Master thesis

The effect of Neurofeedback on perceived sleep quality

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Master Health psychology

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Abstract English

Background: The presence of poor sleep-duration, poor sleep quality or insomnia symptoms, i.e. sleep deficiency, have shown substantial (negative) effects (on overall health). Sleep medication is the most common treatment, but the use of prolonged sleep medication can lead to illness and accidents. Therefore it is important to implement and evaluate non-pharmacological treatments, such as Neurofeedback.

Objectives: The aim of the current study was to evaluate the effect of Bèta and Sensorimotor rhythm (SMR) neurofeedback on different sleep parameters and Health Related Quality of Life in Philips employees with perceived sleep difficulties.

Methods: All participants (N=36 (5 dropped out)) used an innovative self-guided system with water-based electrodes integrated in an audio headset. All subjects performed the training at home (21 days out of 28). Two experimental conditions, i.e. the SMR condition and the Bèta condition were compared to the Sham condition (control group). Whereas the SMR neurofeedback condition was specifically training to enhance the SMR, the Bèta neurofeedback condition to suppress Bèta, and the Sham condition received random feedback (not based on their live signal). Subjective and objective measures were applied.

Results: Preliminary results showed no effect of the neurofeedback training on the primary outcome sleep onset latency. However a significant improvement over time was found. This was also found for the secondary outcome total sleep time. Two other secondary outcomes were significantly different. The Bèta group improved significantly regarding the PSQI-score in comparison to the sham condition and the SMR group improved significantly on the subjectively reported sleep quality in comparison to the sham condition. No effects were found on the objective sleep parameters, measured with the Actiwatch. Only the Health Related Quality of Life concepts 'vitality' and 'general health' improved over time. Significant difference were observed between groups in changes of vitality over time, however post hoc analysis didn't show any significance.

Discussion/conclusion: In some cases the treatment adherence was low, which may have contributed to the fact there are less effects detected. Also only half of the intended amount of participants were included, which lowers the power of the study. Furthermore, there were some problems with the Actiwatch data. Despite these facts, for now we must conclude that the neurofeedback was not effective. Though, the study must be continued to be able to make real conclusions.

Recommendations: It is recommended to continue with the study (RCT), therefore it is important to execute the study the same as is done in the current study. Though it is recommended to use another objective sleep measurement, for example one with more functions (heart rate). Besides it might be good to extent the interview, so make a combination of quantitative and qualitative research (mixed methods). For future research the system need some improvements (make it compact, no cables, in-ear EEG), but also the intervention period need to be extended and the duration of the sessions must be reduced. Further recommendations can be made after the results of the whole study are known.

First steps:

- Choose another objective sleep measurement
- Continue with the study
- Analyse all data that is available (Consensus sleep diary, adherence, interview)

Abstract Dutch

Achtergrond: Te weinig slaap, slechte slaapkwaliteit of insomnie symptomen, i.e. slaapdeficiency, hebben aanzienlijke (negatieve) effecten (op de algehele gezondheid). Slaapmedicatie is de meest voorkomende behandeling, echter heeft langdurig gebruik van slaapmedicatie ziekte en ongelukken als gevolg. Het is daarom van belang om niet-farmaceutische interventies te ontwikkelen, implementeren en evalueren. Een voorbeeld van een dergelijke interventie is Neurofeedback.

Doel: Het doel van het onderzoek was het toetsen van het effect van de Bèta en Sensorimotor rhythm (SMR) neurofeedback op diverse slaapparameters en gezondheid gerelateerde kwaliteit van leven bij Philips medewerkers met ervaren slaapproblemen.

Methode: Alle deelnemers (N=36 (5 dropouts)) hebben een innovatieve 'self-guided system' gebruikt, met een koptelefoon welke was geïntegreerd met 'water-based' EEG elektrodes. Alle deelnemers hebben het systeem 28 dagen mee naar huis gekregen, waarvan zij minimaal 21 dagen het systeem dienden te gebruiken. Twee experimentele condities (SMR en Bèta) zijn vergeleken met de Sham conditie (controle groep). De SMR neurofeedback conditie kreeg de SMR-up training, de Bèta groep kreeg de Bèta-down training en de controle groep kreeg random feedback (dit was niet gebaseerd op het live brein signaal van de desbetreffende persoon). Zowel subjectieve als objectieve metingen zijn uitgevoerd.

Resultaten: Voorlopige resultaten wijzen uit dat er geen effect is van de neurofeedback training op de primaire uitkomstmaat slaaplatentietijd. Echter is er wel een significante verbetering over de tijd waargenomen. Ook de secundaire uitkomstmaat totale slaaptijd is significant over de tijd verbeterd. De Bèta groep verbeterde significant ten aanzien van de globale PSQI-score in vergelijking met de controle groep. De SMR groep verbeterde significant ten opzichte van de controle groep ten aanzien van de subjectief gerapporteerde slaapkwaliteit. Geen effecten zijn gevonden ten aanzien van de objectieve slaapparameters, gemeten met de actiwatch. Alleen de gezondheid gerelateerde kwaliteit van leven concepten 'vitaliteit' en 'algehele gezondheid' zijn verbeterd over de tijd. Er was een significant verschil tussen de groepen in veranderingen over de tijd ten aanzien van vitaliteit. Echter liet de post-hoc test geen significantie zien.

Discussie/conclusie: Bij sommige participanten was de 'treatment adherence' laag, dit kan er aan hebben bijgedragen dat er weinig effecten zijn gevonden. Daarnaast is maar de helft van het voorgenomen aantal participanten geincludeerd, wat de power van de studie verlaagd. Tevens zijn er wat problemen geweest met de actiwatchdata. Voor nu moeten we concluderen dat de neurofeedback interventie niet effectief is gebleken. Echter dient de studie eerst te worden hervat om in staat te kunnen zijn om echte conclusies te kunnen trekken.

Aanbevelingen: Het is aan te bevelen om de de studie te hervatten, daarbij is het van belang dat het zo wordt uitgevoerd als in het verleden is gedaan. Echter is het wel aan te bevelen om een ander objectief slaap intstrument te gebruiken in plaats van de actiwatch, bijvoobeeld met meer functies dan alleen het meten van slaap. Daarnaast is het wellicht mogelijk om het interview wat uit te breiden en een combinatie te maken tussen kwantitatief en kwalitatief onderzoek. Voor onderzoek in de toekomst is het van belang dat het systeem in bepaalde opzichten wordt verbeterd (compacter, kabelloos, in-ear EEG). Ook is het van belang om de interventieperiode uit te breiden en de neurofeedback sessies in te korten.

First steps: *Kies een andere objectief slaap instrument; hervat de studie; analyseer alle data (slaap logboek, adherence en interview).*

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Abbreviations and definitions

Abbreviations

Abbreviation	Description
EEG	Electroencephalography
PSG	Polysomnographic
PSQI	The Pittsburgh Sleep Quality Index
HRQoL	Health Related Quality of Life
SE	Sleep Efficiency
SOL	Sleep Onset Latency
TST	Total Sleep Time
WASO	Wake After Sleep Onset
DIST	Amount of disturbances during the night
Wet AgCl	Silver chloride electrode, water based
SMR	Sensorimotor rhythm

Definitions

Definition	Description
SOL	Sleep onset latency is defined as the time between lights out and sleep onset evidence of sleep onset
SE	The percent of the time asleep out of amount of time spent in bed
WASO	The amount of minutes awake after sleep onset

1. Introduction

1.1 Background

In virtually all organisms sleep is an important part of their life, and it has an important vital function. The most distinctive features of sleep are the loss of behavioral control and consciousness. Although the full function of sleep is not completely understood, one of the most important functions seems to be the establishment of memories (Someren & Cluydts, 2009). Furthermore, sleep is critical for the regulation and maintenance of physiological systems (Buxton et al., 2012). On average adults sleep seven to eight hours per day, children sleep longer, and older people sleep less. One of the simplest functions of sleep is rest. The body requires a safe, stable period of time to be able to recover from a day full activities (Knuistingh Neven et al., 2005). From a physiological point of view, normal sleep is associated with well-described cycles, stages, arousals, and microstructures. A normal sleep pattern consists of 5 stages, which are grouped into the Rapid Eye Movement (REM)-sleep (i.e. dream sleep) and the non-REM sleep. Each cycle is approximately 90-120 minutes and will repeat it selves 4-5 times (Carskadon & Dement, 2011).

The presence of poor sleep-duration, poor sleep quality or insomnia symptoms, i.e. sleep deficiency, have shown substantial (negative) effects on overall health (Mullington et al., 2010). Studies suggest that approximately 30 percent of the general population have symptoms of sleep disruption, and circa 10 percent have associated daytime functional impairments (Janssen, De Vries, Verstappen, & De Leijer, 2011; NIH, 2005; Ohayon, 2002). This can contribute to traffic accidents, mood disorders, impaired social functioning, and a reduced performance at work or school. There are various sleep disorders; the most common is insomnia (Neerings-Verberkmoes, Flat, Lau, & Burger, 2014). Chronic insomnia is defined as a complaint of prolonged sleep latency, difficulties in maintaining sleep, the experience of non-refreshing or poor sleep coupled with impairments of daytime functioning, including reduced alertness, fatigue, exhaustion, and other symptoms. Insomnia will only be diagnosed when complaints endue for at least 4 weeks (Riemann et al., 2010). Chronic sleep difficulties as initiation and maintaining sleep are often associated with psychosocial and occupational impairments.

In the Netherlands approximately 33% of the adult population suffers from insomnia (Neerings-Verberkemoes et al., 2014). People who have an increased risk of getting insomnia are women, older persons, those who are divorced or widowed, persons with lower socioeconomic status (SES) or co-morbid people, and persons who snore. Particular older persons are at risk of insomnia, partly on the basis of age-related changes in sleep physiology (Buscemi et al., 2005; Irwin, Cole, & Nicassio, 2006). They have decreased sleep efficiency and deep sleep, and an increased sleep onset latency (i.e. time until sleep onset). 74% of the patients with sleep problems who visit their general practitioner (GP) for the first time are getting prescribed sleep medication (pharmacotherapy) (Neerings-Verberkemoes et al., 2014). Chronic insomnia and the use of prolonged sleep medication can lead to illness, and accidents like traffic accidents. It's also associated with the metabolic syndrome, hypertension, and cardiovascular disease (Laugsand, Barrels, Platou, & Janszky, 2011; Troxel et al., 2010; Vgontzas, Liao, Bixler, Chrousos, & Vela-Bueno, 2009). As mentioned before, when professional treatment is sought usually the General practitioners prescribe sleep medication (pharmacotherapy), which is the most widely used and often the only recommended treatment (Morin et al., 1999).

Besides the pharmacotherapy, also several non-pharmacological treatments for chronic insomnia exist. Harsora and Kessmann (2009) described non-pharmacologic interventions that have shown to produce reliable and sustained improvements in sleep patterns of patients with insomnia. An effective non-pharmacological treatment for primary insomnia is the Cognitive Behavioral Therapy (CBT). In addition to cognitive therapy, CBT for insomnia includes several techniques for improving

sleep such as sleep hygiene education, stimulus control, sleep restriction, paradoxical intention, and relaxation therapy. The therapy is about to educate patients about good sleep practices, modify maladaptive coping mechanisms, reduce hyper arousal states, and resolve misconceptions about sleep (Harsora & Kessmann, 2009). Another example of a non-pharmacological intervention is neurofeedback, which is a neuroscience-based clinical method (Harsora & Kessmann, 2009; Johnstone, Gunkelman, & Lunt, 2005). Neurofeedback training is a brainwave training, which gives feedback at brain frequencies. Brainwaves occur in various frequencies; some are slow, and some are fast, these can be measured with an electroencephalography (EEG). The classic names of the EEG bands are Delta, Theta, Alpha, sensorimotor rhythm (SMR) and Bèta. These bands are measured in cycles per second or hertz (Hz) (Hammond, 2006). In relation to sleep (deficiency) the Bèta-, and SMR-activities seem to be important. The Bèta brainwaves (14-35) are small and fast brainwaves. They are associated with a state of mental activity/concentration. For example; when someone is trying to resolve a cognitive task the EEG shows a high Bèta activity (Hammond, 2006). The sensorimotor rhythm (SMR) is a brain wave rhythm ranging from 12 to 15 Hz. This brain activity appears to be dominant during quiet but alert wakefulness (Hoedlmoser et al., 2008).

The electrical patterns in the brain are a form of behavior, which can change through "operant conditioning". It allows people to recondition, retrain or learn different brainwave patterns. Excessive brain frequencies can be reduced through a neurofeedback system, and those with a deficit can be increased (Johnstone et al., 2005; Heinrich, Gevensleben, & Strehl, 2007). From a neurocognitive perspective the cortical arousal in insomnia patients is reflected by heightened levels of high frequency EEG activity (Bèta and gamma power) during sleep onset and polysomnographic (PSG) sleep. Insomniacs appear to exhibit higher levels of relative Bèta power during wakefulness and during the sleep attempt. Also higher Bèta and gamma power during NREM sleep especially during the second part of the night as well as during REM sleep are present (Lamarche & Ogilvie, 1997; Perlis, Smith, Andrews, Orff, & Giles, 2001). The neurocognitive perspective posits that the presence of these high EEG frequencies might explain the excessive discrepancies often seen in patients with insomnia between the subjective and objective sleep measurements (Krystal, Edinger, Wohlgemuth, & Marsh, 2002; Pelis et al., 2001). Morin, Rodrigue, and Ivers (2003) described that insomnia patients perceive daily stressors, and major life events as more stressful in comparison to healthy sleepers. This results in higher pre sleep arousal at bedtime, which in turn is correlated with decreased sleep quality, and a high Bèta activity.

Cortoos, de Valck, Arns, Breteler, & Cluydts (2010) concluded there are several studies that have already shown the relationship between SMR and sleep improvement and sleep spindle density (Berner et al., 2006; Hauri, 1981; Hauri et al., 1982; Sterman, Howe, and Macdonald, 1970). In the neurofeedback study of Cortoos et al. (2010) the neurofeedback group had to increase SMR (12-15 Hz) and inhibit high beta power (20-30 Hz) at Cz. Several studies have demonstrated that SMR-neurofeedback results in increased sleep spindle density during sleep, decreased sleep onset latency (SOL), and increased total sleep time. Sterman et al. (1970) were the first who demonstrated that instrumental SMR conditioning (ISC) during wakefulness could improve subsequent sleep in cats. Hauri, Percy, Hellekson, Hartmann, and Russ (1982) demonstrated that patients suffering from primary insomnia specifically had benefits from the SMR training. Hoedlmoser et al. (2008) suggested that SMR-neurofeedback (as compared to a placebo randomized-frequency conditioning protocol) could exert positive effects on sleep quality. In a more recent study of Cortoos et al. (2010) 17 insomniacs were randomly assigned to a neurofeedback protocol (SMR 12-16 Hz) or Biofeedback protocol. This study showed an improvement regarding the subjective sleep measures (also SOL), measured with a sleep wake log, which only was present in the neurofeedback group. Also Hammer, Colbert, Brown, and Ilioi (2011) reported positive outcomes regarding their neurofeedback study by insomniacs. They suggested their neurofeedback system improved the sleep and daytime functioning of insomnia patients. Furthermore, the excessively high levels of Bèta power were significant lower at

post treatment in comparison with the pre-test.

