Regulating Interoception Through Low Frequency Mechanical Dermal Stimulation to Improve Sleep

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Abstract— **More than 50 million adults living in the United States suffer from disordered sleep. Yet few safe, effective, drug-free interventions are available. In this 30-day open-label home study, participants (n=25) reporting poor sleep were recruited to test a novel wearable mechanical stimulation device. The device is designed to modulate the interoceptive network by producing gentle, slow mechanical stimulation. After using the device each night before bed for 30 days, significant improvements in sleep quality were reported. Additionally, participants reported improvements across multiple dimensions of interoception as measured by the Multidimensional Assessment for Interoceptive Awareness. On average, participants (n=22) reported a 43% improvement in the overall quality of their sleep, measured by the Pittsburgh Sleep Quality Index. Participants (n=15) contacted 3 to 7 months after completing the study, maintained improvements in sleep quality and interoceptive regulation. These findings indicate that mechanical stimulation may offer an effective, safe, non-drug alternative to improving sleep via interoceptive regulation and suggest a novel approach to treatment.**

Keywords-sleep; neurostimulation; interoception; affect; c-tactile afferents.

I. INTRODUCTION

The term 'interoception,' coined in 1906, initially described the total afferent input of the viscera to the brain [2]. The concept was mostly dormant until decades later when it evolved and expanded to include all afferent signaling to the central nervous system [3]. Most responses to interoceptive signals are understood to be autonomic, rarely rising to the level of consciousness (e.g., retracting a hand back when touching something hot), while others only indirectly reach awareness (e.g., filtration action of the kidneys only requires a response to the urge to void) [4]. Interoceptive signals such as those associated with emotion, can be mistakenly regarded as instinctual or autonomic; however, they are generally learned habits that remain malleable [5][6].

Methods to assess interoceptive capacity in individuals (e.g., heart rate detection tasks) have been developed, as well as self-report measures to assess various aspects of interoception [7][8][9]. Lower interoceptive awareness (i.e., lack of response to interoceptive signals) and dysregulated interoception (i.e., misinterpretation of the interoceptive signals) are associated with impaired decision making, poor sleep quality, increased psychiatric disorders, and reduced empathy [10] [11]. With that considered, dysregulated interoception is often recognized as a common feature of many affective and somatic disorder and their symptoms, prompting researchers to investigate neural bases of interoception [12]. Studies have shown that areas in the brain such as the anterior insula (IA) and anterior cingulate cortex (ACC), which are essential for processing emotion, affect, and behavior, are also proving to be fundamental in interoceptive processing [17][18]. Multiple studies suggest that modulating activity in these areas through practices such as mindfulness and meditation, appear to improve interoception [19][20][21]. Similarly, the same practices reduce symptomology among many affective and somatic disorders [22][23][24].

Disciplines of the mind and/or body, such as meditation, or yoga, or physical exercise, can improve interoceptive regulation because these activities stimulate the same areas of the brain as those dedicated to specific inputs from the periphery [12][13][15][22]. That specific interoceptive network is comprised of C-tactile afferent (CTAs) nerves [25]. CTAs are dermal mechanoreceptors, found only in hairy skin of mammals. They respond to a narrow range of slow, light touch stimuli, such as the kind of touch seen between a parent and child, the comforting caress of a partner, the grooming of baboons, and similar social behaviors [26]. This type of touch, called affective touch, also modulates areas of the brain involved in interoception, emotional regulation, and related functioning [27][28]. In turn, affective touch is associated with reduced stress, increased relaxation, a sense of belonging, and increased empathy [29][30][31].

1) Interoception and Sleep

Interoceptive signals such as those relating to temperature or pain, have been found to significantly impact sleep. For example, there is strong evidence in support of the relationship between internal body temperature and sleep regulation, where studies have shown that environmental temperature can alter sleep regulation [11] [32]. Similarly, as interoception includes processing nociceptive information, the present literature reveals a strong relationship between pain and sleep [11] [33]. Evidence of the relationship between pain and sleep is often observed in clinical populations such as chronic

pain patients, where one study found that 53% of chronic pain patients reported also suffering from insomnia as well, compared to only 3% of the healthy population [34]. As discussed earlier, dysregulated interoceptive processing can produce a wide range of symptoms, often overlapping in different clinical populations, which may explain the relationship seen among disorders of sleep and chronic pain, as well as with disorders of affect [5][10][35][36][37].

Neuroscience research, both electroencephalogram (EEG) and functional magnetic resonance imaging (fMRI) research, has provided evidence that cortical regions play a role in particular aspects of sleep, help regulate sleep-wake patterns, and are similar to those prominent in regulating the interoceptive system of interest here [38]. The ACC, a brain region found to stimulate wakefulness, AI, and orbitofrontal cortex have all been studied for their roles in insomnia disorder, a highly prevalent sleep disorder associated with impaired functioning during waking hours [38][39][40][41]. For instance, functional neuroimaging studies have found that those with insomnia have an increased insula coactivation with cortical networks associated with salience and arousal, such as the ACC, when compared to healthy controls [38][42]. Interestingly, these same brain regions are also recognized for their involvement in interoceptive processing and affect [10]. Insomnia disorder has also been associated with heightened interoceptive awareness, see [11] for review. When interoception is dysregulated, heightened interoceptive awareness may lead to a hyperawareness of physiological states that becomes disruptive to sleep, especially when falling asleep or staying asleep, as discussed earlier.

The relationship between interoception and sleep quality has been observed in a study investigating the relationship between components of subjective sleep quality, measured by the Pittsburgh Sleep Quality Index (PSQI), and dimensions of interoception, measured by the Multidimensional Assessment for Interoceptive Awareness (MAIA-II) [43]. In that sample of young adults (n=545), ages 18 to 25 years old, 90% were considerably poor sleepers, measured by Global PSQI scores., Poor sleep quality, was found to be significantly negatively correlated with dimensions of interoception including non-distracting and trusting, with the strong effect sizes [43]. These results suggest that those who experience better quality sleep may be more adept at recognizing sensations such as pain and discomfort, and more trusting of the internal bodily information regarding various physiological states, which is consistent with previous work investigating sleep and pain tolerance, as well as subjective hunger [43]. Overall, these findings provide evidence that there is a relationship between perceivably improved sleep and improved interoception. Therefore, considering the overlap of brain regions and cortical networks involved in both interoceptive processing and sleep, as well as the relationship between interoception, disordered sleep, and subjective sleep quality, one may argue that interoceptive processes are salient to at least some sleep disturbances.

2) Impact of Disordered Sleep

Disordered sleep, including insomnia, obstructive sleep apnea, and hypersomnia, impacts between 50 and 70 million Americans each year and an estimated 83.6 million U.S. adults get below the recommended 7 hours of sleep per night [44][45]. Roughly 15% of the U.S. population report insomnia related symptoms, and a quarter of the population are dissatisfied with their sleep. One study found that one in five adult females in Australia experience chronic insomnia, and one in seven experience obstructive sleep apnea [46].

The prevalence of disordered sleep can have a profound impact on both societal and individual levels. For example, insufficient and low-quality sleep decreases workplace productivity, increases the risk of motor vehicle accidents, and elevates the number of risk-factors for health outcomes. Poor-quality sleep and sleep deprivation have also been linked to metabolic dysfunction, cognitive impairment, alterations in neuroendocrine function and affective dysregulation [47][48]. Additionally, disordered sleep has been linked to a reduced quality of life and increases in anxiety related disorders [49].

