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An overview of different techniques of vestibular stimulation used in experimental animals

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ABSTRACT

Even though primarily the function of the vestibular system is the maintenance of balance and equilibrium, it has been found that vestibular stimulation is beneficial even in advanced areas like cognitive neuroscience. The history of the vestibular system only dates back to 18th century, but much before that vestibular stimulation had been used to cure psychiatric disorders. Later vestibular stimulation used as a tool for diagnosing vestibular disorders. However, abundant evidence again proved that this old technique is beneficial in neurological disorders like Alzheimer's and Parkinson's disease. Vestibular stimulation also found to be beneficial in the management of stress, improving diabetics and hypertension, improving sleep quality, improving immunity, improving memory, motor execution during a cognitive task, and reduction in abnormal muscle tone. Further, for normal growth and development, vestibular stimulation is an essential component. The current review article deals with different methods available for vestibular stimulation in experimental animals.

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INTRODUCTION

The vestibular end organs are located within the petrosal bone in close vicinity to the cochlea. This hidden location proximal to the auditory organ and the difficult access considerably delayed our understanding of the functional role of the vestibular system. Vestibular sense is one of the first to develop in a growing fetus and is stimulated by the movement of a carrying mother's body. By only 5 months in utero, this system is well developed and provides a great deal of sensory information to a growing fetal brain (Eva Moeckel and Noori Mitha, 2008). This system is very important to a child's early development (Sylvette *et al.,* 2013). It was only a century back conducted the first systematic behavioural studies on the vestibular system. Even though initially vestibular system was considered as a part of an auditory organ, in 19th-century systematic lesion experiments on the frog, pigeon and dog have proven that vestibular system is important in equilibrium and balance independent of auditory function (Goltz, 1870). The roles of the vestibular system in control of posture, balance and eye movements have been intensively studied. Besides these more basic functions, the investigation of vestibular stimulation has extended and advanced to various fields especially in cognitive neuroscience (Smith and Zheng, 2013).

Research during the past two decades has demonstrated the importance of the vestibular system in topographical orientation and memory and the network of neural structures associated with them. Various clinical and animal studies have proven various benefits of vestibular stimulation like cognitive enhancement (Horii *et al.,* 1994), stress relief (Sailesh *et al.,* 2014), improving sleep quality (Andrew *et al.,* 2010) and immunity (Sailesh and mukkadan, 2013), increased eye contact in autistic children (Slavik *et al.,* 1984) and the report of an instant and complete cure of hysterical deafness (McKenzie, 1912). Earlier researches have highlighted that bilateral loss of vestibular function is associated with hippocampal atrophy and spatial memory deficits (Brand *et al.,* 2005). Now a day's different vestibular stimulation methods are found beneficial in various aspects of neuroscience. Here we review different types of vestibular stimulation methods uses in experimental animals in detail.

Vestibular stimulation

Vestibular system research has started in different vertebrate species, including pigeons and rabbits (Flourens, 1824). Later fish, frog, pigeon, salamanders, cockatoos, dog, cat and rat-mice models were used for thorough understanding of the system and other functions of the vestibular system (Goltz., 1870; Ewald, 1892). Notably, based on their evolutionary proximity to humans, non-human primates have become a standard model for furthering our knowledge of basic vestibular processing and advancing translational research (Cullen, 2012). A comparative approach including studies invertebrate species from fish to mammals was essential to the progress that was made in the early vestibular research of the 19th century. Vestibular stimulation is input that the body receives when it experiences movement or gravity. Vestibular stimulation is a physiological approach and non-expensive, non-invasive therapy which can trigger a range of changes in cognition, emotions, and personality. For many neurodegenerative diseases, only temporary treatments are available but with a lot of side effects (Allan, 2013; Prasan., 2013). Hence, there is a need of alternative therapy which can effectively potentiate improvement and with less or no side effects (Keyvan *et al.,* 2007). Almost all data that have come from animal and human clinical studies support vestibular stimulation as a promising therapy for not only various neurological disorders but helps to improve quality of day to day life.

Different methods of vestibular stimulation for experimental animals

However, as many types of vestibular stimulation methods are available, it is quite essential to explore the efficiency of different types of vestibular stimulation in improving a wide range of functions. Vestibular stimulation can be achieved by spinning or rotatory stimulation, swinging or linear stimulation or by directly stimulating the vestibular nerve with surface electrodes (Galvanic Vestibular Stimulation), or by using cold/hot water/air against the tympanic membrane to stimulate current in the endolymph of the vestibular organs (Caloric Vestibular Stimulation) or stimulate the vestibular apparatus by using magnetic field. Here, we review different possible methods of vestibular stimulation available in different experimental animal models.

