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Enhancing sleep quality and memory in insomnia using instrumental sensorimotor rhythm conditioning

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ABSTRACT

EEG recordings over the sensorimotor cortex show a prominent oscillatory pattern in a frequency range between 12 and 15 Hz (sensorimotor rhythm, SMR) under quiet but alert wakefulness. This frequency range is also abundant during sleep, and overlaps with the sleep spindle frequency band. In the present pilot study we tested whether instrumental conditioning of SMR during wakefulness can enhance sleep and cognitive performance in insomnia.

Twenty-four subjects with clinical symptoms of primary insomnia were tested in a counterbalanced within-subjects-design. Each patient participated in a SMR- as well as a sham-conditioning training block. Polysomnographic sleep recordings were scheduled before and after the training blocks.

Results indicate a significant increase of 12–15 Hz activity over the course of ten SMR training sessions. Concomitantly, the number of awakenings decreased and slow-wave sleep as well as subjective sleep quality increased. Interestingly, SMR-training enhancement was also found to be associated with overnight memory consolidation and sleep spindle changes indicating a beneficial cognitive effect of the SMR training protocol for SMR "responders" (16 out of 24 participants). Although results are promising it has to be concluded that current results are of a preliminary nature and await further proof before SMR-training can be promoted as a non-pharmacological approach for improving sleep quality and memory performance.

1. Introduction

Insomnia is characterized by a complaint of difficulty initiating sleep, maintaining sleep, and/or non-restorative sleep that causes clinically significant distress or impairment in social, occupational or other important areas of functioning (Littner et al., 2003; Riemann et al., 2010). From a psychological perspective insomnia patients typically complain of being unable to stop their reverberating thoughts and "rest their mind" which prevents them from sleeping. Insomnia is considered a significant complaint and is associated with decreased quality of life, absenteeism, increased work and car accidents, as well as increased general health care utilization. Epidemiological research shows the high prevalence of insomnia with about 30% of the general population complaining about some insomnia symptoms and 10% of the population fulfilling criteria for an insomnia syndrome with classical symptoms such as negative daytime consequences (Morin, LeBlanc, Daley, Gregoire, & Merette, 2006). According to DSM-IV criteria the proportion of primary insomnia is estimated to be around 3% (Gallup-Organization, 1995) to 6% (Ohayon, 2002). Empirical data demonstrate that insomnia is most often a chronic condition, defined as an inability to consistently sleep well for a period of at least 1 month. The consequences of chronic insomnia are severe and include adverse effects such as deficits in cognitive efficiency (Nissen et al., 2011), social discomfort and non-specific physical complaints (Gallup-Organization, 1995; Morin, Bootzin, et al., 2006; Stepanski et al., 1989). In addition to the high

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rates of past or present psychopathology, insomnia patients also have an increased risk for the development of *further* psychiatric illnesses (Buysse, 2004; Morawetz, 2003; Weissman, Greenwald, NinoMurcia, & Dement, 1997).

In summary, insomnia is a prevalent and clinically important problem. In fact it is the most commonly reported sleep problem in industrialized nations worldwide (Sateia, Doghramji, Hauri, & Morin, 2000).

Reports from patients with insomnia suggest that the disorder often starts as a stress-related phenomenon (Hauri & Fisher, 1986) with the individual's emotional and behavioral response to the condition playing an important role in the final outcome of the situation. These maladaptive cognitive, behavioral and emotional responses – precipitating and perpetuating insomnia – may be well dealt with non-pharmacological treatments. Indeed, there is promising evidence that non-pharmacological interventions besides hypnotics can be (i) efficient in treating insomnia symptoms (i.e., improving objective sleep measures such as sleep onset latency [SOL], wake after sleep onset [WASO], or total sleep time [TST]) and can also (ii) lead to *subjective* alleviation of patient complaints, with higher measurable quality of life after treatment (Ebben & Spielman, 2009; Morin, Bootzin, et al., 2006; Perlis, Smith, Cacialli, Nowakowski, & Orff, 2003; Van Houdenhove, Buyse, Gabriels, & Van den Bergh, 2011).

According to Freedman (1986) and more recently Perlis, Giles, Mendelson, Bootzin, and Wyatt (1997); Perlis, Kehr, et al. (2001); Perlis, Merica, Smith, and Giles (2001); Perlis, Smith, Andrews, Orff, and Giles (2001) the cognitive hyperarousal associated with insomnia (for review also see Riemann et al., 2010) is reflected in fast brain oscillations (including beta and gamma activity) which are elevated at sleep onset and during shallow NREM sleep stages (e.g., Buysse et al., 2008). The "Neurocognitive Model of Insomnia" (Perlis et al., 1997) proposes that the increase in central nervous system tone results in increased and persistent sensory and cognitive processing also during sleep where under normal circumstances such processes would be vastly attenuated or inhibited. According to the model increased sensory processing and perception thus account for difficulties in sleep initiation and sleep maintenance. This view is also in accordance with positron emission tomography (PET) data from Nofzinger and colleagues (Nofzinger et al., 2006) which show greater brain metabolism in arousal systems during the night in these patients. It is assumed that this cognitive hyperarousal and concomitantly elevated beta and gamma frequencies can be influenced and diminished using instrumental EEG conditioning of slower frequencies.

In the present study we therefore specifically focus on the instrumental conditioning of 12–15 Hz oscillations for improving sleep quality and memory performance in a population of young primary insomnia patients. These 12–15 Hz oscillations are prominent over the sensorimotor cortex – therefore termed sensorimotor rhythm (SMR) – and show a very distinctive pattern. They are (i) dominant during quiet but alert wakefulness and (ii) synchronize when motor behavior is inhibited (Sterman, Howe, & Macdonald, 1970). Interestingly, oscillations in the same frequency range are also abundant during light non-rapid eye movement (NREM) sleep, and overlap with the sleep spindle frequency band. Sterman et al. (1970) were the first to demonstrate that instrumental SMR conditioning (ISC) during wakefulness can improve subsequent sleep in cats. Hauri then used instrumental conditioning of various EEG parameters to treat disordered human sleep (Hauri, 1981; Hauri, Percy, Hellekson, Hartmann, & Russ, 1982) and demonstrated that patients suffering from primary insomnia specifically benefited from the SMR training protocol if they did not also suffer from physiological hyperarousal (i.e., enhanced muscle tension) at study intake. Given these findings (Hauri, 1981; Hauri et al., 1982; Sterman et al., 1970) as well as a meta-analysis on the efficacy of SMR biofeedback for epilepsy (Tan et al., 2009) we followed the rationale that ISC is in good place to directly counteract cognitive hyperarousal by attenuating associated high-frequency EEG oscillations.

In addition we recently found that instrumental SMR conditioning (as compared to a "placebo" randomized-frequency-conditioning protocol) can exert positive effects on sleep quality and even on declarative memory performance in *healthy* individuals (Hoedlmoser et al., 2008). Interestingly, and in accordance with previous literature, sleep spindles were found to be elevated after waking SMR conditioning (Sterman et al., 1970). This is in so far important, as a vast amount of literature points to the direct significance of sleep spindles for "offline" memory consolidation (e.g., Griessenberger et al., 2012; Gais, Mölle, Helms, & Born, 2002; Schabus et al., 2004; Tamaki, Matsuoka, Nittono, & Hori, 2008). With respect to insomnia a recent, exploratory study using "tele-neurofeedback" (i.e., done at home but connected with the therapist via an internet connection) (Cortoos, De Valck, Arns, Breteler, & Cluydts, 2010) indicates that TST improves after SMR tele-neurofeedback (but not after electromyography tele-biofeedback) whereas SOL decreases. Unfortunately, most of these – often termed "neurofeedback" (NFT) – studies lack important controls such as (i) real (sham) conditions or (ii) a convincing demonstration of proposed EEG changes after training.

Therefore, we aim to clarify in a counterbalanced cross-over design the efficacy of instrumental SMR conditioning for insomnia (termed ISC in the following) and start by testing whether patients actually succeed in (waking) SMR enhancement over ISC training sessions and whether such enhancement transfers to spindles during sleep. Last but not least we then assess whether ISC may influence (i) sleep quality and/or (ii) cognitive performance (as evidenced by declarative overnight memory consolidation).