Cortoos, Vertraeten, and Cluydts (2006) reported that neurofeedback is a promising application, and literature shows that neurofeedback might have a 24-h influence. Previous studies with insomnia patients have suggested a possibly significant effect of neurofeedback training on sleep therefore further research in this area should be encouraged (Cortoos et al., 2006).

1.2 Justification

Philips research developed a neurofeedback system (PNFS), which is described in chapter 4.2. Van Boxtel et al. (2012) evaluated this system in their study and showed that the system is capable of improving the relative activity in the EEG alpha band. In their study the alpha activity was increased in the group that actually received the alpha training. In the present study the PNFS will be adapted for people who have difficulties falling asleep.

The effect of the aforementioned PNFS has not yet been investigated regarding the Bèta and SMR activity in the EEG power spectrum. As in the background section is mentioned, previous literature to date shows promising results with a similar device (Van Boxtel et al., 2012). The PNFS is never used training people's Bèta or SMR activity. In the present study the effect of the Bèta and SMR training will be evaluated. Whereby the Beta training is focused on a decrease of the power in the Beta band, and the SMR training on an increase of the power in the SMR band. People with a perceived sleep deficiency will be included in the study. They must have difficulties falling asleep at a desired bedtime, what is called a sleep onset latency (SOL) and/or have a specific score (≥5) on a sleep questionnaire (The Pittsburgh Sleep Quality Index (PSQI)).

In a later stage Philips would like to investigate the effect of the neurofeedback system in a group of individuals suffering from insomnia. Before such a research can be performed, Philips first has to investigate to what extent the neurofeedback system is capable of reducing the SOL and/or PSQI-score in 'healthy people' with perceived sleep difficulties.

1.3 Objectives and outcomes

1.3.1 Primary objective

The primary objective of this study is to evaluate the effect of the Bèta and SMR neurofeedback on subjectively reported Sleep Onset Latency (SOL) in Philips employees with perceived sleep difficulties (PSQI ≥5 and/or SOL ≥20 min.).

1.3.2 Secondary objective(s)

"Is the PNFS capable of improving the total sleep time of Philips employees with perceived sleep difficulties?"

"Is the PNFS capable of improving the sleep efficiency percentage of Philips employees with perceived sleep difficulties?"

"Is the Philips neurofeedback system capable of reducing the PSQI-score of Philips employees with perceived sleep difficulties?"

"Is the PNFS capable of reducing the sleep disturbances of Philips employees with perceived sleep difficulties?"

"Is the PNFS capable of improving the perceived sleep quality of Philips employees with perceived sleep difficulties?"

"Will the Philips neurofeedback intervention improve the Health Related Quality of Life (HRQoL) of Philips employees with perceived sleep difficulties?"

1.4 Structure thesis

The thesis is structured as follows; at first the method section is presented including the study design, study population, measurements, statistical considerations and study procedures. Chapter 3 concerns the result section, in this chapter the results of the subjective and objective sleep data are presented, as well as the health related quality of life data. In the discussion (Chapter 4) the results of the current study are compared to the findings of others (literature), also an interpretation of the researcher is given. Besides the limitations of the current study are reported. With all the information taken into account a conclusion is written and last but not least recommendations are given.

2. Methods

2.1 Study design

Causal research provides an ability to make cause-effect statements. Determining a cause-and-effect relationship is imperative in situations in which an investigator must reveal the true cause(s) when evaluating whether or not an intervention caused the observed changes (Crosby, DiClemente, & Salazar, 2006). In addition causal research allows us to find out if a particular program is helpful in solving a problem. In the present study we want to investigate whether or not the PNFS (independent variable) is capable of improving the perceived sleep quality (dependent variable). The effects of the manipulation can be measured by assessing the designated outcome variables over some specific period of time. The outcome measure is called the dependent variable (Crosby et al., 2006). The major advantage of experimental research over observational research is the strength of causal inference it offers. This implies that a fair conclusion can be made regarding the effect of an independent variable on a dependent variable (Crosby et al., 2006).

A common experimental design is the between-subject design. In this type of experimental design, different groups are exposed to the different levels of the independent variable. The present research consists of three levels, namely the Bèta group, the SMR group, and the sham group. The subjects will be randomly assigned to one of the three groups, which means the design will be a double blind "randomized between groups design", i.e. a true experiment. This kind of research is considered as the "gold standard" in health promotion research (Crosby et al., 2006). Figure 1 is a representation of the study design.

Participants who fulfill the inclusion criteria, were randomly assigned to one of the following conditions:

1. **Bèta-group:** participants in the Bèta condition listened once per day (before they were going to sleep) for 20 minutes over a period of four weeks to their favorite music via the PNFS, in order to end with a total of 21 sessions. The measured Bèta power in the EEG power spectrum (15-30 Hz) determines the music quality: the lower the power in the Bèta band of the EEG spectrum, the more enriched the music sounds.

2. **SMR-group:** participants in the SMR condition listened once per day (before they were going to sleep) for 20 minutes over a period of four weeks to their favorite music via the PNFS, in order to end with a total of 21 sessions. The measured SMR power in the EEG power spectrum (13-15 Hz) determines the music quality: the higher the power in the SMR band of the EEG spectrum, the more enriched the music sounds.

3. **Sham-group (random neurofeedback):** participants in the sham condition, concerns the control group. This group also received the PNFS and listened once per day (before they were going to sleep) for 20 minutes over a period of four weeks to their favorite music via the PNFS, in order to end with a total of 21 sessions. In contrast to the other two groups, the control group received the feedback based on a previously recorded session of another individual, which was randomly picked. So this was not based on their live EEG signal. In order to mimic the dynamics of a normal neurofeedback session the music fluctuates, so it seemed like real feedback.

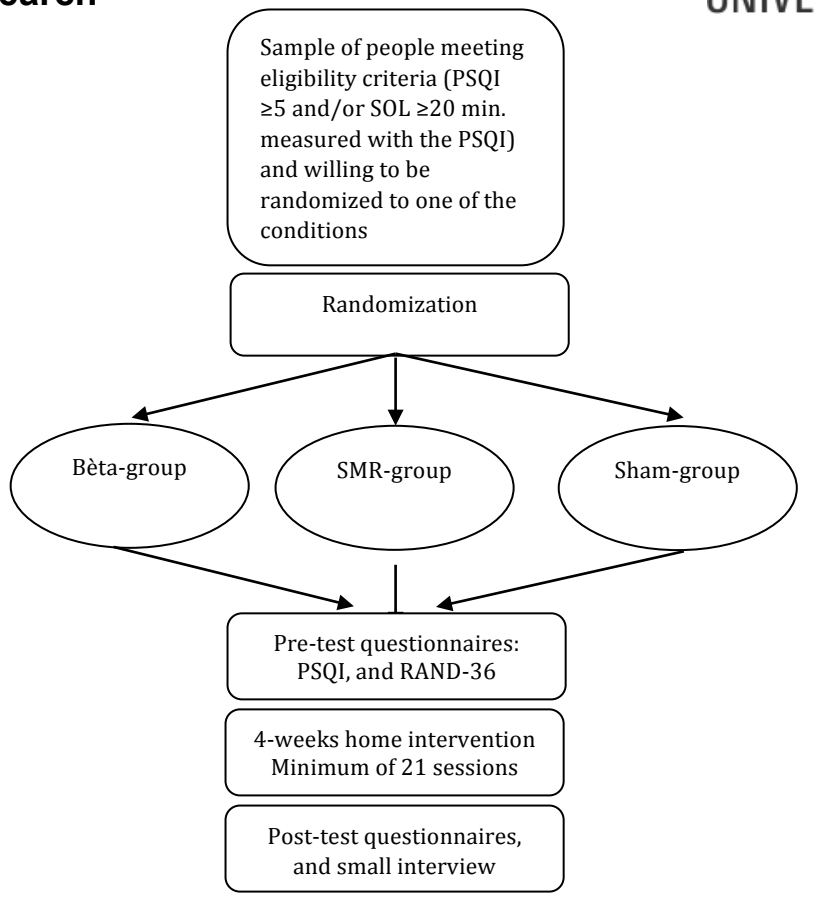


Figure 1. A schematic illustration of the experiment

2.2 Study population

2.2.1 Recruiting procedure

Convenience sampling provides convenient access to a population by using pre-existing groups (Crosby et al., 2006). In this study Philips employees were the pre-existing group. Philips employees were asked to volunteer in the study; they were recruited via flyers. In every Philips building at the High Tech Campus (HTC) the flyers were left on the walls near by; elevators, copy machines and coffee corners. People who were interested did sent an email to the experimenter. At first all participants received extra information, and in case they were still interested they had to fill in the Pittsburgh Sleep Quality Index (PSQI). If they met the criteria, they were invited to participate in the study. Also at the pre-test they had to fill in the PSQI, People were included in the study in case they still met the criteria.

2.2.2 Population characteristics

Only Philips Research employees aged 18-65 years with a perceived sleep deficiency (PSQI ≥5 and/or a SOL score of ≥20min.) were included. Complete inclusion/exclusion criteria are described below.

2.2.3 Inclusion criteria

Participants were qualified for the study if they met the following criteria:

- Aged between 18 and 65 years;
- Have a subjective impaired sleep quality as measured by a PSQI-score of ≥5 and/or a SOL score of ≥20min.

2.2.4 Exclusion criteria

Participants were excluded when they:

- Used sleep medication
- Used different kind of treatments with the intention to treat their sleep deficiency
- Were/ became pregnant and or were breastfeeding

2.2.5 Sample size justification

A priori sample size of N is computed as a function of power level 1-β, significance level α, and the 'to be detected population effect size' (Paul, Erdfelder, Lang, & Buchner, 2007). The results of the study of Cortoos et al. (2010) showed a significant decrease in the Sleep Onset Latency in the neurofeedback group (SOL $X^2 = 4.5$, $p < .05$, $r = .49$). This result indicates a significant effect at the pre-post treatment, not between groups. An effect size of r=0.49 (d=1,12; f=0.56) concerns a very large effect. Since our neurofeedback experiment was different than their experiment, we chose for a more safe effect size, but we still expected a large effect. So the effect size f was set at 0.40. The sample size calculation is conducted with G*power (Paul et al., 2007). Therefore the following values were important to fill in: an α of 0.05, 1-β = 0.80, 3 conditions (SMR, Bèta and Sham), 2 measurements (pre and post), and the statistical test ANOVA repeated measures between factors design (F-test). The calculated sample was 51. Since a dropout rate of 15% must be taken into account, approximately 60 subjects had to be included. The participants of the study could withdraw from participation of the experiment any time, without providing a reason.

2.2.6 Demographics participants

The demographic data of the subjects are displayed in Table 1 and are described in the section below. Thirty-six participants did meet the inclusion criteria and were included. In total thirty-one participants completed the whole study (pre-test, intervention, and post-test). Five participants dropped-out, for different reasons. Table 1 represents the demographics of all the included participants, divided into the different conditions; SMR, Bèta (experimental condition), and Sham group (control condition).

In total twenty-three male (63,9%) and thirteen female (36,1%) participants were included. Eighteen participants (50%) were 40 years old or younger, and eighteen participants were older than 40. In total more Dutch (58,3%) than international (41,7%) participants participated in the study. According to the chi square there were no significant differences on the demographics; gender, X^2 (2, $N = 36$)= 1.211, p>.05; age, X^2 (16, $N = 36$)= 10.231, p>.05; and language, X^2 (2, $N = 36$)= 3.632, p>.05.

Table 1
Demographics participants (N=36)

		Experimental conditions		Control condition
		SMR group (n=11)	Bèta group (n=13)	Sham group (n=12)
Gender	Male	7 (63,6%)	7 (53,8%)	9 (75,0%)
	Female	4 (36,4%)	6 (46,2%)	3 (25,0%)
Age	≤ 40	6 (54,5%)	6 (46,2%)	6 (50,0%)
	> 40	5 (45,5%)	7 (53,8%)	6 (50,0%)
Language	Dutch	9 (81,8%)	6 (46,2%)	6 (50,0%)
	English	2 (18,2%)	7 (53,8%)	6 (50,0%)
Drop-out	Yes	1 (9,1%)	3 (23,1%)	1 (8,3%)
	No	10 (90,9%)	10 (76,9%)	11 (91,7%)

In every group participants dropped out, but in the Bèta condition the most, namely 3. The dropout reason was mostly the lack of motivation (2), or this in combination with system dysfunction (2). There was one participant who dropped out for another reason.

2.3 Measurements

Table 2 presents an overview of the measurements, which were conducted in the study. All questionnaires were digital and available in English and Dutch. Appendix 1 shows the questionnaires used.

Table 2
Experiment measurements

Pre test	***During intervention***	***Post test (4-weeks)***
PSQI *RAND-36*	*Sleep diary (all days)** *Actiwatch (only first and last week)*	*PSQI* *RAND-36* *Small interview**

**results are not reported due to limited time, will be done in the future*

All sleep related outcomes are subjectively measured with the Pittsburgh Sleep Quality Index (PSQI) questionnaire and the Consensus Sleep Diary (CSD). In this study only the data of the PSQI is analysed and reported, the CSD data will be analysed in the future. The outcomes of the PSQI are compared to the objective sleep measurement data (Actiwatch). The results are shown in Chapter 3 'Results'. The subjectively outcomes were leading, but it was also important to take the objective measurement into account. The Health Related Quality of Life (HRQoL) is measured with the RAND-36, all aspects were measured and analysed. The measurements, which are used in the experiment, are described below.

2.3.1 PSQI

The Pittsburgh Sleep Quality Index (PSQI), developed by Buysse, Reynolds, Monk, Berman, & Kupfer (1989), has gained widespread acceptance as a useful tool to measure the sleep quality in different (patient) groups (Backhaus, Junghanns, Broocks, Riemann, & Hohagen, 2002). The PSQI is a short self-report assessment of general sleep quality during the previous month (Sommer, Lavigne, & Ettlin, 2015). The PSQI contains 19 self-rated questions and 5 questions rated by the bed partner or roommate (if one is available). Only self-rated questions are included in the scoring. The response option of items 1-4 has a free entry, item 5 consist of 10 sub questions with a response option on a 4-point Likert scale (0=Not during the past month; 3=Three or more times a week). Item 6 *"During the past month, how would you rate your sleep quality overall?*" has also a response option on a 4-point Likert scale (0=Very good; 3=Very bad). Item 7 and 8 have the same response option as item 5 does. Item 9 has a response option of "0= No problem at all, 3=A very big problem". In case the participant is having a bed partner or roommate the sub questions of item 10 must be filled in. These questions have the same response option as item 5. A few items of the PSQI are shown below:

- *"During the past month, what time have you usually gone to bed at night?"* (BED TIME: 22:30)
- *"During the past month, how often have you had trouble sleeping because you cannot get to sleep within 30 minutes?"* (0. Not during the past month; 1. Less than once a week; 2. Once or twice a week; 3. Three or more times a week).
- *"During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?* (0. Not during the past month; 1. Less than once a week; 2. Once or twice a week; 3. Three or more times a week).
- *"During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done? (0. No problem at all; 1. Only a very slight problem; 2. Somewhat of a problem; 3. A very big problem).*

The 19 self-rated items are combined to form seven component scores, namely; 1) Subjective sleep quality; 2) Sleep latency; 3) Sleep duration; 4) Habitual sleep efficiency percentage = *(Number of hours slept/Number of hours spent in bed) x 100*; 5) Sleep disturbances; 6) Use of sleep medication; and 7) Daytime dysfunction. All component scores have a range of 0-3 points. In all cases, a score of "0" indicates no difficulty, while a score of "3" indicates severe difficulty.

