Heart Rate Dynamics and Burnout

Juney Dijkstra
3365018, Game & Media Technology MSc.
Department of Information and Computing Sciences, Utrecht University

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Abstract

The purpose of this study was to detect a change in the level of burnout in a person through Heart Rate (HR) dynamics, such as HR and Heart Rate Variability (HRV) measures. Research performed so far includes detection through questionnaires and, more recently, through biomarkers such as cortisol, respiration and blood values. However, biomarker findings are inconsistent and hard to compare, likely because research has focused on single HR measurements between different people, which by themselves already vary. This thesis describes a study continuing previous work done at Philips Research, which aspires to differentiate itself from previous burnout research by combining a longitudinal study with nightly and breathing exercise intra-personal photoplethysmogram (PPG) signal measurements obtained from individuals recovering from burnout through therapy. It was hypothesised that the HR and HRV before and after recovery from burnout would have changed, while similar measurements from healthy people would show little to no difference.

This study investigated the correlation of the HR dynamics and the Maslach Burnout Inventory (MBI) scores of a group of 24 healthy participants. As expected, we found no significant difference between the two measurement weeks in the values for the HR at night, the HRV during paced breathing and regular breathing or the MBI scores. We also confirmed the existence of a small HR dip between falling asleep and waking up, and a larger HR dip between the maximum and minimum HR of the night, but we could not find any relation between the extent of this dip and the level of burnout. Furthermore, we showed that the paced breathing exercise HRV feature values were significantly different from the HRV feature values obtained during the regular breathing measurement, but again we found no correlation between the change in any of the paced breathing HRV feature values and the change in burnout level. From the exploratory analysis we conclude that the root mean square of successive differences between adjacent interbeat intervals (RMSSD), high frequency (HF) power and low frequency (LF) power may be interesting to look at throughout the night for data gathered from revalidating burnout participants in future research.

This thesis was written as part of the graduation phase for the Utrecht University Game & Media Technology master degree. The study was performed at Philips Research, Eindhoven, with supervision from Philips Principal Scientist, Dr. Joyce H.D.M. Westerink and Utrecht University professors, Dr. Dr. Egon L. van den Broek (primary supervisor and first corrector) and Dr. Ir. Robbert-Jan Beun (second corrector).

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Chapter 1

Introduction

Burning out from work has serious consequences for both the employee and the organisation they work for. Burnout can cause an increase in sick leave [6], various physical symptoms or even job turnover [48]. It is also a prevalent issue. The Central Bureau for Statistics in the Netherlands reports that between 2007 and 2011 the percentage of burned out employees increased from 11% to 13%. This is supported by similar or higher figures for specific occupations from all over the world [1, 3, 32, 36, 44, 51]. Many companies already provide burnout prevention and detection training [4, 28], because they have become aware of the potential occupational, health and financial risks of their employees burning out. Even so, burnout is not recognised as a disorder by the DSM-V [2], the most used diagnostic and statistical manual for mental disorders, or the ICD-10, the International Statistical Classification of Diseases and Health Related Problems [41].

Burnout can be described as a psychological syndrome, caused by extensive exposure to chronic interpersonal stressors at work [34]. There are multiple recurring symptoms, such as mental exhaustion, physical fatigue, detachment from work, and feelings of diminished competence [48]. Depression [35, 46] and chronic fatigue [13, 15] are most often named as comparative disorders, both of which are recognised in the DSM-V and ICD-10 documents.

An extensive (internal) literature study on burnout and burnout biomarkers performed by Philips in 2012 [14] includes an interview with an occupational health company, which clearly indicates that knowing what employees are risking burnout would help start prevention treatment sooner. They say they would like to know, even if that person would have never developed burnout, because detecting burnout at a later stage makes it much harder to recover. Therefore, it would be ideal to track the 'burned out' state of a person at any given time, and if an increase is detected, to start a prevention trajectory. For example, a person becoming gradually more stressed, or even burned out, due to work could be made aware of this fact with the use of persuasive technology (such as a health tracking app). A review of studies on mental health apps concludes that 'mobile apps for mental health have the potential to be effective in reducing depression, anxiety, stress, and possibly substance use' [17]. The apps coach people on how to change their lifestyle; for example by teaching them how to manage their time better and take more breaks in between stressful tasks. A health tracker could then also provide feedback about whether they are gradually becoming less stressed and are returning to a healthier lifestyle. By intervening early, the effects of stress could be mitigated and a state of burnout may never even be reached.

The techniques most used to diagnose burnout heavily rely on self reported data obtained from questionnaires, such as the Maslach Burnout Inventory (MBI) [34], the Shirom-Melamed Burnout Questionnaire (SMBQ) [33] and the Copenhagen Burnout Inventory (CBI) [30]. The MBI, and in particular the Maslach Burnout Inventory - General Survey (MBI-GS), is most commonly used. There are two other variations of the MBI which are more specific in their application, the Maslach Burnout Inventory - Human Services Survey (MBI-HSS) and Maslach Burnout Inventory - Educators Survey (MBI-ES). The MBI consists of three scales: Emotional exhaustion, depersonalization and personal accomplishment, of which emotional exhaustion is considered the core dimension [54]. Researchers have used the MBI for various purposes, such as to gain knowledge about gender differences in relation to burnout [6], to examine the relation with job performance [54] and to discover early predictors of job burnout or disengagement [35].

As lengthy questionnaires are quite time consuming, it would be a hassle to fill these in regularly, which would be required to keep track of a person's burnout level. Therefore, it would be ideal to use an objective, biological signal, 'biomarker', as an indicator of changes in the burned out state of employees. Attempts to find biomarkers for burnout have already been made, and are highly varied in their approaches. Investigation of the biomarker potential of cortisol levels, the autonomic nervous system, the immune system and many others have already been tried [13]. The available literature suggests Heart Rate (HR) and Heart Rate Variability (HRV) in particular as promising indicators of burnout [29, 37, 39]. HRV 'has become the conventionally accepted term to describe both instantaneous heart rate and RR intervals' [40], and an RR interval is the amount of time between two similar points in successive heart beats. The interval between heart beats is also commonly referred to as the interbeat interval (IBI).

Multiple studies show that the HR of high-trained athletes is lower than that of healthy people [21], and the HR of healthy people tends to be lower than that of people suffering from burnout [15] or similar disorders [8]. De Vente et al. [15] investigated the differences in basal physiological values between burnout patients and healthy controls, measuring their resting HR, blood pressure and cortisol. They found burnout patients had a higher resting HR than healthy controls. Similarly, a study by Boneva et al. [8] found patients of the comparative disorder chronic fatigue syndrome had a higher resting HR than their matched controls.

Night time HR has also been suggested as a potential indicator of changes in health [23]. As shown by Ben-Dov et al. [7], (the lack of) a dip in the HR measured at night can be used as additional prognostic information for all-cause mortality. Night measurements are presumably the most useful because at night there are no external factors (such as exercise or stress) to influence the data, making it easier to compare different nights and discover trends. Additionally, the body uses sleep to rest, which includes bringing the physiological system back to its resting state.

The European Society of Cardiology defined a lot of HRV measures [40] and many have been looked into for their biomarker potential [13]. Multiple time and frequency domain variables show potential, such as in the time domain the average IBI length, the standard deviation of IBIs (SDNN) and the root mean square of successive differences between adjacent IBIs (RMSSD) [29, 39], and in the frequency domain the low frequency (LF) and high frequency (HF) power of the photoplethysmogram (PPG) signal [29, 37]. Sloan et al. [52] measured the effect of mental stress on cardiac autonomic control throughout the day in healthy participants. They looked at the length of the IBI and the power distribution at stressful times in a 24 hour period and found the IBIs to be shorter, HF power to be lower and consequently the ratio between LF and HF power to be higher during stress. These results are supported by a study done by Brosschot et al. [10], who looked at the physiological consequences of stress and found stress is reflected in a higher average HR and shorter RMSSD throughout the day and following night. Barrios-Choplin et al. [4] show similar results in a reversed study, measuring the effect of a stress reducing training on various physiological variables, including the HR standard deviation and power distribution. They found a significant decrease in total power and HR standard deviation, supporting their hypothesis that a reduction of stress would cause a reduction in resting autonomic activity.

The effect of Reiki, another stress reducing training, on various physiological variables such as IBI measures, cortisol, body temperature and MBI score was looked at by Diaz-Rodriguez et al. [16]. They found a significant difference in the SDNN and LF power of the IBIs between the trained and control groups, again indicating the potential of HRV measures. This potential is emphasised by multiple studies done measuring the physiological variables of medical professionals. In 2012, Dutheil et al. [19] found that HRV was lower and the circadian rhythm disturbed during shift work; but also, that these were restored on days off. Natalya et al. [39] and Kotov et al. [29] both measured the differences in HRV parameters between different stages of burnout in medical professionals, and both found these were particularly visible between early stages of burnout.

Breathing exercises also show HR differences between people that are stressed and people that are not. Respiratory sinus arrhythmia, the rhythmic fluctuations of electrocardiographic IBIs observed in healthy resting humans, is found to be smaller during rapid breathing, and larger at slower breathing rates [20]. A study on resonant breathing training for stress reduction [53] showed the training to be useful for the reduction of negative emotional symptoms, and this was supported by a significant improvement in HR physiology.

Overtraining (or 'athlete burnout') is another branch of burnout research that supports the use of HR and HRV measures. Research showed early on that highly-trained athletes have a lower resting HR than sedentary controls [21], and HRV appears to be a good indicator of cumulated training load [42, 45]. Overtraining, however, seems to cause a decrease in HRV [57], similar to the effect of 'regular' burnout. Additionally, Hynynen et al. [26] showed that overtrained athletes have lower LF power in a standing test. Similarly, Mourot et al. [38] tried to characterise the HR profile of athletes suffering from overtraining and found that differences in HRV profiles could be highlighted by a short tilt test. They show the profiles can be found both in linear and non-linear measures, suggesting time and frequency variables are both viable.

Therefore, it seems that there is a definite potential in HR and HRV measures to be able to predict burnout and other health related issues. Sadly, the methods used to measure HR data and results found are often highly incomparable, and when they can be compared, the data turns out to be inconclusive [13, 22]. It can be argued, however, that this may be caused by the studies measuring the HR between people [10], having only single measurements [29] and often only featuring healthy participants [24, 25].

In this study, we try to find out whether or not full PPG signal within an individual allows the detection of a change in burnout level. In particular, it is attempted to find a biomarker in the HR dynamics, such as HR and HRV measures, of a person. This is done by analysing longitudinal changes within people. Based on the above discussed literature, this has led us to multiple hypotheses.

1. A higher MBI-GS score on the Exhaustion and Cynicism scales, and a lower MBI-GS score on the Personal Efficacy scale can indicate burnout symptoms or even clinical burnout [47]. During burnout, we expect the Exhaustion and Cynicism scores to be much higher and the Personal Efficacy much lower than the scores after recovery within individual burned out people (e.g. they are healthy enough to go back to work). Within healthy people, we expect the MBI-GS score difference between measurements to be non-significant.

2. A night time HR dip is considered a sign of good health [7]. We expect no significant HR dip will be detectable during the night in the data collected from burned out people before recovery, and expect to see the return of such a HR dip after recovery. In healthy people, we expect this HR dip will exist and we expect there will be little difference between measurements.

3. Breathing exercises cause large fluctuations in IBI lengths in data collected from healthy people [20]. We expect these fluctuations to be smaller in the data collected from burned out people before recovery than in the data obtained from healthy people, and expect these fluctuations to be similar to data collected from healthy people after recovery. In healthy people, we expect these fluctuations to be large and we expect to see little difference between measurements.

4. The HR of burnout patients is higher [15], and the HRV lower [29, 39] than that of healthy participants. Therefore, we expect a change over time in the HR and HRV variables obtained between measurements to correlate with a change over time in MBI-GS scores.

In general, we expect the MBI-GS score (hypothesis 1, 4) and HR dynamics (hypothesis 2, 3, 4) of burned out people to change after they have recovered. At the same time, we expect the MBI-GS score and HR dynamics of healthy people to stay similar between measurements.

Chapter 2

Methods

Our goal is to identify HR biomarkers that indicate a decrease in burnout from HR data. This study is part of a larger project at Philips Research to find a biomarker to detect burnout. In preparation for the present study, a series of pilot studies were performed by MSc. student Dornostup [18] to look for potential issues in this kind of study. The most important issues that were signaled were with regards to potential loss of data, which were designed around in the creation of the present study.

In this chapter, more details are presented on the study design, after which more information is given about the participants, materials, methods/procedure and the chapter concludes with an overview of the analysis.

2.1 Design

Two sets of unobtrusive measurements of the PPG signal of 20-40 (recovering) burnout patients were planned. The measurements took place during the first and last week of an 18-week burnout therapy. The same measurements were planned for a healthy participant group of the same sample size, to see if there were clear differences in the HR dynamics between the burned out and healthy states of recovering burnout patients, and the HR dynamics of healthy people over the same amount of time.

The measurements took place at night, starting when the participants got in bed, and stopping shortly after the participant got out of bed. Participants were asked to remain seated on the edge of the bed for a few minutes after waking up to obtain a baseline measurement of their waking resting HR. This was followed by a paced breathing exercise, where participants breathe a set amount of times per minute. They also fill in a questionnaire twice a day, and multiple questionnaires at the end of each measurement week.

The study design was approved by the Internal Committee Biomedical Experiments (ICBE). The full process and an overview of the documents that had to be handed in can be found in Appendix A.

