Sai Sailesh Kumar Goothy* and Jason McKeown

Modulation of sleep using electrical vestibular nerve stimulation prior to sleep onset: a pilot study

https://doi.org/10.1515/jbcpp-2020-0019
Received February 9, 2020; accepted June 20, 2020;
published online October 5, 2020

Abstract

Objectives: Electrical stimulation of the vestibular system (VeNS) has been shown to improve Insomnia Severity Index (ISI) when delivered during sleep. We hypothesize that repeated electrical vestibular stimulation, when delivered prior to sleep onset, will improve ISI scores. The primary aim of this study was to assess the effect that VeNS had on ISI scores when delivered prior to sleep onset. A secondary aim was to provide initial data indicating "length of time to effect" that will allow more appropriate design of a larger randomized control trial (RCT).

Methods: The present study was an experimental study (pre and post without control). The participants acted as self-controls. After recording the baseline values, electrical vestibular nerve stimulation was administered as intervention once in a day for 30 min, 1 h prior to sleep onset using ML1000 device (Neurovalens, UK) for 14 days.

Results: There was significant decrease in the ISI scores followed by the electrical vestibular nerve stimulation. Further, participants reported a significant increase in well-rested sleep post the intervention period.

Conclusions: This study supports our hypothesis that VeNS has a positive impact on ISI scores when delivered on a regular basis prior to sleep onset.

Keywords: insomnia; sleep; vestibular stimulation.

***Corresponding author: Sai Sailesh Kumar Goothy**, PhD Medical Physiology, Associate Professor, Department of Physiology, R.D Gardi Medical College, Ujjain, Madhya Pradesh, India, Phone: +91 7382075279, E-mail: dr.saisailesh@gmail.com, https://orcid.org/0000-0002-5838-3994

Jason McKeown, Center for Brain and Cognition, UC San Diego, San Diego, USA; Wellcome-Wolfson Institute for Experimental Medicine, Queen's University Belfast, Belfast, UK; and Neurovalens Ltd., Belfast, UK, E-mail: jmckeown@ucsd.edu

Introduction

Sleep is defined as a natural state of unconsciousness where some of the body functions are active and some are inactive. In fact, sleep is essential for homeostasis and lack of sleep leads to adverse effects on body systems [1]. Sleep loss leads to increases day time sleepiness, depression, mood disorders and decline in the cognitive functions [2]. Further, deprivation of sleep was reported to impair the glucose metabolism and decrease insulin sensitivity which increases the incidence of diabetes [3]. It was reported that 50–70 million Americans chronically suffer from sleep disorders [1]. Though pharmacotherapy is effective in the management of sleep problems, it is often associated with adverse effects like decline in memory, drowsiness, fatigue and even decreased quality of life [4–6].

Therefore, alternative approaches that improve sleep without the use of pharmacotherapy may prove beneficial. The vestibular apparatus is a membranous structure located within the bony labyrinth of the inner ear. It comprises three semicircular canals and two otolith organs on either side. Changes in the rate of linear motion are detected by otolith organs and rotatory or angular acceleration or deceleration is detected by semicircular canals. The vestibular system also contributes to a wide range of functions from level of reflexes to level of cognition and coordination. Given this multi-function integration, the vestibular feedback is often referred to as the sixth sense [8]. It is widely accepted that the vestibular system plays an important role in sleep, particularly when rocking is administered to infants to induce sleep and for calming effects. Further, vestibular stimulation was proven to improve sleep in individuals with weakness of respiratory muscles [7]. Rocking produces relaxation effect that contributes to reduction in the latency of sleep onset and also improves the quality of sleep. Vestibular stimulation may cause both sleep and arousal depending on speed of stimulation [9]. High-speed vestibular stimulation induces wakefulness and lower speed induces sleep, respectively, [10]. Recent research reported that natural vestibular stimulation decreases sleep latency and speed up the transition from wakefulness to sleep [11].

Recent experiments have identified prominent vestibular pathways that project into multiple sleep and circadian-regulating nuclei of the brainstem and hypothalamus. Electrical stimulation of the vestibular system (VeNS) has been shown to improve Insomnia Severity Index (ISI) when delivered during sleep [12]. We hypothesize that repeated electrical vestibular stimulation, when delivered prior to sleep onset, will improve ISI scores. The primary aim of this study was to assess the effect that VeNS had on ISI scores when delivered prior to sleep onset. A secondary aim was to provide initial data indicating "length of time to effect" that will allow more appropriate design of a Randomized Control Trial (RCT).

