Development and evaluation of a HRV Biofeedback System

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KTH Technology and Health

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Utveckling och utvärdering av ett system för HRV biofeedback

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Technology and Health	**Examensarbete inom medicinsk teknik (HL202X) *30hp*** **2014:95** **Development and evaluation of a HRV Biofeedback System** Klara Lindskog

Godkänt	Recensent	Handledare
2014-09-30	Kaj Lindecrantz	Farhad Abtahi
	Uppdragsgivare Mats Nilsson	

Sammanfattning

Det här är en rapport från ett examensarbete på masternivå utfört på KTH, Skolan för teknik och hälsa i Flemingsberg. Arbetet handlar om att vidareutveckla en mobil applikation för surfplattor som utvecklats i ett tidigare masterprojekt. Programmet engagerar användaren i andning efter en specifik metod.

Metoden med HRV biofeedback bygger på att visualisera och träna upp HRV medan man andas. Detta innebär att maximera de varierande tidsintervallen mellan hjärtats slag vilket har potential att fungera som en behandlingsmetod för att reducera stress och bibehålla god hälsa.

Genom att programmera i Java och implementera en ny spelvy i det existerande programmet har applikationen förbättrats. Även andra aspekter av programmet har förbättrats.

Arbetet har också inneburit att hitta svar på frågor om optimal dosering och frekvens för träning med HRV biofeedback för att detta ska kunna ge långsiktiga effekter på HRV. En litteraturstudie utfördes för att finna svar på dessa frågor. Det saknas dock studier som påvisar positiva långvariga effekter på hjärtats variabilitet hos friska personer. Därför har ett testprotokoll föreslagits vilket kan vara en grund för att i framtiden göra en studie för att vidare utforska dessa frågor.

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Abstract

This is a master thesis project written at the School of Technology and Health within KTH, Flemingsberg. It consisted of making improvements in an existing application for tablets used for training HRV biofeedback that was developed as part of an earlier master thesis within the same school. The software involves the user in paced breathing according to an established method.

The method with HRV biofeedback visualises and trains HRV while the user performs paced breathing. This means that the user maximises the variations of time between heart beats which may have potential to reduce stress and sustain health.

To improve the software developed earlier at KTH a new graphical user interface was implemented in form of a simple game. In addition further aspects of the program were improved.

Furthermore, this thesis tried to find evidence for the optimal frequency and duration of HRV biofeedback training for healthy individuals. For this purpose a literature review was performed, showing a lack of evidence for the effectiveness of HRV biofeedback training in healthy individuals. Therefore a study protocol was developed that can be used in future studies aimed at finding the optimal dosage of HRV biofeedback.

Abbreviations

ADT	Android Development Tools
ANS	Autonomous nervous system
App	Application
CPU	Central processing unit
ECG	Electro cardiogram
GPU	Graphics processing unit
HF	High frequency
HR	Heart rate
HRV	Heart rate variability
LF	Low frequency
NN50	NN-pairs where intervals differ 50 ms or more
PSD	Power spectrum density
RAM	Random access memory
RMS	Root mean square
RSA	Respiratory sinus arrhythmia
SDK	Software development kit
SDNN	Standard deviation of the NN-intervals
TEB	Thoracic electrical bioimpedance
VLF	Very low frequency
VM	Virtual machine

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1 INTRODUCTION

1.1 Background

Today's technology facilitates surveillance of our health; mobile devices, apps and sensors available empower people with information about their body's condition. For example a pulse watch during exercise can send data via bluetooth to a mobile device that enables monitoring athletic improvements. Also medical apps and IT technology have the potential to cut costs for healthcare where patients can get information about their current health which may work as a means to prevent sickness.

Today, it is possible and easily accessible to monitor blood pressure and heart rate (HR) by sensors and mobile applications. In addition, Heart Rate Variability (HRV) has the potential to be a future parameter to monitor in order to prevent sickness and to enhance health.

A RR-interval is the time between two adjacent heart beats. A healthy person has variations in RR-intervals during the respiration cycle. These variations are called HRV. A stressed, depressed or a sick person has less variations. A small HRV can therefore be seen as an indicator of poor health. Training of HRV may contribute to better health, it can be used as way to handle stress. [1]

HRV is enhanced by physical exercise, relaxation and paced breathing. A slow and paced breathing technique much like the slow breathing practiced in Yoga, Qigong, and Zen takes a lot of training to master. [2] A mobile device application, based on scientific evidence of HRV enhancement, may promote the same positive health effects as traditional eastern Yoga techniques. An instructive mobile device application can make the training techniques available to anyone.

Today there are mobile applications and computer programs with sensors to measure and train HRV. This might have the potential to maintain and improve health and may also cut cost for healthcare.

1.2 Purpose

In a previous master project performed at KTH, STH in Flemingsberg, Stockholm a biofeedback application for Android systems was developed. [3] This biofeedback application engages the user in following a specific breathing pattern that maximises HRV and may contribute to positive long term effects on health.

This master thesis project contains of two parts. The main goal with this thesis was to improve the application previously developed at KTH and to evaluate it. This thesis also suggests how to find the optimal way to use the biofeedback system in terms of appropriate session length and training frequency in order to see a continuous positive effect on HRV for healthy people.

1.3 Outline

Chapter 2 describes the theoretical background of HRV and explains the specific breathing technique used to maximise HRV. Moreover, an explanation and overview of the topical app is given and how it needs to be further developed.

Chapter 3 contains the methods used for achieving the goals. The details of tools used for software development and how the literature study has been conducted are presented.

Chapter 4 describes the results of the literature study and the outcome from the application improvements. A test protocol for experimental studies on a test group is also suggested to give further answers to the dosage and frequency of training with HRV biofeedback.

Chapter 5 contains the discussion of the results. Also the drawbacks, future recommendations and ethical aspects of using the system are presented.

Chapter 6 summarises the work that has been performed.

Chapter 7 suggests future ideas for developing the work further and some recommendations for similar projects.

2.1 RR interval

The heart muscle cells contract in order to pump blood to the body. The contraction of the heart is created through the electrical activity of the sinoatrial node which generates the pacer of heart beats. A recording of the electrical activity of the heart is called an electro cardiogram (ECG). The ECG is a result of a recorded voltage difference of electrodes placed on the skin of a person´s chest.

The ECG consists of three different patterns; the P wave, QRS complex and the T wave which represent different stages in the heart's polarisation and depolarisation throughout a normal heart beat. When analysing the ECG signal, the R peak can be used for detecting heart beats thanks to its characteristic shape. [4]

The time between two R peaks adjacent to each other is called RR interval and is illustrated in figure 1.

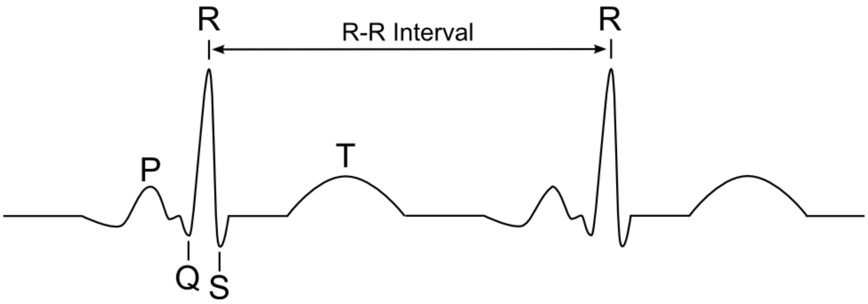

Figure 1. RR interval [5]

2.2 Heart Rate Variability

The heart rate of a healthy person at rest is not entirely regular. The variations of time intervals between heart beats are called heart rate variability (HRV) which is correlated with the breath and controlled by the autonomous nervous system (ANS). [6] Two major mechanisms, affecting the ANS, are known to influence HRV; respiratory sinus arrhythmia (RSA) and the baroreflex. RSA is the primary source of HRV which produces the response of the heart rate (HR) while breathing. Exhaling increases the time intervals between heart beats and inhaling decreases these time intervals. The secondary source of HRV is the baroreflex which is controlled by stretch receptors located in the aortic arch and carotid artery. The baroreceptors trigger the reflex of blood pressure regulation and are affected by HR. The receptors trigger a feedback loop to the heart; an increase in blood pressure would result in a decreasing HR and a blood pressure drop would trigger an increase of HR.