In the primary care setting, patients complaining of sleep dysfunction have become a common occurrence and many people around the country have turned to available treatments. The most common agents of treatment include prescription drugs, such as benzodiazepines and antidepressants, and over the counter options, such as antihistamines and melatonin [50]. Between 1998 and 2006 the number of Americans reliant on sleep aid prescriptions tripled and roughly 4% of the adult population reported use of a prescription sleep aid [44]. A review of 35 studies relating to the effectiveness of melatonin found that most of the studies were inconclusive and melatonin was rarely superior to placebo [51]. Several of the reviewed studies gave weak recommendations for the use of melatonin among healthy volunteers or those with a history of insomnia due to melatonin's lack of effectiveness in initiating sleep or improving the quality of sleep [51]. Prescription drug such as. benzodiazepines leave users with a "hungover" feeling and often result in daytime drowsiness, impaired memory, difficulty concentrating, lack of coordination, amnesia, dizziness, and many other side effects that impact day-to-day activities [52]. Other prescription options, such as antidepressants, can lead to increases in suicidal ideation and mania [49]. The lack of reliable treatment options suggests a need for an alternative approach to a significant public health issue.

Considering the apparent relationship between sleep and interoception, as well as the research showing how practices that improve interoception (e.g., mindfulness,

yoga, and extreme sports/intense exercise), can also improve affective and somatic symptomology, we hypothesized that improving interoception will also improve sleep [22][23][24][53]. To do so, we developed a mechanical stimulation technology targeting CTAs (low intensity and low frequency (~5-15Hz) stimulation) [54]. This technology offers a non-invasive means of activating the affective touch pathway by targeting specific mechanoreceptors in the skin, and in turn, modulating interoceptive processing [1]. The objective of this research was to assess the effects, if any, of a device designed to improve interoceptive regulation via CTAs on symptoms of sleep disorder measured by the Pittsburgh Sleep Quality Index (PSQI) [55].

The rest of this paper is organized as follows. Section II details the nature of our novel approach to improve sleep through regulating interoception. Section III outlines the study method, including a description of the participant sample and eligibility criteria, the device technology, and measures used to assess sleep quality and interoceptive characteristics. Section IV details all study procedures, including a statement of ethics, participant eligibility screening, participant responsibilities, and visit procedures. Section V contains the detailed results of the present study and Section VI closes out the paper with the conclusion and a discussion of future work.

II. State of the Art

Most sleep interventions, aside from known drug or comorbid causes, treat sleep as a primary disorder. Our interest, as in other work, is to approach sleep disturbances as a manifestation of dysregulated interoception and others have done preliminary work looking at that pathway [32] [43] [56]. While some interventions for sleep, such as mindfulness, are also known to improve interoceptive regulation [53], few interventions appear to make the explicit connection, with at least one exception [57]. More specifically, no study, to our knowledge, explicitly approaches sleep as a function of dysregulated interoception and further, none use mechanical stimulation of the affective touch pathway to improve interoceptive regulation.

III. Study Method

This section details the overall method for the 30-day study, including the recruitment of qualifying participants and exclusion criteria, description of our novel mechanical stimulation device, and the measures used to assess sleep quality and characteristics of interoception.

A. Participants

Participants for this trial included healthy adults (mean age=34) with self-reported poor sleep. The subject population included a distribution of female (n=13) and male (n=9) participants. Poor sleep was measured using the PSQI (Global Score >10) [55].

Exclusion criteria included the use of sleep medication, current psychiatric disorder, a skin condition that may be exacerbated with device use, a metal implant in the head/neck region and finally if participants were pregnant or breastfeeding. These exclusion criteria aimed to control for any comorbid psychopathology and for any variance arising from interactions with other drugs.

B. Mechanical Stimulation Device

A simple headband with small piezoelectric actuators at the distal ends, seen in Figure 1 (a), was developed to deliver short bursts of very low intensity, low frequency mechanical stimulation, targeting CTAs associated with the affective touch pathway. The actuators were positioned behind the ears, on the mastoid, for convenience. The specific wave form was derived from a combination of empirical study (changes in alpha power pre/post stimulation in in-lab studies over 2 years) and known response characteristics of the CTA mechanoreceptors (low intensity, low frequency ~10 Hz).

C. Measures

The subsections below describe the measures used to assess sleep, including both behavioral and subjective measures, as well a subjective measure to assess various aspects of interoception.

1) Behavioral Sleep

A daily sleep diary with a 1- item sleep rating scale was used to track sleep quality throughout subject's participation in the study.

A Garmin Vivosmart 4 (https://buy.garmin.com/en-US/US/p/605739) watch was used to measure sleep duration during the study. The Garmin watch uses a wrist-based Pulse Ox sensor to measure sleep activity. Although the watch reports detailed sleep stages as well, that was excluded from this study due to the lack of reliability in those assessments [58][unpublished internal testing].

2) Subjective Sleep

Changes in sleep quality were assessed via PSQI and a 1-Item Sleep Quality Rating Scale. The Pittsburgh Sleep Quality Index (PSQI) is a self-report measure assessing sleep quality and disturbances over a 1-month timeframe. It is an 18-item questionnaire with seven component scores (range 0–3) that result in a global sleep quality score (range 0–21). Scores of five or greater indicate a probable sleep disorder [55]. The seven component measures include subjective sleep quality (PSQI_C1), sleep latency (PSQI_C2), sleep duration (PSQI_C3), habitual sleep efficiency (PSQI_C4), sleep disturbances (PSQI_C5), use of sleep medication (PSQI_C6) and daytime drowsiness (PSQI_C7).

The 1-Item Sleep Quality Rating Scale is a self-report measure utilizing a scale of 1 to 5, where 1 represents little to no sleep at all, and 5 represents great sleep (no problems falling or staying asleep).

An exit interview was conducted by a study coordinator at the end of the study to assess the usability of the device.

3) Affective/Interoception Characteristics

The Multidimensional Assessment of Interoceptive Accuracy (MAIA) is a 32-item self-reported measure of interoception (scale of 0 Never – 5 Always) that tracks changes in interoceptive awareness across eight dimensions [7]. The eight dimensions are Noticing (MAIA_MN), Not-Distracting (MAIA_MND), Not-Worrying (MAIA_MNW), Attention Regulation (MAIA_MAR), Emotional Awareness (MAIA_MER), Self-Regulation (MAIA_MSR), Body Listening (MAIA_MBL), and Trust (MAIA_MT).

IV. Study Procedure

Subjects were enrolled in the sleep protocol for 30 days and instructed to use the device at home at least once a day, within one hour of their regular bedtime. Written informed consent was obtained from all participants. During enrollment, subjects were provided with device instructions, device calibration and their first stimulation session. A subset of participants (n=13) wore a wrist device to track sleep (Garmin VivoSmart 4). Subjects were compensated up to $300 at the end of the study in the form of a gift card. Refer to Figure 1 (b) below for a visualization of the 30-day study protocol. All study procedures were reviewed and approved by Solutions IRB (#: FWA00021831) [59].

A. Screening

Participants were recruited for the study via digital ads on Facebook, as well as flyers posted around the community. Interested subjects were then screened for the use of sleep medication, and participants that did not use any sleep medication were then invited to fill out an application via Google Forms. All applications were reviewed and those subjects meeting the inclusion criteria (n=39) were invited to schedule their enrollment appointments, of whom 25 participants (14 females, 11 males) were enrolled into the study, displayed in Figure 2.

