AUTONOMIC REGULATION VIA DERMAL VIBROTACTILE TRIGGERING OF PIEZOELECTRIC CHANNELS: AN EMERGING NON-MEDICATION APPROACH TO SYMPTOM RELIEF

Peter Hurwitz[1]; Jeffrey Gudin, MD[2]

[1]Clarity Science LLC, Narragansett, Rhode Island USA; [2]Pain and Palliative Medicine, Miller School of Medicine, University of Miami, Miami, USA

Abstract

Overview

The Autonomic Nervous System (ANS) maintains homeostatic balance of the body by controlling involuntary physiological functions such as body temperature. While the brain's hypothalamus and brainstem are primary brain areas that control the ANS, its limbic system is involved in emotional reactions such as anxiety and excitement, which can impart an effect on autonomic responses such as heart rate and blood pressure. Meanwhile, Piezo ion channels enable interpretation of sensory information conveyed through the Somatic Nervous System (SNS) of the Peripheral Nervous System (PNS) to be communicated between neurons in the brain, and also bidirectionally between the brain and the PNS.

Piezo channels allow electrical current to pass through them. In this way, ion channels enable neurons (nerve cells) to communicate with each other, so that the brain's neural networks can properly function. TRP ion channels stimulate neuronal cellular responses, while Piezo channels open in response to mechanical stimuli, so an interrelationship exists between them. Haptic Vibrotactile Trigger Technology (VTT) prompts a sensory response by using electrical current-producing vibrations to stimulate the skin's mechano-receptors and is communicated via the PNS to the brain.

Results

Outcomes from recent research of VTT randomized clinical trials (RCTs) have demonstrated positive effects (*e.g.,* the reduction of anxiety, stress, depression, improvement in sleep, pain relief, balance and stability),which can prompt an ANS response such as lowering heart rate and/or blood pressure.

Conclusions

The bi-directional sensory communication promoted by VTT utilization may be able to boost the functioning of the piezoelectric channels. Evolving VTT treatments may be beneficial in people with diminished functioning of their piezoelectric channels.

Introduction

Ion channels control the transmission of neural impulses in the peripheral and central nervous systems and are responsible for the biology of the senses. Specific ion channels, such as the transient receptor potential (TRP) channel, respond to various stimuli, such as temperature, touch, and vibration, whose responses are conveyed from the skin to the brain [1]. Other ion channels, such as Piezo-1 and 2, are mechano-transducing (mechano-sensitive) and open in response to mechanical stimuli [2,3]. Investigations of Piezo ion channels have revealed that they are trimers and shaped like a three-bladed propeller (see **Figure 1).** Piezo 2 specifically, has been shown to act as a sensor for mechanical stimuli, such as touch or stretching. Mechano-transduction allows living organisms to receive and respond to physical signals from the external and internal environments; Piezo channel research has revealed it to be among the largest mechano-sensitive ion channels [2] than other ion channels (e.g., potassium channels), which may also be large in size but function differently. The brain's ion channels also act on neurotransmitter (e.g., dopamine) release and other secreted biochemicals [4].

Haptic technology creates a sense of touch using vibration, motion, and other forces and has been gaining popularity in medical arenas since the 1980s-1990s. One example in medical education is the use of surgical simulators that enable tactile feedback to surgeons-in-training [5]. Haptic technology has also been incorporated into diverse stroke and traumatic brain injury (TBI) rehab devices, especially in tandem with virtual reality (VR) technology. Furthermore, the "cutting-edge" use of medically focused haptic technology has expanded to include pain, sleep, and anxiety relief [6-8]. Ongoing research will support these advances in haptic technologies and their incorporation into various medical applications.

Haptic Technology and Its Applications

Haptic stimulation is currently being used as a noninvasive treatment for adults living with diverse neurodegenerative disorders. For adults post-stroke or TBI (who often have resulting sensory deficits), haptic stimulation is used as a rehab approach to promote sensory retraining [9]. For people with Parkinson's disease, vibrotactile (VTT) stimulation at gamma frequency has been shown to lessen cognitive decline and improve motor function [10], and haptic stimulation has also been found to attenuate AD symptoms [11]. In addition, the findings of a recent clinical trial of a haptic VTT patch (see **Figure 2**) in adults with symptoms of emotional stress/anxiety showed reduced anxiety and other improved mental health variables [12].

Pain has been a particular focus as a potential for therapeutic VTT haptic sensory stimulation, and numerous studies have shown that mechanical stimuli generate a Piezo channel response that can lessen pain [13]. Vibrating motors were used on the fingers of the remaining hand in research subjects with an amputated hand to reduce the "phantom pain" in the amputated hand [14]. In a different study, a haptic patch was worn and utilized by research subjects diagnosed with pain [15]. The findings pertaining to the use of both of these modalities showed clinically significant reductions in self-perceived pain and functional measurements.