Please note that the present study is best seen as a comprehensive pilot test for upcoming studies addressing the efficacy of ISC training on sleep and memory in an even more controlled manner.

2. Methods and materials

2.1. Participants

Twenty-four subjects (17 female, 7 male) aged between 19 and 50 years ($M = 34.83$, SD = 10.60) were included in the study. Subjects were recruited from the public by radio, newspaper and online advertisements as well as announcements on notice boards at the University of Salzburg and the Christian-Doppler hospital (Salzburg, Austria). Subjects gave written informed consent on study entrance and were refunded €200 – on study completion. Furthermore, participants had to refrain from any drug/medication and limit caffeine use (no caffeine intake for at least 5–6 h prior to sleep laboratory visits) as well as smoking (to a maximum of 4 cigarettes a day) during the complete study period. Subjects were preselected based on questionnaires concerning sleep quality (Pittsburgh Sleep Quality Index, PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989), anxiety (BAI; Beck, Epstein, Brown, & Steer, 1988) and depression (BDI-II; Beck, Steer, & Brown, 1996). On entrance subjects were required to (i) have a global score > 5 on the PSQI to ensure a minimum level of insomnia severity, (ii) have a daytime impairment related to the nighttime sleep difficulty, and show (iii) no signs of a current or past mental or psychiatric disorder (concurrent with insomnia). The latter two criteria are in accordance with the research diagnostic criteria for "primary insomnia" of the American Academy of Sleep Medicine (AASM; Edinger et al., 2004). Furthermore, subjects needed to have a problem in initiating or maintaining sleep, in waking up too early or reporting chronically non-restorative sleep (despite adequate opportunity and circumstances for sleep). Subjects complying with these pre-screening criteria were further evaluated by sleep diaries and a structured clinical interview for sleep disorders (SIS-D; Schramm et al., 1993). Finally, only patients with a primary insomnia complaint (at least 3 times a week over the course of a month) according to SIS-D criteria were included in the study. The mean duration of the current insomnia episode was reported to be about 4 years ($M = 4.08$, SD = 2.33). Lastly, we set a minimum criterion for subjectively impaired sleep quality (SOL or WASO greater than 20 min as derived from sleep diaries). At the subsequent entrance examination patients were asked to fill out the Freiburger Personality Inventory (FPI; Fahrenberg, Hampel, & Selg, 1984), the Wechsler Memory Scale – Revised (WMS-R; Wechsler, 1987), the Brief Symptom Inventory (BSI; Derogatis & Melisaratos, 1983) as well as the WHO

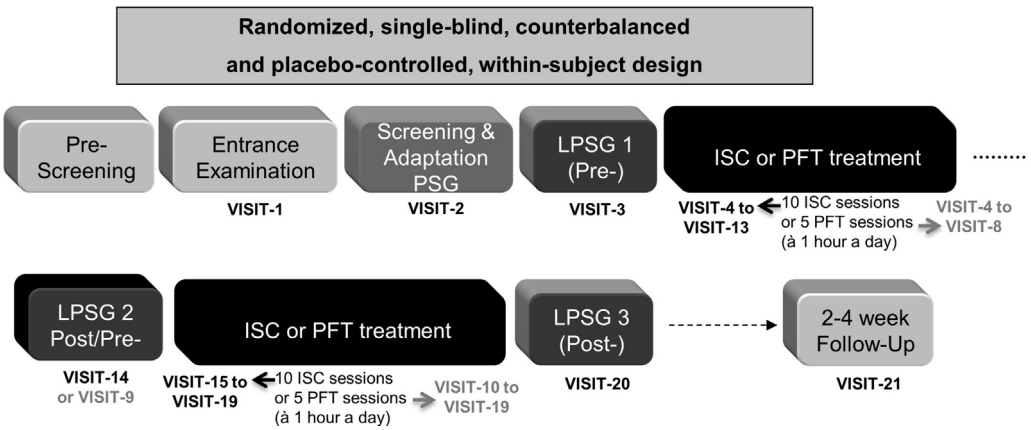

Fig. 1. Study design. Pre-screening was conducted via email and phone consultation. After a screening and adaptation night three more "learning nights" (LPSG) followed. Note that LPSG 2 thereby served as post-treatment (e.g., for ISC treatment in ISC-first condition) and pre-treatment (e.g., for PFT) night at the same time. In addition sleep was continuously monitored by sleep diaries and actigraphy. Eighty word-pairs had to be learned prior to each "learning" night (LPSG 1–3) and were tested by cued recall before and after sleep. Each subject reported to the laboratory 21 times (VISITS). ISC, instrumental SMR conditioning; PFT, pseudo-feedback (placebo); PSG, polysomnography.

Quality of Life Index-Bref (The-WHOQOL-Group, 1998) and were given actigraphs for monitoring sleep-wake cycles throughout the study period.

2.2. PSG and sleep analysis

Polygraphic sleep recordings were conducted using Synamps EEG amplifiers (NeuroScan Inc.). All signals were filtered (0.10 Hz high-pass filter; 70 Hz low-pass filter; 50 Hz notch filter) and digitized online with a 500 Hz sampling rate. Twenty-three Ag–AgCl electrodes were attached according to the international 10–20 system (Fp1, Fpz, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, Oz, O2, as well as A1 and A2 for later re-referencing) and were referenced to Fcz. In addition, four electrooculogram (EOG) channels, one bipolar submental electromyogram channel, one bipolar electrocardiogram channel (ECG) and one bipolar respiratory channel (chest wall movements) were recorded. In the screening/adaptation night a setup with 8 EEG channels, 4 EOG channels, bipolar ECG, 3 bipolar EMG (musculus mentalis and musculus tibialis on both sides) as well as three respiratory channels (chest and abdomen movements, air flow) and pulsoximetry was utilized.

Sleep was visually checked and scored by The Siesta Group© (Somnolyzer 24 × 7; cf., Anderer et al., 2004; Anderer et al., 2005) according to standard Rechtschaffen and Kales (1968) criteria. Spindle detection was based on an automatic algorithm, which is a further development of the bandpass filtering method developed by Schimicek, Zeitlhofer, Anderer and Saletu (1994) and is based on linear discrimination analyses (for further details see Anderer et al., 2004; Anderer et al., 2005). Rather than measuring the mean number of sleep spindles per time (spindle density), the applied algorithm also provides detailed sleep spindle features such as the duration, amplitude and frequency besides the overall number of detections. For the present study we focused on the number of slow (11–13 Hz) and fast (13–15 Hz) sleep spindles on central electrode C3 (cf. Hoedlmoser et al., 2008).

2.3. Instrumental EEG conditioning

Patients were trained to enhance the EEG amplitude within the 12–15 Hz range during 10 ISC sessions. Visual online feedback of the amplitude was provided using the system THERA PRAX® (neuroConn GmbH). Each session was conducted in a standardized procedure and lasted for about 1 h; therein subjects performed eight 3 min blocks of ISC (i.e., 24 min net training time per session).

EEG was recorded using a sampling rate of 512 Hz from C3 and C4 with reference placed on the right earlobe and ground electrode on the left earlobe. For offline artifact rejection a bipolar vertical EOG channel was recorded. The ongoing EEG at site C3 was band-pass filtered to continuously extract SMR (12–15 Hz) components during conditioning. Absolute band amplitude values (μV) were calculated online and used as relevant conditioning parameters. One trial consisted of a 3-s baseline interval followed by a continuous feedback interval lasting until the SMR band amplitude exceeded (for more than 250 ms) the predefined reward threshold measured during the baseline. The instruction given to the subject was simply to try to move the "compass needle" as much as possible to the left to exceed the threshold represented by a green dot on the compass. Subjects were told only that they could find out (by "trial and error") which strategy would help to enhance the SMR amplitude. Once successful, (usually after 2–3 sessions) participants usually maintained their previously found strategy (e.g., trying some kind of relaxation) for the remaining sessions. After the appearance of the reward and a randomized interval lasting for 1–3 s the baseline value was refreshed followed by a new continuous feedback interval until the next reward.

