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Master thesis (25 ECTS)

The Effects of the Philips Audio Neurofeedback System on Sleep

A thesis presented to the department of Psychology, Health and Technology (PGT)
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Abstract

Background: The high prevalence and impact of sleep disorders on individuals and society calls for adequate treatment options. Neurofeedback (NFB) presents an individualized treatment for sleep disorders that could have less adverse effects than pharmaceutical solutions. Its' effects and feasibility should be explored further. For this purpose, knowledge on methods to measure sleep (other than polysomnography) should be increased by comparing different objective and subjective measures.

Objectives: This study aimed to determine the effects of SMR-up and Beta-down audio NFB training on (i) sleep onset latency (SOL), perceived sleep quality, insomnia severity and (ii) total wake time after sleep onset (TWT), fatigue, depression, anxiety and stress. Furthermore, the agreement and differences between a subjective (Consensus Sleep Diary, CSD) and objective (Philips Health Watch, PHW) measure on SOL and TWT were examined.

Methods: Forty-one participants (6 dropped out) were randomly assigned to the SMR-up (n = 13) or beta-down (n = 15) NFB condition or the control condition (n = 13). Participants were asked to conclude at least 21 (at-home) audio neurofeedback (NFB) training sessions using the Philips audio Neurofeedback System (PNFS). Measurements took place pre-, post and during the study phase (which lasted on average 30 days per participant).

Results: A significant improvement over time was found on all primary and secondary outcomes in all conditions, except for SOL and TWT measured through the PHW. However, in the SMR or beta NFB training conditions no larger improvements were found than in the control condition. Yet, a pooled analysis on sleep quality (PSQI score) including data of a similar RCT indicated that beta neurofeedback training worked better in improving sleep quality. The comparison of the (subjective) CSD and the (objective) PHW measurements on SOL and TWT showed high differences (and thus bias) between the two measures, indicating that measurements can only be compared when log10-transformed and not on an absolute level.

Discussion / conclusion: We have to conclude that our study provides no (clear) evidence for the effectiveness of neurofeedback (either SMR up or Beta down) on sleep, depression, anxiety, or stress. Several factors that could have influenced the results were identified such as the amount of NFB sessions; reactivity of outcome measures; treatment effects; the overall effects of listening to music; small sample size; strict inclusion and exclusion criteria; and the lack of knowledge on actual changes in EEG activity.

Recommendations: The following recommendations for future research can be given based on the results of this study:

- Analyze measurements of EEG activity during neurofeedback sessions.
- Include a control condition in which participants wear the Philips Health Watch and fill in the Consensus Sleep Diary but do not receive (pseudo) neurofeedback training.
- Include a follow-up measurement after the study phase.
- Increase sample sizes.
- Take into account the type of neurofeedback and its' potential effects in relation to outcomes in the study design.
- Increase the amount of neurofeedback sessions and duration of study phase.
- Use subjective and objective measures to report sleep and compare these to each other and the "golden standard" in sleep measurement, polysomnography.

Table of Contents

Abbreviations

Abbreviation	Description
NFB	Neurofeedback
EEG	Electroencephalography
SMR	Sensorimotor rhythm
SOL	Sleep onset latency
TWT	Total wake time after sleep onset
PSG	Polysomnography
PNFS	Philips Audio Neurofeedback System
CSD	Consensus Sleep Diary
PHW	Philips Health Watch

1 Introduction

1.1 Background

Sleep disorders are highly prevalent and can have a strong impact on individuals and society. In 2010, the total number of persons with sleep disorders in Europe was estimated around 45 million. In the same year, 1.4 million persons suffered from sleep disorders in the Netherlands (Gustavsson et al., 2011). Sleep disorders are reported to have a significant negative impact on Quality of Life (QoL) (Bolge, Doan, Kannan, & Baran, 2009; Szentkirályi, Madarász, & Novák, 2009). These effects on QoL might be even stronger in specific target groups such as persons suffering from one or more chronic (health) conditions (Chasens, Sereika, Burke, Strollo, & Korytkowski, 2014; Havlikova et al., 2011; McKenna, Tierney, O'Neill, Fraser, & Kennedy, 2018). Sleep disorders also have societal consequences. In 2010, the total societal costs of sleep disorders in the Netherlands were estimated around 1.4 billion euros (Gustavsson et al., 2011). Furthermore, sleep disorders form a risk to society due to an increase in motor vehicle crashes (Gottlieb, Ellenbogen, Bianchi, & Czeisler, 2018). The high prevalence and impact of sleep disorders calls for adequate treatment options.

Current treatment options for sleep disorders are dividable into pharmaceutical and non-pharmaceutical treatments. Neerings-Verberkmoes et al. (2014) found that 74% of persons that visit their general practitioner (GP) for sleep problems are prescribed sleep medication. Treatments by pharmaceutics are effective but have adverse effects to consider such as, dizziness, headache, drowsiness, psychiatric and behavioral problems, hallucinations, and/or weight gain (Ramar & Olson, 2013; Soares & Kanungo, 2018). Prolonged use of sleep medication is also associated with higher mortality hazard and risks for accidents in traffic (Booth et al., 2016; Gustavsen et al., 2008; Kripke, 2016). Examples of non-pharmaceutical treatment options are: sleep hygiene therapy, stimulus control therapy, sleep restriction therapy, relaxation training, and temporal control therapy (Hasora & Kessmann, 2009; Maness & Khan, 2015). Often, these different types of therapy are combined into cognitive behavioral therapy (CBT), in which managing sleep disorders is done by targeting and working on maladaptive thoughts, behaviors and beliefs regarding sleep. CBT has demonstrated to improve sleep, but some researchers such as Fullagar & Bartlett (2016) argue that behavioral therapies like CBT are not geared to the high interpersonal variability of sleep (disorders). The proven adversities of sleep medication and lack of individualized non-pharmaceutical treatments show the need for other types of treatment for sleep disorders.

Neurofeedback (NFB) presents such an individualized treatment for sleep disorders that could have less adverse effects than pharmaceutical solutions. NFB is a method based on the principle of operant conditioning in which individuals train to modulate their own brain activity (Enriquez-Geppert, Huster, & Herrmann, 2017; Reiner, Gruzelier, Bamidis, & Auer, 2018). Feedback on brain activity can be auditory (e.g. improving or reducing music quality or hearing a certain sound), visual (e.g. a bar changing its length or an animated hand changing its posture from open to grasp), or tactile (e.g. feeling a vibration). Feedback can also consist of a combination of these modalities (Enriquez-Geppert et al., 2017). In most types of NFB, electroencephalography (EEG) is used for measuring brain activity. Brain activity measured through EEG takes the shape of brainwaves (or neural oscillations) which can differ in frequency and amplitude. Brainwaves represent simultaneous firing of groups of different kind of neurons in the brain and are generally divided into the following frequency bands: delta (<4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–35 Hz) and gamma (>35 Hz). Sensorimotor rhythm (SMR) consists of the brainwaves ranging from 13 to 15 Hz. SMR activity lies close to alpha and beta activity, but originates from a different region in the brain (Niedermeyer & Silva, 2004).

Brainwaves in the SMR and beta frequency range have specific roles in sleep-related processes. Presence of SMR activity indicates inhibition of motor behavior and sensory input and is of importance due to its role in the sleep onset of humans (Howe & Sterman, 1972). SMR activity is known to play a role in the production of so-called sleep spindles, which are seen in the transition from drowsiness to sleep (De Gennaro & Ferrara, 2003). Increasing SMR activity may therefore decrease sleep onset latency (SOL). Beta activity reflects cognitive load and is of importance due to its role in the development and continuing existence of insomnia. Patients experiencing primary insomnia exhibit higher levels of beta activity during wakefulness in the sleep onset period and during non-rapid eye movement (NREM) and rapid eye movement (REM) sleep (Cortoos, De Valck, Arns, Breteler, & Cluydts, 2010). Inhibiting beta activity may therefore decrease SOL and total wake time after sleep onset (TWT), which might improve sleep quality. The effects and feasibility of the application of audio NFB training enhancing SMR activity and inhibiting beta activity to improve sleep should be explored.

Several studies have examined the potential applications of NFB on improving sleep (Arns, Feddema, & Kenemans, 2014; Cortoos et al., 2010; Hoedlmoser et al., 2008; Schabus et al., 2017, 2014). Arns, Feddema & Kenemans (2014) have examined the effects of visual and

auditory SMR and Theta/Beta (TBR) NFB on sleep onset latency in patients with attention deficit hyperactivity disorder (ADHD). They found a significant decrease on SOL in both the SMR and TBR NFB condition. In the SMR NFB condition, the effects on SOL were most pronounced within the first half of the treatment. Cortoos et al. (2010) compared the effects of at-home visual NFB training (targeting several frequency bands in the EEG spectrum including SMR and Beta) and at-home biofeedback training. This study revealed a decrease in SOL in both treatment groups and a significant improvement in total sleep time only in the NFB condition. Hoedlmoser et al. (2008) tested whether visual NFB enhancing SMR activity had an impact on sleep parameters. Results showed an increase in expression of SMR activity and a shortened SOL only in the SMR-conditioning group. Schabus et al. (2014) examined whether sleep quality in insomnia patients could be improved by enhancing SMR activity. They found a significant decrease of the number of awakenings, a trend towards decreased SOL and a significant improvement in subjective sleep quality as a result of the enhancement. In a subsequent study by Schabus et al. (2017), improvements in subjectively reported sleep quality were seen for participants in the placebo as well as the NFB condition, but no improvements on sleep parameters were measured objectively. The conducted studies provide evidence of the potential beneficial effects of NFB enhancing SMR activity on sleep. Evidence on inhibition of beta activity is limited. The effects of at-home audio NFB training on these frequency bands should be examined further. Previously conducted studies also have some methodological limitations for future studies to address, such as small sample sizes and a lack of adequate control group treatment protocols.

To determine the effects of NFB on sleep, accurate methods to measure sleep are essential. Until today, polysomnography (PSG) remains the golden standard in sleep assessment. However, PSG is costly, exclusive and the assessment of sleep takes place in a potentially stressful environment (e.g. a hospital or a laboratory), which may not reflect real-world circumstances (Ibáñez, Silva, & Cauli, 2018a). Therefore, sleep diaries and questionnaires are used as a substitute or complement. Often, in combination with other objective sleep measurements methods (Ibáñez, Silva, & Cauli, 2018b; Van De Water, Holmes, & Hurley, 2011). There is an ongoing debate on whether available objective measurement methods (e.g. using actigraphy, health trackers, or other hardware devices) and subjective measurements (e.g. sleep diary entries) are reliable, valid, comparable and interchangeable (Cellini, McDevitt, Mednick, & Buman, 2016; Dickinson, Cazier, & Cech, 2016; Razjouyan et al.,

2017). Future studies should address this issue by comparing different methods to measure sleep objectively and subjectively.

1.2 Justification

The Philips Audio Neurofeedback System (PNFS) was developed with the aim to apply instrumental conditioning of brain activity through audio NFB in a consumer product for everyday use. The enhancement of alpha activity using the PNFS was investigated and yielded positive results in studies by van Boxtel et al. (2012) and Dekker et al. (2014). Dam (2016) examined the use of the PNFS to enhance SMR and inhibit beta activity to improve sleep in a double blind randomized controlled trial (RCT) with three arms (control, SMR-up and beta-down). Petit (2018) re-examined the data obtained in this RCT and looked further into the influence of the PNFS on SMR and beta EEG activity by analyzing the EEG recordings of the NFB sessions. Mixed results were found which could be explained by the relatively small sample size (n = 36) and problems with the collection of the objective measurements on sleep. The effects of SMR and beta audio NFB training on sleep have to be examined further to progress the development of the PNFS towards a consumer product.

1.3 Objectives

1.3.1 Primary objective

The primary objective of this study is to evaluate the effects of (beta and SMR) audio neurofeedback training on sleep onset latency (SOL), perceived sleep quality and insomnia severity.

1.3.2 Secondary objectives

The secondary objectives of this study are as follows:

- Evaluating the effect of (beta and SMR) audio neurofeedback training on total wake time after sleep onset (TWT).
- Evaluating the effect of (beta and SMR) neurofeedback training on fatigue levels.
- Evaluating the effect of (beta and SMR) neurofeedback training on depression, anxiety and stress levels.
- Examining the agreement and differences between sleep diary and Philips health watch measurements of sleep onset latency (SOL) and total wake time after sleep onset (TWT).

