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Improvement of Mental Health and Anxiety with Haptic Technology Patch Utilization: Interim Results from an Exploratory Study

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ABSTRACT

Anxiety chronically affects 49.9% of all US adults aged 18-24, 32.3% of all US adults, and an estimated 4% of the global population currently experience an anxiety disorder. Nonpharmacologic, behavioral therapies are useful yet underutilized. Treatment with antidepressants and anxiolytics are the most common pharmacotherapy for anxiety disorders, with variable effectiveness, significant side-effect burden [including being implicated with suicide] and high misuse liability. Identifying alternative treatments, including non-invasive and non-pharmacologic options that are safe, efficacious, and have reduced or limited side effect profiles would be preferred over conventional therapies targeting anxiety-related symptoms.

Ongoing research suggests that brain patterns can be altered in response to various haptic stimuli. A novel patch that delivers haptic vibrotactile trigger technology (VTT) was designed and theorized to target various neural pathways to influence brain centers. The technology is over-the-counter, non-invasive, non-pharmacological and applied topically.

The purpose of this IRB-approved, blinded, minimal-risk observational study was to evaluate and compare patients' experiences, perceptions and response for those who received a haptic vibrotactile trigger technology (VTT) embedded stress and anxiety-relieving patch (PEACE Patch with VTT; Super Patch Company, Srysty Holding Co, Toronto, Canada) with those who received a control patch without the embedded technology.

***Methods:** A total of 65 patients (49 females, 16 males) at 3 US investigator sites who presented with stress and/or anxiety- related issues or associated symptoms were enrolled in the treatment (n=65) arm of the study and completed baseline, day 7, and day 14 surveys. Demographic results were similar for gender and age at the baseline survey. The mean age at baseline was 46.8 years. The study evaluated changes in stress and anxiety symptoms, mental health perceptions and other relevant domains via validated stress and anxiety measurement and symptom scales (e.g., The Perceived Stress Scale (PSS) and the Medical Outcomes Study Short Form-20 (SF-20)) as well as additional survey questions regarding patient satisfaction, patient quality of life, change in medication usage, change in other treatment modalities attempted, and any side effects reported during the study period.*

***Results:** After using the VTT embedded stress and anxiety-relieving patch, results showed statistically significant decreases in stress and anxiety related symptoms, improved mental health scores, and improved perceptions about overall health. At day 14, over 90% of patients in the treatment group indicated that they were satisfied with the patch and approximately 90% of subjects indicated that they would recommend it to others for the treatment of anxiety related symptoms.*

***Conclusions:** Study results indicate that this non-pharmacologic, non-invasive, haptic vibrotactile trigger technology (VTT) embedded topical patch reduces stress and anxiety levels, improves mental health perceptions, and may encourage initiation and incorporation of exercise and other concomitant behavioral activities. These results suggest that further investigation is warranted, and may support the use of this OTC patch as a first-line, noninvasive and nonpharmacological therapy and also as a component of the multimodal treatment approach to anxiety and related symptoms.*

Keywords
Haptic vibrotactile trigger technology, Stress, Anxiety, Perceived Stress Score, PSS, SF-20, Medical Outcome Study Short Form, PEACE PATCH, VTT.

Introduction
Anxiety is also referred to as emotional stress, and chronically affects 49.9% of all US adults aged 18-24, as well as 32.3% of all US adults [1]. A chronic state of anxiety is associated with the persistent over-release of stress hormones such as cortisol, and is linked to adverse effects on the heart, immune system, and overall health [2]. Self-perceived quality-of-life (QoL) is likewise impacted adversely by living with chronic anxiety [3]. Substance abuse has long been recognized as a coping mechanism in adults afflicted with chronic anxiety [4,5], with substance abuse (*e.g.,* alcohol abuse) often diagnosed as a co-disorder in US adults living with an anxiety disorder [6]. Meanwhile, substance abuse is linked bi-directionally to both depleted social support networks and homelessness [7], which can increase feelings of stress.