Instrumental conditioning during the control condition (pseudofeedback, PFT) differed only concerning the rewarded frequency band. Whereas the aim during the experimental condition was to enhance SMR-amplitude throughout all 10 instrumental conditioning sessions, randomized 3 Hz frequency bins between 7 and 20 Hz (except 12–15 Hz) were used as relevant PFT conditioning parameters. Consequently, during every PFT session (5 sessions) subjects had to enhance the amplitude of a new frequency range to avoid enhancement within a specific frequency bin. In order to keep motivation balanced over conditions and training blocks we adjusted the threshold in such a way that within a 3 min block similar amounts of rewards (around 10–15) were always given. If less than 5 rewards were received in a 3 min block we lowered the threshold to-be-exceeded, if more than 15 rewards were achieved we raised the to-be-exceeded threshold. Participants remained blind to the conditioning protocols (ISC or PFT) until being fully debriefed at the end of the investigation.

For offline analysis of SMR activity the Brain Vision Analyzer software (Brain Products GmbH) was used. In a first step, ocular artifacts were automatically minimized and visually controlled. To obtain amplitude values in the frequency domain fast Fourier transformation was applied. By averaging in the frequency domain, amplitude spectra were calculated in steps of 1 Hz for each of the feedback intervals ("Feedback onset" to "Feedback quote") during a 3-min trial. In order to reduce the huge and nonspecific effects of intersubject variation in absolute amplitude values, we obtained *normalized* amplitude values by dividing the mean amplitude during the feedback interval by the mean amplitude during rest with eyes open preceding the instrumental conditioning sessions. These derived relative amplitude values were then averaged across all blocks within one session. In order to compare EEG during early vs. late ISC, EEG data were further averaged across session 2–3 (early conditioning) and session 9–10 (late conditioning) for each subject. The first instrumental conditioning session served as training session and was excluded from analyses. For a complete description of procedures please refer to Hoedlmoser and colleagues (2008).

2.4. Experimental design

We adopted a counterbalanced within-subjects design (21 lab visits over the course of 3–6 weeks; cf. Fig. 1) with 4 polysomnographic recordings (PSG) (starting between 11 pm and midnight) and set the time in bed to 8 h.

After pre-screening (for anamnesis, PSQI, BDI-II and BAI questionnaires) subjects reported to the laboratory for the entrance examination and completed a structured clinical interview (SIS-D) as well as the BSI and FPI-R questionnaire. After at least a week of sleep diary self-assessment participants' reported again to the laboratory for a first *adaptation and screening night*. After that night (and exclusion of sleep disorders besides insomnia), a *pre-treatment PSG* (*LPSG-1*) was conducted in order to objectively assess sleep before treatment start. The LPSG-1 night was conducted within 4 days after screening PSG whenever possible ($M = 3.75$, $SD = 4.16$). After these nights patients started with 10 h of ISC (within 10–35 days; termed "duration ISC" in the following) or 5 h PFT which were followed by another experimental (i.e., post-treatment 1 or pre-treatment 2) night (*LPSG-2*). Thereafter, the second block with either ISC or PFT followed which was concluded with a final post-treatment PSG night (*LPSG-3*). ISC was always composed of 10 blocks of 12–15 Hz training (over C3), whereas PFT included training of 5 randomized frequency bands: 7–9 Hz, 8–10 Hz, 9–11 Hz, 17–19 Hz, and 18–20 Hz (for more details see Hoedlmoser et al., 2008). That is, subjects came 15 times (for 1 h each) to the laboratory for ISC/PFT training (10 times for ISC and 5 times for PFT); no more than one training session per day was permitted.

In order to evaluate stability or recurrence of insomnia symptoms a *behavioral follow-up* with questionnaires (WHOQOL, PSQI), actigraphy and sleep diaries was conducted after 2–4 weeks. ISC and PFT were counterbalanced with subjects being

Table 1
Overview of the objective and subjective sleep data.

	Learning night 1 (LPSG-1)				Learning night 2 (LPSG-2)				Learning night 3 (LPSG-3)				TIME × ISC/PFT-first
	ISC first		PFT first		ISC first		PFT first		ISC first		PFT first		$F(p)$
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age	34.5	11.8	35.2	9.8									
Time in bed	475.6	19.2	473.2	23.8	475.2	20.4	470.4	21.9	471.2	21.4	473.2	17.1	0.45 (n.s.)
Total sleep time	439.7	31.6	413.8	58.5	424.8	37.0	400.0	54.8	424.1	33.6	411.8	58.1	.87 (n.s.)
Number of awakenings	12.8	4.3	14.8	13.1	9.8*	3.5	14.3*	5.8	16.1	7.5	12.2	10.4	4.03 (<.05)
Sleep onset latency	17.6	23.4	18.3	11.7	13.7	11.9	25.6	30.3	13.3	6.9	19.5	13.6	2.28 (0.11)
Sleep efficiency	92.4	5.2	87.4	11.4	89.4	6.7	85.1	11.7	90.1	7.4	86.9	11.0	0.42 (n.s.)
N1 (min)	42.6*	18.4	27.8*	13.1	33.9	7.9	29.0	10.3	41.2*	19.5	26.7*	7.6	1.91 (n.s.)
N2 (min)	210.3	35.3	220.2	53.8	207.8	42.8	204.1	30.2	210.7	41.8	202.4	39.6	0.62 (n.s.)
N3 (min)	101.4	35.1	89.7	47.3	98.7	39.7	84.8	29.5	90.8	33.7	100.7	42.3	4.24 (<.05)
R (min)	85.6	18.6	76.5	21.8	84.8	37.0	82.3	25.0	81.6	22.6	82.2	30.9	0.72 (n.s.)
WASO (min)	19.3	14.5	41.9	47.4	37.3	32.5	45.7	48.2	34.6	34.8	43.3	44.3	0.91 (n.s.)
Awakening Index	1.8	.6	2.4	2.9	1.4*	.5	2.2*	1.0	2.3	1.2	1.9	1.7	1.69 (n.s.)
Shift Index	17.0	4.6	16.3	6.5	16.4	3.9	16.1	2.6	18.3	5.1	15.5	3.7	1.01 (n.s.)
TST_subj	389.3	56.0	336.6	72.0	385.2	62.7	345.8	56.0	390.1	50.0	358.3	74.4	0.01 (n.s.)
SOL_subj	26.8	15.5	35.2	14.2	19.1*	12.6	35.6*	18.8	20.8	9.9	29.5	17.0	0.11 (n.s.)
SEff_subj	84.2	4.7	82.7	8.6	85.5	6.6	81.2	8.0	86.9	6.3	81.5	12.8	1.28 (n.s.)

Please note that the objective sleep data are directly derived from the PSG in the sleep laboratory, whereas subjective sleep quality (shaded gray) is the mean of the last 5 days preceding LPSG 1–3 including the respective laboratory night. Between group differences (ISC first vs. PFT first) are marked within each experimental night (LPSG 1–3): TST_subj, subjective total sleep time; SOL_subj, subjective sleep onset latency; SEff_subj, subjective sleep efficiency.

* $p < .05$ (2-tailed).

randomly assigned to receive either ISC or PFT first. In addition all 3 experimental PSG (*LPSG 1–3*) nights were preceded by a declarative word pair association task (3 different lists of 80 word pairs each, presented twice during encoding; for details see Hoedlmoser et al., 2008; Schabus, Hödlmoser, Pecherstorfer, & Klösch, 2005) in the evening (as well as a cued recall before and after sleep) in order to evaluate overnight memory consolidation.