2.2 Participants

The study population intended to involve two groups of 20-40 participants, of which one group consisted of burnout therapy patients, and one of healthy participants. The burnout therapy patients were referred to us by CIRAN, a revalidation centre that offers multiple revalidation therapies at a fixed length of 18 weeks. This study was completely voluntary and opt-in. Potentially suitable candidates received a flyer with contact information and could contact us if they were interested. Participants were promised financial compensation proportional to the percentage of the study completed, up to a maximum of €50. Travel compensation was also offered: actual cost to a maximum of public transport costs. Healthy participants were recruited at Philips Research by means of flyers and general invitation e-mails, and no individual active recruitment was done. Philips participants did not receive financial compensation.

Subjects from both groups received an informed consent prior to participation and were given sufficient time to consider. After the participants had decided to participate, a first meeting was scheduled in which the informed consent was signed.

There are a few inclusion and exclusion criteria. All participants had to be:

- between 18 and 60
- able to read and understand English

And a burnout patient also had to be:

- at the start of their burnout therapy

Any participant was excluded if they:

- might be, or were, pregnant
- suffered from any chronic disease, such as diabetes, cardiovascular and pulmonary diseases

Furthermore, for the specific groups:

- healthy participants could not have a clinical burnout score as measured by the MBI-GS in both measurement weeks
- burnout patients referred to us by CIRAN could not be Philips Research employees

This study involved patients that were suffering from burnout, which means they belonged to a vulnerable group. CIRAN provided confirmation that the research would not impose on their treatment in such a way that the therapy would be in danger of success.

Participants could opt to withdraw from the study at any time without the need to give a reason. If a participant withdrew from the experiment before the second week, their data was omitted from analysis. If a participant withdrew during the second week, or data was missing, the data was manually checked to see if it was still representative and if there was enough data to perform the analysis.

2.3 Materials

This section gives an overview of the different materials that were used in this study, including the measurement devices, the paper diary, the weekly questionnaires and additional materials.

2.3.1 Measurement Devices

Multiple measurement devices were considered for this study, though only the devices actually used for the study are described in this section. The full overview of devices and the reasoning for our choice to use the modified MIO wristwatch can be found in Appendix B.

The Alpha Watch by MioGlobal is a commercially available Optical Heart Rate Sensor, which measures the HR at the wrist (see Figure 2.1). The 'Optic Heart Rate Logging Device' used in this study was a MioGlobal Alpha Watch, modified by Philips to record the full PPG signal, plus allow the use of the built-in accelerometer and storage of the recorded data on the device. The watch records four interleaved 16 Hz PPG signals, resulting in a combined 64 Hz pulse signal. This device is a prototype and was approved by the ICBE with a Declaration of Conformity for this test.

Figure 2.1: A MioGlobal Alpha Watch

All participants also received a laptop. The laptop contained a program to be used as part of the morning session, which gave instructions for two breathing exercises and handled the daily download of the recorded data from the watch that was worn at night. Details on the program can be found in Appendix C.

2.3.2 Diary

Participants received a paper diary with instructions for the daily procedure and a questionnaire for them to fill in twice a day. The instructions would comprise the daily morning and evening instructions and accompanying help images. The full diary can be found in Appendix E.

The daily questionnaire participants were asked to complete every morning and evening was the Self-Assessment Manikin (SAM) scale [9]. The SAM is a 5-

point bi-directional Likert scale with images to indicate your current emotional state on Pleasure, Arousal and Dominancy scales. In addition to the regular SAM, Energy, Stress and Sleep quality SAMs were added to the base SAM scales. The Energy and Sleep quality SAMs were created for internal Philips Research work [27]. The Stress SAM was created specifically for our study on stress and burnout, but was also inspired by the same internal report [27]. Participants were asked to fill in these scales twice a day, with the exception of the Sleep Quality questionnaire, which was only filled in after waking up. In the questionnaire, they marked their current emotional states by checking one of the five images per scale.

In the diary, the time of waking up, sleeping in and starting both exercises could be noted. An example of a completed morning and evening questionnaire can be found in Appendix E.

2.3.3 Weekly Questionnaires

The four weekly questionnaires the participants were asked to fill in at the end of both test weeks were the MBI-GS [34], Warwick-Edinburgh Mental Well-Being Scale (WEMWBS) [56], the Perceived Stress Scale (PSS) [12] and the Pittsburgh Sleep Quality Index (PSQI) [11]. The full questionnaires can be found in Appendix E. The questionnaires were filled in at the end of the test week to make sure the answers reflected upon the test week in particular.

2.3.4 Other Materials

Participants were recruited with the use of flyers, which were handed out to burnout patients by CIRAN, and distributed in Philips coffee areas for the healthy participant group. As soon as participants indicated they were interested in participating, they would receive the consent form by e-mail. The flyers and consent form can be found in Appendix E.

2.4 Procedure

As soon as a participant had indicated their interest in participating, they would receive the consent form by e-mail. Upon agreeing to participate, a first meeting would be planned, in which the consent form would be presented on paper and signed. Demographic information (and optionally, current medication) would be noted, and then the study would be detailed and the instructions for the devices given. The participant would be walked through the instructions once, and would also receive the diary containing the instructions and daily SAM questionnaires. At the end of each measurement week, another meeting would take place for the participants to return the devices. They would then also be asked to fill in four questionnaires, the MBI-GS, WEMWBS, PSS, and PSQI. These questionnaires were conducted through a Philips approved survey site, which offered survey design tools and allowed downloading of the survey results.

The weekly procedure for test weeks can be found below, with the second week measurements taking place 18 weeks after the first measurement week and being almost identical to the first week.

- First meeting - Sign consent form (first week only). Provide information about age, gender, average hours of sleep per night (first week only) and optionally, current medication. Receive detailed information and instruction manual about the study protocol and details on the use of the devices.
- Throughout the week - Measure PPG signal with modified MIO Alpha wristwatch (dominant arm) for 7 nights, complete the modified SAM every evening and morning, perform breathing exercise in the morning. Otherwise, participants were asked to live as they usually would.
- Second meeting - Return devices and fill in weekly questionnaires.

The breathing exercises included a regular breathing exercise and a paced breathing exercise, each lasting 6 minutes. Both were performed directly after waking up. The regular breathing exercise instructions asked the participants to sit upright and breathe regularly for 6 minutes to provide a baseline measurement. The paced breathing exercise instructions asked the participants to sit upright and breathe according to the instructions shown on the laptop screen, which told the participants to breathe in and out for 5 seconds each, resulting in 6 breaths per minute, also for 6 minutes. For this, two small Java programs were developed. Screenshots of the two programs are found in Appendix C. Code is available upon inquiry. The wristwatch and laptop process was usability tested in a think-aloud session with two healthy participants.

The modified MIO Alpha wristwatch has storage space for about 8-9 hours of data, which is generally enough to record a full night of data, plus breathing exercises. If a participant indicated they sleep longer than 8-9 hours a night on average, they would receive two MIO wristbands. One MIO would be used to record the night data, and one would be used to collect the data for the breathing exercises. As we collected 7 nights of data, the laptop was provided to offload and consecutively erase the data from the watch in the morning. The collected data was encrypted and could not be read from the laptop after being downloaded from the watch.

2.5 Data Acquisition & Analysis

This section gives details on the additional steps taken to prepare the data to be displayed and analysed. The diary and questionnaires are looked at first, followed by the measurements obtained from the watch.

2.5.1 Diary and Questionnaires

The data obtained from the paper diary, the daily questionnaires, and additionally noted timestamps, were entered in a spreadsheet per participant per night. For the SAM questionnaire, the scales were converted to a 1-5 rating.

The results from the weekly questionnaires were processed according to each scale's instructions to get the actual scale data for each participant. For the

MBI-GS, this involved summing the results of different questions to obtain values for all three MBI scales; Emotional Exhaustion, Depersonalisation, and Personal Efficacy. For the PSQI, this involved formatting the submitted time data to all be in the same time format, assigning values to semi-open question responses, assigning values to pre-set question responses and adding, subtracting and dividing the resulting numerical values to obtain the scale scores. For the PSS, this involved changing the pre-set question responses to numerical values and reversing various questions. For the PSQI, this involved changing the pre-set question responses to numerical values.

2.5.2 PPG and Accelerometer Data

The measurement included the retrieval of full PPG and accelerometer signals for the complete night and throughout the breathing exercises. This section shows what the raw PPG and accelerometer signal data looks like and how it was processed in preparation for the analysis.

2.5.2.1 PPG signal

The obtained signal, a PPG, shows the amount of light reflected back through the skin (which varies as blood passes through veins). In our case, this was measured at the wrist.

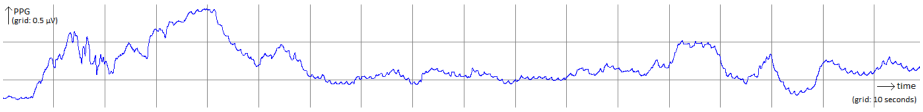

Figure 2.2: A sample PPG signal over 180 seconds, where the x-axis indicates the time passed, and the y-axis the amount of light absorbed by the skin.

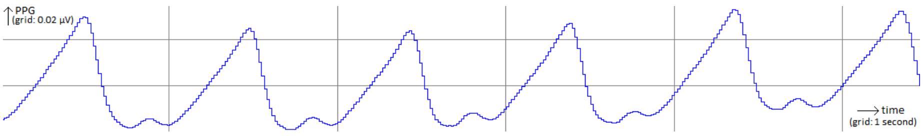

Figure 2.3: Zoomed in example of the PPG signal over 5-6 seconds, where the x-axis indicates the time passed, and the y-axis the amount of light absorbed by the skin.

The PPG signal takes a wave form, as can be seen in Figure 2.2. Zoomed in, the pulse ideally looks like Figure 2.3. In the signal, each peak is detected by means of a second order derivative method. The interbeat intervals are then calculated as the time between two consecutive peaks. If the person moves a lot, however, the PPG signal will be distorted and it becomes much harder to accurately detect interbeat intervals.

2.5.2.2 Accelerometer signal

The accelerometer data consists of three signals based on the x-, y- and z-direction of the watch. It is very sensitive to movement, especially before going to bed and after getting up, or even repositioning during sleep, as can be seen in Figure 2.4 (only shows the X-coordinate, as the Y- and Z-coordinate traces are very similar).

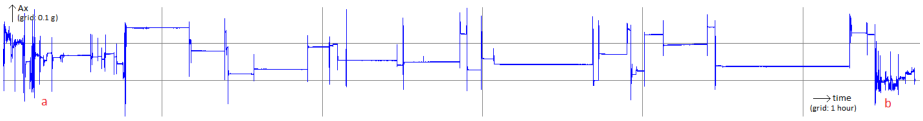

Figure 2.4: X-coordinate accelerometer signal for a full night, including getting in bed (a) and getting up (b). The Y- and Z-coordinate traces are very similar to the X-coordinate signal and are therefore omitted from this example.

From the times the participants wrote down in the paper diary for waking up, getting up and the start of the breathing exercises, it became clear that the accelerometer data clearly indicates the separation between the breathing exercises and the actual night's sleep, as shown in Figure 2.5.

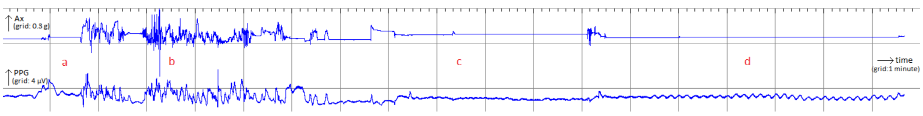

Figure 2.5: X-coordinate accelerometer signal (top) and accompanying PPG signal (bottom) showing waking up (a), getting up (b) and the two breathing exercises (c, d). The Y- and Z-coordinate traces are very similar to the X-coordinate signal and are therefore omitted from this example.

2.5.2.3 Signal Processing

After being downloaded from the laptop, the raw data files were converted into a file containing the PPG and accelerometer signal data (CMP) recorded at 16 Hz and an HR file recorded at 1 Hz, which held the output of a robust HR averaging algorithm and an accompanying Heart Rate Quality (HRQ) value. The HRQ ranged from 1 to 4, where 4 is the best. The HRQ assigned a quality rating to every reported HR, based on how much the participant moved according to the accelerometer data, and was determined by a Philips internal algorithm which combined the HR and accelerometer data. Philips internally defined a HRQ of 4 as the minimum requirement to get accurate IBI values for HRV calculations, 3 is considered reliable enough for HR calculations and 2 or less is considered too unreliable to calculate any values from.

As soon as the 7 nights of data files per participant were identified, they were processed in various ways to obtain the relevant variables. First, the CMP and HR files were combined so the signal could be graphically displayed in an EDF-browser program [5]. A Java program was developed to calculate the rolling mean, minimum, maximum, average of the minimum and average of the maximum of the HR over a three minute interval to get an impression of what the HR file data looked like. Code is available upon inquiry. The CMP files were also separately processed with a Philips internal IBI algorithm, which is still in development and may or may not be published at a later date. The results from the IBI algorithm were then processed with a sleep algorithm, with an interval selection program and a feature selection program. These are detailed in the next sections.

2.5.2.4 Sleep algorithm

Philips internally developed a binary sleep/wake classifier, which uses the output from the Philips internal IBI algorithm. The classifier uses the calculated HR and the accelerometer data to assign an activity value per 30 seconds of data, reporting whether the participant was asleep or awake at that time. The classifier was tested to have a mean error of 7.5 minutes for the accuracy of the detection of sleeping in and waking up. It is still in development and will be published at a later date.