Pharmacotherapy with antidepressants and anti-anxiety medications are the most common treatment modality, besides psychotherapy, for anxiety disorders; Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin and Norepinephrine Reuptake Inhibitors (SSNIs) are the standard medications prescribed [8]. Benzodiazepines, particularly *Alprazolam,* is the anti-anxiety medication most often prescribed to manage moderate-to-severe anxiety episodes, but benzodiazepines are widely considered to have a high misuse liability [9]. Moreover, benzodiazepines have been implicated as the method of choice in one-third of all suicide attempts [10] as well as 21% of annual alcohol overdose deaths [11], and in 2021, nearly 14% of overdose deaths involving opioids also involved benzodiazepines [12].

Psychotherapy can be as effective as pharmacotherapy for some patients, but adherence over time and compliance with treatment are barriers to its effective use. Some patients have contraindications or are intolerant to antidepressants and anxiolytics and may not be suitable candidates for select pharmacotherapies. This is especially so for benzodiazepines (as the most commonly used anti-anxiety medications), due to their widely known addictive properties plus dangerous interactions with alcohol, opiates, and other commonly-abused drugs [13]. In addition, tapering of either benzodiazepines or antidepressants in patients who no longer are experiencing anxiety symptoms can result in anxiety-producing (and other) withdrawal symptoms [14].

Stroke and Traumatic Brain Injury (TBI) survivors frequently experience resulting anxiety and depression, as well as cognitive impairment depending upon the location of the brain injury [15]. Injury to the cerebellum can impair balance, injury to the occipital cortex can result in blindness, and injury to the somatic sensory cortex can impair tactile perception and other higher brain functions [16]. Patients with post-stroke or TBI related deficits can benefit from somatosensory re-learning as a potential cognitive rehabilitation component [17,18].

Among all adults diagnosed with clinical depression, 45-67% meet the criteria for a co-morbid anxiety disorder; for those with an anxiety disorder, up to 63% of adults are diagnosed with clinical depression [19]. Additionally, adults with a co-disorder of depression and anxiety are more likely to be refractory to front-line psychiatric treatments than those diagnosed with solely anxiety or solely depression [20].

An abnormally low level of neurotransmitters including serotonin, norepinephrine, and/or dopamine in the Central Nervous System (CNS) is considered to play a role in modulating depression and anxiety symptoms. Meanwhile, neurons in both the peripheral and central nervous system respond to stimulation and transmit neural "messages" that trigger other brain-activated biochemical responses affecting both mood and anxiety level.

Haptic Vibrotactile Trigger Technology (VTT)
Haptic Vibrotactile Trigger Technology (VTT) generates a feedback response to tactile sensations, with bi-directional communication central to haptic-controlled systems and devices [21]. Diverse pathways of neural networks in the CNS and PNS respond to tactile sensations such as pain, as well as all other kinds of sensory information [22]. Notably, stroke and TBI victims can have resultant cognitive impairments that prevent accurate processing of sensory information inclusive of tactile sensations, with recent inclusion of haptic technology for tactile re-learning within cognitive rehab programs [23].

In the medical realm, haptic technology has been primarily associated with the use of robotic surgical and rehabilitative devices or prosthetics [24]. Haptics can be further categorized into Brain-Computer Interface (BCI) and Neurofeedback (NF) systems/devices. While BCI predominates in the medical (and entire) haptic realm, NF has historically been used to develop human internal control [25]. An example is haptic technology implanted in the footwear of TBI rehab patients, in order to provide NF to these patients to promote better balance when standing [26]. Another example is a VTT-controlled pressure sleeve that produces different tactile sensations in order to trigger improved EEG-evidenced sensation perception [27].