A small HRV is a sign of an imbalance in the parasympathetic nervous system and the sympathetic nervous system which are the two branches of the ANS that are responsible for relaxation and activation respectively. These two branches are believed to activate the “rest and digest” and “fight or flight” psychophysiological response in the body. An imbalance between the two branches may also be a marker for poor cardiovascular health.

Large variations of HRV can be seen as an indicator of good health. A person who is relaxed and healthy produces larger variations in HRV than if that person was unhealthy or stressed. The HRV naturally diminishes with age but this effect might be reduced if a person is performing physical exercise or trains their HRV on a regular basis. [1]

2.3 Resonance frequency breathing and effects on HRV

A specific method to increase HRV is through paced breathing in a resonance frequency. By relaxing and breathing at a frequency of around 6 breaths per minute the breathing synchronises with the variations of blood pressure. HRV maximises as the paced breathing continues. Training on a regular basis makes the baroreceptors more efficient and practice will therefore enhance baroreflex gain.

The motive for a specific resonance frequency is the delayed blood pressure response, resulting from a change in HR. After a rise in HR, triggered by RSA while inhaling, an elevation in blood pressure is executed as a response about 5 seconds later. This delay is due to the inertia of the body’s vascular system. The elevation in blood pressure is then sensed by the baroreceptors that immediately affect the ANS which controls the HR by slowing it down. A decrease in HR would again be sensed after 5 seconds by the baroreceptors. This works the same way for exhaling. While exhaling, the RSA affects HR by slowing it down. The blood pressure drop is detected by the baroreflex after about 5 seconds at which point an increase in HR is executed.

When breathing one cycle (in and out) every 10^{th} second the effects of the delays produce an oscillatory behaviour of the HR. The breathing and blood pressure response are in a 180 degree out of phase pattern. The HR is at its highest state when the blood pressure is at its lowest state. These oscillations are the key to the maximised HRV and training the of the baroreceptors efficiency.

There are differences between resonance frequencies among individuals. Research findings suggest that the resonance frequencies vary from 4.5 to 7 breaths per minute. The individual difference might be related to the volume of vasculature in a person. For example, a larger network of vessels could be a sign of a lower resonance frequency where a blood pressure rise from an increasing HR would demand longer delay due to the inertia of the system. In other words, to create the desired oscillations, time between inhaling and exhaling needs to be longer. [1]

2.4 Biofeedback and Heart Rate Variability

A biofeedback method is about taking some control over the body's physiological functions with some kind of feedback indicator for the user. [7] This could mean that the user can see their own physiological measurements on a computer screen in real time while performing a certain activity with the aim to alter these physiological parameters. In the case of using HRV biofeedback; the user gets information and instructions of how well the paced breathing is followed and about the HRV. By visualising HRV and paced resonance breathing, paced breathing and relaxation can help balance the autonomous nervous system of the user.

2.5 State of the art

2.5.1 Research of HRV biofeedback training

HRV biofeedback training has been proven to give positive results on HRV in the acute timeframe during and immediately after training sessions. Less is known about the long term effects. [8] The question whether biofeedback training can give long term effects on HRV for healthy people remains unanswered. It is not known how long the effects of HRV biofeedback remain after training. Though, there is lacking evidence of effects on healthy people, the HRV biofeedback method has been investigated in studies considering health problems.

HRV biofeedback training in asthma has been evaluated systematically. Studies by Lehrer, Smetankin and Potapova have involved patients with mild asthma. Their studies showed improvements in pulmonary function. Their results included a lower respiratory resistance for those receiving HRV. Moreover, the patients who took HRV biofeedback training did not consume as much medicaments as their control group.

The HeartMath Institute, a nonprofit research and education organization in the United States dedicated to helping people reduce stress, did a study on a workplace where participants used HRV biofeedback. Blood pressure in patients who suffered from hypertension was decreased among those who received HRV biofeedback training.

Cowan, Pike and Budzynski did a study on 129 patients who had survived ventricular fibrillation or asystole. It was shown that the treatment group which received cognitive therapy and HRV biofeedback training had lower risk of mortality than the control group. [1]

2.5.2 Heart Rate Variability biofeedback and apps today

Today there are apps available for measuring HRV in order to keep track of the body's restoration after workout, improving meditation status or managing stress through paced breathing. Two of the apps available today much like the app developed at KTH are MyCalmBeat produced by MyBrain Solution and InnerBalance by HeartMath. They are both stress management biofeedback systems in the form of apps for mobile devices and use an ear clip sensor with pulse oximetry to measure HRV. The systems use the paced resonance frequency breathing methodology explained earlier. [9], [10]

No apps for training of HRV enhancement together with immediate breathing biofeedback exist on the market. The impedance measurement across the chest for breathing movements with its biofeedback feature is unique for the app developed by KTH.

2.6 HRV analysing methods

2.6.1 Measurement methods for HRV

A set of standard measurements for HRV was set out by the European Society of Cardiology and the North American society for Pacing and Electrophysiology in 1996. It was specified that there are short term recordings for measurements up to 5 minutes and long term recordings for measurements more than 24 hours. First, the system needs to detect heart beats, which is the data to be analysed. Two methods to analyse the data are the time domain and frequency domain methods. [11]

2.6.2 Detection of heart beats

The R peak has a characteristic shape that can be automatically detected by ECG analysing systems using an algorithm. A QRS detection algorithm was developed by Pan and Thompkins which derives the R peak from raw ECG data. [12] The RR-intervals are calculated by considering the time between the R peaks.

2.6.3 Common time domain methods

RR-interval can also be called NN-interval and is the time interval between two heart beats. The NN-interval nomenclature stands for that the heart beat is normal. The RR-interval plotted to time is called a tachogram. The standard deviation of the NN-intervals (SDNN) is a common estimate of the HRV. The root mean square (RMS) of successive intervals is a measure based on the differences of RR-intervals. Also, the number of adjacent NN-pairs where intervals differ 50 ms or more is called NN50 count. [11] The advantage of the time domain analysis is that they are easy to compute. On the other hand there are limitations of these methods, they do not reflect the balance between the two branches in the ANS as clearly as an analysis in frequency domain does. [13]

2.6.4 Frequency domain methods

The tachogram signal contains rhythms that correspond to the breathing. Breathing in a certain frequency for example 6 breaths per minute would produce a tachogram signal which for the majority is represented by 0.1 Hz in the frequency domain. The Fourier transform transfers the data from time domain to frequency domain.

In order to use Fourier transform on the tachogram signal it has to be interpolated and resampled. This is due to the uneven sample rate that develops since the tachogram is composed by heart beat intervals. [13] Another solution is to use a Lomb periodogram when analysing the HRV frequency parameters. Lomb estimation does not require resampling meaning it will save computational capacity for the analysing system. The Lomb periodogram has been shown to be a robust method for quantifying frequency parameters. [14]

There are three major spectral components: very low frequency (VLF), low frequency (LF) and high frequency (HF). These components are expressed in ms^2. The physiological factor behind VLF, which lays within the frequency band of 0.003 Hz to 0.04 Hz, is not defined and it is questionable if there are any conclusions to draw from this component.