The seven component scores must be summed to yield a global PSQI score, which has a range of 0-21; higher global scores indicate poorer sleep quality. The PSQI has a Cut-off score which distinguishes the good sleepers from the poor sleepers. When the global score is 5 or more (=severe difficulties in at least two domains, or moderate difficulties in more than three domains) the respondent is a poor sleeper (Sommer et al., 2015). The scoring procedure is shown in Appendix 2.

The PSQI has been widely translated and employed in a wide range of population-based and clinical studies. It has been shown to be a reliable and valid instrument for the assessment of subjective general sleep quality. The questionnaire has a good test-retest reliability (0.85) and internal consistency (α=0.83). Also the criterion validity is good, so the questionnaire distinguishes good sleepers from poor sleepers (Backhaus et al., 2002). The PSQI is easy to handle and can be completed within five-ten minutes (Sommer et al., 2015).

2.3.2 Sleep diary (logbook)

A sleep diary is a daily logbook that can be used to record peoples sleep-wake pattern. It monitors when someone is going to bed and getting up in the morning, how long it takes to fall asleep, how often someone is awake during the night, and how restful his or her sleep is. It also allows recording alcoholic or caffeinated drink intakes that may affect the sleep. The participant needs to fill in the diary in the ***morning*** within one hour after they woke up. The Consensus Sleep Diary (CSD) of Carney et al. (2012) is a sleep diary, which gives insight in at least the following sleep parameters; Sleep Onset Latency (SOL), Wake After Sleep Onset (WASO), Sleep disturbances (DIST) and the Sleep Efficiency percentage (SE%), and the total sleep time (TST). It also gives insight in the alcohol, caffeine, and medication intake *(confounders)*. The CSD has three versions. The version that is used is the CSD-M, which consists of a general instruction and 15 items. The questions have different response options. A few examples are shown below, for insight in the whole questionnaire see Appendix 1.2.

- *"What time did you get into bed?"* (e.g. 22:15)
- *"How long (minutes) did it take you to fall asleep?"* (e.g. 40 min.)
- *"How many times did you wake up, not counting your final awakening?"* (e.g. 5 times)
- *"Did you wake up earlier than you planned?"* (e.g. yes or no)
- *"In total, how long did you sleep?"* (e.g. 5 hours 10 min.)
- *"How would you rate the quality of your sleep?"* (e.g. 1: very poor, 2: poor, 3: fair, 4: good, 5: very good)
- *"How rested or refreshed did you feel when you woke-up for the day?"* (e.g. 1: not at all rested, 2: slightly rested, 3: somewhat rested, 4: well-rested, 5: very well-rested)

During the intervention period (4 weeks) the participants received an automatically generated email at 05.00 in the morning (every day). This email contained a link to the questionnaire, so they were reminded of filling in the questionnaire every day. The diary is used to check the Actiwatch data, e.g in case there were missing markers (time try to sleep, and time of waking up) in the data. In the future the data will also be analysed, but due to the lack of time only the PSQI is analyzed (subjective).

2.3.3 HRQoL, RAND-36

Individual's ability to function and the perceived well-being in physical, mental and social domains of life can be summarized as the health related quality of life (HRQoL). Perhaps the RAND-36 is currently the most widely used HRQoL survey instrument in the world. The RAND-36 is a self-administered questionnaire, which takes about 7-10 minutes (Hays & Morales, 2001).

The RAND-36 is comprised of 36 items that assess eight health concepts, namely physical functioning (10 items), role limitations caused by physical health problems (4 items), role limitations caused by emotional problems (3 items), social functioning (2 items), emotional well-being (5 items), energy/fatigue (4 items), pain (2 items), and general health perceptions (5 items).

Negative formulated items were recoded. After the items were recoded the scale scores was calculated for each health concept. A transformed score is calculated with the following formula: $\left(\frac{raw\ scale\ score - minimum\ raw\ score}{score\ range}\right) x\ 100$. The minimum raw score is the lowest score that can be achieved on the scale. The score range is the difference between the lowest possible scale score and the highest scale score. The scores are calculated for each health concept. The higher the score the better the health status of the person is.

Van der Zee, Sanderman, Heyink, and De Haes (1996) validated the RAND-36 and examined the reliability and the validity of the RAND-36. The internal consistency was high, the Cronbach's alpha ranged from .71 to .93. The test-retest reliability (intervals of respectively two and six months) was satisfactory for an instrument that needs to be susceptible for fluctuations in the health status. Furthermore, does the instrument seem to have a high convergent validity (Van der Zee et al., 1996) See Appendix 1.4 for the used questionnaire.

2.3.4 Actigraphy

The Actigraphy has been used to study sleep/wake patterns for over 20 years. The Philips Respironics Actiwatch 2 monitoring system (Figure 2) is a wrist worn accelerometer and light recorder. It helps to (objectively) assess a subject's sleep/wake pattern and activity in response to the neurofeedback training. It's designed to be comfortable, rugged, and waterproof (IEC Standard 60529 IP52), CE marked and a medical device class II (Ancoli-Israel et al., 2003; Sadeh & Acebo, 2002). It seamlessly fit into the volunteer's lifestyle.

Collected data was downloaded to a computer for display and analysis of activity/inactivity that in turn was analysed to estimate wake/sleep patterns and the SOL. The first Actigraphs were developed in the early 1970's. Over the years there are different types of Actigraphs developed leading to the digital types of today. The Actigraphs have movement detectors (e.g accelerometers) now and sufficient memory to record for up to several weeks (Ancoli-Israel et al., 2003).

The Actigraphy (Actiwatch) was placed on the non-dominant wrist. The participants wore the Actigraphy the whole day (24-hours) during the first and the last week of the experiment. Since only the data of the night was meaningful for this experiment all participants had to push the marker button before they were going to sleep (when switching off the light and closing their eyes). Also when they woke up, and were not trying to sleep anymore they had to push the marker button. After returning the Actigraphy the data was retrieved. If the markers were shown in the data, the intended sleep period of the participants was visible. If not, the CSD was needed to set the markers manually.

The Actiwatch data is analysed regarding the outcomes (sleep onset latency, wake time after sleep onset, sleep efficiency percentage, sleep disturbances, and total sleep time). The data of the first week was compared to the data of the last week; the average of both weeks is taken. In case there were missing markers the investigator used the bedtime and wake time the participants filled in at the CSD. In case the participants forgot to wear the Actiwatch in the period they had to, this data couldn't be taken into account.

The Actiwatch had to record at least four reliable days out of seven for both weeks (first week, and last week). If the Actiwatch did not record at least four days in both weeks, the data of the participant was not analysed.

Figure 2. Philips Respironics Actiwatch 2

2.3.5 Adherence

The neurofeedback system logged the neurofeedback sessions of the participants. In this way it is possible to monitor whether or not the participants adhere to the treatment. All participants needed to end-up with 21 sessions, so at the end the neurofeedback system must logged at least 21 sessions.

Since the data of the logged sessions had some technical problems (which are not fixed yet) the data shown is an estimate of the total amount of sessions. In future research the real data will be analysed.

2.4 Statistical considerations

2.4.1 Bias prevention

In order to minimize bias, the participants were randomized to one of the three groups with treatment allocation balance for gender, age, PSQI-score, and SOL-score. Subjects were allocated to one of the three groups according to a pre-defined randomization schedule. The randomization schedule was generated by a statistician not directly involved with the day-to-day data collection and was not available to the study statistician until database was locked. The study statistician was blinded to subjects' treatment assignment until it was needed for the analysis. Compliance and randomization was monitored for accuracy by the un-blinded Project manager using site source documents. The study statisticians had access to the database for programing purposes but did not have access to the randomization scheme until all efficacy evaluations were completed and the database was locked.

2.4.2 Statistical analysis

It was intended to evaluate the effect of the Neurofeedback training over time (i.e., following 4 weeks and 3 months follow-up) in sixty participants (three conditions; two experimental conditions and one control condition). Due to limited time the analyses is conducted with thirty-six participants, which can be seen as an interim analysis. Only the pre-test, and post-test (4 weeks) data were taken into account. Also only the quantitative data is analysed, the qualitative data will be analysed in the future. An analysis of variance using repeated-measures ANOVA was performed. The data is analysed with the Statistical Package for the Social Sciences (SPSS). Participants who fully completed the experiment (pre-test, intervention, and post-test) were analysed.

Before conducting all analysis a few assumptions regarding the data were checked. At first the normality of the data is tested, therefore the Kolmogorov-Smirnov test, and Shapiro-Wilk test were used. They compare the scores in the sample to a normally distributed set of scores with the same mean and standard deviation. If the test is non-significant $p > .05$ it means that the distribution of the sample is not significantly different from a normal distribution. At least one of the two tests must be non-significant; otherwise the assumption for the parametric test was not met. Second the homogeneity of variance is tested.

This assumption means that the variances should be the same throughout the data. In this study several groups (conditions) of participants were tested, so in this case the assumption means that each of these groups must have the same variance. This is checked with the Levene's test. If the Levene's test was non-significant $p > .05$ the variances were roughly equal and the assumption was tenable. Another rule is that the data should be measured at least at the interval level. If all assumptions were met, the repeated measures ANOVA was conducted. If the normality assumption was not met or when the construct was measured at an ordinal level, the Kruskal-Wallis was conducted. Therefore the difference scores (post-test score (4 weeks) minus pre-test score) were used.

2.5 Study procedures

2.5.1 Roles, responsibilities and legal agreements

Table 3
Role and responsibility regarding the study

Role and responsibility	**Name**
Researchers	**Ad Denissen (0.2 FTE)** Principal scientist **Tim Weysen (0.05 FTE)** Research Scientist **Joëlle Dam (1 FTE)** Intern Philips Research, Student University of Twente
Study sites	**Philips Group Innovation | Research** High Tech Campus 36 5656AE Eindhoven

2.5.2 Devices used

Audio Neurofeedback system

Participants received a complete set of the Philips Neurofeedback System (PNFS), which allowed them to follow the Neurofeedback training at home. The training consists of the following parts;

- Listen to their favorite music for a period of 10 minutes
- Playing a game (flow, angry birds, gravity guy, or mind the gab) for a period of 5 minutes
- Listen to their favorite music for a period of 10 minutes

Figure 3. Schematic overview Neurofeedback intervention

The PNFS consists of two subsystems:

The first subsystem is a complete wireless and battery operate audio headset, EEG water electrodes (measured central), a wireless and battery operated bio acquisition device (Nexus-10) – see Figure 4.

Figure 4. The left picture represents the audio headset and the EEG water electrodes; the right picture is showing the Nexus-10 acquisition device.

The second subsystem is an Android tablet, the 'Samsung Galaxy Tab A', with an Application of the PNFS, which interprets the EEG signal and modulates the audio quality accordingly, see Figure 5.

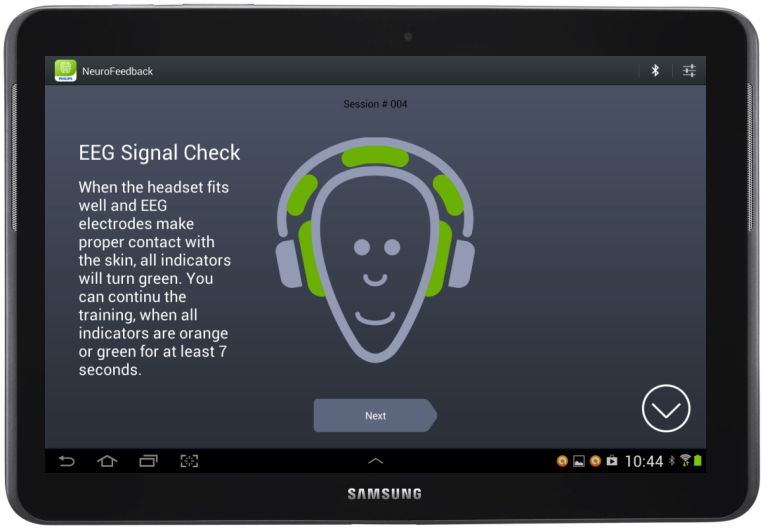


Figure 5. Samsung Galaxy Tab A, runs the Philips Neurofeedback System application.

Explanation neurofeedback system

In the background section (paragraph 1.1) the function and the effect of Neurofeedback is explained. Neurofeedback knows many forms, for instance visual, and audio based. Philips Research developed an audio Neurofeedback system. This PNFS is already used in a previous experiment of Van Boxtel et al. (2012). During the Neurofeedback training people had to listen to their favorite music. Pilot work showed that a simple high-bass filter on the sound had a great impact at the music quality, making the music sound very distant and thin. Van Boxtel et al. (2012) reported this turned out to be the basis of a very intuitive form of feedback, especially because people are very familiar with their own favourite music and recognize when something regarding the music is different. That's why no instructions have to be given to the participant for training to occur. The Neurofeedback system conveyed the feedback via the quality of the music, by removing the low frequency components (bass tones). The cut-off frequency of the filter depends on the amount of power observed in the EEG frequency band of interest (Van Boxtel et al., 2012). For example, when subjects were relaxed during the training, the alpha power in the EEG spectrum was high.

All tones above 2 Hz then passed the filter and the music did sound normal, which is a positive reinforcement. When the Alpha power was too low, the music did sound less comfortable, which is negative reinforcement (Van Boxtel et al., 2012). In the experiment of Van Boxtel et al. (2012) subjects were randomly assigned to one of three following conditions; alpha group, random Bèta group, or the music only group. Their study shows that their PNFS is capable of training the alpha activity, because the alpha activity increased significantly in the group that actually received the alpha training. They also proved the feasibility of the innovative self-guided system (the PNFS) with water-based electrodes fastened in an audio headset.

The PNFS is an *audio* Neurofeedback system, the feedback will be conveyed via the quality of the music by removing the low frequency components (bass tones) with a simple first order high pass filter with a slope of 6 dB/octave (see Figure 6). The cut-off frequency of the filter depends on the amount of power observed in the EEG frequency band of interest. For example for Bèta training 15 to 30 Hz is used. In the 2nd experimental group, feedback is provided on the SMR power (13-15 Hz). When subjects were relaxed, the SMR power in the EEG spectrum was high, and all tones above 2 Hz could pass the filter and the music did sound normal (Van Boxtel et al., 2012). In the present study, feedback will be provided on the Bèta power. When the Bèta power increased the cut-off frequency of the high pass filter did shift upwards up to 2 kHz.

As a result, the music contained mainly high tones because the low tones were filtered out, and this caused a decreased experience: the music sound "thin" and less loud for the reason is that a significant amount of power in the music is present in the lower part of the audio spectrum. In this way, the Bèta level is coupled with the filtering of the music and depending on the Bèta level, the music sounds good or bad, a method used before (Van Boxtel et al., 2012). In summary when the Bèta activity in the Bèta group is high, the participants received feedback through hearing bad music. When their Bèta activity reduced the music did sound well again. This is a continuous process. Concerning the SMR group, they received feedback (bad music) when their SMR power was low. The sham condition did receive random neurofeedback.