3. Statistics

Please note that the nature of our study design precluded analyzing our within-subject design as such, as the LPSG-2 night served as post-treatment for the first feedback condition as well as pre-treatment for the second feedback condition. We therefore chose to analyze our within-subject design (TIME: [LPSG 1, LPSG 2, LPSG 3]) in a more conservative way using an additional between group-factor "ISC/PFT-first" (participants starting with the ISC or PFT condition first). Consequently, we calculated TIME × ISC/PFT-first ANOVAs (with 12 subjects per group) which compromises statistical power. We adopted (1-tailed) *t*-tests for post hoc evaluation of significant ANOVA effects where a priori hypotheses were present (sleep quality changes following SMR conditioning (Cortoos et al., 2010; Hauri, 1981; Hauri et al., 1982; Sterman et al., 1970); SMR training enhancement and spindle (frequency) change (Berner, Schabus, Wienerroither, & Klimesch, 2006; Hoedlmoser et al., 2008); SMR learning and change in memory (Gruzelier, Egner, & Vernon, 2006; Hoedlmoser et al., 2008); (fast) spindles and change in overnight memory consolidation (Nishida & Walker, 2007; Schabus et al., 2004; Schabus et al., 2008; Tamaki et al., 2008). As dependent variables for assessing objective sleep data we used SOL, wake after sleep onset (WASO), N2, N3, REM (all in min), as well as sleep efficiency (in %) and number of awakenings (NOA). In addition we calculated overnight memory change by a 3-way ANOVA with the within-subject factors TIME and EVENING/MORNING (evening or morning recall) as well as the between-subject factor ISC/PFT-first. Pearson correlations (1-tailed) were used where not otherwise specified when previous data indicated the direction of effects of interest (see above). For not normally distributed data we utilized non-parametric Spearman–Rank correlations. ISC or PFT training success was estimated as the difference of ISC sessions 2–3 (pre) to sessions 9–10 (post), or PFT sessions 1–2 to 4–5, respectively.

One of the nights (LPSG-3) was lost in one of the participants (ISC-first group) due to technical problems. Subjective sleep quality was estimated from the last 5 sleep diary days preceding the LPSG nights (i.e., including the respective laboratory night value).

4. Results

4.1. Polysomnography data

Sleep data of the 3 learning nights (LPSGs) are shown for both subjects starting with ISC (ISC-first, $n = 12$) and pseudofeedback (PFT-first, $n = 12$) training (cf. Table 1).

4.2. Behavioral results

Behavioral data revealed significant overnight forgetting ($F_{1,23} = 10.20$, $p < .01$) in two of the three learning nights in insomnia patients (cf. Table 2). Overnight memory change was however unrelated to ISC or PFT preceding the learning night (TIME × EVENING/MORNING × ISC/PFT-first). The order of ISC/PFT neither affected absolute memory performance ($F_{2,44} = 0.88$, $p > .05$) nor overnight (evening to morning) memory change ($F_{2,44} = 0.71$, $p > .05$). An ANOVA TIME × EVENING/MORNING additionally revealed a general trend indicating better overall memory performance with time ("order effect") ($F_{2,46} = 2.76$, $p = .097$).

4.3. Instrumental conditioning

ISC data indicate a linear increase of 12–15 Hz activity over the course of the ten training sessions with significant pre (session 2–3) to post- (session 9–10) treatment changes at C3 ($t_{23} = -2.50$, $p = .02$; Cohen's $d = 0.511$). From the 24 subjects 16 responded with an increase in SMR activity ($M = 12.30\%$, $SD = 7.70\%$). Interestingly, also the higher beta band (16–25 Hz) showed a similar effect ($t_{23} = -3.00$, $p < .01$; Cohen's $d = 0.620$) (cf. Fig. 2). The contralateral (untrained) C4 electrode showed similar yet non-significant effects in the same direction (SMR: $t_{23} = -1.70$, $p = .10$; Cohen's $d = 0.348$ and Beta: $t_{23} = -1.90$, $p = .070$; Cohen's $d = 0.388$, respectively). Pre to post PFT sessions neither revealed significant enhancement in SMR (C3: $t_{23} = -1.62$, $p = .12$; Cohen's $d = 0.341$; C4: $t_{23} = -1.38$,

Table 2
Declarative overnight memory change in insomnia patients.

Memory HITS%		Mean	SD	N	Cohen's *d*	*t*-test	*p*-value
LPSG 1	Evening	59.77	26.85	24	0.472	1.82	.082
	Morning	58.21	29.42	24			
LPSG 2	Evening	65.91	27.62	24	0.966	3.89	.001*
	Morning	63.44	29.32	24			
LPSG 3	Evening	66.62	29.49	24	0.446	2.19	.039*
	Morning	65.03	30.41	24			

HITS% refer to the number of correctly retrieved word-pairs plus 0.5 of semantically correct (e.g., "river" instead of "stream") words. Note that in addition to overnight forgetting a trend toward higher general memory performance with repeated learning is evident (order effect). The declarative material consisted of 3 different word-pair lists with randomized order of (cued) recall at each occasion.

* $p < .05$.

$p = .18$; Cohen's $d = 0.281$) nor BETA power (C3: $t_{23} = -1.09$, $p = .29$; Cohen's $d = 0.224$; C4: $t_{23} = -1.07$ $p = .30$; Cohen's $d = 0.226$).

Furthermore, it becomes evident that the longer subjects needed to complete the 10 SMR training sessions, the higher their overall gain in SMR amplitude ($r_{22} = .66$, $p < .001$, 2-tailed; cf. Fig. 3) was. The variation in the time to complete the 10 ISC sessions was determined by the patients' availability over the course of the study period and could not be imposed experimentally.

4.4. ISC effects on sleep quality

Significant 2-way interactions TIME × ISC/PFT-first and post hoc tests revealed a decrease in the number of awakenings (NOA; $F_{2,40} = 4.03$, $p = .025$) and enhancements of $N3_{min}$ ($F_{2,40} = 4.24$, $p = .021$) following the ISC blocks (cf. Fig. 4). Please refer to the supplementary material for a further trend in SOL. The other sleep stages (N1, N2, REM) as well as total sleep time, waking after sleep onset, and sleep efficiency remained unchanged (cf. Table 1).

4.5. ISC effects on sleep spindles and memory

Most importantly, we also observed a transfer of SMR training success to fast NREM sleep spindles in the way that SMR training enhancement (pre to post) correlated positively with fast spindle number change (pre to post ISC block) (C3: $r_{22} = .38$, $p = .033$; cf. Fig. 5, left) but not slow spindle change (C3: $r_{22} = .-21$, $p = .16$). This correlation also does not change when controlling for changes in N2 and N3 duration (min) (C3: $r_{18} = .39$, $p = .038$). Yet, there is no evidence for an *overall* enhancement of sleep spindles after the ISC as compared to the PFT condition as revealed in a TIME × ISC/PFT-first-ANOVA. Only spindle number (in N3) showed an overall trend for more spindles after the ISC block ($F_{2,42} = 2.45$,

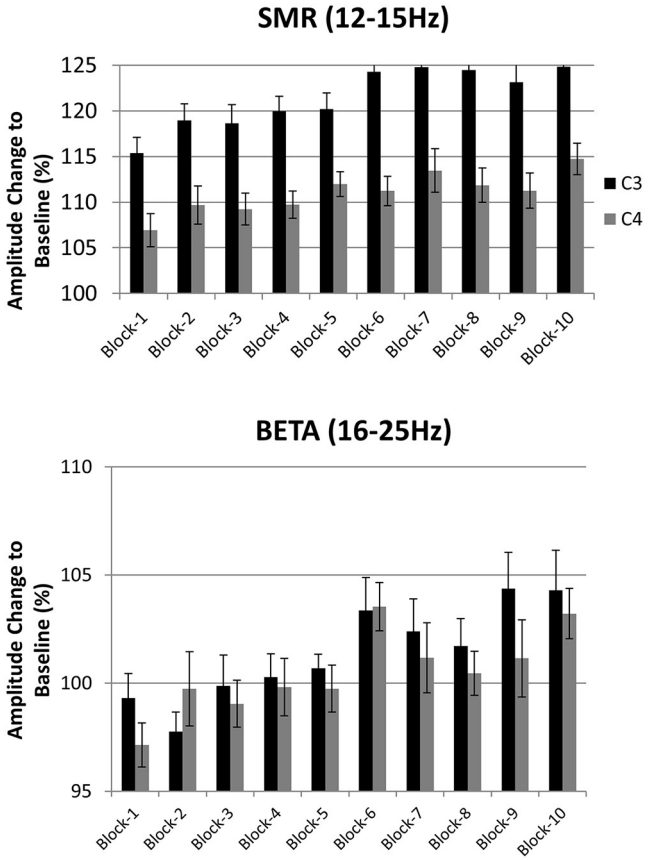

Fig. 2. EEG changes across instrumental SMR conditioning (ISC) sessions. SMR (top) and BETA (bottom) amplitude changes from baseline (100% value) are depicted over the course of the 10 training sessions. Training was done on recording site C3. Note that also the contralateral side shows a trend to increase over time.