LF components lie within the range of 0.04 Hz to 0.15 Hz. It is not clear what this component stands for. Literature claims that this is due to a dominance of the sympathetic branch of the ANS that affects the heart. [6] On the other hand, literature describes the LF component interpretation to be controversial or that it might reflect both parasympathetic and sympathetic branch of the ANS. [11]

HF frequencies range from 0.15 Hz to 0.4 Hz and the interpretation is more clearly stated in the literature. HF frequencies correspond to the respiratory modulation of the time intervals between heart beats. It can be considered as indicator of the vagal influence on the heart which means that it reflects the parasympathetic influence on the heart. [6]

2.7 The topical app and system

A former master thesis project on KTH has resulted in an application for tablets to be used together with a developed bluetooth device. The application was designed as a training tool for HRV using paced breathing and biofeedback. [15] The application is not on the android market since it is under development.

The system uses the R peak detection according to Pan and Thompkins and time domain values such as a tachogram. A Lomb periodogram and frequency band distributions are used as frequency domain methods. [15]

The setup is composed of 7 electrodes attached to the body. Four of them are used for thoracic electrical bioimpedance (TEB) to detect breathing movements and three of them are used for electrocardiography (ECG) to detect RR intervals.

The outcome of the TEB measurement, using two pairs of electrodes, is a difference in impedance in thorax while the user is breathing. A thorax filled with air would create a higher impedance across the electrode pairs while a lower impedance would exists while exhaling. Two electrodes are injecting a single frequency current at 50 kHz. These electrodes are placed on opposite sides of the thorax. Another electrode pair is sensing the current and a voltage difference is measured between the sensing electrodes. The voltage difference changes while the user is breathing. The output signal, a varying impedance can be derived through Ohm's law since the current is known. The output signal represents the breathing movements of the user. The principle for TEB measurement and electrode placement are shown in figure 2.

The ECG measured is a voltage difference across an electrode placed on the neck and an electrode placed on the hip. It is optional to use a reference electrode on the leg or ankle. The driven right leg reference electrode can reduce interference.

The electrodes used for development of the application are ECG electrodes for single use and attached to the body like a patch. The model of the electrode is called 2228 and produced by M3.

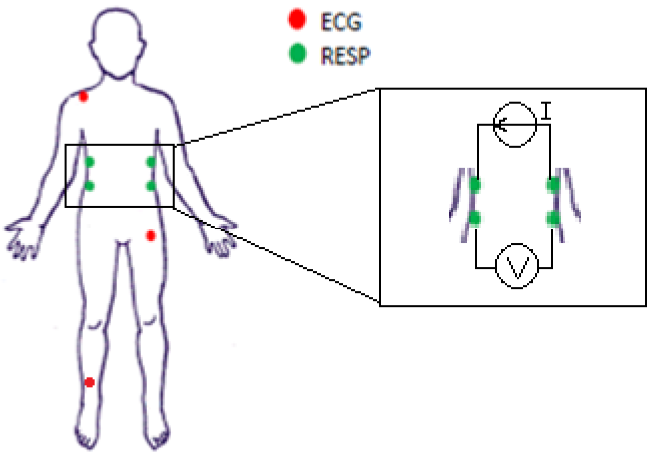

Figure 2. Electrode placement and principle for measuring the TEB.

The wires used have a banana plug connected to a crocodile clip that attach to the electrode knob. Figure 3 shows the wires and the Bluetooth device.

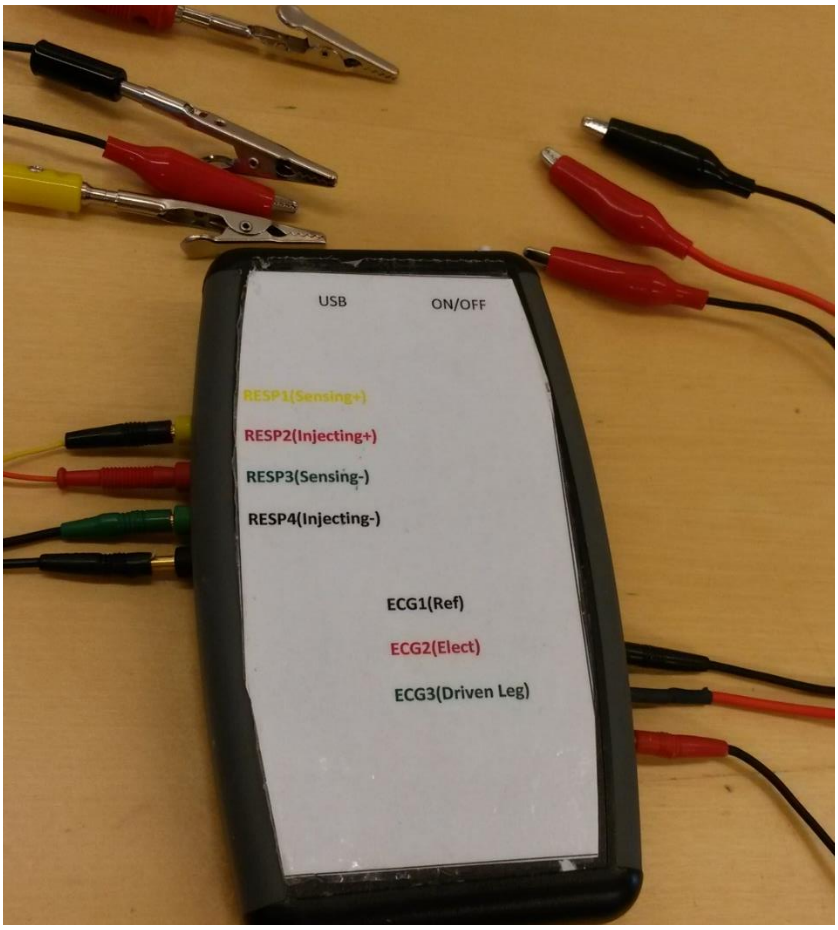

Figure 3. Bluetooth device and wires

The Bluetooth device in figure 3 sends the signal to a tablet with the developed application. In this project the tablet used was a Sony Xperia Z with android version 4.4.2. The system is also compatible with other tablets using a minimum of Android version 4.2.

The developed application has two views. The first view, in figure 4, shows an action bar where the name of the application and two buttons are visible. One button is used to activate the second view and the other to enter calibration mode of the TEB wires.

The calibration of the TEB wires is necessary when the Bluetooth device is switched on and connected to the software. The calibration is made with a 50 ohm resistor. The sensing wires are placed on one side of the resistor and the ejecting wires on the opposite side. After calibration, further activation of the application is needed through the start button in the lower right corner. Then the graph starts to plot from left to right.

Below the action bar the ECG curve and HR are presented. The ECG curve shows red dots where the software distinguishes R-peaks.

The second graph from the top represents the TEB measurement (blue line) and a breathing pacer (green line). The purpose is to adapt the breathing to the pacer as much as possible.

Paced breathing will produce a tachogram which is 180 degrees out of phase in comparison with the breathing movements. The tachogram, the third graph, is the time intervals between R-peaks plotted to time. In other words the red dots represent R-peaks and they vary on the Y-axis depending on the duration from the adjacent R-peak. The data in the tachogram is dependent of the timing of a heartbeat; the tachogram signal is therefore not continuously sampled with time.