2 Methods

2.1 Design

This study concerns a double-blind randomized controlled trial (RCT) with three arms. Eligible participants were randomly assigned to one of the experimental conditions (SMR-up or Beta-down) or the control condition. Measurements took place pre-, post and during the study phase (which lasted on average 30 days per participant). The Internal Committee Biomedical Experiments (ICBE) of Philips Research and the Ethics Committee of the University of Twente approved this study.

2.2 Participants and procedures

In September 2018, targeted advertisements were placed on the Philips Benelux Facebook platform. These advertisements were shown to users fitting the inclusion criteria based on their Facebook activity. By clicking on the advertisement, potential participants were redirected to a webpage displaying information about the study and an e-mail address for application. Each applicant was then provided a participant number and a hyperlink to several intake questionnaires that were used to test for eligibility. Eligible participants were self-selected adults residing in the Eindhoven area; aged 18 to 65 year; with a Pittsburgh Sleep Quality (PSQI) score > 5 or a self-reported sleep onset latency (SOL) > 20 minutes; with regular average working hours: 09:00 – 17:00 and a working week of 24 hours or more. Exclusion criteria were:

- Use of sleep deficiency (self-) treatment (medication, drugs, alcohol, therapy);
- Medical conditions that affect the vestibular system (e.g. Ménière disease);
- Pregnancy or breastfeeding;
- Suffering from traumatic experiences;
- Being a student;
- Travelling to other time zones in the last month and/or during the experiment;
- Unwillingness or inability to provide informed consent;
- A DASS depression score > 27 (indicates extremely severe depression);
- A DASS anxiety score > 19 (indicates extremely severe anxiety);
- A DASS stress score > 33 (indicates extremely severe stress).

Of the 412 applicants, 307 filled in the online intake questionnaires correctly and were assessed for eligibility. The relatively high amount of questionnaires (applicants were asked to fill in six questionnaires) might explain the large number of applicants not completing the online intake questionnaires. 266 participants were excluded of which 231 because they did not meet inclusion criteria (mainly due to irregular working hours and use of sleep medication). After accepting invitations for an on-site intake, 41 participants were randomized over the three conditions (SMR-up, Beta-down or control) using block randomization, based on the following covariates derived from the intake questionnaires (see figure 2.1 for a flowchart of the participants):

- Age
- Gender
- Sleep quality (score on the Pitssburgh Sleep Quality index, PSQI)
- Depression, anxiety and stress level (scores on the Depression Anxiety Stress scales, DASS)
- Insomnia severity (score on the Insomnia Severity Index, ISI)
- Fatigue level (score on the Fatigue Assessment Scale, FAS)

On-site intakes took place in groups of three to six participants. During these intakes, informed consent was obtained from each of the participants. Participants filled in the pre-test questionnaires. Furthermore, each participant received the study equipment, information on the study procedure, and instructions on how to use the equipment. During the study phase, which lasted on average 30 days, participants were actively monitored to encourage data collection and prevent missing data. The responsible researchers actively supported the participants by providing (on-site/at home) technical support and weekly “How are you?”-emails in which they asked for an update of the participants’ progress regarding the training sessions and data collection. The on-site outtake meetings took place individually or in groups of two to six participants. During the outtakes, participants were asked to fill in the post-test questionnaires, which consisted of the same questionnaires as the pre-test with exception of the following items that were added:

- A few questions regarding the experience that the participants had during the study and with the use of the PNFS in general.
- The System Usability Scale (SUS)
- The van Westendorp price sensitivity scale

The results of these extra items were not analyzed for the current study report but were integrated for internal research and development purposes. As an incentive, participants who completed the training phase received 100 euros in VVV vouchers during the outtake meeting. Participants that quit the training before the end of the 4 weeks received a compensation of 50 euros in VVV vouchers.

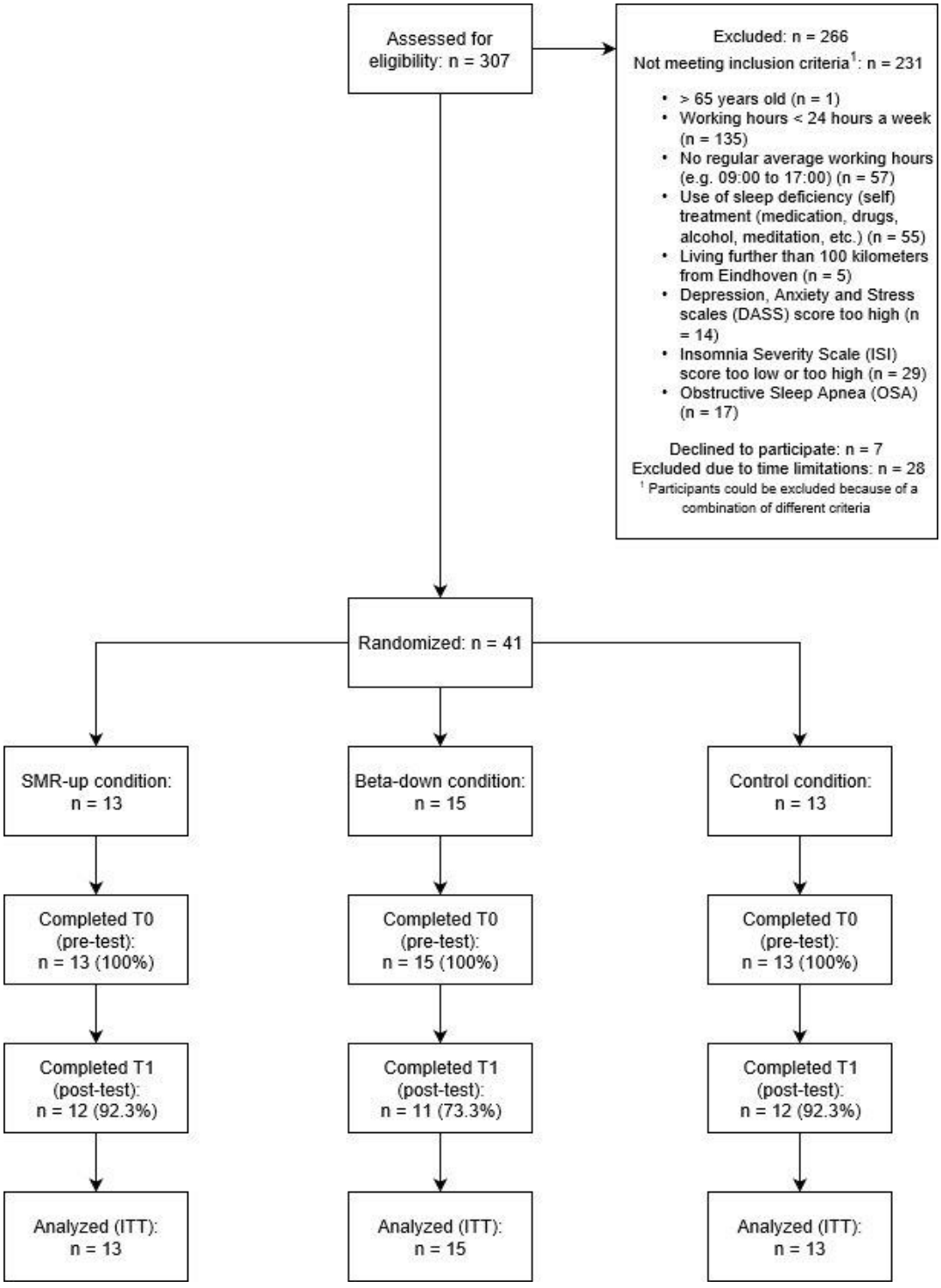

Figure 2.1 Flowchart of participants *Neurofeedback4sleep* study

2.3 The intervention – audio neurofeedback training

During the study phase, participants were asked to conclude at least 21 (at-home) audio neurofeedback (NFB) training sessions using the Philips audio Neurofeedback System (PNFS), which consists of two subsystems:

- A Philips O'Neill the Stretch 2.0 Headband Headset (Black) with five water based AgCI EEG electrodes (figure 2.3). This headset is connected to either a Nexus 10 or a TMSI Mobi Mini EEG data recorder (figure 2.4).
- An android tablet, the 'Samsung Galaxy Tab 2', with a playlist of the participant's favorite music, the Philips Neurofeedback System application and several games (figure 2.5).

Figure 2.2: Complete Philips Neurofeedback System

Figure 2.3: Locations of electrodes on the Philips O'Neill the Stretch 2.0 Headband Headset.

Figure 2.4: The Nexus 10 EEG data recorder

Figure 2.5: Samsung Galaxy Tab running the Philips Neurofeedback System application

Each of the audio NFB sessions consisted of 10 minutes of audio NFB training followed by 5 minutes of playing a game and another 10 minutes of audio NFB training. For participants in all experimental conditions, the intervention structure was the same but different power bands in the EEG-spectrum were stimulated during the session. In the Beta-down condition, a lower power in the beta band of the EEG spectrum was stimulated during received audio NFB training. In the SMR-up condition, a higher power in the SMR band of the EEG spectrum

was stimulated. In the control condition, pre-stored EEG data of other individuals was used to mimic a natural EEG signal to elicit "random" stimulation. The EEG measurements of each session were recorded and stored on a data server. Active monitoring of adherence to the intervention was performed by accessing this data.

A description of the exact functionality of the Philips Neurofeedback System, details on the Philips Neurofeedback System application and a more extensive explanation on the NFB mechanisms in the different conditions is included in appendix 1.

2.5 Measures

The measures used in the current study can be divided into pre- and post-test measures and measures during the training phase of the study.

2.5.1 Pre- and post-test measures

The following pre- and post-test measures were used:

- The Pittsburgh Sleep Quality Inventory (PSQI) (appendix 2)
- The Insomnia Severity Scale (ISI) (appendix 3)
- The Fatigue Assessment Scale (FAS) (appendix 4)
- The Depression Anxiety and Stress Scales (DASS) (appendix 5)

Sleep quality was measured using the Pittsburgh Sleep Quality Inventory (PSQI, appendix 2) (Buysse et al., 1989). The PSQI is a short self-report assessment of general sleep quality during the previous month consisting of 19 self-rated questions and 5 questions to be rated by a bed partner or roommate (if available). Only the self-rated questions are included in the scoring. The PSQI measures different aspects of sleep and results in seven component scores reflecting the following domains: subjective sleep quality; sleep onset latency (i.e., the time it takes to fall asleep); sleep duration; sleep efficiency (i.e., the percentage of time in bed that one is asleep); sleep disturbances; use of sleeping medication; and daytime dysfunction. The items assessing sleep duration, sleep onset latency and sleep efficiency consist of free entry questions such as: *"During the past month, what time have you usually gone to bed at night?"*. Items assessing sleep disturbances, the use of sleep medication and daytime dysfunction have answering options ranging from 0 ("*Not during the past month*") to 4 ("*Three or more times a week*"). An example item is as follows: *"During the past month, how often have you had trouble sleeping because you could not get to sleep within 30 minutes?*". The item assessing sleep quality *"During the past month, how would you rate your sleep*

quality overall?" has answering options ranging from 0 ("*Very good*") to 4 ("*Very bad*"). Each item is weighted on a 0–3 interval scale. The global PSQI score is then calculated by summing the seven component scores, providing an overall score ranging from 0 to 21, with a score > 5 indicating poor sleep quality (Backhaus, Junghanns, Broocks, Riemann, & Hohagen, 2002). The PSQI has been widely translated and employed in a range of population-based and clinical studies. It has shown to be a reliable and valid instrument for the assessment of subjective general sleep quality. The internal consistency ($\alpha = 0.65$) of the PSQI in the current study was lower than the internal consistency reported in the literature ($\alpha = 0.83$) (Backhaus et al., 2002). This difference might have been caused by certain characteristics of the sample population included in the current study (one of the inclusion criteria was a PSQI score of > 5).

Severity of insomnia was measured using the Insomnia Severity Index (ISI, appendix 3) (Morin, Belleville, Bélanger, & Ivers, 2011). The ISI is a self-report, 7-item questionnaire designed in a 5-point Likert frequency scale, with answering options ranging from 0 ("*None/Not at all*") to 4 ("*Very*"). Questions refer to insomnia experiences in the previous two weeks and include questions, such as: "*How satisfied/dissatisfied are you with your current sleep pattern?*" and "*To what extent do you consider your sleep problem to interfere with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) currently?*". The ISI score is determined by adding the scores on the seven items and can range from 0 to 21, with a score > 15 indicating moderate to severe insomnia. The ISI has demonstrated excellent internal consistency ($\alpha = 0.90$) and validity in a validation study by Morin et al. (2011). The internal consistency of the ISI in the current study was lower ($\alpha = 0.77$), but still acceptable.

