The moving history of vestibular stimulation as a therapeutic intervention

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DOI: https://doi.org/10.1163/22134808-00002495

Posted at the Zurich Open Repository and Archive, University of Zurich
ZORA URL: https://doi.org/10.5167/uzh-112439
Accepted Version

Originally published at:
DOI: https://doi.org/10.1163/22134808-00002495
The moving history of vestibular stimulation as a therapeutic intervention

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Abstract
Although the discovery and understanding of the function of the vestibular system date back only to the 19th century, strategies that involve vestibular stimulation were used long before to calm, soothe and even cure people. While such stimulation was classically achieved with various motion devices, like Cox’s chair or Hallaran’s swing, the development of caloric and galvanic vestibular stimulation has opened up new possibilities in the 20th century. With the increasing knowledge and recognition of vestibular contributions to various perceptual, motor, cognitive, and emotional processes, vestibular stimulation has been suggested as a powerful and non-invasive treatment for a range of psychiatric, neurological and neurodevelopmental conditions. Yet, the therapeutic interventions were, and still are, often not hypothesis-driven as broader theories remain scarce and underlying neurophysiological mechanisms are often vague. We aim to critically review the literature on vestibular stimulation as a form of therapy in various selected disorders and present its successes, expectations, and drawbacks from a historical perspective.

Keywords: historical perspective, vestibular system, motion device, caloric vestibular stimulation, galvanic vestibular stimulation, treatment
The moving history of vestibular stimulation

“Nothing happens until something moves.” (Albert Einstein)

 Aristotle’s famous description of the five senses (i.e. sight, audition, smell, touch and taste) has not only informed lay understanding but also “guided the [scientific] study of perception for two thousand years” (Wade, 2003, p. 151). Although phylogenetically very old (e.g. Goldberg and Fernández, 2011), the vestibular system and its functions were discovered and described only in the 19th century, most prominently by Flourens (1830), Purkinje (1820) and Ménière (1861). Marie Jean Pierre Flourens (1830), for example, observed that pigeons showed oscillatory eye movements and postural impairments after a labyrinthectomy. This finding was surprising and informative, because at that time the anatomy of the labyrinth was known, but its function was attributed to auditory perception. Thus, the labyrinth seemed clearly to be implicated in other ways than previously thought of.

Today, the vestibular system, which includes sensors detecting three-dimensional linear (otoliths) and angular (semicircular canals) acceleration, is - at least in the scientific community - accepted as a “sixth sense”. Its important roles in the control of posture, balance and eye movements have been intensively studied. Besides these more basic functions, the investigation of vestibular contributions extends to various fields of clinical and cognitive neuroscience (for reviews, see e.g. Gurvich et al., 2013; Lenggenhager and Lopez, in press; Mast et al., 2014; Palla and Lenggenhager, 2014; Pfeiffer et al., 2014; Smith and Zheng, 2013). Especially the study of the cognitive aspects of vestibular stimulation, though already highlighted by Griffith (1922) has recently gained importance. Despite this new trend, insights and knowledge, especially concerning its cortical representations, are still rather limited compared to other senses (for a brief discussion see e.g. Mast et al., 2014).

Contrasting the late discovery and limited understanding of the neurophysiological mechanisms, vestibular stimulation has often been suggested as a cure for various clinical disorders, and provided some seemingly surprising data suggesting for example increased eye contact in autistic children (Slavik et al., 1984) and the report of an instant and complete cure of hysterical deafness (McKenzie, 1912). In the following, we will describe how vestibular stimulation has been developed and - with varying success - used in therapeutic contexts over more than 2000 years. The advantages of vestibular stimulation as a therapy and its resulting popularity are evident, given that it is usually non-invasive (even if some of the methods used in the early 19th century would nowadays be regarded as torture), rather cheap and easily applicable. Yet, it is often ignored that vestibular stimulation is highly complex because a) its effects
The moving history of vestibular stimulation

depend on the exact application parameters and b) vestibular stimulation is never pure, requiring elaborate and well-controlled studies.

The aim of this review is to outline and critically discuss the use of therapeutic vestibular stimulation in humans in a historical framework. We will first describe the discovery and development of the three main methods of passive vestibular stimulation, i.e. motion devices, caloric vestibular stimulation (CVS) and galvanic vestibular stimulation (GVS). Then, we will review the literature that investigates the effects of vestibular stimulation on various clinical conditions, including sleep difficulties, mood disorders, chronic pain, bodily disorders, schizophrenia, neurodevelopmental and neurodegenerative disorders. Finally, we will provide a short outlook on the potential of vestibular stimulation for cognitive enhancement. It is important to point out that it is by no means possible to cover all the relevant literature from the field within the scope of this review. It thus represents a selection of those topics and studies that seem most relevant and interesting to us.

1. The discovery and development of vestibular stimulation techniques for humans

1.1. Motion devices

Although cradles, which apply a basic form of passive vestibular stimulation, have existed for a very long time (Jütte, 2009), the first documented therapeutic motion device was probably the so-called ‘lectos pensiles’ (hanging beds), built by ancient Greek physician Asclepiades of Bithynia (Vieth, 1795). Based on his observations, Roman physician Aulus Cornelius Celsus prescribed the ‘lectis suspensi motus’ (floating beds) for setting the body in motion to cure ‘phrenesis’, i.e. ‘madness’ (for a more exhaustive historical overview, see Jütte, 2009).

The documentation of motion devices reappeared in the 18th century. Despite the fact that Erasmus Darwin (1801) is typically credited for reintroducing a sketch of a motion device (rotating couch) in his work ‘Zoonomia’ (e.g. Wade, 2005; Wade et al., 2005), it has been argued that it was in fact Christian Gottlieb Kratzenstein and his student Henrico Hövinghoff1 who had described and built the ‘centrifuga’, a therapeutic motion device, in the mid-18th century (Jütte, 2009). While Kratzenstein’s work has rarely been cited, the English physician Joseph Mason Cox became famous with the so-called Cox chair2 that he built according to Darwin’s idea (Wade, 2005; Wade et al., 2005). He used conventional swings, rotating chairs and rotating beds in the treatment of patients with various pathologies of the asylum where he practiced. A short time later, the Irish physician William Saunders Hallaran developed a chair and a bed

1His medical dissertation “Novum medicinae genus nimirum vim centrifugam ad morbos sanandos adplicatam more geometrarum proponit” from 1765 can be found online (http://www.ub.uni-kiel.de/digiport/bis1800/Kd3153.html).
2Pictures from Darwin’s drawings of his rotating couch and a photograph of the Cox chair can be found in Wade et al., 2005.
The moving history of vestibular stimulation

(see Fig. 1A) that could be rotated up to 100 times per minute (Breathnach, 2010).
The use of rotating chairs also fueled scientific theories about the vestibular system (Barany, 1907).
Around 1820, the Czech physiologist Johannes Evangelista Purkinje (1820) observed systematic eye
movement in psychiatric patients during and after their treatment on a rotating chair. He is therefore
often identified as the ‘discoverer’ of the nystagmus (Barany, 1907; Breathnach, 2010), although post-
rotatory eye movements had already been described by Darwin and Wells (Wade, 2000; Wade et al.,
2001). A more detailed description of the vestibular system, including the semicircular canals, was later
provided by Ernst Mach and Alexander Crum Brown (Wade, 2000). To test the semicircular canals in
more detail, Mach (1875) built a chair within a wooden rotatable frame, allowing horizontal and vertical
rotations to investigate the effects of rotations as well as visual orientation in tilted positions (Wade,
2005) (see Fig. 1B). Crum Brown (1874), who was more interested in vestibular thresholds for detecting
body rotation, developed a revolving stool, which was less elaborate than Mach’s device (Wade, 2005,
p. 200). With Robert Bárány (1907, see Fig. 1C), the interest shifted towards the role of eye movements
in vestibular disorders and the rotary chair started being used as a diagnostic tool, which it still is today
(e.g. Valente, 2007).