More recently, haptic technology has been studied as an adjunct or alternative therapy for the treatment of insomnia and/or psychiatric disorders, such as various *DSM-5* described anxiety disorders [28-30]. Haptics involving the use of a head-mounted display plus a specialized interface device to generate a Virtual Reality (VR) environment for receipt of exposure therapy has shown promise in relieving symptoms in people diagnosed with Post-Traumatic Stress Disorder (PTSD), panic attack, specific phobias, and Generalized Anxiety Disorder (GAD) [31-33]. During radiation treatments for cancer, haptic technology has been used to simulate human empathetic touch as a mode to relieve patient anxiety [34].

In this pilot STRAVA (Stress Reduction After Use of a Haptic Vibrotactile Trigger Technology Patch: Analysis and Assessment) minimal risk, controlled, observational, and IRB-approved research

study, we compared and evaluated an over the counter, non-invasive, non-drug, stress and anxiety-supporting patch (PEACE Patch; Super Patch Company, Srysty Holding Co, Toronto, Canada) that incorporates haptic-vibrotactile trigger technology (VTT) with a patch that did not contain VTT in patients with stress and anxiety-related symptoms. This study evaluated subject responses to validated tools including The Perceived Stress Scale (PSS) and the Medical Outcomes Study Short Form-20 (SF-20) to assess patient-reported changes in stress and anxiety related issues and symptoms. Data presented here is for the treatment arm of the study. Future analysis will include control and crossover groups.

Methods

Study Design

This study was a prospective, Institutional Review Board-approved, blinded Observational Study aimed at evaluating patients' experiences and/or perceptions and patient response for those who have received a haptic vibrotactile trigger technology (VTT) embedded patch (PEACE Patch; Super Patch Company, Srysty Holding Co, Toronto, Canada) or an inactive patch, without VTT, by their clinician.

Baseline demographic and clinical characteristics of patients

For this interim analysis, a total of 65 patients (49 females, 16 males) at 3 US investigator sites were enrolled in the treatment (n=65) arm of the study and completed the baseline, day 7, and day 14 surveys. Demographic results were similar for gender and age at the baseline survey. The mean age at baseline was 46.8 years.

Study subjects were given surveys that included validated stress and anxiety measurement and symptom scales (e.g., The Perceived Stress Scale (PSS) and the Medical Outcomes Study Short Form-20 (SF-20)) as well as additional survey questions regarding patient satisfaction, patient quality of life, and resumption of their normal activities.

Patients who met the eligibility criteria and who were treated with the active patch comprised the study's treatment group (TG) and patients given a similar-looking patch without the embedded VTT were assigned to a control group (CG) for which data is still being collected. Patient inclusion criteria were as follows: 1) ages 18 to 85 years, inclusive; 2) ability to provide written informed consent; 3) received the active VTT embedded study patch; and 4) had been diagnosed and presented with stress or anxiety related symptoms. Patients who had a history of use drug or alcohol abuse, patients who had an implantable pacemaker, defibrillator or other electrical devices, or patients who were pregnant, were ineligible to participate in the study. For the control group, the patch given to subjects did not contain the VTT technology. Patients were blinded and were unaware of which patch was given to them. Patches were identified by a number on the external package and were recorded and tracked by the CRO's compliance team. Control Group subjects who completed the study at day 14 were then crossed over into the treatment arm of the study to make up the Crossover Group (CrossG).

Enrolled study subject was identified by an identification number, and a confidential file containing the informed consent forms and patient identification numbers were kept and maintained in a secured cabinet only accessible to the principal investigator and authorized personnel. Patient survey responses were provided with no identifying patient information. Patients could withdraw from this study at any time with the assurance of no unfavorable impact on their medical care. All diagnostic tests and treatment decisions were made at the discretion of clinicians. All patients gave informed and written consent and were provided the patches at no cost without compensation for their participation in the study.

The study protocol was approved by ADVARRA institutional review board and was performed in full accordance with the rules of the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and the principles of the declaration of Helsinki and the international council of Harmonisation/GCP.