Fatigue was measured using the Fatigue Assessment Scale (FAS, appendix 4) (Michielsen, De Vries, Van Heck, Van de Vijver, & Sijtsma, 2004). The FAS is a self-report, 10-item questionnaire designed in a 5-point Likert frequency scale with answering options ranging from 1 ("*Never"*) to 5 ("*Always"*). Questions include statements regarding fatigue experiences in general, such as: *"I get tired very quickly", "I have enough energy for everyday life",* and *"When I am doing something, I can concentrate quite well"*. FAS scores are calculated by summing the scores on all items and can range from 10 to 50, with a score of > 22 indicating substantial fatigue (Michielsen, De Vries, & Van Heck, 2003).The internal consistency of the FAS for the Dutch population was investigated by Michielsen, de Vries & van Heck (2003).

The FAS showed a good internal consistency (α = 0.90). The internal consistency of the FAS in the current study was also good (α = 0.90).

Depression, anxiety and stress were measured using the Depression Anxiety Stress Scales (DASS, appendix 5) (Lovibond & Lovibond, 1995). The DASS is a self-report, 42-item questionnaire designed in a 4-point Likert frequency scale, with answering options ranging from 0 ("*Did not apply to me at al*") to 3 ("*Applied to me very much, or most of the time*"). Questions refer to depression, anxiety and stress experiences in the previous week, such as: "*I found myself getting upset by quite trivial things*", "*I was aware of dryness of my mouth*" and "*I couldn't seem to experience any positive feeling at all*". The scores for the total and the subscales are calculated by determining the sum scores of the constituent items. The score on each subscale of the DASS can range from 0 to 42 with cut-off scores for moderate depression, anxiety and stress respectively lying at > 13, > 9, and > 18 (Lovibond & Lovibond, 1995). The DASS has demonstrated excellent internal consistency on each of the subscales (α = 0.96, 0.89 and 0.93 for Depression, Anxiety, and Stress, respectively) in a validation study by Brown, Chorpita, Korotitsch, & Barlow (1997). In the current study, the internal consistency was slightly lower, but still good (α = 0.90, 0.81 and 0.91 for Depression, Anxiety, and Stress, respectively).

2.5.2 Measures during the training phase

Consensus Sleep Diary

During the study phase, sleep onset latency (SOL), total wake time after sleep onset (TWT) and Sleep Quality (SQ) were (subjectively) measured using an online version of the Consensus Sleep Diary (CSD, appendix 6) (Carney et al., 2012). The CSD is a sleep diary that gives insight in several sleep parameters (e.g. sleep onset latency and number of awakenings) as well as into sleep hygiene habits (e.g. caffeine intake and alcohol intake). The version of the CSD used in the current study (CSD-M) consists of 15 items with different response options. The items from the original questionnaire assessing sleep onset latency, sleep duration and time in bed were merged into three different sliders by which the participants answered the following questions:

- *"At what time did you get into bed and at what time did you get out of bed for the day?"*
- *"At what time did you try to go to sleep and at what time did you finally wake without trying to sleep more?"*

- *"From when to when did you actually sleep?"*

Examples of other items and their responses options were as follows (for the other items, see appendix 6):

- *"How many times did you wake up, not counting your final awakening?"* (e.g. 5)
- *"How would you rate your quality of sleep on a scale from 1 to 10?"* (1: very poor, 10: very good)
- *"How rested or refreshed did you feel when you woke-up for the day?"* (1: not rested at all, 10: very rested)
- *"How many glasses of alcohol did you drink last night?"* (e.g. 3)
- *"At what time did you consume your last alcoholic drink last night?"* (e.g. 22:30)

Findings by Maich, Lachowski & Carney (2018) have provided good support for the validity and utility of the CSD. The internal consistency of CSD is not determined because the sleep diary is not intended to measure one construct, and items are not expected to correlate with one another (e.g., there is no reason to expect that bed time would correlate with number of awakenings).

Philips Health Watch

During the study phase, sleep onset latency (SOL) and total wake time after sleep onset (TWT) were objectively measured using the Philips Health Watch (PHW) by measuring heart rate (variability). The PHW (figure 2.6) is CE marked and can be classified a medical device (FDA class 2). The accuracy of measurements of sleep parameters using the PHW was examined by Hendrikx et al. (2017). Their study showed that total energy expenditure can be estimated by the PHW with an accuracy of 85%. This is an important finding as sleep can be recognized as periods of low total energy expenditure.

Furthermore, the PHW provides insight into sleep parameters due to its photoplethysmography (PPG) functionality. PPG sensors have shown to be able to accurately measure average heart rate and offer the possibility of measuring heart rate variability (HRV) throughout the night. HRV can be used to determine sleep phases as different levels of HRV represent different sleep stages (Fonseca et al., 2017). Philips Research developed a PPG-based sleep staging algorithm that achieved a satisfactory agreement for the following sleep parameters: Total Sleep Time (TST), TWT, and Sleep Efficiency (SE, i.e., the percentage of time in bed that one is asleep)

for more than 70% of the processed recordings (Fonseca et al., 2017). The aforementioned algorithm was used to derive SOL and TWT measurements for the current study.

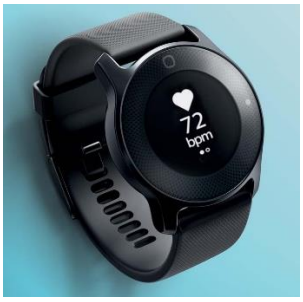

Figure 2.6: the Philips Health Watch

In table 2.1, a visualization of the measures over the time points of the study is given.

Table 2.1 Visualization of measures over time points *Neurofeedback4sleep* study

Measure	T0 (pre-test)	Training phase	T1 (post-test)
Sleep quality (PSQI)	X		X
Fatigue (FAS)	X		X
Depression, anxiety and stress (DASS)	X		X
Insomnia severity (ISI)	X		X
SOL and TWT (PHW)		X	
SOL, TWT, and sleep quality (CSD)		X	

2.5 Sample size calculation

The sample size calculation for the study was conducted using G*power 3 (Faul, Erdfelder, Lang, & Buchner, 2007). The effect size was set to be 0.40 based on reported results of an earlier study by Cortoos et al. (2010). The statistical test for the study was set to an ANOVA repeated measures (pre-test and post-test) between factors (the three experimental conditions). The α value was set to 0.05 and the statistical power 1-β to 0.80. In order to satisfy the above parameter settings, a sample size of at least N = 51 was deemed necessary. Calculating a drop-out rate of about 15%, the final sample size was set to N = 60.

2.6 Statistical analysis

All statistical analyses were performed using R Statistical Software version 3.5.1 (R Core Team, 2012) with 2-tailed tests with a significance level of < .05. Little's MCAR test indicated that missing data were completely at random for pre- and posttest data (X^2 (16) =

18.31, p = .306). Missing Philips Health Watch (PHW) and Consensus Sleep Diary (CSD) data were not completely at random (X^2 (2) = 9.51, p < .01 and X^2 (2) = 31.13, p < .001), indicating that it would not be safe to list wise delete cases with missing values or to singly impute missing values. Therefore, an intention-to-treat analysis (ITT) without imputation was conducted using a linear mixed models (LMM) procedure. We only report the ITT results.

Chi-square tests, one-way analysis of variance (ANOVA) and non-parametrical Kruskal-Wallis rank sum tests were conducted to examine if there were any significant differences between conditions on any of the demographics or pre-test measurements at baseline.

Dropout was defined as early termination of the experiment (before the end of the 30 days). Differences in the amount of dropouts in the three conditions were analyzed using Pearson's chi-square tests with Yates' continuity correction. Differences between dropouts and completers on demographics and baseline measurements were analyzed using Pearson's chi-square tests with Yates' continuity correction, analysis' of variance (ANOVA's) and non-parametrical Kruskal-Wallis rank sum tests.

LMM's allow to account for item-level variability and subject-level variability by including both fixed and random effects as an extension of simple linear models. Mixed models account for missing data using maximum likelihood for the estimation of missing data points (Liu, 2015). LMM's were set-up for all variables and types of data (pre- and post-test, CSD- and HW-data) using the "lme4" -package in R (Bates et al., 2014). These LMM's included time as repeated measures and group, time and group × time interaction as fixed effects. Furthermore, random intercepts for each participant were included as random effects. Each LMM was tested for violations on the assumptions of linearity, homogeneity of variance and normal distribution of model residuals. No clear violations were detected. The "predictmeans" package was used to generate predicted means from each LMM (as displayed in the table 3.3 and table 3.4) (Dongwen, Ganesh, & Koolaard, 2014).

Sleep onset latency (SOL) and total wake time after sleep onset (TWT) measurements (CSD and HW) were log10-transformed in order to meet a normal distribution before setting up the LMM's.

The "lmerTest"-package was used to perform ANOVA's on the LMM's to provide statistical inference on the amount of variance contributed by group and time as main effects and the interaction of group with time (Kuznetsova, Brockhoff, & Christensen, 2017).

Data on disturbance in sleep quality (PSQI) scores of the current study was pooled with data of the almost identical randomized controlled trial (RCT) with the same outcome measure performed by Dam (2016). This approach was chosen because both studies have a too small sample size according to their power analyses. Pooled analysis of the data of both studies allows for the drawing of firmer conclusions regarding the effects of the Philips Audio Neurofeedback System on sleep quality. A separate ITT analysis was performed on this data, following an LMM procedure.

Agreement between the CSD and PHW measures on SOL and TWT was examined by comparing measurements of 760 nights using Bland-Altman analysis. In Bland-Altman plots, the differences between the CSD and HW measurements were plotted against the means of the two measurements. The mean differences between CSD and HW measurements, and limits of agreement (LOA's) were plotted as lines (respectively, blue and red). The LOA's (d – 1.96 * SD and d + 1.96 * SD) were calculated using the mean difference (d) and standard deviation (SD) of the differences. Furthermore, the Confidence Intervals (CI's) were calculated for the LOA's and mean differences. The proportions of measurements outside of the LOA's were also calculated. The degrees of correlation between the means and the differences of the two measurement methods on SOL and TWT were determined using Pearson's product-moment correlation and linear regression. These correlations were plotted as a (dotted) line in the Bland-Altman plots (representing the adjusted R^2 or "line of best fit"). Due to heteroscedascity of the data (SOL and TWT measurements), a log10-transformation was performed and the Pearson's correlation was recalculated to derive proportional bias.

3 Results

3.1 Baseline

3.1.1 Demographics

In table 3.1, the age and gender of the participants are displayed for the three conditions (SMR-up, Beta-down and Control). Most of the participants were female (70.7%). About half of the participants was aged 45 years or older (56.1%).

Table 3.1
Baseline characteristics of participants in the SMR-up, Beta-down, and control group and the total sample.

	SMR-up (*n* = 13)	Beta-down (*n* = 15)	Control (*n* = 13)	Total (*n* = 41)	*P*[1]
Gender, *n* (%)					.982
Female	9 (69.2)	11 (73.3)	9 (69.2)	29 (70.7)	
Male	4 (30.8)	4 (26.3)	4 (30.8)	12 (29.3)	
Age, *n* (%)					.477
≤ 45 years	7 (53.8)	7 (46.7)	9 (69.2)	23 (56.1)	
> 45 years	6 (46.2)	8 (53.3)	4 (30.8)	18 (43.9)	

[1]Chi-square tests.
Note: There were no significant group differences.

3.1.2 Baseline measures (pre-test)

In table 3.2, the baseline measurements on sleep quality (PSQI), insomnia severity (ISI), fatigue (FAS) and depression, anxiety and stress (DASS) are displayed for the three conditions (SMR-up, Beta-down and Control). No significant differences were found between conditions on these measurements. Therefore, the randomization procedure was successful.

Table 3.2
Baseline scores on sleep quality (PSQI), insomnia severity (ISI), fatigue (FAS) and depression, anxiety and stress (DASS) of participants in the SMR-up, Beta-down, and control group.