From the 1920s, Dodge’s experiments to investigate rotation thresholds and habituation to rotation
stand out (Dodge, 1923a, 1923b). To perform such experiments he needed very slow accelerating mo-
tion devices. With the beginning of aeronautic and manned space programs a few decades later, large-
scale centrifuges were built to simulate an increase of gravitational force and to study its influence on
human physiology and cognition (e.g. Graybiel and Brown, 1951; Kunkle et al., 1948). But other motion
devices, such as a slow rotating room, were also developed for the space program (Graybiel et al., 1960).
An extensive list of available motion devices is presented in Guedry and Graybiel (1961). Walsh (1961)
used another notable device, which stimulated participants while they were immersed in water in a
movable tank. This was done in an effort to reduce the co-involvement of the proprioceptive and somatic
system as this is one of the important confounds and thus disadvantage of vestibular stimulation
through motion devices.

Another milestone in the development of modern motion devices was Stewart’s idea of a motion plat-
tform with six degrees of freedom, allowing the application of rotations and translations (Stewart, 1965).
In contrast to early devices that usually allowed movements around one axis only, on this platform par-
ticipants can be moved in different directions to stimulate the otoliths and semicircular canals separate-
ly or in combination. Nowadays, motion devices are increasingly used for vestibular research (for a re-
view of different ways of stimulating the vestibular system see Pall and Lenggenhager, 2014). The ad-
The moving history of vestibular stimulation

Vantage of such devices is that they provide access to precise information about and manipulation of acceleration, acceleration profile and duration of the applied movements.

1.2. Caloric vestibular stimulation (CVS)

Robert Bárány is also credited for introducing CVS as a diagnostic clinical tool. He discovered that irrigating the external ear canals with warm or cold water elicits eye movements in a predictable fashion ([Barany, 1907], see Fig. 2A for a picture of his bedside setup). In fact, exactly 100 years ago, Bárány (1914) was awarded the Nobel Prize of Medicine for his remarkable contributions (Breathnach, 2010; Lopez and Blanke, 2014; Wade, 2005). Thanks to otologists, who routinely prescribed syringing to remove cerumen, it was already known that syringing with warm or cold water could induce vertigo (Goltz, 1870) and provoke eye movements, while use of body temperature water and syringing in an upright position does not lead to these symptoms. Bárány described how one day he irrigated the ear of a patient with cold water. As the patient complained about getting “giddy”, he used warmer (accidentally too hot) water and noticed that, curiously, the nystagmus changed direction (Baloh, 2002). This led him to propose the theory of endolymphatic flow, which is still largely accepted today. It is disputed however, how much his colleagues in Vienna contributed to these developments (see Baloh, 2002 for a detailed account on the controversy surrounding Bárány and the discovery of the caloric test). Importantly, Bárány recognized the value of CVS as a diagnostic tool for peripheral vestibular dysfunctions as it is still used in clinical settings. Bárány himself did not seem to have attributed a therapeutic value to CVS, but such stimulation was later also used in therapeutic settings. Less known is the fact that Bárány (1907) also described the application of galvanic vestibular stimulation (GVS), the history of which we will outline below.

1.3. Discovery and development of galvanic vestibular stimulation (GVS)

The history of GVS (nicely reviewed in Fitzpatrick and Day, 2004) dates back to the beginning of the 19th century. In the context of Alessandro Volta’s discoveries, experiments with application of currents behind the ears have been described to evoke sensations of vertigo (Augustin, 1803), even if the underlying physiological mechanisms were still not known. This finding, as well as the fact that such stimulation induces disturbances of equilibrium, nystagmus, and the specific sensation of an illusory tilt towards the cathode, has later on been described by various authors (e.g. Hitzig, 1874) and was finally identified by Josef Breuer (1874) as a phenomenon of vestibular origin. GVS has been suggested early on as a therapeutic method, although initially as a treatment for deafness and tinnitus (see e.g. Rubinstein and Tyler,
2004, for a discussion of the sudden rise and fall of GVS as a cure for auditory deficits, see Fig. 2B for a picture of the setup). While the devices of the first half of the 19th century all used direct current stimulation (thus galvanization), other stimulation methods, for example, using alternating current, soon evolved (Rubinstein and Tyler, 2004).

Nowadays, it is well-known that GVS, transmitted via two electrodes placed over the mastoid process, stimulates and/or inhibits all peripheral vestibular afferents of both the semicircular canals and the oto-liths (Goldberg et al., 1984), and the type of stimulation depends on the current’s flow (e.g. Fitzpatrick and Day, 2004). The device itself has changed only marginally since its early application, and various relatively cheap, safe and simple stimulators are available, usually consisting of two electrodes and an electrical stimulation device that delivers currents between 0-3 mA. GVS is now increasingly used in cognitive and neuroscientific research to manipulate vestibular signaling in controlled ways, as similar to motion devices but unlike CVS - it allows precise timing and coordination with other stimuli (see e.g. Palla and Lenggenhager, 2014, for a review). Below we will review how GVS has been used as a therapeutic tool for various neurological and psychiatric disorders.

1.4. Future directions

While becoming more high-tech and elaborate, the stimulation techniques have, in principle, not changed radically over the last decades (see e.g. Palla and Lenggenhager, 2014, for an illustration of new applications). Nevertheless, for each method, certain trends might be foreseen.

Motion devices can - due to technical advances - be controlled much more precisely in terms of type of motion, intensity, acceleration profile, and duration. New research trends point in two directions. On the one hand, laboratories have started to use top-notch motion devices like the MPI CyberMotion Simulator, which allows continuous motion in different axes and for which a big hall had to be constructed (e.g. Barnett-Cowan et al., 2012). Such large motions devices present great opportunities in basic research, but are less convenient for therapeutic purposes. On the other hand, there are trends to develop relatively small, affordable and easy to use therapeutic home devices (see e.g. Dyk et al., 2008, for a model specifically designed for children), which are more relevant for therapeutic purposes.

New methods for caloric vestibular stimulation strive to make its application safer. For instance, air caloric devices are gaining importance (for a discussion of air vs. water CVS, see e.g. Barros and Caovilla, 2012). In the same vein, other techniques such as CVS with near infrared radiation (Walther et al., 2011)
The moving history of vestibular stimulation

or wet air (Gudziol et al., 2012) are being investigated. CVS activates the horizontal canal(s) because of the proximity to the external ear canal. It is still debated whether the vertical canals can also be stimulated by CVS (e.g. Ichijo, 2012, 2011; Shen et al., 2013), but if so, it would broaden the possibilities for applications. Particularly, this could a) allow testing the integrity of the vertical canals and thus be interesting for diagnostic purposes and b) allow to assess the implication of the vertical canals, for example, in an emotion or cognition paradigm and thus be interesting for basic research. Furthermore, increased safety could allow the use of home devices for prolonged and repetitive stimulation, which has shown to be important in some therapeutic setups (see below).