2.5.2.5 Interval selection

With the sheer amount of data available it was decided that to compare the nights, we would use intervals of data around specific marker times. These marker times would indicate certain times of the night (e.g., the time of getting in bed or falling asleep). With the use of the graphical representation of the PPG, accelerometer, HR and HRQ data, plus the sleep/wake classification, the marker times were manually placed for each of the nights. The calculation of HR and HRV features requires an interval of at least 3 to 5 minutes of data to be used to get accurate values [40]. After analysis of our week 1 data and based on the minimum interval length recommended by the European Society of Cardiology [40], we chose an interval length of 3 minutes to get a reasonable percentage of usable intervals from the gathered data (see Figure 2.6). The selection of an interval depended on the HRQ, and the HRQ was not always high enough at marker times. Therefore, a time frame was decided upon around the marker time in which we would look for a suitable interval. The markers and the time frames in which we looked for a suitable interval are as follows:

1. Shortly after going to bed (time frame: +10 minutes)
   Placement was done by visually analysing the accelerometer data. The marker would be placed when the accelerometer data showed the participant stopped moving (e.g. got in bed).

2. Shortly after falling asleep (time frame: +10 minutes)
   Placement was done by analysing the sleep/wake classified data, and taking the first epoch that reported the participant to be 'asleep' that was not followed by a period of 'waking' in the next twenty epochs. In ambiguous cases, these were checked against the times reported in the diary.

3. Minimum of the night (time frame: -5, +5 minutes)
   Placement was done by taking the minimum HR value between falling asleep and waking up (markers 2 and 5). All epochs where the participant was reported to be awake in the middle of the night were excluded with a margin of +/- 7.5 minutes from minimum HR selection.

4. Maximum of the night (time frame: -5, +5 minutes)
   Placement was done by taking the maximum HR value between falling asleep and waking up (markers 2 and 5). All epochs where the participant was reported to be awake in the middle of the night were excluded with a margin of +/- 7.5 minutes from maximum HR selection.

5. Shortly before waking up (time frame: -10 minutes)
   Placement was done by analysing the sleep/wake classified data, and taking the last epoch that reported the participant to be 'asleep' (before getting up). In ambiguous cases, these were checked against the times reported in the diary.

6. Shortly before getting out of bed (time frame: -10 minutes)
   Placement was done by visually analysing the accelerometer data. The marker would be placed when the accelerometer data showed the participant started moving (e.g. got up).

7. During regular breathing exercise (time frame: within 6 minute exercise)
   Placement was done by visually analysing the accelerometer data. The marker would be placed when the accelerometer data showed the participant had gotten up, moved around a little, then went reasonably still again (e.g. sat down, started the laptop and started the baseline measurement).

8. During paced breathing exercise (time frame: within 6 minute exercise)
   Placement was done by visually analysing the accelerometer data. The marker would be placed when the accelerometer data showed the participant had reached for the laptop to close the baseline measurement and pressed enter to start the breathing exercise.

Interval	1	2	3	4	5	6	7	8
Placed in a total of ... nights	159	142	145	145	134	148	106	108
Percentage of total nights in which an interval of 3 minutes could be found	99%	98%	100%	100%	96%	96%	69%	71%

Figure 2.6: Percentages of time frames around markers that allowed an interval of 3 minutes per marker for measurements of healthy participants in week 1.

Ideally, the markers would be placed as in Figure 2.7 (a); but, quite often, marker 2 and 5 fall within the 10 minute time frame for markers 1 and 6 (e.g., people fell asleep shortly after going to bed, and got up shortly after waking up). To get an interval as close to the time of getting in bed and getting up as possible, the first and last possible large enough interval were chosen respectively for markers 1 and 6. To make sure the participant was really asleep in the interval chosen after falling asleep and before waking up, for these the last and first possible large enough interval were chosen respectively for markers 2 and 5. This means the selected interval still falls within the 10 minute time frame, but with a preference towards earlier or later in the time frame, which is illustrated in Figure 2.7 (b). Even with with these restrictions on how often an overlap could occur, the chance still existed that some intervals would overlap, but as this ended up only happening in 0.5% of all placed intervals and the HR and HRV values for these intervals would not be compared with each other, this was disregarded.

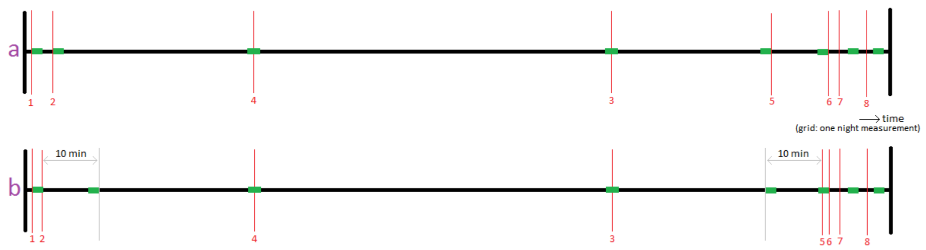

Figure 2.7: Two sets of marker placements, where red indicates a marker time and green are the selected intervals. a) Ideal marker placement for a single night's measurement. b) More realistic marker placement and alteration of preferred interval selection for markers 2 and 6. NB: Markers 3 and 4 could be found anywhere between markers 2 and 5.

A Java program was developed to automatically select 3 minute intervals of data within the mentioned time frame based on the HRQ variable. These intervals were selected such that:

- it fell within the appropriate time frame for the marker time, and for markers 1, 5, 7, and 8, as close to the marker time as possible, and for markers 2 and 6, as far from it as possible (but still within the time frame)
- the HRQ was 4 for the full interval of 180 seconds, as we expect no reliable HRV parameters from traces with lower quality

The algorithm for the first marker can be found in Appendix D, code is available upon inquiry. The algorithm for the other markers is similar, but tweaked based on the size of the time frame, the preferred location of the interval within the time frame (different for markers 2 and 6) and the calculation of the starting time of the time frame in which an interval could be searched for (different for markers 5 and 6).

2.5.2.6 HR and HRV features

The output from the internal IBI algorithm was used to calculate a wide variety of HRV parameters, of which the most commonly used ones as defined by [40] were selected. As previously done by Redmond et al. [43], the selected variables were calculated every 30 seconds over an interval of 3 minutes, and are as follows.

Time domain measures determine the instantaneous HR at any point in time, or the intervals between successive heart beats [40]. The measures we selected to look at were:

- the average HR:

$$\overline{HR} = \frac{1}{N}\sum_{i=1}^{N} HR_i \tag{2.1}$$

with HR_i being the HR per minute for the i'th IBI of N, and with RR_i being the i'th IBI of N:

$$HR_i = \frac{60000}{RR_i} \tag{2.2}$$

- the average IBI:

$$\overline{RR} = \frac{1}{N}\sum_{i=1}^{N} RR_i \tag{2.3}$$

- the SDNN:

$$\sqrt{\frac{1}{N}\sum_{i=1}^{N}(RR_i - \overline{RR})} \tag{2.4}$$

- the RMSSD:

$$\sqrt{\frac{1}{N-1}\sum_{i=1}^{N-1}(RR_{i+1} - RR_i)^2} \tag{2.5}$$

It should be noted that the task force of the European Society of Cardiology [40] raises the issue of SDNN measures being inappropriate to compare between recordings of different durations. However, as we calculate these values over intervals of 3 minutes, the recordings being compared are all of identical length.

Frequency domain measures provide the basic information of how power is distributed as a function of frequency [40]. The frequency distribution of a signal is the result of a spectral analysis (e.g., with a fast fourier analysis, see Figure 2.8). The total power of the individual frequency bands is calculated as $\int_a^b pdf(f)\,\mathrm{d}f$, where *pdf* is the power density function for example calculated with a fast fourier analysis, f is the frequency, a is the lower frequency limit, and b the upper frequency limit belonging to that frequency. The measures (with their respective frequency limits) we chose to look at, are those suggested by [40] for short sections of data. These were calculated as by Teich et al. [55], as the log-ratio of each frequency band. This means the power in each frequency band was divided by the total power in all other frequency bands and the natural logarithm was then taken.

- VLF, very low frequency ($a = 0.003, b = 0.04$; Hz)
- LF, low frequency ($a = 0.04, b = 0.15$; Hz)
- HF, high frequency ($a = 0.15, b = 0.4$; Hz)
- LF/HF ratio (calculated as $\frac{LF}{HF}$)

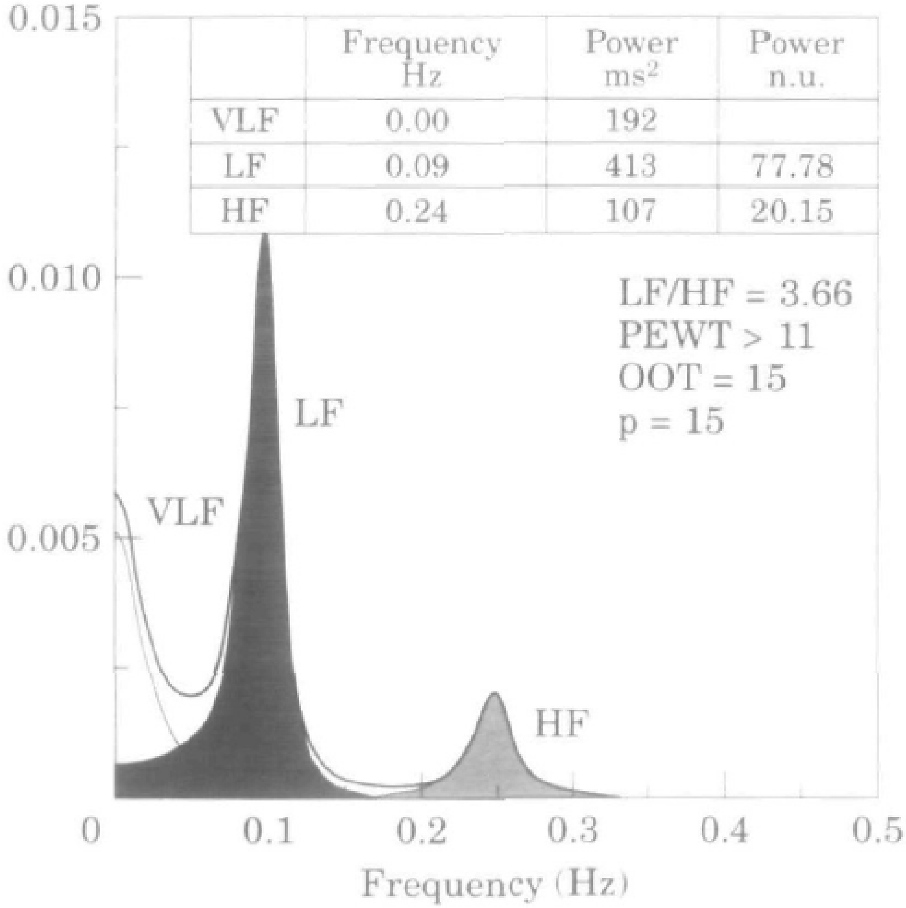

Figure 2.8: Power distribution as a function of frequency of a sample input signal of 5 minutes, divided in three frequency bands; VLF, LF and HF [40].

2.5.2.7 Feature selection

The timestamps for the selected intervals were all set at the start of the 3 minute interval, and the algorithm that calculates the HR and HRV features calculates them over the 90 second before, and 90 seconds after the timestamp. This meant the timestamps of all markers had to be moved (by +1,5 minute) to the middle of the interval, to be sure the appropriate interval was used in the calculation.

Additionally, for markers 1, 6, 7, and 8 the marker times were selected precise up to the second. However, the internal IBI algorithm only reports HR and HRV values every 30 seconds. This meant the times had to be bucketed to the closest 30 second epoch.

A Java program was written to perform both of these tasks, after which for every marker interval, the HR and HRV variables were filtered from the full night's data. Code is available upon inquiry.

The collected variables were then analysed through Repeated Measures MANOVA, One Sample T-Tests, Paired T-Tests and bivariate correlation analyses with the use of statistical program SPSS.

Chapter 3

Results

This chapter gives an overview of the results from the dataset obtained in this study. First, the missing data is discussed, followed by an overview of the definitions used and a short summary of the obtained data to give an impression of what it looks like. Then, the results of the analyses done in support of the hypotheses are shown and the chapter concludes with the results of the exploratory analysis performed afterwards.

3.1 Missing Data

Along the way, we found out that the summer months are not ideal for the recruitment of burnout participants and due to time pressure, we were only able to measure the first week of 6 burnout participants, with the second measurement week falling outside of this study. The collection of data from burnout participants as defined by the design of this study will be continued by Philips after this study is concluded. The burnout participants are matched by age and gender to healthy participants. For the burnout and for their age and gender matched healthy participants, the second week measurement will take place as scheduled after 17-19 weeks.

As the second measurement week for the burnout participants fell outside of this study and more burnout participant data would be collected after this study was finished, their first week measurement data was excluded from this study. The data used for analysis in this study was limited to a group of 24 healthy participants, and due to time pressure, the interval for these (unmatched) participants was reduced to 11-13 weeks.

The data was collected for two weeks of 7 nights per participant. The measurement started when the participant went to bed, and ended after the second breathing exercise was finished. With 24 participants, this resulted in 336 possible nights of data. Due to personal circumstances of the participants, 26 nights were not recorded. Due to a defective MIO, 32 nights consisted of mainly fragmented data, which meant some parameters could not be calculated for them and for 18 of these nights, it was impossible to use the data at all. In 23 cases, participants slept longer than 9 hours, which means the recording cut off before the breathing exercises started, so for these nights the breathing exercise recordings were lost. This means a total of 255 recordings were fully used in the analysis, and 37 were partially used in the analysis.