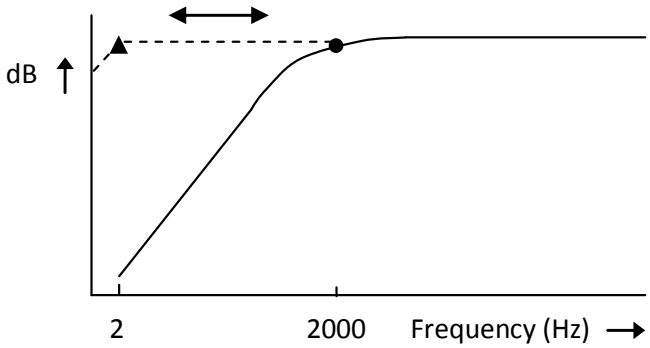


Figure 6. Representation of a high pass filter with a slope of 6dB/octave

EEG power levels are not constant over time. To be able to change the music with the changing power level in the brain, every neurofeedback training period was divided into epochs of 4 seconds. The EEG power was measured during each epoch and depending on the level, the filtering of the music changed or not. Since the EEG power differs a lot between different persons minimum and maximum levels were estimated for the perfect individual training. For a stable estimation the 15% (minimum) and 85% (maximum) percent point of the cumulative distribution of the EEG power over the epochs from the past, which were free from artifacts were used. The system slightly forgets the oldest epochs to adapt for a change in EEG spectrum. When the EEG power is above the 85% point the music sound bad.

However, when the EEG power drops below 15% all tones of the music are allowed to pass the filter, resulting in a perfect music quality. EEG power, ranging between the 15% and 85% point were gradually filtered so that subjects did not notice sudden frequency and volume changes in the music (Source: Private communications with Ad Denissen).

2.5.3 Informed consent procedure

Interested participants received the informed consent letter by email, with the option to be given further information. Volunteers were free to respond at any time, but received a reminder after about one week. The volunteers could read everything in their own pace. During the intake the protocol was repeated orally, accompanied with an explanation of the practical issues of the study before the Informed Consent was signed. This procedure was executed by the study managers/executors (master student). The information is attached in Appendix 3. Study participation was voluntary. The subject could refuse to consent or could withdraw from the study at any time without giving a reason and without any consequences.

2.5.4 Compensation

The Philips employees were compensated for their time and effort with 1000 Recognition@Philips points (100 euros). For more information they could check a Philips webpage. Since only complete datasets were valuable for the study, partial completion of the protocol was compensated likewise. 250 Recognition@Philips points were compensated when participation was stopped during the home sessions, before part 4 of the study.

2.5.5 Privacy considerations

Personal data was collected to be able to contact the participant. These include full name, and email address. Additional personal data was stored (under a randomized participant number) for research purposes, including age and sex. All data collected during the test, including physiological data, questionnaire data and the sleep diary were also stored under a randomized participant code. The document is provided with a password and only two persons had access to this document, namely the Responsible Researcher (Ad Denissen) and the experimenter (Joëlle Dam). All collected data will be stored for 5 years, after this period the data will be destructed.

3. Results

In this chapter the results of the subjective and objective data are shown, also the results of the general health data are described. Only the data of the pre-test and the post-test (4-weeks) are analysed. Due to limited time the consensus sleep diary (CSD) data and the data of the small interview were not analysed, but this will be done in the future as well as the follow up (3 months) data.

3.1 Sleep data

Mean (M) and standard deviation (SD) scores of the subjective and objective sleep evaluations are presented in Table 4. Since some constructs were not normally distributed or were measured at an ordinal level also the median (Mdn) and interquartile range (IQR) are reported, see Appendix 4 (Table 7 and 8).

Table 4
Mean (SD) scores of subjective and objective sleep evaluations for each condition and time separately

Variable	Group				Statistics (*p* values)			
	Time	SMR	Bèta	Sham	Time x group	Time	Group	NP*
Subjective sleep		n= 10	n= 10	n= 11				
SOL	Pre	36.50 (14.35)	30.50 (12.12)	25.00 (18.44)	NS	.000	NS	
	Post	20.00 (13.12)	15.00 (8.50)	15.82 (11.81)				
TST	Pre	5.87 (1.20)	6.03 (1.06)	5.73 (1.06)	NS	.005	NS	
	Post	6.15 (.99)	6.73 (.76)	5.95 (1.21)				
SE%	Pre	76.75 (15.36)	86.11 (16.98)	80.80 (13.60)	NS	NS	NS	
	Post	80.00 (6.00)	89.11 (8.87)	80.34 (12.57)				
PSQI	Pre	10.40 (3.60)	9.80 (2.70)[a]	7.91 (3.11)[a]				.016
	Post	7.40 (2.60)	6.40 (2.21)	6.91 (3.30)				
DIST	Pre	8.70 (4.30)	12.50 (5.44)	6.36 (2.80)				NS
	Post	7.00 (3.20)	9.40 (6.54)	4.45 (2.30)				
SQ	Pre	2.20 (.42)[b]	1.80 (.63)	1.64 (.67)[b]				.036
	Post	1.40 (.84)	1.50 (.53)	1.45 (.52)				
Objective sleep		n= 9	n= 7	n= 8				
SOL	Pre	8.03 (4.60)	8.13 (7.71)	8.00 (7.58)	NS	NS	NS	
	Post	8.49 (4.30)	8.56 (3.95)	7.62 (6.93)				
DIST	Pre	27.87 (6.57)	29.01 (5.46)	24.89 (3.30)	NS	.015	NS	
	Post	31.33 (7.76)	28.89 (7.38)	29.15 (6.58)				
SE%	Pre	87.06 (4.27)	85.51 (3.20)	86.70 (3.66)	NS	NS	NS	
	Post	86.47 (4.94)	86.08 (4.03)	85.71 (5.07)				
WASO	Pre	40.54 (13.57)	40.63 (8.33)	37.50 (6.87)				NS
	Post	45.04 (18.65)	42.81 (16.85)	44.59 (14.66)				
TST	Pre	6.96 (.84)	6.69 (.49)	6.29 (.77)				NS
	Post	7.00 (.70)	6.73 (.49)	6.41 (.68)				

Repeated measures ANOVA; *Kruskal wallis (non-parametric test)
NS no significant effect
[a] Significant difference between Bèta group and the Sham group ($U = 9$, $p = .001$, $r = .72$).
[b] Significant difference between SMR group and the Sham group ($U = 25.50$, $p = .017$, $r = .52$).
Note. SOL=Sleep Onset Latency (min.), SOL is log-transformed for statistical tests; TST=Total Sleep Time (h); SE%=Sleep efficiency percentage; PSQI=Global PSQI score; DIST=Amount of disturbances during night; SQ=Subjective Sleep Quality; WASO= Wake After Sleep Onset.

3.1.1 Subjective sleep data

Sleep onset latency

The primary outcome, sleep onset latency (SOL) improved strongly in all groups. A repeated measures ANOVA was conducted to evaluate the effect among the three neurofeedback conditions (Bèta, SMR, and Sham). The SOL was log-transformed in order to meet a normal distribution. There was a statistically significant effect of time on subjectively reported sleep onset latency, $F(1,28) = 47.764$, $p < .05$. However there was not a significant difference observed between groups in changes of SOL over time $F(2,28) = .879$, $p > .05$. So all participants needed less time to fall asleep, but there was not a significant difference observed between the groups.

Total sleep time

In all conditions the mean of the total sleep time was improved. A statistically significant improvement in time was observed on subjectively reported total sleep time (TST), $F(1,28) = 9.09$, $p < .05$. However there was not a statistically significant difference in improvement of TST between the groups, $F(2,28) = 1.244$, $p > .05$.

Sleep efficiency percentage

A repeated measures ANOVA showed that the sleep efficiency percentage of the first time point, and the second time point were not statistically different, $F(1,28) = .486$, $p > .05$. Also the difference between the groups was not significant, $F(2,28) = .193$, $p > .05$.

Global PSQI-score

The secondary outcome, the global PSQI score, improved also in all groups. A Kruskal-Wallis test was conducted to evaluate differences among the three neurofeedback conditions on median change in the global PSQI-score (PSQI). The test was significant $X^2(2, N = 31) = 8.30$, $p < .05$. Mann-Whitney-U tests were used to follow up this finding. A Bonferroni correction was applied and so all effects are reported at a *(.05/(N test = 2)=* .025 level of significance. It appeared that the improvement in PSQI score was not different in the SMR group compared to the Sham condition ($U = 34.50$, $p = .140$, $r = .32$) However, the PSQI score in the Bèta group was significantly lower compared to the Sham condition ($U = 9$, $p = .001$, $r = .72$).

Sleep disturbances

A Kruskal-Wallis test was conducted to evaluate differences between the three neurofeedback conditions on median change in the amount of sleep disturbances (DIST). The test was not significant, $X^2(2, N = 31) = 2.38$, $p > .05$.

Sleep quality

Since the sleep quality (SQ) was measured on an ordinal level a Kruskal-Wallis test was conducted. The results of the analysis indicates that there are significant differences in the median changes of the sleep quality, $X^2(2, N = 31) = 6.67$, $p < .05$. Follow-up tests (Mann-Whitney-U test) were conducted to evaluate pairwise differences among the three groups, controlling for Type I error across tests by using the Bonferroni approach (.025 level of significance). The results of these tests indicated a significant difference between the SMR group and the Sham group (control) ($U = 25.50$, $p = .017$, $r = .52$). Though the reported sleep quality was not different in the Bèta group compared with the Sham group ($U = 48.50$, $p = .535$, $r = .14$).

3.1.2 Objective sleep data

In Table 4 the means and standard deviations of the constructs of the Actiwatch (objective) sleep data are reported. Since a few constructs were not normally distributed also the median and interquartile range is reported (see Appendix 4).

In total, 31 subjects fully completed the neurofeedback sleep study. Since there were some troubles with collecting the objective data (low adherence and technical problems) only the objective sleep data of 24 subjects were analysed.

No significant differences were detected in the objective sleep parameters, except for the sleep disturbances.

Sleep onset latency

The SOL was log-transformed in order to meet a normal distribution. A repeated measures ANOVA showed that there was not a statistically significant effect of time on sleep onset latency, $F(1,21) = .68$, $p > .05$. Ass well as there was not a statistically significant effect between the groups on sleep onset latency, $F(2,21) = .019$ $p > .05$

Sleep disturbances

The amount of sleep disturbances increased significant in time $F(1,21) = 7.02$, $p < .05$. However there was not a statistically significant difference between the groups in sleep disturbances, $F(2,21) = 1.847$, $p > .05$.

Sleep efficiency percentage

There was not a statistically significant effect of time on the sleep efficiency percentage (SE%), $F(1,21) = .44$, $p > .05$. Ass well as there was not a statistically significant effect between the groups on SE%, $F(2,21) = .774$, $p > .05$.

Wake time after sleep onset

A Kruskal-Wallis test was conducted to evaluate differences among the three neurofeedback conditions on median change of the WASO. The test was not significant, $X^2(2, N = 24) = 1.17$, $p > .05$.

Total sleep time

The differences among the three neurofeedback conditions on median change of the total sleep time was not significant, $X^2(2, N = 24) = .19$, $p > .05$.

3.2 Health related quality of life

In Table 5 the means and standard deviations of the health related quality of life (HRQoL) are displayed, as well as the statistical data. Since some constructs were not normally distributed or were measured at an ordinal level also the median (Mdn) and interquartile range (IQR) are reported, see Appendix 4 (Table 9).

Table 5
Mean (SD) scores of Health Related Quality of Life evaluations for each condition and time separately

Variable	Group				Statistics (*p* values)			
	Time	SMR	Bèta	Sham	Time x group	Time	Group	NP *
HRQoL		n= 10	n= 10	n= 11				
Vitality	Pre	49.00 (23.43)	50.00 (13.74)	56.82 (15.70)	.048	.006	NS	
	Post	60.00 (17.80)	49.50 (16.24)	62.27 (15.55)				
General-health	Pre	54.50 (24.55)	69.00 (15.06)	70.91 (18.55)	NS	.006	NS	
	Post	64.00 (19.83)	71.00 (10.49)	77.27 (16.33)				
Physical-functioning	Pre	92.00 (11.35)	89.50 (10.92)	94.09 (13.38)				NS
	Post	92.00 (12.74)	90.50 (8.64)	94.55 (10.36)				
Social-functioning	Pre	57.50 (34.46)	72.50 (12.91)	78.75 (15.65)				NS
	Post	81.25 (24.47)	81.82 (16.17)	86.36 (16.25)				
Physical-problems	Pre	72.50 (36.23)	80.00 (25.82)	97.73 (7.54)				NS
	Post	80.00 (34.96)	85.00 (24.15)	97.73 (7.54)				
Emotional-problems	Pre	60.00 (40.98)	63.33 (24.60)	69.70 (34.82)				NS
	Post	90.00 (22.50)	86.67 (17.21)	87.88 (22.47)				
Mental-health	Pre	65.60 (21.27)	66.00 (16.47)	76.00 (14.53)				NS
	Post	74.80 (18.19)	66.00 (14.64)	77.45 (17.09)				
Pain	Pre	81.22 (23.97)	84.90 (15.46)	90.35 (10.33)				NS
	Post	90.20 (17.60)	85.92 (12.60)	91.47 (12.31)				
Health-change	Pre	45.00 (10.54)	57.50 (12.08)	52.27 (13.48)				NS
	Post	42.50 (20.58)	55.00 (10.54)	56.82 (16.17)				

Repeated measures ANOVA; *Kruskal wallis (non-parametric test)
NS No significant effect

A repeated measures ANOVA was conducted to evaluate the effect among the three neurofeedback conditions (Bèta, SMR and Sham) on the vitality and general health concepts. There was a statistically significant improvement in time on both respectively, $F(1,28) = 8.96$, $p < .05$ and $F(1,28) = 8.81$, $p < .05$. However there was not a significant difference observed between the groups in changes of general health over time, $F(2,28) = .92$, $p > .05$. There was found a significant interaction effect of vitality, $F(2,28) = 3.386$, $p < .05$. Further analyses were conducted to follow up this finding. However no significant differences between groups in changes over time were found for all other HRQoL constructs.

3.3 Amount of sessions

Table 6 represents an estimate of the minimum, maximum and mean amount of the neurofeedback sessions the participants in each group completed. This gives insight in the adherence of the participants regarding their training sessions. But since it is an estimate we must be careful with draw real conclusions. In future research the real data will be analysed.

Table 6 is dived into the three different groups and represents the first 10 minutes of the neurofeedback training (listening to music), the second 10 minutes (listening to the music, after playing the 5 min. game), and the mean of both. There might be a discrepancy between the values of the first 10 minutes and the second 10 minutes, which can indicate the participants stopped earlier for some reason, or something went wrong with the system.

Table 6
Amount of neurofeedback sessions by group

	SMR group (n=10)			**Bèta group (n=10)**			**Sham group (n=11)**		
	Min	Max	M (SD)	Min	Max	M (SD)	Min	Max	M (SD)
First 10 min.[a]	10.06	26.03	21.18 (5.40)	19.55	26.99	19.55 (4.65)	11.37	28.98	22.87 (5.65)
Second 10min.[b]	8.03	26.03	20.10 (5.93)	11.98	24.15	18.09 (4.38)	7.98	27.99	20.42 (6.64)
Mean of both[c]	9.05	26.03	20.64 (5.60)	12.50	25.57	18.82 (4.47)	11.18	27.99	21.64 (5.84)

[a] First 10 minutes of the neurofeedback session (listening to music). [b] Second 10 minutes of the neurofeedback session (listening to music, after playing the 5 min. game).[c] Mean of first 10 minutes and last 10 minutes.

