Therapeutic effectiveness and patient acceptance of a vestibular nerve activation intervention in chronic insomnia

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Defined as: “Complaints of disturbed sleep in the presence of adequate opportunity and circumstance for sleep”, insomnia is one of the most common presenting symptoms in the primary care setting [1, 2]. The disturbance may consist of one or more of three features:

• difficulty in initiating sleep
• difficulty in maintaining sleep
• waking up too early [3].

Insomnia can have a serious impact on work performance and maintaining healthy social relationships [4]. Chronic insomnia is differentiated from acute insomnia by individuals experiencing at least one of the symptoms described above for a minimum of 30 days [3].

Predictably, there has been a wealth of research in the areas of assessment and treatment for this sleep disorder, given the impact insomnia has been shown to have on mental and physical health and wellbeing [3-5]. Incidence rates are routinely around 9% of the general population, escalating to 30% for those who report occasional suffering [6]. Many individuals continue to report symptoms of insomnia for many years after initial onset [7]. Areas of particular interest to clinicians, health-care professionals and insomnia sufferers include implementation, acceptance and adherence to therapies that provide effective long-term management.

Conventional treatments include prescription medications (sedative-hypnotics), cognitive-behavioral therapy (CBT) and other alternative therapies (e.g. alcohol, herbal remedies and off-label use of other medicines) [3]. While sedative-hypnotics and CBT have been shown to be effective in the treatment of insomnia [3,8], expert opinion counsels against long-term use of sedative-hypnotics due to residual sedation, rebound insomnia, memory impairment, dependency and withdrawal difficulties [9, 10]. In addition, CBT is not easily accessed and patients frequently have difficulty adhering to the strict behavioral program that is typically prescribed [11]. A further area of concern is the limited evidence supporting the efficacy and safety of alternative therapies, despite their widespread use [3].

One promising approach to managing chronic insomnia is non-invasive mechanical vestibular nerve stimulation, which has been demonstrated to affect sleep [12-17]. The vestibular apparatus, in conjunction with visual and proprioceptive inputs, is responsible for maintaining balance under all conditions. Previous studies have used a mechanical rocking motion to induce vestibular activation, mimicking the sensation of infants being comforted by their parents. Improvements in sleep architecture and increased Total Sleep Time, Sleep Efficiency, Rapid Eye Movement and decreased Sleep Onset Latency have been demonstrated when using this technique [12-17].

A unique therapy, designed to non-invasively stimulate the vestibular nerve to promote sleep onset, has recently been developed. As an alternative to the rocking motion delivered by mechanical action, a swaying sensation is artificially created through mild electrical stimulation. Clinical studies have been previously conducted to investigate both the safety and efficacy of this medical device for the treatment of insomnia via a transient insomnia model, with positive outcomes [18, 19].

Individuals with chronic insomnia report similar issues in sleep disturbance to those in transient insomnia, but persistent in nature. Given the limitations of current effective therapies, and the recent emphasis on patient-centered care [20], there is an increasing need for an alternative treatment for insomnia symptoms. It has been shown that patient preference for non-pharmacological treatment was over three times greater than prescription medications [21]. Thus many would prefer a non-pharmaceutical approach if an effective one were available [11]. Vestibular nerve activation may provide such a treatment for chronic insomnia.
Design and methods

Objectives
An open-label trial, without control, of 30 days’ non-invasive vestibular nerve stimulation in adults with self-reported chronic insomnia was conducted in order to examine the acceptance and effectiveness of a novel medical device as a treatment for managing chronic insomnia symptoms.

Participants
Participants between 21 to 65 years of age who reported a history of chronic insomnia were recruited to the study. Excluded from the study were persons:
• taking medications, including over-the-counter or herbal medicines, which affected sleep/wake function (unless the medication was used to promote sleep)
• with unstable or untreated psychiatric illness
• with a diagnosis of, or highly likely to have, a sleep disorder that was unstable or untreated
• with pre-existing medical conditions contraindicated for vestibular nerve stimulation
• with any disorder initiating seizures
• with an electronic implanted device or hearing aid
• who were pregnant
• who were currently under going electrical monitoring
• with a history of falls, or who had previously participated in a vestibular nerve stimulation study.

All participants enrolled into the study provided informed, written consent.

The protocol was approved by the appropriate Institutional Review Board at each investigative site.

Intervention
Non-invasive electrical vestibular nerve stimulation was applied via the Philips SleepWave device (Figure 1). Stimulation was initiated by participants, as required, to expedite sleep onset. The stimulating electrode is shielded in an ear spiral fitted behind the ear. Once activated, each stimulation had a one-hour duration. The device was programmed to deliver a peak current from 0.1–1.0 mA at a frequency of 0.5 Hz.