A similar trend towards easier and safer application can be seen for galvanic vestibular stimulation. This technique also appeals to developers of virtual reality applications, who see in it a method to increase the feeling of presence in virtual reality (Maeda et al., 2005). This might also be important for the emerging field of VR-based therapeutic interventions and rehabilitation. In this context, GVS as a ‘remote-control’ has already been used to steer human walking (Fitzpatrick et al., 2006). Apart from such integrative methods, the main progress of GVS over the past might lie in the shift of application and stimulation parameters towards stochastic and sub-threshold galvanic stimulation (see e.g. Oppenländer et al., 2014 for the treatment of visual neglect). Such stimulation does not induce the side-effects typically associated with GVS, like pain on the skin (Lenggenhager et al., 2008), therefore allowing prolonged stimulation duration (e.g. Yamamoto et al., 2005) and allowing vestibular and sham stimulation to switch without the participants’ awareness.

2. The use of vestibular stimulation as a therapeutic intervention

The use of vestibular stimulation as a therapeutic instrument dates back to a time long before the physiology and function of the vestibular system were known. Yet, the interest in vestibular stimulation and its potential use in various therapeutic settings strongly increased in the 19th and 20th centuries. In the following chapters, we discuss a selection of interesting observations and studies in which vestibular stimulation has been used as a therapeutic method. We thereby try to judge its success and failure from today’s perspective and knowledge.

2.1. Vestibular stimulation for general soothing effects and improving sleep quality

The use of cradles to induce sleepiness in children has already been described in ancient times (Jütte, 2009). Such knowledge of the hypnagogic effect of passive rocking seems culturally universal. There are,
The moving history of vestibular stimulation

for example, reports about its early usage in the Himalaya (Burrows, 1828). However, empirical data on the topic are inconclusive. Some studies found prolonged quiet sleep during vestibular stimulation (Barnard and Bee, 1983; Johnston et al., 1997; Korner et al., 1990), while other studies found that it promoted wakefulness (Campos, 1994; Gregg et al., 1976), which is also in line with literature suggesting an influence of vestibular cues on arousal and sleep regulation (e.g. Horowitz et al., 2005). The velocity of rocking has been suggested to be crucial (Johnston et al., 1997): slower speed is thought to promote sleep (Gregg et al., 1976) while faster speed or a fall is thought to promote wake states (Campos, 1994) or even wake an organism from sleep (Horner et al., 1997). On a neurophysiological level, an animal model showed that the medial vestibular nucleus projects onto hypocretin neurons and thus regulates sleep and arousal (Horowitz et al., 2005).

The first documented use of moving or rocking as a formal treatment probably dates back to the ancient Greek physician Asclepiades of Bithynia (Vieth, 1795). He invented hanging beds (‘lectos pensiles’) in which people could be rocked to reduce pain and induce sleep. Rocking was probably used as a sedative throughout the next centuries (Jütte, 2009), but only regained popularity with the construction of more sophisticated rotary chairs. In the beginning of the 19th century, Trommsdorf (1811) writes about the soothing effect of the rotary machines that were first recommended by Kratzenstein and, later, by Erasmus Darwin. Darwin thought that the rotatory movements would increase pressure on the patient’s brain and therefore induce sleep (Wade, 2005). Joseph Mason Cox (1806) was probably the first to implement those ideas more systematically in clinical settings. While curing patients in an English institution known as the Fishpond asylum, Cox observed and described the soothing effect of his swing in patients with various disorders. Apart from vertigo, the treatment on the swing was followed by “the most refreshing slumbers” (Cox, 1806, p. 140), a characteristic which he considered highly valuable to cure his patients. Interestingly, subjective drowsiness is nowadays listed as a cardinal symptom of motion sickness as well as the so-called “sopite syndrome”, a reaction in response to prolonged motion (Graybiel, 1969; Graybiel and Knepton, 1976; Guedry and Graybiel, 1961; Lawson and Mead, 1998), which matches Cox’s observations of patients’ becoming sleepy after having experienced his treatment.

While investigating habituation to rotation, Dodge (1923a) reported that his participants described the experiment as having a “soothing and soporific character, both during and immediately after rotation” (Dodge, 1923a, p. 21). In the past 60 years, sleep researchers have developed an increasing interest in the effects of vestibular stimulation on sleep physiology and quality. As an example, the first manned space flights fueled the interest in the effects of a lack of gravity on sleep and motion sickness (e.g. Graybiel, 1969; Graybiel et al., 1968, 1960; Oosterveld et al., 1973).
A more recent study which focused on the intrinsic properties of sleep found that natural vestibular stimulation speeds up transition from wake to sleep and increases sleep stage N2 in daytime naps (Bayer et al., 2011). Vestibular stimulation was obtained using a bed that swung with a moderate to low frequency of 0.25 Hz and a peak horizontal acceleration of 0.1 m/s². Older studies have reported anecdotal but not statistical evidence for similar effects (Woodward et al., 1990). Bayer and colleagues (2011) argue that vestibular stimulation may enhance synchronicity in thalamo-cortical networks, caused by vestibular and somatosensory input to the thalamic nuclei, which could promote onset and maintenance of sleep. In a more therapeutic approach, Krystal and colleagues (2010) set out to investigate vestibular stimulation as a treatment of insomnia. They used GVS on normal sleepers with a model of transient insomnia, but found that it had an effect on sleep onset latency in only a specific subset of participants who had a sleep onset latency above the median (≥ 14 minutes). In an experiment on herself, Vose (1981), previously a poor sleeper, describes deeper and longer sleep days after vestibular stimulation.

Vestibular stimulation seems to influence not only sleep characteristics but also properties of dreams (Leslie and Ogilvie, 1996). Indications about a connection arise from patients with vestibular disorders reporting strong vestibular imagery while dreaming (Doneshka and Kehaiyov, 1978). Additionally, in the aforementioned study by Woodward and colleagues (1990), participants claimed to have experienced intense dreams of a sexual nature after a night of vestibular stimulation. In this study, increased REM sleep density was measured. Longer and denser REM bursts after vestibular stimulation have also been found in children (Ornitz et al., 1973). On a side note, lucid dreaming is apparently more pronounced in young children (Voss et al., 2012). Interestingly, the frequency of lucid dreams seems to be related to the vestibular activity in sleep (Gackenbach et al., 1986). In a similar vein, Leslie and Ogilvie (1996) showed that vestibular stimulation lead to changes in dream mentation, including increased bizarreness and vestibular imagery. They hypothesized that activity of vestibular nuclei may contribute to lucid dreaming. Lucid dreaming is a promising treatment in various psychiatric conditions such as depression or post traumatic stress disorder, but induction of lucid dreaming is not always successful (Voss et al., 2014). Based on those findings, we speculate that vestibular stimulation during REM sleep could be an interesting way to induce lucid dreams (Noreika et al., 2010).