A Kruskal-Wallis test was conducted to evaluate differences among the three neurofeedback conditions on median change of the neurofeedback sessions. The tests were not significant.

4. Discussion

Subjective sleep parameters

No significant effects of Bèta or SMR neurofeedback are found on the primary outcome subjectively reported sleep onset latency (SOL). The current study showed an improvement over time on the SOL. However, this result was seen in all groups, so in all groups it took the participants less time to fall asleep. Though no group improved significantly more in comparison to the control group. This is in line with Hauri et al. (1982), they also reported an overall improvement in SOL. However Cortoos et al. (2010) reported a significant improvement in SOL in the neurofeedback group only. Which is in contradiction with our findings. This discrepancy can be due to different reasons. One of the differences between Cortoos et al. (2010), Hauri et al. (1982) and the current study is the way in which feedback is given. Cortoos et al. (2010) and Hauri et al. (1982) gave visual feedback and in the current study people had to listen to their favourite music. The feedback is given through the change in music quality. Literature showed that only listening to music already improves the sleep quality (Lai & Good, 2006; Levin 1998; Mornhinweg & Voignier 1995; Zimmerman et al. 1996). This is probably what we see. In all groups the SOL improves over time, but no differences between groups were found. The only thing that is different between the experimental conditions and the control condition is the neurofeedback element. In this case there is no effect of the neurofeedback element.

Another difference between our study and the study of Cortoos et al. (2010) and Hauri et al. (1982) is that they analysed the subjective sleep data of the sleep diary. In the current study the subjective sleep is also measured with a sleep diary, but due to the lack of time only the PSQI data is reported. One of the advantages of the sleep diary is that the recall bias is minimized. The subjects needed to fill in the diary within one hour after they woke up. This is much easier than give an estimate over the previous month. The sleep diary data also gives more insight in the progress over time of the participants regarding the subjective sleep parameters, since it is measured at more time points. Also the study design differs. Hauri et al. (1982) had no control group at all, and Cortoos et al. (2010) had a health sleepers control group. Our study design is more suitable to make conclusions whether or not neurofeedback helps.

Also the study population differs, Cortoos et al. (2010) and Hauri et al. (1982) recruited diagnosed insomnia patients, via clinical sleep centres and primary care physicians. Those participants have more sleep problems than our participants (people who had perceived sleep problems, but were not diagnosed insomnia patients, recruited at Philips). And there is a big difference in study design. Hauri et al. (1982) didn't have a control group at all, and Cortoos et al. (2010) had a 'healthy sleep' control group, which is not comparable with population poor sleepers.

It is hard to compare the results of the current study to the results of the study of Cortoos et al. (2010) and Hauri et al. (1982) since there are a lot of differences. Besides only the preliminary results of the current study are presented. Real conclusions can be made when the study is finished.

The secondary outcome total sleep time (TST) also improved in all groups, but no differences between the groups were found. This result is in line with Cortoos et al. (2010) and Hauri et al. (1982). This means that in all studies there is no effect of the neurofeedback on the TST.

In spite of the results above a significant difference in improvement between the groups was detected on the global PSQI-score (score of overall reported sleep problems) and the sleep quality, both measured with the Pittsburgh Sleep Quality Index (PSQI). The Bèta group improved significantly regarding the PSQI-score compared to the sham group. The SMR group improved significantly regarding the sleep quality. Arns, Feddema, and Kenemans (2014) studied SMR and Theta/Bèta ratio neurofeedback in ADHD patients. They reported only a time effect (improvement) of the PSQI score. This contradiction can be due to the different population and a different neurofeedback protocol.

Sleep quality is commonly used in sleep medicine, sometimes it is used to refer to a collection of sleep measures including TST, SOL, degree of fragmentation, total wake time, sleep efficiency, and sometimes sleep disruptive events such as apnea or spontaneous arousals. The Pittsburgh sleep Quality Index (PSQI), is widely employed and provides a measure of global sleep quality based on a respondent's retrospective appraisal (past month) of an array of sleep parameters, including SOL, TST, habitual SE, sleep disturbances, use of sleep medication, and daytime dysfunction (Kristal & Edinger, 2008). The current study presents a significant improvement of the global PSQI score, which means that in the Bèta group the respondent's retrospective appraisal of the past month on an array of sleep parameters (sleep quality) is improved. This is a positive result for Philips that provides perspective, but the fact remains that a few improvements need to be done. These are described in the 'recommendations' part.

Objective sleep parameters

In contrast to the subjective sleep parameters, no significant improvement of the objective sleep parameters was found. It is even remarkable that in the objectively measured sleep parameter 'sleep disturbances' an aggravate was shown. This means that in the last week the participants woke up more often in the middle of the night, compared to the first week. However no significant differences between the groups were found. This is in contradiction with Cortoos et al. (2010), they showed that a specific neurofeedback protocol induced greater objective changes in comparison to EMG biofeedback. They observed an overall improvement in SOL and WASO, irrespective of training group. Also the insomnia group received a neurofeedback training focusing on inhibition of Theta and high Bèta, as well as reinforcement of SMR, showed a significant increase in TST. This means that they found an effect of the neurofeedback on the objective sleep parameters. So, there is a huge discrepancy between their findings and our findings.

The contradiction between the studies could be attributed to the use of different measurements. Cortoos et al. (2010) measured the objective sleep with a polysomnography (PSG) at an experimental sleep laboratory. In the current study an Actiwatch is used. Since the introduction of the PSG in the 1950s, it has been regarded as the gold standard for objective assessment of sleep. In addition to classification of sleep stages the PSG provides measures of both sleep and wake time. It offers extensive information on sleep behavior and sleep physiology, but is also very expensive, time consuming and can sometimes be too invasive to use in clinical studies (Silvertsen et al., 2006). Therefore the Actigraphy has been suggested as an alternative assessment method to PSG. The Actigraphy (used in the current study) consists of an accelerometer and memory storage. Based on differences in movements associated with wakefulness and sleep, Actigraphy provides an estimate of sleep-wake schedules. Morgenthaler et al. (2007) reported that the Actigraphy was useful in assessing treatment response in patients with insomnia. Others found that the Actigraphy was useful for measuring insomnia disorder treatment response (Vallieres & Morin, 2003). The Actigraphy has a high level of sensitivity (95.2%), however the specificity of Actigraphy, ie. the ability to detect wakefulness, was much lower (36.3%).

Since the Actiwatch is a wrist worn watch and measures activity of wrist movements, it gives inaccurate information if the person is awake but lying still (Hammer et al., 2011; Paquet et al., 2007; Silvertsen et al., 2006). Since this is a commonly known behavior of people with insomnia, it might overestimate their sleep duration, and underestimates the SOL, WASO, and wake-bouts. This could explain why there is a huge discrepancy between the objective and subjective sleep results. A discrepancy between objective and subjective measures is often reported in studies, and neurofeedback research is not an exception. This phenomenon was already reported by Cortoos et al. (2010), Egner et al. (2002), and Egner and Gruzelier (2003). The Actiwatch used in the current study doesn't seem accurate. Therefore it is recommended to use another instrument instead of the Actiwatch in future research.

Finally, there were also a few technical and adherence problems. The participants had to wear the Actiwatch 24/7 in the first and the last week of the experiment, and had to push the marker button twice (when they had the intention to fall asleep, and when they woke up in the morning). The Actiwatch had to record at least four nights in the first week, and four nights in the last week otherwise the data wouldn't be analysed. Since some participants forgot to wear the Actiwatch a few times and/or forgot to push on the marker button (low adherence), these data couldn't be taken into account. Also a few Actiwatches seemed to have technical problems, so were not analysed. Therefore a lot of the objective data was lost, and therefore the power reduced a lot.

Health related quality of life parameters and treatment adherence

The neurofeedback had no effect on the Health Related Quality of Life concepts. Two concepts, namely 'vitality' and 'general health' did improve over time, but no differences were found between the experimental conditions and the control condition.

The first studies that used the SF-36 in insomnia populations consistently demonstrated lower scores (greater impairment in health status of HRQoL) on all domains, relative to normal sleepers (Hajak & Sine, 2001; Hatoum, Kong, Kania, Wong, & Mendelson, 1998; Zammit, Weiner, Damato, Sillup, & McMillan, 1999). Kyle, Morgan, and Espie (2010) reported that from the limited treatment studies an improvement in sleep, in some cases, could lead to statistical improvements in aspects of HRQoL. However, it isn't clear whether the improvements are *clinically meaningful*: do they really matter to the patient? In the literature they are not consistent, that's why they say 'could lead'.

Since no literature is found regarding neurofeedback and HRQoL, the results of Cognitive Behavioral Therapy (CBT) are described. CBT is as well as neurofeedback a non-pharmacological treatment and there are a few studies that examined the effect of CBT on sleep quality and the HRQoL. Verbeek, Konings, Aldenkamp, Declerck, & Klip (2006) reported data from their CBT study on outcomes of both sleep and HRQoL parameters. As measured by the sleep logs they found a significant time effect for SOL, TST, SE, and WASO, but there was no significant group effect, only for WASO there was a modestly significant Group x Time effect. The HRQoL was measured with the RAND-36, both treatment groups showed comparable improvements in 'global' scores of the RAND-36, however they did not detail scores for each subscale. So it is impossible to identify what specific HRQoL components were most sensitive to the CBT intervention. They also had no control group in their study, so maybe something else caused the improvement instead of the intervention.

Espie et al. (2007) conducted a RCT of CBT versus 'treatment as usual' in general practice. After 6 months they found sleep improvements in the CBT condition which were accompanied by small, but significant improvements in the energy/vitality and mental healh subscales of the SF-36.

Also Soeffing et al. (2008) conducted a RCT of a cognitive behavioral intervention group and a sham biofeedback group. At post-treatment significant effects were detected in the experimental group (CBT) at SOL, WASO, and SE (medium to large effects), but no improvements were found in SF-36 scores (mean dimension/ component scores were not reported).

The studies described above are all CBT interventions, eventhough a non-pharmacological treatment is used, it is not a neurofeedback intervention. So we can take the results into account, but it is also very important to keep in mind that it is a different intervention. What can be conclude is that improvement in sleep could lead to improvements of HRQoL, but does not have to be so. The quality of sleep is intrinsically linked to quality of life (Kyle et al., 2010; Reimer & Flemons, 2003). So it is expected that when the sleep quality improves, also the HRQoL will improve. Since in the current study the effect on the sleep parameters was disappointing, it is comprehensible that there are no significant improvements on the HRQoL. It might be different when the sleep quality does improve significantly, then it is possible that also the HRQoL will improve. Therefore it is important that the study will be continued and that the participants adhere to the treatment. Reimer and Flemons (2003) stated that the impact of sleeping problems on the quality of life is usually the reason for people to

seek and adhere to treatment. In contrast to what they pronounce, adherence to the treatment seemed to be hard for the participants in the current study. All participants needed to end up with 21 neurofeedback sessions out of 28 days, but for a lot of the participants this was not achievable. This might be the reason for the disappointing results.

Limitations

There are some limitations that need to be accounted before interpreting the results. First of all, the sample sizes of the groups were small, which affects the power of the study. Instead of sixty participants, only thirty-six were included from which five dropped out. Drop out reasons were; due to personal reasons, a lack of motivation, problems with the system or a combination of both. These participants filled in the first questionnaires (at pre-test) and started with the intervention. Since there was no post-test data available, the participants were not analysed. Usually randomized controlled trials are less prone to selection bias, but since we didn't analyse all subjects we included, it is possible that selection bias occurred. However, the dropout rate was approximately the same in each group. No intention-to-treat analyse is done, but might be a recommendation for the future. There are two main reasons why a study may not show a significant difference between groups. One, there really was no significant difference (a true negative). Two, there was a difference but the study failed to detect it (false negative). It is possible that we didn't find a significant effect because of the small sample size. Further research is needed to check whether there isn't a significant effect on some sleep parameters due to the small sample size or because there simply is no significant effect. The analyses were conducted with approximately half of the sample, so the study must be continued.

Secondly, a few participants had some troubles with the neurofeedback system, which was really inconvenient. In some cases it was (too) hard to reach the connection with the EEG. It took them too long, which resulted in frustration, and skipped sessions. The subjects had to complete 21 neurofeedback sessions within 28 days. Results showed that in all groups some participants were not able to achieve that. A few participants in each group completed more than 21 sessions, but also some completed less. However, all subjects were analysed, so also the ones who completed less than 21 sessions. Therefore it is possible that there isn't found a significant effect at some parameters, due to the low adherence of some subjects.

All subjects performed the training at home, as such being less time consuming than conducting it in a hospital setting. The participants were also able to schedule their own sessions, which is an advantage. In case the system worked well mostly participants were able to keep sufficiently motivated to complete such an intensive program (21 sessions within 28 days). Even though the home intervention has a lot of advantages, it holds also a few disadvantages. Although all participants received a lot of instructions, some things can't be controlled. For example; the environment is not controlled for all participants, e.g. the way that participants paid attention to the training (feedback) and/or disruptive influences from distraction factors as; noise, children, family are not known in such a home protocol. This might influence the neurofeedback training.

The troubles with the Actiwatch were already discussed. Because of the lack of more objective measurements it is not possible to compare the Actiwatch results with some other objective measures. Since it was hard for the Actiwatch to detect wakefulness it is recommended to use (also) other objective measures as a PSG and EEG.

At last, the long-term effects are not reported yet, since not all follow-up data is collected and analysed. Also the results of the interviews are not analysed yet. This will be done in the future.

Relevance

Besides Cortoos et al. (2010), also the current study evaluates a neurofeedback home intervention in people with sleep problems. The current study is innovating in two ways. First of all the participants listen to *music* and receive feedback via changes in the music quality, instead of getting visual feedback which others use. Secondly, we tested three groups, two experimental conditions and one control condition. All conditions listened to their favourite music and received feedback; only the kind of feedback was different. Since also the control condition received feedback and could not know in which group they were in, the study was double blind. The fact that everything within all groups was the same, except for the type of feedback, the *neurofeedback element* can be tested. So there are a lot of elements that make the design very strong. This isn't seen in other studies. It is important that the study will be continued and that other analyses will be done to be scientific relevant.

For Philips the study is really relevant. It depends on the outcome of the study if they will continue with this type of neurofeedback. Since we can't draw real conclusions yet, it is important to continue with the study. Since the current study is only halfway they must continue with the study the same way as was done (only other objective measure). Otherwise it is not possible to use the current data with future data to make real conclusions. After finishing this study, depending on the outcome, it might be interesting to evaluate the system in a population of real insomnia patients. Another important element is the adherence to the treatment, which must be evaluated. Since Philips is a real innovative company it also might be interesting to evaluate the neurofeedback with in-ear, instead a headphone integrated with EEG electrodes. This would be way more convenient for the participants.

Also for people with sleep problems/insomnia patients this study is relevant, because 30 percent of the general population has symptoms of sleep disruption. The presence of poor sleep duration, sleep quality or insomnia symptoms have shown substantial (negative) effects. Chronic insomnia and the use of prolonged sleep medication can lead to illness and accidents. Therefore it is very important to implement effective non-pharmacological treatments. That's why it is important to do such research and make improvements. Those improvements are described below.