B. Study Visits

Eligible participants were enrolled via a written informed consent in the lab. They completed a set of baseline questionnaires, which included demographic information, subjective sleep measures and interoception measures. Upon completion of these assessments, all participants were instructed on device use and went through calibration to find the lowest level at which they could perceive the stimulation. Participants then had their first 20-minute stimulation session in the lab to ensure proper training and use of the device. Participants in the cohort with the Garmin sleep tracker were given additional instruction.

Participants returned to the lab after 30 days of home use for the final assessment of sleep and interoception measures and an exit interview was conducted with a study coordinator to discuss usability of the device.

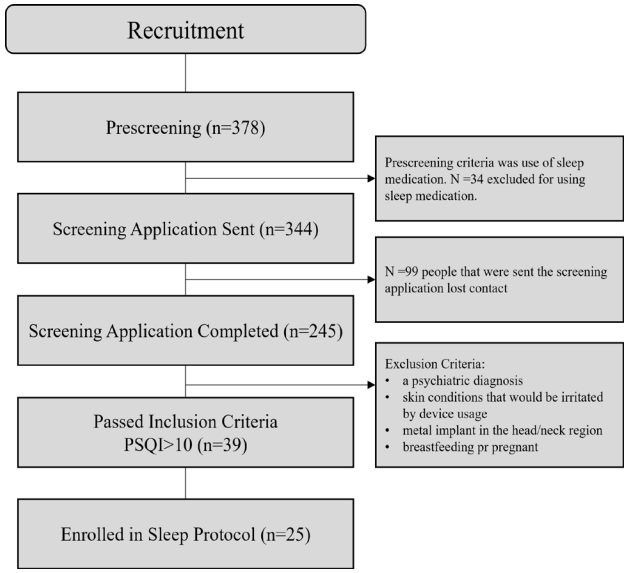

Figure 1: Participant Recruitment and Screening Procedure.

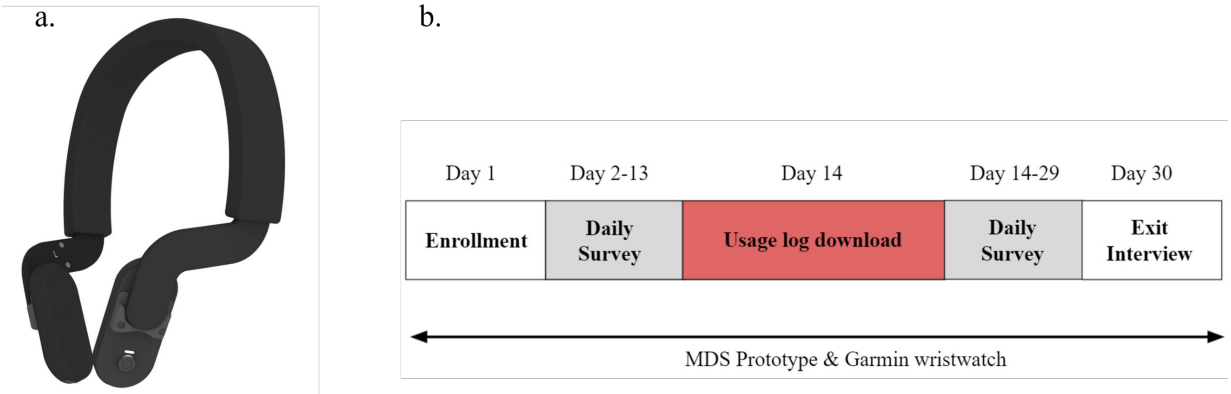

Figure 2: (a) Mechanical Dermal Stimulation Device Prototype (b) 30-Day Study Protocol.

C. Protocol

All participants were instructed to use the stimulation device for 30 days at home within one hour of their regular bedtime. Participants received a text message each morning with a link to fill in their daily sleep diary via Google Forms. Participants in the Garmin tracker cohort were asked to wear the Garmin watch each day and night during the 30-day study, and data from the watch was collected at the end of the study.

D. Analysis

Data analysis was performed on MATLAB and Microsoft Excel. Due to the small sample size of the study, t tests were conducted, and p values (with a 95% confidence interval) are reported as outcome measures in the following section.

V. Results

This section outlines the detailed results of the 30-day study, including descriptive characteristics of the participant sample, observed changes in sleep quality via self-report measures and a wearable sleep tracking device, as well as changes in aspects of interoception.

A. Descriptive Characteristics of Participants

In the sample of 25 participants, 3 were excluded from the primary analysis due to lack of compliance with the 30-day study protocol (i.e., device usage, completing the study). More specifically, those that used the device less than 33% of the time (based on usage 1x/day for 30 days) were considered noncompliant and removed from analysis. The results discussed in this section will be reported as mean ± standard deviation. The characteristics of the sample of compliant participants (n=22) are displayed in Table 1. In short, the sample (n=22) included 13 females and 9 males with ages ranging from 24 to 60 years old (34.27 ± 9.64).

B. Sleep Characteristics

After using the MDS device before bed for 30 days, 86% of participants (n=22) reported an overall improvement in sleep, measured by Global PSQI scores seen in Figure 3 (a), where lower scores indicate improvement in symptoms. Global PSQI scores improved significantly by 43% on average (Pre: 9.77 ± 3.04, Post: 5.18 ± 2.58, p=0.00), displayed in Table 2. In terms of individual characteristics of sleep measured by the PSQI (PSQI component scores), we observed significant improvements in Subjective Sleep Quality (p=0.00), Sleep Latency (p=0.00), Sleep Disturbances (p=0.04), and Daytime Drowsiness (p=0.00), shown in Table 2. On average, Subjective Sleep Quality improved by 67% (Pre: 2.0 ± 0.53, Post: 0.64 ± 0.58), Sleep Latency improved by 51% (Pre: 1.32 ± 0.48, Post: 1.05 ± 0.38), Sleep Disturbances improved by 14% (Pre: 1.86 ± 0.89, Post: 0.86 ± 0.64) and Daytime Drowsiness improved by 45% (Pre: 1.86 ± 0.89, Post: 0.86 ± 0.64), seen in Figure 3 (a). Similarly, we saw significant improvements in sleep quality ratings after 30 days of device use (p=0.00), displayed in Table 2. On average, sleep quality ratings increased by 45% (Pre: 3.09 ± 0.53, Post: 0.64 ± 0.58), shown in Figure 3 (b) (c), where higher scores indicate better sleep quality.

Sleep hours were assessed via a commercial wrist Photoplethysmography (PPG) device (Garmin VivoSmart 4) for a subset of compliant participants (n=13). This PPG device was chosen as it was most reliable for sleep time based on earlier studies, where we found that no devices to our knowledge appeared to accurately measure sleep stages, nor is PPG a suitable substitute for a hypnogram. After 30 days of using the MDS device, sleep hours increased by 65 minutes on average (Pre: 6.60 ± 0.29, Post: 7.45 ± 0.45), shown in Figure 3 (d).

