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Review Article

Controlled Vestibular Stimulation: A Novel Treatment for Insomnia

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ABSTRACT

Everyday activities such as running, dancing, swinging, falling aside, or driving cars may exert positive and negative effects on subjective well-being. Rocking is soothing because it is similar to the movements in utero. A thorough review of literature revealed that vestibular system is having extensive interactions with hypothalamus, dorsal raphe nucleus, nucleus tractus solitarius, locus coeruleus, hippocampal formation and promotes sleep. Vestibular stimulation promotes sleep by relieving pain and reducing stress. Vestibular stimulation also promotes sleep by regulating growth hormone and thyroid hormones. The purpose of this article is to review research reports related to vestibular stimulation and its role in sleep and to establish a hypothesis that controlled vestibular stimulation can be used for treatment of insomnia and to suggest translational research in this area.

Keywords: Controlled vestibular stimulation, Insomnia.

INTRODUCTION

Chronic sleep disorders have impaired daily functioning, compromised health status, and diminished quality of life.[1] Insomnia in general is described as a sleeping disorder in which patient has inability to fall asleep and or the inability to remain asleep for a reasonable amount of time. Insomnia, the most frequently reported sleep disorder, is characterized as a state of hyper arousal in which stress is believed to activate the hypothalamic-pituitary-adrenal axis.[2] 10%–20% of adults have suffered from moderate to severe insomnia. Insomnia may result from psychiatric illness, sociopsychological stress, a medical problem, poor sleep habits or a primary sleep disorder. Pain has been reported to be a leading cause of insomnia in medical illness, where >70% of the patients complain of sleep problems. Hormones shift naturally during menstruation and menopause causing some degree of insomnia in females. Sometimes due to disturbances of the circadian rhythm such as shift work and jet lag can cause an inability to sleep at some times of the day and excessive sleepiness at other times of the day. Neurological disorders such as brain tumors, trauma can lead to chronic insomnia. Diseases such as hyperthyroidism and Wilson's disease have been reported to

cause insomnia. Insomnia is often precipitated by stress and diagnosis of cancer itself is a stressful event so this stress continues throughout the disease process including treatment. Finding the underlying cause of insomnia is usually necessary to cure it. The primary goal of insomnia treatment should first be to relieve any underlying disorder (e.g., cancer pain, depression, anxiety) that may be causing the sleep disturbance.[3]

An epidemiological study has shown that persons with insomnia are at a higher risk of developing depression and anxiety disorders.[4] If insomnia remains untreated for a long time, it can lengthen the depressive illness as well as the current depressive episode and increases frequency of depressive disorders.[5]

Although antidepressants, anti-psychotics, and anticonvulsants are often prescribed for the treatment of insomnia, they are not approved by the U.S. Food and Drug Administration for this indication and have side effects that are sometimes severe.[6]

Extensive projections are identified from the vestibular nucleus to regions mediating arousal and sleep-related functions, most of which receive immune-histochemically identified projections from the lateral hypothalamic hypocretin (orexin) neurons. These include the locus coeruleus, dorsal and pedunculopontine tegmental nuclei, dorsal raphe, and lateral preoptic area.[7] Vestibular stimulation excites sleep inducing areas like nucleus tractus solitarius (NTS) [8, 9] and Serotonergic dorsal raphe nucleus.[10,11]

MATERIALS AND METHODS

Searches of the review study register articles from google.com, pubmed.com, British medical journal.com, Medline, ERIC, frontiersin.org, hindawi.com and online standardized journals.

Controlled vestibular Stimulation modulates sleep through hypothalamus

Vestibular projections to the intergeniculate leaflet IGL were confirmed by using anterograde tracer injection into the medial vestibular nucleus. The intergeniculate leaflet (IGL) has widespread projections to the basal forebrain and visual midbrain, including the suprachiasmatic nucleus (SCN). IGL may be part of the circuitry governing visuomotor activity and further indicate that circadian rhythmicity might be influenced by head motion or visual stimuli that affect the vestibular system.[12,13]

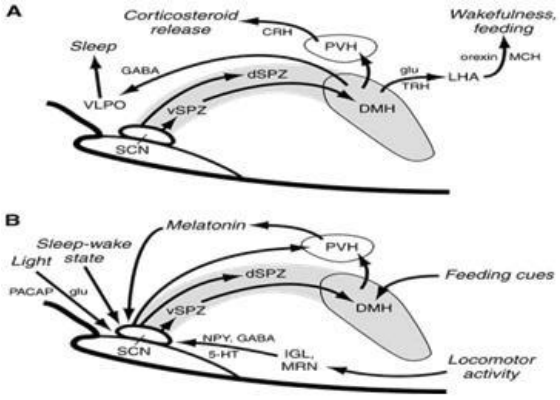

Figure: 1. Circadian regulation of sleep wake cycle.