Topical Intervention

The active patches (Photo 1) have an adhesive backing on one side and contain no drug or energy source. The non-invasive, 2 x 2-inch non-pharmacological patches are embedded with proprietary sensory pattern imprints making up/compiling the haptic vibrotactile trigger technology (VTT). Study participants were instructed to wear a patch on their forearm each day, and placement was the same for the active and non-active treatment arms. The non-active patch looked similar to the active patches but did not incorporate the VTT.

Photo 1

Study procedures and assessments

Following enrollment, all study subjects were asked to complete surveys of the PSS and SF-20 at baseline (day 0) and follow-up surveys on days 7 and 14 of the study period. The surveys were comprised of questions to address and document stress and anxiety symptoms and how it interferes and impacts their quality-of-life components and in their daily lives.

The Perceived Stress Scale (PSS) is a classic stress assessment instrument. The tool, originally developed in 1983, remains a

popular choice for helping understand how different situations affect our feelings and our perceived stress. The Perceived Stress Scale (PSS) is the most widely used psychological instrument for measuring the perception of stress [35]. It is a measure of the degree to which situations in one's life are appraised as stressful. Items were designed to assess how unpredictable, uncontrollable, and overloaded respondents find their lives. The scale also includes a number of direct queries about current levels of experienced stress [35].

The Medical Outcomes Study Short Form-20 (SF-20) questionnaire is a 20- item instrument recommended for health-related quality of life research. It is also a commonly used outcome measurement tool with substantial evidence for its reliability and validity [36]. This is a general health measurement, but has been referred to as a functional measure, a measure of health status, and a quality-of life measure [36].

Patients were also asked to indicate their preference between the patch they were given and any other medications that they had been taking for stress and anxiety relief at the time of the baseline, day 7, and day 14, as well as their satisfaction and ease of use of the patch. Any reported side effects were also documented.

Study End Points

The primary endpoints included changes in patient responses to The Perceived Stress Scale (PSS) and The Medical Outcomes Study Short Form-20 (SF-20) scores among the treatment group, control, and crossover groups, differences between the treatment, control, crossover groups, preference in the use of prescription and OTC medications versus the patch, and differences in other treatments tried. We also assessed patient satisfaction with patch treatment and any side effects reported by patients during the trial.

Statistical Analysis

For all variables, descriptive statistics were calculated, including frequencies and percent for categorical variables and means with standard deviation (SD) for continuous variables. The maximum sample size available was used for each statistical analysis. Changes from baseline to day 7, and to day 14, in PSS and SF-20 scores were analyzed using the paired *t*-test to identify any statistically significant differences within the treatment and control groups. Each survey collected responses to questions regarding patient satisfaction and side effects of assigned treatment. Descriptive statistics were used to determine patient satisfaction with the patch within the treatment, control, and crossover groups. Descriptive statistics were also used to report any side effects experienced by patients. A two-tailed alpha was set to 0.05 for all statistical comparisons. SPSSv. 27 was used for all analyses.

Results

For this report, only patients that completed 14 days of treatment were included in the analysis.

Perceived Stress Scale Score (PSS)

PSS categorizes stress levels as either high (scores of between 27-40), moderate (scores between 14-26), or low (scores between 0-14). For the treatment group, after 14 days, the mean PSS score decreased 33% (21.05 to 13.95/40;P< .001), indicating a reduction from a moderate to low stress level. At Baseline, patients reported a mean stress level of 21.05, indicating a moderate level of stress. At day 14, the mean reported stress level was reduced to 13.95, a 7.0-point decrease on the PSS (out of 40 points), indicating a low perceived stress level (Figure 1). The Effect Size (Cohen's d) was 1.14 (large effect) for Baseline to F1, 0.86 (large) for F1 to F2, and 1.29 (large) for Baseline to F2.