Additionally, because of a loss of connection between the skin and the MIO watch due to movement in sleep, gaps appeared in data throughout the night. These gaps ranged from a few seconds to hours and occurred in a lot of nights. We expect these gaps are most frequently caused by the MIO not being strapped on very tightly (which causes discomfort at night and was therefore advised against by CIRAN). Consequently, when a participant moved at night (turned over, repositioned their arm under their pillow, etc.), the MIO would move a fraction and the different angle meant the reflected light could no longer be picked up by the MIO. It is a general problem, as 60% of nights had gaps, and these gaps occurred for 87.5% of the participants. If a night had gaps, it would on average have 2-3 gaps. Gaps range between 1 second and 4 hours, and their average, median and mode length are 9.6 epochs, 1 epoch and 1 epoch respectively, where 1 epoch covered 30 seconds. This means the average gap is 9.6 / 2 = 4.8 minutes, but over half of all gaps are 30 seconds or less. Consequently, this means we are unsure of the reliability of the variables obtained for the minimum/maximum intervals of the night.

For the weekly questionnaires, 6 people forgot to enter a reply to single questions in the MBI or WEMWBS. Of these, 3 people skipped a total of 4 questions in the first week MBI, 1 person skipped 1 question in the second week MBI and 2 people skipped 1 question each in the second week WEMWBS. As these are all healthy participants and we expect to see no change in their values between the weeks, the omitted value was filled in with the value entered for that question in the other week.

3.2 Definitions

This section details the definitions of the abbreviations that will be used in the hypotheses and results.

MBI scale scores

The MBI-GS has three scales, which were obtained twice: once at the end of both measurement weeks. The scales will be referenced as follows:

- MBI-PE: MBI-GS Personal Efficacy scale
- MBI-EX: MBI-GS Exhaustion scale
- MBI-CY: MBI-GS Cynicism scale

HR dip values

For each night recorded for each participant, we calculated three HR dips. We also calculated the average values for all three dips per participant per measurement week.

- HR_{dip1}, the difference in HR between getting in bed and getting up (as indicated by markers 1 and 6)
- HR_{dip2}, the difference in HR between falling asleep and waking up (as indicated by markers 2 and 5)
- HR_{dip3}, the difference in HR between the maximum HR and minimum HR of the night (as indicated by markers 4 and 3)

Paced Breathing and Regular Breathing IBI values

In addition, for each night recorded for each participant, we calculated three HRV values during the Paced Breathing and Regular Breathing measurements. We also calculated the average values for both exercises per participant per measurement week. The three HRV values we look at are the RMSSD of adjacent IBIs, the HF power and the LF power.

- PB_{rmssd}, the RMSSD of adjacent IBIs during the Paced Breathing exercise
- PB_{hf}, the HF power during the Paced Breathing exercise
- PB_{lf}, the LF power during the Paced Breathing exercise
- RB_{rmssd}, the RMSSD of adjacent IBIs during the Regular Breathing exercise
- RB_{hf}, the HF power during the Regular Breathing exercise
- RB_{lf}, the LF power during the Regular Breathing exercise

Δ MBI scores, Δ HR-dip values and Δ PB values

Based on the average values per week, we calculated the change over time between the two measurement weeks for each of these parameters, where week 2 was measured 11-13 weeks after week 1:

ΔMBI-EX = MBI-EX (week 2) - MBI-EX (week 1)
ΔMBI-PE = MBI-PE (week 2) - MBI-PE (week 1)
ΔMBI-CY = MBI-CY (week 2) - MBI-CY (week 1)
$\Delta HR_{dip1} = HR_{dip1}$ (week 2) $-HR_{dip1}$ (week 1)
$\Delta HR_{dip2} = HR_{dip2}$ (week 2) $-HR_{dip2}$ (week 1)
$\Delta HR_{dip3} = HR_{dip3}$ (week 2) $-HR_{dip3}$ (week 1)
$\Delta PB_{rmssd} = PB_{rmssd}$ (week 2) $-PB_{rmssd}$ (week 1)
$\Delta PB_{hf} = PB_{hf}$ (week 2) $-PB_{hf}$ (week 1)
$\Delta PB_{lf} = PB_{lf}$ (week 2) $-PB_{lf}$ (week 1)

3.3 Summary of the Data

To give an impression of what the data looks like, this section gives some descriptive values about the shape of the data. We collected data for 24 participants, resulting in 48 weeks of data, or 336 possible nights. In the collected 292 nights, participants were in bed an average of 7 hours and 11 minutes, and they actually slept 6 hours and 53 minutes. On week nights, participants were in bed 7 hours and 2 minutes and slept 6 hours and 45 minutes on average, while on weekend nights they were in bed 8 hours and 22 minutes and slept 7 hours and 32 minutes.

The maximum heart rate of the night took place on average 2.5 hours after falling asleep, and the minimum heart rate of the night took place on average 4,5 hours after falling asleep. The time between waking up and starting the breathing measurements was 6.5 minutes on average, although we found this was strongly influenced by a few nights where the participant did not stick to the instructions of starting the breathing exercises directly after waking. In 19 nights, people started the breathing exercises after 15 minutes, and without these, the average drops to 5 minutes.

Of the 24 participants, 3 were female and 21 were male. The average age was 43.3, with a standard deviation of 11 years. The first week measurements were done spread across a period of seven weeks, and the second week measurements took place on average 90 days (or 12.8 weeks) later.

3.4 Hypotheses

This section provides more detail on the four hypotheses, the adjustments that were made based on the exclusion (for this study) of the burnout participant data, the analyses that were done after the healthy participant data was obtained and the results from these analyses.

3.4.1 Hypothesis 1

"A higher MBI-GS score on the Exhaustion and Cynicism scales, and a lower MBI-GS score on the Personal Efficacy scale can indicate burnout symptoms or even clinical burnout [47]. During burnout, we expect the Exhaustion and Cynicism scores to be much higher and the Personal Efficacy much lower than the scores after recovery within individual burned out people (e.g. they are healthy enough to go back to work). Within healthy people, we expect the MBI-GS score difference between measurements to be non-significant."

As for this study we are only looking at the data collected from healthy participants, this hypothesis has been split up in the following sub-hypotheses.

Hypothesis 1a. There is no difference in MBI scores between week 1 and week 2 for healthy participants.

Hypothesis 1b. The MBI scores for healthy participants indicate they are healthy.

The descriptives of the MBI scores can be found in Figure 3.1. A Repeated Measures MANOVA was done between the scores for each MBI scale from week 1 and 2. This tested whether there was a difference in MBI scores between week 1 and 2 for all scales (hypothesis 1a), and the result was not significant, F(3,

18) = 1.243, n.s.

	N	Mean	Std. Deviation
W1_MBI_PE_avg	24	4.8403	.64358
W1_MBI_EX_avg	24	1.7917	1.42826
W1_MBI_CY_avg	24	1.3917	1.01378
W2_MBI_PE_avg	21	4.6825	.74704
W2_MBI_EX_avg	21	1.5143	1.18755
W2_MBI_CY_avg	21	1.2476	.91631
Valid N (listwise)	21		

Figure 3.1: N, mean and standard deviation of the averaged week 1 and 2 MBI scores for all three scales. The scores were calculated by summing the questions per scale and dividing by the amount of questions in the scale.

To test whether our participants are healthy (hypothesis 1b), we checked the Maslach Burnout Inventory Manual [47] for the procedure. According to the manual, burnout scores differ per country and when trying to decide on cut-off scores, those most relevant to your country should be taken into account. In the Netherlands, a Dutch translation of the MBI called the Utrechtse BurnOut Schaal (UBOS) is most often used, with the UBOS-A being the 15-item Dutch translation of the 16-item MBI-GS. This means there are little to no relevant studies with MBI-GS cut-off scores for Dutch study participants. We have therefore chosen to do test whether our participants were healthy against the cut-off values for the UBOS-A based on those used by Mohren et al. [36]. These cut-off scores are given as average scores of the questions per MBI scale, so the questions per scale were summed and divided by the amount of questions in the scale.

As suggested by the UBOS manual [49], Mohren et al. [36] use respectively the upper and bottom quartile values as cut-off values to determine burnout Level 1, at which subjects have burnout complaints:

1. Exhaustion > 2.40 and
2. Cynicism > 2.25 or Personal Efficacy < 3.5

This resulted in a count for week 1 of 5 participants with some burnout symptoms, and 4 of these participants also did the second week measurements and retained these levels of burnout symptoms.

3.4.2 Hypothesis 2

"A night time HR dip is considered a sign of good health [7]. We expect no significant HR dip will be detectable during the night in the data collected from burned out people before recovery, and expect to see the return of such a HR dip after recovery. In healthy people, we expect this HR dip will exist and we expect there will be little difference between measurements."

As for this study we are only looking at the data collected from healthy participants, this hypothesis has been split up in the following sub-hypotheses.

Hypothesis 2a. There is no difference between the weekly average HR_{dip} values for healthy participants.

Hypothesis 2b. There is a detectable HR_{dip} for healthy participants.

The descriptives for the HR_{dip} values can be seen in Figure 3.2. A Repeated Measures MANOVA was done between the week 1 and week 2 HR values for HR_{dip1}, HR_{dip2} and HR_{dip3}. This tested whether there was a difference between the weekly averages for the HR_{dip} values (hypothesis 2a), and the result was not significant, F(3, 18) = 1.328, n.s.

	Mean	Std. Deviation	N
W1_HR_dip1	1,710245457	4,196154535	21
W2_HR_dip1	1,362004443	4,661419631	21
W1_HR_dip2	1,724006871	3,004161631	21
W2_HR_dip2	1,922349931	3,023723290	21
W1_HR_dip3	12,13894891	2,735867799	21
W2_HR_dip3	13,21878412	2,635035492	21

Figure 3.2: N, mean and standard deviation of the three HR_{dip} values for week 1 and 2.

As the differences between week 1 and week 2 for the HR_{dip} values were not significant, the calculations done to check if the HR_{dip} values were detectable (hypothesis 2b), we calculated the average of the scores over all measurement days for both weeks. Figure 3.3 shows the descriptives for the dip values averaged over both weeks. The hypothesis was tested with the use of One Sample T-Tests, where the HR_{dip} values were tested against 0, as a value of 0 would indicate no detectable dip was present.

	N	Mean		Std. Deviation
	Statistic	Statistic	Std. Error	Statistic
HR_dip1	24	,6762152925	,9421044095	4.615350176
HR_dip2	24	1.716335365	,6108823955	2.992700324
HR_dip3	24	12.76765884	,4610817260	2.258829917
Valid N (listwise)	24			

Figure 3.3: N, mean and standard deviation of the three HR_{dip} values averaged over all measured days.

- HR_{dip1} was not significantly different from 0:
  t(23) = .718, n.s.

- HR_{dip2} was significantly different from 0:
  t(23) = 2.810, p < .05

- HR_{dip3} was significantly different from 0:
  t(23) = 27.691, p < .001

For dip 3, out of 289 discovered minimum and maximum values, 207 times (or 72%) the maximum took place before the minimum. Additionally, we calculated the average HR_{dip} values over all weekdays and weekend days in both measurement weeks. We then checked the difference between HR_{dip} values on week nights and on weekend nights with a Repeated Measures MANOVA, but this did not result in significance, F(3, 20) = .532, n.s.

3.4.3 Hypothesis 3

"Breathing exercises cause large fluctuations in IBI lengths in data collected from healthy people [20]. We expect these fluctuations to be smaller in the data collected from burned out people before recovery than in the data obtained from healthy people, and expect these fluctuations to be similar to data collected from healthy people after recovery. In healthy people, we expect these fluctuations to be large and we expect to see little difference between measurements."

As for this study we are only looking at the data collected from healthy participants, this hypothesis has been split up in the following sub-hypotheses.

Hypothesis 3a. There is no difference in the PB_{rmssd}, PB_{hf} and PB_{lf} values during the paced breathing exercises done in week 1 and week 2 for healthy participants.

Hypothesis 3b. There is a significant difference in RMSSD, HF and LF values between the Paced Breathing exercise and the Regular Breathing measurement for healthy participants.

The descriptives for the HRV values can be seen in Figure 3.4 and Figure 3.5. To test whether the breathing exercises were different between the two measurement weeks, a Repeated Measures MANOVA was done with Week as a factor (two levels: week 1 and 2) and with Mode as a factor (two levels: Regular and Paced Breathing), comparing the regular breathing measurement with the paced breathing exercise for each of the chosen measures.

- The week factor did not cause a significant difference in HRV features:
  F(3, 16) = 1.477, n.s.

- The mode of breathing exercise caused a significant difference in HRV features:
  F(3, 16) = 33.957, p < .001.

- The interaction effect of the week and the mode of breathing exercise caused a significant difference in HRV features:
  F(3, 16) = 4.595, p < .05.

	N	Mean	Std. Deviation
W1_PB_RMSSD	21	3,959234001	,4160288996
W2_PB_RMSSD	21	3,882196564	,4106268038
W1_PB_HF	21	-2,50136276	,6190119616
W2_PB_HF	21	-2,59667314	,5849480830
W1_PB_LF	21	-,1548839271	,1116702016
W2_PB_LF	21	-,1389230100	,0995983118
Valid N (listwise)	19		

Figure 3.4: N, mean and standard deviation of the Paced Breathing HRV-feature values for week 1 and 2.

	N	Mean	Std. Deviation
W1_RB_RMSSD	20	3,622899012	,4618359683
W2_RB_RMSSD	20	3,847859012	,4326164556
W1_RB_HF	20	-1,45345575	,4458065332
W2_RB_HF	20	-1,44760104	,4339310198
W1_RB_LF	20	-,4020034095	,1874371709
W2_RB_LF	20	-,3923851735	,1649315873
Valid N (listwise)	19		

Figure 3.5: N, mean and standard deviation of the Regular Breathing IBI-feature values for week 1 and 2.