Conclusion and recommendations

Despite some significant effects in subjective sleep parameters the effect of the neurofeedback is disappointing. We can conclude that in this study the neurofeedback was not effective. However, since only the preliminary results are reported we must be careful with draw conclusions. The execution of the study is halfway and does not have a lot of power, it is important to continue with the study. Only when 60 participants are included real conclusions can be made. Though it is important to think of recommendations already.

Due to the low adherence of some participants it might be an idea to give the participants **more time** to complete their neurofeedback sessions. Since it was expected to see an effect if they ended up with approximately 21 sessions it is important to adhere to that. In the current study is seen that for a few participants it was not possible, and less effects were detected. Another possibility is to **shorten the time of the neurofeedback sessions**. In the current study the neurofeedback sessions endured for 25 minutes (10 minutes listening to music, 5 minutes playing a game, 10 minutes listening to music). It might be good to let it endure for only 15 minutes (6 minutes listening to music, 3 minutes playing a game, 6 minutes listening to music. Maybe then it is easier to schedule the sessions and adhere to the treatment. What this will do to the effect of the intervention is not clear.

In the current study the Consensus Sleep Diary (CSD) data is only used for correcting the Actiwatch data. The CSD might be really useful since in contrast to the PSQI data the CSD data gives insight in the sleep parameters of more time points (participants filled it in every day during the experiment). A disadvantage of the PSQI is that it is based on a respondent's retrospective appraisal of an array of sleep parameters; it asks participants questions about the *previous month.* So there might

occur recall bias. Besides, when at the post-test the participants must respond to questions that refer to their sleep about the previous month, also the intervention period is within that month. This means that the responses at the post-test were also about the period that the participants were improving their sleep. This might give some bias. In the future it might be better to add another measurement point between the post-test and the follow-up. For example, the participant must fill in the PSQI at the following time points; pre-test (the start of the study), then right after the intervention period, one month later and at last the follow-up (long-term effect). In contrast to the PSQI questionnaire, the CSD gives insight in the progress over time, so you can also see when the participants improved the most (which part of the intervention). The recall bias for the CSD is minimized, since the participants had to fill it in within one hour after they woke up. Since the data of the CSD is collected it is recommended to **analyse the CSD data** and compare it with our other findings.

Since there was a big discrepancy between the Actiwatch (objective) data and the subjective data, and the Actiwatch was not able to really detect wakefulness, **using another objective measurement** it is recommended in the future. It might be useful to use a measurement, which is not only measuring sleep but also for example the heart rate.

The last recommendation is about the **interview data**. At the post-test a small interview was conducted to get some insight in the experiences of the participants and to receive some feedback. This data isn't described in this thesis, but will be used by Philips. Recommendations are: extend the interview in the future and make a combination of **qualitative** and **quantitative** research (mixed-method approach). In this way you might also get insight in the **relevance** for the participants. It is possible that there is found an effect on a specific sleep parameter, but that isn't really meaningful for them. It is also possible that it is the other way around. It might be interesting to look into that.

Philips also must improve the system. During the intervention period some participants had some troubles with the system, for example it was hard to get connected with the EEG electrodes. This costs the participants a lot of time, which is very frustrating. This could have led to the low adherence. Measuring EEG in the ear is up coming; it would be great if the EEG of the participants can be measured via their ears and could listen to the music and receive feedback via the same in-ear. It also has the preference to make the system without all the cables, and make it more compact. For future research it might be interesting to evaluate the usability of the system.

Summary of the recommendations

Current study

- Continue with the study
- Use another objective measure (with more functions e.g. hearth rate)
- Measure the adherence
- Analyse the results of the consensus sleep diary

Future research

- Longer intervention period (for example; 1.5 month)
- Shorten the time of the neurofeedback sessions (6 minutes – 3 minutes – 6 minutes)
- Mixed model approach
- Improve the system (EEG, in-ear, compact)
- Population: insomnia patients

References

Ancoli-Israel, S., Cole, R., Alessi, C., Chambers, M., Moorcroft, W., & Pollak, C. (2003). The role of actigraphy in the study of sleep and circadian rhythms. American Academy of Sleep Medicine Review Paper. *Sleep, 26* (3), 342-392.

Backhaus, J., Junghanns, K., Broocks, A., Riemann, D., & Hohagen, F. (2002). Test-retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. *Journal of Psychosomatic Research, 53* (3), 737-740.

Buscemi, N., & et al. (2005). Manifestattions and management of chronic insomnia in adults. *Evidence Report Technological Summaries, 125*, 1-10.

Buxton, O. M., & et al. (2012). Relationship of sleep deficiency to perceived pain and functional limitations in hospital patient care workers. *Journal of occupational and environmental medicine, 54* (7), 851-858.

Buysse, D., Reynolds, C., Monk, T., Berman, S., & Kupfer, D. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry research, 28* (2), 193-213.

BioSemi. (2007). *ActiveTwo User Manual.* Amsterdam: BioSemi.

Carney, C. E., & et al. (2012). The Consensus Sleep Diary: Standardizing Prospective Sleep Self Monitoring. *Sleep, 35* (2), 287-302.

Cluydts, R., & van Someren, E. (2009). Slaap en slaapstoornissen. *Neuropraxis, 13* (6), 153-167.

Cortoos, A., de Valck, E., Arns, M., Breteler, M. H., & Cluydts, R. (2010). An exploratory study on the effects of tele-neurofeedback and tele-biofeedback on objective and subjective sleep in patients with primary insomnia. *Applied Psychophysiology and Biofeedback, 35*, 125-134.

Cortoos, A., Verstraeten, E., & Cluydts, R. (2006). Neurophysiological aspects of primary insomnia: Implications for its treatment. *Sleep Medicine Reviews, 10* (4), 255-266.

Crosby, R., DiClemente, R., & Salazar, L. (2006). *Research Methods in Health Promotion.* San Francisco: John Wiley & Sons.

Egner, T., & Gruzelier, J. H. (2003). Ecological validity of neurofeedback: modulation of slow wave EEG enhances musical performance. *Cognitive Neuroscience and Neuropsychology, 14* (9), 1221-1224.

Espie, C. A., MacMahon, K. M., Kelly, H. L., Broomfield, N. M., Douglas, N. J., & Engleman, H. M. (2007). Randomized clinical effectiveness trial of nurse-administered small-group cognitive behavior therapy for persistent insomnia in general practice. *Sleep, 30*, 574–584.

Hauri, P., Percy, L., Hellekson, C., Hartmann, E., & Russ, D. (1982). The treatment of psychophysiologic insomnia with biofeedback: a replication study. *Biofeedback and self-regulation, 7* (2), 223-235.

Hajak, G., & Sine, S. G. (2001). Epidemiology of severe insomnia and its consequences in Germany. *European Archives of Psychiatry and Clinical Neurosciences, 251*, 49-56.

Hammer, B., Colbert, A., Brown, K. A., & Ilioi, E. C. (2011). Neurofeedback for Insomnia: A Pilot Study of Z-Score SMR and Individualized Protocols. *Applied Psychophysiology and Biofeedback, 36*, 251 264.

Harsora, P., & Kessmann, J. (2009). Nonpharmacologic Management. *American Family Physician, 79* (2), 125-130.

Harrison, M. (1994). *Diagnosing Organizations: Methods, Models, and Processes.* Thousand Oaks: Sage.

Hatoum, H. T., Kong, S. X., Kania, C. M., Wong, J. M., & Mendelson, W. B. (1998). Insomnia, health related quality of life and healthcare resource consumption - A study of managed-care organisation enrollees. *Pharmacoeconomics , 14*, 629–637.

Hays, R., & Morales, L. (2001). The RAND-36 measure of health-related quality of life. *Annals of medicine , 33* (5), 350-357.

Heinrich, H., Gevensleben, H., & Strehl, U. (2007). Annotation: Neurofeedback - train your brain to train behaviour. *Journal of Child Psychology and Psychiatry, 48* (1), 3-16.

Hoedlmoser, K., Pecherstorfer, T., Gruber, G., Anderer, P., Doppelmayr, M., Klimesch, W., et al. (2008). Instrumental conditioning of human sensorimotor rhythm (12-15 hz) and its impact on sleep as well as declarative learning. *Sleep, 31*, 1401-1408.

Irwin, M. R., Cole, J. C., & Nicassio, P. M. (2006). Comparative meta-analysis of behavioral interventions for insomnia and their efficacy in middle-aged adults and in older adults 55+ years of age. *Health Psychology, 25* (1), 3-14.

Janssen, R., de Vries, S. J., Verstappen, C. C., & de Leijer, C. (2011). De epidemiologie van slaapstoornissen. *Bijblijven, 27* (1), 7-16.

Johnstone, J., Gunkelman, J., & Lunt, J. (2005). Clinical database development: Characterization of EEG Phenotypes. *Clinical EEG and Neuroscience, 36* (2), 99-107.

Klem, G., Lüders, H., Jasper, H., & Elger, C. (1999). The ten-twenty electrode system f the International Federation. The International Federation of Clinical Neurophysiology. *Electroencephalography and clinical neurophysiology. Supplement, 52*, 3-6.

Knuistingh Neven, A., Lucassen, P. L., Bonsema, K., Teunissen, H., Verduijn, M. M., & Bouma, M. (2005). *NHG-Standaard Slaapproblemen en slaapmiddelen*. Retrieved Mei 1, 2015, from Nederlands huisartsen genootschap: https://www.nhg.org/standaarden/volledig/nhg-standaard slaapproblemen-en-slaapmiddelen#idp9684176

Krystal, A. D., & Edinger, J. D. (2008). Measuring sleep quality. *Sleep Medicine, 9* (1), 10-17.

Lai, H. L., & Good, M. (2006). Music improves sleep quality in older adults. *Journal of Advanced Nursing, 53* (1), 134-146.

Lamarche, C., & Ogilvie, R. (1997). Electrophysiological changes during the sleep onset period of psychophysiological insomniacs, psychiatric insomniacs, and normal sleepers. *Sleep, 20* (9), 724-733.

Laugsand, L. E., Vatten, L. J., Platou, C., & Janszky, I. (2011). Insomnia and the risk of acute myocardial infarction: a population study. *Circulation, 124* (19), 2073-2081.

Levin, Y. I. (1998). 'Brain music' in the treatment of patients with insomnia. *Neuroscience and Behavioral Physiology, 28* (3), 330-335.

Morgenthaler, T., & et al. (2007). Practice parameters for the use of actigraphy in the assessment of sleep and sleep disorders: an update for 2007. *Sleep, 30* (4), 519-529.

Morin, C. M., & et al. (1999). Nonpharmacologic Treatment of Chronic Insomnia. *Sleep, 22* (8), 1134 1156.

Morin, C., Rodrigue, S., & Ivers, H. (2003). Role of stress, arousal, and coping skills in primary insomnia. *Psychosomatic medicine, 65* (2), 259-267.

Mornhinweg, G. C., & Voignier, R. R. (1995). Music for sleep disturbance in the elderly. *Journal of Holistic Nursing, 13* (3), 248-254.

Mullington, J. M., Simpson, N. S., Meier-Ewert, H. K., & Haack, M. (2010). Sleep loss and inflammation. *Best practice & research. Clinical endocrinology & metabolism, 24* (5), 775-784.

Neerings-Verberkmoes, N. E., Vlak, M. H., de Lau, L. M., & Hamburger, H. L. (2014). Chronische insomnie: niet altijd psychofysiologisch. *Nederlands Tijdschrift voor Geneeskund, 158*, 1-5.

Ohayon, M. (2002). Epidemiology of insomnia: what we know and what we still need to learn. *Sleep Medicine Review, 6* (2), 97-111.

Paul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods , 39*, 175-191.

Perlis, M. L., Merica, H., Smith, M., & Giles, D. E. (2001). Beta EEG activity and insomnia. *Sleep Medicine Reviews, 5* (5), 365-376.

Sadeh, A., & Acebo, C. (2002). The role of actigraphy in sleep medicine. *Sleep Medicine Reviews, 6* (2), 113-124.

Scammell, T. (2015). Overview of sleep: the neurologic processes of the sleep-wake cycle. *The Journal of clinical psychiatry, 76* (5), e13.

Sivertsen, B., & al., e. (2006). A Comparison of Actigraphy and Polysomnography in Older Adults Treated for Chronic Primary Insomnia. *Sleep , 29* (10), 1353-1358.

Soeffing, J. P., Lichstein, K. L., Nau, S. D., McCrae, C. S., Wilson, N. M., Aguillard, R. N., et al. (2008). Psychological treatment of insomnia in hypnotic-dependant older adults. *Sleep Medicine, 9*, 165–171.

Sommer, I., Lavigne, G., & Ettlin, D. (2015). Review of self-reported instruments that measure sleep dysfunction. *Sleep medicine, 16* (1), 27-38.

Sterman, M. B., Howe, R. C., & Macdonald, L. R. (1970). Facilitation of spindleburst sleep by conditioning of electroencephalographic activity while awake. *Science, 167*, 1146-1148.

Rangaswamy, M., & et al. (2002). Beta Power in the EEG of Alcoholics. *Biological Psychiatry, 52* (8), 831–842.

Reimer, M. A., & Flemons, W. W. (2003). Quality of life in sleep disorders. *Sleep Medicine Reviews, 4* (7), 335-349.

Riemann, D., & et al. (2010). The hyperarousal model of insomnia: A review of the concept and its evidence. *Sleep Medicine Reviews, 14*, 19-31.

Troxel, W. M., Buysse, D. J., Matthews, K. A., Kip, K. E., Strollo, P. J., Hall, M., et al. (2010). Sleep symptoms predict the development of the metabolic syndrome. *Sleep, 33* (12), 1633-1640.

Vallieres, A., & Morin, C. M. (2003). Actigraphy in the assessment of insomnia. *Sleep, 26*, 902-906.

Van Boxtel, G., & et al. (2012). A novel self-guided approach to alpha activity training. *International Journal of Psychophysiology, 83* (3), 282-294.

Van der Zee, K. I., Sanderman, R., Heyink, J. W., & De Haes, H. (1996). Psychometric qualities of the RAND 36-item health survey 1.0: A multidimensional measure of general health status. *International Journal of Behavioral Medicine, 3* (2), 104-122.

Verbeek, I. H., Konings, G. M., Aldenkamp, A. P., Declerck, A. C., & Klip, E. C. (2006). Cognitive behavioral treatment in clinically referred chronic insomniacs: group versus individual treatment. *Behavioral Sleep Medicine, 4*, 135-151.

Vgontzas, A. N., Liao, D., Bixler, E. O., Chrousos, G. P., & Vela-Bueno, A. (2009). Insomnia with objective short sleep duration is associated with a high risk factor for hypertension. *Sleep, 32* (4), 491 497.

Zammit, G. K., Weiner, J., Damato, N., Sillup, G. P., & McMillan, C. A. (1999). Quality of life in people with insomnia. *Sleep, 22*, 379–385.

Zimmerman, L., Nieveen, J., Barnason, S., & Schmaderer, M. (1996). The effects of music interventions on postoperative pain and sleep in coronary artery bypass graft (CABG) patients. *Scholarly Inquiry for Nursing Practice, 10* (2), 153-170.

Appendix I Questionnaires

I.I General information

This survey uses cookies to implement functionality for this survey only. Cookies are not tracked between surveys or after the survey is complete.