Materials and methods

Study participants: 20 adults were part of the study after obtaining the written informed consent. The following criteria were used in recruiting the participants.

Inclusion criteria

(1) Adults
(2) Both genders
(3) Self-reported chronically disrupted sleep
(4) Score of eight or greater in the insomnia severity index questionnaire
(5) Willingness to participate in the study.

Exclusion criteria

(1) Use sleep medication
(2) Ear problems
(3) Under any kind of treatment
(4) Practicing sleep improving techniques
(5) Any other significant health-related problems.

Study design

The present study was an experimental study (before and after without control). The participants acted as self-controls. After recording the baseline values, electrical vestibular nerve stimulation was administered as intervention once in a day for 30 min, 1 h prior to sleep onset using ML1000 device (Neurovalens, UK) for 14 days.

Study setting

The study was conducted at Neurovalens lab, UK.

Electrical vestibular nerve stimulation

Bilateral application of electrical vestibular nerve stimulation (VeNS) using battery-powered vestibular nerve stimulator (ML1000, Neurovalens, UK) was practiced [13]. Insomnia Severity Index (ISI) score: ISI is a standardized, self-reported questionnaire to assess the nature, severity and impact of insomnia [14] (see Figure 1).

Self-rated assessment of "next day restfulness"

Participants were asked to score how "well rested" they felt on a scale of 0 (not at all rested) to 4 (very well rested).

Statistical analysis

Data were analyzed using SPSS 20.0. Probability value less than 0.05 was considered as significant.

Ethical consideration

Appropriate ethical consideration was taken following assessment based on guidance by the Central Office for Research Ethics Committees (COREC) and amended by the National Research Ethics Service (NRES) of the Health Research Association (UK). Confidentiality of data was maintained as per the regulations.

Results

Figure 4 displays the mean subjective score of "how well rested" the participants felt on a daily basis. Baseline was recorded for 14 days, with daily VeNS delivery for a further 14 days. Self-reported feeling of next day "restfulness" (range 0–4) was calculated at 1.6 (SD 0.63) for baseline, with and increase to 2.01 (SD 0.79) by during Week 1 and

Figure 1: Battery-powered vestibular nerve stimulator (ML1000, Neurovalens, UK).

2.67 (SD 0.56) during Week 2. No significant adverse events were reported.

ISI scores for all 20 participants

Figure 2 shows the mean ISI scores for all 20 participants taken at Day 0 and again at Day 14.95% confidence intervals are displayed. Mean baseline ISI was calculated as 15.7 (SD 4.7) (moderate insomnia). Repeat ISI score, after 14 days of VeNS sessions, was calculated at 8.15 (SD 3.6) (subclinical insomnia). This result was statistically significant ($p<0.00001$).

ISI distribution against insomnia subcategories

Figure 3 displays the ISI distribution against insomnia subcategories as recorded at Day 0 and again at Day 14.

Mean subjective score of "how well rested" the participants felt on a daily basis

Figure 3 displays the mean subjective score of "how well rested" the participants felt on a daily basis. Baseline was recorded for 14 days, with daily VeNS delivery for a further 14 days. Self-reported feeling of next day "restfulness" (range 0–4) was calculated at 1.6 (SD 0.63) for baseline, with and increase to 2.01 (SD 0.79) by during Week 1 and 2.67 (SD 0.56) during Week 2. No significant adverse events were reported.

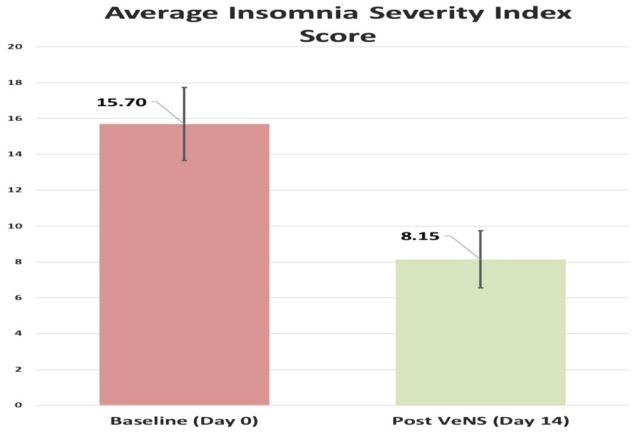

Figure 2: ISI scores for all 20 participants. This graph shows the mean ISI scores for all 20 participants taken at Day 0 and again at Day 14.95% confidence intervals are displayed.