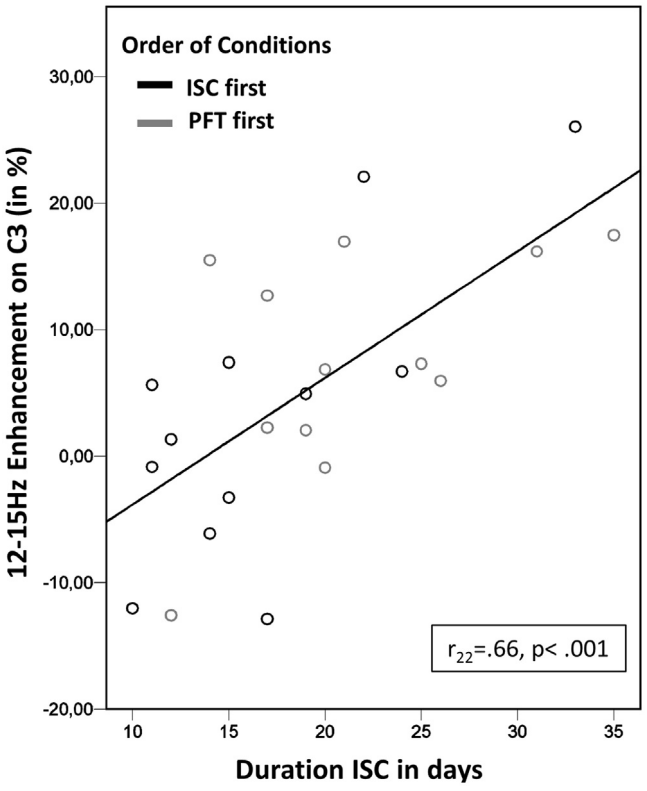

Fig. 3. ISC training time and SMR amplitude enhancement. Note that ISC training duration is strongly related to higher SMR enhancement (in %) suggesting a beneficial effect of an extended ISC training period. ISC training duration was not experimentally controlled but determined by the patients' availability for the 10 ISC sessions (10–35 days). The order of ISC/PFT conditions (ISC-first, black; ISC-first, gray) is not related to ISC training success.

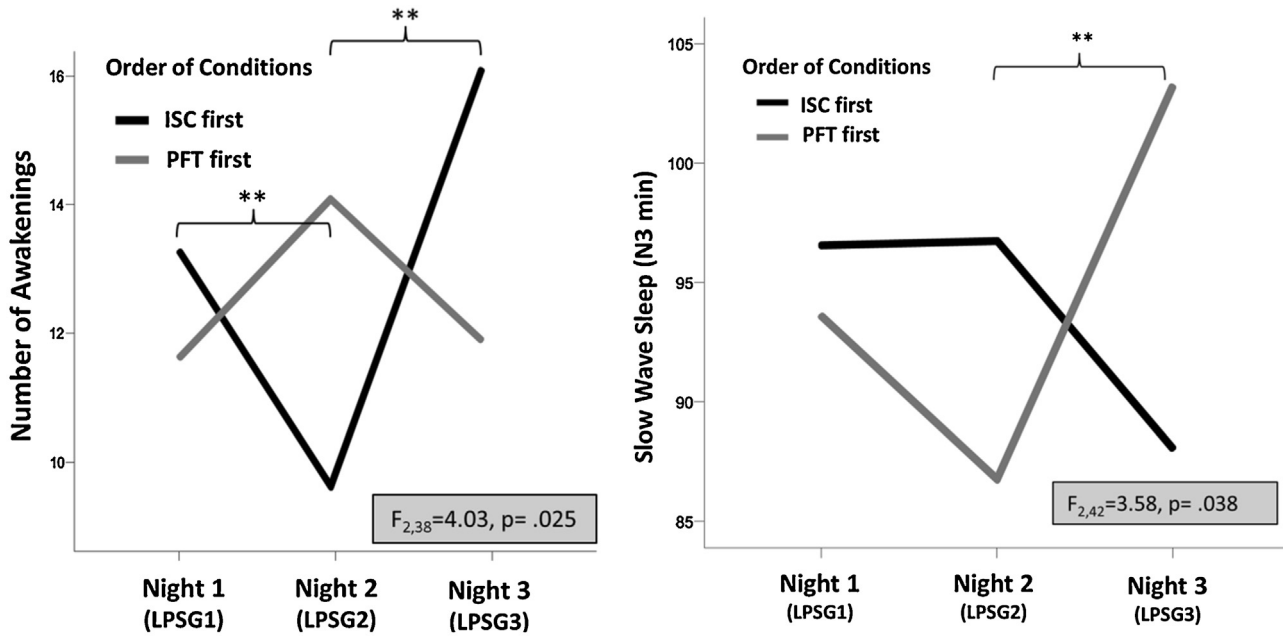

Fig. 4. Objective sleep quality changes following ISC and PFT training. Note significant changes (**, $p < .05$) in the number of awakenings (left) and slow-wave sleep (right) following ISC but also PFT training.

$p = .10$), yet this effect is also mediated by higher N3 amounts after ISC.

Although there is no overall effect of ISC vs. PFT on overnight memory change or absolute memory performance, linear correlations reveal an interesting association of *individual* ISC training success and consolidation changes (evening to morning changes in performance). Specifically, data indicate that the amount of 12–15 Hz enhancement over the ISC sessions correlates with the change in overnight memory consolidation pre to post ISC block ($r_{22} = .40$, $p = .027$, cf. Fig. 5, right). Last but not least, a significant correlation between these changes in memory consolidation (pre to post ISC block) and the change in fast (NREM) spindle numbers reveals that memory consolidation changes are associated with the fast spindle enhancement ($r_{22} = .35$, $p = .049$) but not with slow spindle changes ($r_{22} = -.25$, $p = .12$).

4.6. ISC effect on subjective well being

The PSQI score from entrance ($M = 10.83$, SD = 1.99) to follow-up examination ($M = 7.00$, SD = 2.67) revealed a reduction in subjective sleep complaints ($t_{23} = 7.74$, $p < .001$) in all but one subject. Seven of the participants scored at or below a value of 5 indicating clinically significant improvement after the completion of both ISC and PFT. Yet note that we do not have separate evaluations of subjective

