The Lateralized Vestibular Stimulation: Effect on Mood, Cognition, and Autonomic States in Mental Disorders

A.M. Soza Ried[1,2,*] and Catalina Arrau[1]

[1]*Vest Brain, Neurovestibular Center, Chile*

[2]*Universidad de Chile, Adjunct Professor, Psychiatry & Mental Health Department, Chile*

Abstract: The vestibular system in the inner ear senses the body's movements, which is essential for regulating reflex movements and body balance at the brain stem level. Still, it is also critical in regulating high brain functions, including mental states, motivation, mood, cognition, and reasoning. This article reviews the neuro-functional effects of lateralized vestibular stimulation in three main brain areas involved in mental disorders: the parieto–insular–vestibular cortex (PIVC), the hippocampus, and the hypothalamus. We discuss its implications for the performance of high-demanding works and possible therapeutic applications in psychiatric patients.

Keywords: Lateralization, Depression, Vestibular stimulation.

INTRODUCTION

Mental illnesses show alterations in self-perception, cognitive dysfunctions, and a variety of bodily symptoms, such as sleep disturbances and symptoms of autonomic dysregulation. The insular cortex (PIVC), the hippocampus, and the hypothalamus are central to these functions. Although the mechanisms that regulate their activity are still uncertain, it is proposed that alterations in the normal lateralization of these neuronal centers could have a role in mental illnesses such as depression. In this regard, besides its importance in the body balance, the vestibular system has unique capacities to produce lateralized modulation of brain areas.

Brain Lateralization and Mental States

The lateralization of brain functions has been primarily discussed, suggesting that the right or left hemisphere is linked with different moods and cognitive styles. For example, visual dichoptic tests show that both hemispheres constantly deal with each other for dominance, giving rise to perceptual ocular rivalry [1]. Various experiments demonstrate that normal rivalry can be shifted towards either the right or the left hemisphere after unilateral vestibular stimulation [2].

Although there is not enough evidence about the lateralization of mood functions [3], some reports demonstrate that unilateral vestibular stimulation can elicit visible mood changes, turning from mania to euthymia after a few minutes [4].

Sad mood, cognitive impairment, sleep disturbances, and endocrine and autonomic dysfunction characterize major depression. Despite functional studies have not been conclusive in describing abnormal brain asymmetries in depression, the auditive and vestibular systems (which have no clear symptomatic relation with depression) have shown abnormal lateralization. Specifically, Bruder has demonstrated lateralization in the auditive function using dichotic techniques [5, 6], and Soza Ried showed that vestibular functional studies are also abnormally lateralized in depression [7].

Cognitive lateralized abilities have also been studied after the application of vestibular stimulation, showing the improvement of right or left brain functions depending on which side the stimulation is applied.

This article provides an overview of the vestibular system's neuronal centers and of the main techniques of lateralized vestibular stimulation available. We show evidence of abnormal lateralization of that brain areas involved in mental disorders which also receive vestibular modulation: the insular cortex, the hippocampus, and the hypothalamus, highlighting the different neuronal effects depending on the side Figure **1**.

The Vestibular System

The vestibular system is a sensory system responsible for detecting motion, spatial orientation, and balance. Located in the inner ear, the semicircular canals, the utricle, and the saccule detect head movements and position relative to gravity. The semicircular canals are sensitive to rotational movements, while the utricle and saccule detect linear

*Address correspondence to this author at the Universidad de Chile, Adjunct Professor, Psychiatry & Mental Health Department, Chile;
E-mail: amsozaried@vestbrain