	SMR (*n* = 13) *M* (*SD*)	Beta (*n* = 15) *M* (*SD*)	Control (*n* = 13) *M* (*SD*)	*P*[1]
Disturbance in sleep quality (PSQI)	7.15 (2.88)	8.53 (2.85)	8.00 (2.20)	.401
Insomnia Severity (ISI)	14.69 (2.72)	14.79 (4.46)	15.08 (3.20)	.960
Fatigue (FAS)	21.17 (7.02)	18.53 (4.91)	20.92 (7.57)	.503
Depression (DASS)	3.31 (4.07)	4.73 (4.30)	4.15 (5.64)	.452
Anxiety (DASS)	3.15 (3.72)	3.27 (3.53)	1.85 (1.77)	.563
Stress (DASS)	9.31 (6.64)	9.33 (5.69)	9.92 (7.41)	.994

[1] Non-parametrical Kruskal-Wallis rank sum tests for DASS subscales, one-way ANOVA's for the other variables.
Note: PSQI = Pittsburgh Sleep Quality Index score (0 – 21), ISI = Insomnia Severity Index (0 – 28), FAS = Fatigue Assessment Scale (10 – 50), DASS = Depression Anxiety Stress Scales, Dep = Depression scale of the DASS (0 – 42), Anx = Anxiety scale of the DASS (0 – 42), Str = Stress scale of the DASS (0 – 42).
Note: There were no significant group differences.

According to the generally accepted cut-off score (PSQI > 5), the average PSQI score of participants in all groups (7.92) indicates poor sleep quality in the sample. However, the average score on insomnia severity (ISI, 14.85) is close to, but does not indicate clinical insomnia in the sample as the cut-off score lies at 15. The average fatigue (FAS) score (20.1) also lies close to the cut-off score (> 21), but does not indicate substantial fatigue in the sample. Average depression (4.10), anxiety (2.78) and stress (9.51) scores as measured by the DASS show normal levels as the cut-off scores for clinically relevant issues respectively lie at > 10, > 7, and > 11.

3.1.3 Drop-out

Forty-one participants started the study by participation in the on-site intake. In total, 35 participants completed the study phase (30 days). Six participants dropped out for different reasons (e.g. technical issues, personal issues, etc.). Dropouts and completers did not differ significantly on demographics. It appeared that dropouts were more inclined to have lower depression scores and lower fatigue levels than adherers. However, the number of participants (and dropouts) was too low to perform reliable statistical analyses on these differences.

3.2 Primary outcomes

Table 3.3 shows that a significant improvement over time was found for sleep quality (PSQI and sleep diary) and insomnia severity (ISI), but not for health watch and sleep diary measurements on sleep onset latency (SOL). Comparisons between the experimental groups and the control group only showed a significant condition-by-time interaction effect between the Beta-down and control group on SOL measured by the health watch, indicating a marginally significant improvement over time on SOL in the control condition as opposed to a deterioration in the Beta-down condition. No other significant condition-by-time interactions were found, thus showing that one treatment does not work better than another in improving the primary outcomes.

Table 3.3
Primary outcome measures and results of mixed model analysis.

								Time effect, *F* (*P*)	Condition-by-time interaction, *F* (*P*)	
Outcome	Time	SMR-up (*n* = 13)		Beta-down (*n* = 15)		Control (*n* = 13)		SMR-up - Beta-down - Control	SMR-up - Control	Beta-down - Control
		M	SE	M	SE	M	SE			
Sleep onset latency (SOL) – Philips Health Watch ↓	Wk. 1	14.43	3.30	14.67	3.56	19.18	3.08	1.28 (.280)	0.62 (.604)	2.78(.040)*
	Wk. 2	16.44	3.02	22.71	3.49	16.45	2.88			
	Wk. 3	12.21	2.87	21.78	3.34	16.37	2.83			
	Wk. 4	16.11	2.95	25.06	3.35	15.21	2.85			
Sleep onset latency (SOL) – Consensus Sleep Diary ↓	Wk. 1	31.89	7.39	40.42	6.98	24.87	7.47	1.98 (.116)	1.23 (.298)	0.32 (.810)
	Wk. 2	19.07	7.61	31.15	6.98	28.57	7.52			
	Wk. 3	21.79	7.46	30.04	7.18	22.30	7.65			
	Wk. 4	19.56	7.40	31.96	7.42	22.23	7.67			
Disturbance in Sleep Quality (PSQI) ↓	Pre	7.15	0.80	8.54	0.74	8.00	0.80	16.40 (.000)***	1.96 (.174)	0.35 (.560)
	Post	6.59	0.82	5.91	0.78	5.93	0.82			
Sleep Quality (Sleep diary) ↑	Wk. 1	4.96	0.33	5.40	0.31	5.60	0.34	6.58 (.000)***	1.69 (.169)	0.15 (.927)
	Wk. 2	5.80	0.34	5.64	0.31	5.83	0.34			
	Wk. 3	5.69	0.34	5.90	0.32	5.98	0.34			
	Wk. 4	5.74	0.34	5.82	0.33	5.83	0.34			
Insomnia Severity (ISI) ↓	Pre	14.69	1.08	14.80	1.04	15.07	1.08	28.53 (.000)***	0.40 (.535)	0.05 (.824)
	Post	11.40	1.12	9.99	1.08	10.71	1.12			

Note: PSQI = Pittsburgh Sleep Quality Index score (0 – 21), ISI = Insomnia Severity Index (0 – 28).
Note: Means and standard deviations displayed in the table are predicted from linear mixed models containing all groups.
Note: Sleep onset latency measurements (health watch and sleep diary) were log10 transformed for the analysis.
Note: Arrows (↑ or ↓) indicate the desirable direction of change for each of the outcome measures.
* $p < .05$, ** $p < .01$, *** $p < .001$ (two-tailed)

3.2.1 Pooled analysis

Table 3.4 shows the results of a pooled analysis on sleep quality (PSQI score) including data of an almost identical randomized controlled trial (n = 36) performed by Dam (2016) that examined the use of the Philips Neurofeedback System (PNFS) to enhance SMR and inhibit beta activity to improve sleep. A significant improvement over time was found for sleep quality (PSQI), indicating that scores improved in all groups. The pooled analysis shows a significant condition-by-time interaction for the beta-down and control group, indicating that sleep quality improved significantly more in the beta-down group than in the control group. This implies that the beta-down neurofeedback (NFB) condition works better than the SMR-up condition and control condition in improving sleep quality.

Table 3.4
Pooled PSQI scores and results of mixed model analysis.

								Time effect, F, (P)	Condition-by-time interaction, F (P)	
Outcome	Time	SMR-up (n = 23)		Beta-down (n = 25)		Control (n = 24)		SMR-up - Beta-down - Control	SMR-up - Control	Beta-down - Control
		M	SE	M	SE	M	SE			
Disturbances in Sleep Quality (PSQI) ↓	Pre	8.83	0.52	8.88	0.50	7.83	0.51	49.17 (.000)***	0.62 (.434)	11.00 (.002)**
	Post	7.13	0.53	6.09	0.51	6.09	0.51			

Note: PSQI = Pittsburgh Sleep Quality Index score (0 – 21).
Note: Means and standard deviations displayed in the table are predicted from linear mixed models containing all groups.
Note: The arrow (↓) indicates the desirable direction of change.
* $p < .05$, ** $p < .01$, *** $p < .001$ (two-tailed)

3.3 Secondary outcomes

Table 3.5 shows a significant improvement over time on total wake time after sleep onset (TWT) as measured by the sleep diary, fatigue (FAS), depression (DASS), anxiety (DASS) and stress (DASS) in all groups. No significant improvement or deterioration was found for TWT as measured by the health watch. Comparisons between the experimental groups and the control group showed no significant condition-by-time interaction effect on any of the secondary outcome measures. These results indicate that all groups showed significant improvements on most of the variables, but none of the groups, and thus treatments, were better than another in improving the secondary outcomes.

Table 3.5
Secondary outcome measures and results of mixed model analysis.

								Time effect, *F*, (*P*)	Condition-by-time interaction, *F* (*P*)	
Outcome	Time	SMR-up (*n* = 13)		Beta-down (*n* = 15)		Control (*n* = 13)		SMR-up - Beta-down - Control	SMR - Control	Beta - Control
		M	SE	M	SE	M	SE			
Total wake time after sleep onset (TWT) – Philips Health Watch ↓	Wk. 1	20.63	6.67	21.19	7.27	27.43	6.30	0.08 (.971)	0.72 (.540)	1.54 (.202)
	Wk. 2	23.09	6.20	29.62	7.15	33.13	5.96			
	Wk. 3	21.56	5.94	27.25	6.91	28.98	5.87			
	Wk. 4	20.32	6.08	36.02	6.92	28.95	5.90			
Total wake time after sleep onset (TWT) – Consensus Sleep Diary ↓	Wk. 1	43.87	6.90	37.67	6.53	50.66	6.97	4.66 (.003)**	0.25 (.864)	0.48 (.695)
	Wk. 2	25.99	7.13	40.72	6.53	38.43	7.01			
	Wk. 3	27.19	6.97	32.68	6.74	38.81	7.15			
	Wk. 4	36.83	6.91	32.55	6.99	49.96	7.18			
Fatigue (FAS) ↓	Pre	20.96	1.67	18.53	1.53	20.92	1.65	17.40 (.000)***	0.91 (.351)	1.34 (.259)
	Post	18.99	1.67	16.62	1.57	17.34	1.67			
Depression (DASS) ↓	Pre	3.31	1.09	4.73	1.01	4.15	1.09	13.33 (.000)***	0.76 (.393)	0.53 (.475)
	Post	2.53	1.11	2.06	1.05	2.47	1.11			
Anxiety (DASS) ↓	Pre	3.15	0.80	3.27	0.75	1.85	0.80	4.95 (.032)*	1.70 (.205)	1.63 (.214)
	Post	2.36	0.82	1.52	0.78	1.70	0.82			
Stress (DASS) ↓	Pre	9.31	1.64	9.33	1.53	9.92	1.64	16.18 (.000)***	0.21 (.647)	0.01 (.932)
	Post	6.35	1.66	7.18	1.57	7.60	1.66			

Note: FAS = Fatigue Assessment Scale (10 – 50), DASS = Depression Anxiety Stress Scales, Dep = Depression scale of the DASS (0 – 42), Anx = Anxiety scale of the DASS (0 – 42), Str = Stress scale of the DASS (0 – 42).
Note: Means and standard deviations displayed in the table are predicted from linear mixed models containing all groups.
Note: Total wake time measurements (health watch and sleep diary) were log10 transformed for the analysis.
Note: Arrows (↑ or ↓) indicate the desirable direction of change for each of the outcome measures.
* $p < .05$, ** $p < .01$, *** $p < .001$ (two-tailed)

3.4 Agreement between measurement methods

A Pearson's product-moment correlation test shows a correlation of 0.33 ($p < .001$) between Consensus Sleep Diary (CSD) and Philips Health Watch (PHW) measurements on SOL and a correlation of 0.42 ($p < .001$) between CSD and PHW measurements on TWT. These correlations both indicate a weak to moderate positive relationship between the CSD and PHW measurements.

Table 3.5 Agreement between Consensus Sleep Diary (CSD) and Philips Health Watch (PHW) measurements

	Mean CSD measurements	Mean PHW measurements	Mean differences (Confidence intervals)	Lower limit of agreement (Confidence intervals, % lower)[2]	Upper limit of agreement (Confidence intervals, % higher)[2]	r^3(*P* value)
Sleep Onset Latency (SOL)[1]	24.05	18.45	5.69 (3.33 to 7.87)	-57.00 (-60.94 ± -53.06, 0.9%)	68.20 (64.27 ± 72.14, 3.8%)	0.49 (< 0.001)***
Total Wake Time (TWT)[1]	37.24	29.29	7.94 (5.04 to 10.85)	-72.16 (-77.20 ± -67.12, 2.6%)	88.05 (83.01 ± 93.09, 3.0%)	0.20 (< 0.001)***

[1] In minutes.

[2] Proportion of measurement differences outside of limits of agreement.

[3] *r* =Pearson correlation between difference and mean of the CSD measurements and the HW measurements.

As can be seen in table 3.5 and figures 3.1 and 3.2, the CSD and PHW measurements on SOL and TWT were generally close to each other. The CSD measurements were on average 5.69 minutes higher than PHW measurements on SOL and 7.94 minutes higher on TWT, indicating that participants' subjective CSD reports of SOL and TWT were on average higher than what objective PHW measurements indicated.

