution's website or the Author's personal website, in each case provided that a link to the Article on the JoVE website is provided and notice of JoVE's copyright in the Article is included. All non-copyright intellectual property rights in and to the Article, such as patent rights, shall remain with the Author.

5. Grant of Rights in Video – Standard Access. This **Section 5** applies if the "Standard Access" box has been checked in **Item 1** above or if no box has been checked in **Item 1** above. In consideration of JoVE agreeing to produce, display or otherwise assist with the Video, the Author hereby acknowledges and agrees that, Subject to **Section 7** below, JoVE is and shall be the sole and exclusive owner of all rights of any nature, including, without limitation, all copyrights, in and to the Video. To the extent that, by law, the Author is deemed, now or at any time in the future, to have any rights of any nature in or to the Video, the Author hereby disclaims all such rights and transfers all such rights to JoVE.

6. Grant of Rights in Video – Open Access. This **Section 6** applies only if the "Open Access" box has been checked in **Item 1** above. In consideration of JoVE agreeing to produce, display or otherwise assist with the Video, the Author hereby grants to JoVE, subject to **Section 7** below, the exclusive, royalty-free, perpetual (for the full term of copyright in the Article, including any extensions thereto) license (a) to publish, reproduce, distribute, display and store the Video in all forms, formats and media whether now known or hereafter developed (including without limitation in print, digital and electronic form) throughout the world, (b) to translate the Video into other languages, create adaptations, summaries or extracts of the Video or other Derivative Works or Collective Works based on all or any portion of the Video and exercise all of the rights set forth in (a) above in such translations, adaptations, summaries, extracts, Derivative Works or Collective Works and (c) to license others to do any or all of the above. The foregoing rights may be exercised in all media and formats, whether now known or hereafter devised, and include the right to make such modifications as are technically necessary to exercise the rights in other media and formats. For any Video to which this Section 6 is applicable, JoVE and the Author hereby grant to the public all such rights in the Video as provided in, but subject to all limitations and requirements set forth in, the CRC License.

7. Government Employees. If the Author is a United States government employee and the Article was prepared in the course of his or her duties as a United States government employee, as indicated in **Item 2** above, and any of the licenses or grants granted by the Author hereunder exceed the scope of the 17 U.S.C. 403, then the rights granted hereunder shall be limited to the maximum rights permitted under such

statute. In such case, all provisions contained herein that are not in conflict with such statute shall remain in full force and effect, and all provisions contained herein that do so conflict shall be deemed to be amended so as to provide to JoVE the maximum rights permissible within such statute.

8. Likeness, Privacy, Personality. The Author hereby grants JoVE the right to use the Author's name, voice, likeness, picture, photograph, image, biography and performance in any way, commercial or otherwise, in connection with the Materials and the sale, promotion and distribution thereof. The Author hereby waives any and all rights he or she may have, relating to his or her appearance in the Video or otherwise relating to the Materials, under all applicable privacy, likeness, personality or similar laws.

9. Author Warranties. The Author represents and warrants that the Article is original, that it has not been published, that the copyright interest is owned by the Author (or, if more than one author is listed at the beginning of this Agreement, by such authors collectively) and has not been assigned, licensed, or otherwise transferred to any other party. The Author represents and warrants that the author(s) listed at the top of this Agreement are the only authors of the Materials. If more than one author is listed at the top of this Agreement and if any such author has not entered into a separate Article and Video License Agreement with JoVE relating to the Materials, the Author represents and warrants that the Author has been authorized by each of the other such authors to execute this Agreement on his or her behalf and to bind him or her with respect to the terms of this Agreement as if each of them had been a party hereto as an Author. The Author warrants that the use, reproduction, distribution, public or private performance or display, and/or modification of all or any portion of the Materials does not and will not violate, infringe and/or misappropriate the patent, trademark, intellectual property or other rights of any third party. The Author represents and warrants that it has and will continue to comply with all government, institutional and other regulations, including, without limitation all institutional, laboratory, hospital, ethical, human and animal treatment, privacy, and all other rules, regulations, laws, procedures or guidelines, applicable to the Materials, and that all research involving human and animal subjects has been approved by the Author's relevant institutional review board.

