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Reducing bedtime physiological arousal levels using immersive audio-visual respiratory bio-feedback: a pilot study in women with insomnia symptoms

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Abstract Hyperarousal is a critical component of insomnia, particularly at bedtime when individuals are trying to fall asleep. The current study evaluated the effect of a novel, acute behavioral experimental manipulation (combined immersive audio-visual relaxation and biofeedback) in reducing bedtime physiological hyperarousal in women with insomnia symptoms. After a clinical/adaptation polysomnographic (PSG) night, sixteen women with insomnia symptoms had two random-order PSG nights: immersive audio-visual respiratory bio-feedback across the falling asleep period (manipulation night), and no pre-sleep arousal manipulation (control night). While using immersive audio-visual respiratory bio-feedback, overall heart rate variability was increased and heart rate (HR) was reduced (by $\sim$ 5 bpm; $p < 0.01$), reflecting downregulation of autonomic pre-sleep arousal, relative to no-manipulation. HR continued to be lower during sleep, and participants had fewer awakenings and sleep stage transitions on the manipulation night relative to the control night ($p < 0.05$). The manipulation did not affect sleep onset latency or other PSG parameters. Overall, this novel behavioral approach targeting the falling asleep process emphasizes the importance of pre-sleep hyperarousal as a potential target for improving sleep and nocturnal autonomic function during sleep in insomnia.

Keywords Relaxation · Falling asleep · Insomnia · Biofeedback · Polysomnography · Heart rate variability

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Introduction

One-third of the general adult population complains of insomnia symptoms, while as a clinical disorder, insomnia has a prevalence of 6–10%, and is more common in women (Morin et al., 2006; Ohayon, 2002; Ohayon & Reynolds III, 2009). Insomnia is a major public health concern and an economic burden for individuals and society (Léger & Bayon, 2010), with growing data supporting insomnia as an independent risk factor for the development of severe mental (e.g. depressive disorders) (Baglioni et al., 2011; Riemann, 2007) and physical (e.g. cardiovascular diseases) (Sofi et al., 2014) conditions.

Insomnia can be broadly conceptualized within the theoretical framework of behavioral models like the 3P Spielman model, a widely accepted model viewing insomnia as resulting from the interaction among predisposing, precipitating and perpetuating factors. Predisposing factors include all biopsychosocial factors increasing the vulnerability to insomnia (e.g. the female sex, tendency to worry and rumination); the precipitating factors are acute events or stressor triggering the manifestation of insomnia (e.g. job loss), while the perpetuating factors refer to all the maladaptive behaviors, psychophysiological and environmental factors implicated in the chronicity of the disorder. Several other models exist and emphasize different aspects

of the disorder like cognitive alterations (intrusive thoughts, worry about sleep and rumination in the cognitive models) and/or neurobiological aspects of the disorder (e.g. neurocognitive and neurobiologic models). Still, there is not an exhaustive model of insomnia capturing the heterogeneity of the disorder (see Perlis et al., 2017). Across different models, a chronic abnormal state of heightened psychological (elevated worry, rumination, negative thoughts) and physiological (abnormal cortical and autonomic activity, elevated cerebral metabolism, raised inflammatory markers) arousal (i.e., *hyperarousal*) is proposed as a significant pathophysiological mechanism underlying the etiology of insomnia (Bonnet & Arand, 2010; Riemann et al., 2010).

Hyperarousal seems to be a constant trait of insomnia involving multiple psychophysiological domains (Bonnet & Arand, 2010; Riemann et al., 2010); however, a state level of hyperarousal exists and is magnified under insomnia-specific circumstances [e.g. when individuals are trying to sleep (Robertson et al., 2007)]. Insomnia sufferers show a pattern of elevated worry, rumination, and intrusive thoughts at bedtime (Harvey, 2000, 2002). They also show central nervous system (CNS) alterations including lower power in the electroencephalographic (EEG) low frequencies (e.g. lower delta activity) and higher power in the EEG high frequencies (e.g. higher beta activity) before sleep, and/or slower increases in EEG low frequency power and slower reductions in EEG high frequency power in the wake-to-sleep transition, compared to controls (Cervena et al., 2014; Freedman, 1986; Lamarche & Ogilvie, 1997; Merica & Gaillard, 1992; Staner et al., 2003). Autonomic nervous system (ANS) upregulation during the pre-sleep period in insomnia is supported by evidence of persistent cardiac sympathetic hyperactivation (de Zambotti et al., 2011) and elevated heart rate (HR) (de Zambotti et al., 2011, 2013, 2014; Farina et al., 2014). These data corroborate early studies in which physiological alterations (high frontalis and chin electromyographic activity, HR and respiratory rate, and lower finger temperature) in insomnia sufferers were evident before sleep and diminished as sleep approached (Freedman & Sattler, 1982).

From a clinical point of view, the centrality of hyperarousal in the pathophysiology of insomnia can have strong therapeutic implications. In fact, insomnia should not be exclusively viewed as a disorder in which sleep disruption is the primary symptom, but rather it should be viewed as a more complex disorder in which multiple systems are altered (hyperaroused), chronically and in response to insomnia specific circumstances (e.g. bedtime). The pre-sleep period is a critical time in which an individuals' psychophysiological state influences onset and maintenance of sleep. We and others have shown that pre-sleep manipulation using situational stressors (e.g. anticipatory psychosocial stress) increases pre-sleep arousal, impacting sleep and the recovery function of sleep in both healthy sleepers (de Zambotti et al., 2016; Hall et al., 2004) and insomnia sufferers (de Zambotti et al., 2016). Further, increasing pre-sleep cognitive arousal (induced cognitive load) delays sleep onset latency and results in increased CNS arousal during sleep (elevated relative EEG beta power) in healthy sleepers (Wuyts et al., 2012).

Few studies have investigated the effect of acute down-regulation of pre-sleep arousal on subsequent sleep. Sakakibara et al. (2013) reported that acute selective pre-sleep HR variability (HRV) bio-feedback (performed for about 20 min before bedtime) was effective in improving cardiorespiratory function during sleep in healthy young adults. Pre-sleep HRV bio-feedback also improved polysomnographic (PSG) sleep in healthy participants on their first night in the laboratory (reduced "first night effect") (Ebben et al., 2009). Pre-sleep imagery distraction (imagining interesting and engaging, but also pleasant and relaxing situations) was effective in reducing distress related to unwanted thoughts and shortened self-report sleep onset latency in university students with insomnia symptoms (Harvey & Payne, 2002). Critically, applying relaxation strategies before sleep is one of the elements of cognitive behavioral therapy for insomnia (CBTi), the recommended first line treatment for insomnia (Schutte-Rodin et al., 2008). CBTi has proven efficacy in reducing insomnia symptoms and improving sleep quality in insomnia sufferers, with greater efficacy than drug therapy, particularly when considering the sustained benefits (van Straten et al., 2017). Web-based CBTi approaches are growing and show effects comparable with traditional CBTi. The advantage of these methods is a cost reduction and increased treatment accessibility, compared to traditional face-to-face approaches (Zachariae et al., 2016). However, internet-based CBTi still requires multiple sessions and engagement from individuals, challenging treatment adherence. Thus, alternative behavioral treatment options should be investigated.