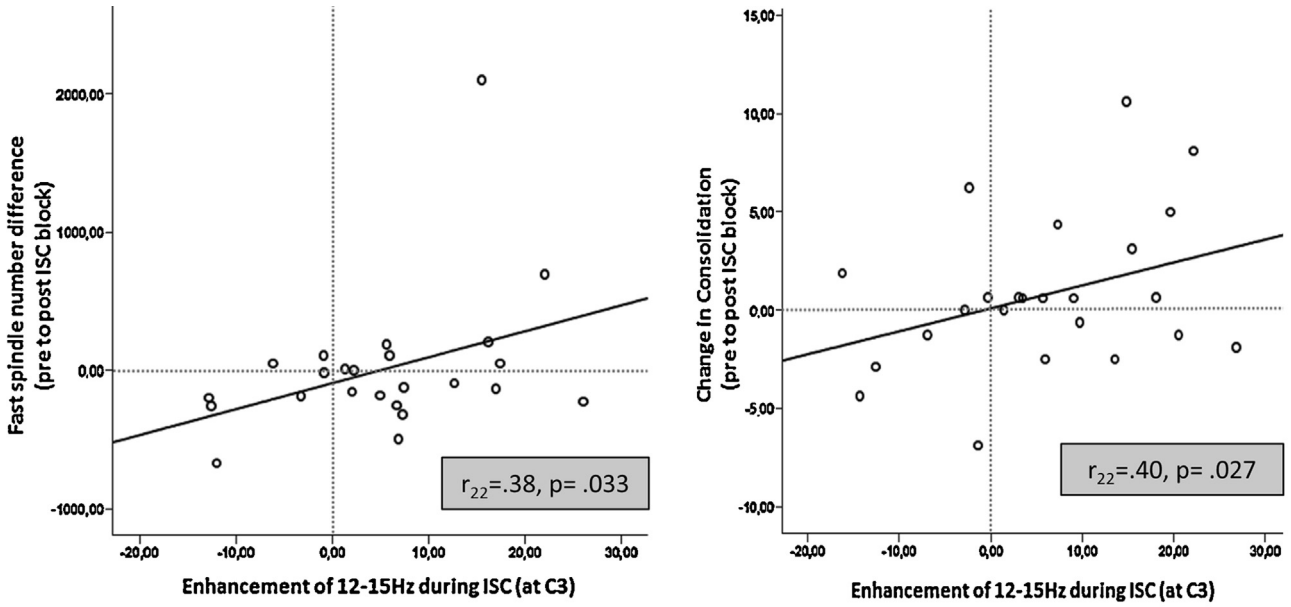

Fig. 5. Association of SMR enhancement, memory consolidation and spindle change. Note the association of SMR training success in the ISC condition, which is significantly related to (i) concomitant enhancement of fast sleep spindles (left) as well as (ii) improvement of declarative memory consolidation overnight (right). Note that the effect appears specific to the fast spindle type on recording (and ISC feedback) site C3. Changes in absolute spindle numbers across (N2 and N3) NREM sleep are depicted.

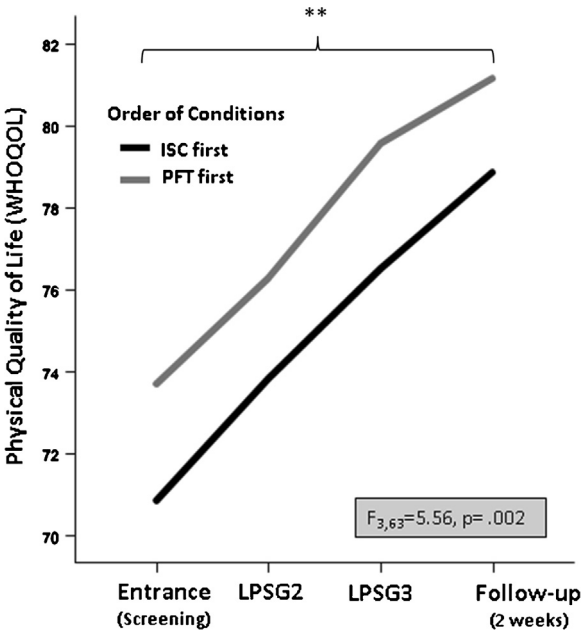

Fig. 6. Subjective quality of life changes following ISC and PFT treatment. Note that physical quality of life changes as a function of time irrespective of ISC or PFT trainings. **, significant ($p < .05$) difference between entrance examination and follow-up irrespective of the treatment condition.

sleep quality after the ISC and PFT condition and can thereby only state that there appears to be a beneficial NFT effect non-specific to the training type (cf. Suppl. Fig. 2).

Interestingly, WHOQOL physical quality of life (assessing domains such as energy and fatigue, sleep and rest, or work capacity) was also enhanced over time ($F_{3,63} = 5.56$, $p = .002$). Absent interactions with the factor ISC/PFT-first however indicate that the subjective change is unrelated to ISC or PFT training ($F_{3,63} = .015$, $p = .99$). Post hoc *t*-tests revealed that there is a significant increase from entrance examination to follow-up irrespective of the treatment condition ($t_{22} = -3.20$, $p < .01$; Cohen's $d = -0.667$) suggesting a placebo effect (cf. Fig. 6).

5. Discussion

In healthy individuals we reported earlier that SMR during wakefulness and subsequent spindle activity can be increased using ISC and that this training elicits positive changes in various sleep parameters as well as declarative memory performance (Hoedlmoser et al., 2008). In the current study we now applied ISC to people suffering from insomnia based on the assumption that these individuals would specifically benefit from such a non-pharmacological treatment alternative (Hoedlmoser, Dang-Vu, Desseilles, & Schabus, 2011).

Results reveal that – beside healthy subjects – people also suffering from primary insomnia increase their SMR amplitude over the ISC training period but do not show such changes in a randomized-frequency conditioning protocol (PFT) (cf. Fig. 2).

Previous studies using an identical word-pair task in healthy individuals reported overnight consolidation without forgetting (Berner et al., 2006; Hoedlmoser et al., 2008) or even (tendencies toward) overnight memory improvement (Schabus et al., 2004; Schabus et al., 2005). In contrast, we report here significant overnight forgetting in young insomnia patients (cf. Table 2). This latter finding is of importance as results regarding cognitive functioning in primary insomnia are highly inconsistent with subjective complaints often being more pronounced than neuropsychological test outcomes would suggest (for reviews see Fortier-Brochu, Beaulieu-Bonneau, Ivers, & Morin, 2012; Orff, Drummond, Nowakowski, & Perils, 2007).

Although ISC training in our insomnia patients did not generally enhance declarative memory performance as previously found in healthy individuals (Hoedlmoser et al., 2008), we do find correlative associations between ISC and memory consolidation. Specifically, we found linear relationships between individual SMR-enhancement, (i) overnight memory consolidation and (ii) fast NREM sleep spindle changes (cf. Fig. 5). Yet note that overall, found associations are moderate and overnight forgetting could not be stopped using 10 ISC sessions. In addition the change in (fast) sleep spindles appears to be related to changes in memory performance overnight as reported earlier in healthy individuals (Morin et al., 2008; Schabus et al., 2004; Schabus et al., 2008; Tamaki et al., 2008). Interestingly we found that this effect is most pronounced for fast (N2 and N3) NREM spindles on recording site C3 which is in agreement with the place where (and the frequency in which) SMR feedback was provided. Given this we speculate that ISC might be beneficial for sleep-dependent memory consolidation by increasing (fast) sleep spindles in the first instance.

Most importantly, and in addition to this beneficial cognitive effect, results reveal a significant effect of ISC on objective sleep quality. Specifically, data indicate a decrease in the number of awakenings, a trend toward decreased sleep onset latency as well as an increase in slow wave sleep (N3) after ISC but not PFT training (cf. Fig. 4 and suppl. material). Last but not least subjective sleep quality (cf. Suppl. Fig. 2) as well as life quality (cf. Fig. 6) appear to change in the course of the study. In this context it is critical to note that placebo effects might have significantly mediated some of these subjective changes as indicated by physical quality of life improvements which are identical after ISC as well as PFT training blocks (cf. Fig. 6) and which remain at follow-up testing. One therefore cannot stress sufficiently the importance of accurately controlling for placebo effects in biofeedback studies as the time and instrument intensive approach itself may likely result in unspecific (placebo) effects (e.g., Lansbergen, van Dongen-Boomsma, Buitelaar, & Slaats-Willemse, 2011). Also note that among the few well-controlled double-blind "neurofeedback" studies beneficial effects (Keizer, Verschoor, Verment, & Hommel, 2010) are found as often as pure null results (for review see Hoedlmoser et al., 2011; Logemann, Lansbergen, Van Os, Bocker, & Kenemans, 2010).

In the present experimental approach we intended to apply an as much as possible unbiased ISC training, checking for ISC efficacy by purely training 12–15 Hz over sensorimotor regions and in the absence of any pre-selection of patients. Given the evident concomitant beta change (cf. Fig. 2, lower panel) and its reported association with (hyper-) arousal during sleep (Perlis, Merica, et al., 2001; Wuyts et al., 2012) it is possible that some of the patients may have trained a maladaptive beta EEG change compromising the overall beneficial ISC effect in our study.

