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Peripheral Somatosensory Stimulation in the Treatment of Post-Traumatic Stress Disorder: A Clinical Trial

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Abstract

Objective: Posttraumatic Stress Disorder (PTSD) is a complex condition that represents a significant burden in terms of individual disability and societal costs. Despite decades of research investigating treatment options, PTSD remains a major cause of quality-of-life impairment. We hypothesized that patients with PTSD might benefit from peripheral somatosensory stimulation (PSS) therapy.

Methods: 6 adult patients with clinically diagnosed PTSD were enrolled to undergo daily PSS therapy over a 4-week period. Patients completed two surveys evaluating satisfaction with treatment and overall well-being (Survey 1) and severity of PTSD symptoms (Survey 2). Survey 1 was completed weekly during the course of the study. Survey 2 was based on the 9-question National Stressful Events Survey PTSD Short Scale (NSESSS) and was completed as a baseline prior to initiation of therapy and then at the conclusion of the trial. All data were analyzed by an independent statistician.

Results: 6 male patients were enrolled in the study; all completed the trial. All patients demonstrated a decrease in symptoms within one week of initiation of therapy. This benefit was sustained and appeared to further improve over the course of the trial. For Survey 1, the overall median scores demonstrated a significant time-dependent improvement across measurement times ($p<0.001$). For Survey 2, patients had statistically significant improvements from baseline regarding feelings of being emotionally upset and being overly alert. Results from a cumulative link mixed model demonstrated that treatment yielded a 38.2-fold higher likelihood of transitioning from a higher PTSD score at baseline to a lower (improved) score at week 4. No adverse events were described by the patients.

Conclusion: PSS stimulation appeared to improve symptoms in all six patients with PTSD symptoms in this trial. Patients had unanimous and clinically meaningful improvement in overall PTSD symptoms with treatment. By week 4, all patients responded that they enjoyed the treatment and would like to keep their device. We suggest that further investigation into the potential usefulness of PSS therapy in patients with PTSD is warranted.

Keywords: Anxiety • Neuromodulation • Post-traumatic stress disorder • Somatosensory • Stimulation

Introduction

Post-traumatic stress disorder (PTSD) may develop in select individuals after exposure to extreme traumatic events and has been associated with "hyperarousal" and increased sympathetic output [1-6]. It has been estimated that more than 7 million Americans are diagnosed with PTSD every year [7]. In addition to pharmacotherapy and psychological interventions, treatment for PTSD has included various methods of relaxation including yoga and deep breathing exercises [2-5,8]. Nevertheless, PTSD remains a major cause of quality-of-life impairment for patients and a significant societal burden in terms of medical costs [3-7]. Peripheral Somatosensory Stimulation (PSS) therapy is a non-invasive technique which may be beneficial to patients with a variety of neurological disorders [9-13]. The current trial was undertaken to evaluate the potential benefit of such PSS therapy in patients with PTSD.

Data and Methods

Study description

NeuroGlove is a non-invasive device that provides PSS stimulation in the form of pneumatic puffs of air directed at the volar surface of the distal forearm, the palm, and the fingers. This study was designed as a prospective, single center trial enrolling six patients to explore the effect of PSS therapy on symptoms and quality-of-life measures in patients with PTSD. Men and women between the ages of 18 and 85 years with an active diagnosis of PTSD who were able to provide informed consent were considered eligible for trial enrollment. Patients who were unable to comprehend or follow instructions or unable to use the device due to physical limitations of the upper extremity including fracture, joint deformity, severe spasticity/contracture, or skin breakdown were excluded from participation.

Device use

Subjects were instructed to use the device at home for 1 hour of therapy per day (30 minutes using each hand) for 4 weeks. Subjects were directed to synchronize their breathing to the firing (on/off cycle) of the machine to encourage relaxation during device use. At the conclusion of the trial, compliance was determined based on patient reporting and using an internal computerized system that allowed the investigators to track device use during the course of the trial.