Galvanic vestibular stimulation

Luigi Galvani (1791) demonstrated electrical conductivity of nerves and muscles and Count Alessandro Volta had built the first "voltaic" battery. The same bioelectric potentials sought by Galvani and debunked by Volta continue to be used in the present day because they are an easy, non-invasive approach to activate the vestibular nerve (s). Galvanic vestibular stimulation (GVS) has been used to activate fibres of the vestibular nerve in humans and experimental animals by applying 0.1–4 mA DC currents through the skin over the mastoid processes (Fitzpatrick and Day, 2004; Curthoys, 2009). Steps of current are used most often, causing continuous activation of the entire vestibular nerve and this stimulation excites a wide range of central vestibular neurons, including those related to both the semicircular canals and the otolith organs. The preponderance of physiological data supports the view that GVS is primarily an otolithic stimulus (Cohan., 1965). It has been proven that GVS modulates posture and balance relationship (Balter *et al.,* 2004), oculo- kinetic responses (Murofushi *et al.,* 2002) and spatial orientation (Moore *et al.,* 2006). Emerging evidence shows that GVS does improve cognition by increasing the Ach release in CA1 and CA3 regions of the hippocampus (Mochizuki *et al.,* 1994; Wilkinson *et al.,* 2008). GVS is a unique technique with maximum benefits and avoiding unwanted side effects of vertigo, nausea and nystagmus (Day, 1999).

Sinusoidal galvanic vestibular stimulation (sGVS)

Evidence proves that sinusoidal galvanic vestibular stimulation (sinusoidal GVS, sGVS) has been used in humans long ago to explore new areas of benefits in vestibular research (Dzendolet, 1963; James *et al.,* 2010). sGVS is a variant of GVS utilising sinusoidal currents and it was introduced by Macefield and colleagues (Grewal and James, 2009; Cohen *et al.,* 2011). sGVS is given using a computer-controlled stimulator and the current delivered via two Ag/AgCl needle electrodes inserted into the skin over the mastoids, behind the external auditory meatus. Sinusoidal currents of 1–4 mA and frequencies of 0.008 to 0.5 Hz is applied (Kaufman *et al.,* 2002; Cohen *et al.,* 2011). sGVS is applied to anaesthetised rats. It can also induce sudden decreases in blood pressure and heart rate that resemble human vasovagal syncope (Cohen *et al.,* 2010a).

Further research should be done to explore more beneficial effects of this technique

Noisy galvanic vestibular stimulation/stochastic vestibular stimulation

The principle of galvanic stimulation of the vestibular nerve/end organs is a long-established technique. The speciality with stochastic vestibular stimulation is that the currents delivered are stochastic and activate the vestibular system without creating an illusion of movement (Mark *et al.,* 2011) most likely via the phenomenon of stochastic resonance. Stochastic vestibular stimulation is low levels of bipolar binaural white noise based imperceptible stochastic electrical stimulation to the vestibular system. The basic assumption is that noise in the environment, through the perceptual system introduces into the neural system. Stochastic resonance is the counterintuitive statistical phenomena where signals that are too weak to be detected become detectable when a random (stochastic) noise is added. According to the SR phenomenon moderate noise is beneficial for cognitive performance whereas both excessive and insufficient noise is detrimental (Göran and Sverker, 2008; Yamamoto *et al.,* 2005). Noisy Galvanic stimulation can improve motor performance in healthy as well as patients with neurodegenerative diseases (Pal *et al.,* 2009; Bottini *et al.,* 2013).

Caloric vestibular stimulation

Caloric vestibular stimulation (CVS) has traditionally been used as a tool for neurological diagnosis. This method was developed by Robert Bárány who won a Nobel Prize in 1914 for this discovery. More recently; however, it has been applied to a range of phenomena within the cognitive neurosciences. Caloric vestibular stimulation consists of water irrigation of the external auditory canal, which induces a change in the temperature that leads to convection currents in the semicircular canals. This evokes slow-phase nystagmus toward the stimulated ear and it elicits sensations of virtual body rotations and vertigo (Nishiike *et al.,* 1996). Caloric vestibular stimulation is a safe non-invasive method of stimulating the vestibular system. The procedure is done either by using a syringe or by inserting a Teflon tube surgically. The temperature of water for hot water vestibular stimulation is 45°C (Horii *et al.,* 1993) and cold water at 4°C (Angelaki *et al.,* 2004). In all irrigation, the flow rate was fixed at 5 ml/min with a peristaltic pump, and each of the irrigation periods lasted for 15 min. Vestibular system is extensively connected to various brain areas related to cognition and interacts with various cognitive processes such as spatial navigation (Ferre *et al.,* 2013), space perception (Lopez *et al.,* 2010) body representation (Lenggenhager *et al.,* 2008), mental imagery (Figliozzi *et al.,* 2008), attention (Smith *et al.,* 2010), memory (Lopez *et al.,* 2013)and even social cognition (Horii *et al.,* 1994). Animal experimental studies have been proven that caloric vestibular stimulation modulates cognition by increasing acetylcholine release from rat hippocampus and also enhances long-term potentiation via activation of cholinergic septo-hippocampal cells (Albernaz and Ganança, 1972).