APPROVAL

- I have read the informed consent and agree the information I leave will be used for the stated purpose(s)
- Exit survey (in this case you choose not to participate)

Back Next

Demographics

ID# (Participant code):

Gender:
0 Male 0 Female

Age:
0 16-20
0 21-25
0 26-30
0 31-35
0 36-40
0 41-45
0 46-50
0 51-55
0 56-60
0 61-65
0 65>

I.II PSQI

ID#_____Date_____Time_____AM PM

PITTSBURGH SLEEP QUALITY INDEX

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

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

   BED TIME _____

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

   NUMBER OF MINUTES _____

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

   GETTING UP TIME _____

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

   HOURS OF SLEEP PER NIGHT _____

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

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

a) Cannot get to sleep within 30 minutes

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Wake up in the middle of the night or early morning

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Have to get up to use the bathroom

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Cannot breathe comfortably

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

e) Cough or snore loudly

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

f) Feel too cold

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

g) Feel too hot

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

h) Had bad dreams

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

i) Have pain

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

j) Other reason(s), please describe_____

_____

How often during the past month have you had trouble sleeping because of this?

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

6. During the past month, how would you rate your sleep quality overall?

Very good _____

Fairly good _____

Fairly bad _____

Very bad _____

7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all _____

Only a very slight problem _____

Somewhat of a problem _____

A very big problem _____

10. Do you have a bed partner or room mate?

No bed partner or room mate _____

Partner/room mate in other room _____

Partner in same room, but not same bed _____

Partner in same bed _____

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

a) Loud snoring

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

b) Long pauses between breaths while asleep

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

c) Legs twitching or jerking while you sleep

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

d) Episodes of disorientation or confusion during sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Other restlessness while you sleep; please describe_____

_____

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: Psychiatry Research, 28:193-213, 1989.

I.III The Consensus Sleep Diary (CSD-M)

Sleep Diary Instructions (CSD-M)

General Instructions

What is a Sleep Diary? A sleep diary is designed to gather information about your daily sleep pattern.

How often and when do I fill out the sleep diary? It is necessary for you to complete your sleep diary every day. If possible, the sleep diary should be completed within one hour of getting out of bed in the morning.

What should I do if I miss a day? If you forget to fill in the diary or are unable to finish it, leave the diary blank for that day.

What if something unusual affects my sleep or how I feel in the daytime? If your sleep or daytime functioning is affected by some unusual event (such as an illness, or an emergency) you may make brief notes on your diary.

What do the words "bed" and "day" mean on the diary? This diary can be used for people who are awake or asleep at unusual times. In the sleep diary, the word "day" is the time when you choose or are required to be awake. The term "bed" means the place where you usually sleep.

Will answering these questions about my sleep keep me awake? This is not usually a problem. You should not worry about giving exact times, and you should not watch the clock. Just give your best estimate.

Sleep Diary Item Instructions

Use the guide below to clarify what is being asked for each item of the Sleep Diary.

Date.: Write the date of the morning you are filling out the diary.

1. What time did you get into bed? Write the time that you got into bed. This may not be the time you began "trying" to fall asleep.

2. What time did you try to go to sleep? Record the time that you began "trying" to fall asleep.

3. How long did it take you to fall asleep? Beginning at the time you wrote in question 2, how long did it take you to fall asleep.

4. How many times did you wake up, not counting your final awakening? How many times did you wake up between the time you first fell asleep and your final awakening?

5. In total, how long did these awakenings last? What was the total time you were awake between the time you first fell asleep and your final awakening. For example, if you woke 3 times for 20 minutes, 35 minutes, and 15 minutes, add them all up (20+35+15= 70 min or 1 hr and 10 min).

6a. What time was your final awakening? Record the last time you woke up in the morning.

6b. After your final awakening, how long did you spend in bed trying to sleep? After the last time you woke-up (Item #6a), how many minutes did you spend in bed trying to sleep? For example, if you woke up at 8 am but continued to try and sleep until 9 am, record 1 hour.

6c. Did you wake up earlier than you planned? If you woke up or were awakened earlier than you planned, check yes. If you woke up at your planned time, check no.

6d. If yes, how much earlier? If you answered "yes" to question 6c, write the number of minutes you woke up earlier than you had planned on waking up. For example, if you woke up 15 minutes before

the alarm went off, record 15 minutes here.

7. What time did you get out of bed for the day? What time did you get out of bed with no further attempt at sleeping? This may be different from your final awakening time (e.g. you may have woken up at 6:35 a.m. but did not get out of bed to start your day until 7:20 a.m.)

8. In total, how long did you sleep? This should just be your best estimate, based on when you went to bed and woke up, how long it took you to fall asleep, and how long you were awake. You do not need to calculate this by adding and subtracting; just give your best estimate.

9. How would you rate the quality of your sleep? "Sleep Quality" is your sense of whether your sleep was good or poor.

10. How restful or refreshed did you feel when you woke up for the day? This refers to how you felt after you were done sleeping for the night, during the first few minutes that you were awake.

11a. How many times did you nap or doze? A nap is a time you decided to sleep during the day, whether in bed or not in bed. "Dozing" is a time you may have nodded off for a few minutes, without meaning to, such as while watching TV. Count all the times you napped or dozed at any time from when you first got out of bed in the morning until you got into bed again at night.

11b. In total, how long did you nap or doze? Estimate the total amount of time you spent napping or dozing, in hours and minutes. For instance, if you napped twice, once for 30 minutes and once for 60 minutes, and dozed for 10 minutes, you would answer "1 hour 40 minutes." If you did not nap or doze, write "N/A" (not applicable).

12a. How many drinks containing alcohol did you have? Enter the number of alcoholic drinks you had where 1 drink is defined as one 12 oz beer (can), 5 oz wine, or 1.5 oz liquor (one shot).

12b. What time was your last drink? If you had an alcoholic drink yesterday, enter the time of day in hours and minutes of your last drink. If you did not have a drink, write "N/A" (not applicable).

13a. How many caffeinated drinks (coffee, tea, soda, energy drinks) did you have? Enter the number of caffeinated drinks (coffee, tea, soda, energy drinks) you had where for coffee and tea, one drink = 6-8 oz; while for caffeinated soda one drink = 12 oz.

13b. What time was your last caffeinated drink? If you had a caffeinated drink, enter the time of day in hours and minutes of your last drink. If you did not have a caffeinated drink, write "N/A" (not applicable).

14. Did you take any over-the-counter or prescription medication(s) to help you sleep? If so, list medication(s), dose, and time taken: List the medication name, how much and when you took EACH different medication you took tonight to help you sleep. Include medication available over the counter, prescription medications, and herbals (example: "Sleepwell 50 mg 11 pm"). If every night is the same, write "same" after the first day

15. *Comments*: If you have anything that you would like to say that is relevant to your sleep feel free to write it here.

Consensus Sleep Diary-M (Please Complete Upon Awakening) **ID** ____________________

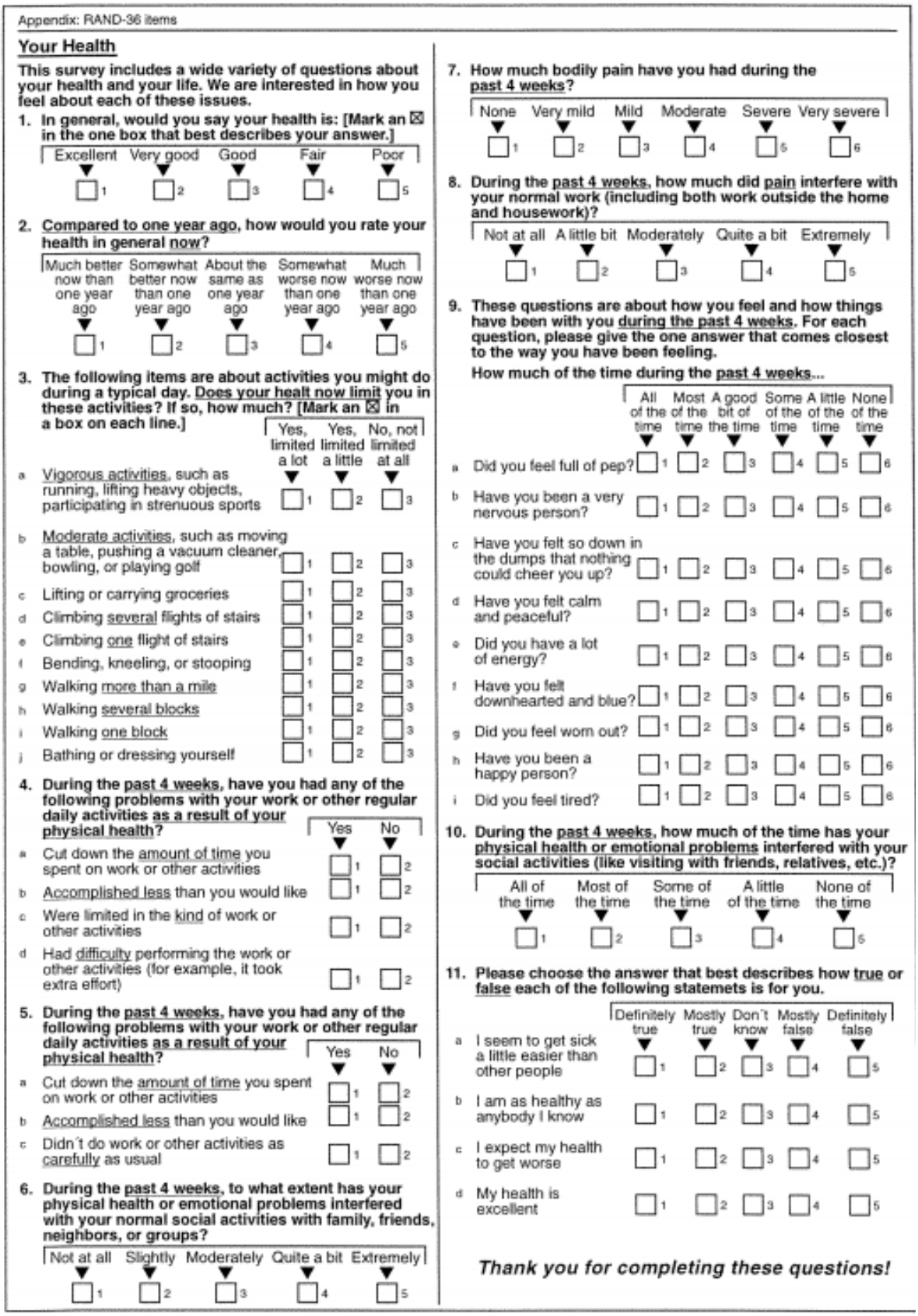
	Sample							
Today's Date	4/5/08							
1. What time did you get into bed?	10:15 p.m.							
2. What time did you try to go to sleep?	11:30 p.m.							
3. How long did it take you to fall asleep?	55 min.							
4. How many times did you wake up, not counting your final awakening?	6 times							
5. In total, how long did these awakenings last?	2 hours 5 min.							
6a. What time was your final awakening?	6:35 a.m.							
6b. After your final awakening, how long did you spend in bed trying to sleep?	45 min.							
6c. Did you wake up earlier than you planned?	☑ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
6d. If yes, how much earlier?	1 hour							
7. What time did you get out of bed for the day?	7:20 a.m.							
8. In total, how long did you sleep?	4 hours 10 min.							
9. How would you rate the quality of your sleep?	☐ Very poor ☑ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good
10. How rested or refreshed did you feel when you woke-up for the day?	☐ Not at all rested ☑ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested

Consensus Sleep Diary-M Continued

ID: _____

	Sample							
Today's Date	4/5/10							
11a. How many times did you nap or doze? 11b. In total, how long did you nap or doze?	2 times 1 hour 10 min.							
12a. How many drinks containing alcohol did you have? 12b. What time was your last drink?	3 drinks 9 :20 p.m.							
13a. How many caffeinated drinks (coffee, tea, soda, energy drinks) did you have? 13b. What time was your last drink?	2 drinks 3 :00 p.m.							
14. Did you take any over-the-counter or prescription medication(s) to help you sleep? If so, list medication(s), dose, and time taken	☑ Yes ☐ No Medication(s): Relaxo-Herb Dose: 50 mg Time(s) taken: 11 pm	☐Yes ☐No Medication(s): Dose: Time(s) taken:	☐Yes ☐No Medication(s): Dose: Time(s) taken:	☐Yes ☐No Medication(s): Dose: Time(s) taken:	☐Yes ☐No Medication(s): Dose: Time(s) taken:	☐Yes ☐No Medication(s): Dose: Time(s) taken:	☐Yes ☐No Medication(s): Dose: Time(s) taken:	☐Yes ☐No Medication(s): Dose: Time(s) taken:
15. Comments (if applicable)	I have a cold							

I.IV RAND-36



Appendix: RAND-36 items

Your Health

This survey includes a wide variety of questions about your health and your life. We are interested in how you feel about each of these issues.

1. In general, would you say your health is: [Mark an ☒ in the one box that best describes your answer.]

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. Compared to one year ago, how would you rate your health in general now?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. The following items are about activities you might do during a typical day. Does your healt now limit you in these activities? If so, how much? [Mark an ☒ in a box on each line.]

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
b Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d Climbing several flights of stairs	☐ 1	☐ 2	☐ 3
e Climbing one flight of stairs	☐ 1	☐ 2	☐ 3
f Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g Walking more than a mile	☐ 1	☐ 2	☐ 3
h Walking several blocks	☐ 1	☐ 2	☐ 3
i Walking one block	☐ 1	☐ 2	☐ 3
j Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	Yes	No
a Cut down the amount of time you spent on work or other activities	☐ 1	☐ 2
b Accomplished less than you would like	☐ 1	☐ 2
c Were limited in the kind of work or other activities	☐ 1	☐ 2
d Had difficulty performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	Yes	No
a Cut down the amount of time you spent on work or other activities	☐ 1	☐ 2
b Accomplished less than you would like	☐ 1	☐ 2
c Didn´t do work or other activities as carefully as usual	☐ 1	☐ 2

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very severe
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a Did you feel full of pep?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
b Have you been a very nervous person?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
c Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
d Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
e Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
f Have you felt downhearted and blue?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
g Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
h Have you been a happy person?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
i Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

11. Please choose the answer that best describes how true or false each of the following statemets is for you.

	Definitely true	Mostly true	Don´t know	Mostly false	Definitely false
a I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Thank you for completing these questions!

Appendix II Scoring procedure PSQI

SCORING INSTRUCTIONS FOR THE PITTSBURGH SLEEP QUALITY INDEX:

The Pittsburgh Sleep Quality Index (PSQI) contains 19 self-rated questions and 5 questions rated by the bed partner or roommate (if one is available). Only self-rated questions are included in the scoring. The 19 self-rated items are combined to form seven "component" scores, each of which has a range of 0-3 points. In all cases, a score of "0" indicates no difficulty, while a score of "3" indicates severe difficulty. The seven component scores are then added to yield one "global" score, with a range of 0-21 points, "0" indicating no difficulty and "21 " indicating severe difficulties in all areas.