In the current pilot study, we investigated the effect of an acute direct manipulation of pre-sleep arousal on pre-sleep and sleep cardiac autonomic functioning, and PSG sleep macrostructure in women with insomnia symptoms. A novel approach using immersive, audio-visual, respiratory bio-feedback was used to reduce pre-sleep arousal levels. The novelty of the approach consists of creating an immersive and relaxing audio-visual experience at bedtime using a sleeping mask that provides audio and visual stimulation in co-ordination with respiratory bio-feedback control. This approach targets both cognitive and physiological hyperarousal: individuals are immersed in a peaceful scenario disconnected from current worry and rumination and cardiac effort is reduced and heart rate

variability is increased via slow diaphragmatic breathing, guiding individuals across the falling asleep period, from lights-off to the onset of sleep.

Methods

Participants

Sixteen women complaining of insomnia symptoms, participated in the study. Recruitment targeted women complaining of trouble sleeping in the San Francisco Bay Area community via local flyers, social media, and word of mouth. The study was reviewed and approved by SRI International's Institutional Review Board. All participants were informed about the purpose of the study and they gave written informed consent.

A phone screen was used to determine eligibility. Women were included if they self-reported prominent difficulty in falling asleep (all women but one reported typically spending more than 30 min to fall asleep) and/or maintaining sleep, with sleep difficulties occurring at least 3 times per week and for at least 1 month, and interfering with daytime functioning (e.g. fatigue, poor mood, difficulty in concentration). Six women were pre-menopausal (regular menstrual cycle with periods), six women were peri-menopausal (irregular menstrual cycles with periods becoming farther apart or closer together by more than 7 days), and 4 women were post-menopausal (periods had stopped completely for at least 1 year), according to the Stages of Reproductive Aging Workshop (STRAW) criteria (Soules et al., 2001).

Women were excluded if they currently used psychotropic (e.g. antidepressants, antipsychotics) and/or sleeping (e.g. hypnotics) medication, self-reported severe physical health (e.g. Diabetes) and/or mental health (e.g. depression) conditions, or reported sleep disorders other than insomnia (e.g. breathing-related and/or leg-movement related disorders). Absence of these disorders was confirmed with a clinical in-lab PSG evaluation (all women had an apnea–hypopnea index ≤ 5 and a periodic limb movement index ≤ 10).

Details about sample characteristics including demographics, self-reported sleep quality [Pittsburgh Sleep Quality Index, PSQI (Buysse et al., 1989)], bedtime cognitive intrusion [Glasgow Content of Thought Inventory, GCTI (Harvey & Espie, 2004)], insomnia severity [Insomnia Severity Index, ISI (Bastien et al., 2001)], symptoms of depression [Beck Depression Inventory, BDI-II (Beck et al., 1996)], anxiety [State-Trait Anxiety Inventory, STAI-Y2 (Spielberger et al., 1983)], general health and health related behaviors, are provided in Table 1.

Experimental design

This was an experimental within-subject design study conducted in the Human Sleep Research Laboratory at SRI International. After screening, eligible women had a laboratory clinical/adaptation overnight PSG recording to exclude the presence of sleep disorders other than insomnia (e.g. breathing and leg movement disorders) and to adapt women to the sleep lab environment and staff. Then, eligible participants were randomly assigned to either *pre-sleep arousal immersive, audio-visual, respiratory bio-feedback* (manipulation night) or *no pre-sleep manipulation* (control night) conditions. Six women had their manipulation night first (the order of nights was used as a factor in the analyses). On both nights, PSG signals including electrocardiogram (ECG) were continuously assessed.

Nights were scheduled on non-consecutive days (number of days between PSG nights, mean $\pm$ SD: 12.9 $\pm$ 10.1 days; $\pm$ 95% CI 7.5–18.3 days). Cycling women were studied irrespective of menstrual cycle phase. Before each night, participants were instructed to refrain from consuming alcohol or caffeine after 3 pm. Women arrived about 3 h before bedtime and were prepared for recordings. Lights-off and lights-on times were self-selected by participants based on their typical weekly routine. Participants slept in temperature-controlled and sound-attenuated bedrooms.

Pre-sleep immersive audio-visual respiratory bio-feedback

Participants were trained how to perform audio-visual respiratory bio-feedback during a brief ($\sim$ 10 min) training session when they first arrived in the laboratory on the manipulation night. The training sessions were delivered by a trained sleep lab research assistant, who followed a standardized script. The research assistant instructed the participants on how to perform slow diaphragmatic breathing and explained the basic bio-feedback control loop between breathing and audio-visual immersion. When participants began the audio-visual respiratory bio-feedback, the research assistant qualitatively checked if participants understood and were comfortable with the apparatus and the task. None of the women had trouble in using the audio-visual respiratory bio-feedback apparatus.

The apparatus consisted of a customized sleeping mask, which provided audio-visual immersion, and a smartphone placed on the abdomen, which detected respiration. Audio-visual stimulation was provided through Vuzix Wrap 1200VR Video Eyewear (16:9 widescreen head-mount display with 1280 $\times$ 720 resolution and an equivalent of 35 degrees field of view) embedded in the mask. The video

Table 1 Sample characteristics

	Mean (SD)	± 95% CI	Range (min–max)
Age (year)	43.44 (13.31)	36.34–50.53	22–60
Body Mass Index (kg m^{-2})	25.09 (3.96)	22.98–27.20	18.15–34.28
Race			
Caucasian, No.	11/16		
Asian, No.	3/16		
Black, No.	2/16		
Hispanic, No.	2/16		
Sleep Quality (PSQI), total score	10.94 (3.04)	9.32–12.56	6–16
Bedtime cognitive intrusion (GCTI), total score	58.00 (9.96)	52.70–63.30	33–68
Insomnia symptoms			
Difficulty falling asleep (yes), No.	16/16		
Difficulty staying asleep (yes), No.	12/16		
Waking up early in the morning (yes), No.	8/16		
Insomnia Severity (ISI), total score	16.31 (4.39)*	13.97–18.65	8–23
Depressive symptoms (BDI-II), total score	8.19 (7.95)	3.95–12.42	0–26
Trait anxiety symptoms (STAI-Y2), total score	40.00 (9.85)	34.75–45.25	27–60
Perceived health and health related behaviors			
Health status (Likert scale: 1, "poor" to 5, "excellent")	3.88 (0.96)	3.36–4.39	2–5
Physical activity (days/week of > 30 min physically active)	3.44 (2.48)	2.12–4.76	0–7
Current smoker (yes), No.	2/16		
Caffeine Consumption, N cups/day	1.47 (1.18)	0.84–2.09	0–4
Alcohol consumption, N drinks (8 oz)/week	2.27 (3.88)	0.20–4.33	0–14
Blood pressure[a]			
Systolic blood pressure (mmHg)	113.08 (13.16)	106.06–120.09	85.00–136.50
Diastolic blood pressure (mmHg)	72.34 (10.52)	66.74–77.95	58.25–97.5