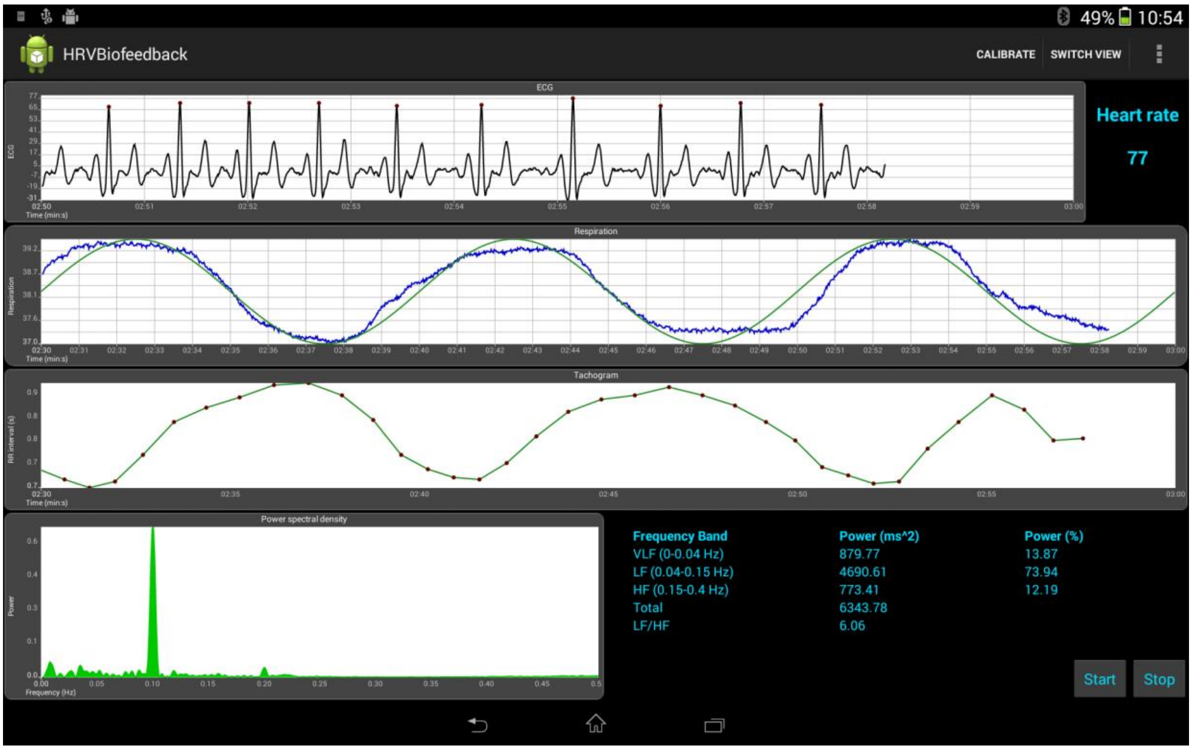

Figure 4. First view of the application

Moreover there is a Power Spectrum Diagram (PSD) presented in the first view. It displays the power spectrum from the tachogram, the signal frequency disposition. The power spectrum in figure 4 shows that the tachogram, the middle graph, mainly consist of a signal of 0.1 Hz corresponding to the heart beats reaction to 6 breaths per minute. This peak in the power spectrum will continue to grow as long as the user breathes in that pace.

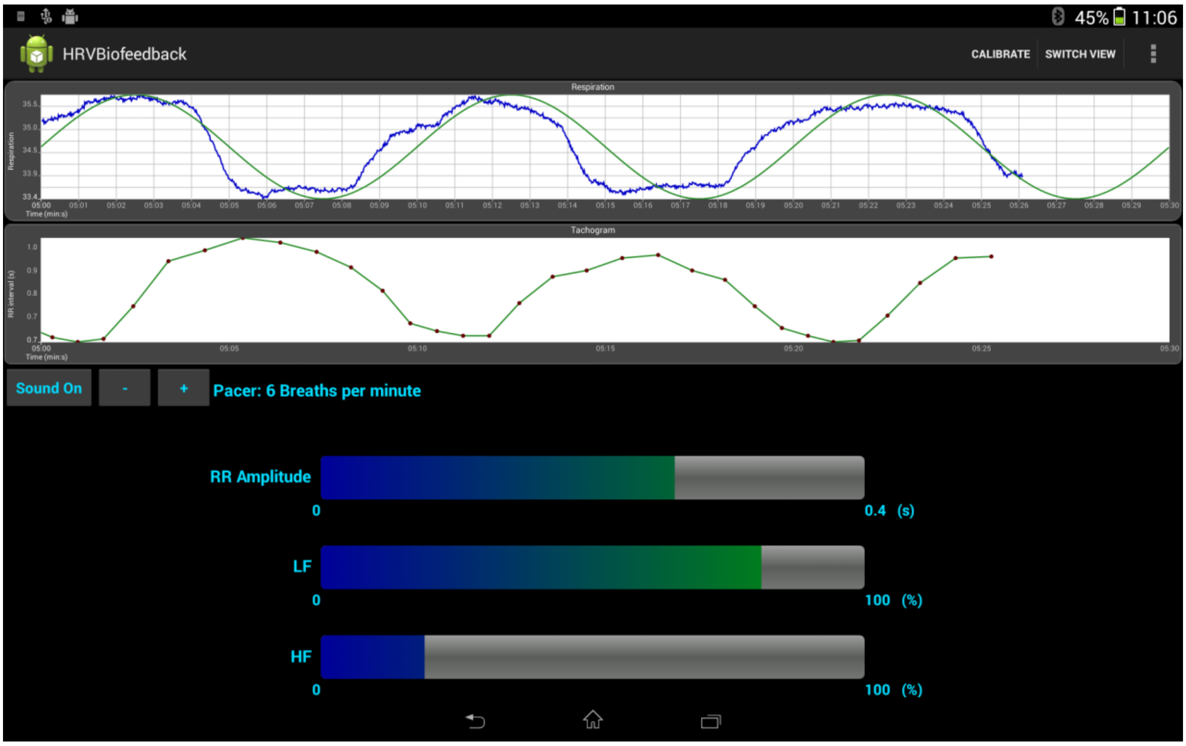

Figure 5. Second view of the application

The bars in the second view, shown in figure 5, are an indication of how well the user is doing. A goal for the user is to make the uppermost bar fill up to the right. A filled bar means that the maximum and minimum time intervals between heart beats within one respiration cycle differs 0.4 s or more. The other two bars indicate the normalized powers of the LF and HF frequency bands, in other words; shows the frequency distributions of the tachogram. [15]

2.7.1 Developing platform and software

The app is developed for Android systems and programmed in Java. The development environment used is Eclipse and Android software development kit (SDK) is used which is comprised of tools for software development.

Java is an object oriented programming language. Objects can be said to have a state and behaviour described in the object class. Classes are the description of how an object is going to be created and what kind of actions it will be involved in. [16]

A thread is an executional part of a program. Actions in the program do not need to be performed one after the other. By implementing actions in different threads, the actions can be executed simultaneously. [17]

Memory garbage collection is performed automatically with the Dalvik Virtual Machine (VM). The Dalvik VM is Android's software based processor that executes files. When an object is no longer in use, the garbage collector reuses the memory. [18]

However, if memory is allocated in classes that are used globally, for example classes used in other threads, the memory might not be returned to random access memory (RAM) causing a memory leakage when new memory needs to be allocated. A memory leakage could lead to poor performance and automatic shutdown of the program. [19]

The software is composed by classes such as the main activity, classes for plotting the ECG, TEB, tachogram and power density spectrum. There are also classes for the bluetooth connection and the peak detection.

There are four threads for plotting the data. Communication between the threads is supported by handlers. Handlers are designated to a single thread and place the message to be sent to another thread in a message queue. [20] There are methods describing when to send in the thread and what to do with the information in the thread of the recipient.