Vestibular system is having projections to serotonergic dorsal raphe nucleus. Vestibular stimulation activates midbrain. Electrical stimulation of the dorsal and median raphe nuclei (DRN and MRN, respectively) induced 5-HT release in the SCN. Electrical stimulation of the DRN induces phase-resetting of the circadian activity rhythm.[14] Fibers from suprachiasmatic nucleus terminate in intermediolateral gray column of the thoracic spinalcord that in turn project to superior cervical ganglion from where fibers originate to end in the pinealgland.[15] Melatonin may be involved in physiologic sleep onset.[16] The circadian rhythm of pineal melatonin secretion, which is

controlled by the suprachiasmatic nucleus (SCN), is reflective of mechanisms that are involved in the control of the sleep/wake cycle. The hypnotic and rhythm-regulating properties of melatonin and its agonists (ramelteon, agomelatine) make them an important addition to the armamentarium of drugs for treating primary and secondary insomnia and circadian rhythm sleep disorders.[17]

Insomnia activates the hypotha-lamic-pituitary-adrenal axis.[18,19] Vgontzas *et al*. demonstrated that, compared with healthy subjects, those with chronic insomnia had increased secretion of corticotropin and cortisol throughout the sleep-wake cycle.[20]

Controlled vestibular Stimulation modulates sleep through dorsal raphe nucleus

Vestibular stimulation activates midbrain. Activation of neurons in the midbrain periaqueductal gray matter excites neurons of the rostral medulla, some of which contain serotonin. Serotonin has been known for many years to play a role in the modulation of sleep; however, it is still very controversial how and where serotonin may operate this modulation. Early studies suggested that serotonin is necessary to obtain and maintain behavioral sleep (permissive role on sleep).[21]

The apparent inconsistency between an inhibitory and a facilitatory role played by serotonin on sleep has at least two possible explanations. On the one hand serotonergic modulation on the sleep/wake cycle takes place through a multitude of post-synaptic receptors which mediate different or even opposite responses; on the other hand the achievement of a behavioral state depends on the complex interaction between the serotonergic and other neurotransmitter systems.[22] Serotonergic activity may be accompanied by waking or sleep depending on the brain area and receptor type involved in the response, on the current behavioural state and on the concomitant agonism/antagonism of other neurotransmitter systems.[23] Pineal gland converts serotonin into melatonin through a two step process that involves serotonin's N-acetylation and then its methylation.[24] Nocturnal melatonin secretion may be involved in physiologic sleep onset and that exogenous melatonin may be useful in treating insomnia.

Controlled vestibular Stimulation modulates sleep through nucleus tractus solitarius

Anatomical studies demonstrated that the vestibular nuclei project to nucleus tractus solitarius (NTS). The activity of more than one-third of NTS neurons was modulated by vertical vestibular stimulation, with most of the responsive cells having their firing rate altered by rotations in the head-up or head-down directions.[25,26] Anterogradely labeled axons from the caudal medial vestibular nucleus (cMVN) and inferior vestibular nucleus (IVN) could be traced bilaterally to nucleus tractus solitarius (NTS). Fewer axons ended near the somata of neurons in the dorsal motor nucleus of the vagus nerve (DMX). Cholinergic activation of the NTS, may affects sleep.[27] Furthermore, microinjection of morphine into the NTS provokes an enhancement of SWS and this effect is blocked by naloxone,[28] suggesting the somnogenic effect of opioidergic system in the NTS.