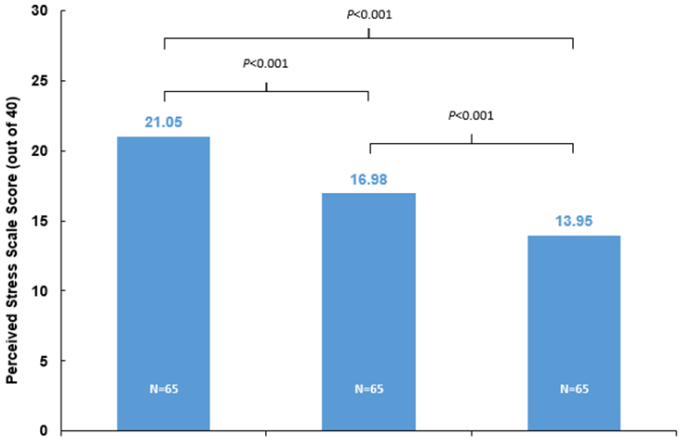

Figure 1. Treatment Group Mean Perceived Stress Scale Score (PSS) at Baseline, F1 and F2

Medical Outcomes Study Short Form-20 (SF-20) Scores

There are 6 domains in the SF-20 that are measured including Physical Functioning, Role Functioning, Social Functioning, Mental health, Health perceptions, and Pain. Except for the Pain domain, the higher the percentage, the better the quality of life. For the Pain domain, the lower the percentage, the lower the amount of bodily pain. For the Mental Health domain, the analysis represents the four major mental health dimensions (anxiety, depression, loss of behavioral-emotional control, and psychological well- being). The most notable positive change reported was a 23.8% relative increase in the percent score for the Mental Health domain from Baseline (64.2%) to the 14-day Follow-up Survey (F2) (79.5%) (Figure 2), indicating that study subject's Mental Health status improved significantly (P<.001) while using the active patch. Results also showed a positive outcome and statistically significant percentage increase (83.6% to 86.5%; P<.001) from Baseline to F2 in the Health Perception domain, indicating that respondents perceived that their health improved over the 14 days of active patch use. There were no significant differences in perceptions of physical functioning, role functioning, or social functioning, and although there was a slight decrease in reported pain levels over 14 days (34.4% to 31.8%), the difference was not significant.

Changes in Prescription or Over the Counter (OTC) Medication Usage

At Baseline, 17% of patients (11/65) indicated that they were taking prescription or OTC medication for their stress or anxiety-related symptoms. After 14 days, there were no significant changes in prescription or OTC medication usage.