Survey 1: Patient satisfaction

The primary objective of Survey 1 (Table 1) was to evaluate overall patient satisfaction scores on a weekly basis during the trial. Each question was answered using the following ordinal scoring system: "Strongly Disagree"=1, "Disagree"=2, "Neutral"=3, "Agree"=4, and "Strongly Agree"=5. Simple descriptive statistics were calculated for individual scores at each timepoint, including median and interquartile ranges (IQR). A composite score of all questions using the pooled median value of patient-specific survey questions was also generated and compared between patient visits. Additionally, for in-text summaries, scores were trichotomized as ≥ 4 (positive), 3 (neutral), and <2 (negative). For trichotomized scores, counts and percentage of total

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were calculated. Friedman's test was used to determine if ordinal response scores significantly changed over time from week 1 to week 4. Box and whisker plots were generated in order to visually show overall and patient-specific results across timepoints.

Table 1. Questions from survey 1

Question	Description
Q1	My Memory is better
Q2	I'm more relaxed
Q3	My thoughts are more positive
Q4	It's easier to concentrate
Q5	I'm less irritable
Q6	I feel better about myself
Q7	My thinking ability is better
Q8	I'm using less alcohol and/or drugs
Q9	I look forward to and enjoy using the device
Q10	My PTSD Symptoms are reduced
Q11	I would like to keep the device

Survey 2: Severity of PTSD symptoms

The primary objective Survey 2 (Table 2) was to evaluate change from baseline severity of posttraumatic stress symptoms. Survey 2 was based on the National Stressful Events Survey PTSD Short Scale (NSESSS) and was administered at baseline and at week 4 after consistent use of the device. Each question was answered using the following ordinal scoring system: "Not At All" = 0, "A Little Bit"=1, "Moderately"=2, "Quite a Bit"=3, and "Extremely"=4.

We assessed changes in ordinal response scores from patient-specific matched pairs using Wilcoxon's signed-rank test to determine if there were significant improvements from baseline to week 4. A composite score of all questions using the pooled median value of patient-specific survey questions was also generated and compared between baseline and week 4. Effect sizes from Wilcoxon's signed rank tests were reported as the median of differences alongside approximates of the 95% confidence interval. Since this nonparametric test works with ranks, it is typically not possible to derive a confidence interval with exactly 95% confidence; instead, the closest approximate was calculated, corresponding to true CIs calculated with 96.88% confidence; for simplicity these are reported as 95% CIs in text.

To formally analyze overall cumulative probability of improved scores across measurement times, we employed a Cumulative Link Mixed Model (CLMM) with a logit link function. The model was specified with the following formula using the clmm () function in the 'ordinal' package for R: Score ~ Visit + (1 | Subject), where, 'Score' represents individual ordinal-scale responses, 'Visit' is the predictor variable of interest (baseline or week 4), and '(1 | Subject)' indicates the inclusion of random intercepts for individual subjects to account for within-subject variability. Laplace approximation was employed to estimate the model parameters due to its suitability for handling ordinal response data. Predicted probabilities and 95% CIs for each score at a given timepoint were extracted from the model. Overall effect sizes from the CLMM model are reported as cumulative odds ratios.

Table 2. Questions from survey 2

Question	Description
Q1	Having "flashbacks", that is, you suddenly acted or felt as if a stressful experience from the past was happening all over again (for example, you re-experienced parts of a stressful experience by seeing, hearing, smelling, or physically feeling parts of the experience)?
Q2	Feeling very emotionally upset when something reminded you of a stressful experience?
Q3	Trying to avoid thoughts, feelings, or physical sensations that reminded you of a stressful experience?
Q4	Thinking that a stressful event happened because you or someone else (who didn't directly harm you) did something wrong or didn't do everything possible to prevent it, or because of something about you?
Q5	Having a very negative emotional state (for example, you were experiencing lots of fear, anger, guilt, shame, or horror) after a stressful experience?
Q6	Losing interest in activities you used to enjoy before having a stressful experience?
Q7	Being "super alert," on guard, or constantly on the lookout for danger?
Q8	Feeling jumpy or easily startled when you hear an unexpected noise?
Q9	Being extremely irritable or angry to the point where you yelled at other people, got into fights, or destroyed things?

