Galvanic vestibular stimulation: a novel modulatory countermeasure for vestibular-associated movement disorders

Estimulação galvânica vestibular para corrigir transtornos neurológicos associados à disfunção vestibular

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ABSTRACT
Motion sickness or kinetosis is the result of the abnormal neural output originated by visual, proprioceptive and vestibular mismatch, which reverses once the dysfunctional sensory information becomes coherent. The space adaptation syndrome or space sickness relates to motion sickness; it is considered to be due to yaw, pitch, and roll coordinates mismatch. Several behavioural and pharmacological measures have been proposed to control these vestibular-associated movement disorders with no success. Galvanic vestibular stimulation has the potential of up-regulating disturbed sensory-motor mismatch originated by kinetosis and space sickness by modulating the GABA-related ion channels neural transmission in the inner ear. It improves the signal-to-noise ratio of the afferent proprioceptive volleys, which would ultimately modulate the motor output restoring the disordered gait, balance and human locomotion due to kinetosis, as well as the spatial disorientation generated by gravity transition.

Keywords: kinetosis, spatial orientation, galvanic vestibular stimulation, movement disorders, space adaptation syndrome, GABA.

RESUMO
A cinetose ou doença do movimento resulta de uma resposta neural anormal originada do desequilíbrio entre estímulos visuais, proprioceptivos e vestibulares, que melhora quando esse desequilíbrio é corrigido. A síndrome de adaptação espacial ou doença do espaço está relacionada à doença do movimento e é desencadeada por mudanças bruscas de direção, inclinação e rotação da cabeça. Têm sido propostas várias medidas comportamentais e farmacológicas para controlar esses transtornos do movimento associados com o sistema vestibular, mas sem sucesso. A estimulação galvânica vestibular pode regular o desequilíbrio sensitivo-motor causado pela cinetose e pela doença do espaço modulando os canais iônicos GABA, relacionados à transmissão de impulsos nervosos no ouvido interno. Essa estimulação melhora a relação sinal-ruído dos impulsos proprioceptivos que acabam modulando a resposta motora, restabelecendo o equilíbrio e a marcha, recuperando a desorientação espacial causada pelos diversos gradientes de gravidade.

Palavras-chave: enjoo de movimento, orientação aeroespacial, estimulação galvânica vestibular, distúrbios do movimento, síndrome de adaptação aeroespacial, GABA.
in up to 70% of civilian and military airplane pilots while they are under training in flight simulators. Although a good number of investigations have been done, the pathophysiology of MS is far from understood.

Space adaptation syndrome (SAS) or space sickness, on the other hand, is a disorder that relates to MS, which is experienced by almost 50% of people traveling out of the Earth. It is believed that SAS is due to yaw, pitch, and roll coordinates mismatch. SAS accentuates with longer exposure to the stimulus that generates it, a situation that may lead to quitting the career of the pilot at earlier times than planned. In addition, SAS possesses a risk of sudden disability in flight, as well as in the cabin of the plane, among other menaces.

Current interventions in MS and SAS

When individuals develop MS they show self-consistent patterns of pathophysiological variations that constitute a personal signature, which remains unchanged across multiple provocative exposures. Thus, autogenic feedback training has been proposed as a measure to prevent space and terrestrial MS. Using this technique, individuals are trained to detect subtle changes in heart rate, respiration, and skin temperature among other parameters. People trained to keep in balance these physiological parameters are believed to become resistant to MS. In theory, motion abnormalities originated by kinetosis should revert when visual, proprioceptive and vestibular input becomes coherent, which is the main goal of this type of intervention. However, current studies indicate that astronauts do not benefit from autogenic feedback training, thus providing little hope that SAS as well as MS could be prevented or attenuated by this type of intervention.

Pharmacological approaches have also been undertaken to control kinetosis and SAS, without success. For example, medications prescribed to airplane pilots for short periods of time during commercial flights, and under strict medical supervision have impaired their flight performance. Promethazine, the most common medication used to treat space sickness, prevents adaptation or hinders learning. Thus, there is still concern that medications would delay sensory-motor adaptation in people exposed to aerospace environments, among other side effects.

Similarly, interventions proposed to improve the quality of life of people suffering SAS have fallen short to prevent it; further, they have also been inefficient to improve spatial disorientation and flight maneuverability. Else, they are expensive and may affect aviation safety. Of note, SAS re-appears on veteran astronauts during subsequent flights. It means that this condition is resistant to habituation procedures, which parallels kinetosis-resistant habituation.