E-ISSN: 2313-1047/24

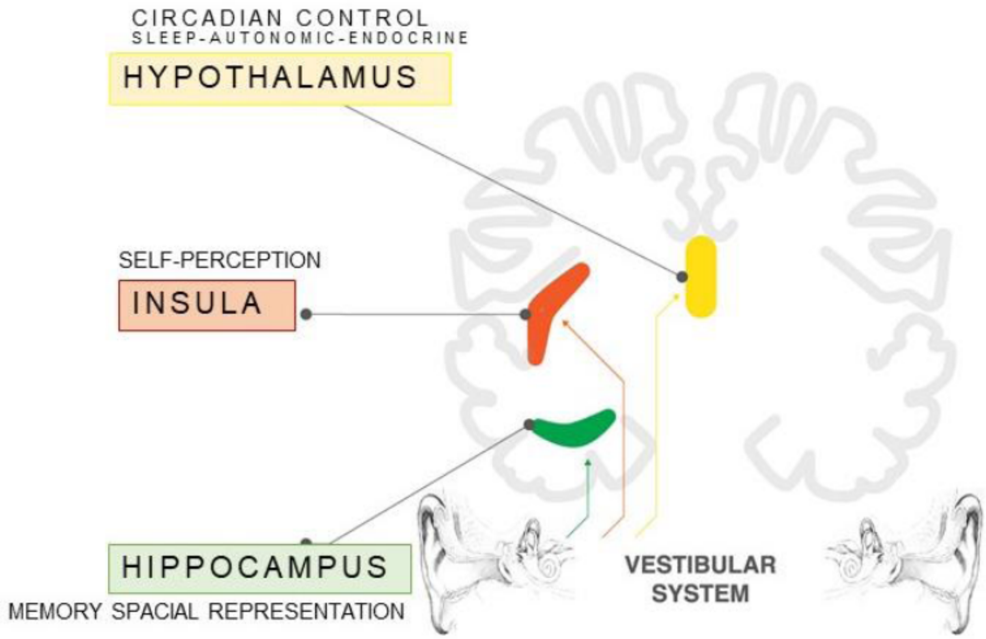

Figure 1: Brain areas/functions involved in mental disorders receive lateralized modulation from the vestibular system.

acceleration and gravitational forces. These structures send signals via the vestibular nerve to the brain, where the information is integrated with input from other sensory systems (*e.g.*, visual and somatosensory systems) to help maintain equilibrium and coordinate eye and head movements. The primary functions of the vestibular system include stabilizing vision during head movements (via the vestibulo-ocular reflex), maintaining posture and balance, and contributing to the perception of body movement in space. It plays a crucial role in everyday activities such as walking, driving, or even standing still, as it helps the body adjust to changes in position and movement. Dysfunction of the vestibular system can lead to vertigo, dizziness, and balance disorders, highlighting its importance for normal motor and sensory functioning.

Ciliary cells in macular epitheliums of semicircular canals respond to angular acceleration of the head. Meanwhile, utricular and saccular ciliary macular cells are correspondingly sensitive to horizontal and vertical linear acceleration. For the physiological acquisition of movement and positional information, both sides, right and left vestibular receptors, must be equally sensitive. Vestibular nerves and nuclei also must be symmetrically functioning; otherwise, the unilateral diminution or enhancement of their function will give rise to vertigo and dizziness.

Three semicircular canals containing endolymph register movements in three different orientations. Sensitive hair cells of the ampulla are stimulated with ampullipetal or inhibited by ampullifugal inclination of cilia. Physiological stimuli for the vestibular system are rotations in the correspondent three-dimensional orientation of the semicircular canal, although other artificial methods for stimulating the vestibular receptors have been developed; unilateral caloric stimulation of the ear that can induce stimulation of receptors with warm or inhibition with cold irrigation of the ear, also galvanic stimulation in which the cathode stimulates vestibular receptors and the anode inhibit them during the application of the electrodes to the vestibular nerve [8], (Figure **2**).

The four vestibular nuclei at the brain stem, superior, medial, lateral, and inferior, receive sensorial information from semicircular canals, utricles, and saccules. Neural fibers from the cerebellar vermis also raise vestibular nuclei, giving them mainly inhibitory inputs. Efferents from vestibular nuclei reach contralateral vestibular nuclei through commissural fibers. Vestibule spinal neurons also influence alpha and gamma motoneurons' activity in the anterior horn of the spinal cord, enhancing antigravity muscular activity and neck muscle contraction.