PSQI Pittsburgh Sleep Quality Index, *GCTI* Glasgow Content of Thought Inventory, *ISI* Insomnia Severity Index, *BDI* Beck Depression Inventory, *STAI* State-Trait Anxiety Inventory

[a]Sphygmomanometric blood pressure readings were taken on two different days in the evening lying in bed (blood pressure was taken three times on each visit; the first reading of each day was discharged, and the final value was obtained by averaging the other measurements)

*All women but one had a ISI total score ≥ 10, optimal cut-off for detecting insomnia cases in a community sample (Morin et al., 2011)

content consisted of an underwater high definition video exploring sea life, and the audio consisted of a classical music soundtrack (all participants received the same audio–video content). The closed loop control feedback mechanism consisted of changing the level of audio-visual immersion based on the participants' breathing pattern. From an initial no-feedback condition (blank screen and no audio stimulation) when breathing normally, participants were guided to reach an optimal audio-visual environment presented at a respiratory frequency of 0.1 Hz (6 breath per min). A schematic representation of the audio-visual respiratory bio-feedback under normal and slow breathing conditions is provided in Fig. 1.

The respiratory signal used for the biofeedback loop was obtained from an Android phone, placed on the individual's abdomen, through a customized algorithm that uses the Integrated Measurement Unit (IMU) sensor with accelerometers and gyroscopes to detect real-time breathing frequency via periodic abdomen motion patterns (see Liu et al., 2011).

On the manipulation night, participants began using the audio-visual respiratory bio-feedback apparatus at lights-out (beginning of the pre-sleep arousal manipulation). They could use it for as long as they wanted and did not have to remove the sleeping mask before falling asleep; according to the closed loop control feedback mechanism, when an individual fell asleep and breathing returned to a normal rate (faster than when performing respiratory bio-feedback), the audio-visual stimulation stopped (blank screen and no audio stimulation). On the control night, participants were told to follow their typical bedtime routine and received no manipulation.

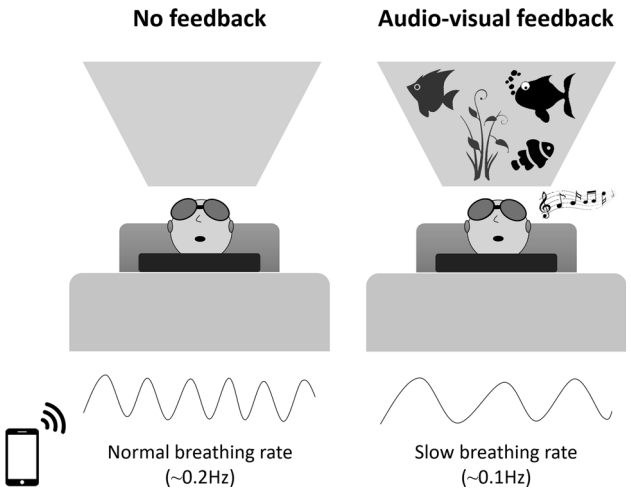


Fig. 1 Schematic representation of the audio-visual respiratory biofeedback apparatus operating under normal (no feedback) and slow (immersive audio-visual feedback) breathing conditions. Breathing rate was detected by a phone placed on the individual's abdomen

The general in-lab procedure is illustrated in Fig. 2.

Polysomnographic sleep assessment

Standard PSG included the measurement of electroencephalography (EEG; $F_{3/4}$, $C_{3/4}$, $O_{3/4}$ referenced to the contralateral mastoids), bilateral electrooculography (placed 1 cm lateral and below the outer canthus of left and right eyes) and submental electromyography according to American Academy of Sleep Medicine (AASM) criteria (Iber, 2007) using a Grael^{TM} system and Profusion PSG3^{TM} software (Compumedics, Abbotsford, Victoria, Australia). EEG signals were sampled at 256 Hz and band-pass 0.3–35 Hz filtered. PSG wake, and sleep stages N1, N2, N3, and REM were scored in 30 s epochs. Arousals ($\geq$ 3 s, $<$ 15 s) were marked according to AASM criteria (Iber, 2007). The following standard PSG parameters were calculated: total sleep time (TST, min), sleep onset latency (SOL, min; time from lights-out to the first epoch of any sleep stage), total amount of wake after sleep onset (WASO, min), time spent in N1, N2, N3 and REM sleep (calculated as a percentage of TST), sleep efficiency (SE, percentage of TIB spent asleep), awakening index (number of awakenings per hour of sleep; awakenings were counted as any transitions to a wake epoch from a sleep epoch of any stage across the night) and arousal index (number of arousals per hour of sleep), and fragmentation index (calculated as the proportion of the total number of sleep stage transitions including wake-to-sleep, sleep-to-wake, as well as transitions between stages of sleep, over the TIB).

Cardiac autonomic assessment

The ECG signal was collected at 512 Hz using Ag/AgCl Meditrace surface spot electrodes in a modified lead II Einthoven configuration. R-waves were automatically detected and manually adjusted when necessary and normal-to-normal interbeat-intervals (IBIs, ms) were calculated.