Simple descriptive statistics were also calculated, including median and IQRs. Additionally, for in-text summaries, scores were dichotomized as ≤ 1 (positive) or >1 (negative). Box and whisker plots were generated in order to visually show overall and patient-specific results across timepoints.

Software

All analyses were conducted in RStudio (2023.06.2 Build 561), running on R version 4.2.2. CLMM analyses were performed using the 'ordinal' package (version 2022.16). Figures were generated using the 'ggplot2' package (version 3.4.0). All data were analyzed by an independent statistician at the conclusion of the trial.

Results

6 patients with a formal diagnosis and active symptoms of PTSD were consented and enrolled in the trial. All patients were men, and all patients completed the trial. Compliance with device use was greater than 95% based on self-reporting and internal control checks at the conclusion of the trial. No patient reported an adverse event related to use of the device. All patients reported enjoying using the device and wished to keep the device at the conclusion of the trial. One patient was bothered by the noise level associated with device use, but othes found the background noise calming.

Survey 1

By week 4, all 6 patients (100%) had positive scores (scores 4 and 5) for feelings of relaxation (Q2), positive thoughts (Q3), enjoying using the device (Q9), and wanting to keep the device (Q11). Regarding feeling better about oneself (Q6) and reduction in PTSD symptoms (Q10), 5 out 6 patients (83%) showed positive scores. Regarding memory (Q1), concentration (Q4), and irritability (Q5), 4 patients (67%) had positive scores. Half of the patients had improved thinking ability (Q7). Patients exhibited the lowest scores regarding using less alcohol and/or drugs (Q8), with 2 out 6 (33%) having positive scores, and the remaining had neutral scores. Of note, no individual patient reported scores of 1 or 2 for any of the questions by week 4, suggesting that no patients disagreed with improved satisfaction scores, and either felt improved or at least neutral.

The pooled median score by week 4 was 4 (IQR: 4-4), and ranged from 3 to 5, suggesting a typically positive outcome and significantly improved overall score over time (p<0.001) (Table 3). The question that had the largest upward trend from week 1 was regarding improved memory (Q1), showing a statistically significant improvement by week 4 (p<0.001). Other individual questions did not demonstrate significant time-dependent improvements. Patients had the lowest upward trend regarding thinking ability (Q7) and use of drugs/alcohol (Q8), exhibiting slight, albeit not significant, reductions in score on week 4 compared to week 1.

Table 3. Summary of Survey 1 results across timepoints

Survey Question	Week 1 Median (IQR)	Week 2 Median (IQR)	Week 3 Median (IQR)	Week 4 Median (IQR)	P-value for time-dependent trend of improvement
Q1	3 (2–3)	3 (2.75–3)	3.5 (3–4)	4 (3–4)	0.007
Q2	4 (3.5–4)	4.5 (3.75–5)	4 (4–4)	4 (4–5)	0.266
Q3	3.5 (3–4)	4 (4–4)	4 (3–4)	4 (4–4)	0.125
Q4	3 (3–4)	3 (3–4)	3 (3–4)	4 (3–4.25)	0.561
Q5	3.5 (2.75–4)	4 (3–4)	3.5 (3–4)	4 (3–4.25)	0.438
Q6	3 (3–4)	3 (3–4)	4 (3.75–4)	4 (3.75–4.25)	0.146
Q7	4 (3–4)	3 (3–4)	3 (3–4)	3.5 (3–4)	0.719
Q8	3.5 (3–4)	3 (3–3.25)	3 (3–4)	3 (3–4)	0.917
Q9	4 (3.5–4.25)	5 (3.5–5)	4 (3.75–4.25)	4 (4–5)	0.305
Q10	3 (2.75–4)	4 (4–4)	4 (3.75–4)	4 (3.75–4)	0.133
Q11	4 (3.75–4)	4 (4–5)	4 (4–4.25)	4 (4–5)	0.333
Overall*	4 (3–4)	4 (3–4)	4 (3–4)	4 (4–4)	<0.001
*Overall scores correspond to pooled median value from patient-specific questions.					