Remarkably, results also indicate that randomized frequency PFT did not only have *no effect* on some variables but even led to considerable negative sleep quality changes (cf. Fig. 4). We hypothesize that PFT probably led to a subjective loss of self-efficacy. In general it is already quite difficult for participants to come up with an efficient training strategy for a given EEG frequency band. If this (unconscious) strategy then becomes ineffective from session to session it may inevitably lead to subjective loss of control and consequently decreases in sleep quality as well as well-being. An alternative would be to just train one specific other frequency band systematically but then the protocol faces the problem that another frequency band might itself trigger distinct (yet unspecified) changes in sleep quality or cognition. However note that in order to keep motivation balanced as much as possible we did

control for equal amounts of rewards within each ISC and PFT session.

It should also be mentioned that for economic reasons we had to somewhat limit the complexity of our study protocol which even in the current form was rather extensive. Already this "preliminary" protocol required a minimum number of 21 laboratory visits (15 ISC/PFT sessions, 4 PSG nights, entrance and follow-up examination) per subject spanning over 4–8 weeks. The main limitations of the current study are certainly the 5 PFT vs. 10 ISC sessions with the LPSG-2 night having to serve as post-treatment night for treatment 1 and at the same time as pre-treatment night for treatment 2. As a consequence we also were not able to statistically take advantage of the built-in within-subject design and had to adopt a statistically less sensitive between-group analysis.

With respect to the transfer of SMR training to sleep spindles it is evident that our previous study using an identical ISC protocol with healthy individuals (Hoedlmoser et al., 2008) was more successful which likely is related to the slower ISC learning curve of insomnia patients and the relatively low ISC dosage (10 blocks á 24 min net training time) for patient populations. It also important to note that we did not find an overall beneficial effect of ISC training on sleep spindle enhancement or memory consolidation but rather linear relationships indicating that some patients may benefit from ISC ("responders") whereas others may not be responding in desired directions.

Future studies will have to meet these shortcomings, enhance the training amount and consider scattering training over time as present data suggest benefits for an extended ISC training schedule (cf. Fig. 3). Furthermore, upcoming studies should consider adding multiple nights before and after ISC training blocks as well as to add a delayed follow-up (6–9 months) using objective PSG recordings throughout. Last but not least studies are awaited which address in which way ISC training exerts its effects on sleep and memory, that is which specific mechanisms or brain regions are altered over the course of ISC training which then mediate sleep quality changes (such as NOA decreases or N3 enhancements). An interesting observation in this respect is that some patients tended to even decrease SMR amplitude in the baseline interval which set a lower "to-be-exceeded" threshold for the following "reward period." In this sense patients may not necessarily learn to up-regulate SMR amplitude but rather to control at will SMR activity and related mental relaxation.

In general we believe that biofeedback studies have to ensure that they accurately disentangle real from placebo effects if they intend to promote this promising method as a real non-pharmacological treatment alternative for various disorders. Demonstrating that after a given ISC protocol related EEG data actually changes is as important as comparing the treatment group to a serious sham-condition of identical duration and instrumental setup. Unfortunately this latter approach is adopted very rarely (for review see Hoedlmoser et al., 2011) in the field. It is therefore to date also practically impossible to tailor ISC or "neurofeedback" protocols to individual patients' needs as reliable scientific evidence in this respect is basically absent.

6. Conclusion

In summarizing, current results indicate that people suffering from primary insomnia can experience subjective as well as objective benefits from SMR conditioning. Yet more than 10 SMR training sessions are recommended in order to find robust and widespread effects in EEG and well-being even in patient populations. If it can be confirmed that ISC effects are indeed durable in treating primary insomnia ISC might qualify as a cost-effective, non-pharmacological treatment alternative also suited for patients non-compliant to psychotherapeutic intervention or pharmacotherapy.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.biopsycho.2013.02.020.

References

Anderer, P., Gruber, G., Parapatics, S., Woertz, M., Miazhynskaia, T., Klösch, G., et al., 2005. An E-health solution for automatic sleep classification according to Rechtschaffen and Kales: Validation study of the Somnolyzer 24 × 7 utilizing the siesta database. Neuropsychobiology 51, 115–133.

Anderer, P., Saletu, B., Saletu-Zyhlarz, G.M., Gruber, G., Parapatics, S., Miazhynskaia, T., et al., 2004. Recent advances in the electrophysiological evaluation of sleep. In: Drinkenburg, W., Ruigt, G., Jobert, M. (Eds.), Essentials and applications of EEG research in preclinical and clinical pharmacology. Unipublish Verlag für Studium & Praxis OHG, Berlin, pp. 307–339.

Beck, A.T., Epstein, N., Brown, G., Steer, R.A., 1988. An inventory for measuring clinical anxiety: Psychometric properties. Journal of Consulting and Clinical Psychology 56, 893–897.

Beck, A.T., Steer, R.A., Brown, G.K., 1996. Manual for the Beck Depression Inventory-II. Psychological Corporation, San Antonio, TX.

Berner, I., Schabus, M., Wienerroither, T., Klimesch, W., 2006. The significance of sigma neurofeedback training on sleep spindles and aspects of declarative memory. Applied Psychophysiology and Biofeedback 31, 97–114.

Buysse, D.J., 2004. Insomnia, depression, and aging – Assessing sleep and mood interactions in older adults. Geriatrics 59, 47–51.

Buysse, D.J., Germain, A., Hall, M.L., Moul, D.E., Nofzinger, E.A., Begley, A., et al., 2008. EEG spectral analysis in primary insomnia: NREM period effects and sex differences. Sleep 31, 1673–1682.

Buysse, D.J., Reynolds 3rd., C.F., Monk, T.H., Berman, S.R., Kupfer, D.J., 1989. The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. Psychiatry Research 28, 193–213.

Cortoos, A., De Valck, E., Arns, M., Breteler, M.H.M., 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 Biofeedback 35, 125–134.

Derogatis, L.R., Melisaratos, N., 1983. The Brief Symptom Inventory: An introductory report. Psychological Medicine 13, 595–605.

Ebben, M.R., Spielman, A.J., 2009. Non-pharmacological treatments for insomnia. Journal of Behavioral Medicine 32, 244–254.

Edinger, J.D., Bonnet, M.H., Bootzin, R.R., Doghramji, K., Dorsey, C.M., Espie, C.A., et al., 2004. Derivation of research diagnostic criteria for insomnia: Report of an American Academy of Sleep Medicine Work Group. Sleep 27, 1567–1596.

Fahrenberg, J., Hampel, R., Selg, H., 1984. Freiburger Persönlichkeitsinventar – Revision (FPI-R). Manual. Hogrefe, Göttingen.

Fortier-Brochu, E., Beaulieu-Bonneau, S., Ivers, H., Morin, C.M., 2012. Insomnia and daytime cognitive performance: A meta-analysis. Sleep Medicine Reviews 16, 83–94.

Freedman, R.R., 1986. EEG power spectra in sleep-onset insomnia. Electroencephalography and Clinical Neurophysiology 63, 408–413.

Gais, S., Mölle, M., Helms, K., Born, J., 2002. Learning-dependent increases in sleep spindle density. Journal of Neuroscience 22, 6830–6834.

Gallup-Organization, 1995. Sleep in America. Gallup Organization, Princeton, NJ.

Griessenberger, H., Hoedlmoser, K., Heib, D.P., Lechinger, J., Klimesch, W., Schabus, M., 2012. Consolidation of temporal order in episodic memories. Biological Psychology 91, 150–155.

Gruzelier, J., Egner, T., Vernon, D., 2006. Validating the efficacy of neurofeedback for optimising performance. Event-Related Dynamics of Brain Oscillations 159, 421–431.

Hauri, P., 1981. Treating psychophysiologic insomnia with biofeedback. Archives of General Psychiatry 38, 752–758.

Hauri, P., Fisher, J., 1986. Persistent psychophysiologic (learned) insomnia. Sleep 9, 38–53.

Hauri, P.J., Percy, L., Hellekson, C., Hartmann, E., Russ, D., 1982. The treatment of psychophysiologic insomnia with biofeedback: A replication study. Biofeedback and Self Regulation 7, 223–235.