Table 1: Compliant Study Sample Demographics

Demographics	N = 22
Age	34.27 ± 9.64
Gender	
Female	13
Male	9
Ethnicity	
Hispanic	2
White / Caucasian	7
Black or African American	3
Prefer not to say	1
Asian / Pacific Islander	7
Hispanic and Middle-Eastern American	1
Mixed Race	1

Table 2: Compliant Study Sample Results

	Pre	**Post**		
	Mean ± SD	*Mean ± SD*	*pvalue*	*tstat*
Sleep Rating	3.09 ± 0.75	4.27 ± 0.63	**0.000001**	-5.654
PSQI_C1	2 ± 0.53	0.64 ± 0.58	**0.000000**	8.101
PSQI_C2	2.05 ± 0.72	0.95 ± 0.9	**0.000064**	4.439
PSQI_C3	1.32 ± 1.09	0.82 ± 0.96	0.112858	1.619
PSQI_C4	0.82 ± 0.91	0.64 ± 0.9	0.508631	0.667
PSQI_C5	1.32 ± 0.48	1.05 ± 0.38	**0.040966**	2.109
PSQI_C6	0.41 ± 0.73	0.23 ± 0.53	0.351170	0.943
PSQI_C7	1.86 ± 0.89	0.86 ± 0.64	**0.000105**	4.283
PSQI_Global	9.77 ± 3.04	5.18 ± 2.58	**0.000003**	5.406
MAIA_MN	3.34 ± 0.79	3.8 ± 0.84	0.070784	-1.854
MAIA_MND	2.18 ± 1.04	2.05 ± 1.15	0.681956	0.413
MAIA_MNW	2.61 ± 1.45	2.62 ± 1.16	0.969703	-0.038
MAIA_MAR	2.69 ± 0.91	2.98 ± 0.96	0.307309	-1.033
MAIA_MEA	3.69 ± 1.14	3.8 ± 1.17	0.756368	-0.312
MAIA_MSR	2.76 ± 1.01	2.91 ± 1.15	0.653277	-0.452
MAIA_MBL	2.47 ± 1.07	3.02 ± 1.16	0.111566	-1.625
MAIA_MT	3 ± 1.42	3.23 ± 1.04	0.547755	-0.606

C. *Affective/Interoception Characteristics*

After 30 days of using the MDS device, on average participants (n=22) reported an overall improvement in interoception, measured by the MAIA, displayed in Table 2. Most notably, participants improved in the following dimensions of interoception: Noticing (Pre: 3.34 ± 0.79, Post: 3.8 ± 0.84), Not Worrying (Pre: 2.61 ± 1.45, Post: 2.62 ± 1.16), Attention Regulation (Pre: 2.69 ± 0.91, Post: 2.98 ± 0.96), Body Listening (Pre: 2.47 ± 1.07, Post: 3.02 ± 1.16), and Trusting (Pre: 3 ± 1.42, Post: 3.23 ± 1.04), shown in Figure 3 (e).

D. *Follow Up Results*

Approximately 3 to 7 months following the 30-day study, a subgroup of compliant participants (n=15) completed follow-up assessments. The follow-up sample (n=15) included 8 females and 7 males, with ages ranging from 24 to 44 years old (31.73 ± 5.71), shown in Table 3.

Despite discontinued use of the MDS device for 3 to 7 months, participants (n=15) maintained some improvements in sleep from their 30-day study participation. When compared to baseline scores, participants reported significant improvements in overall sleep quality (p=0.03), represented by Global PSQI scores displayed in Table 4. On average, Global PSQI scores at follow up improved by 26% when compared to baseline (Pre: 9.93 ± 3.15, Post: 5.4 ± 2.8, Follow Up: 7.07 ± 3.75), where lower scores represent improved sleep, displayed in Figure 4(a). Apart from Global PSQI scores, significant improvements were also found in Subjective Sleep Quality (p=0.04), and Sleep Duration (p=0.00) when comparing follow-up PSQI component scores to baseline, displayed in Table 4. On average, Subjective Sleep Quality improved by 22% (Pre: 2.07 ± 0.59, Post: 0.67 ± 0.62, Follow Up: 1.53 ± 0.74) and Sleep Duration improved by 53% (Pre: 1.27 ± 1.16, Post: 0.93 ± 1.03, Follow Up: 0.2± 0.41), and although not significant, Daytime Drowsiness improved by 22% (Pre: 2.07 ± 0.88, Post: 0.87 ± 0.64, Follow Up: 1.47± 1.13), shown in Figure 4(a). Similarly, on a scale of 1 to 10, where higher scores indicate better sleep, sleep quality ratings did not return to baseline, shown in Table 4. On average, participants (n=15) reported an improvement in sleep by 12% at follow up when compared to baseline (Pre: 3.07 ± 0.8, Post: 4.33 ± 0.62, Follow Up: 3.27± 0.96), displayed in Figure 4(b).

Overall, the improvements reported in interoception following 30 days of MDS device use were maintained following cessation of the MDS device for 3 to 7 months, shown in Table 4. Most notably, participants (n=15) maintained an improvement in not distracting, attentional regulation, self-regulation, body listening, and trusting dimensions of interoception, measured by the MAIA. On average, participants reported a 28% improvement in Not Distracting (Pre: 2.36 ± 1.16, Post: 2.13 ± 1.19, Follow Up: 2.41 ± 1.05), 20% improvement in Attentional Regulation (Pre: 2.7 ± 0.86, Post: 3.22 ± 0.99, Follow Up: 2.96 ± 1.03), a 28% improvement in Self-Regulation (Pre: 2.83 ± 1.18, Post: 3.03 ± 1.28, Follow Up: 3.03 ± 1.23), a 38% improvement in Body Listening (Pre: 2.53 ± 1.15, Post: 2.98 ± 1.16, Follow Up: 3.08 ± 0.57), and 32% improvement in Trusting (Pre: 2.89 ± 1.45, Post: 3.09 ± 1.07, Follow Up: 3.17 ± 1.23), displayed in Figure 4(c).

Table 3: Follow Up Sample Demographics

Demographics	N = 15
Age	31.73 ± 5.71
Gender	
Female	8
Male	7
Ethnicity	
Hispanic	2
Caucasian	4
African American	2
Prefer not to say	1
Asian / Pacific Islander	4
Mixed Race	2

Table 4: Follow Up Results

	Pre	**Post**	**Follow-up**	**Pre vs Follow Up**
	Mean ± SD	*Mean ± SD*	*Mean ± SD*	*pvalue*
Sleep Rating	3.07 ± 0.8	4.33 ± 0.62	3.27 ± 0.96	0.540
PSQI_C1	**2.07 ± 0.59**	**0.67 ± 0.62**	**1.53 ± 0.74**	**0.039**
PSQI_C2	2.07 ± 0.8	0.93 ± 0.88	1.6 ± 0.83	0.127
PSQI_C3	**1.27 ± 1.16**	**0.93 ± 1.03**	**0.2 ± 0.41**	**0.002**
PSQI_C4	0.8 ± 0.94	0.8 ± 1.01	1.07 ± 1.28	0.521
PSQI_C5	1.33 ± 0.49	1.07 ± 0.26	1.07 ± 0.59	0.190
PSQI_C6	0.33 ± 0.72	0.2 ± 0.56	0.33 ± 0.82	1.000
PSQI_C7	2.07 ± 0.88	0.87 ± 0.64	1.47 ± 1.13	0.116
PSQI_Global	**9.93 ± 3.15**	**5.4 ± 2.8**	**7.07 ± 3.75**	**0.031**
MAIA_MN	3.3 ± 0.76	3.87 ± 0.94	3.33 ± 0.88	0.930
MAIA_MND	2.36 ± 1.16	2.13 ± 1.19	2.41 ± 1.05	0.889
MAIA_MNW	2.91 ± 1.23	2.82 ± 0.95	2.48 ± 1.08	0.320
MAIA_MAR	2.7 ± 0.86	3.22 ± 0.99	2.95 ± 1.03	0.473
MAIA_MEA	3.6 ± 1.21	3.61 ± 1.31	3.63 ± 1.09	0.950
MAIA_MSR	2.83 ± 1.18	3.03 ± 1.28	3.03 ± 1.23	0.653
MAIA_MBL	2.53 ± 1.15	2.98 ± 1.16	3.08 ± 0.57	0.109
MAIA_MT	2.89 ± 1.45	3.09 ± 1.07	3.17 ± 1.23	0.567

VI. Conclusion and Future Work

To our knowledge, this is the first human study to evaluate mechanical stimulation of the affective touch pathway in a sleep-disordered population. Although the trial is small, open-label, and used early prototypes, the results were significant, and participants benefited from the use of the MDS device [1]. Overall sleep quality, represented by Global PSQI scores, significantly improved after using the MDS device for 30 days. Participants reported falling asleep faster, experiencing fewer sleep disturbances, and experiencing less daytime drowsiness. Participants also reported an overall improvement in

aspects of interoception. These findings suggest that mechanical stimulation of CTAs can lead to improvements in sleep. There is a need for further research to better understand the relationship between sleep, sleep disorders and interoception, and more robust clinical trials to assess the effects of mechanical stimulation on sleep and other symptoms of dysregulated interoception.