Frequency domain HRV analysis was performed on consecutive 2 min bins from lights off to the first epoch of sleep (pre-sleep–wake), and on artifact-free 2 min bins of NREM (N2 + N3) and REM sleep selected throughout the night according to modified rules described by Trinder et al. (2001). For each bin, IBIs were re-sampled (4 Hz) and 3rd order polynomial filtered to remove the slow non-stationary trend. Total power (TP, 0–0.5 Hz) was divided into 0.02 Hz bands and an algorithm found the highest value in the 0.03–0.15 Hz to identify the low frequency (LF) component, and in the 0.15–0.40 Hz to identify the high frequency (HF) component. Absolute integrated

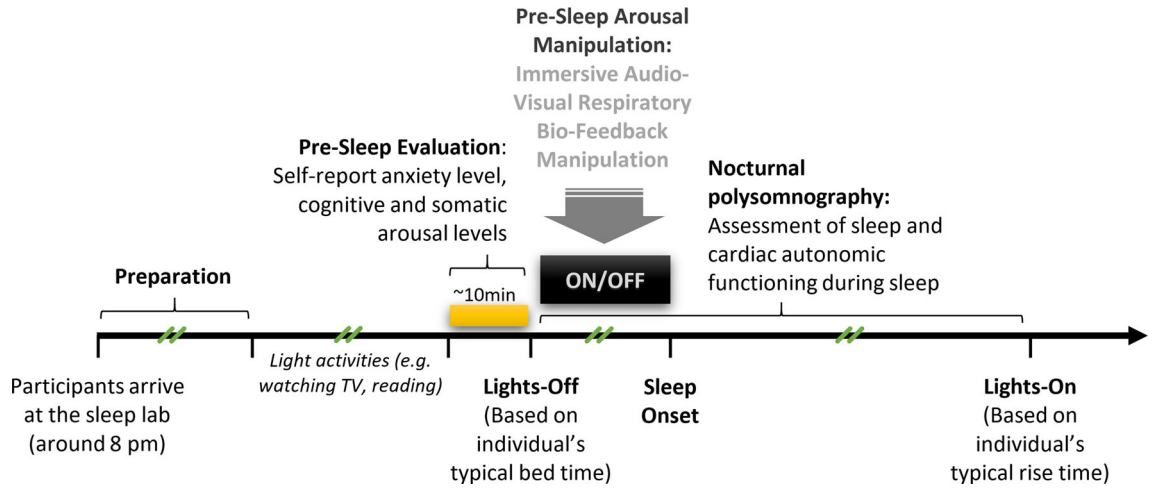


Fig. 2 Overview of the in-lab experimental procedure

power was quantified for LF and HF bands as the area between the first frequency bands on either side of the peak to fall to 50% of the peak value [see (2001) for details]. HR (bpm), absolute LF integrated power in the narrow band (LF_{na}, ms^2; though to reflect both sympathetic and vagal influences), absolute HF integrated power in the narrow band (HF_{na}, ms^2; an indicator of vagal activity), and total absolute integrated power (0.03–0.4 Hz, ms^2; a measure of total HRV), were calculated. TP, LF_{na}, HF_{na} have been log-transformed before analysis. The inclusion of LF allows measurement of the effect of slow breathing (targeting 0.1 Hz) on HRV within the expected low frequency range.

Statistical analyses

Paired t-tests were used to compare all measures between the manipulation and control nights. Repeated measure ANOVA models with 2 within *nights* (manipulation and control nights) × 2 within *sleep stages* (REM and NREM) were used to analyze nocturnal cardiac ANS measures. If significant, all models were then re-run by adding the dichotomous factor *order of nights* as a potential confounding factor.

All analyses were performed using STATISTICA 64 v13 (Dell Inc.) for Windows. Significance was set at $p < 0.05$ for all models. Values are reported as mean ± SD. On the significant ANOVA models, partial eta squared (η^2p) was reported as measures of effect size.

Results

Prior-night sleep and pre-manipulation arousal state

Upon arrival at the lab, on each recording night participants completed a questionnaire about their previous night's sleep. There were no differences in self-reported amount of total time slept and time spent awake over the prior-night between manipulation and control nights ($p > 0.05$).

Participants were also asked to rate their level of state anxiety [State-Trait Anxiety Inventory, STAI-Y1 (Spielberger et al., 1983)], and their cognitive and somatic arousal levels [Pre-Sleep Arousal Scale, PSAS (Nicassio et al., 1985)]. Ratings were similar on both nights (STAI-Y1 scores, control night: 35 ± 7; manipulation night: 34 ± 9; cognitive PSAS arousal scores, control night: 18 ± 4; manipulation night: 17 ± 4; somatic PSAS scores, control night: 11 ± 2; manipulation night: 11 ± 2) reflecting a similar arousal state at the laboratory admission, on both recording nights.

Pre-sleep ANS measures

On the manipulation night when women performed immersive audio-visual respiratory bio-feedback across the wake-to-sleep transition, compared to the control night, HRV TP ($t = -3.79$, $p = 0.002$) and LF power ($t = -4.60$, $p < 0.001$) were higher, and HR was lower by ~ 5 bpm ($t = 4.46$, $p < 0.001$; see Fig. 3) during the pre-sleep–wake period. Pre-sleep HRV HF power did not differ between manipulation and control nights.

PSG sleep and ANS functioning during sleep

PSG variables are shown in Table 2. Women had a lower awakening index ($p = 0.010$) and fewer sleep stage transitions (fragmentation index, $p = 0.008$), on the manipulation night compared to the control night. The results were still significant after adding the order of nights as a factor. None of the other PSG measures differed significantly between nights.

ANS variables are shown in Table 3. Women had a lower average HR in both NREM and REM sleep on the manipulation night relative to the control night (*nights* main effect: $F_{1,15} = 6.80$, $p = 0.020$, $\eta^2p = 0.31$; see Fig. 3). Results were still significant after controlling for the order of nights. None of the other variables (TP, LF_{na}, HF_{na}) showed *nights* main effects and/or *nights* × *sleep stage* interactions.

As expected, there was a *sleep stage* main effect for both HR ($F_{1,15} = 10.74$, $p = 0.005$, $\eta^2p = 0.42$) and HF_{na} ($F_{1,15} = 74.14$, $p < 0.001$, $\eta^2p = 0.83$) indicating higher HF_{na} (elevated vagal activity) and lower HR in NREM sleep compared to REM sleep.

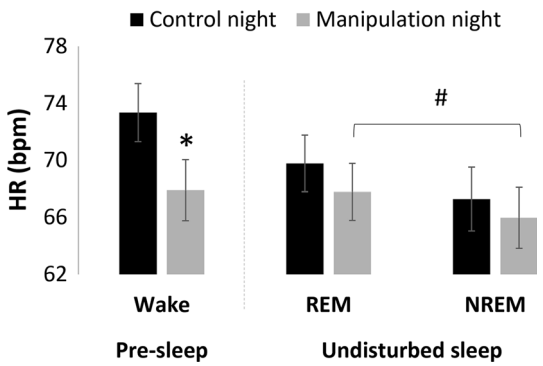


Fig. 3 Effect of an audio-visual respiratory bio-feedback manipulation (manipulation night) relative to no manipulation (control night) on heart rate (HR) during the pre-sleep–wake period and during undisturbed artifact- and arousal-free rapid-eye-movement (REM) and non-REM (NREM) sleep during the night in 16 women with insomnia symptoms. Error bars represent standard errors. * $p < 0.01$, compared to pre-sleep period on control night; # $p = 0.02$, compared to REM and NREM periods on control night (ANOVA main effect)