Hoedlmoser, K., Dang-Vu, T.T., Desseilles, M., Schabus, M., 2011. Non-pharmacological alternatives for the treatment of insomnia – Instrumental EEG

conditioning, a new alternative? In: Soriento, Y.E. (Ed.), Melatonin, sleep and insomnia. Nova Science Publishers, Inc., New York.
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, 1401–1418.
Keizer, A.W., Verschoor, M., Verment, R.S., Hommel, B., 2010. The effect of gamma enhancing neurofeedback on the control of feature bindings and intelligence measures. International Journal of Psychophysiology 75, 25–32.
Lansbergen, M.M., van Dongen-Boomsma, M., Buitelaar, J.K., Slaats-Willemse, D., 2011. ADHD and EEG-neurofeedback: A double-blind randomized placebo-controlled feasibility study. Journal of Neural Transmission 118, 275–284.
Littner, M., Hirshkowitz, M., Kramer, M., Kapen, S., Anderson, W.M., Bailey, D., et al., 2003. Practice parameters for using polysomnography to evaluate insomnia: An update. Sleep 26, 754–760.
Logemann, H.N., Lansbergen, M.M., Van Os, T.W., Bocker, K.B., Kenemans, J.L., 2010. The effectiveness of EEG-feedback on attention, impulsivity and EEG: A sham feedback controlled study. Neuroscience Letters 479, 49–53.
Morawetz, D., 2003. Insomnia and depression: Which comes first? Sleep Research Online 5, 77–81.
Morin, A., Doyon, J., Dostie, V., Barakat, M., Hadj Tahar, A., Korman, M., et al., 2008. Motor sequence learning increases sleep spindles and fast frequencies in post-training sleep. Sleep 31, 1149–1156.
Morin, C.M., Bootzin, R.R., Buysse, D.J., Edinger, J.D., Espie, C.A., Lichstein, K.L., 2006a. Psychological and behavioral treatment of insomnia: Update of the recent evidence (1998–2004). Sleep 29, 1398–1414.
Morin, C.M., LeBlanc, M., Daley, M., Gregoire, J.P., Merette, C., 2006b. Epidemiology of insomnia: Prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. Sleep Medicine 7, 123–130.
Nishida, M., Walker, M.P., 2007. Daytime naps, motor memory consolidation and regionally specific sleep spindles. PLoS ONE 2, e341.
Nissen, C., Kloepfer, C., Feige, B., Piosczyk, H., Spiegelhalder, K., Voderholzer, U., et al., 2011. Sleep-related memory consolidation in primary insomnia. Journal of Sleep Research 20, 129–136.
Nofzinger, E., Nissen, C., Germain, A., Moul, D., Hall, M., Price, J., et al., 2006. Regional cerebral metabolic correlates of WASO during NREM sleep in insomnia. Sleep 29, A260.
Ohayon, M.M., 2002. Epidemiology of insomnia: What we know and what we still need to learn. Sleep Medicine Reviews 6, 97–111.
Orff, H.J., Drummond, S.P., Nowakowski, S., Perils, M.L., 2007. Discrepancy between subjective symptomatology and objective neuropsychological performance in insomnia. Sleep 30, 1205–1211.
Perlis, M.L., Giles, D.E., Mendelson, W.B., Bootzin, R.R., Wyatt, J.K., 1997. Psychophysiological insomnia: The behavioural model and a neurocognitive perspective. Journal of Sleep Research 6, 179–188.
Perlis, M.L., Kehr, E.L., Smith, M.T., Andrews, P.J., Orff, H., Giles, D.E., 2001a. Temporal and stagewise distribution of high frequency EEC activity in patients with primary and secondary insomnia and in good sleeper controls. Journal of Sleep Research 10, 93–104.
Perlis, M.L., Merica, H., Smith, M.T., Giles, D.E., 2001b. Beta EEG activity and insomnia. Sleep Medicine Reviews 5, 365–376.
Perlis, M.L., Smith, M.T., Andrews, P.J., Orff, H., Giles, D.E., 2001c. Beta/gamma EEG activity in patients with primary and secondary insomnia and good sleeper controls. Sleep 24, 110–117.
Perlis, M.L., Smith, M.T., Cacialli, D.O., Nowakowski, S., Orff, H., 2003. On the comparability of pharmacotherapy and behavior therapy for chronic insomnia – Commentary and implications. Journal of Psychosomatic Research 54, 51–59.
Rechtschaffen, A., Kales, A.A., 1968. A manual of standardized terminology techniques and scoring system for sleep stages of human subjects. US Department of Health, Education, and Welfare Public Health Service – NIH/NIND, Bethesda.
Riemann, D., Spiegelhalder, K., Feige, B., Voderholzer, U., Berger, M., Perlis, M., et al., 2010. The hyperarousal model of insomnia: A review of the concept and its evidence. Sleep Medicine Reviews 14, 19–31.
Sateia, M.J., Doghramji, K., Hauri, P.J., Morin, C.M., 2000. Evaluation of chronic insomnia. Sleep 23, 243–308.
Schabus, M., Gruber, G., Parapatics, S., Sauter, C., Klosch, G., Anderer, P., et al., 2004. Sleep spindles and their significance for declarative memory consolidation. Sleep 27, 1479–1485.
Schabus, M., Hödlmoser, K., Pecherstorfer, T., Klösch, G., 2005. Influence of midday naps on declarative memory performance and motivation. Somnology 9, 148–153.
Schabus, M., Hoedlmoser, K., Pecherstorfer, T., Anderer, P., Gruber, G., Parapatics, S., et al., 2008. Interindividual sleep spindle differences and their relation to learning-related enhancements. Brain Research 1191, 127–135.
Schimicek, P., Zeitlhofer, J., Anderer, P., Saletu, B., 1994. Automatic sleep-spindle detection procedure – Aspects of reliability and validity. Clinical EEG (Electroencephalography) 25, 26–29.
Schramm, E., Hohagen, F., Grasshoff, U., Riemann, D., Hajak, G., Weess, H.G., et al., 1993. Test-retest reliability and validity of the Structured Interview for Sleep Disorders according to DSM-III-R. American Journal of Psychiatry 150, 867–872.
Stepanski, E., Koshorek, G., Zorick, F., Glinn, M., Roehrs, T., Roth, T., 1989. Characteristics of individuals who do or do not seek treatment for chronic insomnia. Psychosomatics 30, 421–427.
Sterman, M.B., Howe, R.C., Macdonald, L.R., 1970. Facilitation of spindle-burst sleep by conditioning of electroencephalographic activity while awake. Science 167, 1146–1148.
Tamaki, M., Matsuoka, T., Nittono, H., Hori, T., 2008. Fast sleep spindle (13–15 Hz) activity correlates with sleep-dependent improvement in visuomotor performance. Sleep 31, 204–211.
Tan, G., Thornby, J., Hammond, D.C., Strehl, U., Canady, B., Arnemann, K., et al., 2009. Meta-analysis of EEG biofeedback in treating epilepsy. Clinical EEG and Neuroscience: Official Journal of the EEG and Clinical Neuroscience 40, 173–179.
The-WHOQOL-Group, 1998. Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. Psychological Medicine 28, 551–558.
Van Houdenhove, L., Buyse, B., Gabriels, L., Van den Bergh, O., 2011. Treating primary insomnia: Clinical effectiveness and predictors of outcomes on sleep, daytime function and health-related quality of life. Journal of Clinical Psychology in Medical Settings 18, 312–321.
Wechsler, D., 1987. Wechsler memory scale-revised. The Psychological Corporation, San Antonio, TX.
Weissman, M.M., Greenwald, S., NinoMurcia, G., Dement, W.C., 1997. The morbidity of insomnia uncomplicated by psychiatric disorders. General Hospital Psychiatry 19, 245–250.
Wuyts, J., De Valck, E., Vandekerckhove, M., Pattyn, N., Bulckaert, A., Berckmans, D., et al., 2012. The influence of pre-sleep cognitive arousal on sleep onset processes. International Journal of Psychophysiology 83, 8–15.