Assessment and measures
Eligible participants were asked to complete a baseline sleep journal for one week prior to an orientation and training session, in order to determine baseline measurements before the commencement of the study. The sleep journal included self-reports pertaining to:
• time of sleep onset
• number of awakenings during night and the reason for this
• final time of awakening
• total sleep time and total time in bed.

Also explored were participants’ opinions of their waking state and energy levels for the previous day. These journals were to be completed on awakening to minimize recollection errors.

Orientation and training on the SleepWave were managed in two ways: at a central site, or remotely. All participants were encouraged to attend central sites, located in Pittsburgh, Chicago, Dallas, New York, and San Francisco. Completed baseline sleep journals were recovered where available. Participants completed a baseline questionnaire including demographic data, current sleep habits and the Insomnia Severity Index (ISI) [22]. The ISI is a seven-item questionnaire assessing the nature, severity, and impact of sleep difficulties for the preceding month. A Likert scale is used to rate each item, with a possible score between 0–28. Scores can be classified into 4 categories: absence of insomnia (0-7); sub-threshold insomnia (8-14); moderate insomnia (15-21) and severe insomnia (22-28). In addition to determining the baseline severity, the ISI is sensitive enough to measure treatment outcome [23].

Comprehensive training on operating the SleepWave was given. For those participants who did not attend one of the central sessions, a DVD training guide was provided and telephone support was offered in addition to the training materials.

Sleep journals were completed daily for the duration of the study. In addition, telephone interviews exploring experiences using the medical device were conducted on day 7 and day 14 of the study. An on-line questionnaire was provided as an alternative for participants who were unable to complete the interviews by telephone.

A final interview was held for all participants on completion of the 30-day study. These were held at the five central sites for the majority of participants. The final interview consisted of a questionnaire incorporating questions recorded in previous interviews which examined their sleep habits, frequency of device usage, and use of alternative interventions (medications or other) taken during the study. A post intervention ISI was also completed.
Adverse events
A 24/7 toll-free helpline number was provided to all participants for technical, medical or general issues during the study period. Previously reported adverse events using the SleepWave included headaches, nausea, dizziness, and skin irritation causing tingling, warmth or itching. No serious adverse events had been reported in previous studies [14, 15].

Results

Baseline data
In total, 105 participants were enrolled into the study. Five participants (all female) withdrew from the study within the first week of data collection. Of these, three reported an inability to tolerate treatment and two withdrew without giving a reason. Mean age at entry (n = 86) was 43.8 years (SD ± 10). Gender data were available for 91 participants (59/91 female), resulting in a 2:1 female: male ratio.

The majority (75/105) attended a face-to-face centrally conducted orientation and training session held at one of the five US city sites, with the remaining participants being instructed via telephone and a DVD training aid.

Seven-day baseline sleep journal data and ISI scores was collected from 43/105 and 89/105 respectively, confining our pre/post analysis to 41% and 85% of our sample population.

SleepWave intervention usage
Sleep journal data were available for 100 individuals. These data showed that the device was initiated once per night during 61% of the nights; twice per night during 11% of the nights; 3 or more times 4% of nights and not used at all during 24% of the total nights (n = 2525).

Outcomes
The primary outcome was evidenced by means of the ISI data sets at baseline and at 30 days post intervention (n = 89). Comparison of pre and post ISI scores using Wilcoxon Signed Ranks test (nonparametric) showed a statistically significant improvement in this study population (Mean(SD) 17.8(4.0) and 11.8(5.4) p<.001). Additionally, the insomnia severity distributions differed significantly between baseline and 30 days post intervention (Figure 2, McNemar Test, p< .001), showing a significant improvement in the group ISI scores pre-and post-intervention.

Secondary outcome measures of participant recorded and investigator calculated sleep variables demonstrated statistically significant improvement in sleep onset latency, total sleep time, wake after sleep onset and sleep efficiency was shown between baseline and 30 days (Table 1).

As baseline data limited the analysis of this study population, comparisons between subjects with and without baseline data was explored for recorded sleep onset latency measures to try to determine whether the reported improvement was comparable between groups. A mixed model was performed including those subjects with and without baseline data, and the repeated measures factor of time (weeks 1-4). No significant difference was observed between those with baseline data and those without (p=.983). Furthermore, there was no significant interaction between subject group and time (p=.933), suggesting that the change in sleep onset latency
It is important to note that this study employed a purely “as required” therapy regimen. Giving individuals complete autonomy to determine whether or not to activate the SleepWave resulted in variable use of the medical device by participants in this study. While it is common for prescription medication management to be of a fixed nightly dose, participants did not necessarily feel the need to use the device every night. This is possibly due to the waxing and waning nature of insomnia symptoms and appears to be beneficial compared to that of fixed dosing as it empowers individuals in managing their symptoms. This autonomy potentially provides a more realistic approach to insomnia management [24].