Survey 2

By week 4, all 6 patients (100%) had positive scores (0 and 1) for having flashbacks (Q1) and negative emotional state (Q5). Regarding stressful events (Q4), losing interest in activities (Q6), being super alert (Q7), being easily startled (Q8), and being irritable or angry (Q9), 5 out 6 (83%) had positive scores, while 1 patient had moderate severity. No individual patient reported adverse scores of 3 or 4, suggesting no severe symptoms by week 4 (Table 4).

Table 4. Summary of survey 2 questions at baseline and at week 4

Survey Question	Baseline Median (IQR)	Week 4 Median (IQR)	Median of differences [95% CI]	p-value
Q1	2 (0.75–2.25)	0 (0–1)	-1 [-3; 0]	0.063
Q2	3 (1.75–4)	0 (0.75–2)	-1.5 [-3; -1]	0.031
Q3	4 (1.75–4)	1 (0.75–1.5)	-2.5 [-3; 0]	0.063
Q4	2 (0–2.5)	0 (0–1.25)	-1 [-4; 1]	0.250
Q5	4 (2.5–4)	0.25 (0–1)	-3.25 [-4; 0]	0.063
Q6	3.5 (0.75–4)	0.5 (0–1.25)	-2 [-4; 0]	0.063
Q7	4 (3.75–4)	1 (0.75–1.25)	-3 [-3; -2]	0.031
Q8	4 (2.5–4)	1 (0.75–1.25)	-2.5 [-3; -1]	0.031
Q9	2.5 (0.75–3.25)	0.5 (0–1.25)	-2 [-2; 0]	0.063
Overall*	**3 (2–4)**	**1 (0–1)**	**-2 [-3; -2]**	**<0.001**
*Overall scores correspond to pooled median value from patient-specific questions.				

Of the individual survey questions, patients had statistically significant improvements regarding feelings of being emotionally upset (Q2: MD=-1.5, p=0.031) and being overly alert (Q7: MD=-3, p=0.031; Table 5). Although not statistically significant for all individual questions, all patients uniformly had numerically improved scores by week 4. The composite score was substantially improved from baseline, with an overall median score of 3 (IQR: 2-4) at baseline to 1 (IQR: 0-1) by week 4 (MD=-2 [95% CI: -3; -2], p<0.001). Overall, the predicted probability of obtaining the best outcome (score=0) was 2% at baseline vs. 43% by week 4. Conversely, the predicted probability of obtaining the worst outcome (score=4) was 39% at baseline vs. 2% at week 4. The overall cumulative odds ratio was 38.2 (p<0.001), suggesting that on average, the odds of moving from one score to a lower (improved) score at week 4 compared to the baseline are 38.2 times higher. The significant decrease in symptoms based on Survey 2 over time is illustrated in Figures 1 and 2.