Mental health disorders have been another focus as a potential for therapeutic VTT haptic sensory stimulation [16], as well as VR devices with vibrotactile platforms [17]. These disorders have ranged from anxiety and phobias to schizophrenia [17]. Since the perception of pain can be distorted (either abnormally increased or decreased) in some adults diagnosed with psychiatric disorders [18], chronic pain as a VTT target can be investigated as a distinct therapeutic target (in and of itself) or included as a possible future therapy aimed at persons living with a mental health disorder resulting in pain perception distortions.

Moreover, since chronic depression has been linked to increased pain perception [19], the use of VTT haptic sensory stimulation for the treatment of chronic depression in these people may help alleviate their pain, resulting in lessened depression.

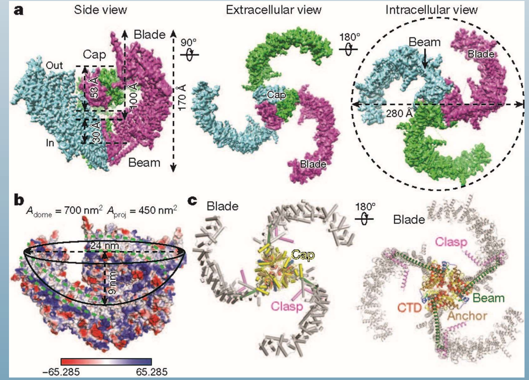

Figure 1 The homotrimeric structure of Piezo-2

Neural Networks and Haptics

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 [20]. Brodmann areas 1, 2, and 3 (See **Figure 3**) make up the primary somatosensory cortex and are responsible for processing touch and sensation. This part of the brain is located in the postcentral gyrus, which sits in the parietal lobe, and it's where your brain processes sensory information coming from your body. These three areas work together as a team, processing sensory signals from the thalamus – a relay station for information coming from your skin, muscles, and joints.

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 [21].

Figure 2 Haptic Vibrotactile Trigger Technology Patch (Srysty Holdings, Toronto, Canada; The SuperPatch Co).

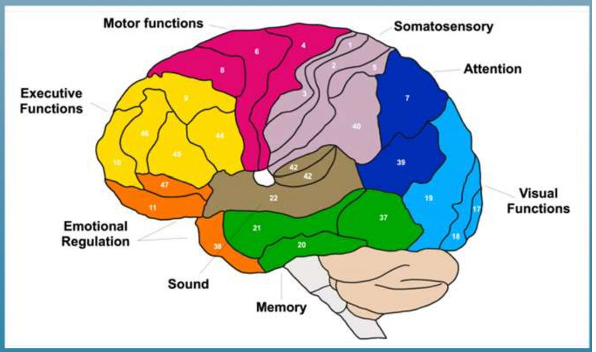

Figure 3 Brodmann Areas of the Brain

Conclusion

Since its discovery in 2010, research investigations on the Piezo ion channel's impact on the brain and nervous system have increased, as have studies focused on TRP V1 and TRP M8. The ability to detect and respond to changes in the extracellular environment is critical for all neuronal cells, so determining the sensory roles of specific ion channels is an important scientific breakthrough with huge potential medical intervention implications.

VTT haptic technology is grounded in an understanding that TRP ion channels stimulate the brain's sensory (and other) responses to peripheral nerve stimuli, such as those that exist in the skin. Touch perceptions are bidirectional, and VTT-induced sensations on the skin can promote brain neurotransmitter reactivity, brain "neuroplasticity," and improved cognitive functioning.

Overall, VTT haptic technology in the form of a noninvasive patch is especially promising for self-use by people living with various physical and/or mental health disorders. Further investigation is warranted to determine the best types of haptic stimulation, locations for those stimuli, and other to-be-determined markers that will affect the potential success of topical Piezo-modulating haptic therapies. Rapid breakthroughs in the emerging neuroscience field of connectomics, combined with the current developments in AI aimed at the medical arena, suggest that the future is bright for developing diverse, noninvasive, drug-free technologies, such as VTT haptics, that can be used to improve the symptoms of patients living with diverse disorders.

Outcomes from recent research of VTT randomized clinical trials (RCTs) have demonstrated positive effects (*e.g.,* the reduction of anxiety, stress, depression, improvement in sleep, pain relief, balance and stability). This will be especially useful for disorders where the currently available treatments (e.g., pharmacological, surgical procedures, acupuncture, and other complementary therapies) are suboptimal, may have significant side effects, and provide only limited relief.