The Repeated Measures MANOVA also shows the significant difference the mode of breathing exercise causes in the HRV features, which covers the test for hypothesis 3b. Upon closer inspection of the interaction effect between the week and mode of breathing exercise, we discovered that the RB_{rmssd} was significantly different between the the two weeks, $F(1, 18) = 13.831$, $p < .01$. This interaction effect is illustrated in Figure 3.6.

3.4.4 Hypothesis 4

"The HR of burnout patients is higher [15], and the HRV lower [29, 39] than that of healthy participants. Therefore, we expect a change over time in the HR and HRV variables obtained between measurements to correlate with a change over time in MBI-GS scores."

Hypothesis 4a. There is a correlation between the change in MBI scores and the change in HR_{dip} values for healthy participants.

Hypothesis 4b. There is a correlation between the change in MBI scores and the change in PB HRV values for healthy participants.

A bivariate correlation analysis was done between the ΔMBI scales and each

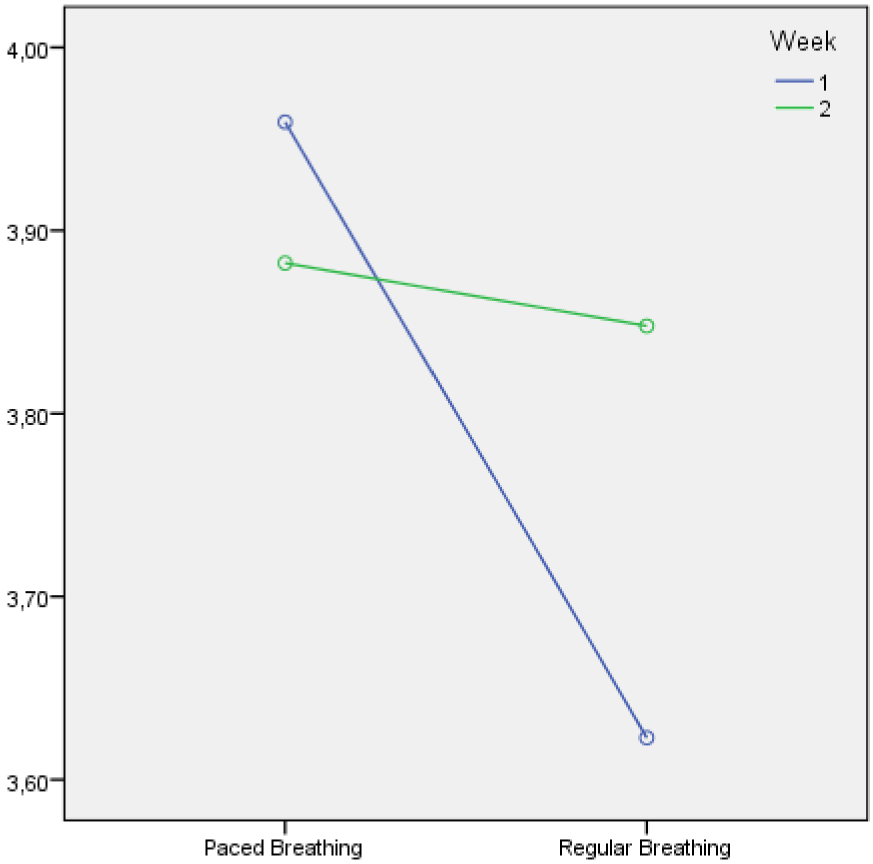

Figure 3.6: Interaction graph of the effects of the Week*Mode interaction of Paced Breathing and Regular Breathing RMSSD.

individual ΔHR_{dip} or ΔPB HRV value to see if any significance or trends could be discovered. This was not the case. As the results between the scales are fairly similar, only the results of the MBI-EX scale are reported here as they are of the most interest to us.

- ΔMBI-EX was not significantly related to ΔHR_{dip1}:
  r = -.04, p > .05
- ΔMBI-EX was not significantly related to ΔHR_{dip2}:
  r = .190, p > .05
- ΔMBI-EX was not significantly related to ΔHR_{dip3}:
  r = .422, p > .05
- ΔMBI-EX was not significantly related to ΔPB_{rmssd}:
  r = .091, p > .05
- ΔMBI-EX was not significantly related to ΔPB_{hf}:
  r = .301, p > .05

- ΔMBI-EX was not significantly related to ΔPB_{lf}:
  r = -.229, p > .05

3.5 Additional Exploratory Analysis

As the MIO watch measures the full PPG signal and the internal Philips algorithm provides more features than were essential to test our hypotheses, we have extra data to explore for possible biomarker potential. Additionally, we collected SAM data in the paper diaries, and had participants fill out three extra weekly questionnaires, which we would also like to take a look at. Any significance found in this section would have to be confirmed by future research, but could point out other interesting factors to look at. This section first gives an overview of the SAM data, followed by the data from the weekly questionnaires and extra data available from the HR and HRV features. The section concludes with a series of correlations between the questionnaires and HR and HRV data.

3.5.1 SAM

Every day and every morning we gathered information about the participant's mood via the SAM questionnaire, but this information was not needed for our hypotheses. However, they do provide information about how the participants felt throughout the week on a more detailed level than the weekly questionnaires provided, and this section gives an overview of some of the interesting results we found when looking at this data more closely.

As we collected data for 7 consecutive nights twice, that meant we had data for up to ten week days and up to four weekend days. To test whether anything significant could be found in the SAM data, a Repeated Measures MANOVA was done with Type of Day as a factor (two levels: weekday and weekend day), and Time of Day as a factor (two levels: Evening and Morning).

- The type of day did not cause a significant effect on the SAM values:
  $F(5, 19) = 1.768$, n.s.
- The time of day caused a significant effect on the SAM values:
  $F(5, 19) = 7.300$, $p < .01$
- The interaction effect of the type of week day and time of day caused a significant effect on the SAM values:
  $F(5, 19) = 2.795$, $p < .05$

The other interaction effects were not significant. For individual scales, we found that the Pleasure and Energy SAMs were significantly different between the morning and evening, Pleasure: $F(1,23) = 10.467$, $p < .01$ (see Figure 3.7) and Energy: $F(1,23) = 19.461$, $p < .001$ (see Figure 3.8).

3.5.2 Weekly Questionnaires

In addition to the MBI-GS, we also asked participants to complete the WEMWBS, PSS and PSQI at the end of each measurement week. This data was not used

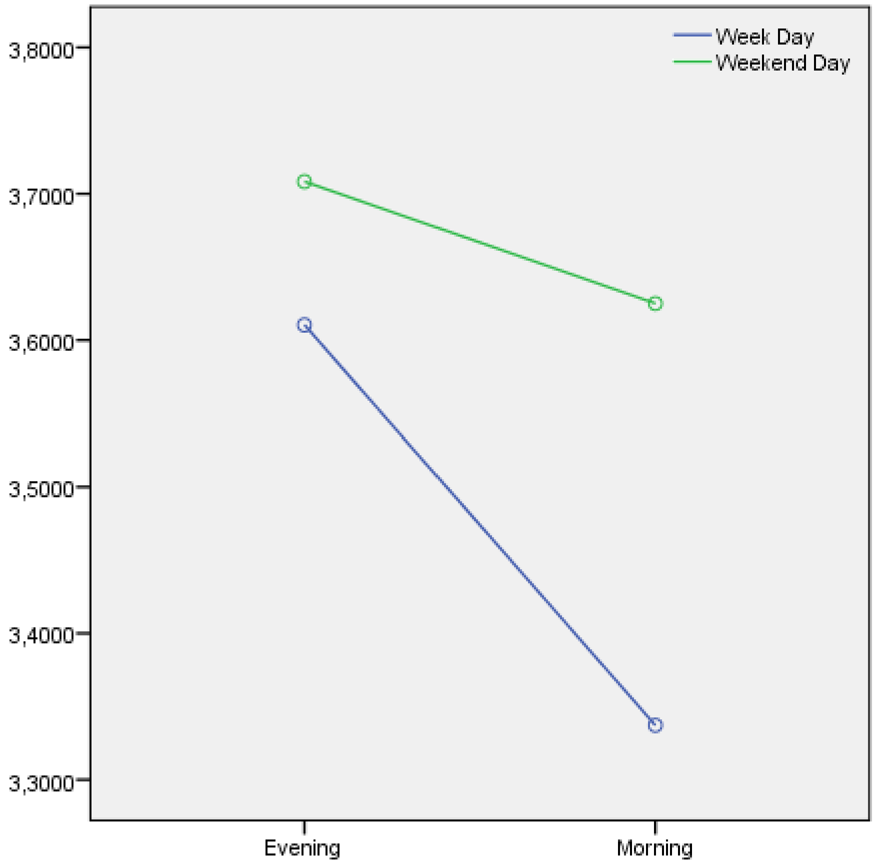

Figure 3.7: Interaction graph of the effects of the Time of Day*Week interaction of the Pleasure score in the mornings and evenings of week days and weekend days.

for any of the hypotheses, but to be sure there were no significant differences, we did a Paired T-Test between the week 1 and week 2 values obtained for each of these questionnaires. The results from these analyses were all not significant.

3.5.3 HR and HRV features

The close observer may have noticed that in hypothesis 2 we only looked at the HR values, and in hypothesis 3 we only looked at the Paced Breathing and Regular Breathing HRV values, which means we did not look at the HRV values throughout the night, nor the HR values during Paced Breathing and Regular Breathing. However, it could be interesting to look at both of these situations as well, as perhaps the HRV values could differ at different points of the night, and the HR could be different between the Paced Breathing and Regular Breathing exercises. We therefore did a Repeated Measures MANOVA between the different intervals for the HR dips with the HRV features and a Repeated Measures MANOVA between the different intervals for the Paced Breathing and Regular Breathing measurements with the HR features.

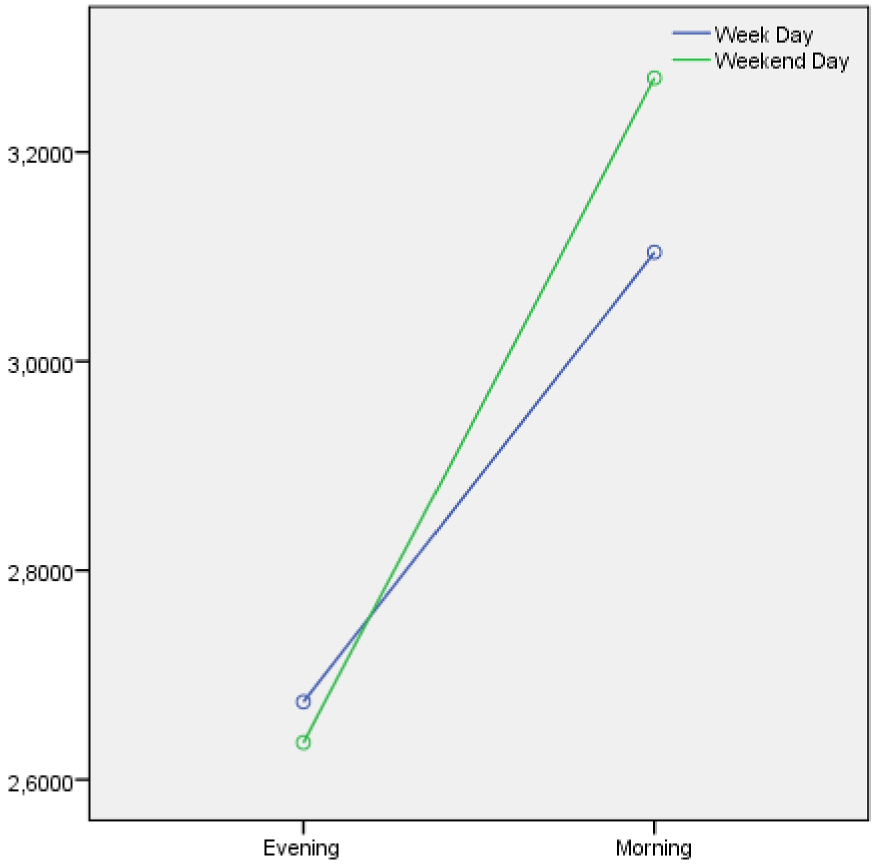

Figure 3.8: Interaction graph of the effects of the Time of Day*Week interaction of the Energy score in the mornings and evenings of week days and weekend days.

Going to bed (M1) vs. getting up (M6)

Figure 3.9 shows the descriptives of the RMSSD, HF power and LF power, averaged over all days in both measurement weeks for both going to bed (M1) and getting up (M6). The results of a Repeated Measures MANOVA with a factor for the Interval (two levels: Going to bed and Getting up) for the three HRV measures RMSSD, HF power and LF power was significant, $F(3, 21) = 22.801$, $p < .001$. The results of the individual HRV measures show that the RMSSD is significantly lower, $F(1, 23) = 26.760$, $p < .001$, the HF power is significantly higher, $F(1, 23) = 52.309$, $p < .001$ and the LF power is significantly higher, $F(1, 23) = 22.844$, $p < .001$ when getting in bed than when getting up.