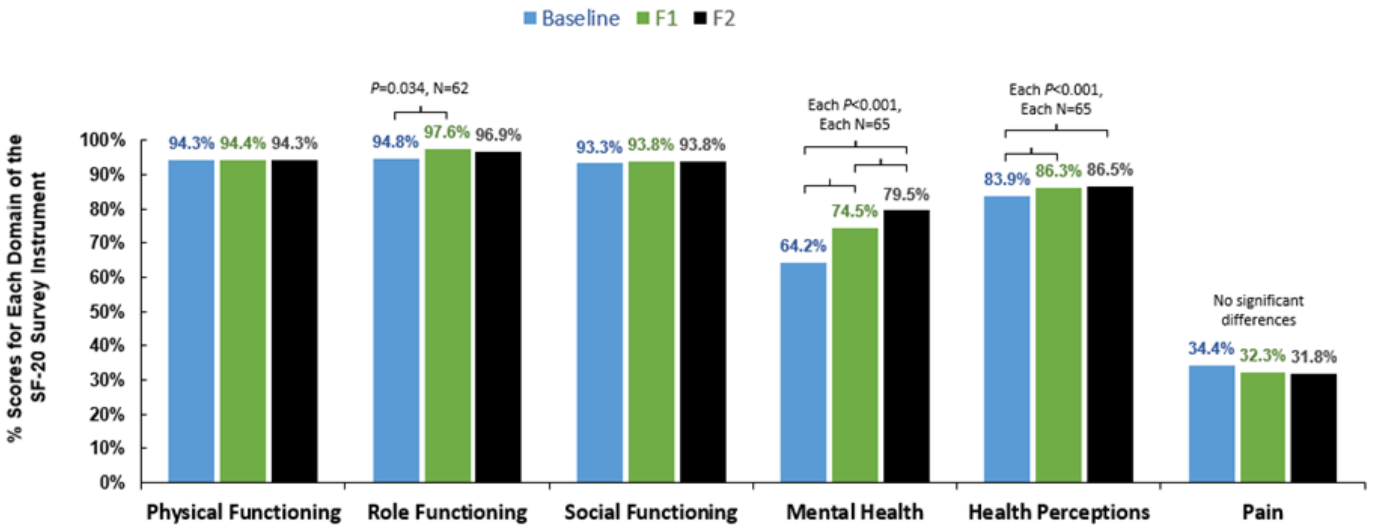

Figure 2. Treatment Group Percent Scores for Each of 6 Domains of the SF-20 Survey Instrument at Baseline, F1, and F2

Other Treatments

At Baseline, 26% (17/65) of subjects reported that they were incorporating other treatments to address their stress and/or anxiety related symptoms. These included such things as massage, exercise, behavioral therapy, physical therapy, yoga, and meditation. After 14 days, there was a 35% increase in the number of study subjects (17 to 23) who undertook or began these other forms of treatment, including exercise, massage, yoga, and swimming (Figure 3).

Baseline (N=65)	F1 (N=65) DAY 7	F2 (N=65) DAY 14
• None (48) • Massage (5) • Exercise (4) • Behavioral Therapy, gym • Exercise, shopping • Physical Therapy • Workout • Therapy (Non-Behavioral) • Yoga • Yoga, massage, exercise • Yoga, exercise • **17 total patients (26%) with a combined total 22 other treatments**	• None (44) • Exercise (7) • Yoga, exercise (3) • Massage (2) • Behavioral Therapy • Massage, exercise classes • Massage, Physical Therapy • Massage, Pilates • Therapy (Non-Behavioral) • Walking • Walking, swimming • Yoga, massage, exercise • Yoga, exercise, Pilates, shopping • **21 total patients (32%) with a combined total 33 other treatments**	• None (42) • Exercise (7) • Yoga, exercise (3) • Massage (2) • Behavioral Therapy (2) • Yoga, massage, exercise (2) • Massage, Physical Therapy • Massage, Pilates • Exercise (Zumba) • Swim, walk, acupuncture • Therapy • Walking, meditation • Yoga, exercise, Pilates, shopping • **23 total patients (35%) with a combined total 38 other treatments**

Figure 3. Other Treatments, besides Prescribed or OTC medications, reported from Baseline to Day 14

Satisfaction of Patch

Subjects were queried on specific satisfaction rating aspects regarding use of the patch (scale: 1 = Not at All, 2 = Not Very, 3 = Somewhat, 4 = Very, 5 = Extremely). At day 14, over 90% of patients in the treatment group indicated that they were satisfied with the patch and approximately 90% of subjects indicated that they would recommend it to their family and friends.

Safety

Patients reported no side effects or serious adverse events while being treated with the active patch.

Discussion

Here we report the interim results of this STRAVA study, a prospective, blinded, non-randomized observational study evaluating the safety and efficacy of a patch with VTT in patients presenting with stress or anxiety-related symptoms. Future analyses will compare these results to a control group who received a patch without the embedded technology, and a crossover group of patients, who received an active patch after completing the Control Group arm of the study. For the treatment group data evaluated, results showed positive outcome measurements in the PSS scores, with a decrease in stress level, from moderate to low, and positive outcomes in the SF-20 Mental Health and Health Perception domains. In addition, after 14 days of using the PEACE patch, patients reported an increase and initiation of concurrent and complimentary activities, including massage, exercise, and yoga.