Table 5. Cumulative link mixed model results of overall improvement in PTSD symptoms

Survey Score	Baseline Probability [95% CI]	Week 4 probability [95% CI]	Cumulative odds ratio [95% CI]	P-value
Score 0	2% [0–5%]	43% [13–74%]	38.2 [13.8–105.5]	<0.001
Score 1	13% [0–27%]	43% [24–63%]		
Score 2	28% [10–47%]	10% [0–21%]		
Score 3	18% [6–29%]	2% [0–4%]		
Score 4	39% [9–68%]	2% [0–4%]		

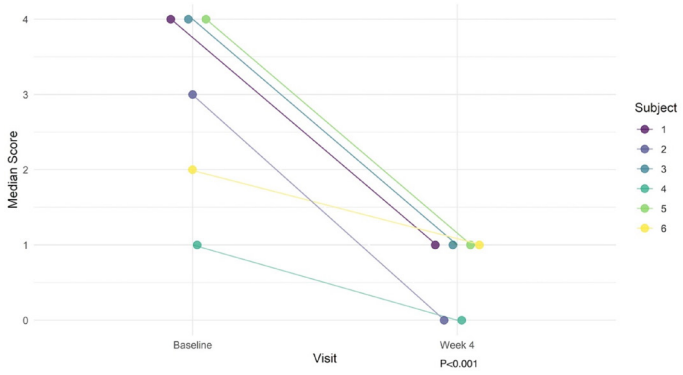

Figure 1. Illustration of changes in PTSD symptom severity in 6 patients over the course of the study

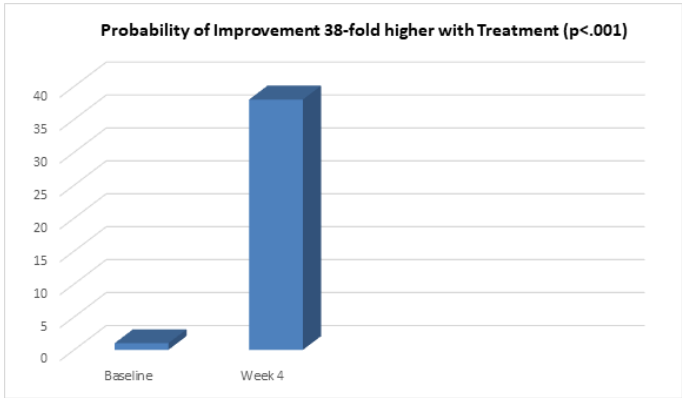

Figure 2. Bar Graph showing cumulative odds ratio of improvement with treatment

Discussion

PTSD is a prevalent and potentially disabling condition that appears to represent a form of anxiety disorder associated with hypervigilance and increased sympathetic output [1-7]. Although the mainstay of treatment for PTSD was originally pharmacologic, an increasing emphasis has been placed on psychological interventions and various relaxation techniques such as yoga and deep breathing exercises [3-8]. Despite ongoing research into newer treatment options, PTSD remains a major cause of individual disability, quality-of-life impairment, and significant medical and societal costs [3,4,6].

A variety of physiological alterations within the brain have been associated with PTSD, and increasing evidence suggests that impaired sensory processing may play a critical role in the development and pathophysiology of this disorder. As early as 1972, Ayres suggested that sensory processing forms a significant basis for an individual's physiological state [14]. Haricharichan et al. postulated that alterations in the neural pathways important for processing sensory input have a cascading effect on the ability to perform higher cognitive functions implying that abnormal sensory processing may be contributory and associated with PTSD [15]. In addition, it has been shown that individuals with PTSD have decreased prefrontal cortex activation resulting in impaired sensory integration and emotional regulation [2,16-18]. Engel-Yeger et al. identified reproducible patterns of sensory hypersensitivity in patients suffering from PTSD [19]. Based upon these findings, we hypothesized that impaired sensory perception and processing, which may play a role in PTSD, might also represent a potential treatment avenue using PSS therapy in this patient population.

It has been shown that PSS significantly improves neurological outcomes following ischemic injury in rodent models of stroke [20-22]. Potential suggested mechanisms for this benefit include improved regional cerebral perfusion through the recruitment of local collateral blood supply and/or delayed neuronal reorganization allowing for better neural "learning" and functional recovery [10]. Preliminary clinical experience in stroke patients has suggested that such peripheral sensory stimulation can improve recovery and rehabilitation in stroke survivors [9,10,23-33]. Interestingly, similar benefits have been demonstrated in patients with Parkinson's disease, and PSS has also shown promise following traumatic brain injury and in inflammatory, auto-immune conditions such as multiple sclerosis [34-39].