However, the limits of agreement (LOA's) are wide for both variables, ranging from -57.00 to 68.20 minutes for SOL and from -72.16 to 88.05 minutes for TWT. This indicates high differences (and thus bias) between subjective (CSD) and objective (PHW) reports of SOL and TWT. A higher percentage of differences between the CSD and PHW measurements were above the upper LOA (3.8% for SOL and 3.0% for TWT) than below the lower LOA (0.9% for SOL and 2.6% for TWT). Indicating again that participants' subjective reports (CSD) on SOL and TWT were on average higher than the objective reports (PHW).

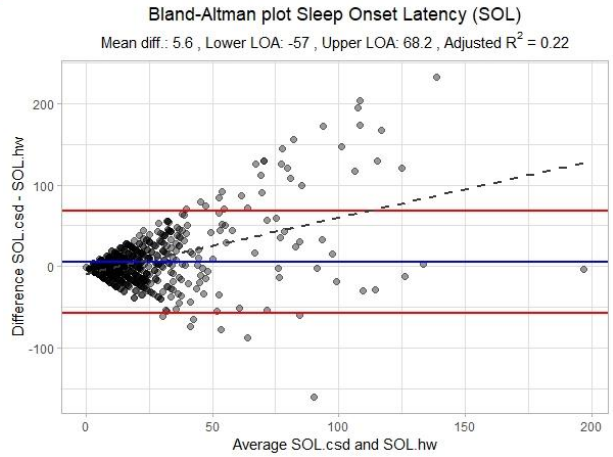

Figure 3.1 Bland-Altman plot Sleep Onset Latency (SOL)

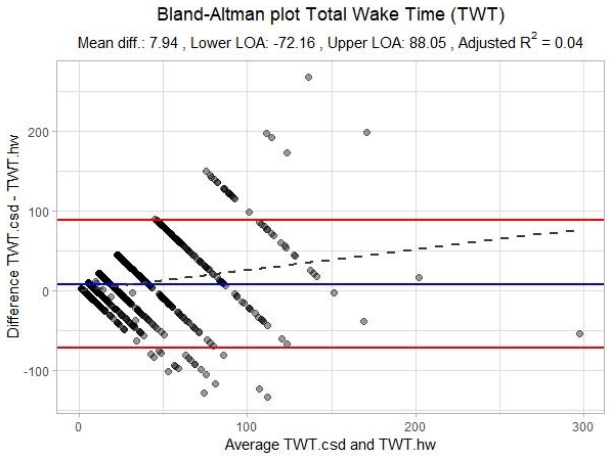

Figure 3.2 Bland-Altman plot Total Wake Time (TWT)

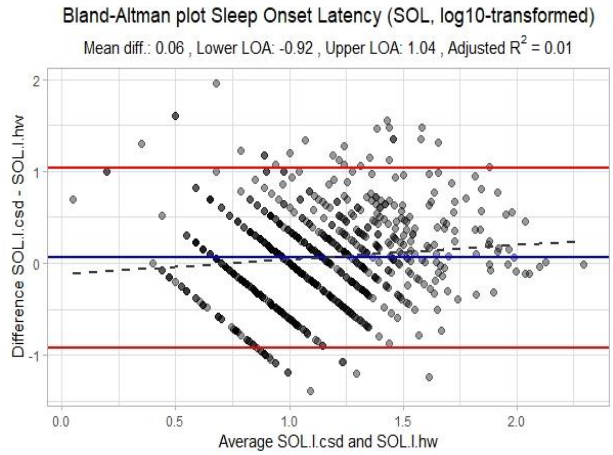

Figure 3.3 Bland-Altman plot Sleep Onset Latency (SOL, log10)

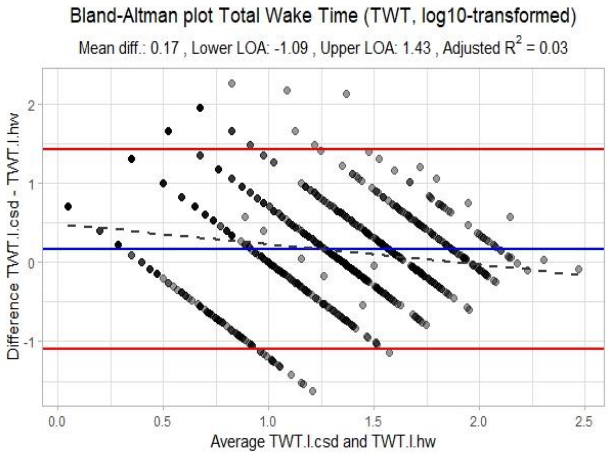

Figure 3.4 Bland-Altman plot Total Wake Time (TWT, log10)

The degree of correlation between differences and the mean of the CSD and PHW measurements is 0.49 with $p < .001$ on SOL and 0.20 with $p < .001$ for TWT, indicating a proportional bias between subjective (CSD) and objective (PHW) measurements on both variables. However, the scatter of values of differences increases progressively as average values increase (figures 3.1 and 3.2), indicating heteroscedascity of the data and revealing that higher differences and bias between the subjective (CSD) and objective (PHW) measurements were found on higher average measurements.

Therefore, the data was log10-transformed (figures 3.3 and 3.4) and the Pearson correlation recalculated, resulting in a correlation of 0.10 with $p < .01$ for SOL and -0.18 with $p < .001$ for TWT, still indicating a proportional, but smaller, bias on both variables.

4 Discussion

In this study, we investigated the effects of SMR-up and Beta-down audio neurofeedback (NFB) training on (i) sleep onset latency (SOL), perceived sleep quality, insomnia severity and (ii) total wake time after sleep onset (TWT), fatigue, depression, anxiety and stress. Furthermore, the agreement and differences between a subjective (Consensus Sleep Diary, CSD) and objective (Philips Health Watch, PHW) measure on SOL and TWT were examined.

A significant improvement was found in all conditions on sleep quality and insomnia severity, but not on sleep onset latency. However, in the SMR or beta NFB training conditions no larger improvements were found on these primary outcomes than in the control condition. Yet, the pooled analysis on sleep quality (PSQI score) including data of an almost identical randomized controlled trial (n = 36) performed by Dam (2016) showed a significant condition-by-time effect for the beta down condition, indicating that beta neurofeedback training worked better in improving sleep quality. A significant improvement in all groups was found for all secondary outcomes, except total wake time measured through the Philips Health Watch. Nevertheless, both of the NFB training protocols did not lead to significantly stronger improvements on the secondary outcomes compared to the control condition protocol. The comparison of the (subjective) Consensus Sleep Diary and the (objective) Philips Health Watch measurements on sleep onset latency and total wake time showed high differences (and thus bias) between the two measures. Subjective (CSD) reports by participants on the sleep parameters were on average higher than what was objectively measured (through the PHW). In addition, differences in measurements were larger for higher average measurements.

4.1 Primary outcomes

The results regarding sleep onset latency (SOL) are not in-line with expectations, as we expected SOL to decline significantly more in the SMR-up condition as opposed to the control condition based on previously conducted studies and findings (Arns et al., 2014; Cortoos et al., 2010; De Gennaro & Ferrara, 2003; Hoedlmoser et al., 2008; Howe & Sterman, 1972; Schabus et al., 2014). However, the findings on SOL were in line with results of a study by Schabus et al. (2017). A possible explanation for the differences in the results found in this study and the aforementioned studies could be related to differences in the study protocols. All of the aforementioned studies, including the study by Schabus et al. (2017), use different types of neurofeedback (audiovisual feedback) and other protocols (in terms of

frequency, duration, control condition protocol and spread of neurofeedback sessions). In addition, each of these studies used different inclusion and exclusion criteria. Arns et al. (2014) even recruited from a completely different sample population (adults with Attention Deficit Hyperactivity Disorder, ADHD). Measurement methods and intervals also varied strongly. The study by Schabus et al. (2017) followed a similar neurofeedback protocol as the studies by Hoedlmoser et al. (2008) and Schabus et al. (2014), but a different experimental set-up provided for a more rigorously controlled study then the previous. This can explain its' different outcomes compared to the previously conducted studies by Schabus et al. (2014) and the similarities of the results to the outcomes of the current study. The variation in study protocols of studies examining the effects of neurofeedback in general, makes it hard to compare results.

For expectations regarding sleep onset latency improved by beta neurofeedback, evidence was limited, but it indicated potential improvement (Arns et al., 2014). Sleep onset latency did not decline significantly more in the beta NFB condition than in the SMR NFB or control condition, which was therefore against expectations. The results on improvements in sleep quality and insomnia severity were in line with results found by Schabus et al. (2017, 2014), but against the expectation that these outcomes would improve more in both the SMR-up and beta-down condition than in the control condition. These differences may be due to differences in the study protocol of the current study as opposed to the protocols of the aforementioned reference studies (Arns et al., 2014; Schabus et al., 2017, 2014).

The results of this study regarding the primary outcomes may have been influenced by several factors. Schabus et al. (2017) found that persons with substantial sleep issues exhibit a lower ability to learn (and take-up the learning mechanism of neurofeedback) in comparison to "healthy" persons. This may have had an influence on the uptake of neurofeedback and therefore the results on the primary outcomes in this study. Results on the primary outcomes could also have been negatively influenced by a lack of neurofeedback training sessions, since Hammond et al. (2011) argued that it could take up to 50 sessions for neurofeedback to be effective. The objective EEG measurements were not analyzed, therefore it cannot be determined to what extent SMR EEG activity was enhanced or beta activity inhibited and the relation of these changes with the outcomes cannot be established. In addition, we cannot confirm or deny if the amount of NFB sessions should be increased or not. The absence of differential effects of the SMR and beta NFB can also be caused by the type of neurofeedback, since listening to music alone is reported to have positive effects on sleep

(Chang, Lai, Chen, Hsieh, & Lee, 2012; Feng et al., 2018; Lai & Good, 2005). The measures used to report sleep during the study phase (Consensus Sleep Diary and Philips Health Watch) may have also caused an improvement on the primary outcome measures in all groups, since filling a sleep diary or indicating the intention to sleep on the health watch may have effects on sleep already (Goelema, Willems, Haakma, & Markopoulos, 2016). Furthermore, non-specific effects such as treatment effects (e.g., induced by weekly "How are you?" mails send by the researchers) may have caused a placebo effect in the control condition for some of the outcomes. This makes it harder to distinguish the effects of the NFB training protocols on the outcomes measured. The strict inclusion and exclusion criteria of the current study may have had influenced the outcomes of his study as well.

Future research should take into account several methodological aspects, such as the reactivity of the measures to report sleep and the effects of the music component of the neurofeedback training on outcomes. The latter could be done by including a control condition in which participants wear the Philips Health Watch and fill in the Consensus Sleep Diary but do not receive (pseudo) neurofeedback training. To rule out part of the treatment effects, it would be interesting to see which effects on the outcomes endure after the study phase and if these effects are stronger in one of the NFB conditions as opposed to the control condition. Sending a follow-up questionnaire a few months after the end of the study phase would be a solution to rule out treatment effects and reactivity of the measures used to report sleep during the study. The results of the pooled analysis show the potential of a bigger sample size to determine the effects of the beta NFB on sleep quality.

4.2 Secondary outcomes

A significant improvement in all conditions was found for all secondary outcomes, except total wake time measured through the Philips Health Watch (PHW). Nevertheless, both of the NFB training protocols did not lead to significantly stronger improvements on the secondary outcomes compared to the control condition protocol. A condition-by-time effect was found for total wake time as measured by the PHW, but in the opposite direction: a deterioration in the beta-down condition as opposed to an improvement in the control condition.

The evidence-base for expectations regarding the secondary outcomes is limited. A study by Schabus et al. (2014) indicated a potential decrease in the number of awakenings as a result of enhancement of SMR activity. Findings by Cortoos et al. (2010) regarding the role of beta activity in wakefulness suggest that inhibition of beta activity may decrease total wake time.

However, an unexpected opposite effect was found in the beta condition in total wake time measured through the Philips Health Watch and no significant effects were found on total wake time measured through the Consensus Sleep Diary. Against expectation, fatigue did not improve significantly more in the NFB conditions as opposed to the control condition. Since we expected insomnia severity and sleep quality to improve and since depression, anxiety and stress levels can be linked to insomnia severity (Baglioni, Spiegelhalder, Lombardo, & Riemann, 2010), an improvement on these outcomes was expected, especially in the NFB conditions.