Table 2 Polysomnographic sleep measures on manipulation (immersive audio-visual respiratory biofeedback) and control nights in 16 women with insomnia symptoms

	Manipulation night		Control night		t value	*p* value
	Mean (SD)	± 95% CI	Mean (SD)	± 95% CI		
Lights-off (hh:mm)	23:38 (01:29)	22:51–00:26	23:26 (01:25)	22:40–00:12	− 1.38	0.188
Lights-on (hh:mm)	06:08 (01:20)	5:25–6:51	05:57 (01:00)	5:25–6:29	− 1.01	0.325
Time in bed (hh:mm)	06:30 (01:13)	5:51–7:08	06:32 (01:06)	5:56–7:07	0.14	0.892
Total sleep time (min)	341 (59)	310–372	342 (69)	306–379	0.08	0.940
Sleep efficiency (%)	88.1 (5.7)	8.5–9.1	87.2 (7.4)	83.2–91.1	− 0.64	0.534
Sleep onset latency (min)	24 (18)	14–33	20 (20)	10–30	− 0.98	0.343
Wake after sleep onset (min)	24 (17)	14–33	29 (23)	17–42	1.39	0.185
Time in N1 (%)	6.6 (3.5)	4.8–8.5	7.9 (5.0)	5.3–10.6	1.53	0.146
Time in N2 (%)	50.0 (9.7)	44.8–55.1	49.8 (8.3)	45.4–54.2	− 0.09	0.931
Time in N3 (%)	19.8 (9.1)	15.0–24.7	20.1 (7.9)	15.9–24.3	0.19	0.850
Time in REM (%)	23.6 (7.3)	19.7–27.5	21.9 (7.5)	17.9–25.9	− 1.31	0.209
Awakening index[a]	2.5 (1.0)	1.9–3.1	3.3 (1.5)	2.5–4.1	2.95	0.010
Arousal index[b]	7.8 (3.1)	6.1–9.4	9.8 (6.1)	6.5–13.0	1.69	0.112
Fragmentation index	0.25 (0.08)	0.21–0.30	0.30 (0.09)	0.25–0.35	3.03	0.008

REM rapid-eye-movement-sleep

[a]Number of awakenings per hour of sleep

[b]number of arousals per hour of sleep

Table 3 Autonomic measures during the pre-sleep, rapid-eye-movement (REM) sleep and non-REM (NREM) sleep periods on manipulation (immersive audio-visual respiratory biofeedback) and control nights in 16 women with insomnia symptoms

	Pre-sleep		REM sleep		NREM sleep	
	Mean (SD)	± 95% CI	Mean (SD)	± 95% CI	Mean (SD)	± 95% CI
HR (bpm)						
Manipulation night	67.9 (8.5)	63.4–72.5	67.8 (8.0)	63.5–72.1	66.0 (8.6)	61.4–70.5
Control night	73.4 (8.2)	69.0–77.7	69.8 (7.9)	65.6–74.0	67.3 (8.9)	62.5–72.0
HRV TP (log ms^2)						
Manipulation night	2.6 (0.5)	2.3–2.9	2.2 (0.5)	1.9–2.4	2.2 (0.4)	2.0–2.4
Control night	2.3 (0.6)	1.9–2.6	2.1 (0.5)	1.9–2.4	2.2 (0.5)	2.0–2.5
HRV LF_{na} (log ms^2)						
Manipulation night	2.1 (0.6)	1.7–2.4	1.5 (0.5)	1.2–1.7	1.3 (0.4)	1.1–1.5
Control night	1.5 (0.7)	1.1–1.9	1.4 (0.5)	1.2–1.7	1.3 (0.5)	1.1–1.6
Manipulation night	1.3 (0.6)	1.0–1.6	1.1 (0.5)	0.8–1.3	1.5 (0.5)	1.2–1.7
HRV HF_{na} (log ms^2)						
Control night	1.3 (0.7)	1.0–1.7	1.1 (0.6)	0.8–1.4	1.5 (0.5)	1.2–1.8

See text for details of significant effects. *HRV* heart rate variability, LF low frequency, *HF* high frequency, *na* narrow absolute

Discussion

This pilot study shows that immersive audio-visual respiratory bio-feedback applied across the wake-to-sleep transition was effective in lowering pre-sleep physiological arousal, as reflected by a lower HR and higher HRV, relative to no manipulation in women with insomnia symptoms. After falling asleep on the manipulation night, women continued to have a lower HR, reduced number of awakenings per hour of sleep and decreased sleep fragmentation, relative to the control night (no pre-sleep arousal manipulation). These pilot data suggest that when performing immersive audio-visual bio-feedback across the wake-to-sleep transition, women entered into sleep in a physiologically less aroused state (see Fig. 4), and that this state persisted during sleep.

The experimental manipulation had both an immediate effect during use and a prolonged effect during the night on

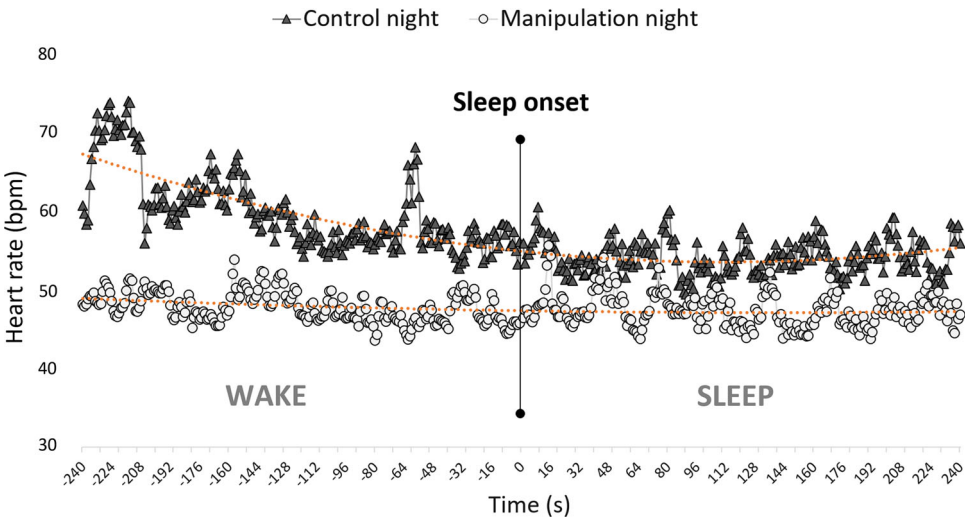


Fig. 4 Heart rate changes across the onset of sleep (4 min before and 4 min after), in a representative participant. The black triangles represent the beat-to-beat heart rate changes while the woman was normally falling asleep (control night), and the empty circles represent the heart rate changes while the same woman was continuously using audio-visual respiratory bio-feedback across the wake-to-sleep transition (manipulation night). In the latter, the woman was entering sleep in a "physiologically less aroused state"