Noteworthy, using a computational model, we recently demonstrated that gravity changes affect semicircular canals similarly as galvanic vestibular stimulation (GVS) does in humans, which in turn simulates SAS-like effects. Of remark, the scientific literature is plenty of reports demonstrating the disordered motor output effects generated by GVS, and it is very scarce on the benefits that this non-invasive intervention may produce to humans.

Interestingly, there is growing scientific evidence that supports the use of GVS as a novel and powerful neurorehabilitation measure in a number of movement disorders. Therefore, we anticipate that customized GVS can restore the abnormal human balance, gait and locomotion happening in the Earth, the moon, Mars and elsewhere.

Technical aspects of GVS

GVS is a non-invasive neural intervention developed since several centuries ago that is still overlooked in modern textbooks. The galvanic stimulus is delivered by a controlled current source by means of a switch and a battery which usually does not exceed 9 V. The current is delivered transcutaneously at levels of ~1 mA, which reaches vestibular afferents, modulating neural firing. Although the stimulators used to generate the GVS are essentially similar, the changes in body perception, movement and spatial location that GVS produces are based upon wave configuration, polarity, intensity, duration, timing and frequency of the stimulation, and number and placement of the stimulating electrodes.

Briefly, bilateral bipolar GVS is the mode most commonly used (Figure 1). In this case, the anode is placed on the mastoid process behind one ear, and the cathode behind the other ear. The reference or ground signal is usually placed at the forehead. The signal originated from the semicircular canals during bilateral bipolar GVS mode originates a large roll and small yaw, both toward the cathodal side. Hence, the observed sway toward the anodal side appears to be the...
appropriate balance response. Another type of stimulation is called bilateral monopolar. In this case, electrodes with the same polarity are placed in both ears, and a distant reference electrode is used. This type of GVS mode produces a semicircular canal signal of a small backward pitch with no roll component. Thus, the subjects sway forward with cathodal GVS on both sides and backward with anodal GVS on both sides. Another stimulation mode is called unilateral GVS mode. In this instance, the stimulating electrode is placed in one mastoid and the nonstimulating electrode is placed on the forehead, or in more distant regions such as the arm.31 This mode of GVS evokes sway responses with an oblique trajectory.32,33 The lateral component of the oblique sway produced by unilateral GVS mode is either toward an anodal electrode or away from a cathodal electrode; however, the amount of sway is similar.

The galvanic current can also be modulated, with modifications owed to the aims of the study. In some cases, the stimulus is delivered in a continuous varying sinusoidal form.34,35 In other occasions stochastic waveforms of alternating polarity have been used. These stimuli roughly modulateafferent firing similarly to the action exerted by the continuous tonic stimulus originated by the other modes of stimulation above mentioned.

Neurofunctional aspects of GVS

Very few or none adverse effects have been reported in humans; if any, they consist of mild sensations of transient retroauricular vibrations.38-41 This makes GVS unique, compared to other vestibular modulatory stimulations such as the caloric one.38-40 GVS polarizes the vestibular nerves, which means that GVS separates and accumulate positive and negative electric charges in two distinct regions of the mentioned nerves. This process activates the semicircular canals, otolith organs, and the adjacent vestibular nerves.26,27 Thus, GVS modulates posture and balance relationship, oculokinetic responses, and spatial orientation. The action of GVS has been modeled using vector summation, following stimulation of the pars medialis, bilateral utricular macular and semicircular canals.50 Such modeling has demonstrated that vector summation from utricular afferents does not explain the observed sway in people exposed to GVS. Therefore, new hypotheses have been proposed. Some of them have suggested that the otolithic component involved in the balance response originates only from the pars medialis of the utricular macula.26 Further, functional neuroimaging studies have revealed the existence of a complex network of multisensory cortical areas activated by GVS in healthy and ill populations. Such areas include the insular and retrolenticular regions, the superior temporal gyrus, temporo-parietal cortex, the basal ganglia and the anterior cingulate gyrus.36,47 The parieto-insular vestibular cortex and the temporo-parietal junction area are activated as well in healthy subjects. Interestingly, bilateral activations of vestibular cortices are obtained by applying left-cathodal/right-anodal GVS, whereas unilateral, right-hemispheric activations are induced by right-cathodal/left-anodal GVS.46,48