A confirmatory Randomized Control Trial (RCT) is underway to address limitations such as sample size and inclusion of a control group, which will be completed in late 2021.

An abundance of sleep research has provided evidence suggesting that impaired sleep has potentially serious implications on a wide variety of health conditions involving cardiovascular, immune, endocrine, and nervous systems [43]. Even in healthy populations, insufficient and disordered sleep can still have profound impacts on health. For example, in a sample of healthy adolescents, sleep deprivation was found to induce mood deficits [60]. These findings are supported by how the same brain structures recognized for their roles in interoception and regulating mood and emotion, such as the insula, have also shown evidence to be sensitive to sleep-dependent modulation [2][61] [62]. Clinically diagnosed sleep disorders, especially Insomnia Disorder, are commonly comorbid to other conditions like chronic pain, as well as affective disorders, all of which have been associated with dysregulated interoception [11]. The relationship between chronic pain and subjective sleep quality is well-established, where those reporting poor sleep quality also report an increased level of pain, and vice-versa [11] [43] [63]. In a sample of patients with affective disorders, including anxiety and major depression, those who reported poor sleep quality via PSQI, performed worse on a measure of interoception (heart-rate discrimination task), representing a reduction in interoceptive accuracy when compared to healthy controls [56]. With consideration of the above research findings regarding the relationship between sleep and various health conditions, disorders, and physiological processing, it is worth investigating what may be the underlying connection: dysregulated interoception.

In this pilot trial of sleep-disordered subjects, regular use of the mechanical dermal stimulation device appears to have produced significant improvements in sleep and related areas. What is of potential interest to others in the nascent field of affective touch therapeutics is that the proposed underlying mechanism of action is not particularly salient to sleep. The intervention is not designed to specifically and differentially affect sleep. The intent is to improve interoceptive regulation. In the course of our work, we have used other markers of interoception, like stress, fear, depression, and anxiety, as outcome measures. In general, we find that improving interoceptive regulation in some domain is correlated with improvements in the specific feature of interest.

It should be the case that improving interoceptive regulation would lead to improvements in function in multiple domains as interoception is a key driver of emotional responses. The current, dominant psychiatric and even lay nosology around distress has a variety of classifications based on symptoms and complaints. A nosology based on mechanisms of action, such as dysregulated interoception, collapse many of the older 'symptom-based' nosology into that singular category. Although much of the therapeutic 'infrastructure' in psychiatry and psychology is rooted in the distinctiveness of disorders, practitioners recognize that, in the clinic, there is vast overlap among disorders and many comorbidities [10]. As we continue to work in developing therapeutic interventions around interoceptive regulation, we will continue to report using the existing symptom-based nosology, but always tie that back into the larger goal of improving interoceptive regulation. Future work that can help tie many currently disparate disorders (anxiety, eating disorders, sleep disturbances, etc.) to a common mechanism will help forge more common treatment methodologies and measures of improvement.

Conflicts of Interest

The authors declare the following financial interests which may be considered as potential competing interests: Gina Sensale, Sahithi Garikapati, Angelina Distefano and Sean Hagberg are employees of the Company. Jean-Marie Toher and Hanna Villa were employees of the Company. All authors hold stock ownership in the Company. Sean Hagberg has patent No. 16/241,227 pending to Affect Neuro, and a patent 10,786,666 issued to Affect Neuro. Sahithi Garikapati has patent No. 16/241,227 pending to Affect Neuro.

References

[1] G. Sensale, S. Garikapati, J. Toher, H. Villa, and S. Hagberg, "Mechanical Dermal Stimulation to Modulate the Interoceptive Network in Sleep-disordered Populations," The Sixth International Conference on Neuroscience and Cognitive Brain Information (BRAININFO 2021) IARIA, Jul. 2021, pp. 23–25, ISSN: 2519-8653, ISBN: 978-1-61208-885-3.

[2] E. F. Pace-Schott, "Chapter 48 - The Neurobiology of Dreaming," Principles and Practice of Sleep Medicine (Fifth Edition), pp. 563–575, Oct. 2011, doi: 10.1016/B978-1-4160-6645-3.00048-7.

[3] S. C. Sherrington, The Integrative Action of the Nervous System. New Haven, CT: Yale University Press, 1906.

[4] G. G. Berntson and S. S. Khalsa, "Neural Circuits of Interoception," Trends in Neurosciences, vol. 44, no. 1, pp. 17–28, Jan. 2021, doi: 10.1016/J.TINS.2020.09.011.

[5] P. Duquette, M. Tamietto, S. Gajraj Tewari, and L. Sun, "Increasing Our Insular World View: Interoception and Psychopathology for Psychotherapists," Frontiers in Neuroscience, vol. 11, p. 135, 2017, doi: 10.3389/fnins.2017.00135.

[6] L. F. Barrett and W. K. Simmons, "Interoceptive predictions in the brain," Nature Reviews Neuroscience, vol. 16, no. 7, pp. 419–429, 2015, doi: 10.1038/nrn3950.

[7] W. E. Mehling, C. Price, J. J. Daubenmier, M. Acree, E. Bartmess, and A. Stewart, "The Multidimensional Assessment of Interoceptive Awareness (MAIA)," PLOS ONE, vol. 7, no. 11, p. 48230, Nov. 2012, doi: 10.1371/JOURNAL.PONE.0048230.

[8] W. E. Whitehead, V. M. Drescher, P. Heiman, and B. Blackwell, "Relation of Heart Rate Control to Heartbeat Perception," Biofeedback and Self-Regulation, vol. 2, no. 4, Dec. 1977, doi: 10.1007/BF00998623.

[9] S. N. Garfinkel, M. F. Manassei, G. Hamilton-Fletcher, Y. In den Bosch, H. D. Critchley, and M. Engels, "Interoceptive dimensions across cardiac and respiratory axes," Philosophical transactions of the Royal Society of London, Series B, Biological Sciences, vol. 371, no. 1708, Nov. 2016, doi: 10.1098/RSTB.2016.0014.

[10] S. S. Khalsa et al., "Interoception and Mental Health: A Roadmap," Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, vol. 3, no. 6, pp. 501–513, Jun. 2018, doi: 10.1016/J.BPSC.2017.12.004.

[11] Y. Wei and E. J. van Someren, "Interoception relates to sleep and sleep disorders," Current Opinion in Behavioral Sciences, vol. 33, pp. 1–7, Jun. 2020, doi: 10.1016/J.COBEHA.2019.11.008.