The graph plotting for ECG, TEB and tachogram is built on the android open source library for dynamic plots: androidplot-core-0.5.2.

More details about the software can be found in the master thesis of Andreas Berndtsson. [15]

2.7.2 Areas of software improvements

The visualisation for the user in the second view is not clear and can be improved. Confusion can arise whether the user is supposed to fill up both the LF and HF bars to the right, which is not possible since the signal consists of both bands. For example: as the user relaxes the HF band would be greater, making the HF bar grow to the right, since it describes the parasympathetic influence of the heart. A resonant frequency breathing of 6 breaths per minute produces a peak in the LF band making LF bar grow to the right. A growing LF bar would produce a shrinking HF bar and vice versa. Therefore the representation of the distributions does not give the user information of how well the tachogram follows the paced breathing.

Inverse effects of the TEB signal could develop if the electrodes for TEB are placed lower on the user's abdomen. An inverse effect means that the impedance is lowered when inhaling and increased when exhaling. The signal is also affected by movements such as change of body posture, coughing and sneezing. If the electrodes are placed too high, the heart activity would create peaks in the signal. This affects the scaling of the TEB signal and makes it more difficult for the user to follow the pacer curve. Figure 6 shows a TEB signal affected by spikes resulting from impedance affected by heart beats.

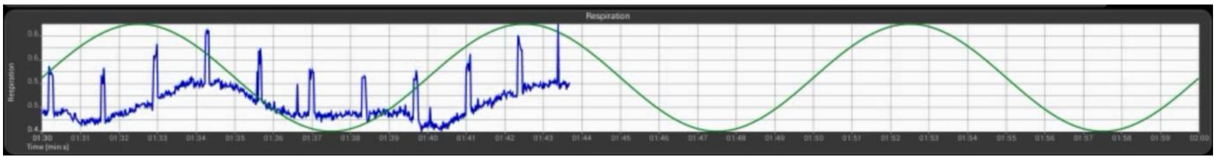

Figure 6. TEB signal affected by heart beats.

The saving of data files was set to a folder that was not easily accessible on the tablet. The recorded files were hard to find. The files were too large to store and retrieve for analysis when performing the 20 minute training period.

The peak detection sometimes stopped working for longer periods. When the peak detection of the R peaks is not working the tachogram is not displayed. This can be seen in the ECG when the red dots disappear. This situation could arise in the middle of biofeedback training forcing a reset of the training session. To reset it and making it work again an electrode replacement or a restart of the application was necessary.

3.1 Eclipse SDK

The platform used for software development was Eclipse. The Eclipse Android Development Tools (ADT) with the Android SDK bundle was downloaded from the Android development site. The continuous development tests were performed with the tablet connected to the development platform. This allows debugging by stepping forward in the software while the software is running on the tablet. The method was used when testing small portions of new developed code but could not be used for complete testing of the application. This was due to the fast continuous sending of data with the bluetooth device compared to the slow debugging process.

3.2 Software development

All of the code was written in Java since the existing code was written in that programming language. The code from the previous master thesis was available and examined. The software developed in this project was implemented into the existing code. The new code was iteratively developed with continuous functional testing.

3.3 Open GL

To develop a new interface that could visualise how the user was doing, a game view was considered. A more graphical interface on the application could cause a decreased performance of the program if it is implemented to use the central processing unit (CPU). Using the graphics processing unit, the GPU, of the tablet would let the calculations for graphics run on a different processing unit than the CPU. The graphics would not burden the CPU and the performance of the device would not decrease. Open GL (Open graphics library) is a library that targets the GPU and it comes in three versions: Open GL 1.0, 2.0 or 3.0. Open GL 3.0 is rather new and not compatible with older devices, therefore Open GL 2.0 was used which according to literature seems to be compatible with most of the devices running Android systems. [21]

3.4 Tracking memory leaks

Running an application on a device connected to Eclipse provides information about the processes the device is going through. The Logcat window, in the development platform, displays numerous activities that are performed by the running application. It is possible to filter messages by setting a tag filter which enables the developer to get an overview of a certain process. Memory leaks were discovered with this method.

3.5 Literature study

To be able to decide the duration and frequency of the training sessions with HRV biofeedback a literature study was performed. The source for finding literature was through KTH library search tool: KTHB Primo. This search tool uses the common databases for published articles within the field of medicine and technology. More information about included databases for KTHB Primo can be found on the website of the KTH library. [22]

The search phrase for the literature study search in those databases was “Heart Rate Variability Biofeedback” which yielded 606 found items. The search was limited to show only articles that were available in full text and to show publications from the year 2000 and forward. This search criterion reduced the number to 284 articles.

The articles were read briefly to identify relevant information. Articles that only included short term effects of HRV Biofeedback were excluded. Only studies conducted on a test group of healthy people with the resonance breathing methodology were included. Studies that were printed in several journals were only considered once. The title and the abstract of the article were read to decide if the article should be included. This resulted in 5 articles that were studied and summarized.

The information studied in the articles was: how the study was conducted and if the result produced long term effects on HRV. The purpose of this was to find a general idea of duration and frequency of training.

4.1 Improvements to the app

The graphical interface was improved with a prototype game view. The game mainly consists of a running pacer, a tracker and feedback when time interval between heartbeats is complying with the frequency of breathing.

4.2 Graphical interface

The pacer is a moving sine wave and the indicator is a balloon. It is the user's task to move the indicator in line with the sine wave by using breathing movements. The sine wave moves from right to left and has the period of the desired breathing frequency. When the user inhales the balloon should move upwards and exhaling causes the balloon to descend. However this is dependent on the electrode placement. If the electrodes are placed more on the abdomen, reverse effects could appear. If reverse effects appear, the balloon still moved in opposite directions when exhaling and inhaling and the effects of controlling the game remained.

When the user is performing a peak in the power spectrum that corresponds to the resonance breathing frequency stars in the background are starting to light up. As long as the user is keeping this pattern the stars will remain, otherwise they will disappear until the trend is positive again. This stimulates and indicates to the user that the process is going well. Figure 7 shows the game view.

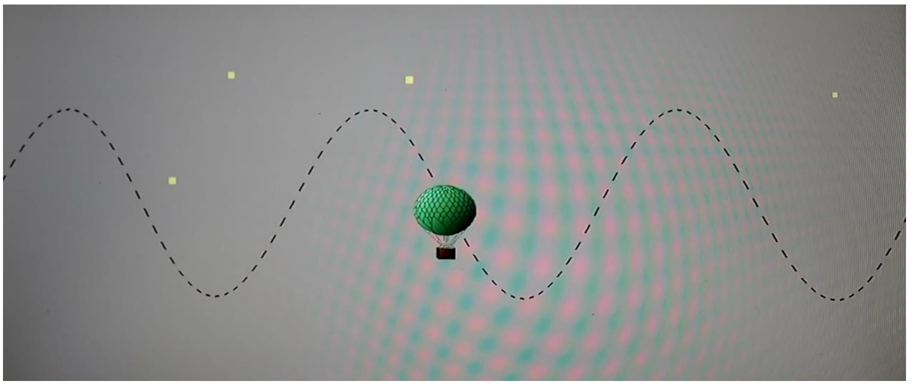

Figure 7. The game view.

4.3 Software development

This game implementation works in the main thread, in the main activity. The game view is implemented through a view flipper which is activated by clicking the button called "Game" from the first or the second view. A view flipper changes the view that the user is looking at, it does not start a new activity. This feature was implemented in order to let the user freely choose the view most suitable during HRV biofeedback.

