

Nachrichten der Arbeitsgemeinschaft Autonomes Nervensystem



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Vagal nerve stimulation may improve post-stroke motor recovery

The Vagus Nerve Stimulation (VNS) may promote reorganization of motor networks via engaging a variety of molecular and neuronal mechanisms through ascending neuromodulatory systems. A recently published review from *Frontiers in Neuroscience* (N. D. Engineer et al. Targeted Vagus nerve stimulation for rehabilitation after stroke, *Front Neurosci.* 2019, 29;13:280) is laid out how recent experimental and clinical studies are providing increasing evidence for a beneficial effect of vagus nerve stimulation for the motor recovery after stroke of both, ischemic and hemorrhagic origin. Two multi-site, randomized controlled pilot trials have suggested that when paired with neurorehabilitation, VNS stimulation may generate temporally precise neuromodulatory feedback within the synaptic eligibility trace and may hence, drive synaptic plasticity.

A single-blinded, randomized feasibility study evaluating VNS paired with motor rehabilitation was performed by Dawson et al. (2016) in 20 participants > 6 months after ischemic stroke who had moderate to severe upper limb weakness. Subjects were randomized to VNS paired with rehabilitation (n = 9; implanted) or rehabilitation alone (n = 11; not implanted). VNS was triggered by a physiotherapist pushing a button during task-specific movements. The main outcome measures were a change in upper extremity Fugl-Meyer Assessment (FMAUE) score and response rate – FMA-UE change ≥ 6 points was considered clinically meaningful. After 6 weeks of in-clinic rehabilitation, participants in the paired VNS group showed a 9.6-point improvement from baseline while the control group improved by 3 points in the per-protocol analysis (between group difference = 6.5 points, CI: 0.4

to 12.6, $p = 0.038$). The response rates were 66 and 36.4% in VNS and control groups, respectively. No serious adverse device effects were reported.

The second study was a multicenter, fully blinded and randomized study (Kimberley et al., 2018). All participants were implanted with the VNS device, which allowed the control group to crossover to receive paired VNS therapy after completion of blinded follow-up. This permitted a within subject comparison of gains. To evaluate the lasting effects of VNS stimulation combined with home-based physiotherapy was included as part of the study. Seventeen participants who had moderate to severe upper extremity impairment after stroke were enrolled at four sites. Both groups had 1 month of at-home exercises with no VNS followed by 2 months of home-based therapy. During home therapy, participants in both groups activated the VNS device at the start of each 30-min session via a magnetwipe over the implanted pulse generator to deliver either Active or Paired VNS (0.8 mA) or Control VNS (0 mA), respectively. After 2 months of home-based therapy, the Paired VNS group continued the VNS therapy while the Control Group switched over to receive paired VNS. After 6 weeks of in-clinic therapy, the FMA-UE score increased by 7.6 points for the VNS group and 5.3 points for controls. Three months after the end of in-clinic therapy (post-90), the FMA-UE increased by 9.5 in the paired VNS group and 3.8 points in controls. At post-90, response rate (FMA-UE change ≥ 6 points) was 88% in the VNS group and 33% in controls ($p = 0.03$).

Noteworthy in both studies was the greater improvement of the upper limb function when physiotherapy was applied simultaneously with vagal nerve stimulation. VNS likely supported the recovery of upper limb functions via activation of multiple neuro-

modulatory networks that regulate synaptic plasticity. This may include the noradrenergic, cholinergic, and serotonergic systems (Nichols et al., 2011; Hulseley et al., 2017). These neuromodulators, in turn, act synergistically to alter spike-timing dependent plasticity (STDP) properties in active networks. The studies above align well with the time scale of the synaptic eligibility trace and provide a means by which VNS may drive temporally precise neuromodulatory release to reinforce ongoing neural activity related to the paired event. An open question is whether similar improvement can be achieved using non-invasive vagal nerve stimulation. To this moment, the identifying and consistently delivering stimulation within a particular range of parameters appears to be of greater challenge with non-invasive VNS than with the implanted VNS device.

Physiotherapy combined with vagal nerve stimulation seems to be a new and promising approach to enhance the functional recovery after stroke.

Arbeitsgemeinschaft Autonomes Nervensystem vergift 2 Reisestipendien für die aktive Teilnahme am 6. Kongress der EAN in Paris

Vom 23. bis 26.5.2019 findet in Paris der 6. Kongress der European Academy of Neurology statt. Als Arbeitsgemeinschaft Autonomes Nervensystem wollen wir unseren wissenschaftlichen Nachwuchs fördern und die Gelegenheit zu internationalem Austausch und „networking“ mit Wissenschaftlern und Arbeitsgruppen verschiedenster Forschungsgebiete ermöglichen.



Mit der Vergabe von 2 Reisestipendien in Höhe 750 Euro an Bewerber, die bisher noch keine Mitglieder der Arbeitsgemeinschaft sind, wird die AGANS in diesem Jahr Studenten, junge Wissenschaftler, Kollegen in der ärztlichen Ausbildung unterstützen, welche sich mit Vorträgen oder Postern rund

um das Autonome Nervensystem am Meeting beteiligen.

Bitte senden Sie uns per E-Mail Ihre Bewerbung um eines dieser Travel Grants mit Ihrem kurzen Lebenslauf, Ihrem Abstract und mit der Bestätigung Ihrer Anmeldung zur Kongressteilnahme spätestens bis zum 28. Februar 2020 an: Prof. Dr. med. Jens Jordan, Sprecher der Arbeitsgemeinschaft Autonomes Nervensystem, E-Mail: jens.jordan@dlr.de

Allen Bewerbern um einen Travel Grant bieten wir zudem die kostenlose Mitgliedschaft in der Arbeitsgemeinschaft Autono-

mes Nervensystem für das Jahr 2020 an. Natürlich würden wir uns freuen, wenn Sie auch über dieses Jahr hinaus bei uns mitwirken würden.

IMPRESSUM

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