2.2. Vestibular stimulation in mood, anxiety, mania and depression

Next to calming effects, vestibular stimulation has been proposed to induce more specific mood changes. Early on, starting in ancient Greece, commonalities between vestibular related symptoms such as
The moving history of vestibular stimulation

vertigo or dizziness and anxiety were noticed (see e.g. Balaban and Jacob, 2001 for a historical perspective). Even Sigmund Freud (1962) listed ‘locomotor vertigo’, defined as illusory movement, as an important symptom in anxiety neurosis (‘Angstneurose’), a disorder described by him. During the 20th century, vestibular functions began to be objectively quantified by measuring the vestibulo-ocular reflex elicited by caloric, galvanic and natural stimulation (Balaban and Jacob, 2001). As a consequence, there was a first report about abnormal vestibular functioning in patients with anxiety neurosis (Hallpike et al., 1951). Interestingly, the unusual vestibular situation experienced in space was reported to result in emotional disturbances amongst other alterations (Guedry and Graybiel, 1961). Moreover, it was found that patients with a vestibular disorder have a higher risk of suffering from depression, panic and anxiety disorders (e.g. Eagger et al., 1992; Godemann et al., 2004).

Strikingly, and besides the long known relationship between affective disorders and vestibular disturbances, there are only few records of attempts to use vestibular stimulation as a therapeutic tool in anxiety or related disorders. From the analysis of Cox’s (1806) case reports it seems that he also treated patients with anxiety disorders on his swing, even if it is difficult to determine a clear psychopathological diagnosis based on his descriptions. He and also Hallaran further mention the cure of mania with motion devices (Breathnach, 2010), but again there is reasonable doubt as to whether their definition of mania would transfer to modern diagnostic criteria. Kelly (1989) describes a therapeutic approach in which rotation and spinning were applied in various body positions to provide complete vestibular stimulation of the semi-circular canals in order to treat agoraphobia. In one reported case, this treatment improved quality of life profoundly. Moreover, there is one study in which vestibular stimulation was used to test the integrity of the vestibular system in patients with a major depression (Soza Ried and Aviles, 2007) and two case studies that used CVS in patients with mania (Dodson, 2004; Levine et al., 2012). Those showed that right hemispheric activation through left CVS alleviated manic symptom severity (Dodson, 2004; Levine et al., 2012) and increased (but non-significantly) bilateral frontal and central alpha EEG band activation (Levine et al., 2012). Inspired by the anecdotal knowledge of mood enhancing swinging and rocking, a study in patients with dementia found that the use of a glider swing improved mood and relaxation (Snyder et al., 2001).

The mood altering effects of vestibular stimulation have also been described in healthy participants and seem to depend strongly on the type of motion applied. Using a motion device, passive yaw rotation elicited more comfortable feelings; pitch rotations elicited more alert and energetic feelings, and roll rotation elicited less comfortable feelings. Passive heave translation evoked more alert, less relaxed and less comfortable feelings, and surge translation more alerting feelings (Winter et al., 2012). Based on
those findings and inspired by Cox’ chair (cp. chapter 1.1), Winter and colleagues (2013) set out to look more closely at the effects of yaw rotation on mood. But in contrast to their previous findings, yaw rotation diminished positive mood. No study tried to use such knowledge yet for more specific, hypothesis-driven stimulation in patients with mood disorders.

Next to inducing specific emotions, vestibular stimulation has been suggested to alter affect control. Preuss and colleagues (2014a) showed an improvement of affect control during right cold CVS when positive stimuli were presented and an increased positive mood rating, while positive mood decreased during left cold stimulation. In a similar vein, left cold CVS was shown to reduce the desirability of a product (Preuss et al., 2014b) and to attenuate unrealistic optimism (McKay et al., 2013). Overall, activation of the right hemisphere through left cold CVS lowers the mood and vice versa. In conclusion, lateralized vestibular stimulation has been found to modulate mood in healthy participants, but clinical studies are scarce.

In a recent review, Coelho and Balaban (2014) hypothesize that visuo-vestibular conflicts are involved in a continuum of fear ranging from a lack of fear to panic attacks or exaggerated fear. Because in clinical practice fear-evoking visuo-vestibular cues are often neglected, they propose the construction of new visuo-vestibular expectations as a possible treatment. With technical progress and thus affordable head-mounted displays, virtual reality has become a valid alternative to in vivo exposure therapy in acrophobia (fear of heights) (for a review see Coelho and Balaban, 2014). They also hypothesize that a visuo-vestibular reconfiguration might be involved in the effectiveness of virtual reality therapy.

On a side note, we would like to point out that devices for vestibular stimulation are not only used in scientific and clinical settings but also for amusement. Hallaran noted, 200 years ago, that a few psychiatric patients used the motion device in the asylum for amusement (Breathnach, 2010). Today, they are an inherent part of playgrounds (swings, seesaw, rocking horses) and amusement parks (carousel, ferris wheel, roller coasters, graviton, tilt-a-whirl, drop tower). Interestingly, loud music with low frequencies, as played at rock concert or in clubs, has shown to activate the vestibular system. Based on this finding, listening to such loud music is hypothesized to be partly just another form of vestibular-mediated amusement seeking (Todd and Cody, 2000). Since bone-conducted vibration results in vestibular-evoked myogenic potentials and thus acts in a similar way on the vestibular system (e.g. Curthoys et al., 2014), it would be interesting to investigate the effect of bone-conducted vibration on mood.

2.3. *Analgesic effects of vestibular stimulation*

One thing that is sometimes mentioned together with the soothing effect of vestibular stimulation is its
The moving history of vestibular stimulation

analgesic impact. Despite the early use of hanging beds to reduce pain (see above), the ‘spin doctors’ of the 19th century did not seem to apply their rotating chairs and moving beds primarily to alleviate pain. To our knowledge, renewed interest in the use of vestibular stimulation to alleviate pain is fairly recent. Kolev (1990) reports that cold CVS reduced the symptoms of pain during a migraine attack in 11 out of 12 participants. The success of the stimulation varied. In some participants the symptoms completely disappeared while others only noticed a slight decrease, and the duration of the effect varied, lasting from only a few minutes to several days. Reduced pain after CVS has also been reported in amputees (André et al., 2001b) and paraplegics (Le Chapelain et al., 2001) with phantom limb pain - possibly mediated by a modification and normalization of the body schema by vestibular stimulation (see chapter 2.4. below). Further analgesic effects of CVS, which were still reported during follow-up several weeks later, were also found in two patients with central post-stroke pain (Ramachandran et al., 2007a, 2007b). These findings were replicated shortly thereafter; seven out of nine patients with central post-stroke pain reported decreased pain after CVS. The duration varied from only transient relief to several weeks (McGeoch et al., 2008). The analgesic effects were noticed mostly in the face and arms and less in the legs. The authors propose that this reflects the topographical map for pain in the posterior insula (Ramachandran et al., 2007a, 2007b). Alternatively, we speculate that it could reflect more generally the enlarged somatotopic representation of the face and arms on which CVS can act upon. Finally, these authors also successfully applied a similar CVS treatment in one patient with central post-stroke pain and tactile allodynia (McGeoch et al., 2009), as well as in a patient with unilateral central pain of spinal cord origin (McGeoch and Ramachandran, 2008).