10. JoVE Discretion. If the Author requests the assistance of JoVE in producing the Video in the Author's facility, the Author shall ensure that the presence of JoVE employees, agents or independent contractors is in accordance with the relevant regulations of the Author's institution. If more than one author is listed at the beginning of this Agreement, JoVE may, in its sole discretion, elect not take any action with respect to the Article until such time as it has received complete, executed Article and Video License Agreements from each such author. JoVE reserves the right, in its absolute and sole discretion and without giving any reason therefore, to accept or decline any work submitted to JoVE. JoVE and its employees, agents and independent contractors shall have

ARTICLE AND VIDEO LICENSE AGREEMENT

full, unfettered access to the facilities of the Author or of the Author's institution as necessary to make the Video, whether actually published or not. JoVE has sole discretion as to the method of making and publishing the Materials, including, without limitation, to all decisions regarding editing, lighting, filming, timing of publication, if any, length, quality, content and the like.

11. **Indemnification.** The Author agrees to indemnify JoVE and/or its successors and assigns from and against any and all claims, costs, and expenses, including attorney's fees, arising out of any breach of any warranty or other representations contained herein. The Author further agrees to indemnify and hold harmless JoVE from and against any and all claims, costs, and expenses, including attorney's fees, resulting from the breach by the Author of any representation or warranty contained herein or from allegations or instances of violation of intellectual property rights, damage to the Author's or the Author's institution's facilities, fraud, libel, defamation, research, equipment, experiments, property damage, personal injury, violations of institutional, laboratory, hospital, ethical, human and animal treatment, privacy or other rules, regulations, laws, procedures or guidelines, liabilities and other losses or damages related in any way to the submission of work to JoVE, making of videos by JoVE, or publication in JoVE or elsewhere by JoVE. The Author shall be responsible for, and shall hold JoVE harmless from, damages caused by lack of sterilization, lack of cleanliness or by contamination due to the making of a video by JoVE its employees, agents or independent contractors. All sterilization, cleanliness or decontamination procedures shall be solely the responsibility of the Author and shall be undertaken at the Author's


expense. All indemnifications provided herein shall include JoVE's attorney's fees and costs related to said losses or damages. Such indemnification and holding harmless shall include such losses or damages incurred by, or in connection with, acts or omissions of JoVE, its employees, agents or independent contractors.

12. **Fees.** To cover the cost incurred for publication, JoVE must receive payment before production and publication the Materials. Payment is due in 21 days of invoice. Should the Materials not be published due to an editorial or production decision, these funds will be returned to the Author. Withdrawal by the Author of any submitted Materials after final peer review approval will result in a US\$1,200 fee to cover pre-production expenses incurred by JoVE. If payment is not received by the completion of filming, production and publication of the Materials will be suspended until payment is received.

13. **Transfer, Governing Law.** This Agreement may be assigned by JoVE and shall inure to the benefits of any of JoVE's successors and assignees. This Agreement shall be governed and construed by the internal laws of the Commonwealth of Massachusetts without giving effect to any conflict of law provision thereunder. This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together shall be deemed to me one and the same agreement. A signed copy of this Agreement delivered by facsimile, e-mail or other means of electronic transmission shall be deemed to have the same legal effect as delivery of an original signed copy of this Agreement.

A signed copy of this document must be sent with all new submissions. Only one Agreement required per submission.