HR. However, HRV changes were limited to the period when women performed bio-feedback in which the respiratory sinus arrhythmia (RSA; reflecting the oscillations of HR during the breathing cycle with increases in HR during inhalation and decreases in HR during exhalation) was maximized in response to slow breathing (Song & Lehrer, 2003). The increase in HRV LF with no change in HRV HF in response to direct audio-visual respiratory bio-feedback reflects the main effect of slowing one's breathing rate on the HRV spectrum within the LF range (the average peak frequency while performing slow breathing was 0.11 ± 0.01 Hz, falling within the 0.04–0.15 Hz LF range). In contrast, the effect on HRV of breathing under normal conditions is mainly evident in HF power measures, given that an individual's breathing rate normally lies within the HF range (0.15–0.40 Hz) (Krasnikov et al., 2013; Lehrer & Gevirtz, 2014; Song & Lehrer, 2003).

Importantly, differently from normal breathing conditions where RSA reflects cardiac vagal modulation, the increase in HRV and the reduction in HR under slow breathing frequencies does not necessarily result from an increase in vagal trafficking (Song & Lehrer, 2003). Lehrer and Gevirtz (2014) hypothesized that different processes are involved in the effect of HRV bio-feedback or respiratory bio-feedback on HRV, potentially including a phase relationship between HR oscillations with breathing as well as with blood pressure at different frequencies, baroreceptors, and the resonance proprieties of the cardiovascular system. With this in mind, HR is influenced by both sympathetic and vagal branches of the ANS, and sleep-dependent changes in HR are determined by both an increase in vagal tone and a reduction in tonic sympathetic activity across the night and in response to sleep stage changes (Baust & Bohnert, 1969; Trinder, 2007). Elevated HR (even if not always reaching a level of statistical significance) and cardiac sympathetic ANS, particularly in the pre-sleep period (de Zambotti et al., 2011), are evident in insomnia sufferers compared to healthy sleepers. In contrast, data supporting specific alterations in vagal-related HRV measures in insomnia are inconsistent (Dodds et al., 2017). Thus, it is possible that the "relaxation effect" of the immersive audio-visual respiratory bio-feedback may have contributed to inhibit the pronounced tonic sympathetic activation typical of insomnia. Sympathetic activity cannot be derived from HRV measures (see de Zambotti et al., 2018), therefore, further work is necessary to measure SNS activity [e.g. by using the pre-ejection period, a noninvasive measure inversely related to the cardiac SNS activity, derived from impedance cardiography (see de Zambotti et al., 2018)] in insomnia sufferers while using our approach to determine its acute effects during use as well as across the subsequent night.

Sakakibara et al. (2013) reported a significant increase in HF (vagal) components of HRV during the night following pre-sleep HRV bio-feedback in healthy sleepers, which we did not find. Possible reasons for the different findings between studies include the different populations studied (insomnia vs. good sleepers) and variations in methodology of the biofeedback manipulation. Also, in our study, the effective time participants performed the respiratory bio-feedback varied between participants (for most users, < 10 min) and was mainly determined by the time participants spent to fall asleep. In contrast, participants in the study of Sakakibara et al. (2013) performed HRV bio-feedback continuously for a relatively fixed time ($\sim$ 20 min) before their habitual bedtime. It is possible that the duration of the bio-feedback application and the timing, with respect to sleep onset, may have accounted for differences in HRV results across the night and could be a critical factor to explore in relation to bio-feedback-related outcomes.

Although we targeted the pre-sleep period, and the sample was recruited based on self-reported difficulties falling asleep, the pre-sleep manipulation did not lead to a reduction in SOL. Women spent, on average, < 30 min to fall asleep, even on the control night. This is in line with a meta-analysis of laboratory PSG-defined SOL in insomnia populations, which is reported to be, on average, < 30 min (Baglioni et al., 2014). Sleep in insomnia sufferers is highly variable, and this high night-to-night variability in PSG sleep patterns, in addition to the laboratory environment (see Edinger et al., 1997), may have masked the potential effect of the pre-sleep downregulation on SOL. Future work is needed to investigate the effect of this manipulation on sleep outside the laboratory environment, over multiple nights (to capture nights in which the sleep complaint may objectively manifest, as well as potential oscillations in pre-sleep arousal levels), and also considering self-report assessments of sleep quality and measures other than PSG. Although SOL was not affected, there was some improvement in aspects of PSG sleep consolidation after using the intervention (manipulation night), with participants having fewer awakenings and less sleep stage transitions relative to the control night. These findings are similar to those of Ebben et al. (2009) who employed 20 min of HRV bio-feedback before bedtime in healthy sleepers. They found no impact of the HRV bio-feedback device on SOL, but an overall improvement in sleep quality (as evaluated by a composite scale including different PSG outcomes: SE, REM latency, N1 sleep, and WASO) on a single night of use of the device. Possibly, lowering pre-sleep ANS arousal is a mechanism for leading to a more consolidated sleep, however, since our manipulation also targeted cognitive arousal (using an audio-visual relaxing environment), we cannot isolate the mechanism for the improvements in ANS function and sleep. Repetto et al. (2013) used virtual immersion in conjunction with, or without, bio-feedback (the target parameter for the feedback loop was HR), in the treatment of individuals with generalized anxiety disorder. Interestingly, both applications resulted in pre-post session reductions in HR and state anxiety, but the effects were greater in the virtual immersion bio-feedback group. Further work is needed that separates the components of the manipulation (slow diaphragmatic breathing, immersive audio-visual experience, biofeedback control) to determine how the single and combined components are implicated in lowering hyperarousal and improve sleep consolidation.

A novel aspect of our approach relies on the use of virtual immersion. The use of a pleasant immersive audio-visual scenario and blocking external stimulation is based on the rationale that by immersing individuals with insomnia in a relaxing virtual environment would help them to disconnect from the current environment (bring them away from worry and rumination), overall improving their cognitive relaxation. The addition of a respiratory bio-feedback component allows maintenance of a passive engagement with the virtual environment and further enhances ANS relaxation across the entire wake-to-sleep transition. Whether a fully immersive virtual reality system (e.g. head mounted display) could really "encapsulate" a person in a novel, virtual environment by completely eliminating the actual surroundings (allowing a person to believe they are falling asleep in a virtual dimension), is still an open question.