Next to these effects of vestibular stimulation on chronic pain in patients, a recent experimental study in healthy participants found increased pain thresholds shortly after left cold CVS (Ferrè et al., 2013). It is not known, however, how long this effect lasts. Moreover, a study that investigated the effect of “simulated rocking” on the pain response to the so-called heelstick procedure in infants, found inconclusive results (Johnston et al., 1997), which could suggest that artificial stimulation is more likely to alleviate pain than natural vestibular stimulation due to its hemisphere specific (lateralized activation) nature.

While these analgesic effects of vestibular stimulation are potentially very important, more well-controlled studies with adequate sample sizes are needed, and imaging or electrophysiological studies should be done in order to reveal the underlying mechanisms. An interaction between vestibular and nociceptive stimuli seems neurophysiologically plausible due to shared information processing (Balaban, 2011) particularly in the insula (zu Eulenburg et al., 2013) and/or the anterior cingulate cortex (McGeoch et al., 2009; Miller and Ngo, 2007); see Lenggenhager and Lopez (in press) and Mast and colleagues
The moving history of vestibular stimulation

(2014) for a more thorough discussion of underlying physiological mechanisms. Furthermore, Rama-chandran and colleagues (2007a) provide an interesting evolutionary and functional speculation on the link between pain and the vestibular system, in which they propose that activating the vestibular system is often a useful strategy to escape pain, which makes an interaction between the two systems plausible. Moreover, an interaction between pain and the vestibular system could generally be mediated by changes in the awareness of the bodily self, as hypothesized in a recent review (Lenggenhager and Lopez, in press; see also next chapter).

2.4. Vestibular stimulation in neurological body disorders of the bodily self and space

From the beginning of the 20th century on – especially with the early work of Bonnier (1905, 1893) and later with the one of Lhermitte (1939) and Schilder (1935), a strong link between the vestibular system and the experience of the space, the body and the self has been suggested. For example, Bonnier (1905) described various body perception alterations in patients with vertigo. Such a link between the vestibular system and the sense of an embodied self was later confirmed and strengthened by various findings showing, for example, body misperception in patients with peripheral vestibular disturbances as well as in healthy participants during artificial vestibular stimulation (Jauregui-Renaud et al., 2008; Sang et al., 2006; see also Lopez, 2013 for a review). These patients describe feelings like being separated from the body, not being in control of their own body and changes in the size of body parts. Such symptoms overlap with the experiences of patients with psychiatric or neurologically-caused disorders of the perception of the body, the self and space (see e.g. de Vignemont, 2010 for a comprehensive list of clinical syndromes). These disorders are traditionally related to right parietal dysfunctions (e.g. Critchley, 1953, 1950), although similar experiences have been described with lesions in other brain areas (e.g. Lopez et al., 2010a).

With the relatively early recognition of the importance of vestibular signaling in the representation of body and space, the use of vestibular stimulation to treat various disorders of the bodily self has increased slowly but steadily during the 20th century. In fact, Bonnier noticed already 1893 that the bodily illusions he observed in vestibular patients transiently decreased during vestibular stimulation (i.e. head shaking) (Bonnier, 1893). In 1941, Silberpfennig describes two patients with ‘pseudo-hemianopic’ disorder, i.e. a problem of drawing attention to the contralesional space, which was clearly attenuated during CVS (Silberpfennig, 1941). Since then the use of vestibular stimulation to increase spatial functioning in hemineglect has gained importance, and while early studies report short-term effects during single applications (e.g. Cappa et al., 1987; Rubens, 1985), more recent studies suggest that long-term effects can
be induced using multiple sessions of artificial vestibular stimulation (Wilkinson et al., 2014). Alongside successful application of vestibular stimulation to normalize space awareness (see e.g. Chokron et al., 2007 for a review and a list of relevant studies), artificial vestibular stimulation has been used and suggested to be used as a therapeutic measure for patients with various bodily disorders. It has successfully been used to alleviate somatosensory hemi-inattention (Bottini et al., 2005; Schmidt et al., 2013), motor neglect (Vallar et al., 2003), anosognosia and personal neglect (Cappa et al., 1987), somatoparaphrenia (Rode et al., 1992), macrosomatognosia (Rode et al., 2012) as well as phantom limb sensation and pain (André et al., 2001a; Le Chapelain et al., 2001). Next to these positive (albeit not well-controlled findings), vestibular techniques have been enthusiastically propagated to treat a variety of other bodily disorders of both, neurological or psychiatric origin (Ramachandran et al., 2007a, 2007b; Ramachandran and McGeoch, 2007).

While most of these studies lack an explicit functional hypothesis, the effects are commonly ascribed to an activation of a higher-level, multisensory body representation by vestibular stimulation, which presumably restores the body representations and triggers a more accurate body perception through unification of multisensory input. Vestibular stimulation has been shown to activate predominantly retroin-sular and temporo-parietal areas (e.g. Lopez et al., 2010b), areas that have generally shown to be important in multisensory and higher-level body and space representation (Blanke, 2012; Pfeiffer et al., 2014 for reviews). Importantly, almost all of these studies are single case studies, many do not include any sham stimulation (see e.g. Schmidt et al., 2013 for an exception) and have other methodological flaws. Furthermore, the effectiveness of the method might be overestimated due to publication bias (see Mast et al., 2014 for a brief discussion). For example, recent empirical evidence in a group of patients with a complex body disorder did not show any normalization during or after artificial vestibular stimulation (Lenggenhager et al., 2014). It remains to be seen whether other stimulation paradigms and types such as prolonged noisy GVS, used quite successfully in neurodegenerative patients so far (see chapter 2.8.), could increase effectiveness compared to traditional stimulations in certain psychiatric or neurological disorders such as body integrity identity disorder.

2.5. The use of vestibular stimulation to treat conversion disorders

Conversion disorders cover a range of symptoms such as blindness or deafness, paralysis, numbness, motor deficits, and other neurological symptoms that cannot be fully explained by physiological findings. Historically, the term ‘hysteria’ was used until Freud progressively introduced the term ‘conversion’, which refers to his theory that psychological symptoms are converted into physical symptoms (Bo-
The moving history of vestibular stimulation

gousslavsky, 2011). Ernst Horn (1818; see also Harsch, 2006) described the use of his rotating bed (and chair) to treat hysteria with considerable success. However, Horn’s apparatus was particularly unpleasant as it applied substantial g-force and the fear of repeated spinning was considered as therapeutically valuable (Harsch, 2006). Hundred years later, just shortly after Bárány published his book on caloric stimulation (1907), Abercrombie and McKenzie (1910) suggested that CVS might be a useful diagnostic tool to differentiate between hysterical and organic deafness. McKenzie (1912) reports that he therefore applied CVS in a woman who had been deaf in her right ear since childhood and recently started to show signs of hysterical deafness in her left ear. Curiously, after the procedure, the woman was able to hear well again on her left side, while the impairment on the right remained unchanged. McKenzie (1912, p. 19) states the following reasoning regarding the positive effect: “The patient then volunteered the information that she had several times lost her voice, and had had it restored “by the battery.” And there can be no doubt that it was the memory of this previous successful treatment, coupled with the profound mental shock of the violent vestibular stimulation, which cured her deafness on this occasion.”