In this study, we encountered a significant early response to PSS treatment as evidenced by the improvement in symptoms just one week after initiating therapy. This benefit appeared to be sustained and to further increase over the course of the study. Interestingly, multiple patients reported that when they were challenged by a stress-inducing event, they used the device to help them achieve a calmer state and mitigate their symptoms.

Our survey results suggest promising preliminary evidence of improved PTSD scores and high user satisfaction after 4 weeks of PSS therapy. Regarding Survey 1, patients seemed most improved regarding feelings of relaxation, positive thoughts, enjoying using the device, and wanting to keep the device. The pooled median scores on Survey 1 demonstrated significant and time-dependent overall improvement. No patients demonstrated negative survey responses by the week 4 survey. Regarding Survey 2, patients demonstrated unanimous improvement by week 4, with composite scores substantially improved from baseline. By week 4, all patients agreed that they enjoyed the treatments and wanted to keep their device.

Conclusion

We describe the results of a clinical trial evaluating the impact of one month of treatment with PSS on symptoms in patients with a diagnosis of PTSD. All patients completed the trial, and all appeared to benefit from the therapy. The improvement in symptomatology was apparent at one week of device use and was sustained and typically increased through the course of the trial. A significant reduction in symptoms was achieved in all patients when comparing baseline (pre-trial) and 4-week (post-trial) assessment using the NSESSS Scale. We suggest that further investigation into the potential use of PSS in the treatment of patients with PTSD is warranted.

Limitations

The main limitation of our study is the small sample size evaluated in this trial. Data are also limited to self-reported survey questions and may, therefore, fail to capture other clinically important outcomes. In addition, the exact mechanism by which patients in this study benefitted from device use is unclear. This is a small trial with a small sample size representing a preliminary investigation of the potential benefit of PSS in patients with PTSD.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Acknowledgement

None.

Conflict of Interest

Dr. Eric Nussbaum is a shareholder in NeuroGlove, LLC.

References

1. "American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders," 2000.
2. Yehuda, R, Hoge CW, McFarlane AC and Vermetten E, et al. "Post-traumatic Stress Disorder." *Nat Rev Dis Primers* 1(2015):15057.

