June 3rd, 2024

STROKE SPECIAL INTEREST GROUP

Academy of Neurologic Physical Therapy

In this newsletter...

- ***NEW Article Review
- Congratulations to our new Stroke SIG Secretary and Nomination Committee Board Members!!
- ANPT Annual Conference – September 19th - 21st in Columbus, OH
- All Members Meeting Thursday June 13, 2024
- Check out our latest podcast episode!

Completed by: Swapna Balakrishnan, PT, DPT
Thank you, Swapna!

Overseen by: Daniel Dray, PT, DPT, NCS

Summary topic title: Non-Invasive Vagus Nerve Stimulation in Cerebral Stroke: Current Status and Future Perspectives

Article reference: Li L, Wang D, Pan H, et al. Non-invasive Vagus Nerve Stimulation in Cerebral Stroke: Current Status and Future Perspectives. *Front Neurosci*. 2022;16:820665. Published 2022 Feb 16. doi:10.3389/fnins.2022.820665

Link to full article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8888683/

Abbreviations:
VNS: Vagus nerve stimulation
iVNS: Invasive Vagus Nerve Stimulation.
nVNS: Non-invasive Vagus nerve stimulation.
BDNF: Brain derived neurotrophic factor
cAMP: cyclic adenosine monophosphate
PKA: Protein Kinase A

pCREB: Phosphorylated cyclic AMP-responsive element binding protein

Purpose of article: Non-invasive Vagus Nerve Stimulation (nVNS) is a type of neural stimulation that utilizes non-invasive devices to stimulate the vagus nerve transcutaneously. Current research studies show that nVNS coupled with rehabilitation is a promising therapeutic option for ischemic stroke. The purpose of this critical review is to describe the findings of studies conducted using nVNS in stroke to provide a narrative account of its therapeutic potential, and mechanisms of action that may facilitate its therapeutic effects.

Article review: Invasive vagus nerve stimulation (iVNS) has been used historically and involves a pulse generator implanted beneath the skin along with electrodes connected to the vagus nerve. Common sites for iVNS are cervical spine and the auricular region administered either transcutaneously or percutaneously. The vagus nerve is a mixed cranial nerve that maintains parasympathetic system functioning and regulates functioning of body systems such as the cardiovascular and the digestive system. Compared to iVNS, nVNS is easier to use, access and is tolerated better by patients. VNS is found to cause change in neural activity of different regions of the brain which has been successfully used in the past to treat conditions such as cluster headaches, tinnitus migraines, seizures and depression.

Animal studies utilizing nVNS have demonstrated the reduction of cerebral infarction size resulting in improved forelimb function retained even after the stimulation was stopped. In addition, nVNS helps heal damaged neurons by promoting blood vessel growth around the ischemic area as noted by increased expression of endothelial growth factors and Brain Derived Neurotrophic Factor (BDNF). After a stroke, breakdown of the blood brain barrier (BBB) and subsequent brain edema are associated with poor clinical outcomes. VNS was found to reduce permeability of BBB and prevent its breakdown by reducing the enzymes that degrade the tight junction proteins of the BBB. VNS additionally has a neuromodulatory and anti-inflammatory effect in the brain. VNS reduces the release of pro-inflammatory enzymes and promotes activation of microglia which help perform tasks such as synaptic organization, phagocytosis of apoptotic cells and neuronal excitability regulation. After a stroke, the ischemic site often causes these microglia to damage the functioning neural cells which is reduced by VNS. VNS also promotes axonal plasticity in the central nervous system as seen by elevated levels of BDNF, cyclic adenosine monophosphate, Protein Kinase A, and phosphorylated cyclic AMP-responsive element binding protein among rats with cerebral injury. Spreading depolarizations are grey matter depolarizations in different areas of an ischemic brain caused by failure of sodium pump in the ischemic penumbra which cause edema, disrupt blood flow which further worsens infarction of viable neuronal tissue. Spreading depolarizations are important contributors of infarct generation, cell death and injury expansion. nVNS or iVNS reduced frequency of spreading depolarizations in the peri-infarct area.

Studies show that rehabilitation paired with VNS improved upper extremity motor function after stroke as observed by improvements in Fugl Meyer assessment of the upper extremity score compared to stroke survivors who did not receive iVNS. Similar improvements in other upper extremity functional tests such as the Wolf motor function test , Box and Block test and nine hole peg have also been observed in other studies.