Another hundred years later, Noll-Hussong and colleagues (2014) reported a case study of a young man with conversion disorder showing involuntary movements of the upper body. Left cold CVS of varying duration was applied three times. According to the patient’s report, the stimulation helped to attenuate the involuntary movements. Remarkably, after the third stimulation, these beneficial effects were still noticed three days later. Those authors assume that CVS - due to its cortical hemispheric lateralization - activates (and deactivates) critical brain areas (especially temporo-parietal areas, the anterior cingulate cortex, and insula) that drive the effects (compare also Lopez and Blanke, 2011).

2.6. Vestibular stimulation in schizophrenia

Surprisingly, schizophrenia emerged as a specific disorder relatively late in psychiatric history. Only in the late 19th century did Emil Kraepelin define ‘dementia praecox’ more closely, and shortly thereafter, in the early 20th century, Eugen Bleuler introduced the term ‘schizophrenia’. Before this introduction, schizophrenic symptoms may have been classed under more general concepts like ‘madness’ or even just ‘insanity’ (Bürgy, 2008; Heinrichs, 2003). This makes it difficult to trace the use of therapeutic vestibular stimulation in patients with schizophrenia through time. However, a few case reports and mental states have been described that possibly allude to schizophrenia as we know it today. Cox (1806), for example, describes some case studies (e.g. cases XVI, XVII and XX) that might be diagnosed as schizophrenia today. Another physician during Cox’s era, Horn (1818; see also Harsch, 2006), reports using the rotating bed during acute episodes of ‘raving madness’. But again, given the changing understanding of
The moving history of vestibular stimulation

terms and definitions, interpretations are difficult.
Since the 1920’s, vestibular dysfunctions have been repeatedly observed in children and adults with schizophrenia, especially abnormal eye movement responses; yet, some studies also failed to find significant differences compared to a control group (for an overview see e.g. Hixson and Mathews, 1984; Kelly, 1989; Levy et al., 1983). With the onset of Anna Jean Ayres’s postulation of the sensory integration theory (e.g. Ayres and Heskett, 1972), which she started developing in the 1950’s, sensory stimulation became the focus of different therapy interventions. Vestibular stimulation was typically an integral part in sensory integration therapies. Since the work of Schilder (1933), the vestibular system had been considered to help organize other sensory information and to have direct influences on both emotion, through the limbic system, and the experience of a coherent unified self. Furthermore, together with tactile and proprioceptive input, these ontogenetically earlier sensory systems were the focus because sensory integration aimed at promoting sequential development. However, because sensory integration therapy - as the name suggests - applies other sensory stimulation (typically tactile and proprioceptive) and also the vestibular stimulation often involves passive (e.g. swinging in a hammock) as well as active (e.g. riding a scooterboard) components (Ayres and Heskett, 1972), further elaboration is beyond the scope of this review (see instead Hixson and Mathews (1984) and Kelly (1989) for a review on the use of vestibular stimulation in this context).

Only recently, CVS was applied in two patients with schizophrenia (Levine et al., 2012). Interestingly, the results show transiently decreased delusions and decreased lack of insight-judgment as measured with the Positive and Negative Symptoms Scale after left cold CVS but not after right cold CVS (see also chapter 2.2.). Moreover, vestibular stimulation has been suggested to help improving the motor symptoms of catatonia (Miller and Ngo, 2007, see also chapter 2.8) and it may also help to improve cognitive functions (see chapter 2.9.). It should, however, be noted that administering vestibular stimulation may be counter-indicative, at least during an acute phase, among other concerns, because visual hallucinations have been reported after CVS in healthy participants (Kolev, 1995) and overstimulation could exacerbate the symptoms. Generally, again, the underlying mechanisms by which vestibular stimulation should improve symptoms of schizophrenia is not well understood and vestibular and even multisensory stimulation remain negligible in the treatment of schizophrenia.

2.7. Vestibular stimulation in neurodevelopmental disorders
Following Alexander Crum Brown’s suggestion (1878), William James (1881) conducted early experiments with deaf children who “were whirled in a rotary swing” (p. 412). He observed that they were
often less prone to motion sickness compared to hearing children. Despite these early (and questionable) scientific investigations in children and the fact that children often seek the pleasure of movement (e.g. playgrounds are full of vestibular stimulation devices, see also chapter 2.2.) vestibular treatment of children seemed (luckily) less ‘fashionable’ than for adults in the first half of the 19th century.

This changed in the second half of the 20th century, during which vestibular processes have increasingly been suggested to play an important role in a broad variety of developmental disorders (see e.g. Kelly, 1989 for an impressive list of disorders with presumable vestibular deficits) including dyslexia (Frank and Levinson, 1973), attention deficit hyperactivity disorder (ADHD) (Bhatara et al., 1978), autism (Ritvo et al., 1969), as well as more general learning deficits (Ayres and Heskett, 1972). Interestingly, some of their core symptoms have shown to be present in patients with vertigo (e.g. dyscalculia Risey and Briner, 1990; Smith, 2012 for a discussion), suggesting a mutual interaction between these symptoms and vestibular signaling. As a consequence, vestibular stimulation - at the time mostly delivered by motion devices - was increasingly used to treat children. While such approaches are interesting in the context of this paper and will therefore be reviewed briefly below, it is important to note that within the huge research field on neurodevelopmental disorders, they play a rather minor role.

In dyslexia, parallels have been drawn between various symptoms associated with developmental dyslexia (e.g. problems with postural stability, spatial orientation and eye movements) and the vestibular system, leading to the so-called cerebellar-vestibular dysfunction hypothesis of dyslexia (e.g. Levinson, 1988). Early therapies included treatment with anti-motion sickness medication (Levinson, 1991) as well as specific motion stimulation (e.g. Silver, 1986) and combined multisensory integration therapies (Ayres, 1978). Yet, these findings were already at that time heavily debated and even considered wrong (see Pope and Whiteley, 2003; Silver, 1986 for reviews), and have largely lost their influence on current models of dyslexia.

Similarly, ADHD is often associated with poor balance control and postural coordination, suggesting a vestibular and cerebellar contribution (e.g. Sergeant et al., 2006). Such interaction might be mediated by vestibular contributions to the parasympathetic and sympathetic systems (see Clark et al., 2008 for an extensive explanation). Corroboratively, several studies found a positive effect on attention disorder during vestibular stimulation treatment using motion devices (e.g. Arnold et al., 1985; Bhatara et al., 1981, 1978). However, a recent well-controlled study with a relatively large sample of patients concluded that these results were probably due to nonspecific effects, such as experimenter expectancy or attention given to the child, as they found improvement both in the experimental (rotation on a chair) and the control condition (sitting on the chair watching a video and hearing the same noise) (Clark et al.,...
About at the same time, a vestibular dysfunction theory was also proposed for autism, after data showed altered nystagmus response (Ornitz, 1970; Ritvo et al., 1969) as well as altered REM sleep in people with autism, and after vestibular stimulation was found to affect REM (Ornitz EM et al., 1973; see also chapter 2.1.). Most important in the context of this review, repeated rotatory stimulation has shown to improve motor skills of young autistic infants (Kantner et al., 1976).