Citations

1. Levine JD, Alessandri-Haber N: TRP channels: targets for the relief of pain . Biochim Biophys Acta. 2007, 1772:989-1003. 10.1016/j.bbadis.2007.01.008
2. Qin L, He T, Chen S, Yang D, Yi W, Cao H, Xiao G: Roles of mechanosensitive channel Piezo1/2 proteins in skeleton and other tissues. Bone Res. 2021, 9:44. 10.1038/s41413-021-00168-8
3. Shin SM, Moehring F, Itson-Zoske B, Fan F, Stucky CL, Hogan QH, Yu H: Piezo2 mechanosensitive ion channel is located to sensory neurons and non-neuronal cells in rat peripheral sensory pathway: implications in pain. Pain. 2021, 162:2750-68. 10.1097/j.pain.0000000000002356
4. Juárez Olguín H, Calderón Guzmán D, Hernández García E, Barragán Mejía G: The role of dopamine and its dysfunction as a consequence of oxidative stress. Oxid Med Cell Longev. 2015, 2016:9730467.
5. Stone RJ: The (human) science of medical virtual learning environments . Philos Trans R Soc Lond B Biol Sci. 2011, 366:276-85. 10.1098/rstb.2010.0209
6. Teh JJ, Pascoe DJ, Hafeji S, et al.: Efficacy of virtual reality for pain relief in medical procedures: a systematic review and meta-analysis. BMC Med. 2024, 22:64. 10.1186/s12916-024-03266-6
7. Haynes AC, Lywood A, Crowe EM, Fielding JL, Rossiter JM, Kent C: A calming hug: design and validation of a tactile aid to ease anxiety. PLoS One. 2022, 17:e0259838. 10.1371/journal.pone.0259838
8. Doghramji P, Janet Fason, Peter Hurwitz: Reducing sleep disorder and insomnia related symptoms with haptic technology. Int J Family Med Healthcare. 2024, 3(1): 1-9.
9. Villar Ortega E, Aksöz EA, Buetler KA, et al.: Enhancing touch sensibility by sensory retraining in a sensory discrimination task via haptic rendering. Front Rehabil Sci. 2022, 3:929431. 10.3389/fresc.2022.929431
10. Suk H-J, Buie N, Xu G, et al.: Vibrotactile stimulation at gamma frequency mitigates pathology related to neurodegeneration and improves motor function. Front Aging Neurosci. 2023, 15:1129510. 10.3389/fnagi.2023.1129510
11. Hossain SR, Karem H, Jafari Z, Kolb BE, Mohajerani MH: Tactile stimulation improves cognition, motor, and anxiety-like behaviors and attenuates the Alzheimer's disease pathology in adult APP(NL-G-F/NL-G-F) mice. Synapse. 2023, 77:e22257. 10.1002/syn.22257
12. Fason J, Gudin J, Hurwitz P: Improvement of mental health and anxiety with haptic technology patch utilization: interim results from an exploratory study. Int J Psychiatry Res. 2024, 7:1-8.
13. Savadipour A, Palmer D, Ely EV, et al.: The role of PIEZO ion channels in the musculoskeletal system. Am J Physiol Cell Physiol. 2023, 324:C728-40. 10.1152/ajpcell.00544.2022
14. Sano Y, Wake N, Ichinose A, et al.: Tactile feedback for relief of deafferentation pain using virtual reality system: a pilot study. J Neuroeng Rehabil. 2016, 13:61. 10.1186/s12984-016-0161-6
15. Gudin J, Fason J, Hurwitz P: Using haptic technology for pain reduction and functional improvement. Anesth Pain Res. 2024, 8:1-8.
16.Deusdado LD, Antunes AFJ: Virtual reality haptic device for mental illness treatment. Procedia Comput Sci. 2023, 219:1112-9.
17. Maples-Keller JL, Bunnell BE, Kim SJ, Rothbaum BO: The use of virtual reality technology in the treatment of anxiety and other psychiatric disorders. Harv Rev Psychiatry. 2017, 25:103-13. 10.1097/HRP.0000000000000138
18. Kim DJ, Mirmina J, Narine S, et al.: Altered physical pain processing in different psychiatric conditions. Neurosci Biobehav Rev. 2022, 133:104510. 10.1016/j.neubiorev.2021.12.033
19.Hermesdorf M, Berger K, Baune BT, et al.: Pain sensitivity in patients with major depression: differential effect of pain sensitivity measures, somatic cofactors, and disease characteristics. J Pain. 2016, 17:606 16. 10.1016/j.jpain.2016.01.474
20. Melzack R. Pain and the neuromatrix in the brain. J Dent Educ. 2001; 65: 1378-1382.
21. Haddad JJ, DeBrincat M, North DM, Dhaliwal J, Hurwitz P. Cognitive Network Changes After Exposure to Haptic Vibrotactile Trigger Technology: Results From The ENHANCE Study. Neurol Neurosci. 2023; 4(3):1-15.

#1816: Poster and Oral Presentation at the 25th World Congress of Psychiatry, Prague, Czech Republic

5 - 8 October 2025