Explanations for the results on the secondary outcomes could be found in the same factors as mentioned in the discussion of the primary outcomes (lower learning ability in the sample population; too few NFB sessions; lack of knowledge on actual changes in EEG activity; reactivity of outcome measures; overall effects of listening to music; treatment effects and the small sample size). Solutions and recommendations to address these factors in future research would therefore be similar:

- Analysis of EEG activity measures during neurofeedback sessions to determine the actual effects of the neurofeedback on activity in the frequency bands of interest, to investigate how changes in the EEG activity relate to outcomes and to examine the learning curve of participants in relation to the neurofeedback training.
- Include a control condition in which participants wear the Philips Health Watch and fill in the Consensus Sleep Diary but do not receive (pseudo) neurofeedback training.
- Include a follow-up measurement after the study phase to rule out treatment effects, reactivity of measures used to report sleep and to examine the endurance of effects of the neurofeedback training on outcomes.
- Increase sample sizes.

4.2.1 Comparison of measures

Research indicates that it is to be expected that subjective reports on sleep parameters are higher than what is objectively measured and that these differences increase with higher average measures (Baker, Maloney, & Driver, 1999). The comparison of the subjective Consensus Sleep Diary (CSD) and the objective Philips Health Watch (PHW) measurements on sleep onset latency (SOL) and total wake time (TWT) in the current study showed high differences (and thus bias) between the two measures. Subjective reports by participants on sleep parameters (through the CSD) were on average higher than what was objectively

measured (through the PHW). This indicates similar results as in the study by Baker, Maloney & Driver (1999). In addition, differences in measurements were larger for higher average measurements.

A finding by Fonseca et al. (2017) could have influenced the latter. They found that the Philips Health Watch and the PPG-based sleep-staging algorithm used in the current study have the tendency to underestimate sleep onset latency and total wake time when they increase beyond 15 minutes. This may have caused a higher difference in the measurements. Results of the current study indicate that measurements of the Consensus Sleep Diary and the Philips Health Watch differ substantially and should not be compared on an absolute level. However, they can be compared when log10-transformed (e.g., for describing the effects of an intervention). This is an important finding for clinical practice as it is advised that both objective and subjective measures are incorporated into clinical studies, due to their complementary aspects (e.g. in measuring sleep quality) (Van De Water et al., 2011; Zhang & Zhao, 2007). In addition, a recommendation for future research would be to compare Philips Health Watch and Consensus Sleep Diary measurements to polysomnography measurements to examine how these alternative methods to measure and report sleep relate to the "golden standard".

4.3 Strengths and limitations

This study has various strengths and limitations. The use of objective and subjective methods to measure sleep and describe effects of neurofeedback is a strength. The comparison of the two methods may improve interpretation of results. Furthermore, the neurofeedback control protocol can be seen as a strength since it allows participants in the control condition to receive a similar intervention as participants in the experimental conditions, even though they receive pseudo neurofeedback training. Another strength of this study is that it is one of the first studies exploring at-home audio neurofeedback training to enhance SMR activity and inhibit beta activity. The high amount of applications (412) for this study shows an interest of the target population in the application of neurofeedback for improving sleep. This reflects the need for development of alternative methods to improve sleep (besides pharmaceutical and non-pharmaceutical options) and therefore confirms the relevance of this study. Another strength of this study is the inclusion of a follow-up measurement two months after the outtake. By including this measurement, we can examine if effects on the outcomes endure after the study phase and if these effects are stronger in one of the NFB conditions as opposed to the control condition. The follow-up measurements for this study are ongoing. Initial

preliminary analyses indicate stronger enduring effects on some of the outcomes in the Beta NFB condition as opposed to the SMR NFB and the control condition.

Limitations of this study lie in the relatively small sample and the potential reactivity of the measurement methods. Besides being a strength of the study, the neurofeedback control protocol may be a limitation as well, due to the positive effects that music can have on sleep. Even though participants in the control condition were receiving pseudo neurofeedback, they listened to music just like the participants in the NFB conditions. This makes the effects of the neurofeedback training as opposed to the effects of listening to music alone hard to distinguish. Another limitation is that EEG measurements were not analyzed and that it cannot be determined if participants had "enough" neurofeedback training sessions, if brain activity was actually influenced and in which way, and how the changes in brain activity are related to the outcomes. Another limitation lies in the strict inclusion and exclusion criteria, which might negatively affect generalizability of the results of this study.

The changes in the study protocol after the RCT examining the use of the Philips audio Neurofeedback System to enhance SMR and inhibit beta activity to improve sleep performed by Dam (2016) had several advantages and disadvantages. The inclusion of the Philips Health Watch instead of the Philips Respironics Actiwatch 2 has provided better objective measurements of sleep. Furthermore, the inclusion of the Insomnia Severity Index (ISI), Fatigue Assessment Scale (FAS) and Depression Anxiety and Stress Scales (DASS) as outcomes led to a more complete view of the problems of the sample population and the effects of neurofeedback training on these issues. However, the changes in the protocol ensured that comparisons of effects and combination of data to draw firmer conclusions (e.g., using pooled analysis) was not possible for most of the outcomes.

4.4 Conclusion and recommendations for future research

Our study provides no (clear) evidence for the effectiveness of neurofeedback (either SMR up or Beta down) on sleep (sleep onset latency, perceived sleep quality, insomnia severity, total wake time, or fatigue), depression, anxiety, or stress. The comparison of the Consensus Sleep Diary (CSD) and the Philips Health Watch (PHW) measurements on sleep onset latency and total wake time in the current study has led to several findings that are important for the use of (a combination of) the CSD and PHW in clinical practice. This study shows that potential effects of SMR and/or beta neurofeedback on sleep might be revealed after addressing several methodological issues. The following recommendations for future research can be given based on the results of this study:

- Analysis of EEG activity measures during neurofeedback sessions to determine the actual effects of the neurofeedback on the frequency bands of interest, to investigate how changes in the EEG activity relate to outcomes and to examine the learning curve of participants in relation to the neurofeedback training.
- Include a control condition in which participants wear the Philips Health Watch and fill in the Consensus Sleep Diary but do not receive (pseudo) neurofeedback training.
- Include a follow-up measurement after the study phase to rule out treatment effects, reactivity of measures used to report sleep and to examine the endurance of effects of the neurofeedback training on outcomes.
- Increase sample sizes.
- Take into account the type of neurofeedback and its' potential effects in relation to outcomes in the study design.
- Increase the amount of neurofeedback sessions and duration of study phase.
- Use subjective and objective measures to report sleep and compare these to each other and the "golden standard" in sleep measurement, polysomnography.

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Appendices

Appendix 1: The Philips Audio Neurofeedback System

Description of functionality

The Philips Audio Neurofeedback System (PNFS) conveys real-time feedback on activity in certain bands in the EEG-spectrum through changes in quality of music, specifically by removing the low frequency components of the music (bass tones) in the audio output of the tablet on which participants listen to their favorite music. The removing of the low frequency components occurs with a simple first order high pass filter with a slope of 6 dB per octave (figure A.1).

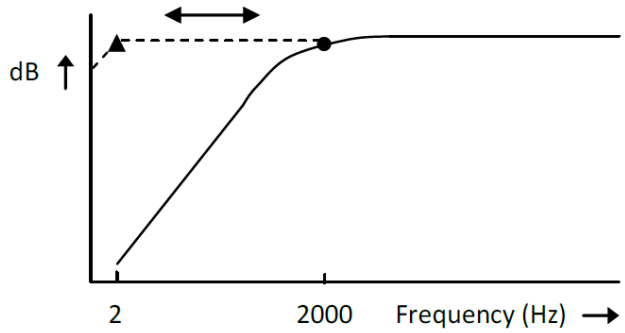

Figure A.1: Representation of a high pass filter with a slope of 6dB per octave (Dam, 2016)

The cut-off frequency of the high pass filter depends on the amount of power (or 'activity') observed in the EEG frequency band of interest. In the current study, the frequency band of interest lies in the range of 13 to 15 Hz for the sensorimotor rhythm (SMR-up) training and at 15 to 30 Hz for the Beta (Beta-down) training. For the SMR-up training this means that when activity in the SMR frequency band is high, the high-pass filter is not applied and participants will hear music containing all components resulting in a more pleasant music experience. A lower activity in the SMR frequency band results in the application of a high-pass filter leading to music sounding less loud, "thin", and therefore much less pleasant. For the Beta-down training this means the opposite. High activity in the Beta frequency range results in the application of the high-pass filter, whereas low activity is stimulated and trained by not applying a high-pass filter. In the control condition, the cut-off frequency shifts in accordance with pre-recorded EEG-recordings of another individual than the participant using the PNFS. Therefore, stimulation of activity in the EEG frequency bands is "random".

EEG power levels are not constant over time. To be able to change the music with changing power levels in the brain, the EEG signal is divided into epochs of four seconds, each containing 8 measurement points per second. Since EEG power differ between persons, minimum and maximum (acceptable) levels were estimated per person using the 15% (minimum) and 85% (maximum) percent point of the cumulative distribution of the EEG power over the previous epochs of the session (Figure

A.2). The weight of the previous EEG power in the distribution is subject to exponential decay. That is, as time that has passed since the previous epoch increases, the weight decreases exponentially (Figure A.3). As a result, the distribution of the previously measured EEG power is influenced more by recent epochs, than by past epochs.

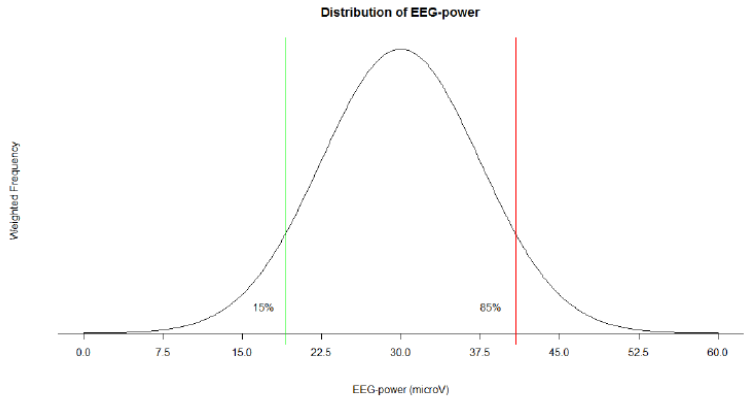

Figure A.2: Weighted distribution of the means of the previous four epochs (Petit, 2017).

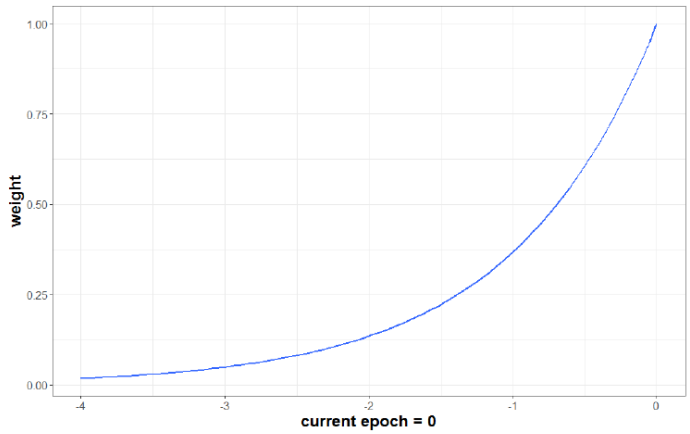

Figure A.3: Exponential decay of the weights of previous epochs (Petit, 2017).

Eight times per second it is measured whether the current EEG power exceeds or falls behind the previously measured 15% and 85% percent points of the cumulative distribution of the EEG power. Depending on the condition, the high-pass filter is then either applied or not resulting in a better or worse experience of music quality.

Description of the Philips Audio Neurofeedback application

The Philips Audio Neurofeedback application starts with a short explanation and a mood assessment questionnaire (figure A.4). Next, a schematic drawing of the headphone and the electrodes is displayed. The panes, that represent the electrodes, turn green when disruptions of the EEG signal are minimal (figure A.5). If disruptions in the signal are substantial, the pads in figure A.5 will stay red and the participant cannot start the training until the signal is of good quality. When the pads have not turned red for 10 seconds, the audio neurofeedback training session can start. The participant is then directed to a screen where he or she can see what song is playing, choose a playlist and navigate back and forth between songs (figure A.6). The participant will then listen to his or her favorite music, while audio neurofeedback is provided as described in the previous section. The participant can view his or her EEG signal during the audio neurofeedback session by clicking on the arrow displayed in figure A.6 (figure A.7).