In the current study, several limitations need to be mentioned. The lack of a comparison group of women without insomnia symptomatology (controls) prevented important between-group comparisons about the presence and quantification of pre-sleep hyperarousal. Also, while the women in our study all reported significant insomnia symptoms, they did not receive a clinical diagnosis of the disorder. Further studies are needed to assess the effect of a pre-sleep arousal manipulation in a sample with a formal clinical diagnosis of insomnia disorder, and considering factors reflecting both chronicity (e.g. length of the disorder) and severity (e.g. severity of daytime dysfunction, objective quantification of sleep impairment), as well as demographics (e.g. age, gender). We did not control for menstrual cycle phase in cycling women, which may have confounded the within-night comparisons due to the associations of menstrual cycle phases with sleep (de Zambotti et al., 2015) and ANS function alterations during sleep (de Zambotti et al., 2017). The lack of control conditions where components of hyperarousal (e.g. cognitive vs. somatic) could be selectively manipulated (e.g. using respiratory bio-feedback or virtual immersion only) did not allow us to quantify the potential effect of selective cognitive and somatic downregulation on sleep and ANS function during sleep. Future work should investigate the effect of the manipulation in comparison with active controls. Also, the implementation of the proposed selective pre-sleep arousal downregulation within a multiple sessions treatment protocol (see Cortoos et al., 2010, for an example) may ultimately be able to unveil the clinical effectiveness of the intervention. Overall, this pilot study emphasizes the importance of the sleep onset process in the context of hyperarousal and insomnia symptoms, as a potentially critical window for intervention that deserves further attention.

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Compliance with ethical standards

Conflict of interests Massimiliano de Zambotti, Fiona C. Baker, and Ian M. Colrain have received research funding unrelated to this work from Fitbit Inc., Ebb Therapeutics Inc., and International Flavors & Fragrances Inc. Mikhail Sizintsev, Stephanie Claudatos and Giacinto Barresi declared no conflict of interest.

Human and animal rights and informed consent All procedures followed were in accordance with ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients for being included in the study.

References

Baglioni, C., Battagliese, G., Feige, B., Spiegelhalder, K., Nissen, C., Voderholzer, U., et al. (2011). Insomnia as a predictor of depression: A meta-analytic evaluation of longitudinal epidemiological studies. *Journal of Affective Disorders, 135*(1–3), 10–19.

Baglioni, C., Regen, W., Teghen, A., Spiegelhalder, K., Feige, B., Nissen, C., et al. (2014). Sleep changes in the disorder of insomnia: A meta-analysis of polysomnographic studies. *Sleep Medicine Reviews, 18*(3), 195–213.

Bastien, C., Vallières, A., & Morin, C. (2001). Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Medicine, 2*(4), 297–307.

Baust, W., & Bohnert, B. (1969). The regulation of heart rate during sleep. *Experimental Brain Research, 7*(2), 169–180.

Beck, A., Steer, R., & Brown, G. (1996). *Beck depression inventory-II (BDI-II)*. San Antonio, TX: Psychological Corporation.

Bonnet, M., & Arand, D. (2010). Hyperarousal and insomnia: State of the science. *Sleep Medicine Reviews, 14*(1), 9–15.

Buysse, D., Reynolds, C., III, 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.

Cervena, K., Espa, F., Perogamvros, L., Perrig, S., Merica, H., & Ibanez, V. (2014). Spectral analysis of the sleep onset period in primary insomnia. *Clinical Neurophysiology, 125*(5), 979–987.

Cortoos, A., De Valck, E., Arns, M., Breteler, 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 and Biofeedback, 35*(2), 125–134.

de Zambotti, M., Cellini, N., Baker, F., Colrain, I., Sarlo, M., & Stegagno, L. (2014). Nocturnal cardiac autonomic profile in young primary insomniacs and good sleepers. *International Journal of Psychophysiology, 93*(3), 332–339.

de Zambotti, M., Covassin, N., De Min, T. G., Sarlo, M., & Stegagno, L. (2011). Sleep onset and cardiovascular activity in primary insomnia. *Journal of Sleep Research, 20*(2), 318–325.

de Zambotti, M., Covassin, N., Sarlo, M., De Min, T. G., Trinder, J., & Stegagno, L. (2013). Nighttime cardiac sympathetic hyperactivation in young primary insomniacs. *Clinical Autonomic Research, 23*(1), 49–56.

de Zambotti, M., Sugarbaker, D., Trinder, J., Colrain, I., & Baker, F. (2016). Acute stress alters autonomic modulation during sleep in women approaching menopause. *Psychoneuroendocrinology, 66,* 1–10.

de Zambotti, M., Trinder, J., Colrain, I., & Baker, F. (2017). Menstrual cycle-related variation in autonomic nervous system functioning in women in the early menopausal transition with and without insomnia disorder. *Psychoneuroendocrinology, 75,* 44–51.

de Zambotti, M., Trinder, J., Silvani, A., Colrain, I., & Baker, F. C. (2018). Dynamic coupling between the central and autonomic nervous systems during sleep: A review. *Neuroscience and Biobehavioral Reviews, 90,* 84–103. https://doi.org/10.1016/j.neubiorev.2018.03.027

de Zambotti, M., Willoughby, A. R., Sassoon, S. A., Colrain, I. M., & Baker, F. C. (2015). Menstrual cycle-related variation in physiological sleep in women in the early menopausal transition. *Journal of Clinical Endocrinology and Metabolism, 100*(8), 2918–2926.

Dodds, K. L., Miller, C. B., Kyle, S. D., Marshall, N. S., & Gordon, C. J. (2017). Heart rate variability in insomnia patients: A critical review of the literature. *Sleep Medicine Reviews, 33,* 88–100.

Ebben, M., Kurbatov, V., & Pollak, C. (2009). Moderating laboratory adaptation with the use of a heart-rate variability biofeedback device (StressEraser). *Applied Psychophysiology and Biofeedback, 34*(4), 245–249.

Edinger, J., Fins, A., Sullivan, R., Jr., Marsh, G., Dailey, D., Hope, T., et al. (1997). Sleep in the laboratory and sleep at home: Comparisons of older insomniacs and normal sleepers. *Sleep, 20*(12), 1119–1126.

Farina, B., Dittoni, S., Colicchio, S., Testani, E., Losurdo, A., Gnoni, V., et al. (2014). Heart rate and heart rate variability modification in chronic insomnia patients. *Behavioral Sleep Medicine, 12*(4), 290–306.

Freedman, R. (1986). EEG power spectra in sleep-onset insomnia. *Electroencephalography and Clinical Neurophysiology, 63*(5), 408–413.

Freedman, R., & Sattler, H. (1982). Physiological and psychological factors in sleep-onset insomnia. *Journal of Abnormal Psychology, 91*(5), 380–389.