Although this study was open-label and without a control it has been suggested that: “optimal trial conditions (efficacy) misrepresents the real world (effectiveness) where variations in clinical skills, the intensity and duration of interventions, patient adherence, and local resources influence outcomes” [25]. Considering this, and the limitations in current treatments, a non-invasive “as required” treatment, such as the SleepWave medical device, may prove to be an effective solution.

Potential limitations of this study include the absence of sleep data derived by polysomnography; consequently, the findings are entirely reliant on subjective assessment. Also, the sub-sample population from which the study cohort was obtained and the resulting number of participants who provided complete data sets for analysis, may have created bias. A further limitation is the lack of a control group.

**Conclusions**

At study completion, all sleep parameters appeared to have improved significantly. Considering the ISI as a measure of treatment outcome, results over time did not differ significantly between participants with and without baseline data.

Of note, participants who were instructed remotely did not demonstrate a reduction in effectiveness of the SleepWave compared to those with face-to-face instruction when comparing pre and post ISI scores (p=.438). From this it appears that the participants were well motivated and the instruction via telephone and the DVD training aid was fully adequate.

### Adverse events

Two adverse events were reported to the study investigators. One participant experienced a petit mal seizure which did not occur while using the device but during the following day. This participant had a previous history of medical and psychiatric conditions that could not be excluded as the origin of the event.

The second adverse event reported was tinnitus-like symptoms. On further investigation this individual had concurrently undergone extensive dental treatment at the same time as entering the study. Therefore the cause of tinnitus could not be unequivocally attributed to device use.

Neither of the reported adverse events in this study are believed to be associated with the device, but as the study provided no control group, no comparison could be made. Both adverse events are currently being evaluated to determine conclusively that these events are not device-related.

**Discussion**

This study provides new evidence supporting vestibular nerve stimulation as a therapeutic intervention for chronic insomnia, with significant improvement in ISI mean scores and classifications, sleep onset latency, total sleep time, wake after sleep onset and sleep efficiency.

<table>
<thead>
<tr>
<th>Sleep measures</th>
<th>Baseline</th>
<th>Day 30</th>
<th>Day 30 - Baseline</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recorded Sleep onset latency (mins) †</td>
<td>46.6 ± 28.5 (40.8)</td>
<td>28.3 ± 21.1 (22.5)</td>
<td>-18.3 ± 22.1 (-17.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Recorded total sleep time (mins) †</td>
<td>376.9 ± 63.3 (378.8)</td>
<td>415.6 ± 62.2 (413.6)</td>
<td>38.7 ± 67.1 (42.0)</td>
<td>=.001</td>
</tr>
<tr>
<td>Calculated total sleep time (mins) π</td>
<td>371.5 ± 72.8 (373.7)</td>
<td>418.0 ± 65.0 (420.9)</td>
<td>46.5 ± 69.4 (44.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Recorded wake after sleep onset (mins) †</td>
<td>30.5 ± 21.9 (26.3)</td>
<td>13.2 ± 15.7 (9.3)</td>
<td>-17.3 ± 23.2 (-13.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Recorded sleep efficiency †</td>
<td>0.8 ± 0.1 (0.8)</td>
<td>0.9 ± 0.1 (0.9)</td>
<td>0.1 ± 0.1 (0.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Calculated sleep efficiency π</td>
<td>0.8 ± 0.1 (0.8)</td>
<td>0.9 ± 0.1 (0.9)</td>
<td>0.1 ± 0.1 (0.1)</td>
<td>&lt;.001</td>
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# For the majority of the endpoints, distributions of the paired differences exhibited a departure from the normality; therefore, change from baseline was assessed using the non-parametric Wilcoxon Signed Ranks test.
† Participant documented times in sleep journal.
π Investigator calculations from time stamps recorded by participants in sleep journals.
suggest that using the SleepWave as a form of therapy is effective in individuals with chronic insomnia symptoms. However, the subjective data on sleep and functioning needs to be supplemented by objective measures.

As insomnia is one of the most common presenting symptoms in the primary care setting, control and long-term management of symptoms is of great concern with a high economic burden [26]. This type of therapy could be valuable and well positioned in the Primary Health Care sector, as it does not appear to have the resource-intensive nature, risks and side effects of existing insomnia therapies.

References