The data and parameters that the game is dependent on are provided by the handlers that communicate with the different threads. The balloon is controlled by the same parameters that plot the respiration curve in the original view. The only alteration is smoothing and scaling to the larger window. The smoothing of the TEB signal is a solution to the signals sudden disturbance from heart beats, see figure 6. The curve that visualises the respiration is smoothed by a mean value filter. Before the new value is plotted to the curve, the last 10 values are taken into account and the mean value of these is calculated. The mean value is the new value to be plotted. In this way temporary alterations such as a chough, sneeze or heart beat alterations are not that disturbing for the user and the curve is smoother.

The saving of data has been made simpler. The application stores the TEB values, ECG values and tachogram values in two separate files that later can be examined through for example Matlab for statistical results of the training. The files were hard to find within the tablet's memory folders. This was helped by storing the files in an easily accessible folder designated for the application. The folder creates itself if it has not been created before, for example when the application is running for the first time on the tablet. Also, the saving of data is made continuously, in multiple files that contain 2 minute episodes, if the user wishes to save all data when performing the biofeedback training. There are therefore two ways of saving data: one where the user on beforehand types in the wish to save data continuously. On the other hand the user could choose to save the data after performing the training. If performing training sessions longer than 5 minutes a continuous saving of data is recommended due to the long time it can take for the files to be stored afterwards.

Some memory leaks were suggested by the Eclipse SDK. The software platform can automatically detect code that can yield memory leaks. Partly the memory leaks were reduced by implementing the handler functions in a slightly different way than before. This stopped the warnings from the Eclipse SDK. However the software implementation still contains a growing lag that causes the views to pause. After 20-25 minutes of use, the application would miss out on data frames sent by the bluetooth device and could self-terminate. This limitation of the software was discovered by the Logcat window and tagging keywords during software tests.

The peak detection became more stable when altering the threshold for detecting R-peaks. The problem with missing R-peaks was not discovered again after that.

4.4 Conclusions of the literature study

In this thesis, the area of interest is the dosage of HRV biofeedback training that produces long term effects on the HRV. The aim of this literature study was to investigate the methodology of the studies described in the articles regarding long term effects on HRV achieved by biofeedback training with resonance breathing. Short term effects, alterations of HRV biofeedback in the acute timeframe after training are not investigated in this literature study.

A summary of the conclusions of the 5 relevant articles can be found below. A summary of the results can be seen in table 1.

Often, studies related to HRV biofeedback have other primary targets than a specific dosage of training and effects on HRV, yet it is common to present HRV measurements as a secondary result for the investigated aim. For example, if the effects of HRV biofeedback on asthma are investigated, the peak expiratory flow is the primary outcome measurement investigated. However, HRV before and after biofeedback can also be presented such as reported results in the study by Lehrer, 2003.

This study led by Lehrer shows long term effects of HRV biofeedback and resonant breathing method. The outcome of the study showed a significant improvement of the baroreflex gain but no long term effects on HRV. The test subjects were followed for a 10 week period with a training and measurement session once a week. Before and after the 30 minute training and measurement session the test subjects had a 5 minute relaxation period. The participants were asked to train paced breathing for 20 minutes twice daily with longer exhalation period than inhalation. [23] Although the study did not prove any long term effects on HRV, positive effects from increased baroreflex gain were shown. This article shows positive effects on blood pressure regulation by training HRV biofeedback for 20 minutes twice a day for at least 10 weeks. The baroreflex is closely related to HRV. A more sensitive baroreflex is said to enhance HRV. [1] The authors did not discuss why they could not find any long term effects of HRV although they found an increased baroreflex gain.

In a study by Paul and Garg the effects of HRV biofeedback on psychological performance of basketball players was studied. The baseline of HRV was assessed by an initial session followed by a 10 consecutive day period with daily practice of HRV biofeedback for 20 minutes. A follow up session was also performed one month later. The participants were engaged in slow shallow breathing together with the resonance breathing methodology. The outcome showed a difference on HRV from baseline compared to the follow up session one month after the biofeedback training. Total HRV and the percentage of LF frequency in the power spectrum increased after biofeedback training and the effect persisted on the follow up session one month later. [24] This article does not reveal if the participants continued practicing HRV biofeedback until the follow up session. This article might indicate that training 20 minutes of HRV biofeedback 10 days in a row gives a long term effect of HRV for basketball players.

A pilot study by Siepmann investigated the effects of HRV biofeedback in patients with depression and healthy subjects. It did not conclude any effects on HRV in healthy individuals after 2 weeks of HRV biofeedback training 3 times a week. The participants practiced the resonance breathing for 25 minutes during these sessions. These authors suggest that a larger study must be performed and the results did not show any long term effects on HRV. [25]

Sutarto investigated workers cognitive skills and HRV biofeedback. The conclusion was that 30-50 minutes weekly training for 5 weeks produced higher scores in an attention test accompanied with a higher percentage of LF range when comparing first week of training with the last week of training. The baseline from the first week was measured before biofeedback training. It is not clear whether rest of the PSD measurements were taken before or immediately after biofeedback training sessions. [26] Therefore it is unclear if the results gave long term effects on HRV.

The effectiveness of a HRV biofeedback device called emWave Pro was investigated in a study by Whited. Participants attended 32 minutes long sessions once weekly for 4-8 sessions. The number of sessions was dependent on each participant's progress. They were instructed to practice the breathing technique with the device at home for 10 minutes each day and to send logs to the experimenter. The measurements were made in resting condition with pre-treatment and post-treatment HRV comparison. The outcome of the study did not show any significant alterations of HRV between pre-treatment and post-treatment. [27]

Table 1. Summary of the outcome from the literature study.

Author	Primary target investigated	Duration for the HRV biofeedback session	Frequency	Total duration of the experiment	Duration and frequency of homework	Long term effects on HRV	Effects on primary target investigated
Lehrer, 2003. [23]	Asthma, baroreflex gain	30 minutes	Once a week	10 weeks	20 minutes twice daily	No	Yes
Paul and Garg, 2012. [24]	Basketball performance	20 minutes	Every day	10 days	No homework was described	Yes	Yes
Siepmann, 2008. [25]	Depression	25 minutes	3 times a week	2 weeks	No homework described	No	No
Sutarto, 2010. [26]	Cognitive skills/attention test	30-50 minutes	Once a week	5 weeks	No homework described	Not clear	Yes
Whited, 2014. [27]	Effectiveness of the Biofeedback system emWave Pro	32 minutes	Once a week	4-8 weeks	10 minutes once daily	No	No

Due to the small number of studies investigating long term effects of HRV biofeedback, it is not possible to draw conclusions from the literature study.

The literature did not clearly point out any suitable answers to the questions of optimal duration and frequency of biofeedback training. Therefore, a test protocol was developed which allows for a continuation of the project in order to do experiments to find a suitable duration and frequency of the biofeedback sessions.

4.5 Test protocol

Lehrer and his research team have described a 5 visit program to teach a person the HRV biofeedback technique. [28] Lehrer has previously described a 10 session long study protocol for HRV biofeedback which is a protocol widely used by other authors in their studies of HRV biofeedback in people with illness. [2] The 5 visit program's purpose is to teach the user the technique of frequency breathing as well as estimating the breathing resonance frequency while the 10 session program previously described provides a ten week long study period.

The authors describe the 5 session program as a way to give the HRV biofeedback subject the means to significantly improve conditions such as pain, anxiety, asthma, chronic obstructive pulmonary disease, food cravings or hypertension. The article describes all visits and provides a manual of how to instruct the person under test and what parameters to consider when establishing the resonance frequency. [28]

It is suggested to follow Lehrer's protocol for the ten week program as it enables the experimenter to compare results with previous studies related to HRV biofeedback. The instructions and the procedure of finding the resonance frequency can be taken from the 5 session program. However, the procedure and protocol need to be modified to adapt the current biofeedback system.