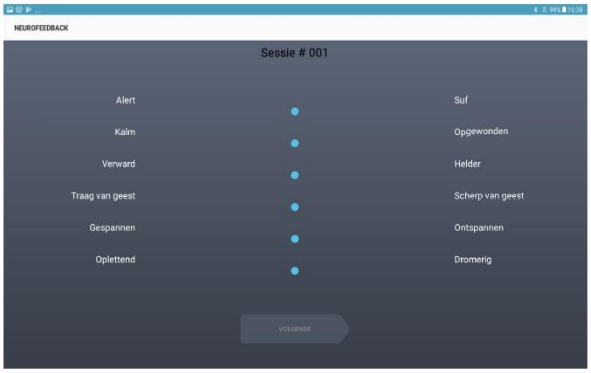

Figure A.4: Mood assessment questionnaire screen (Petit, 2017)

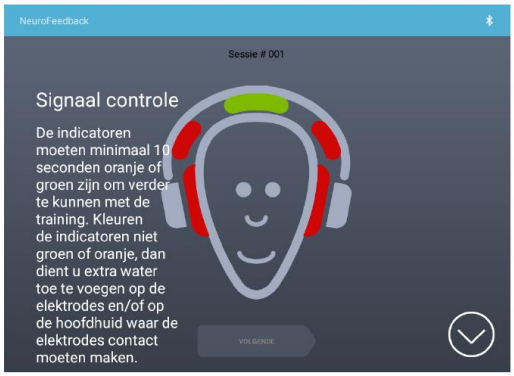

Figure A.5 : Signal check screen (Petit, 2017)

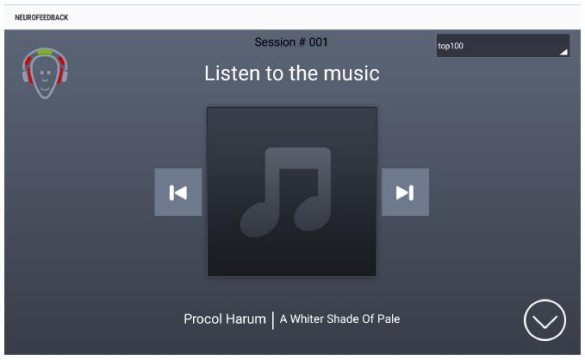

Figure A.6 : Audio neurofeedback training screen (Petit, 2017)

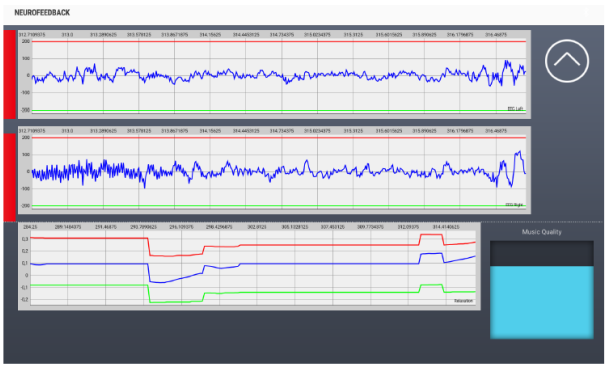

Figure A.7 : EEG signal screen (Petit, 2017)

After ten minutes of audio neurofeedback, participants are automatically directed to a screen where a game can be chosen. Consequently, they play the chosen game for 5 minutes. After 5 minutes, participants are automatically redirected back to the audio neurofeedback training screen (figure A.6). After completing another 10 minutes of audio neurofeedback training, participants are directed to the mood assessment questionnaire (as displayed in figure A.4). After completion of the questionnaire, the application logs out itself.

Note: Parts of the description of the functionality of the PNFS and the description of the application are taken from the following reports:

- Dam, J. (2016). *The effect of Neurofeedback on perceived sleep quality* (Master thesis). Retrieved from: https://essay.utwente.nl/70960/1/DAM_MA_BMS.pdf
- Petit, F. (2017). *The effect of the Philips Audio Neurofeedback System on Sleep* (Unpublished Bachelor thesis). Universiteit Utrecht, Utrecht, the Netherlands.

Appendix 2: Pittsburgh Sleep Quality Inventory (PSQI) questionnaire

Pittsburgh Sleep Quality Index

De volgende vragen hebben betrekking op uw slaapgewoonten gedurende de afgelopen maand. Noteer het antwoord dat voor u het meest van toepassing was gedurende de afgelopen maand. Beantwoord alstublieft alle vragen. Het invullen van deze vragenlijst duurt ongeveer 5 minuten

1. Deelnemersnummer *
Het deelnemersnummer dat u bij Philips hebt gekregen.

2. Datum
Vandaag (yyyy-mm-dd)
2019-04-19

3. Hoe laat ging u 's avonds gewoonlijk naar bed gedurende de afgelopen maand? *
24-uurs formaat (hh:mm). Gebruik 23:00 voor elf uur 's avonds, 00:00 voor middernacht.

4. Hoeveel minuten duurde het de afgelopen maand gewoonlijk voordat u 's nachts in slaap viel? *
Minuten
0

5. Hoe laat stond u tijdens de afgelopen maand 's morgens gewoonlijk op? *
24-uurs formaat (hh:mm). Gebruik 23:00 voor elf uur 's avonds, 00:00 voor middernacht.

6. Aan hoeveel uren slaap kwam u per nacht in tijdens de afgelopen maand? *
Dat aantal kan verschillen van het aantal uren dat u in bed doorbracht. Maak een schatting met minimaal 1 cijfer achter de komma, waarbij je de komma moet vervangen door een punt.
0

7. Hoe vaak had u tijdens de afgelopen maand moeilijkheden met slapen, omdat u niet in slaap kon vallen binnen 30 minuten? *
Niet Minder dan éénmaal per week Eén of tweemaal per week Drie of meermaals per week

8. Hoe vaak had u tijdens de afgelopen maand moeilijkheden met slapen, omdat u midden in de nacht of in de vroege morgen wakker werd? *
Niet Minder dan éénmaal per week Eén of tweemaal per week Drie of meermaals per week

9. Hoe vaak had u tijdens de afgelopen maand moeilijkheden met slapen, omdat u naar het toilet moest gaan? *
Niet Minder dan éénmaal per week Eén of tweemaal per week Drie of meermaals per week

10. Hoe vaak had u tijdens de afgelopen maand moeilijkheden met slapen, omdat u niet gemakkelijk kon ademhalen? *
Niet Minder dan éénmaal per week Eén of tweemaal per week Drie of meermaals per week

11. Hoe vaak had u tijdens de afgelopen maand moeilijkheden met slapen, omdat u luid hoestte of snurkte? *
Niet Minder dan éénmaal per week Eén of tweemaal per week Drie of meermaals per week

12. Hoe vaak had u tijdens de afgelopen maand moeilijkheden met slapen, omdat u het te koud had? *
Niet Minder dan éénmaal per week Eén of tweemaal per week Drie of meermaals per week

13. Hoe vaak had u tijdens de afgelopen maand moeilijkheden met slapen, omdat u het te warm had? *
Niet Minder dan éénmaal per week Eén of tweemaal per week Drie of meermaals per week

14. Hoe vaak had u tijdens de afgelopen maand moeilijkheden met slapen, omdat u nachtmerries had? *
Niet Minder dan éénmaal per week Eén of tweemaal per week Drie of meermaals per week

15. Hoe vaak had u tijdens de afgelopen maand moeilijkheden met slapen, omdat u pijn had? *
Niet Minder dan éénmaal per week Eén of tweemaal per week Drie of meermaals per week

16a. Hoe vaak had u tijdens de afgelopen maand moeilijkheden met slapen, om een andere reden? *
Niet Minder dan éénmaal per week Eén of tweemaal per week Drie of meermaals per week

16b. Omschrijf deze reden:

17. Hoe zou u uw slaapkwaliteit tijdens de voorbije maand beoordelen? *

○ Zeer goed ○ Redelijk goed ○ Eerder slecht ○ Zeer slecht

18. Hoe vaak nam u gedurende de afgelopen maand geneesmiddelen in (al dan niet voorgeschreven) als hulp bij het slapen? *

○ Niet ○ Minder dan éénmaal per week ○ Eén of tweemaal per week ○ Drie of meermaals per week

19. Hoe vaak had u het de afgelopen maand moeilijk om wakker te blijven tijdens het autorijden, het eten of deelname aan een sociale activiteit? *

○ Niet ○ Minder dan éénmaal per week ○ Eén of tweemaal per week ○ Drie of meermaals per week

20. In welke mate was het de afgelopen maand voor u een probleem om met voldoende enthousiasme uw dagelijkse activiteiten uit te voeren? *

○ Helemaal geen probleem ○ Een klein beetje een probleem ○ Een beetje een probleem ○ Een heel groot probleem

21. Heeft u een bedpartner of een kamergenoot? *

○ Geen bedpartner of kamergenoot (ga verdert naar 'Submit') ○ Partner of kamergenoot in een andere kamer
○ Partner in dezelfde kamer, maar niet in hetzelfde bed ○ Partner in hetzelfde bed

22. Indien u een bedpartner of kamergenoot heeft, vraag deze hoe vaak u tijden de afgelopen maand luid snurkte?

○ Niet ○ Minder dan éénmaal per week ○ Eén of tweemaal per week ○ Drie of meermaals per week

23. Indien u een bedpartner of kamergenoot heeft, vraag deze hoe vaak u tijden de afgelopen maand lange ademhalingspauzes had tijdens het slapen?

○ Niet ○ Minder dan éénmaal per week ○ Eén of tweemaal per week ○ Drie of meermaals per week

24. Indien u een bedpartner of kamergenoot heeft, vraag deze hoe vaak u tijden de afgelopen maand trekkende of schoppende benen had tijdens het slapen?

○ Niet ○ Minder dan éénmaal per week ○ Eén of tweemaal per week ○ Drie of meermaals per week

25. Indien u een bedpartner of kamergenoot heeft, vraag deze hoe vaak u tijden de afgelopen maand periodes van verwardheid had tijden het slapen?

○ Niet ○ Minder dan éénmaal per week ○ Eén of tweemaal per week ○ Drie of meermaals per week

26a. Indien u een bedpartner of kamergenoot heeft, vraag deze hoe vaak u tijden de afgelopen maand een andere rusteloosheid had tijdens het slapen?

○ Niet ○ Minder dan éénmaal per week ○ Eén of tweemaal per week ○ Drie of meermaals per week

26b. Omschrijf deze andere rusteloosheid die u had tijdens het slapen de afgelopen week volgens uw bedpartner of kamergenoot:

Verzenden

Appendix 3: Insomnia Severity Index (ISI) questionnaire

Insomnia Severity Index

Geef bij elke vraag het antwoord dat het meest nauwkeurig overeenkomt met je slaappatroon in de afgelopen maand.

Deelnemersnummer *

Het deelnemersnummer dat u bij Philips hebt gekregen.

Datum

Vandaag (yyyy-mm-dd)

2019-04-19

1. Moeite met in slaap vallen. *

Geen Licht Matig Ernstig Zeer ernstig

2. Moeite met doorslapen. *

Geen Licht Matig Ernstig Zeer ernstig

3. Problemen met te vroeg wakker worden. *

Geen Licht Matig Ernstig Zeer ernstig

4. Hoe tevreden ben je met je huidige slaappatroon? *

Zeer tevreden Tevreden Neutraal Ontevreden Zeer ontevreden

5. In hoeverre vind je dat je slaapprobleem je dagelijks functioneren VERSTOORD? *

Helemaal niet Een klein beetje Enigzins Erg Heel erg

6. Hoe MERKBAAR is het voor anderen dat je slaapproblemen je kwaliteit van leven verslechteren? *

Helemaal niet Een klein beetje Enigzins Erg Heel erg

7. Hoe BEZORGD ben je over je huidige slaapproblemen? *

Helemaal niet Een klein beetje Enigzins Erg Heel erg

Verzenden

Appendix 4: Fatigue Assessment Scale (FAS) questionnaire

Fatigue Assessment Scale

De volgende vragen gaan over hoe u zich normaal gesproken voelt. U kunt per uitspraak kiezen uit vijf antwoordcategorieën, variërend van 'nooit' tot 'altijd'. Wilt u het antwoord dat het beste bij uw gevoel past kiezen?

Deelnemersnummer *
Het deelnemersnummer dat u bij Philips hebt gekregen.