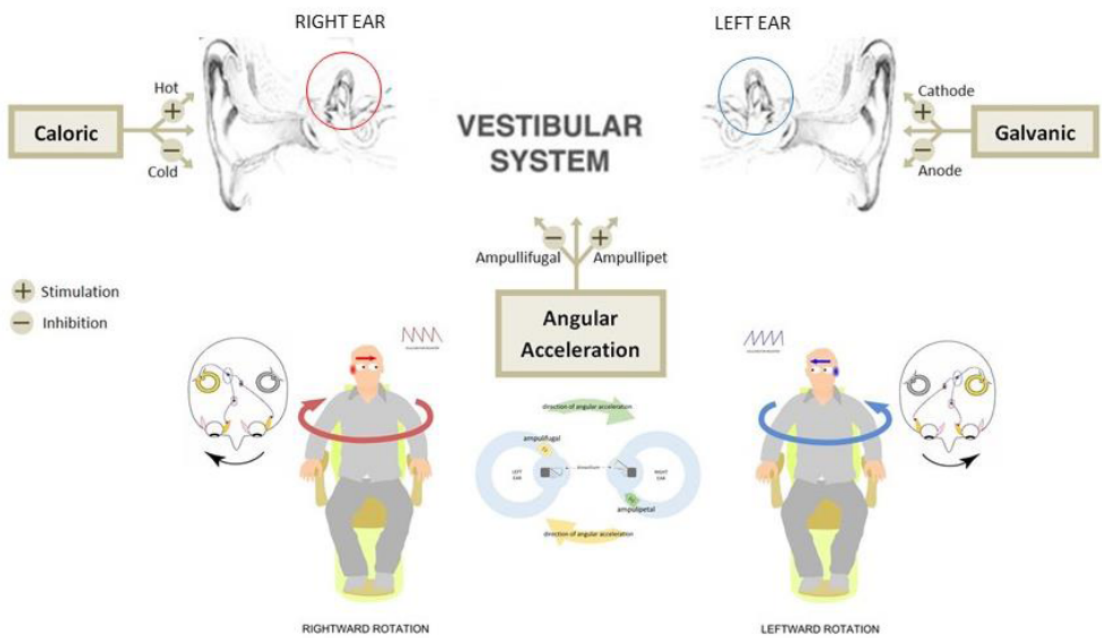

Figure 2: Stimulatory/inhibitory effect of the right/left ear´s vestibular system with different kinds of vestibular stimulation.

Taken together, the utricular, saccule, and semicircular canals give information about our actual position; the integration of that information, in addition to the cerebellar and raphe nuclei afferents, allows us to respond with adequate body and eye movements to stabilize our corporal position.

Vestibular-Brain Ascending Neuronal Pathways

The Modulatory Effect of the Vestibular System on Brain Activity

Vestibular nuclei stimulation also induces widespread brain activation. The primary vestibular cortex, first described in macaca, corresponds in humans to the parietal insular vestibular cortex (PIVC), which is also responsible for the perception of dizziness. In addition, prefrontal, hypothalamic, thalamic, and hippocampal areas are also activated by head position changes sensed by the vestibular system [9]. In physiologic conditions, natural body movements stimulate the right or left vestibular system randomly, and usually, both brain hemispheres have an equal probability of being activated.

Vestibular Modulation of the Parieto Insular Vestibular Cortex (PIVC): Effect on Self-Perception

Role of the PIVC

The enlargement of the brain during the evolution process gave rise to various new, modern, and complex functions, including the conscience. The development of the vestibular cortex in the parietal insular area, known as the parieto-insular vestibular cortex (PIVC), makes it possible to be aware of our body movements and plays an important role in interoceptive activity.

The insular cortex, located deep within the lateral sulcus of the brain, is a critical structure involved in a wide range of physiological, emotional, and cognitive functions and contributes to different aspects of sensory processing and integrative functions [10]. The parieto-insular vestibular cortex (PIVC) plays a crucial role in processing vestibular information, essential for balance, spatial orientation, and the perception of body movement in space [11]. Vestibular afferents, primarily relayed via the vestibular nuclei and thalamus, provide the PIVC with sensory input regarding head motion, gravitational forces, and spatial orientation, allowing it to integrate this information with other sensory modalities [12]. Also, Critchley *et al*. demonstrated a function of the insular cortex in decision-making [13, 14]. The insula receives afferent projections from sensory regions of the brainstem and thalamus, including somatosensory, gustatory, and viscerosensory pathways, which relay information about bodily sensations and visceral states [15]. Efferent projections from the insula target several regions, including the prefrontal cortex, amygdala, and anterior cingulate cortex, highlighting its role in mediating emotional and autonomic responses to sensory input and influencing higher-order cognitive functions such as emotional awareness, empathy, and self-regulation [16, 17].