An additional measurement of HRV 30 minutes after training sessions can be conducted in order to see if the acute effects after HRV biofeedback training still persist shortly after training.

This study protocol can be seen as a pilot study because the focus on effects 30 minutes after training has not yet been investigated. A test group of 12 people for a pilot study is described in the literature as beneficial in the perspectives of feasibility, precision about mean and variance as well as regulatory considerations. [29] A control group of 12 people not receiving HRV biofeedback would also be beneficial. In this way it is possible to see natural variations from different measurements and help to conclude where the results are significant.

The participants should be healthy and it is favourable if a wide span of ages is represented. The participants should not be informed which group they belong to, in this way the study could be conducted as a single blind study. Also, the participants must give their informed consent before taking part in the experiment.

4.5.1 Session 1 and resonance frequency estimation

Session 1 should include information and instructions of the daily homework that Lehrer's protocol also suggests. [2] The participant could in the first session try the device for HRV biofeedback and get familiar to the electrodes and different views on the tablet. Instructions for paced breathing and not breathing too deeply, in order to avoid dizziness, would be given.

Resonance frequency for each individual should be assessed during the first session as well. Lehrer's protocol for the 5 session HRV biofeedback describes how to find the participants resonance frequency. [28] The protocol contains a resonance frequency worksheet where parameters from testing different frequencies are recorded. The protocol by Lehrer suggests that the participant try breathing with the pace of 4.5, 5, 5.5, 6, 6.5 respiration cycles per minute. The device developed by KTH can only use integers for the breathing frequency. Therefore this protocol suggests to only search for the resonance frequency of 4, 5, 6 or 7 breaths per minute. The different frequencies should be tested for at least one minute in order to stabilise the values.

All the parameters in Lehrer's worksheet cannot be recorded by the device. Lehrer's article recommends that as many as possible are used. The checkpoints for evaluation of resonance frequency that comply with the developed device are described below in italic and the adjusted worksheet for assessing resonance frequency can be seen in table 2.

i) *The best phase coherence between TEB diagram and tachogram is established.*

This means that the experimenter estimates where the phase correlation between the tachogram and TEB plots are in a 180 degrees relation to each other. This estimation is done by looking at view 1 or 2 on the application while breathing. Figure 8 shows how the phase relation can be estimated.

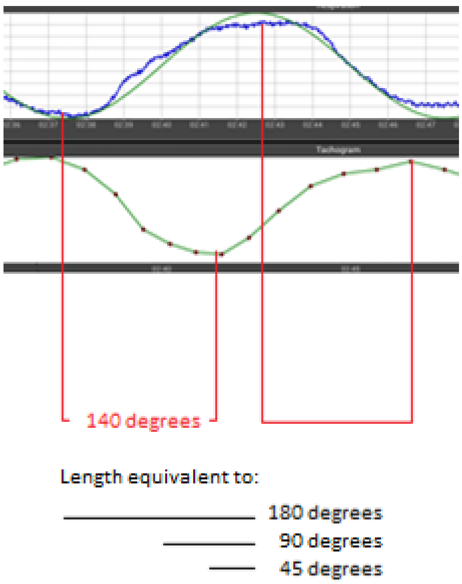

Figure 8. Estimation of phase correlation between the TEB plot and tachogram. This phase relation can be estimated to 140 degrees.

ii) *Highest LF percentage of the total spectrum is noted.*

iii) *Maximum height of peak in the PSD is found.*

A higher peak means a better coherence of the tachogram with the breathing frequency.

Table 2. Adjusted worksheet to estimate the resonance frequency.

Breathing frequency [breaths /minute]	Phase coherence between TEB diagram and tachogram [degrees]	LF percentage of total spectrum [%]	Maximum height of peak in PSD. [ms^2]
4			
5			
6			
7			

The homework would consist of training the breathing technique according to a metronome or a watch at the resonance frequency found. Lehrer's protocol involves two 20 minute sessions of homework each day. The total training of 40 minutes a day could be hard to accomplish for the test subjects as training requires active relaxation and concentration. This protocol therefore suggests 20 minutes of relaxing and resonance breathing only once a day. This modification of Lehrer's protocol is also in line with the study performed by Paul and Garg where they could conclude a long term effect on HRV with 20 minutes of HRV biofeedback training each day. [24] It is advisable to use a logbook to encourage and track the participant's activities of homework training.

4.5.2 Workflow of session 2 to 10

The following sessions are conducted in a similar manner and presented in a workflow scheme in figure 9 and could involve the following steps:

5 minutes of rest are taken before measurement of baseline. This brings the participant to a relaxed state and errors that depend on physical activity beforehand are minimised.

Next, blood pressure is measured in order to be able to evaluate if the subject has been relaxed or stressed during the HRV biofeedback. The connector, wires and electrodes could cause stressed emotions for the participant which can cause a higher blood pressure. Comparing blood pressure values before and after the training session may indicate if the subjects is experiencing stress induced by the biofeedback.

Measurement of baseline HRV before training is then performed for 5 minutes. This is the target value to be compared with the measurement 30 minutes after training. It is also possible to compare these values between sessions which may give an answer to the number of sessions needed in order to see effects on HRV.

After the baseline HRV measurement a 20 minute session of HRV biofeedback with the device is performed. The instructions for how to use the device and how to breathe have already been given in the first session but can be repeated prior to biofeedback.

Immediately after training, a 5 minute measurement can be performed to compare if the acute effects of HRV are enhanced from session to session.

After that, the blood pressure post training may be taken.

To see if the acute effect diminishes 30 minutes after training a 25 minute break is suggested with a 5 minute pause in rest at the end. During the break the participant should not perform heavy work.

The end HRV measurement is recorded during 5 minutes. This value can be compared between sessions to see if the effects of training are stronger after 10 weeks of training.

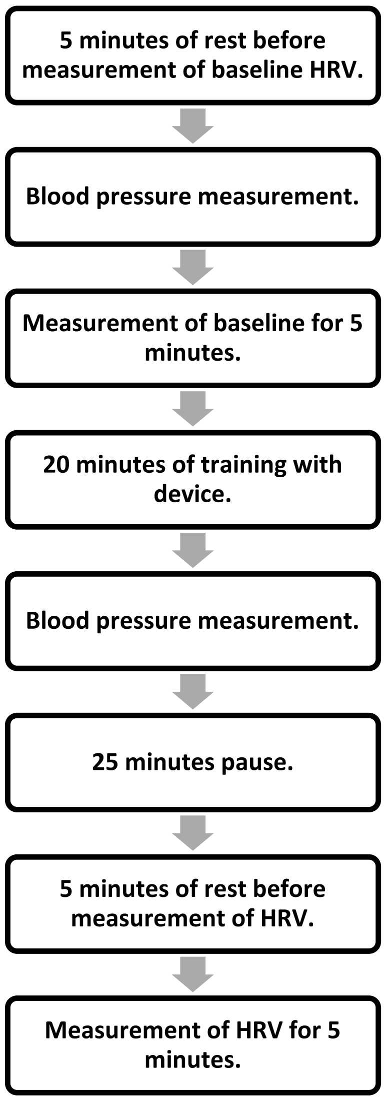

Figure 9. Protocol workflow of session 2-10.

5 DISCUSSION

5.1 Results from the literature study

Long term effects have been shown in one study by Paul and Garg [24] while other studies have not been successful in proving them. However the majority of the studies investigated showed a positive effect on their primarily outcome measure.

The articles investigated had different protocols. Therefore it is hard to make any conclusions and compare the studies with each other. If more studies were conducted in a similar way as the protocol suggested by Lehrer or the protocol suggested in this thesis, stronger conclusions may be derived.