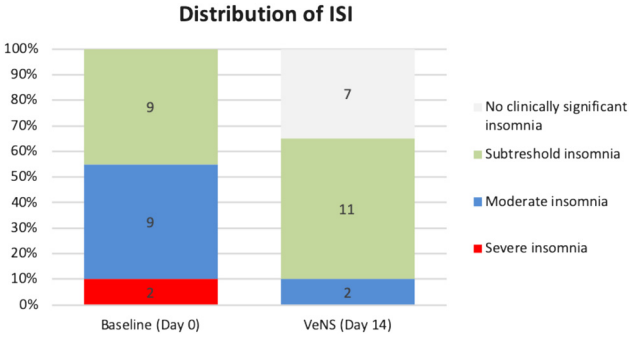

Figure 3: ISI distribution against insomnia subcategories. This chart displays the ISI distribution against insomnia subcategories as recorded at Day 0 and again at Day 14.

Discussion

Decreased sleep duration is a growing public health issue throughout the world [15]. Sleep deprivation has deleterious effects on physical and psychological health of and also decreases the attention and concentration [16]. Sleep deprivation also increases risk of daytime sleepiness and noncommunicable diseases like metabolic syndrome and psychiatric illness like depression [17].

Though the pharmacotherapy is effective in improving the sleep quality, but is associated with significant side effects [18]. This gap in the literature demands development of alternative therapies which are effective and have no side effects.

The primary aim of this study was to assess the effect that VeNS had on ISI scores when delivered prior to sleep onset. A secondary aim was to provide initial data indicating "length of time to effect" that will allow more appropriate design of an RCT. There was significant decrease in the ISI scores followed by the electrical vestibular nerve stimulation. Further, participant's self-reported feeling of being "well rested" showed a significant improvement following the intervention. Vestibular stimulation through rocking is well-known method to induce sleep in infants and also in adults in both healthy and disease conditions [19]. Vestibular stimulation offers relaxation which decreases the sleep latency. Also, as vestibular stimulation has been shown to be well tolerated, it may be incorporated in everyday life style [20]. It was reported that rapid eye movement bursts was observed in the electroencephalogram recordings followed by the rotational vestibular stimulation in normal adults [21]. Synchronization of brain wave activity was reported followed by the vestibular stimulation through rocking [22].

A recent animal study demonstrated that linear vestibular stimulation was effective in promoting sleep in

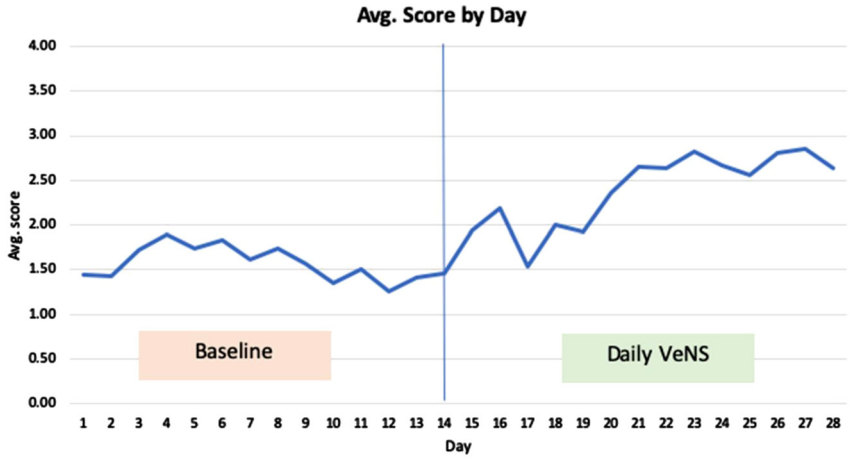

Figure 4: The mean subjective score of "how well rested" the participants felt on a daily basis. Baseline was recorded for 14 days, with daily VeNS delivery for a further 14 days.