Falling asleep (M2) vs. waking up (M5)

Figure 3.10 shows the descriptives of the RMSSD, HF and LF features, averaged over all days in both measurement weeks for both falling asleep (M2) and waking up (M5). The results of a Repeated Measures MANOVA with a factor for the

	Mean	Std. Deviation	N
RMSSD_M1	3,636573312	,4426719298	24
RMSSD_M6	3,899357093	,3802675800	24
HF_M1	-1,03460863	,3608235631	24
HF_M6	-1,41153938	,4140557057	24
LF_M1	2,872328197	3,355908027	24
LF_M6	-,4188838717	,2171582566	24

Figure 3.9: Descriptives for the average over all days in both measurement weeks of RMSSD, HF power and LF power for both going to bed (M1) and getting up (M6).

Interval (two levels: Falling asleep and Waking up) for the three HRV measures RMSSD, HF power and LF power was significant, $F(3, 21) = 8.333$, $p < .01$. The results of the individual HRV measures show that the LF power is significantly lower, $F(1, 23) = 24.656$, $p < .001$, and the HF power is significantly higher, $F(1, 23) = 17.847$, $p < .001$, when falling asleep than upon waking.

	Mean	Std. Deviation	N
RMSSD_M2	3,838069364	,4160033654	24
RMSSD_M5	3,848025240	,4388444793	24
HF_M2	-1,13940082	,4266022020	24
HF_M5	-1,38559006	,4741382484	24
LF_M2	-,5669008621	,2765522121	24
LF_M5	-,4383593421	,2394664444	24

Figure 3.10: Descriptives for the average over all days in both measurement weeks of RMSSD, HF power and LF power for both falling asleep (M2) and waking up (M5).

Maximum (M4) vs. Minimum (M3)

Figure 3.11 shows the descriptives of the RMSSD, HF and LF features, averaged over all days in both measurement weeks for both the maximum HR of the night (M4) and the minimum HR of the night (M3). The results of a Repeated Measures MANOVA with a factor for the Interval (two levels: Maximum HR of the night and Minimum HR of the night) for the three HRV measures RMSSD, HF power and LF power was significant, $F(3, 21) = 22.173$, $p < .001$. The results of the individual HRV measures show that the RMSSD is significantly lower, $F(1, 23) = 68.998$, $p < .001$, and HF are significantly lower, $F(1, 23) = 9.858$, $p < .01$ at the maximum HR than at the minimum HR of the night.

	Mean	Std. Deviation	N
RMSSD_M4	3,446823550	,4841581456	24
RMSSD_M3	4,071944771	,4220614940	24
HF_M4	-1,45943017	,5263695647	24
HF_M3	-1,22047614	,4129990300	24
LF_M4	-,4491316438	,2204524515	24
LF_M3	-,5187337263	,2888191478	24

Figure 3.11: Descriptives for the average over all days in both measurement weeks of RMSSD, HF power and LF power for both the maximum HR of the night (M4) and the minimum HR of the night (M3).

Regular Breathing (M7) vs. Paced Breathing (M8)

Figure 3.11 shows the descriptives of the HR and IBI features, averaged over all days in both measurement weeks for both the regular breathing measurement interval (M7) and the paced breathing measurement interval (M8). The results of a Repeated Measures MANOVA with a factor for the Interval (two levels: regular breathing and paced breathing) for the two HR measures HR and IBI was not significant, $F(2, 19) = .122$, n.s.

	Mean	Std. Deviation	N
HR_M7	65,02174132	7,128127155	21
HR_M8	65,15482390	6,040354603	21
IBI_M7	936,8583891	93,01021411	21
IBI_M8	933,7910168	83,39322657	21

Figure 3.12: Descriptives for the average over all days in both measurement weeks of HR and IBI for both the regular breathing (M7) and paced breathing exercises (M8).

3.5.4 Weekly Questionnaires vs. HR and HRV features

Literature has previously shown that the resting HR of burnout patients is significantly higher than that of control participants, and we therefore also looked at a potential correlation between the weekly questionnaire scores and the regular breathing HR values. To do so, we performed a bivariate correlation between the ΔMBI scales, ΔWEMWBS, ΔPSS, ΔPSQI and ΔHR RB. The results were overall mostly insignificant, but we did stumble upon a positive correlation between ΔPSS and ΔHR RB, $r = .488$, $p < .05$ (two-tailed). This indicates that when the HR goes up over time, the PSS score does so as well. A higher PSS score indicates more stress.

Chapter 4

Discussion & Conclusion

The purpose of this study was to detect a change in the level of burnout in a person through HR dynamics, such as HR and HRV measures. As questionnaires are time consuming and a hassle to fill in frequently, it would be ideal to have a biomarker to detect changes in health within a person. A lot of biomarker research for burnout has already been done, but these studies are often inconclusive or incomparable [13]. This study tried to combine longitudinal nightly and breathing exercise intra-individual measurements with a group of revalidating burnout and matched healthy participants. It was hypothesised that we could find a correlation between the change in HR dynamics with a change in burnout score, as given by the MBI [34]. For this study the participant group consisted of 24 healthy participants, who were measured twice over a period of 11-13 weeks.

This study investigated the following four hypotheses, of which the first hypothesis was as follows, *"A higher MBI-GS score on the Exhaustion and Cynicism scales, and a lower MBI-GS score on the Personal Efficacy scale can indicate burnout symptoms or even clinical burnout [47]. During burnout, we expect the Exhaustion and Cynicism scores to be much higher and the Personal Efficacy much lower than the scores after recovery within individual burned out people (e.g. they are healthy enough to go back to work). Within healthy people, we expect the MBI-GS score difference between measurements to be non-significant."* This hypothesis was divided into two parts that were relevant to the healthy participants we collected data from in this study. First we checked whether the scores were different between the two weeks and we found no significant difference. Then we checked whether our participants were actually healthy against the cut-off scores reported for the Dutch translation of the MBI-GS, the UBOS [50]. We saw that five participants showed burnout symptoms during week 1, and these symptoms persisted for four of these participants who also participated in week 2. This means that 20.8% of our study population was burned out during week 1, and 16.7% was burned out during week 2, which in comparison with previously reported figures is high. Langelaan [31] reports 8-11% as a percentage of burned out participants in a normal sample from the Dutch population, so we conclude that our participants showed significantly more burnout symptoms than a normal sample.

We then moved on to look at the HR dips at night in the second hypothesis. *"A night time HR dip is considered a sign of good health [7]. We expect no significant HR dip will be detectable during the night in the data collected from burned out people before recovery, and expect to see the return of such a HR dip after recovery. In healthy people, we expect this HR dip will exist and we expect there will be little difference between measurements."* It has previously been shown that a HR dip can be used as an indicator of health [23], and therefore we calculated three HR dips per recorded night per participant. Our hypothesis was split up in two parts that were relevant to the healthy participants in this study. In the first we checked whether the average HR dips over the individual measurement weeks were different and found no significant difference between the two weeks. We then proceeded with testing whether the HR dips actually existed, by checking if they were significantly different from 0, and discovered that the HR_{dip1} was not. HR_{dip2} was significantly different from 0, but only by an average of 1-2 heart beats, which means the effect is too small to be relevant. HR_{dip3} was measured between the maximum and minimum and is therefore by definition positive, although this does not yet say anything about whether the maximum took place before the minimum, which would be required to classify it as a 'dip' (otherwise it would be a 'rise'). In 72% of nights, the maximum took place before the minimum, indicating that the third dip has at least some credibility. Further analysis could be done too see what kind of an effect the nights where the minimum takes place before the maximum had on the values we found for HR_{dip3}, but that was outside the scope of this study. We also mentioned that there are gaps in the data, which in particular affect the values of the minimum of the maximum, as a minimum or maximum could have been missed in the missing data. However, a missed minimum or maximum could only be smaller (resp. larger) than the current values found, which means the dip could only become larger. In conclusion, we found no HR dip of the kind that both Hozawa et al. [23] and Ben-Dov et al. [7] report between the day time HR and the night time HR, but as we only compared between the HR upon going to bed and getting up, a discrepancy exists in the calculation of the dip. However, we did find some evidence for the existance of the decline of HR during the night, both between falling asleep and waking up, and between the maximum and minimum HR of the night. In addition, from the exploratory analysis in which we investigated the biomarker potential of the other calculated HR and HRV measures between the same intervals used for the HR dips, we discovered that while the HR dip is not always significant or large, the RMSSD, LF power and HF power do show promise in these intervals.

The third hypothesis looked at the differences in HRV fluctuations between a regular breathing measurement and a paced breathing exercise. *"Breathing exercises cause large fluctuations in IBI lengths in data collected from healthy people [20]. We expect these fluctuations to be smaller in the data collected from burned out people before recovery than in the data obtained from healthy people, and expect these fluctuations to be similar to data collected from healthy people after recovery. In healthy people, we expect these fluctuations to be large and we expect to see little difference between measurements."* This hypothesis was also divided in two parts that were relevant for the healthy participants included in this study. The first part addressed whether the HRV features calculated over the Paced Breathing measurement interval were different between the two weeks and we found no significant differences. We then looked at whether the paced breathing exercise actually caused fluctuations in HRV features as opposed to the regular breathing measurement. The repeated measures MANOVA showed that the mode of breathing exercise indeed had a significant effect on the HRV features, as the RMSSD was significantly higher, the HF significantly lower and the LF significantly higher between the two modes of measurements. This is surprising, as Eckberg [20] expected all fluctuations to be larger during paced breathing than during regular breathing, and we only found the RMSSD and LF to be higher. The MANOVA also showed that there was a significant effect of the week, which contradicted the results for the first part of this hypothesis, and upon closer inspection we discovered that there was a significant difference between the RMSSD obtained during regular breathing between weeks 1 and 2. We conclude that the mode of breathing exercise had a significant on all three HRV measures.

The last hypothesis combined the first three hypotheses in an attempt to find a correlation between the change in HR and HRV data and the change in MBI scores. *"The HR of burnout patients is higher [15], and the HRV lower [29, 39] than that of healthy participants. Therefore, we expect a change over time in the HR and HRV variables obtained between measurements to correlate with a change over time in MBI-GS scores."* As we did not have access to a sufficient amount of revalidating burnout participants throughout the duration of this study, we focused only on the data gathered from healthy participants. To test the hypothesis for healthy participants, we therefore correlated the change in MBI-GS scale scores with the change in HR dip values and the change in paced breathing HRV values, but none of these turned out to be significant. It can be argued, however, given that our tests for hypothesis 1 supported that there was no difference in MBI-GS score between the weeks, and given that our tests for hypothesis 2 and 3 supported that there were no significant differences in HR dip values and Paced Breathing HRV values between the weeks, the changes were simply too small to find anything. As the measurements of the burnout participants are still ongoing at Philips Research, we do therefore recommend looking into these differences once more when the gathering of that data is completed. From the exploratory analysis, we conclude that the HR may not be the most ideal variable to look into when correlating with the MBI, so we therefore recommend taking a closer look at the other features (RMSSD, LF power and HF power in particular) both throughout the night and between regular breathing and paced breathing in the future. We also found that the resting HR measured during regular breathing correlates positively with the PSS score, confirming findings in literature that when stress goes up, the resting HR goes up accordingly [10, 52]. We therefore also recommend looking at these two variables once the burnout participant data has come in.

In summary, this study investigated the HR dynamics and the correlation with their MBI-GS scores of a group of 24 healthy participants. As expected, we found no significant difference between the two measurement weeks in the values for the HR at night, the HRV during paced breathing and regular breathing or the MBI-GS scores. We also confirmed the existence of a small HR dip between falling asleep and waking up, and a larger HR dip between the maximum and minimum HR of the night but we could not find any relation between the extent of this dip and the level of burnout. Furthermore, we showed that the paced breathing exercise HRV feature values were significantly different from the HRV feature values obtained during the regular breathing measurement, but again we found no correlation between the change in any of the paced breathing HRV feature values and the change in burnout level. From the exploratory analysis we conclude that the RMSSD, HF power and LF power may be interesting to look at throughout the night for data gathered from revalidating burnout participants in future research.

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Appendix A

ICBE

It is very important to Philips, and Philips Research, that all research done is performed under a strict set of ethical rules. The ICBE requires all studies to be submitted and approved at one of their monthly meetings. The first step for this study was to be classified as a study type, and it was considered to be either a type G, or type I study. The type of study defines which documents need to be created.

A type G study is a non-medical study using existing market available devices and a type I study is a variation of type G that uses prototypes or alterations of existing products. The Optical Heart Rate Logging Device is a prototype, but it has a standard Declaration of Conformity that guarantees its safety, which meant the additional documents for a type I study did not have to be handed in.

Type G studies require the following document set to be handed in:

- Study Overview
- Study Protocol
- Information Letter & Informed Consent
- Short Form Risk Analysis
- Human Studies Privacy Self Assessment

These documents give a general, and a more in-depth overview of the exact contents of the study design, methods used and participants. They also cover the risks for the participant's privacy, use of the devices and general study risks.

For this study, the following documents were created and approved.

- Full Type G document set, including differing information letters for burnout and healthy participants
- Declaration of Conformity for the MioGlobal Alpha Watch

Appendix B

Overview of considered devices

Multiple devices were considered for this study, and the decision was made based on availability and ease of use. Two devices are prototypes and were accompanied by an approved Declaration of Conformity, containing the guarantee from the ethical committee of their safety in use. A full overview of the devices that were considered can be found in Table B.1.

Table B.1: Overview of considered devices

Device Name	Brand	Intended Use
MioGlobal Alpha Watch	MioGlobal	HR measurement at the wrist
Optic Heart Rate Logging Device (Modified MioGlobal Alpha Watch)	MioGlobal, Philips	Full PPG measurement at the wrist, accelerometer, internal data storage
RS800CX	Polar	HR measurement at the chest, data storage on external Polar device
Zephyr HxM Smart	Zephyr	HR measurement at the chest data storage on external device
Garmin HRM	Garmin	HR measurement at the chest data storage on external device
wGT3x-BT	ActiGraph	Detect sleeping in and waking up, internal data storage
Discrete Tension Indicator (DTI-2)	Philips Research	Detect sleeping in and waking up

The MioGlobal Alpha Watch (see Figure B.1) is a commercially available product, which allows the recording of the HR at the wrist. It enables the storage of the data on an external device such as an iPod or iPhone through transmission via BlueTooth. The battery lasts around 24 hours.