CORRESPONDING AUTHOR:

Name:	Patricia A. Shewokis, PhD	
Department:	Nutrition Sciences Department, CNHP (primary appt.) / School of Biomedical Engineering, Sciences and Health Systems	
Institution:	Drexel University	
Article Title:	Calculating Heart Rate Variability from ECG Data from Youth with Cerebral Palsy during Active Video Game Sessions	
Signature:		Date: 3/13/2017

Please submit a signed and dated copy of this license by one of the following three methods:

- 1) Upload a scanned copy of the document as a pdf on the JoVE submission site;
- 2) Fax the document to +1.866.381.2236;
- 3) Mail the document to JoVE / Attn: JoVE Editorial / 1 Alewife Center #200 / Cambridge, MA 02139

For questions, please email submissions@jove.com or call +1.617.945.9051

Your manuscript, JoVE59230 "Calculating Heart Rate Variability from ECG Data from Youth with Cerebral Palsy during Active Video Game Sessions," has been editorially and peer reviewed, and the following comments need to be addressed. Note that editorial comments address both requirements for video production and formatting of the article for publication. Please track the changes within the manuscript to identify all of the edits.

After revising and uploading your submission, please also upload a separate rebuttal document that addresses each of the editorial and peer review comments individually. Please submit each figure as a vector image file to ensure high resolution throughout production: (.svg, .eps, .ai). If submitting as a .tif or .psd, please ensure that the image is 1920 x 1080 pixels or 300 dpi.

Your revision is due by **Jan 02, 2019**.

To submit a revision, go to the [JoVE submission site](#) and log in as an author. You will find your submission under the heading "Submission Needing Revision".

Best,

Nam Nguyen, Ph.D.
Manager of Review

[JoVE](#)

617.674.1888

Follow us: [Facebook](#) | [Twitter](#) | [LinkedIn](#)

[About JoVE](#)

Editorial comments:

1. Please highlight 2.75 pages of the protocol text for inclusion in the protocol section of the video. This is a hard production limit to ensure that videography can occur in a single day.

There are 44 single spaced lines per page, thus there will be 121 lines of protocol text for inclusion in the protocol section of the video. As requested, the information is highlighted.

2. Figure 1: Please provide units for the time in the X-axis.

Completed.

3. Figure 2: Please define the x and y axes. Please provide units as well.

Completed.

4. Figure 3: The y-axis title is cut off.

The Figure now has a the y-axis and appropriate abbreviations.

5. Please use SI abbreviations for time throughout (s instead of sec).

Completed.

6. Please use the Greek symbol mu throughout for the microvolts abbreviations.

Completed.

Reviewers' comments:

Reviewer #1:

Manuscript Summary:

The study is interesting and proposes a new method for calculating HRV during active video games. However, introduction should address why calculating HRV during exercise is important for this population, despite all the possible limitations present in the method (e.g. signal interference, nonstationary signals, ectopic heart beats etc) and considering that simple methods for monitoring the HR are effective. Please, find below more detailed comments.

Major Concerns:

INTRODUCTION

-Introduction is superficial and fails to provide rationale behind HRV calculation during AVGs for CP patients.

-Considering only the introduction and the abstract, it seems to be a misinterpretation regarding HRV concept. The authors do not mention anything related to HRV indices, but instead comment about the HR, mHR and target HR during exercise. So, it is not clear why it is relevant monitoring HRV in CP patients during AVG. Moreover, several papers have addressed the limitations on quantifying HRV during short no continuous activities. This point could also be addressed in the introduction.

-Finally, the introduction leads the reader to suppose that one of the goals of the study was also to assess the effectiveness of the KOLLECT in improving fitness and aerobic capacity in CP children. So, I suggest the authors reformulate it.

We appreciate the reviewers' interest in highlighting HRV and a clinical perspective. We have addressed the reviewers' suggestions within the Long Abstract and the Introduction.

PROTOCOL

-Provide the model and the brand of the HR monitor used in the study.

We appreciate that the reviewer is interested in the brand of the HR monitor (Bioharness). Do note that JOVE requests that brand information of the equipment is not presented in 10.1186/particular information submitted with the document.

-Provide more details about the HRV analysis: E.g. number of points/beats considered for analysis (e.g.: FFT should be applied on segments with 256 beats or multiples).

Please see the HRV calculations via MATLAB that are posted at the end of this response to this document. The majority of information is noted already in the paper – including the fact that we used a FFT for the measures (see line 256).