Hall, M., Vasko, R., Buysse, D., Ombao, H., Chen, Q., Cashmere, J., et al. (2004). Acute stress affects heart rate variability during sleep. *Psychosomatic Medicine, 66*(1), 56–62.

Harvey, A. (2000). Pre-sleep cognitive activity: A comparison of sleep-onset insomniacs and good sleepers. *British Journal of Clinical Psychology, 39,* 275–286.

Harvey, A. (2002). A cognitive model of insomnia. *Behaviour Research and Therapy, 40*(8), 869–893.

Harvey, K., & Espie, C. (2004). Development and preliminary validation of the Glasgow Content of Thoughts Inventory (GCTI): A new measure for the assessment of pre-sleep cognitive activity. *British Journal of Clinical Psychology, 43*(Pt 4), 409–420.

Harvey, A., & Payne, S. (2002). The management of unwanted pre-sleep thoughts in insomnia: Distraction with imagery versus general distraction. *Behaviour Research and Therapy, 40*(3), 267–277.

Iber, C. (2007). *The AASM manual for the scoring of sleep and associated events: Rules, terminology and technical specifications*. Darien: American Academy of Sleep Medicine.

Krasnikov, G., Tyurina, M., Tankanag, A., Piskunova, G., & Chemeris, N. (2013). Analysis of heart rate variability and skin blood flow oscillations under deep controlled breathing. *Respiratory Physiology & Neurobiology, 185*(3), 562–570.

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.

Léger, D., & Bayon, V. (2010). Societal costs of insomnia. *Sleep Medicine Reviews, 14*(6), 379–389.

Lehrer, P. M., & Gevirtz, R. (2014). Heart rate variability biofeedback: How and why does it work? *Frontiers in Psychology, 5,* 756.

Liu, G.-Z., Guo, Y.-W., Zhu, Q.-S., Huang, B.-Y., & Wang, L. (2011). Estimation of respiration rate from three-dimensional acceleration data based on body sensor network. *Telemedicine and E-Health, 17*(9), 705–711.

Merica, H., & Gaillard, J. (1992). The EEG of the sleep onset period in insomnia: A discriminant analysis. *Physiology & Behavior, 52*(2), 199–204.

Morin, C. M., Belleville, G., Bélanger, L., & Ivers, H. (2011). The Insomnia Severity Index: Psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep, 34*(5), 601–608.

Morin, C., LeBlanc, M., Daley, M., Gregoire, J., & Mérette, C. (2006). Epidemiology of insomnia: Prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. *Sleep Medicine, 7*(2), 123–130.

Nicassio, P., Mendlowitz, D., Fussell, J., & Petras, L. (1985). The phenomenology of the pre-sleep state: The development of the pre-sleep arousal scale. *Behaviour Research and Therapy, 23*(3), 263–271.

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

Ohayon, M. M., & Reynolds, C. F., III. (2009). Epidemiological and clinical relevance of insomnia diagnosis algorithms according to the DSM-IV and the International Classification of Sleep Disorders (ICSD). *Sleep Medicine, 10*(9), 952–960.

Perlis, M. L., Ellis, J. G., Kloss, J. D., & Riemann, D. W. (2017). Chapter 82—Etiology and pathophysiology of insomnia. In M. Kryger, T. Roth, & W. C. Dement (Eds.), *Principles and practice of sleep medicine* (6th ed., pp. 769–784). Amsterdam: Elsevier.

Repetto, C., Gaggioli, A., Pallavicini, F., Cipresso, P., Raspelli, S., & Riva, G. (2013). Virtual reality and mobile phones in the treatment of generalized anxiety disorders: A phase-2 clinical trial. *Personal and Ubiquitous Computing, 17*(2), 253–260.

Riemann, D. (2007). Insomnia and comorbid psychiatric disorders. *Sleep Medicine, 8,* S15–S20.

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*(1), 19–31.

Robertson, J., Broomfield, N., & Espie, C. (2007). Prospective comparison of subjective arousal during the pre-sleep period in primary sleep-onset insomnia and normal sleepers. *Journal of Sleep Research, 16*(2), 230–238.

Sakakibara, M., Hayano, J., Oikawa, L., Katsamanis, M., & Lehrer, P. (2013). Heart rate variability biofeedback improves cardiorespiratory resting function during sleep. *Applied Psychophysiology and Biofeedback, 38*(4), 265–271.

Schutte-Rodin, S., Broch, L., Buysse, D., Dorsey, C., & Sateia, M. (2008). Clinical guideline for the evaluation and management of chronic insomnia in adults. *Journal of Clinical Sleep Medicine, 4*(5), 487–504.

Sofi, F., Cesari, F., Casini, A., Macchi, C., Abbate, R., & Gensini, G. (2014). Insomnia and risk of cardiovascular disease: A meta-analysis. *European Journal of Preventive Cardiology, 21*(1), 57–64.

Song, H., & Lehrer, P. (2003). The effects of specific respiratory rates on heart rate and heart rate variability. *Applied Psychophysiology and Biofeedback, 28*(1), 13–23.

Soules, M., Sherman, S., Parrott, E., Rebar, R., Santoro, N., Utian, W., et al. (2001). Executive summary: Stages of reproductive aging workshop (STRAW). *Climacteric, 4*(4), 267–272.

Spielberger, C., Gorsuch, R., Lushene, R., Vagg, P., & Jacobs, G. (1983). *Manual for the state-trait anxiety inventory: STAI (Form Y)*. Palo Alto: Consulting Psychologists Press.

Staner, L., Cornette, F., Maurice, D., Viardot, G., Le Bon, O., Haba, J., et al. (2003). Sleep microstructure around sleep onset differentiates major depressive insomnia from primary insomnia. *Journal of Sleep Research, 12*(4), 319–330.

Trinder, J. (2007). Cardiac activity and sympathovagal balance during sleep. *Sleep Medicine Clinics, 2*(2), 199–208.

Trinder, J., Kleiman, J., Carrington, M., Smith, S., Breen, S., Tan, N., et al. (2001). Autonomic activity during human sleep as a function of time and sleep stage. *Journal of Sleep Research, 10*(4), 253.

van Straten, A., van der Zweerde, T., Kleiboer, A., Cuijpers, P., Morin, C., & Lancee, J. (2017). Cognitive and behavioral therapies in the treatment of insomnia: A meta-analysis. *Sleep Medicine Reviews, 38,* 3–16.

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*(1), 8–15.

Zachariae, R., Lyby, M., Ritterband, L., & O'Toole, M. (2016). Efficacy of internet-delivered cognitive-behavioral therapy for insomnia-A systematic review and meta-analysis of randomized controlled trials. *Sleep Medicine Reviews, 30,* 1–10.

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