[12] H. Y. Weng, J. L. Feldman, L. Leggio, V. Napadow, J. Park, and C. J. Price, "Interventions and Manipulations of Interoception," Trends in Neurosciences, vol. 44, no. 1, pp. 52–62, Jan. 2021, doi: 10.1016/J.TINS.2020.09.010.

[13] H. Schwarzmeier, N. I. Kleint, H. U. Wittchen, A. Ströhle, A. O. Hamm, and U. Lueken, "Characterizing the nature of emotional-associative learning deficits in panic disorder: An fMRI study on fear conditioning, extinction training and recall," European Neuropsychopharmacology, vol. 29, no. 2, pp. 306–318, Feb. 2019, doi: 10.1016/J.EURONEURO.2018.11.1108.

[14] C. Lamm and T. Singer, "The role of anterior insular cortex in social emotions," Brain Structure and Function, vol. 214, no. 5, pp. 579–591, Apr. 2010, doi: 10.1007/S00429-010-0251-3.

[15] J. Gibson, "Mindfulness, Interoception, and the Body: A Contemporary Perspective," Frontiers in Psychology, vol. 0, p. 2012, Sep. 2019, doi: 10.3389/FPSYG.2019.02012.

[16] E. Kuehn, K. Mueller, G. Lohmann, and S. Schuetz-Bosbach, "Interoceptive awareness changes the posterior insula functional connectivity profile," Brain Structure and Function, vol. 221, no. 3, pp. 1555–1571, Jan. 2015, doi: 10.1007/S00429-015-0989-8.

[17] K. S. Young et al., "The impact of mindfulness-based interventions on brain activity: A systematic review of functional magnetic resonance imaging studies," Neuroscience & Biobehavioral Reviews, vol. 84, pp. 424–433, Jan. 2018, doi: 10.1016/J.NEUBIOREV.2017.08.003.

[18] S. Guendelman, S. Medeiros, and H. Rampes, "Mindfulness and Emotion Regulation: Insights from Neurobiological, Psychological, and Clinical Studies," Frontiers in Psychology, vol. 0, p. 220, Mar. 2017, doi: 10.3389/FPSYG.2017.00220.

[19] N. M. Khoury, J. Lutz, and Z. Schuman-Olivier, "Interoception in Psychiatric Disorders: A Review of Randomized Controlled Trials with Interoception-based Interventions," Harvard Review of Psychiatry, vol. 26, no. 5, p. 250, Sep. 2018, doi: 10.1097/HRP.0000000000000170.

[20] N. Neukirch, S. Reid, and A. Shires, "Yoga for PTSD and the role of interoceptive awareness: A preliminary mixed-methods case series study," European Journal of Trauma & Dissociation, vol. 3, no. 1, pp. 7–15, Jan. 2019, doi: 10.1016/J.EJTD.2018.10.003.

[21] B. Bornemann, P. Kovacs, and T. Singer, "Voluntary upregulation of heart rate variability through biofeedback is improved by mental contemplative training," Scientific Reports, vol. 9, no. 1, pp. 1–13, May 2019, doi: 10.1038/s41598-019-44201-7.

[22] A. Wallman-Jones, P. Perakakis, M. Tsakiris, and M. Schmidt, "Physical activity and interoceptive processing: Theoretical considerations for future research," International Journal of Psychophysiology, vol. 166, pp. 38–49, Aug. 2021, doi: 10.1016/J.IJPSYCHO.2021.05.002.

[23] H. Olausson, J. Wessberg, I. Morrison, F. McGlone, and Å. Vallbo, "The neurophysiology of unmyelinated tactile afferents," Neuroscience & Biobehavioral Reviews, vol. 34, no. 2, pp. 185–191, Feb. 2010, doi: 10.1016/J.NEUBIOREV.2008.09.011.

[24] L. S. Löken, J. Wessberg, I. Morrison, F. McGlone, and H. Olausson, "Coding of pleasant touch by unmyelinated afferents in humans," Nature Neuroscience, vol. 12, no. 5, pp. 547–548, Apr. 2009, doi: 10.1038/nn.2312.

[25] P. Wei and R. Bao, "The Role of Insula-Associated Brain Network in Touch," BioMed Research International, vol. 2013, p. 11, 2013, doi: 10.1155/2013/734326.

[26] M. Björnsdotter, I. Morrison, and H. Olausson, "Feeling good: On the role of C fiber mediated touch in interoception," Experimental Brain Research, vol. 207, no. 3–4, pp. 149–155, Dec. 2010, doi: 10.1007/S00221-010-2408-Y.

[27] J. S. Feinstein et al., "Examining the short-term anxiolytic and antidepressant effect of Floatation-REST," PLoS ONE, vol. 13, no. 2, Feb. 2018, doi: 10.1371/JOURNAL.PONE.0190292.

[28] A. J. Arnold, P. Winkielman, and K. Dobkins, "Interoception and Social Connection," Frontiers in Psychology, vol. 0, p. 2589, Nov. 2019, doi: 10.3389/FPSYG.2019.02589.

[29] J. Ernst, G. Northoff, H. Böker, E. Seifritz, and S. Grimm, "Interoceptive awareness enhances neural activity during empathy," Human Brain Mapping, vol. 34, no. 7, pp. 1615–1624, Jul. 2013, doi: 10.1002/HBM.22014.

[30] Y. Wei et al., "I Keep a Close Watch on This Heart of Mine: Increased Interoception in Insomnia," Sleep, vol. 39, no. 12, p. 2113, Dec. 2016, doi: 10.5665/SLEEP.6308.

[31] D. Whibley et al., "Sleep and Pain: A Systematic Review of Studies of Mediation," The Clinical Journal of Pain,

vol. 35, no. 6, p. 544, Jun. 2019, doi: 10.1097/AJP.0000000000000697.

[32] N. K. Y. Tang, K. J. Wright, and P. M. Salkovskis, "Prevalence and correlates of clinical insomnia co-occurring with chronic back pain," Journal of sleep research, vol. 16, no. 1, pp. 85–95, Mar. 2007, doi: 10.1111/J.1365-2869.2007.00571.X.

[33] C. A. Palmer and C. A. Alfano, "Sleep and emotion regulation: An organizing, integrative review," Sleep Medicine Reviews, vol. 31, pp. 6–16, Feb. 2017, doi: 10.1016/J.SMRV.2015.12.006.

[34] M. E. Rumble, K. H. White, and R. M. Benca, "Sleep Disturbances in Mood Disorders," Psychiatric Clinics of North America, vol. 38, no. 4, pp. 743–759, Dec. 2015, doi: 10.1016/J.PSC.2015.07.006.

[35] V. Lo Martire, D. Caruso, L. Palagini, G. Zoccoli, and S. Bastianini, "Stress & sleep: A relationship lasting a lifetime," Neuroscience & Biobehavioral Reviews, vol. 117, pp. 65–77, Oct. 2020, doi: 10.1016/J.NEUBIOREV.2019.08.024.

[36] M. C. Chen et al., "Anterior Insula Regulates Multiscale Temporal Organization of Sleep and Wake Activity," Journal of Biological Rhythms, vol. 31, no. 2, pp. 182–193, Jan. 2016, doi: 10.1177/0748730415627035.

[37] D. Stoffers et al., "Orbitofrontal Gray Matter Relates to Early Morning Awakening: A Neural Correlate of Insomnia Complaints?," Frontiers in Neurology, vol. 3, p. 105, Jun. 2012, doi: 10.3389/FNEUR.2012.00105.