Did the authors record ECG or RR intervals using a validated equipment (e.g. Polar V800) and analyzed HRV using a validated software (e.g. Kubios) in order to check for reliability and agreement between the new proposed method and a previous validated method?

The Zephyr Bioharness, a physiological monitoring telemetry device, consists of a chest strap and an electronic sensor that is attached to the strap. The device transmits a radio frequency (transmission mode) or stores data (logging mode). The biosignals of interest while HR is sampled at 1 Hz.

The device that we used, Zephyr Bioharness, is considered a reliable and valid tool for obtaining HR and then making the necessary calculations for HRV. Nazari and colleagues (2018) reported a systematic review of 10 studies that used the device. Intraclass correlation coefficients ranged from 0.85-0.95. Comparisons of construct validity coefficients to gold standard measures ranged from 0.74-0.99. Agreement error for the Zephyr Bioharness ranged from approximately 5 beats/min underestimation to 3 beats/min overestimation. Based on the findings, the authors suggested that the Zephyr Bioharness can provide reliable and valid measures of heart rate across varying contexts.

Nazari, G., Bobos, P., MacDermid, J.C., Sinden, K.E., Richardson, J., Tang, A. Psychometric properties of the Zephyr bioharness device: A systematic review. *BMC Sports Science, Medicine and Rehabilitation* 10,6. DOI: doi.org/10.1186/13102-018-0094-4 (2018).

-How the authors solved the problem of nonstationary signals?

We reviewed and determined the minimum height for the R peak and the minimum distance between peaks. If there were unusual, elongated distances between R peaks then further inspection was done to ensure that the ECG sample was sufficient as well as setting a threshold for data to reduce false-positive detection of from T peaks.

Ideally, another post-processing method of addressing nonstationary signals is to plot the R-R interval time series as a function of the respiratory rate for each of the different AVG phases. This may be an interesting assessment of the role of nonstationary signals during fitness conditioning with deconditioned performers.

DISCUSSION

-HRV has been studied in CP patients. So, providing more details about each participant (e.g.: age, GMFCS, Limb distribution etc...) might be important in order to compare the values reported with the values presented in the literature.

Participant Demographic Table has been created with individual patient information included

-Authors should discuss why quantifying HRV indices during exercise is important for this population, and what these measures add to the measurement of HR, considering that usually aerobic exercises are prescribed based on HR of reserve. Also, since we present the "inherent variability", as recognized by the authors, the exercise intensity prescription usually considers a range or target HR zone (e.g. 50-70%HRR). So, why HRV during exercise would be better?

HRV may not be better, it provides a different method to examine exercise response and unlike straight HR, HRV does allow for some information on autonomic nervous system responses

-How long it takes for performing all the protocol?

Did the authors believe this method would be feasible to be used in a clinical setting? Please, comment about it.

The game play session was 60 minutes (3 games at 20 minutes each). The rest time between games to wait until the child HR was back to baseline was about 3-5 minutes. The AVG set up and getting the HR monitor on the child is another 20 minutes – So the session was close to 2 hours. However, in the clinic, there would not be three games in one session, so that may leave time for donning the HR monitor and using AVGs. Another perk of the HR monitor is that we can download the HR data into an Excel file and save these data. Most HR monitors used in clinics do not have this feature.

Minor Concerns:

None

Reviewer #2:

Manuscript Summary:

Authors have described the protocol to measure HRV during Active video game sessions in cerebral palsy participants.

Authors have primarily addressed how movement artifacts are corrected.

Major Concerns:

Nil

Minor Concerns:

LF/HF ratio of ECG is not clear from physiological point of view since it is not mentioned in the task force guidelines for HRV measurement.