Haptic input stimulates higher brain centers. A significant amount of research is underway to gain a better understanding of how haptics interact with different brain centers and the potential therapeutic role that haptics may play [37-45]. Research has shown that when a person is exposed to VTT, there are changes in their EEG patterns [46,47]. In addition, researchers have advanced their theoretical understanding and how neural networks are impacted by VTT [37-40,46-48]. Brain centers have been shown to be responsive to external stimuli that incorporate the VTT technology and have produced positive outcomes in balance and stability measurements [46,49].

As a way to explain the cognitive, emotional, and motor modalities through which humans experience sensations, Ronald Melzack hypothesized that specific regions of the brain communicate with networks of neurons in looping pathways: 1) a traditional sensory pathway with neural projections routed through the thalamus, 2) one that follows a path through the brainstem and parts of the limbic system, and 3) one associated with pathways that are routed through different Brodmann Areas (BA), particularly the somatosensory cortex [48].

Changes in EEG patterns have been reported after exposure to VTT, and the sensory patterns within the studied VTT patches are designed and thought to be in close symmetry between known EEG patterns and their role in modulating EEG and neuronal circuits within higher brain centers [46].

Although non-pharmacological approaches, such as Cognitive Behavioral Therapy (CBT), has shown success in treating patients with anxiety disorders [50-54], there remains a significant unmet need for alternative treatment options for those patients experiencing stress/anxiety-related symptoms and issues that do not respond to CBT. Gaining a better understanding of how the brain interacts with external stimuli, such as through VTT, may lead to viable, safe and effective, non-invasive, drug-free treatment options, with limited or no side effects. This may avoid or reduce conventional pharmacological antidepressant and anxiolytic treatments that are associated with toxic and potentially harmful adverse effects [13,14].

In this analysis, subjects in the treatment group of STRAVA (Stress Reduction after Use of a Haptic Vibrotactile Trigger Technology Patch: Analysis and Assessment) reported a statistically significant decrease in stress and anxiety related symptoms, improved mental health scores and improved perceptions about their health. These results add to the growing body of evidence that incorporating VTT into a multi-modal treatment strategy elicits successful outcomes in the symptoms that patients experience across a wide variety of disorders. Future research is encouraged to confirm and document real-time changes and support the use of VTT for anxiety and other medical conditions.

Limitations

This was a nonrandomized, blinded, observational IRB-approved study based on a sample of patients attending diverse clinical settings for the treatment of stress and/or anxiety-related symptoms who consented to participate in this study. This interim analysis reported on a group of 65 patients who were treated with the VTT embedded study patch. Ongoing study and data collection of a control group and crossover group of patients is ongoing and will be reported in upcoming months.

The data of those patients who did not complete the follow up surveys after baseline, or patients who indicated that they did not use the patch after the baseline visit were removed from evaluation. Due to patients having different stress or anxiety-related symptoms and differences in how they report their symptoms may impact the quality, overall generalization, and consistency of results. Although there were shown to be significant and positive outcomes in those subjects in the treatment group, without comparison to a control group, it difficult to draw absolute conclusions about the effects of the VTT embedded patch. We have attempted to accurately evaluate and provide the most detailed reporting of the data while considering these limitations. Further research and randomized control, double-blinded trials are suggested to reinforce, confirm, and support the use of this novel VTT technology.

Conclusion

Study results indicate that this non-pharmacologic, non-invasive, haptic vibrotactile trigger technology (VTT) embedded topical patch reduces stress and anxiety levels, improves mental health perceptions, and may encourage initiation and incorporation of exercise and other concomitant activities. Future concordant results may support use of this technology as first-line treatment combined with a behavioral and pharmacological multimodal treatment approach.

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Disclosure

Jeffrey Gudin MD has received compensation from Clarity Science LLC for his role as principal investigator and for providing protocol-required services for the study. Janet Fason DO was compensated for her role as a study investigator. Peter L Hurwitz is President of Clarity Science LLC. The authors report no other disclosures.

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