Scoring proceeds as follows:

Component 1: Subjective sleep quality

Examine question #6, and assign scores as follows:

Response	Component 1 score
"Very good"	0
"Fairly good"	1
"Fairly bad"	2
"Very bad"	3

Component 1 score:_____

Component 2: Sleep latency

1. Examine question #2, and assign scores as follows:

Respo\nse	Score
≤15 minutes	0
16-30 minutes	1
31-60 minutes	2
> 60 minutes	3
Question #2 score:	_____

2. Examine question #5a, and assign scores as follows:

Response	Score
Not during the past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3
Question #5a score:	_____

3. Add #2 score and #5a score

Sum of #2 and #5a: _____

4. Assign component 2 score as follows:

Sum of #2 and #5a	Component 2 score
0	0
1-2	1
3-4	2
5-6	3

PSQI Page 3

Component 2 score:_____

Component 3: Sleep duration

Examine question #4, and assign scores as follows:

Response	Component 3 score
> 7 hours	0
6-7 hours	1
5-6 hours	2
< 5 hours	3

Component 3 score: _____

Component 4: Habitual sleep efficiency

1. Write the number of hours slept (question #4) here: _____
2. Calculate the number of hours spent in bed:

   Getting up time (question #3): _____

   Bedtime (question #1): _____

   _____

   Number of hours spent in bed: _____

3. Calculate habitual sleep efficiency as follows:

   (Number of hours slept/Number of hours spent in bed) X 100 = Habitual sleep efficiency (%)

   (_____/_____) X 100 = %

4. Assign component 4 score as follows:

Habitual sleep efficiency %	Component 4 score
> 85%	0
75-84%	1
65-74%	2
< 65%	3

Component 4 score: _____

Component 5: Step disturbances

1. Examine questions #5b-5j, and assign scores for each question as follows:

Response	Score
Not during the past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

5b score: _____
5c score: _____
5d score: _____
5e score: _____
5f score: _____
5g score: _____
5h score: _____
5i score: _____
5j score: _____

2. Add the scores for questions #5b-5j:

Sum of #5b-5j: _____

3. Assign component 5 score as follows:

Sum of #5b-5j	Component 5 score
0	0
1-9	1
10-18-4	2
19-27	3

Component 5 score: _____

Component 6: Use of sleeping medication

Examine question #7 and assign scores as follows:

Response	Component 6 score
Not during the past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Component 6 score: _____

Component 7: Daytime dysfunction

1. Examine question #8, and assign scores as follows:

Response	Score
Never	0
Once or twice	1
Once or twice each week	2
Three or more times each week	3

Question#8 score: _____

2. Examine question #9, and assign scores as follows:

Response	Score
No problem at all	0
Only a very slight problem	1
Somewhat of a problem	2
A very big problem	3

Question #9 score: _____

3. Add the scores for question #8 and #9:

Sum of #8 and #9: _____

4. Assign component 7 score as follows:

Sum of #8 and #9	Component 7 score
0	0
1-2	1
3-4	2
5-6	3

Component 7 score: _____

Global PSQI Score

Add the seven component scores together:

Global PSQI Score: _____

Appendix III Information letter and informed consent

INFORMATION LETTER FOR VOLUNTEERS

Study Title: The effect of Neurofeedback on the perceived sleep quality

Dear sir/madam,

This information letter is intended to help you decide about your participation in this clinical study. It describes the study, what you may expect if you decide to take part, and important information to help you make your decision.

- Participating in this study is voluntary – it is your choice;
- If you join this study, you can change your mind and withdraw at any time;
- It is important you understand why and how this study will be conducted;
- The potential benefits and risks are described.

Please take time to read this information, and if you like, discuss it with friends or family to the extent necessary to decide about your participation. Contact the Responsible Researcher if you do not understand something or if you need more information. The names and contact details can be found under "Contact Information" below in this document.

Only participate in this study if your questions have been answered sufficiently, and you voluntarily decide that you want to be part of this study.

Thank you for reading this information and for considering your participation.

Joëlle Dam

High Tech Campus 36

5656 AE Eindhoven

What is the purpose of this study?

The purpose of this study is to evaluate the effect of Neurofeedback on subjectively reported Sleep Onset Latency (Time to Fall Asleep) and perceived sleep quality in Philips employees between the age of 18 – 65 years.

Where will the study be conducted?

The study will take place at Philips Research at the High Tech Campus (HTC), building 36, and at your home. When you decide to participate, more details will follow regarding the exact time and location.

Duration of your participation in the study

Your participation in this study will take about twelve hours of your time (spread over one month). During the study you will be asked to visit the HTC 36 two times. The first visit (pre-test) will take 60-75 minutes of your time. If you decide to participate we must explain the study protocol, you must sign the informed consent, and fill in two questionnaires. At the end of the first session you will receive the Actiwatch and the Philips Neurofeedback System for a period of four weeks. Within these weeks you are requested to use the system in the evening, and end up with a minimum of 21 sessions, occupying 25 minutes per session. You also must fill in a sleep diary each morning, this will take about 5 minutes of your time. The second visit (post-test) will approximately take about 30 minutes. During this visit you are requested to fill in two questionnaires. At your second visit (post-test) you will return the equipment you had received at the beginning of the experiment.

Who organized and paid for the study?

This study is organized and paid for by Philips Nederland B.V. ("Philips").

Philips has carefully prepared this study and the set-up has been reviewed by an independent internal review committee. Special attention has been given to the safety of the devices used in the study.

What are the steps in the study and what is expected from me?

1. The experiment will start with signing the informed consent
2. You are requested to fill in two questionnaires
3. You will receive an actiwatch which you will wear the first week and the last week of the experiment
4. Every night when you are willing to sleep you must push the markerbutton on the actiwatch
5. Every morning when you wake up you must push the markterbutton on the actiwatch
6. You will receive the neurofeedback system, and you are requested to use the system 25 minutes for a period of four weeks (end up with 21 sessions out of the 28). The training must be applied in the evening in the time window of 3 hours to 1 hour prior bedtime.
7. You are requested to fill in a sleep diary each morning (within one hour after you woke up) for a period of four weeks.
8. After those four weeks you will be invited for the posttest. During this meeting you will fill in two questionnaires and will return the whole equipement you received at the beginning, so it can be used for other participants.

In total, approximately 60 volunteers **(all Philips employees)** will participate in this study.

Which equipment will be used in this study?

Audio Neurofeedback system

This is a research prototype, and is not commercially available.

- Philips audio headphone (left side)

- Wet EEG electrodes (left side)

- Data recorder for measuring EEG (right side)

Samsung Tab2 10 inch Android tablet:

Commercially available

Actigraphy:

Philips Respironics Actiwatch 2 monitoring system helps us to (objectively) assess your sleep/wake pattern. Designed to be comfortable, rugged, and waterproof.

All devices are CE approved, and are safe for use.

Can I stop my participation?

You can stop your participation in the study at any time without giving reasons. The Responsible Researcher may ask why you decided to stop but you are entitled to refuse giving an answer.

The Responsible Researcher may end your participation if:

- Further participation may cause harm to you
- You did not comply with the instructions for participation given to you
- You no longer meet the criteria for participation
- Philips decided to stop the study.

If your participation is no longer possible due to the results of the sleep questionnaire, the Responsible Researcher will inform you.

Please read each of the following statements carefully and consider if it applies to you:

- Are you using sleep medication at the moment?
- Do you use different kind of treatments with the intention to treat your sleep deficiency?
- Are you suffering from a medical condition that affects the vestibular system (e.g. Ménière disease)?
- Are you suffering from traumatic experiences?

[ ] None of the above statements applies to me.

If you could not check the checkbox, stop here: you can not continue with the study. You may of course always quit the study even if you can check the checkbox.

Please note, in case your participation stops, personal data already collected about you will be further processed by Philips as described in this information letter, however, you always have the right to have it deleted if you wish so.

What are the potential risks of participating in the study?

- All ambulatory devices are battery operated and as such only have a marginally small risk on electrical problems. Please note that all devices are FDA approved/CE marked and used within intended use.

Can I participate when I am pregnant or breastfeeding a baby?

Because we do not know if the procedure used in the experiment and/or the device being tested in this study has any impact on your unborn baby or infant, participation in this study is not allowed when you are pregnant or breastfeeding.

What happens if I get pregnant?

If you become pregnant when you are still participating in the study, you must stop your participation. You do not have to inform the Responsible Researcher that you are pregnant if you not want to do so. If you decide to inform the Responsible Researcher, she/he will exclude you from further participation.

What are the benefits of participating in the study?

It is expected that the mental well-being improves upon completion of the intervention. Furthermore, your participation will help to get insights regarding improvements to help other people in the future.

It is the view of the research team that the benefits outweigh the risks.

Insurance

General liability insurance for this study is arranged by Philips.

Compensation

You (Philips employee) will be compensated with 1000 Recognition@Philips points. Check for more information https://philips.rewardstation.com/default.aspx.

Since only complete datasets are valuable for us, partial completion of the protocol will be compensated likewise. 250 Recognition@Philips points will be compensated when participation is stopped during the home sessions, before part 4 of the study.

Will my participation be kept confidential?

Your identity and your participation in this study will be kept strictly confidential. Philips is committed to respect your privacy rights.

If you decide to participate in the study, the minimum necessary personal data about you will be collected, regarding your gender, age, health or other sensitive aspects. To protect your privacy, the following process will be applied: All of your directly identifying personal data (e.g., name, address, etc.) will be separated from the research data (e.g., your measurement data, etc.) and replaced by an assigned code. The directly identifying data will be only used to contact you. Access to the link between the assigned code and your identity will be limited to the Responsible Researcher and might only be disclosed to auditing bodies, if required.

In case any directly identifying data cannot be removed and coded as indicated above due to reporting requirements or due to technical limitations, the Responsible Researcher will inform you about the personal data that will not be coded and also why this will not be done.

As a record of your participation, your personal data (such as the signed consent form) will be stored as long as is required by local regulations and practice. You have the right at any time to request an overview of your identifiable personal data that has been collected, and to have inaccurate, incomplete or irrelevant data corrected or deleted (if applicable). To do so, please contact the Responsible Researcher.

What happens if relevant information about my health status is found during the study?

It is possible that during the study some information is discovered about your medical condition that you were not aware of. If this happens, we must inform you about this. If you do not want to be informed and hence do not agree, you cannot participate as a volunteer in the study.

What happens with the results of this study?

The data collected in this study will only be used for research and development purposes. In addition, the data may be used for the development of or improvements to existing products.

The results may be published (e.g. scientific publications, presentations or reports). Publications will not disclose your identity. Also, the results from this study may be used in the future for secondary purposes and research and development purposes where anonymized, de-identified or coded data may be shared with third parties. It will be ensured that the receiving party cannot, and is contractually prohibited to, trace the data back to an individual.

Confidentiality of Philips' confidential information

During the study you might come across confidential information of Philips. The information brochures, study descriptions, equipment, user manuals, instructions, together with information generated by you during the study, e.g. measurement results, user feedback, is confidential information belonging to Philips. You agree to keep the secrecy and confidentiality of such information and use it only for the purpose of your participation in the study.

Thank you very much for reading this information letter and for considering your participation in the study. If you decide to participate you will get a copy of this information letter and a copy of the signed informed consent.

Contact Information

If you have any questions regarding this study including requests for additional information about the study or your rights as a participant (before, during or after your participation), please contact Joëlle Dam. In the unlikely event of an injury, please contact Joëlle Dam.

Study Sponsor	Philips Electronics Nederland B.V. ("Philips")
Responsible Researcher	**Ad Denissen (Philips Research)** High Tech Campus 36 P 5656 AE Eindhoven
Cooperating Researchers	**Joëlle Dam (Intern University of Twente)** High Tech Campus 36 K 5656 AE Eindhoven **Tim Weysen (Philips Research)** High Tech Campus 36 5656 AE Eindhoven

INFORMED CONSENT **The effect of Neurofeedback on the perceived sleep quality**

Volunteer

- √ I have read and understood the information letter about this study and all my questions have been answered by the Responsible Researcher.

- √ I had sufficient time to consider my participation in this study and I am fully aware that my participation in this study is voluntary.

- √ I agree to participate in this study and follow the Responsible Researcher's instructions.
- √ I know that I can decide not to participate or stop my participation at any time without giving any reason for this decision.

- √ I understand and agree that my personal data will be collected, used and processed, for the purposes of the study, by the Responsible Researcher and other parties involved in the study. The personal data may be related to my health or other sensitive aspects. I understand that my directly identifying personal data (e.g., name, address, etc.) will be separated from the research data and replaced by an assigned code. Access to the link between the assigned number and my identity will be limited to the Responsible Researcher and might only be disclosed to auditing bodies, if necessary.

- √ I agree to the use of my data for other research and development purposes.

- √ I know that I have the right to request an overview of the personal data collected about me and can have it corrected or deleted.

- √ I understand that all devices used in this study must be returned to the Responsible Researcher at the end of my participation in the study.

- √ I understand that any and all information related to the study, including anything in writing and verbally communicated to me is confidential information belonging to Philips. I hereby agree to keep the aforesaid information confidential, use it exclusively for the purpose of deciding on my participation in the study.

- √ I agree to participate as a volunteer in this study.

_____ _____ _____

Name (Participant) Signature Date

Responsible Researcher

I have answered all questions about the study and discussed the meaning and scope of this informed consent and signed it in the presence of the volunteer.

_____ _____ _____

Name Signature Date

Appendix IV Median and interquartile range nonparametric parameters

Table 7 Median and IQR subjective sleep data

	SMR group (n=10)		**Bèta group (n=10)**		**Sham group (n=11)**	
	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test
	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)
PSQI	9 (6)	8 (7)	9.5 (3)	6 (3)	7 (7)	7 (7)
DIST	9 (8)	8 (6)	12 (7)	7 (9)	5 (4)	4 (3)
SQ	3 (0)	2 (1)	3 (1)	2.5 (1)	3 (1)	2 (1)

Note. PSQI=Global PSQI score; DIST=Amount of disturbances during night; SQ=Subjective Sleep Quality

Table 8 Median and IQR objective sleep data

	SMR group (n=9)		**Bèta group (n=7)**		**Sham group (n=8)**	
	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test
	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)
WASO	39.29 (23,55)	41.57 (34.02)	37.71 (12.86)	36.17 (31.71)	37.43 (8.14)	40.79 (28.70)
TST	7.15 (1.21)	7.15 (.65)	6.63 (.32)	6.71 (.98)	6.16 (1.21)	6.30 (.60)

Note. WASO= Wake time after sleep onset (min.); TST=Total Sleep Time.

Table 9 Median and IQR HRQoL

	SMR group (n=10)		Bèta group (n=10)		Sham group (n=11)	
	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test
	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)	Mdn (IQR)
PF	97.50 (15.00)	97.50 (15.00)	92.50 (21.25)	87.50 (16.25)	100.00 (5.00)	100.00 (5.00)
SF	62.50 (59.38)	87.50 (28.13)	68.75 (15.63)	75.00 (18.75)	75.00 (37.50)	87.50 (37.50)
PP	87.50 (56.25)	100.00 (50.00)	87.50 (31.25)	100.00 (50.00)	100.00 (.00)	100.00 (.00)
EP	66.67 (75.00)	100.00 (8.33)	66.67 (41.67)	100.00 (33.33)	66.67 (66.67)	100.00 (33.33)
MH	70.00 (36.00)	80.00 (24.00)	74.00 (27.00)	68.00 (21.00)	84.00 (28.00)	84.00 (28.00)
P	83.67 (25.00)	100.00 (13.27)	84.69 (25.00)	79.59 (22.45)	89.80 (10.20)	100.00 (10.20)
HC	50.00 (6.25)	50.00 (25.00)	50.00 (25.00)	50.00 (6.25)	50.00 (.00)	50.00 (25.00)

Note. PF=Physical functioning; SF=Social functioning; PP=Physical problems; EP=Emotional problems; MH=Mental health; V=Vitality; P=Pain; GH=General health; HC=Health change.