We appreciate that the reviewer pointed out the lack of clarity of LF/HF ratio and have addressed this point in the review. Shaffer, McCraty and Zier (2014) note that autonomic balance hypothesis is associated with the LF/HF ratio. This hypothesis assumes that the sympathetic nervous system and parasympathetic nervous system are in competition to regulate SA node firing. The authors note that the LF/HF ratio needs to be interpreted with caution while noting the context of obtaining information as well as reviewing the LF and HF values. Concerning the application of LF/HF ratio to AVG games in short-term episodes of HR measurements and HRV, a high LF/HF ratio may indicate higher sympathetic activity that may be observed when meeting a challenge that requires effort and increases the sympathetic nervous system activation.

%%HRV Measure Calculations, Corey Landis 6 / 3 / 16

%% Calculate RR Intervals

%Separate out peaks and loc arrays for calculation

loc = Detection(:,1);

peaks = Detection(:,2);

count = length(loc);

interval = [i,1];

%Calcualte time between peaks ('peak intervals')

for i = 1:count-1

 t1 = datevec(time(loc(i),1),'mm / dd / yyyy HH:MM:SS.FFF'); %obtain time of the peak

 t2 = datevec(time(loc(i+1),1),'mm / dd / yyyy HH:MM:SS.FFF'); %obtain time of
 susequent peak

 diff = t2 - t1; %find difference for RR interval in matrix form

 dif = (diff(4) * 3600) + (diff(5) * 60) + diff(6); %difference in seconds accurate to 4 ms

 if dif < 1.5

 interval(i) = dif;

 end

end

if min(interval) < 0

 [m, Check] = min(interval);

 Warning = sprintf('Data Entered Incorrectly. Please Check the row %d of the Detection
 Variable. Once fixed, rerun this program.', Check);

 disp(Warning);

end

% Replot time corrected graphs

locs = loc * Freq;

```

times = 0:Freq:(E-S) * Freq;
plot(times,ECG(S:E))
hold on
plot(locs , peaks, 'ro')
hold off
title('KOLLECT 12 AVG4') %Should be changed based on subject being used
xlabel('Time (sec)')
ylabel('uV')

```

```

%% Calculate RMSSD & NN50

```

```

count = length(interval) + 1;

```

```

rSum = 0;

```

```

NNfif = 0;

```

```

% Calculate difference between successive intervals

```

```

for j = 1:count - 2

```

```

    r = interval(j+1) - interval(j); %Square of successive RR difference

```

```

    rSum = rSum + r^2;

```

```

    if abs(r) > 0.05

```

```

        NNfif = NNfif + 1;

```

```

    end

```

```

end

```

```

RMSSD = sqrt((1/(count-1))*rSum) * 1000;

```

```

pfifty = (NNfif / count)*100;

```

```

SDNN = std(interval(interval~=0)) * 1000; %Find SDNN in ms

```

```

MRR = mean(interval(interval~=0));

```

```

AvgHR = 60 / MRR;

```

```

MRR = mean(interval(interval~=0)) * 1000; % Set to ms

```

%% LF / HF Calculations

X = ECG(S:E);

Fs = 250; %Set sampling rate

t = 0:1/Fs:300; %Set time frame (5 minutes or 300 seconds) to length of observed session
incremented by frequency

L = length(t); %Find length of time frame

n = 2^nextpow2(L);

Y = fft(X,n); %Calculate the FFT for ECG signal

P = abs(Y/n); %Find absolute value of power

LF = sum(P(22:77)); %Sum of Low Frequency Powers

HF = sum(P(78:205)); %Sum of High Frequency Powers

RatioECG = LF / HF;

X = interval;

Y = fft(X,n); %Calculate the FFT for RR interval

P = abs(Y/n); %Find absolute value of power

LF = sum(P(22:77));