2.8. Vestibular stimulation in neurodegenerative disorders
A relatively early, uncontrolled study reported that rotatory vestibular stimulation improved initiation of movement and a better posture in patients with Parkinson’s disease (McNiven, 1986). However, Kelly (1989) also mentions unpublished work of Young (1987) that provides empirical support for the therapeutic success of vestibular stimulation in Parkinson’s measured by an increase in step length. Recent attempts have used GVS, since it includes activation of the vestibular nerve, which innervates autonomic and limbic-to-motor functions, and the regulation of dopamine and noradrenaline in those areas (Albert et al., 1985; Anderson et al., 2002). GVS was therefore hypothesized as possible treatment in neurodegenerative diseases targeting those areas like Parkinson’s Disease and multiple system atrophy (Yamamoto et al., 2005). However, because constant GVS causes unilateral oculomotor and postural responses (Fitzpatrick and Day, 2004) and would therefore limit the benefit of such a stimulation, stochastic/noisy GVS was used in all studies on neurodegenerative disorders that we know of (Pal et al., 2009; Pan et al., 2008; Yamamoto et al., 2005). In their pioneering study, Yamoto and colleagues (2005) found that noisy GVS alleviated autonomic and motoric disturbances in Parkinson’s Disease and multi system atrophy, and that it decreased reaction time in an attention and response control task but did not modulate cognitive performance. Moreover, stochastic GVS was found to stabilize small sway in Parkinson’s Disease (Pal et al., 2009). In conclusion, the underlying mechanisms are still largely unknown (Kim et al., 2013).

2.9. Cognitive enhancement through vestibular stimulation?
There is now accumulating evidence that impaired or absent vestibular input (e.g. vestibular deficits, during weightlessness, or complete vestibular loss) can negatively affect cognitive functioning and has even found to result in hippocampus atrophy (for a review see e.g. Smith and Zheng, 2013). The question might therefore be if, conversely, additional vestibular stimulation can improve such functions. Here we briefly discuss studies that suggest that vestibular stimulation, beyond its therapeutic effects,
functions. Especially, memory - visual memory recall (Wilkinson et al., 2008), and depending on stimulation side, verbal or spatial recall (Bachtold et al., 2001) - was found to be improved (for a review see Smith et al., 2010). Similarly, a recent EEG study suggested improved memory as well as altered frontal beta power after GVS (Lee et al., 2014). Given the positive effect of arousal on memory retention (e.g. Sharot and Phelps, 2004), one could speculate that such results might be explained by arousal caused by vestibular stimulation (Horowitz et al., 2005, see also chapter 2.1). To further investigate this interesting question on the influence of vestibular-induced arousal, one could use different strengths of vestibular stimulation to see whether the positive effect on memory depends on stimulation parameters. Furthermore stochastic galvanic stimulation has been shown to alter modulation of synchrony patterns in the EEG across a broad range of oscillations (i.e. frequency bands), possibly due to stochastic facilitation/resonance (Kim et al., 2013). Such biologically relevant noise may enhance neural information processing and computational goals (McDonnell and Ward, 2011).

Besides these positive effects on perceptual and cognitive processes, vestibular stimulation has been shown to decrease pain (Ferrè et al., 2013, see chapter 2.3) and - depending on the side of stimulation - improve affect control (Preuss et al., 2014a), alter mood (Winter et al., 2012) and decrease unrealistic optimism (McKay et al., 2013, see chapter 2.2). Moreover, there are some hints that vestibular stimulation has positive effects on sleep characteristics (see chapter 2.1.). All these outcomes are also linked to cognitive functioning, and cognitive enhancement after vestibular stimulation could be mediated by these positive effects on various states. Yet, it will probably play a minor role in the future compared to other neurocognitive enhancers, such as tDCS, that directly modulate cortical activation. Furthermore, most studies have not looked at long-term effects, and long-lasting improvements are unexplored.

3. Discussion

The aim of this review was to recapitulate the therapeutic use of vestibular stimulation. We introduced the origins and developments of the three main methods to passively stimulate the vestibular system (i.e. motion devices, CVS and GVS) and presented a selection of topics from psychiatric and neurological research, in which it is suggested that vestibular stimulation may be beneficial. We critically reassessed history, success and effectiveness of vestibular stimulation. Although this literature review covers a broad range of applications, it is by far not complete. Disorders that we have not discussed, but which
we would like to mention here in order to provide a better appreciation of how widely vestibular stimulation has been applied, include also: pusher behavior (Krewer et al., 2013; Nakamura et al., 2014), aphasic syndrome (Wilkinson et al., 2013), prosopagnosia (Wilkinson et al., 2005) and figure-copying deficit after right hemispheric stroke (Wilkinson et al., 2010), intellectual disability (Dave, 1992) and Down’s syndrome (e.g. Brocklehurst-Woods, 1990). Moreover, we only briefly mention the effects of vestibular stimulation on hemispatial neglect, albeit this is probably one of the most promising and thus already most discussed (Schmidt et al., 2013; Utz et al., 2010; Wilkinson et al., 2014) research branch of this field.

### 3.1. Methodological and ethical considerations of vestibular stimulation

The advantages and the resulting popularity of vestibular stimulation as a therapy are evident: it is usually non-invasive, rather cheap and easily applicable. Yet, while most of the studies reviewed here report a positive effect of vestibular stimulation (which might partly be due to publication bias), many of them need to be regarded with caution as they are often associated with methodological problems and their results might be heavily confounded by other effects. Furthermore, even if generally non-invasive, there are still counter indications of therapeutic vestibular stimulation. Already in the early 19th century it was for example not recommended to use vestibular stimulation in fragile, fearful, paranoid or hypochondriac patients nor in patients with organic disease (e.g. Horn, 1818). It was further only recommended in hopeless cases (Cox, 1806) or if no other less stressful methods could be used (Harsch, 2006), which has to be seen in the context of other medical treatments of that time. A contemporary view is important, as some of the former procedures would nowadays be regarded as torture. Such procedures were typically performed without the participant’s consent and in the case of vestibular stimulation purposefully intense and nauseating. In fact, during the first half of the 19th century, the peak period of therapeutically applied motion devices, it was deliberately intended to induce motion sickness, vertigo, nausea and vomiting. The latter was a desired method for treatment during this time, along with others, such as, purging, bleeding, bathing, blistering, and the use of sedatives and stimulants (Cox, 1806; Harsch, 2006; Wade, 2005). Therefore, what is now viewed as the undesired side effects of vestibular stimulation were at the time actually intended. With the change of perspective on psychiatric patients and the call for more ethical treatments introduced by Philippe Pinel at the end of the 18th century and the resulting growth of his followers in the 19th century, the use of such methods decreased, including the use of motion devices (Jütte, 2009).