There are two anatomically distinct -endorphin pathways in the brain; the major pathway originates in the arcuate nucleus and the minor one is in the area of the NTS of the caudal medulla.[29] Endorphin concentrations may increase in the caudal NTS after the vestibular stimulation. Single shock vestibular stimulation evokes response from the ipsilateral but not from

the contralateral vagus nerve[30] and vagal afferents activate the-endorphin system in the NTS. However opioids such as morphine have the interesting property of causing sedation and wakefulness,[31] so it should not be surprising that the effects of opioids on sleep are site receptor-and dose-dependent.[32]

Controlled vestibular Stimulation modulates sleep through locus coeruleus

Caloric stimulation (CS) of the vestibular apparatus inhibits noradrenergic neuronal activity in the locus coeruleus (LC) in urethane-anaesthetized rats.[33] Noisy galvanic vestibular stimulation promotes GABA release in the substantia nigra in animals. GABA inhibits LC noradrenergic neurons during slow wave sleep (SWS) and paradoxical sleep (PS).[35] GABA effects on LC neurones result from a direct action since they persist in low-Ca2+ and high-Mg2+ media which block synaptic transmission. The primary action of GABA on LC neurones is to increase Cl- conductance by activation of bicuculline-sensitive GABAA receptors. The effects of GABA were concentration dependent and antagonized by bicuculline (10 microM).[36] Inhibition of locus coeruleus significantly decreases wakefulness and significantly increases NREM sleep.[34]

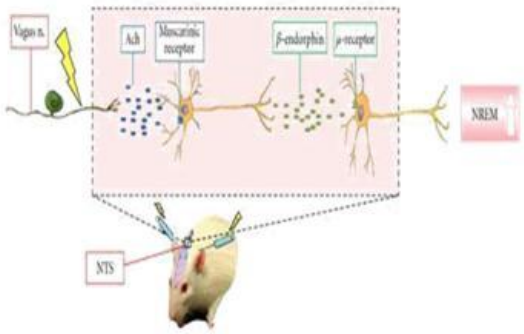

Figure 2: A hypothetical model by which vestibular stimulation may alter NREM sleep through vagal activation.

Controlled vestibular Stimulation modulates sleep through hippocampal formation

High frequency electrical stimulation of specific vestibular sensory regions of the right labyrinth in anaesthetized guinea pigs induced an evoked field potential in the hippocampal formation bilaterally with a latency with a latency of about 40ms following stimulation onset.[37]

Neurons containing immunoreactive delta sleep-inducing peptide (IDSIP) are distributed in the hippocampal formation.[38] Many compounds were proposed as sleep-factors, but only two of the sleep-peptides have been purified to homogeneity and characterized, so far. One of them, DSIP, was shown to be a nonapeptide of MW 849 and to induce mainly delta-sleep in rabbits, rats, mice, and humans, whereas in cats, the effect on REM sleep was more pronounced.[39]

Controlled vestibular Stimulation modulates sleep by relieving pain

Experience of pain impairs sleep.[40] Moreover pain causes stress and stress impairs sleep. A thorough review of literature revealed that vestibular system is having extensive interactions with thalamus, hypothalamus, periaqueductal grey, parabrachial nucleus, cerebellum, nucleus tractus solitarius and raphe nuclei and modulates the activity of these areas to initiate pain modulatory responses. Vestibular stimulation also modulates somato-sensory perception and attention and increases threshold for pain sensation.[41]

Controlled vestibular Stimulation modulates sleep by relieving stress

People who are under considerable stress can have insomnia.[42] Vestibular stimulation inhibits both HPA axis and SAM axis and decreases stress.[43]

Controlled vestibular Stimulation modulates sleep through growth hormone

Vestibular stimulation evokes response from the ipsilateral but not from the contralateral vagus nerve.[44] The influence of vagal stimulation on somatostatin release varies with species. Vagal stimulation inhibits somatostatin release in rat.[45] Vestibular stimulation increases serotonin release. In conscious rats, serotonin microinjected into the basal hypothalamus caused secretion of GH maximal within 10-25 min.

It is concluded that activation of serotonin receptors, probably type I, on or near GH releasing factor neurons in the arcuate nucleus causes secretion of GH.[47,46] Growth hormone-releasing hormone (GHRH) promotes rapid-eye-movement (REM) and non-REM sleep in animals and also in young adults, particularly when given at a time of decreased sleep propensity.[48]

CONCLUSION

From the above discussion we conclude that vestibular stimulation can be used to treat insomnia. It is the need of time to identify the importance of vestibular stimulation and to start translational research in this area.

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