Air caloric vestibular stimulation

Initially, water was the only element employed for caloric vestibular stimulation, but later Ether and ethyl chloride (Aantaa., 1966) have also been used instead of water. Aantaa published a preliminary report on the biphasic caloric test with air using a system which included a thermally adjustable air compressor in which hot and cold temperatures were used (Zapala *et al.,* 2008). Air irrigators were commercially available around the 60's and are widely used today (Albernaz and Ganança., 1972). Air is more comfortable and safer even for patients with eardrum perforations, patients with external otitis media and mastoidectomy cavities (Harsch., 2008). Further standardization and many more experimentations are required to prove its benefits over water in stimulating vestibular system.

Rotatory vestibular stimulation

The vestibular system is stimulated when the head changes position such as when rotating in a swing or rotating disk, jump circling, somersault, side rolling or front rolling etc. More of a part of the day to day life. The history of rotatory vestibular stimulation in humans begins way back to 1800 which were called centrifuge therapy which is used to treat phylacteric patients (Harsch., 2006). Later Joseph Cox had developed Cox's chair and it reemerged as Barany's chair for the clinical assessment of vestibular function (Bárány., 1907). Rotary movement is one of the most potent forms of vestibular stimulation because it causes rapid changes in head position. Hippocampal place cells are found to be activated by vestibular sensory input during rotation or translation in animals (Peter *et al.,* 2000). Rotatory vestibular stimulation is achieved in animals by a specific rotatory vestibular device which works on electricity and the speed is regulated by a modulator (Devi and mukkadan., 2017). Consideration of the speed (rpm) at which vestibular organ that is predominantly activated by the stimulator, as well as the perceived direction of the induced movement and time of stimulation, is crucial. Low vestibular stimulation has no effect and overstimulation may cause nausea, vomiting and radical rise and fall in pulse and respiration (Sailesh *et al.,* 2013a). At 50 revolutions per minute, it has found more beneficial in improving cognition than 25rpm and 75 rpm which was found ineffective (Devi and mukkadan., 2017). Rotatory vestibular stimulation is found to be effective in improving motor skills in autistic children (Kantner 1976) and improving the initiation of movement and a better posture in Parkinsons' patients (McNiven., 1986). Rotatory vestibular stimulation is a safe, inexpensive and non-invasive technique to stimulate the vestibular system and easy to incorporate in our daily life.

Linear vestibular stimulation

Rocking, swinging, bouncing, sliding etc. are simple forms of liner vestibular stimulation Linear Vestibular stimulation is also a very powerful method and easily modulated to be therapeutic. Controlled Back and forth motion provides vestibular wake-up punch. The speed of movement (i.e. slow vs fast) and amplitude of front and back direction should be considered in linear stimulation (Sailesh and Mukkadan., 2015). A specially designed swing is used for the linear vestibular stimulation in rodents. Lowest frequency oscillations are found beneficial in reducing forced swing induced stress in Wister albino rats (Smitha *et al.,* 2015). Conclusions drawn from studies with infants treated with vestibular stimulation have been known to increase arousal, visual exploration, motor development, and reflex integration visual pursuit and visual alertness (Knickerbocker and Barbara, 1980; Fisher *et al.,* 1991). Cuddling a simple form of linear vestibular stimulation through which it has been proven that infant experience increased relaxation and long calm sleep and a decrease in crying (Sailesh and Mukkadan., 2014). Swings are a part of Indian tradition and readily available. As Swinging is a simple method which decreases stress, enhances mood state and lot other benefits, this method should adopt and incorporate in our day to day activities.

Magnetic vestibular stimulation

Vestibular stimulation by using the magnetic field is relatively a new technique. It was recently known that strong magnetic field affects humans as well as animals. It was found that high-strength MRI machines induce nystagmus in normal humans (Robert *et al.,* 2011) and this effect is due to the Lorentz force resulting from the interaction of a strong static magnetic field with naturally occurring ionic currents flowing through the inner ear endolymph into vestibular hair cells. This force pushes on the semicircular canal cupula, leading to nystagmus in normal mice and humans (Horwitz *et al.,* 2014). Strong Nuclear magnetic resonance (NMR) (Houpt *et al.,* 2003) scanner or MRI were used in earlier studies in order to evaluate the impact of strong static magnetic fields on the vestibular system. Furthermore, animal experimentation is required for the establishment of the technique and exploration of new areas of benefits.

CONCLUSION

The current review aims to portray details of different vestibular stimulation methods some of which are already established and some are yet to be established. Past 400 years of study on the vestibular system had proven that it is not only the sensory organ for equilibrium and balance but a lot of astounding and perplexing effects on various systems. Further experimentation in animals and humans are required in the vestibular area to explore maximum benefits. As vestibular stimulation is readily available easily incorporated with minimal time, natural with minimum side effects and maximum benefits, it can be used in many prevalent disorders like Alzheimer's, Parkinson's etc.

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