The Optic Heart Rate Logging Device is a MioGlobal Alpha Watch, modified by Philips to record the full PPG signal, which can be used to calculate both the HR and the HRV, plus allow the use of the accelerometer and the storage of the recorded data on the device. The battery duration is over 24 hours, and the memory can hold between 8 and 9 hours. This device is a prototype and has an approved Declaration of Conformity.

Figure B.1: A MioGlobal Alpha Watch

The RS800CX Chest Strap by Polar (see Figure B.2) is a HR Sensor that measures the HR at the chest. It is accompanied by a watch for the storage of the HR data. The battery duration is a few weeks, but the storage device needs to be charged more often.

The Zephyr HxM Smart Chest Strap by Zephyr (see Figure B.3) is a HR Sensor that measures the HR at the chest. It is accompanied by either an ActiGraph device or iPod for the storage of the HR data via BlueTooth. The battery duration is around a week or two, but the storage device needs to be charged more often.

Figure B.2: The RS800CX Polar Chest Strap

Figure B.3: The Zephyr HxM Smart Chest Strap

The ActiGraph wGT3X-BT (see Figure B.4) serves as an accelerometer and as a data storage device via BlueTooth transmission. The accelerometer detects movement, which can be used to detect sleeping in and waking up. The battery and memory duration are a few days, at least.

The Discrete Tension Indicator (DTI-2) (see Figure B.5) is a prototype developed by Philips Research, which was then approved as a CE-marked device with a Declaration of Conformity. It is used as an accelerometer to detect movement, which can be used to detect sleeping in and waking up. The main purpose of the device is to measure skin conductance, which was not needed for this study.

Figure B.4: The ActiGraph wGT3X-BT

Figure B.5: The Discrete Tension Indicator

Initially, using a chest strap seemed a better option, as their battery duration is much longer than that of the MIO wristbands. After discussing with CIRAN, however, it became clear that the risk of the chest straps chafing or becoming uncomfortable at night was too big in burnout patients, so we decided to go with a wristwatch.

This left the option of either the commercially available MioGlobal Alpha Watch in combination with either the wGT3x-BT or the DTI-2 and an iPod/iPhone, or the Optic Heart Rate Logging Device (being the modified MioGlobal Alpha Watch). The choice for the modified MIO was then made by the desire to also measure the HRV, and the preference to only use one device that had to be worn on the body (instead of two/three) or carried around during the measurement. The regular MIO only transmits the HR, not the HRV, and even that is not completely reliable, plus, as the pilot study showed (see [18]), there is quite a big risk of data loss if the participant forgets to wear or stay in the vicinity of the storage device. The modified MIO is just as easy, or even easier to use (due to the absence of an extra device), than the regular MIO and is equally reliable as the most reliable of the chest belts (see [18]). The downside of our choice was that the Optic Heart Rate Logging Device only has 8-9 hours of internal storage, which meant we had to also provide a laptop to offload the data every morning, but this was considered to be less obtrusive than wearing a storage device on the body.

Appendix C

Data Retrieval Program

The modified MioGlobal Alpha Watch is accompanied by an internally developed Philips Research program to offload the recorded data. The program offloads the data as a raw data file, which may not be used off premises. On top of that, the program is quite complicated and offers a lot of features, which can be confusing to patients. Therefore, a new program was developed by Ad Denissen, Philips Research, using the core of the original program to offload the data, but writing the data as an illegible file that can be downloaded with one button press.

The new program was wrapped in a Perl script (see Figure C.1), and as the participants also have to perform two breathing exercises, the decision was made to give visual feedback of these exercises in the script as well. To do so, two small Java programs were developed; One for the regular breathing exercise (see Figure C.2), which was just a 6 minute timer, and one for the paced breathing exercise C.3, which graphically shows the participant when to breathe in, and when to breathe out. The paced breathing exercise also lasts 6 minutes, and is currently set to 6 breaths per minute, which is a variable that can easily be changed in the code.

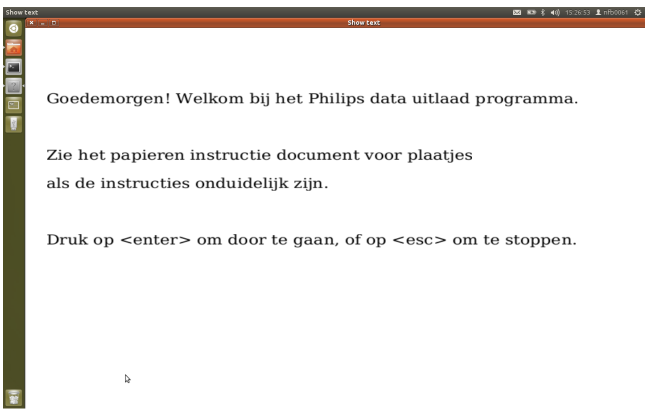

Figure C.1: The Perl script wrapped around the Data Retrieval Program

The complete program was user tested with two participants that matched the demographics of the expected target participant (between the age of 50-60, with limited computer experience) to iron out some usability issues, such as changing the phrasing of the instructions to be less ambiguous and adding photos and images to the instructions document.

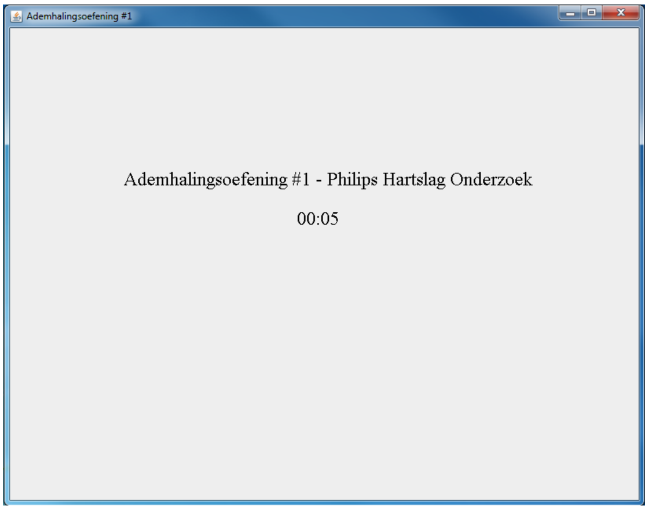

Figure C.2: The Regular Breathing Exercise Program

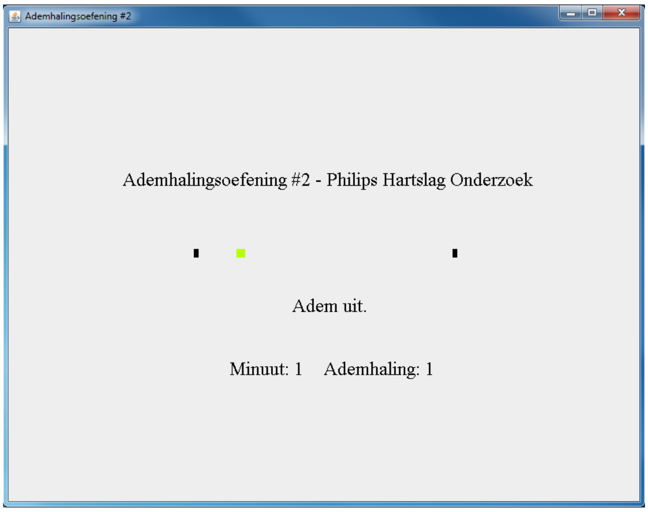

Figure C.3: The Paced Breathing Exercise Program

Appendix D

Interval Selection Program

The HR files were read into HR objects with a timestamp, a HR, a HR status and a HRQ. Then, a text file with 8 marker times was read in. For every marker and marker type (e.g. time frame size, interval location preference -beginning or end of time frame-, start of the time frame -beginning or end of the time frame-), an algorithm was created to grab the appropriate interval. Only the algorithm for marker 1 is shown here, the others are omitted as they are fairly redundant.

$\triangleright$ find start of time frame in seconds
$\triangleright$ calculate total seconds in measurement
  $timeFrameStart \leftarrow markerTime - fileStartTime$
  $totalSeconds \leftarrow fileEndTime - fileStartTime$

$\triangleright$ initialise values
  $beginSecond \leftarrow timeFrameStart$
  $bestBegin \leftarrow -1$
  $bestInterval \leftarrow 0$
  $secondsInCurrentInterval \leftarrow 0$

$\triangleright$ set timeFrameEnd as $min(totalSeconds, timeFrameStart{+}600)$
  if $timeFrameStart + 600 > totalSeconds$ **then**
    $timeFrameEnd \leftarrow totalSeconds$
  else
    $timeFrameEnd \leftarrow timeFrameStart + 600$
  end if

$\triangleright$ $\forall$ *seconds* in *totalSeconds*

- as long as the HRQ is 4 and $bestInterval < 180$ seconds
- update current interval
- update best interval if current interval is new best interval
- move on if interval found is not longer than 180 seconds

```
for i ← timeFrameStart; i < timeFrameEnd; i++ do
  if i.HRQ = 4 and bestInterval < 180 then
    secondsInCurrentInterval++
    if secondsInCurrentInterval > bestInterval then
      bestBegin ← beginSecond
      bestInterval ← secondsInCurrentInterval
    end if
  else
    beginSecond ← i + 1
    secondsInCurrentInterval ← 0
  end if
end for
```

Appendix E

Other Used Materials

Other documents that were used for this study can be found in the following pages and include:

- flyers,
- an instructions document,
- a completed example of the daily questionnaire and
- the four questionnaires to be filled in at the end of the measurement week.

PHILIPS

Would you like to participate in a study about your heart rhythm during your sleep?

The study involves wearing a comfortable wristband at night, during your sleep, which measures your heart rate. It must be worn two weeks of seven consecutive nights; one week at the beginning of your revalidation period at CIRAN, and one week at the end. We will also ask you to fill in a short diary every day, and a few questionnaires at the end of both weeks. The collected information will be made anonymous and cannot be traced back to you.

The study is performed by Philips, and is therefore completely independent from CIRAN. CIRAN will only provide a room at the CIRAN facility (when you are there anyway) so we can give you the wristband and some instructions.

Your participation in this experiment is not part of your treatment at CIRAN and is completely voluntary. It will not influence your revalidation process at CIRAN in any way.

If you decide to participate, we will give you a financial compensation of 50 Euros in gift vouchers for your participation.

If you are interested to get more information, please contact:

Juney Dijkstra
Philips Research
juney.dijkstra@philips.com

Joyce Westerink
Philips Research
joyce.westerink@philips.com
06 316 28 153

Would you like to participate in a study about your heart rhythm during your sleep?

The study involves wearing a comfortable wristband at night, during your sleep, which measures your heart rate. It must be worn two weeks of seven consecutive nights; with 16 weeks in between measurement weeks. We will also ask you to fill in a short diary every day, and a few questionnaires at the end of both weeks. The collected information will be made anonymous and cannot be traced back to you.

If you are interested to get more information, please contact:

Juney Dijkstra
Philips Research
juney.dijkstra@philips.com

Joyce Westerink
Philips Research
joyce.westerink@philips.com
06 316 28 153

Heart Rate Dynamics and Burnout
Juney Dijkstra
juney.dijkstra@philips.com

Heart Rate Dynamics and Burnout
Juney Dijkstra
juney.dijkstra@philips.com

Heart Rate Dynamics and Burnout
Juney Dijkstra
juney.dijkstra@philips.com

Heart Rate Dynamics and Burnout
Juney Dijkstra
juney.dijkstra@philips.com

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Heart Rate Dynamics and Burnout
Juney Dijkstra
juney.dijkstra@philips.com

Heart Rate Dynamics and Burnout
Juney Dijkstra
juney.dijkstra@philips.com

Philips Heart Rate Measurement Study

Instructions and Diary

Researcher Contact information

Juney Dijkstra
Philips Research
juney.dijkstra@philips.com

Joyce Westerink
Philips Research
joyce.westerink@philips.com
06 316 28 153

Instructions for every evening

1. First, just before going to bed, please fill in the “Night” Questionnaire in the diary.

2. You may now strap on the watch.

   TWO MIO

   a. Strap the "Night" MIO around the wrist of your dominant arm, above your wrist bone (see Figure 1). The strap should wrap around your arm snugly, but should not feel uncomfortable (you should be able to fit at most one finger between the strap and your wrist). If you have slim wrists, feel free to wear the watch higher on your arm.

   ONE MIO

   b. Strap the MIO around the wrist of your dominant arm, above your wrist bone (see Figure 1). The strap should wrap around your arm snugly, but should not feel uncomfortable (you should be able to fit at most one finger between the strap and your wrist). If you have slim wrists, feel free to wear the watch higher on your arm.

Figure 1 Photo of MIO location on wrist

3. To start measuring, please hold down the "HR" button (see Figure 2) until the MIO says "FIND" and beeps. The watch will now try to find your pulse and record it.

Figure 2 Photo of “HR” button location on MIO

4. Please write down the approximate measurement starting time in the diary, above the questionnaire.

5. Please wear the watch during the night and follow the “Every Morning” instructions when you wake up.

Instructions for every morning

1. Upon waking, please write down the approximate time of waking up and please fill in the "Morning" Questionnaire in the diary. Going to the bathroom first is allowed, but please finish the instructions before heading to breakfast.