[38] H. S. Gompf et al., "Locus Ceruleus and Anterior Cingulate Cortex Sustain Wakefulness in a Novel Environment," The Journal of Neuroscience, vol. 30, no. 43, p. 14543, Oct. 2010, doi: 10.1523/JNEUROSCI.3037-10.2010.

[39] Y. Wei, T. F. Blanken, and E. J. W. Van Someren, "Insomnia Really Hurts: Effect of a Bad Night's Sleep on Pain Increases With Insomnia Severity," Frontiers in Psychiatry, vol. 0, p. 377, Aug. 2018, doi: 10.3389/FPSYT.2018.00377.

[40] M. C. Chen, C. Chang, G. H. Glover, and I. H. Gotlib, "Increased insula coactivation with salience networks in insomnia," Biological Psychology, vol. 97, pp. 1–8, Mar. 2014, doi: 10.1016/J.BIOPSYCHO.2013.12.016.

[41] T. Arora, M. Barbato, S. Al Hemeiri, O. M. Omar, and M. A. AlJassmi, "A mysterious sensation about sleep and health: the role of interoception," BMC Public Health, vol. 21, p. 1584, Dec. 2021, doi: 10.1186/s12889-021-11603-0.

[42] Y. Chong, C. D. Fryar, and Q. Gu, "Prescription sleep aid use among adults: United States, 2005-2010," Hyattsville, MD, Aug. 2013. [Online]. Available: https://www.cdc.gov/nchs/data/databriefs/db127.pdf. [Accessed: 2021.12.10].

[43] Y. Liu, "Prevalence of Healthy Sleep Duration among Adults — United States, 2014," MMWR. Morbidity and Mortality Weekly Report, vol. 65, no. 6, pp. 137–141, Feb. 2019, doi: 10.15585/MMWR.MM6506A1.

[44] N. McArdle et al., "The prevalence of common sleep disorders in young adults: a descriptive population-based study," Sleep, vol. 43, no. 10, p. zsaa072, Oct. 2020, doi: 10.1093/SLEEP/ZSAA072.

[45] J. Labad et al., "The Role of Sleep Quality, Trait Anxiety and Hypothalamic-Pituitary-Adrenal Axis Measures in Cognitive Abilities of Healthy Individuals," International Journal of Environmental Research and Public Health, vol. 17, no. 20, p. 7600, Oct. 2020, doi: 10.3390/IJERPH17207600.

[46] N. Darchia et al., "Relationship between Sleep Disorders and Health Related Quality of Life—Results from the Georgia SOMNUS Study," International Journal of Environmental Research and Public Health, vol. 15, no. 8, p. 1588, Jul. 2018, doi: 10.3390/IJERPH15081588.

[47] S. Wilson and S. Argyropoulos, "Antidepressants and sleep: a qualitative review of the literature," Drugs, vol. 65, no. 7, pp. 927-947, May 2005, doi: 10.2165/00003495-200565070-00003.

[48] T. Fitzgerald and J. Vietri, "Residual Effects of Sleep Medications Are Commonly Reported and Associated with Impaired Patient-Reported Outcomes among Insomnia Patients in the United States," Sleep Disorders, vol. 2015, pp. 1–9, 2015, doi: 10.1155/2015/607148.

[49] R. B. Costello et al., "The effectiveness of melatonin for promoting healthy sleep: a rapid evidence assessment of the literature," Nutrition Journal, vol. 13, no. 1, pp. 1–17, Nov. 2014, doi: 10.1186/1475-2891-13-106.

[50] J. Glass, K. L. Lanctôt, N. Herrmann, B. A. Sproule, and U. E. Busto, "Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits," BMJ, vol. 331, pp. 1169–1173, Nov. 2005, doi: 10.1136/BMJ.38623.768588.47.

[51] H. L. Rusch et al., "The effect of mindfulness meditation on sleep quality: a systematic review and meta-analysis of randomized controlled trials," Annals of the New York Academy of Sciences, vol. 1445, no. 1, pp. 5–16, Jun. 2019, doi: 10.1111/NYAS.13996.

[52] R. Ackerley, I. Carlsson, H. Wester, H. Olausson, and H. Backlund Wasling, "Touch perceptions across skin sites: Differences between sensitivity, direction discrimination and pleasantness," Frontiers in Behavioral Neuroscience, vol. 8, p. 54, Feb. 2014, doi: 10.3389/FNBEH.2014.00054/BIBTEX.

[53] D. J. Buysse, C. F. Reynolds, T. H. Monk, S. R. Berman, and D. J. Kupfer, "The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research," Psychiatry Research, vol. 28, no. 2, pp. 193–213, May 1989, doi: 10.1016/0165-1781(89)90047-4.

[54] D. L. Ewing, M. Manassei, C. G. van Praag, A. O. Philippides, H. D. Critchley, and S. N. Garfinkel, "Sleep and the heart: Interoceptive differences linked to poor experiential sleep quality in anxiety and depression," Biological Psychology, vol. 127, p. 163, Jul. 2017, doi: 10.1016/J.BIOPSYCHO.2017.05.011.

[55] J. A. Brewer, A. Roy, A. Deluty, T. Liu, and E. A. Hoge, "Can Mindfulness Mechanistically Target Worry to Improve Sleep Disturbances? Theory and Study Protocol for App-Based Anxiety Program," Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association, vol. 39, no. 9, p. 776, Sep. 2020, doi: 10.1037/HEA0000874.

[56] D. Fuller et al., "Reliability and Validity of Commercially Available Wearable Devices for Measuring Steps, Energy Expenditure, and Heart Rate: Systematic Review," JMIR Mhealth and Uhealth, vol. 8, no. 9, Sep. 2020, doi: 10.2196/18694.

[57] "Solutions IRB." [Online]. Available: https://www.solutionsirb.com/. [Accessed: 2021.12.10].

[58] M. A. Short and M. Louca, "Sleep deprivation leads to mood deficits in healthy adolescents," Sleep Medicine, vol. 16, no. 8, pp. 987–993, Aug. 2015, doi: 10.1016/J.SLEEP.2015.03.007.

[59] E. F. Pace-Schott et al., "Physiological feelings," Neuroscience & Biobehavioral Reviews, vol. 103, pp. 267–304, Aug. 2019, doi: 10.1016/J.NEUBIOREV.2019.05.002.

[60] E. A. Nofzinger et al., "Increased Activation of Anterior Paralimbic and Executive Cortex From Waking to Rapid Eye Movement Sleep in Depression," Archives of General Psychiatry, vol. 61, no. 7, pp. 695–702, Jul. 2004, doi: 10.1001/ARCHPSYC.61.7.695.

[61] A. G. Doufas, "Chapter 133 - Pain and sleep," Principles and Practice of Sleep Medicine (Sixth Edition), Elsevier, pp. 1313-1322, 2017, doi: 10.1016/B978-0-323-24288-2.00133-1.