mice [30]. The possible explanation for sleep promoting effect of vestibular stimulation may be due to modulation of sensory processing [23]. The action on vestibular stimulation on sleep may be a multi-modal effect acting on different areas of the brain responsible for sleep. The vestibular system has profound projections to the intergeniculate leaflet which influence the suprachiasmatic nucleus which is important nuclei in the retinohypothalamic tract [24, 25]. Increase in the secretion of serotonin from dorsal raphe nucleus was observed followed by the vestibular stimulation. The sleep promoting effects of serotonin are well documented [26]. The neurons of nucleus of tractus solitaries (NTS) showed burst of potentials followed by the vestibular stimulation [27]. Stimulating vestibular system activates hippocampus which influences REM sleep [28, 29, 31]. Gentle rocking movements were reported to ease the transition from wakefulness to sleep [30].The study results supports earlier studies as there was a significant sleep promoting effect observed followed by the electrical vestibular nerve stimulation.

In contrast, another study reported that no significant effect was observed on sleep quality followed by vestibular stimulation using rocking bed [29]. The possible reason may be activation of multiple receptors along with the vestibular system. Hence, it may be understood that the method of stimulation should be very specific that is it should stimulate specifically the vestibular system. Further, it is well noted in the earlier studies that optimal vestibular stimulation is essential to elicit a positive response. In the present study, the mode of stimulation used is electric vestibular nerve stimulation which specifically stimulates the vestibular nerve. Further, the intensity of the stimulation also is adjustable to offer the optimal stimulation.

Conclusions

This present study supports our hypothesis that VeNS has a positive impact on ISI scores when delivered on a regular basis prior to sleep onset. Therefore, we propose that the mechanism of action is more complex than that of a nonspecific rocking motion and may be secondary to the direct influence that the vestibular system has on the circadian pacemaker and other sleep-regulating nuclei in the brainstem. Although a subjective measurement, it was interesting to note that the feeling of "next day restfulness" appeared to improve significantly within the 2-week VeNS period. As a next step, detailed studies to better understand the underlying mechanism of action whereby VeNS improves ISI scores will be carried out. Further to this, a large, double-blind RCT will be used to assess the clinical efficacy of VeNS stimulation in the setting of clinical Insomnia (ISI 15 and above).

Research funding: None declared.
Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
Competing interests: The VeNS devices (ML1000) were provided to this study by Neurovalens Limited, Belfast, UK. Dr Jason McKeown is a co-founder & CEO of Neurovalens Limited. These data were originally presented via poster presentation at the British Sleep Society Annual Conference. Birmingham, 2019.
Informed consent: Informed consent was obtained from all individuals included in this study.
Ethical approval: Appropriate ethical consideration was taken following assessment based on guidance by the Central Office for Research Ethics Committees (COREC) and amended by the National Research Ethics Service (NRES) of

the Health Research Association (UK). Confidentiality of data was maintained as per the regulations.