3. Sherin, JE and Nemeroff CB. "Post-traumatic Stress Disorder: The Neurobiological Impact of Psychological Trauma." *Dialogues Clin Neurosci* 13(2011): 263-278.
4. Bryant, RA, Friedman MJ, Spiegel D and Ursano R, et al. "A Review of Acute Stress Disorder in DSM-5." *Depress Anxiety* 28(2011): 802-817.
5. Qi, W, Gevonden M and Shalev A. "Prevention of Post-Traumatic Stress Disorder After Trauma: Current Evidence and Future Directions." *Curr Psychiatry Rep* 18(2016): 20.
6. Blechert, J, Michael T, Grossman P and Lajtman M, et al. "Autonomic and Respiratory Characteristics of Posttraumatic Stress Disorder and Panic Disorder." *Psychosom Med* 69(2007): 935–943.
7. National Institute of Mental Health.
8. Descilo, T, Vedamurtachar A and Gerbarg PL. "Effects of a Yoga Breath Intervention Alone and in Combination with an Exposure Therapy for Post-traumatic Stress Disorder and Depression in Survivors of the 2004 South-East Asia Tsunami." *Acta Psychiatr Scand* 121(2010): 289–300.
9. Celnik P, Hummel F, Harris LM and Wolk R, et al. "Somatosensory Stimulation Enhances the Effects of Training Functional Hand Tasks in Patients with Chronic Stroke." *Arch Phys Med Rehabil* 88(2007): 1369–1376.
10. Nussbaum, ES, Janjua TM, Lowary J and Defillo A, et al. "Peripheral Sensory Stimulation of the Hand in the Treatment of Stroke: A preliminary Study of Safety and Effectiveness." *J Neurol Disord* 11(2023): 1-5.
11. Nussbaum, HA and Nussbaum ES. "Peripheral Sensory Stimulation for Neurological Disorders. A Novel, Non-invasive Therapeutic Option. Review Article." *J Neurosci and Neurol Surgery* 13(2023): 267-271.
12. Kristina, JP, Kromer JA, Cook AJ and Hornbeck T, et al. "Coordinated Reset Vibrotactile Stimulation Induces Sustained Cumuluative Benefits in Parkinson's Disease." *Front Physiol* 12(2021): 624317.
13. Lucente, G, Valls-Sole J, Murillo N and Rothwell J, et al. "Noninvasive Brain Stimulation and Noninvasive Peripheral Stimulation for Neglect Syndrome Following Acquired Brain Injury." *Neuromodulation* 23(2020): 312-323.
14. Ayres, AJ. "Treatment of Sensory Integrative Dysfunction." *A J Occ Ther* 19(1972): 1440.
15. Harricharan, S, McKinnon MC and Lanius RA. "How Processing Sensory Information from Te Internal and External Worlds Shape the Perception and Engagement with the World in the Aftermath of Trauma: Implications for PTSD." *Front Neurosci* 15(2021): 88.
16. Etkin, A and Wager TD. "Functional Neuroimaging of Anxiety. A Metanalysis of Emotional Processing in PTSD, Social Anxiety Disorder, and Specific Phobia." *Am J Psychiatr* 164(2007): 1476-1488.
17. Nicholson, AA, Friston KJ, Zeidman P and Harricharan S, et al. "Dynamic Causal Modeling in PTSD and its Dissociative Subtype: Bottom-up vs Top-down Processing within Fear and Emotional Regulation Circuitry." *Human Brain Mapp* 38(2017): 5551-5561.
18. Shin, LM, Rauch SL and Pittman RK. "Amygdala, Medial Prefrontal Cortex and Hippocampal Function in PTSD." *Ann NY Acadd Sci* 1071(2006): 67-79.
19. Engel-Yager, B, Palgy-Levin D and Lev-Wiesel R. "The Sensory Profile of People with PTSD." *Occup Ther Ment Health* 29(2013): 266-278.
20. Lay, CC, Jacobs N, Hancock AM and Zhou Y, et al. "Early Stimulation Treatment Provides Complete Sensory-induced Protection from Ischemic Stroke Under Isoflurane Anesthesia." *Eur J Neurosci* 38(2013): 2445-2252.
21. Frostig, RD, Lay CC and Davis MF. "A Rat's Whiskers Point the Way toward a Novel Stimulus-dependent Protective Stroke Therapy." *Neuroscientist* 19(2012): 313-328.
22. Hancock, AM, Lay CC, Davis MF and Frostig RD. "Sensory Stimulation-Based Complete Protection from Ischemic Stroke Remains Stable at 4 Months Post-Occlusion of MCA." *J Neurol Disord* 1(2013): 135.