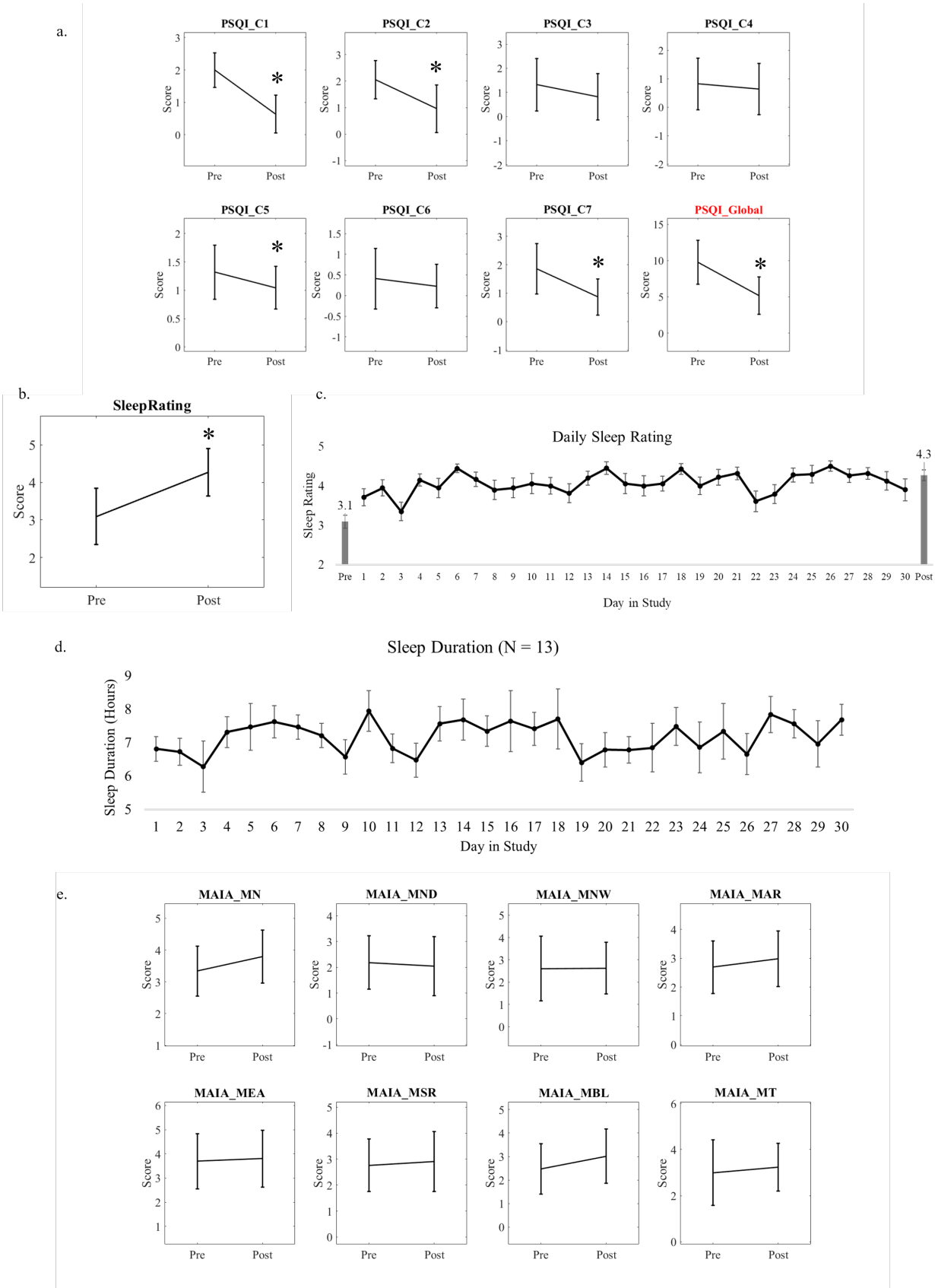

Figure 3: (a) Average PSQI Scores (b) Average Sleep Quality Rating Scores (c) Average Daily Sleep Quality Ratings (d) Average Sleep Duration measured via Garmin (n=13) (e) Average MAIA Scores.

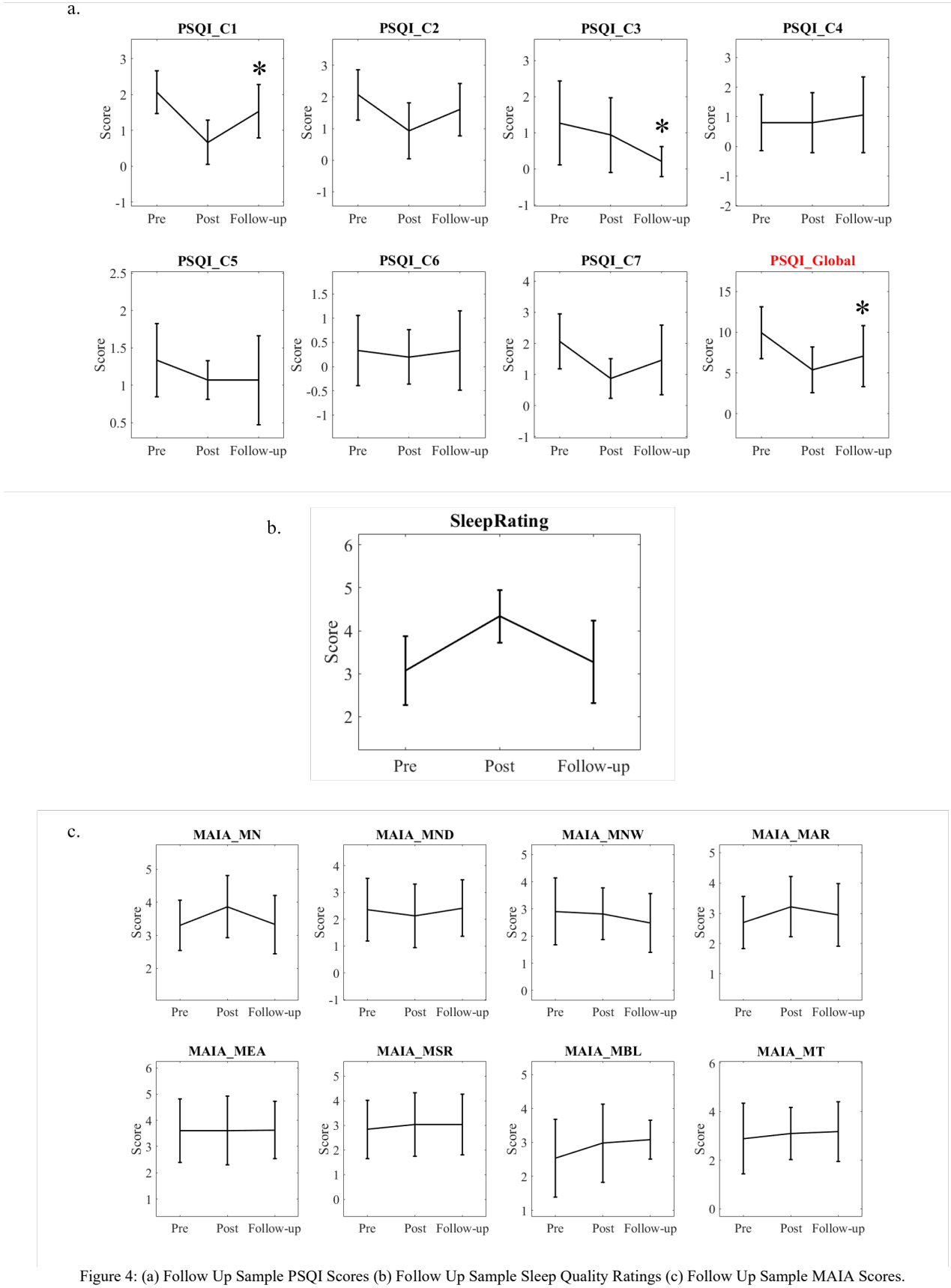

Figure 4: (a) Follow Up Sample PSQI Scores (b) Follow Up Sample Sleep Quality Ratings (c) Follow Up Sample MAIA Scores.