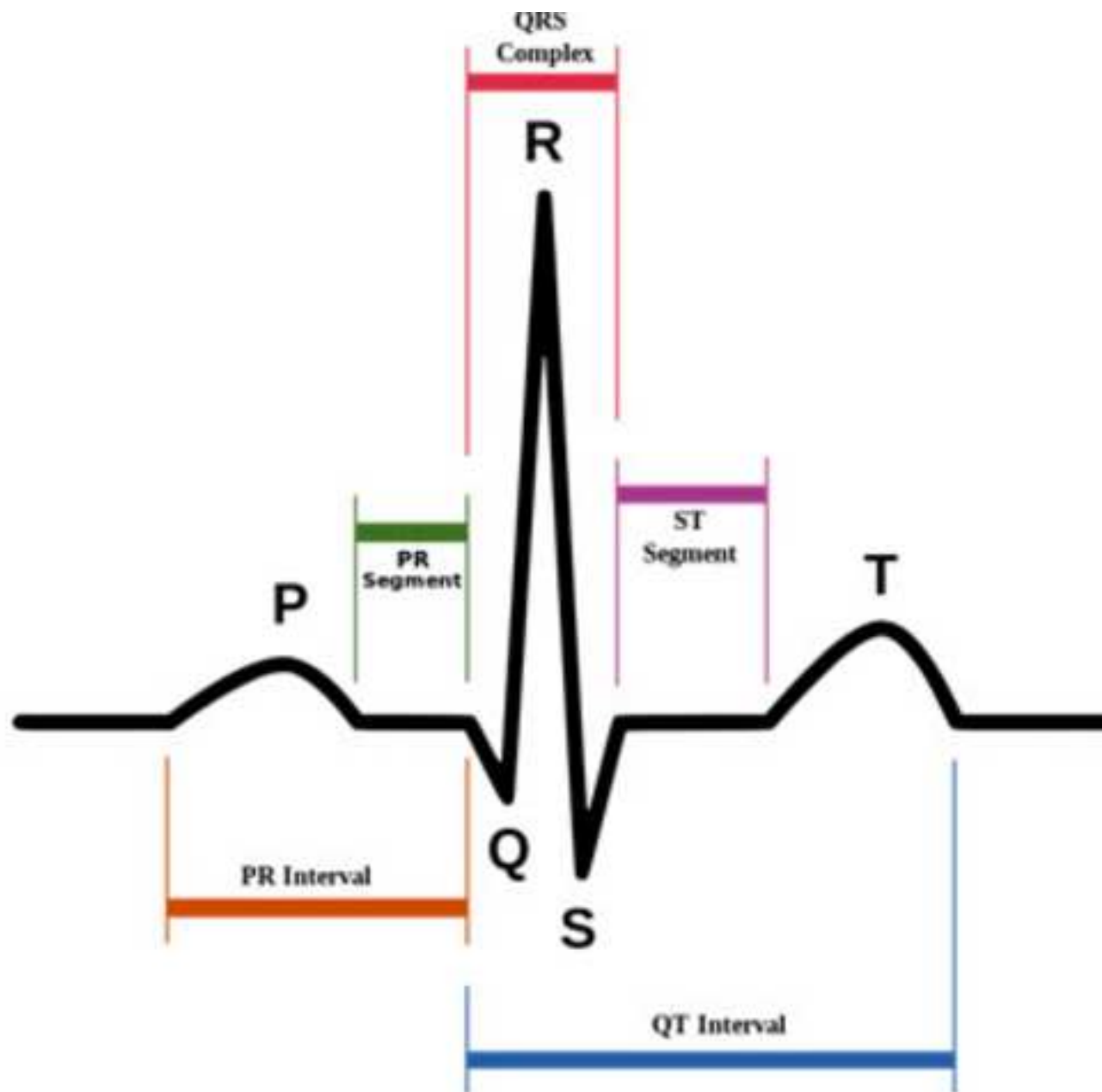
HF = sum(P(78:205));

RatioRR = LF / HF;

%Place all HRV measures in one matrix for ease of access

HRV = [MRR, AvgHR, RMSSD, SDNN, NNfif, pfifty, RatioECG, RatioRR, LF, HF];

%'Mean RR', 'Average HR', 'RMSSD', 'SDNN', 'NN50', 'pNN50', 'LF/HF ECG', 'LF/HF RR',
'LF Power RR', 'HF Power RR'



<https://commons.wikimedia.org/wiki/File:SinusRhythmLabels.svg>