References

1. NHLBI (National Heart, Lung, and Blood Institute). National sleep disorders research plan. Bethesda, MD: National Institutes of Health; 2003. 2003.
2. Dinges D, Rogers N, Baynard MD. Chronic sleep deprivation. In: Kryger MH, Roth T, Dement WC, editors Principles and practice of sleep medicine, 4th ed. Philadelphia: Elsevier/Saunders; 2005: 67–76.
3. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. Oct. Lancet 1999;354: 1435–9.
4. Roth AJ, Mccall WV, Liguori A. Cognitive, psychomotor and polysomnographic effects of trazodone in primary insomniacs. J Sleep Res 2011;20:552–8.
5. Poceta JS. Zolpidem ingestion, automatisms, and sleep driving: a clinical and legal case series. J Clini Sleep Med 2011;7:632–8.
6. Fitzgerald T, Vietri J. Residual effects of sleep medications are commonly reported and associated with impaired patient-reported outcomes among insomnia patients in the United States. Sleep Disord 2015;2015:607148.
7. Iber C, Davies SF, Mahowald MW. Nocturnal rocking bed therapy: improvement in sleep fragmentation in patients with respiratory muscle weakness. Sleep 1989;12:405–12.
8. Goldberg JM. The vestibular system: a sixth sense. Oxford; New York: Oxford University Press; 2012.
9. Horowitz SS, Blanchard J, Morin LP. Medial vestibular connections with the hypocretin (orexin) system. J Comp Neurol 2005;487:127–46.
10. Horner RL, Sanford LD, Pack AI, Morrison AR. Activation of a distinct arousal state immediately after spontaneous awakening from sleep. Brain Res 1997;778:127–34.
11. Bayer L, Constantinescu I, Perrig S, Vienne J, Vidal PP, Mühlethaler M, et al. Rocking synchronizes brain waves during a short nap. Curr Biol 2011;21:R461–462.
12. Zhang H. Therapeutic effectiveness and patient acceptance of a vestibular nerve activation intervention in chronic insomnia. Medicamundi 2010;54:89–93.
13. Sailesh Kumar Goothy S, Goothy S, Mckeown J. Electrical vestibular nerve stimulation for the management of tension headache. Asian J Pharmaceut Clin Res 2020;13:1–3.
14. Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med 2001;2:297–307.
15. Abdulghani HM, Alrowais NA, Bin-Saad NS, Al-Subaie NM, Haji AMA, Alhaqwi AI. Sleep disorder among medical students: relationship to their academic performance. Med Teach 2012;34: 37–41.
16. Giese M, Unternaehrer E, Brand S, Calabrese P, Holsboer-Trachsler E, Eckert A. The interplay of stress and sleep impacts BDNF level. PloS One 2013;8:e76050.
17. Giri P, Baviskar M, Phalke D. Study of sleep habits and sleep problems among medical students of pravara institute of medical sciences loni, Western Maharashtra, India. Ann Med Health Sci Res 2013;3:51–4.
18. Lieberman JA. Update on the safety considerations in the management of insomnia with hypnotics: incorporating modified-release formulations into primary care. Prim Care Companion J Clin Psychiatry 2007;9:25–31.
19. Iber C, Davies SF, Mahowald MW. Nocturnal rocking bed therapy: improvement in sleep fragmentation in patients with respiratory muscle weakness. Sleep 1989;12:405–12.
20. Woodward S, Tauber ES, Spielmann AJ, Thorpy MJ. Effects of otolithic vestibular stimulation on sleep. Sleep 1990;13:533–7.
21. Tauber ES, Handelman G, Handelman R, Weitzman ED. Vestibular stimulation during sleep in young adults. Arch Neurol 1972;27: 221–8.
22. Bayer L, Constantinescu I, Perrig S, Vienne J, Vidal PP, Mühlethaler M, et al. Rocking synchronizes brain waves during a short nap. Curr Biol 2011;21:R461–2.
23. De Gennaro L, Ferrara M. Sleep spindles: an overview. Sleep Med Rev 2003;7:423–40.
24. Omlin X, Crivelli F, Näf M, Heinicke L, Skorucak J, Malafeev A, et al. The effect of a slowly rocking bed on sleep. Sci Rep 2018;8:2156.
25. Jacob N, Vuillez P, Lakdhar-Ghazai N, Paul P. Does the intergeniculate leaflet play a role in the integration of the photo period by the suprachiasmatic nucleus?. Brain Res 1999;828: 83–90.
26. Snowball RK, Dampney RA, Lumb BM. Responses of neurons in the medullary raphe nuclei to inputs from visceral nociceptors and the ventrolateral periaqueductal gray in the rat. Exp Physiol 1997;82:485–500.
27. Sugiyama Y, Suzuki T, DeStefino VJ, Yates BJ. Integrative responses of neurons in nucleus tractus solitaries to visceral afferent stimulation and vestibular stimulation in vertical planes. Am J Physiol Regul Integr Comp Physiol 2011;301:1380–90.
28. Cuthbert P, Gilchrist DP, Hicks SL, MacDougall HG, Curthoys IS. Electro physiological evidence for vestibular activation of the Guinea pig hippocampus. Neuroreport 2000;11:1443–7.
29. Graf MV, J Kastin A. Delta sleep inducing peptide (DSIP): a review. Neurosci Biobehav Rev 1984;8:83–93.
30. van Sluijs R, Wilhelm E, Rondei Q, Omlin X, Crivelli F, Straumann D, et al. Gentle rocking movements during sleep in the elderly. J Sleep Res 2020:e12989. https://doi.org/10.1111/jsr.12989.
31. Kompotis K, Hubbard J, Emmenegger Y, Schwartz S, Bayer L, Paul F. Rocking promotes sleep in mice through rhythmic stimulation of the vestibular. Sys Current Biology 2019;29:392–401.