2. Then, please start the laptop. Let the laptop start up until you see the desktop (see Figure 3). If the laptop requests you to log in, use the following log in information.

   Username:
   Password:

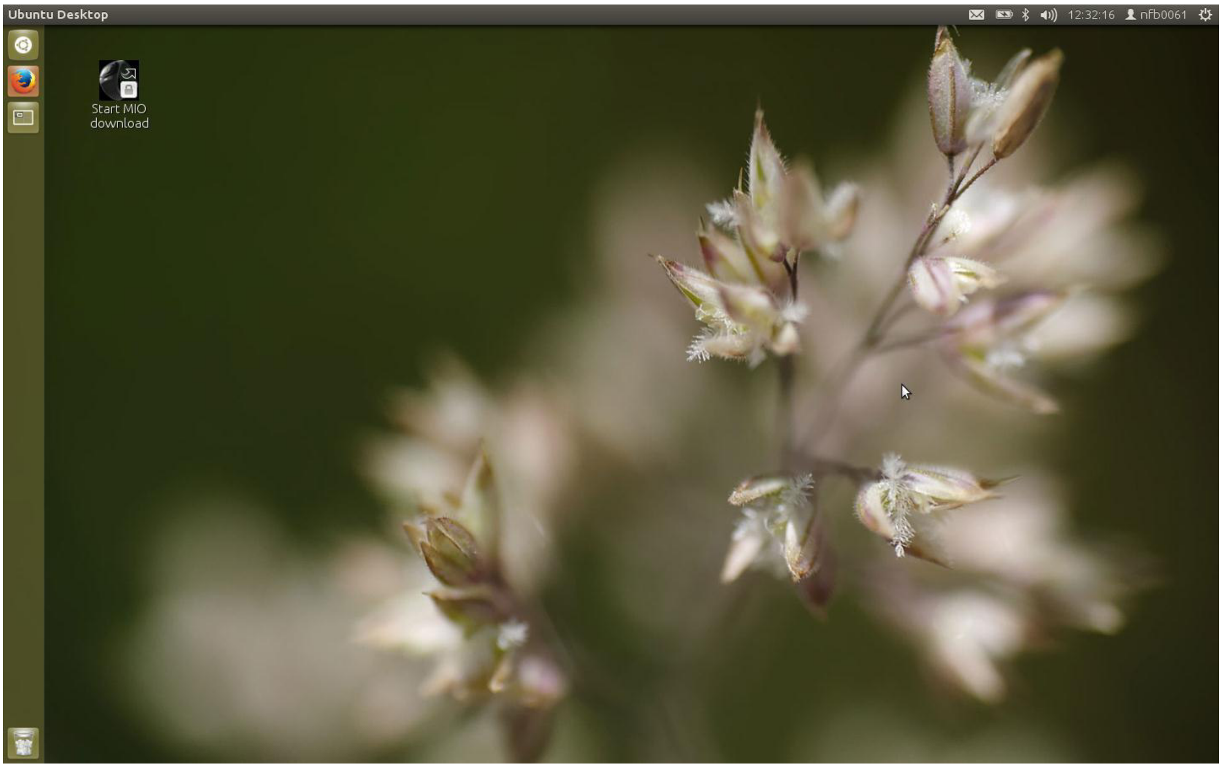

Figure 3 Screenshot of the Laptop Desktop with "Start MIO Download" icon

3. Double click the "Start MIO Download" icon on the desktop (see Figure 3) with your left mouse button to start the program (see Figure 4).

4. Please follow the instructions on the screen until the program lets you know you're finished (the program on screen will report "Download done!"). The instructions will include walking you through connecting to the MIO to the laptop and performing the two breathing exercises.

5. When the downloading and erasing of the MIO memory is finished leave the MIO and dongle attached to the USB port and leave the laptop turned on. The MIO will be fully charged after approximately 3 hours. After the MIO is fully charged, you may shut down the laptop once you are in its vicinity again, or when you go to bed.

   (Alternatively, if you feel uncomfortable leaving the laptop turned on in your absence, you can charge the MIO by unplugging the USB cable and plugging it into the USB adapter, fit for any power socket. The MIO will be fully charged after approximately 3 hours.)

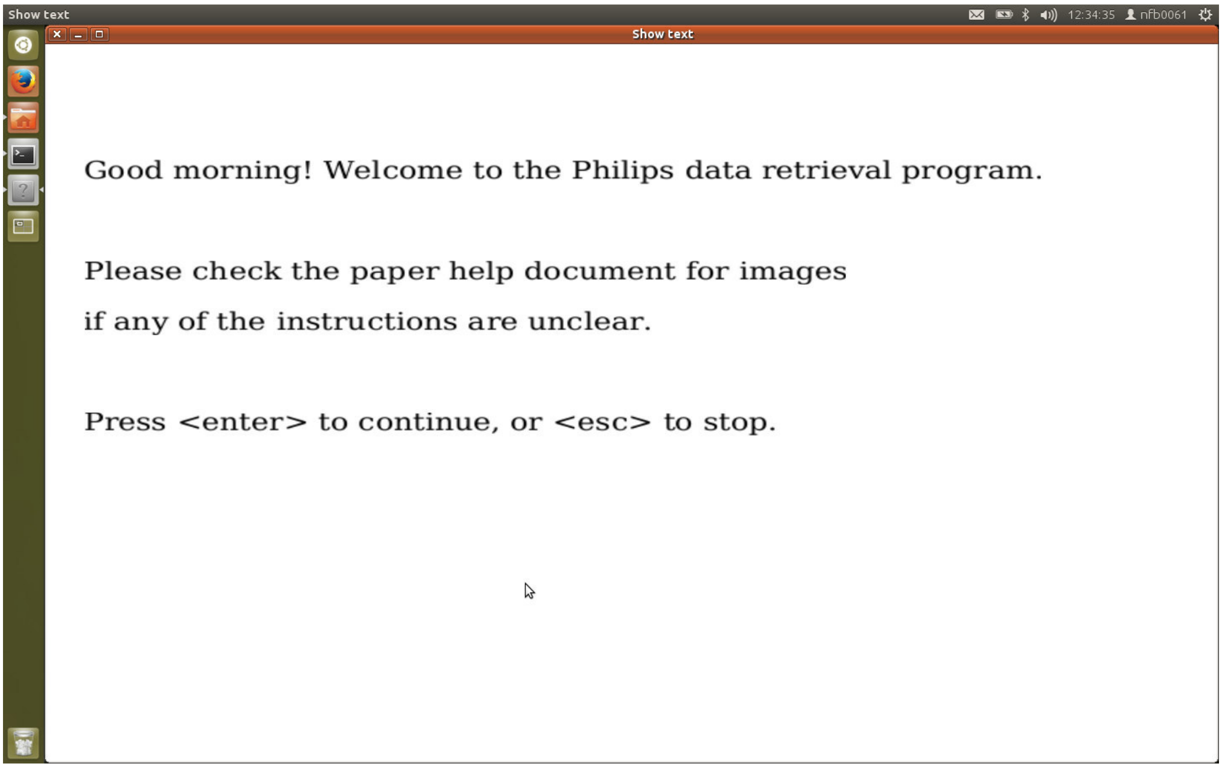

Figure 4 Screenshot of the first screen of the program

Figure 5 Photo of the USB cable location on the laptop

Figure 6 Photo of the MIO attached to the dongle, resting on its side or upside down

Morning questionnaire

Date 4-June Time of waking 7 : 45

	1	2	3	4	5	
Unhappy			✓			Happy
Calm		✓				Excited
Exhausted				✓		Energetic
Submissive				✓		Dominant
Relaxed		✓				Stressed
Bad sleep				✓		Good sleep

How much time have you spent outside of bed before starting this task since waking up? 3min

Starting time breathing exercise #1 7 : 48am **Starting time breathing exercise #2** 7: 54am

Evening questionnaire

Date 5-June **Measurement starting time** 00:01

	1	2	3	4	5	
Unhappy				✓		Happy
Calm			✓			Excited
Exhausted		✓				Energetic
Submissive				✓		Dominant
Relaxed		✓				Stressed

How often:	0	1	2	3	4	5	6
	Never	A few times a year or less	Once a month or less	A few times a month	Once a week	A few times a week	Every day

	Statements	How often						
1.	I feel emotionally drained from my work.	0	1	2	3	4	5	6
2.	I feel used up at the end of the workday.	0	1	2	3	4	5	6
3.	I feel tired when I get up in the morning and have to face another day on the job.	0	1	2	3	4	5	6
4.	Working all day is really a strain for me.	0	1	2	3	4	5	6
5.	I can effectively solve the problems that arise in my work.	0	1	2	3	4	5	6
6.	I feel burned out from my work.	0	1	2	3	4	5	6
7.	I feel I am making an effective contribution to what this organization does.	0	1	2	3	4	5	6
8.	I've become less interested in my work since I started this job.	0	1	2	3	4	5	6
9.	I have become less enthusiastic about my work.	0	1	2	3	4	5	6
10.	In my opinion, I am good at my job.	0	1	2	3	4	5	6
11.	I feel exhilarated when I accomplish something at work.	0	1	2	3	4	5	6
12.	I have accomplished many worthwhile things in this job.	0	1	2	3	4	5	6
13.	I just want to do my job and not be bothered.	0	1	2	3	4	5	6
14.	I have become more cynical about whether my work contributes anything.	0	1	2	3	4	5	6
15.	I doubt the significance of my work.	0	1	2	3	4	5	6
16.	At my work, I feel confident that I am effective at getting things done.	0	1	2	3	4	5	6

PITTSBURGH SLEEP QUALITY INDEX (PSQI)

INSTRUCTIONS: The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

1. During the past month, when have you usually gone to bed at night?

   USUAL BED TIME ____________________

2. During the past month, how long (in minutes) has it usually take you to fall asleep each night?

   NUMBER OF MINUTES ____________________

3. During the past month, when have you usually gotten up in the morning?

   USUAL GETTING UP TIME ____________________

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.)

   HOURS OF SLEEP PER NIGHT ____________________

INSTRUCTIONS: For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you...

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(a) ...cannot get to sleep within 30 minutes	☐	☐	☐	☐
(b) ...wake up in the middle of the night or early morning	☐	☐	☐	☐
(c) ...have to get up to use the bathroom	☐	☐	☐	☐
(d ...cannot breathe comfortably	☐	☐	☐	☐
(e) ...cough or snore loudly	☐	☐	☐	☐
(f) ...feel too cold	☐	☐	☐	☐
(g) ...feel too hot	☐	☐	☐	☐
(h) ...had bad dreams	☐	☐	☐	☐
(i) ...have pain	☐	☐	☐	☐

(j) Other reason(s), please describe

____

____

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
How often during the past month have you had trouble sleeping because of this?	☐	☐	☐	☐

	Very good	Fairly good	Fairly bad	very bad
6. During the past month, how would you rate your sleep quality overall?	☐	☐	☐	☐

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
7. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?	☐	☐	☐	☐
8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?	☐	☐	☐	☐

	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?	☐	☐	☐	☐

	No bed partner or roommate	Partner/ roommate in other room	Partner in same room, but not same bed	Partner in same bed
10. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?	☐	☐	☐	☐

If you have a roommate or bed partner, ask him/her how often in the past month you have had...

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(a) ...loud snoring	☐	☐	☐	☐
(b) ...long pauses between breaths while asleep	☐	☐	☐	☐
(c) ...legs twitching or jerking while you sleep	☐	☐	☐	☐
(d) ...episodes of disorientation or confusion during sleep	☐	☐	☐	☐
(e) Other restlessness while you sleep; please describe	☐	☐	☐	☐

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate *how often* you felt or thought a certain way. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each question fairly quickly. That is, don't try to count up the number of times you felt a particular way, but rather indicate the alternative that seems like a reasonable estimate.

For each question, choose from the following alternatives:

0. Never
1. Almost never
2. Sometimes
3. Fairly often
4. Very often

Questions

1. In the last month, how often have you been upset because of something that happened unexpectedly?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

2. In the last month, how often have you felt that you were unable to control the important things in your life?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

3. In the last month, how often have you felt nervous and 'stressed'?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

4. In the last month, how often have you dealt successfully with irritating life hassles?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

5. In the last month, how often have you felt that you were effectively coping with important changes that were occurring in your life?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

6. In the last month, how often have you felt confident about your ability to handle your personal problems?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

7. In the last month, how often have you felt that things were going your way?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

8. In the last month, how often have you found that you could not cope with all the things that you had to do?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

9. In the last month, how often have you been able to control irritations in your life?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

10. In the last month, how often have you felt that you were on top of things?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

11. In the last month, how often have you been angered because of things that happened that were outside of your control?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

12. In the last month, how often have you found yourself thinking about things that you have to accomplish?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

13. In the last month, how often have you been able to control the way you spend your time?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

14. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

    0. Never
    1. Almost never
    2. Sometimes
    3. Fairly often
    4. Very often

QUESTIONS

1. I’ve been feeling optimistic about the future

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

2. I’ve been feeling useful

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

3. I've been feeling relaxed

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

4. I’ve been feeling interested in other people

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

5. I've had energy to spare

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

6. I’ve been dealing with problems well

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

7. I've been thinking clearly

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

8. I’ve been feeling good about myself

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

9. I’ve been feeling close to other people

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

10. I've been feeling confident

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

11. I’ve been able to make up my own mind about things

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

12. I’ve been feeling loved

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

13. I’ve been interested in new things

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time

14. I've been feeling cheerful

a) None of the time
b) Rarely
c) Some of the time
d) Often
e) All of the time