Today, measures are taken to minimize those undesired effects. For example, the proposed intensity of
The moving history of vestibular stimulation

real motion stimulation is now usually a calming rocking instead of vertiginous swinging and efforts are made to investigate and apply GVS at a sub-sensory threshold with remarkable results (Wilkinson et al., 2010). But even above threshold, if GVS is applied with caution, there are mild side effects and these are of transient nature (Utz et al., 2011). Moreover, repeated treatment sessions may be needed for a satisfying outcome and the safety seems to be warranted when using “low-intensity” (1 mA) GVS (Wilkinson et al., 2009). Yet, even if vestibular treatments today are much more humane, it should be noted that depending on stimulation parameters vestibular stimulation (especially artificial) might still induce considerable side effects (e.g. Lenggenhager et al., 2008). Independent of the side effects, it is important that the methods are carefully evaluated before suggesting vestibular stimulation as a therapy ‘for everything’ (e.g. see chapter 2.7.). Placebo effects as well as co-stimulation of other sensory systems (e.g. touch, pain) need to be considered as explanatory models and protocols should be hypothesis-driven rather than based on trial and error (Kelly, 1989). In addition, there are non-specific effects like stress (e.g. stress-induced analgesia, see Ossenkopp et al., 1988) which might influence the results. Importantly, such effects might not occur in a linear way. Low to modest intensity stimulation might for example lead to decreased stress-immune responses while high intensity may lead to increased stress-immune response compared to no stimulation. Moreover, the duration and repetition of the stimulation needs to be taken into account. In fact, talking about ‘vestibular stimulation’ as it is often done in the present review is an oversimplification, because the vestibular system is a complex system and its responsivity can change depending on the stimulation parameters and the targeted organs (otoliths and/or semicircular canals). Importantly, GVS can be applied by varying intensity, pulse profile and duration, and modern motion devices allow to deliver vestibular stimulation in a similarly precise fashion while CVS does not have these characteristics (Palla and Lenggenhager, 2014). A clear, detailed and ideally a priori defined and hypothesis-driven protocol and selection of the method to stimulate the vestibular organ is thus indispensable. In this context it is interesting to note that historically there seems to have been a tendency to use ‘natural’ vestibular stimulation through the use of motion devices to treat psychiatric disorders and artificial vestibular stimulation (CVS, GVS) to treat neurological disorders – a distinction which seems not justified by any functional or physiological hypothesis.

Furthermore, studies need to show that the effect of ‘vestibular stimulation’ is indeed due to the vestibular activation and not due to any co-activation of other sensory systems (e.g. touch, proprioception) or other unspecific effects. This is among the reasons why this review article focuses on passive vestibular stimulation as opposed to active vestibular stimulation (e.g. slack-lining or rocking in a rocking chair), which may be beneficial due to other and difficult-to-control effects, especially motor activation. We
The moving history of vestibular stimulation

also did not mention optokinetic stimulation, which has often proven useful in similar therapeutic approaches (e.g. Kerkhoff et al., 2006), but is not a genuine vestibular stimulation.

3.2. What neurophysiological mechanisms can explain the effect of vestibular stimulation?

While this review contains a list of beneficial effects of vestibular stimulation on various conditions and disturbances, the reasons for such effects are still far from understood. Explicit explanation of underlying mechanisms of the positive effect is often lacking, and if present, the mechanism might just target a very specific effect of the vestibular stimulation. In fact, different core mechanisms have been proposed to explain potential therapeutic effects of vestibular stimulation, most prominently probably a) relocation of attention, b) multisensory integration, c) hemisphere specific activation, d) neurotransmitter release.

Relocation of attention, could be induced both by the directional nystagmus (for a discussion see Figliozzi et al., 2005) or by activation of attentional networks overlapping with brain areas targeted by vestibular stimulation (Oppenländer et al., 2014). This mechanism has particularly been put forward to help explain the positive effects on neglect and similar symptoms (see e.g. Karnath and Dieterich, 2006; Wilkinson et al., 2014). Such an attention shift could be caused by an unspecific activation of parieto-temporal cortical areas contralateral to the stimulated ear. However, an attention shift due to CVS does not seem to always occur in healthy participants (e.g. Rorden et al., 2001). Recently, Ferrè and colleagues (2014) showed that the effect of vestibular stimulation on somatosensory detection was modulated by multimodal interaction rather than spatial attention. The integration and activation of multisensory processing areas (e.g. insula, parietal operculum, anterior cingulate cortex) by vestibular stimulation has been proposed to be the underlying factor in disorders of the bodily self (e.g. Bottini et al., 2013). The vestibular system is intrinsically multisensory because of its neuroanatomical connections and a vestibular percept is thus rarely experienced purely (Angelaki et al., 2009; Blanke, 2012; Ferrè et al., 2012). Moreover, it has been hypothesized that the vestibular system and emotional circuits overlap (Preuss et al., 2014a) or that CVS would target the inferior frontal gyrus, a region involved in unrealistic optimism (McKay et al., 2013). On an lower level, the medial vestibular nucleus located in the medulla oblongata is connected to different brain areas associated with nociception, sleep and arousal, homeostasis and eye movements (Horowitz et al., 2005). It remains to be seen how those structural connections translate to a more functional level. The hemispheric specific activation/deactivation pattern has been suggested to enhance or hinder specific lateralized brain processes (McKay et al., 2013; Noll-Hussong et al., 2014; Preuss et al., 2014b) . On a smaller scale, vestibular stimulation influences neuro-
transmitter release (for a discussion see Gurvich et al., 2013; Mast et al., 2014). The alteration of specific neurotransmitters such as dopamine, serotonin and GABA are thus crucial for understanding the influence of vestibular stimulation on cognition. For example GVS increases GABA release in rats (Samoudi et al., 2012). But also the sleep-wake system is influenced by vestibular input as projections of the medial vestibular nucleus to hypocretin neurons and vice versa have been found (Horowitz et al., 2005).

Of course, such explanatory models act on differently scaled levels and are not mutually exclusive but may represent different aspects of a shared underlying mechanism.

Finally, as already pointed out, non-specific effects like stress, general arousal, or placebo effects need also to be considered.

The question remains whether there is a more general/common mechanism underlying all these effects and if so, which would be the most promising. Yet, given the broad spectrum of disorders targeted with different underlying dysfunctions, pursuing a ‘one-size-fits-all’ approach might be too ambitious.

3.3. Outlook

This literature review shows that vestibular stimulation has been, and still is, a popular method and certainly contributed to the understanding and treatment of certain disorders. However, since most studies discussed in this review are case or small-scale studies, and often never replicated, an overestimation of its efficiency due to publication bias needs to be considered. This is especially important, because publication bias mostly affects exactly such studies, while sufficiently powered studies are usually published disregarding the actual outcome (Egger et al., 1997; Thornton and Lee, 2000). Therefore, large-scale studies including clinical trials and/or randomized control trials are needed. Such studies are feasible since vestibular stimulation is readily available, inexpensive and many of the discussed disorders, like sleep disorders, chronic pain, depression and anxiety, are unfortunately very prevalent.

Acknowledgments

We are grateful to Nicholas J. Wade and the other (anonymous) reviewer, as well as Victoria J. Madden, Leslie Russek and Peter Brugger for proofreading and their helpful suggestions on the manuscript. The authors are supported by the Swiss National Science Foundation (grant 142601 awarded to B.L. and G.M.; postdoctoral fellowship 144848 awarded to L.G.).
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The moving history of vestibular stimulation


The moving history of vestibular stimulation


The moving history of vestibular stimulation


The moving history of vestibular stimulation

**Figure captions**

Figure 1. A) a picture of Hallaran’s bed and chair used for therapeutic purposes in an asylum in the beginning of the 19th century (Breathnach, 2010), B) the device used by Ernst Mach for experimental purposes (Mach, 1875) and C) Bárány’s rotating chair that he used for clinical diagnostics (Barany, 1907).

Figure 2. A) Bárány’s (1907) bedside caloric test showing a rubber bag to collect the water, b nozzle for water irrigation, and c balloon filled with water (see also Baloh, 2002). B) Early galvanic stimulation device; here used in order to cure tinnitus (Grapengiesser, 1801).