23. Conforto, AB, Cohen LG, Dos Santos RL and Scaff M, et al. "Effects of Somatosensory Stimulation on Motor Function in Chronic Cortico-Subcortical Strokes." *J Neurol* 254(2007): 333–339.
24. Conforto, AB, dos Anjos SM, Bernardo WM and Silva AA, et al. "Repetitive Peripheral Sensory Stimulation and Upper Limb Performance in Stroke: A Systematic Review and Meta-analysis." *Neurorehabil Neural Repair* 32(2018): 863–871.
25. Conrad, MO, Scheidt RA and Schmidt BD. "Effects of Wrist Tendon Vibration on Targeted Upper-arm Movements in Poststroke Hemiparesis." *Neurorehab Neurol Repair* 25(2011): 61-70.
26. Maeda, M, Mutai H, Toya Y and Maekawa Y, et al. "Effects of Peripheral Nerve Stimulation on Paralysed Upper Limb Functional Recovery in Chronic Stroke Patients Undergoing Low-Frequency Repetitive Transcranial Magnetic Stimulation and Occupational Therapy: A Pilot Study." *HK J Occ Ther* 33(2020): 3-11.
27. Nasrallah, FA, Mohamed AZ, Hong KY and Hwa SL, et al. "Effect of Proprioceptive Stimulation Using a Soft Robotic Glove on Motor Activation and Brain Connectivity in Stroke Survivors." *J Neural Eng* 18(2021): 1.
28. Seo, NJ, Enders LR, Fortune A and Cain S, et al. "Phase I Safety Trial: Extended Daily Peripheral Sensory Stimulation Using a Wrist-worn Vibrator in Stroke Survivors." *Transl Stroke Res* 11(2019): 204–213.
29. Seo, NJ, Woodbury ML, Bonilha L and Ramakrishnan V, et al. "Therabracelet Stimulation During Task-practice Therapy to Improve Upper Extremity Function after Stroke: A Pilot Randomized Controlled Study." *Physical Therapy* 99(2019): 319–328.
30. Vatinno, AA, Hall L, Cox H. "Using Subthreshold Vibratory Stimulation during Post-stroke Rehabilitation Therapy: A Case Series." *OTJR* 42(2021): 30-39.
31. Carrico, C, Chelette KC, Westgate PM and Salmon-Powell E, et al. "A Randomized Trial of Peripheral Nerve Stimulation to Enhance Modified Constraint-Induced Therapy after Stroke." *Am J Phys Med Rehabil* 95(2016): 397-406.
32. Carrico, C, Chelette KC, Westgate PM and Salmon-Powell E, et al. "Nerve Stimulation Enhances Task-oriented Training in Chronic, Severe Motor Deficit after Stroke: A Randomized Trial." *Stroke* 47(2016): 1879–1884.
33. Serrada, I, Hordacre B and Hillier SL. "Does Sensory Retraining Improve Sensation and Sensorimotor Function Following Stroke: A Systematic Review and Meta-analysis." *Front Neurosci* 13(2019): 402-415.
34. Pfeifer, KJ, Cook AJ, Yankulova JK and Mortimer BJP, et al. "Clinical Efficacy and Dosing of Vibrotactile Coordinated Reset Stimulation in Motor and Non-motor Symptoms of Parkinson's Disease: A Study Protocol." *Front Neurol* 12(2021): 758481.
35. Tas,s PA. "Vibrotactile Coordinated Reset Stimulation for the Treatment of Parkinson's Disease." *Neural Regen Res* 17(2021): 1495-1497.

36. Tramontano, M, Morone G, De Angelis S and Conti L, et al. "Sensor-based Technology for Upper Limb Rehabilitation in Patients with Multiple Sclerosis: A Randomized Controlled Trial." *Restor Neurol Neurosci* 38(2020): 333-341.

37. Hall, KD and Lifschitz J. "Diffuse Traumatic Brain Injury Initially Attenuates and Later Expands Activation of the Rat Somatosensory Whisker Circuit Concomitant with Neuroplastic Responses." *Brain Res* 1323(2010): 161-173.

38. Lew, HL, Weihing J, Myers PJ and Pogoda TK, et al. "Dual Sensory Impairment (DSI) in Traumatic Brain Injury (TBI)--An Emerging Interdisciplinary Challenge." *Neurorehabilitation* 26(2010): 213-222.

39. Zheng, Z, Dong X, Li Y and Gao W, et al. "Electrical Stimulation Improved Cognitive Deficits Associated with Traumatic Brain Injury in Rats." *Brain Behav* 7(2017): e00667.

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