Side-effects of VNS: Some side-effects noted with VNS include itching, redness,

tingling and pain around the stimulation site. Presence of nausea, vomiting, headache, facial drooping, dizziness vocal hoarseness have also been reported. Few studies have reported side-effects such as palpitations, arrhythmia, bradycardia and hypotension. Among patients with asthma lowering of heart rate was seen following nVNS. More needs to be understood with relation to VNS stimulation parameters and rate of side effects experienced.

Stimulation Parameters: The intensity of VNS directly impacted motor plasticity seen. Since the vagus nerve originates from the right side, stimulating the left ear was thought to reduce risk of cardiac side effects. Common frequency used for nVNS was 20-25 Hz. Participant tolerance level was adjusted to just below the pain threshold by gradually raising the stimulation intensity with wide variability noted across studies.

Discussion, take home message: Studies are increasingly demonstrating that iVNS and nVNS have similar effects and produce similar therapeutic results. Auricular and cervical branches of vagus nerve are commonly targeted with nVNS. There is a need for stronger clinical evidence on the role of nVNS in stroke rehabilitation. There is still a lot of variability in knowledge about parameters, protocols and best location of nVNS. There is need for additional knowledge of frequency, number of doses and treatment tolerance of nVNS. A limited understanding of the mechanism of action by which nVNS works along with ideal stimulation mode is also evident. Most studies using nVNS have been conducted on smaller study samples therefore reducing generalization. Since nVNS can be provided in a non-hospital setting, its effects on stroke and other forms of brain injury should be explored. nVNS has the potential to significantly improve motor outcomes for patients following stroke, reducing burden of care, healthcare costs, and quality of life/participation level of patients.

Prior Stroke SIG Article Summary Focused on VNS:

1. Vagus Nerve Stimulation Paired with Rehabilitation for Upper Limb Motor Function After Ischaemic Stroke (VNS-REHAB): A Randomized, Blinded, Pivotal, Device Trial
URL: https://neuropt.org/docs/default-source/stroke-sig/november-2023-vagus-nerve-stimulation-with-rehab-for-upper-limb-function-after-stroke.pdf?sfvrsn=3a8c5b43_1

Additional references:

1. Anatomy of the ear: National Institutes of Health (NIH). National Human Genome Research. Anatomy of the Ear. Accessed Jan 5, 2023. URL: https://elementsofmorphology.nih.gov/anatomy-ear.shtml.

2. Breit S, Kupferberg A, Rogler G, Hasler G. Vagus Nerve as Modulator of the Brain-Gut Axis in Psychiatric and Inflammatory Disorders. *Front Psychiatry*. 2018;9:44. Published 2018 Mar 13. doi:10.3389/fpsyt.2018.00044

3. Bermejo P, López M, Larraya I, et al. Innervation of the Human Cavum Conchae and Auditory Canal: Anatomical Basis for Transcutaneous Auricular Nerve Stimulation. *Biomed Res Int*. 2017;2017:7830919. doi:10.1155/2017/7830919

CONGRATULATIONS to our Newest Stroke SIG Board Members!

Term Begins July 1st, 2024

Ben Lindaman, PT, DPT – Secretary

Dennis Fell MD, PT – Nominating Committee Member

Join us for the ANPT Annual Conference!

The ANPT 4th Annual Conference will be held in Columbus, Ohio from **September 19th-21st.**

Registration for the ANPT Annual Conference is now open!

For more information and registration, **click here!** There are both in-person and on-demand registration options available!

Join Us for Our Next Stroke SIG All Members Meeting!

June 13, 2024 from 7:30-8:30 pm EST

https://us06web.zoom.us/meeting/register/tZUsfuuvrj8iG9QWDHTa3GZxTy4n4FQqMvIE
Meeting%20ID:

Check Out our Newest Podcast Episode!

Pelvic Health across the Continuum of Care for Patients with Neurologic Conditions: Episode 24

In this episode, host Marissa Moran, PT, DPT is joined by Ariana Jones, PT, DPT, Board-Certified Clinical Specialist in Women's Health Physical Therapy, and Gillian McLean, PT, DPT, Board-Certified Clinical Specialist in Neurologic Physical Therapy, to discuss pelvic health therapy across the continuum of care for the neurologic population, particularly those following a stroke. In this podcast, you may expand your knowledge on the pelvic floor and normal urination/bowel movements. Listen to learn how pelvic health and neurologic physical therapists can collaborate to deliver the effective and holistic care to patients, as well as education you can provide to patients regarding pelvic health concerns/when to see a pelvic health specialist to

promote optimal well-being.

Link: https://www.neuropt.org/education/anpt-podcasts

You can also listen across multiple podcast platforms - search for the ANPT Stroke Special Interest Group!

VISIT THE STROKE SIG ONLINE!

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