In the study by Paul Lehrer long term effects of HRV and biofeedback were examined with the conclusion that no long term effects could be shown. However the article proved long term effects on the baroreflex gain when comparing the first and last training sessions. [23] The baroreflex is a major contributor to HRV. [1] The authors did not discuss why they could not find any long term effects of HRV.

The protocol and worksheet for evaluating the resonance frequency are only suggestions and should be tested, evaluated and adjusted if necessary before performing experiments. Moreover, it does not give a solution for performing the study single or double blinded. This is an important question to consider as placebo effects for the test group could arise. Details of how to perform a single blinded experiment should be further investigated.

5.2 The app and the software development

The application is still in a technical development phase. Before it can become a commercial product it needs to be enhanced both technically and from a user experience point of view.

The application is limited to approximately 20 minutes of use due to the fact that it accumulates too much memory from the tablet's RAM. The time it needs to complete its garbage collection, clean up memory that is no longer in use, is increasing during operation. This growing pause during garbage collection is up to 400 ms which then leads to that the app starting to miss out data frames sent by the bluetooth device. Eventually the application shuts itself down. This memory leakage is a problem if the application is to be used for a longer time than 20 minutes.

It is advisable that the application is systematically tested in smaller parts to fully identify the problem areas for the memory leakage.

The peak detection threshold was altered to remove the problem with missing R-peaks. It is advisable that the new modifications can be evaluated with a Matlab prototype to see if there are missing or double R-peaks.

Considering the user experience, the setup is difficult. The wires easily nestle up and the ECG signal can be affected by the 50 Hz from the power outlet. Wearable electrodes with shorter wires can be used which will facilitate the setup for the user. The electrodes and wires can also be implemented in garments. Also, the connections would not be so vulnerable to movements.

The graphical interface has been enhanced by a balloon and a moving pacer. The balloon travels through the air which is the element that the user is manipulating to move it. The balloon could be considered to be something joyful but it can easily be replaced by another marker in the future if desirable. The user may also choose a character that he or she finds soothing and relaxing. The OpenGL library facilitates a further development of the game with many possibilities of graphical enhancements and effects. Instead of having a sine wave there are many possibilities to use a tracked route for the balloon or the object used as a marker. For example mountains and clouds could form the pacer.

5.3 HRV as a health indicator

Many articles describe HRV to be positive if the variations in time between heart beats are large but a figure or definition of what large variations are for individuals is absent in the literature. The HRV is dependent on age and cannot be compared between individuals which make the concept of large variations vague. HRV measurements must be put in relation to numerous measurements on the same persons to determine trends of HRV and health for a particular individual. In other words, it is hard to use a single HRV measurement as a precise parameter for health conditions.

The results in the literature study did not show reliable evidence that there is a possibility for healthy adults to enhance their HRV with biofeedback. Therefore, the question whether the HRV biofeedback method can be used by healthy adults as a way to prevent sickness remains unanswered. However, in studies considering unhealthy subjects there are results of positive effects on the health by using HRV biofeedback.

The outcome of this thesis result has pointed towards that the HRV biofeedback method could be a successful intervention if a person is suffering from stress or having milder health problems. This might be a way for a patient to learn self-treatment just as physical exercise can be helpful to these symptoms. A HRV biofeedback game application might be easily accessible and a more joyful tool for self-treatment for some patients. For example, a HRV biofeedback game might be used as another treatment option for patients not following their physiotherapy training. Thus, there are reasons to believe that a HRV biofeedback game can be successful in restoring health. A game, that is freely available, might be a cost effective alternative to traditional healthcare. Also, it may lessen the burden on public healthcare.

5.4 Ethical aspects of using the app

This app is not seen as a medical device in the current state. It is advisable that information about this reach the user. Intended use is only for health purposes, not to provide a ground for diagnosis or to indicate unhealthy users. The user of the app is supposed to be a healthy individual. In the situation where a certain heart condition is present, the app will not be able to detect it. If an experimenter is present he or she may not have the clinical background and education to detect it from the ECG representation in the app.

A user might be interested to know whether or not he or she is in good health. This app will not be able to give an answer to those kind of questions. The app can only show what the user is doing, not provide an indication of the user's health condition. It is up to the user to make conclusions about his or her progress when training HRV. This must be provided in some form of information to the user before it can be released as commercial product.

If the user starts up the training by breathing very deeply, the app will adjust to those values and scale the window accordingly. The user can then be fooled to continue to breathe very deep. This can cause dizziness or for the user. The user must be provided with instructions of how to breathe in order to not cause a negative health effect or feeling of unease.

Using a test group for finding the most appropriate time interval of training will also develop situations where ethical aspects must be of concern. The persons under test must be provided with information about the experiment and informed about their own voluntary participation. The test group must also be able to understand and be able to take on decisions about participation.

6 CONCLUSIONS

The HRV biofeedback application for tablets previously developed at KTH has been enhanced by several aspects.

The main improvement consists of a new graphical interface which has been implemented as a game view to stimulate the user to biofeedback training. The simple game view has great potential to be further developed.

Other improvements involve the saving of data which now is more convenient and has options dependent on how the user choose to measure. Moreover, smoothing of the TEB curve has been done to minimise disturbances that may come from movements of electrodes, heart beats or sneezing or coughing. Also, more reliable peak detection is implemented to eliminate the problem with interruptions and restart of the application due to missing peaks.

Although the new features and improvements, the application needs to be investigated further to deal with technical disadvantages such as memory leaks. Testing and further graphical improvements need to be performed before the application can become available on the market.

This thesis has also investigated the dosage and frequency of HRV biofeedback training with the specific method for resonance breathing. There is no clear evidence in the literature of dosage and frequency in order to get a long term positive alteration of HRV. This thesis has therefore suggested a study protocol in order to evaluate the effects of training. This protocol describes the number of participants in the groups, test conditions for participants, preparation of test, duration of measurement and training.

This thesis suggest that doing experiments with this biofeedback system and the test protocol could give indication of how long the acute positive effect remains and thereby give clues to the optimum frequency and duration to train HRV to gain long-term effects.

7 FUTURE WORK

7.1 Further development

The project consisted of two parts. The programming part and the questions about the dosage of HRV biofeedback training could be split into two different areas of work, letting the both parts be further and more deeply investigated. There are many aspects that can be added to the both parts respectively.

For the programming part the game view could be developed further, a study protocol for the software could be used to evaluate the performance of the program. Also, a usability study could also be performed and the already existing HRV biofeedback systems could be compared with the one developed by KTH in order to find pros and cons with the different systems. Moreover, questions about the system as a medical device could be investigated from different perspectives.

The whole system including the Bluetooth device and wires could be evaluated from the user's point of view.

The other part of the project could also contain areas such as evaluating the methods of the studies found in the literature study. Also one can perform the study with the proposed study protocol that focuses on the questions about frequency and duration of HRV biofeedback training. The possibility of performing the study single or double blinded could be further investigated.

7.2 Experience gained and suggestions for similar project

During the work with this thesis, experience within the fields of programming and the function of HRV were learned.

The basics of programming in Eclipse were learned and the existing code was interpreted since major parts of it lacked comments or explanations. Suggestions for similar programming projects would be to learn Eclipse and Java programming in an early stage. Also, the existing code should be tested for errors before implementing the new functionality. A more experienced programmer or tester could help out with their opinions about the existing code and implementation strategies before the new program is implemented.

Concerning the literature search, there are more articles and books available within this area. This master thesis work had to limit the literature search to only use one search phrase. Other combinations of search terms would yield more hits in the database search tool used. It is advisable to be at least two persons to perform a larger literature study. In this way, there are more areas to consider as two people working together can generate more discussions compared to only one investigator.

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