Mechanisms of GVS

GVS applied at spaced intervals may control abnormal movements secondary to MS, SAS and the like. This would be possible by modulating aberrant action potentials that happen in the sensory-motor mismatch, which follows the abnormal neural re-firing originated by these disorders.4,49,50 The restorative action of GVS can be due to the time dependent electric field embedded system that has the potential of modulating GABA receptor signaling given its electromagnetic properties.51 As it is widely known, GABA is the main inhibitory neurotransmitter of the mammalian central nervous system that regulates neuronal excitability.52 In the vestibular end organ, in particular, GABA modulates vestibular afferent nerve firing.50,52 Recent research demonstrated that the GABAergic component of the olivocochlear system also contributes to the long-term homeostasis of key hair cells and related neuronsin the inner ear, which are needed to keep human balance in place.53 Likewise, GVS modulates inhibitory activity recorded from the lateral vestibulo-spinal tract and from the spinal motor neuron activity, all of which is linked to GABAergic neural distribution.54 Furthermore, the GABAergic system found in the cholea
and inner ear also plays an important role in the efferent modulation of balance and locomotion, postural stability and muscle tone, which has been measured by different means including transcranial magnetic stimulation.

Of remark, GVS would also help to restore balance, gait, equilibrium and locomotion in humans affected not only by MS or SAS, but also by the sensory and motor mismatch following neurodegenerative conditions. The fact that GVS improves the disordered sensorimotor activity by modulating the abnormal sensoperceptual afferent information along with the disturbed motor output in patients with disabling neural disorders, including Parkinson’s disease, normal pressure hydrocephalus (Leon-Sarmiento et al., unpublished observations), and focal dystonia supports this view. To prove more efficiently these assumptions, we re-analyzed the results of the effects of GVS in a patient with cervical dystonia.

GVS and movement disorders

The effects of GVS in the neck muscles of a patient with focal dystonia were mathematically calculated. We measured the number of spikes of at least 50 μV of amplitude before and after the application of GVS. The galvanic stimuli were up to 2.5 mA square wave direct current steps of 20-msec duration. The stimuli were generated by an isolated stimulator (Model DS2A; Digitimer, Ltd., Hertfordshire, UK) and delivered to the mastoid processes at a rate of 3 Hz, by means of 20 cm² self-adhesive electrodes, which were cut from electrosurgical plating (3M, St. Paul, MN) and coated with electrode gel. The current was delivered with the cathode at the left mastoid and anode at the right, or vice-versa. After GVS intervention, it was very impressive to observe that the muscle activity displayed by this patient before the intervention, which was 9.2 Hz, was significantly reduced to 1.4 Hz, after intervention (t test, p<0.05) (Figure 2). The most likely explanation for such improvement seemed to be on the benefits exerted in the short latency afferents of the vestibule and trigeminal cervical pathways of this patient. Of remark, these neural pathways use GABA as one of their main neurotransmitters as well.

Recently, limited studies also reported the benefits exerted by the application of GVS in patients with Parkinson’s disease. In one case, a patient who complained of camptocornia received a single session of GVS. Binaural monopolar GVS was applied for 20 minutes. In this stimulation mode, the cathode electrode was placed over each the mastoid process and the anode electrode over the trapezius muscle. Immediately after GVS application, the trunk flexion angle was reduced by 32.1% compared with the values obtained before GVS. This improvement lasted for a month. Another study used bicathodal GVS in five patients with Parkinson’s disease. This GVS configuration employs two cathodal mastoid electrodes and one anodal electrode at the C7 vertebra. It was found that 0.1 mA stochastic current reduced the body sway of the patients. The aforementioned results are encouraging to implement novel GVS methodologies looking to improve balance and gait in Parkinson’s disease via modulation of the cholinergic system, without the side effects brought about by classical pharmacological interventions.

Concluding remarks

The easiness, low cost and portability makes GVS a novel countermeasure for restoring abnormal balance, gait and human locomotion in individuals living in different gravity conditions, including the Earth, the moon and elsewhere. In addition, given the encouraging results of GVS in improving motor function in humans, we stress out the potential of employing GVS in the rehabilitation of hypokinesia and hyperkinetic disorders, including those associated to brain and spinal cord injury as well as neurodegeneration that happens at different levels of the neuroaxis. We
anticipate that novel vestibular neurorehabilitation and sensorimotor control of human balance, gait and locomotion would be at hand in a near future by customizing GVS interventions. Sooner than later, turning GVS devices ON will make a good number of disabling vestibular-associated neural disorders to turn OFF! (Figure 3).

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