Datum
Vandaag (yyyy-mm-dd)
2019-04-19

1. Ik heb last van vermoeidheid. *
Nooit Soms Regelmatig Vaak Altijd

2. Ik ben gauw moe. *
Nooit Soms Regelmatig Vaak Altijd

3. Ik vind dat ik weinig doe op een dag. *
Nooit Soms Regelmatig Vaak Altijd

4. Ik heb genoeg energie voor het leven. *
Nooit Soms Regelmatig Vaak Altijd

5. Lichamelijk voel ik me uitgeput. *
Nooit Soms Regelmatig Vaak Altijd

6. Ik heb problemen om met dingen te beginnen. *
Nooit Soms Regelmatig Vaak Altijd

7. Ik heb problemen om helder na te denken. *
Nooit Soms Regelmatig Vaak Altijd

8. Ik heb geen zin om iets te ondernemen. *
Nooit Soms Regelmatig Vaak Altijd

9. Geestelijk voel ik me uitgeput. *
Nooit Soms Regelmatig Vaak Altijd

10. Als ik ergens mee bezig ben, kan ik mijn gedachten er goed bijhouden. *
Nooit Soms Regelmatig Vaak Altijd

Verzenden

Appendix 5: Depression Anxiety Stress Scales (DASS) questionnaire

Depression Anxiety Stress Scale

Geef voor ieder van de onderstaande uitspraken aan in hoeverre de uitspraak de afgelopen week voor u van toepassing was. Er zijn geen goede of foute antwoorden. Besteed niet te veel tijd aan iedere uitspraak, het gaat om uw eerste indruk.

Deelnemersnummer *
Het deelnemersnummer dat u bij Philips hebt gekregen.

Datum
Vandaag (yyyy-mm-dd)
2019-04-19

1. Ik merkte dat ik overstuur raakte van onbelangrijke zaken. *
Nooit Soms Vaak Meestal

2. Ik merkte dat mijn mond droog aanvoelde. *
Nooit Soms Vaak Meestal

3. Ik was niet in staat om ook maar enig positief gevoel te ervaren. *
Nooit Soms Vaak Meestal

4. Ik had moeite met ademhalen (bijv. overmatig snel ademen, buiten adem zijn zonder me in te spannen). *
Nooit Soms Vaak Meestal

5. Ik kon maar niet op gang komen. *
Nooit Soms Vaak Meestal

6. Ik had de neiging om overdreven te reageren op situaties. *
Nooit Soms Vaak Meestal

7. Ik voelde me beverig (bijv. onvast ter been zijn). *
Nooit Soms Vaak Meestal

8. Ik vond het moeilijk me te ontspannen. *
Nooit Soms Vaak Meestal

9. Er waren situaties die me zo angstig maakten dat ik erg opgelucht was wanneer het ophield. *
Nooit Soms Vaak Meestal

10. Ik had het gevoel dat ik niets had om naar uit te kijken. *
Nooit Soms Vaak Meestal

11. Ik merkte dat ik gemakkelijk overstuur raakte. *
Nooit Soms Vaak Meestal

12. Ik was erg opgefokt. *
Nooit Soms Vaak Meestal

13. Ik voelde me verdrietig of depressief. *
Nooit Soms Vaak Meestal

14. Ik merkte dat ik erg ongeduldig werd van oponthoud (bijv. wachten op een lift, stoplichten, file). *
Nooit Soms Vaak Meestal

15. Ik had het gevoel flauw te gaan vallen. *
Nooit Soms Vaak Meestal

16. Ik had mijn interesse in zo'n beetje alles verloren. *
Nooit Soms Vaak Meestal

17. Ik had het gevoel dat ik als persoon niet veel voorstel. *
Nooit Soms Vaak Meestal

18. Ik merkte dat ik nogal licht geraakt was. *
Nooit Soms Vaak Meestal

19. Ik transpireerde merkbaar (bijv. zweethanden) terwijl het niet warm was en ik me niet inspande. *
Nooit Soms Vaak Meestal

20. Ik was angstig zonder enige reden. *
Nooit Soms Vaak Meestal

21. Ik had het gevoel dat mijn leven niet de moeite waard was. *
Nooit Soms Vaak Meestal

22. Ik vond het moeilijk op verhaal te komen. *
Nooit Soms Vaak Meestal

23. Ik had moeite met slikken. *
Nooit Soms Vaak Meestal

24. Ik was niet in staat om enig plezier te hebbem bij wat ik deed. *
Nooit Soms Vaak Meestal

25. Ik was me bewust van mijn hartslag terwijl ik me niet fysiek inspande (bijv. het gevoel van een versnelde hartslag of het overslaan van het hart). *
Nooit Soms Vaak Meestal

26. Ik voelde me zwaarmoedig. *
Nooit Soms Vaak Meestal

27. Ik merkte dat ik erg snel prikkelbaar was. *
Nooit Soms Vaak Meestal

28. Ik had het gevoel dat ik bijna in paniek raakte. *
Nooit Soms Vaak Meestal

29. Ik vond het moeilijk tot rust te komen nadat iets me overstuur had gemaakt. *
Nooit Soms Vaak Meestal

30. Ik was bang dat ik van mijn stuk zou raken bij een eenvoudige nieuwe bezigheid of taak. *
Nooit Soms Vaak Meestal

31. Ik was niet in staat om over ook maar iets enthousiast te worden. *
Nooit Soms Vaak Meestal

32. Ik vond het moeilijk tot rust te komen nadat iets me overstuur had gemaakt. *
Nooit Soms Vaak Meestal

33. Ik was erg nerveus. *
Nooit Soms Vaak Meestal

34. Ik had het gevoel niets waard te zijn. *
Nooit Soms Vaak Meestal

35. Ik had volstrekt geen geduld met dingen die me hinderden bij iets dat ik wilde doen. *
Nooit Soms Vaak Meestal

36. Ik voelde me ontzettend angstig. *
Nooit Soms Vaak Meestal

37. Ik kon niets in de toekomst zien om me op te verheugen. *
Nooit Soms Vaak Meestal

38. Ik had het gevoel dat mijn leven geen zin had. *
Nooit Soms Vaak Meestal

39. Ik merkte dat ik erg onrustig was. *
Nooit Soms Vaak Meestal

40. Ik maakte me zorgen over situaties waarin ik in paniek zou raken en mezelf belachelijk zou maken. *
Nooit Soms Vaak Meestal

41. Ik merkte dat ik beefde (bijv. met de handen). *
Nooit Soms Vaak Meestal

42. Ik vond het moeilijk om het initiatief te nemen om iets te gaan doen. *
Nooit Soms Vaak Meestal

Verzenden

Appendix 6: Consensus Sleep Diary (CSD) questionnaire

Slaapdagboek 2019-04-19

- Vul het slaaplogboek alstublieft elke dag in; het liefst binnen 1 uur nadat u bent opgestaan.
- Het gaat over de nacht van gisteren op vandaag. U hoeft zich geen zorgen te maken over het opgeven van exacte tijdstippen
- Kijk ook niet de hele tijd op de klok. Als u een tijd niet meer weet, geef dan uw beste schatting.
- Let op: de vragen die naar een tijdstip vragen dienen te worden ingevuld met een 24-uurs tijdsaanduiding (bijvoorbeeld 23:00 is elf uur 's avonds)

Deelnemersnummer *
Het deelnemersnummer dat u bij Philips hebt gekregen.

Datum
Vandaag (yyyy-mm-dd)
2019-04-19

1. Hoe laat ging u naar bed en hoe laat bent u opgestaan? *
Markeer het tijdstip waarop u in bed ging liggen. Dit hoeft niet het tijdstip te zijn waarop u daadwerkelijk probeerde te gaan slapen.
Markeer het tijdstip dat u uit bed ging en u geen poging meer heeft gedaan om te slapen. Dit kan afwijken van het tijdstip dat u wakker werd.
2019-04-18 18:00 | 2019-04-18 23:00 | 2019-04-19 07:30 | 2019-04-19 18:00

2. Hoe laat sloot u uw ogen om te gaan slapen en hoe laat bent u gestopt om nog proberen te slapen? *
Markeer het tijdstip waarop u uw ogen sloot om in slaap te vallen.
Het eerste tijdstip komt overeen met het moment waarop u de 'slaap intentie' op de Health Watch heeft aangezet.
Het tweede tijdstip komt overeen met het moment waarop u de 'slaap intentie' op de Health Watch heeft uitgezet.
2019-04-18 18:00 | 2019-04-18 23:10 | 2019-04-19 07:15 | 2019-04-19 18:00

3. Vanaf hoe laat tot hoe laat heeft u geslapen? *
Het eerste tijdstip markeert het moment waarop u denkt in slaap gevallen te zijn.
Het tweede tijdstip komt overeen met het moment waarop u uiteindelijk wakker werd (en waarna u dus niet meer geslapen hebt).
2019-04-18 18:00 | 2019-04-18 23:20 | 2019-04-19 07:00 | 2019-04-19 18:00

4a. Hoelang heeft in totaal wakker gelegen tussen het moment van inslaap vallen tot het uiteindelijke wakker worden? *
○ 0 - 5 min ○ 5 - 15 min ○ 15 - 30 min ○ 30 - 60 min ○ 1 - 2 uur ○ 2 - 3 uur ○ 3 - 4 uur ○ meer dan 4 uur

4b. Hoe vaak werd u wakker (het uiteindelijke ontwaken niet meetellend)? *
Hoeveel keer werd u wakker tussen het tijdstip waarop u voor het eerst in slaap viel en het moment dat u uiteindelijk wakker werd?
Aantal keer:
0 | 10

5. Hoe beoordeelt u de kwaliteit van uw slaap?
'0' staat voor heel slecht en '10' staat voor heel goed.
Kwaliteit:
0 | 10

6. In welke mate voelde u zich uitgerust toen u opstond?
'0' staat voor helemaal niet uitgerust en '10' staat voor helemaal uitgerust.
Mate van uitgerustheid:
0 | 10

7a. Hoe vaak heeft u een dutje gedaan? *
Een dutje is een bewuste keuze om overdag even te slapen. Dit kan zowel in bed of ergens anders zijn.
Aantal keer:
0 | 6

7b. Hoeveel uur heeft u in het totaal gedut?
○ 0 - 5 min ○ 5 - 15 min ○ 15 - 30 min ○ 30 - 60 min ○ 1 - 2 uur ○ 2 - 3 uur ○ 3 - 4 uur ○ meer dan 4 uur

8a. Hoe vaak bent u ingedommeld? *

Indommelen vindt plaats als u per ongeluk even indut, zonder dat dit uw bedoeling was

Aantal keer:

0 — 6

8b. Hoeveel uur bent u in het totaal ingedommeld?

○ 0 - 5 min ○ 5 - 15 min ○ 15 - 30 min ○ 30 - 60 min ○ 1 - 2 uur ○ 2 - 3 uur ○ 3 - 4 uur ○ meer dan 4 uur

9a. Hoeveel standaard glazen alcohol heeft u gisteren gedronken? *

Een standaard bierglas is 250ml, een standaard wijnglas 100ml, en een glas sterke drank 35ml.

Aantal standaard glazen:

0 — 15

9b. Hoe laat heeft u gisteren de laatste alcoholische drank genuttigd? (hh:mm)

2019-04-18 07:00 — 2019-04-18 23:20 — 2019-04-19 07:00

10a. Hoeveel cafeïnehoudende dranken heeft u gisteren genuttigd? *

Denk hierbij aan koffie, thee, frisdranken en energy dranken

Aantal koppen of glazen:

0 — 15

10b. Hoe laat heeft u gisteren de laatste cafeïnehoudende drank genuttigd? (hh:mm)

2019-04-18 07:00 — 2019-04-18 21:00 — 2019-04-19 07:00

11a. Heeft u geneesmiddelen ingenomen (al dan niet voorgeschreven) als hulp bij het slapen? *

○ Ja ○ Nee

11b. Indien u 'Ja' heeft geantwoord bij vraag 11a, noem hier de namen van alle medicijnen die u ingenomen heeft, bij elke naam de dosis (mg) die u genomen heeft en het tijdstip waarop u het medicijn genomen heeft.

Bijvoorbeeld: Sleepwell, 25, 21:00; Valeriaan, 20, 22:00; Melatinone, 60, 23:08; Sleepzz, 15, 23:22, etc.

12. Opmerkingen:

Verzenden