Different Forms of Vestibular Stimulation can Induce Lateralized Activity at the Insular Cortex (PIVC)

The neuronal pathways of the ascending connections from vestibular nuclei to parieto insular vestibular cortex (PIVC) still need to be better understood. Registers of individual neurons in the vestibular cortex in macaca show that PIVC is stimulated by the vestibular nuclei in the brain stem.

Different inputs can activate the vestibular nuclei: the vestibular stimuli (physiologic or non-physiologic stimulation) and visual stimuli, like optokinetics.

Studies in humans demonstrate that *galvanic* vestibular stimulation activates the parieto insular cortex bilaterally [18]. Meanwhile, Dietrich *et al*. [19, 20] described that stimulation of the right vestibular nuclei (through caloric stimulation with warm water in the right ear) activates the right PIVC in right-handed people. Also, Marcelli *et al*. [21] showed contralateral activation of PIVC after cold water stimulation (inhibitory effect). The ipsilateral activation with warm or inhibition with cold water, respectively, was proved by Naito *et al*. [22] using warm water in the right ear or cold in the left, eliciting activation of the right insula, right parietal inferior lobe and right temporal inferior girus in PET study in humans.

Optokinetic horizontal stimuli produce a coherent activation of the right and left vestibular nuclei and PIVC [23]. According to this, most of the studies in humans show bilateral activation of brain structures in rightward or leftward optokinetic nystagmus [24-28] and just one [29] demonstrate ipsilateral (to the visual stimuli direction) brain activation. A recent article [30] demonstrates bilateral activation of cortical areas related to visual motion processing and bilateral deactivation of PIVC in fMRI in humans. The PIVC is also directly stimulated by visual stimuli coming from superior colliculus.

Different Effects on Self-Perception after Right and Left Insular Activation

The effects of unilateral PIVC activation are complex, and a variety of different sensations have been reported in humans. Direct current application on the right PIVC in a tinnitus patient produced an out-of-body experience [31]. Le Chapelain *et al*. [32] described the apparition of phantom limbs after cold irrigation of the left ear (which inhibits left PIVC activity). MRI abnormalities in the right temporoparietal junction in people with schizophrenia with space hallucinations [33] also illuminate the role of the PIVC in self-perception.

Craig AD [34] suggested that the right anterior insula seems to provide the basis for the subjective image of the material self as a feeling (sentient) entity, that is, emotional awareness, and Lopez *et al*. [35] discuss the importance of the vestibular cortex on embodiment and self-consciousness.

The Insular Cortex in Mental Disorders

Functional asymmetry of the insula has been consistently observed in mental disorders and patients with depression, with growing evidence suggesting that this brain region plays a pivotal role in the pathophysiology of the disorder. Several neuroimaging studies have reported altered activity in the left and right insular cortices in depressed individuals, which is associated with deficits in emotional processing, self-awareness, and regulation [36, 37]. For example, in schizophrenia, there is often a relative hypoactivity of the left insula linked to deficits in self-monitoring and emotional regulation [38].

Similarly, in anxiety disorders, asymmetries in insular activity may reflect heightened sensitivity to emotional stimuli and altered interoceptive awareness [39]. Major depressive disorder also has demonstrated an imbalance between the two insular cortices [40]. Furthermore, research using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) has shown that these asymmetries are not only linked to mood symptoms but may also serve as potential biomarkers for treatment response and illness severity [41].

In conclusion, the PIVC plays an essential role in interoception and subjective perception and can be modulated by ipsilateral vestibular activity. The lateralized activation of the PIVC produces altered mental states, like depression and other mental health disorders.

Vestibulo-Hippocampal Modulation: Effect on Cognition, Memory, and Spatial Abilities

The Role of the Hippocampus

Despite the ancient evolutionary origin of the hippocampus, its role in mental function has been widely described. Closely related to learning and memorizing environmental cues such as odor or internal chemical signals of the blood, the hippocampal areas also seem important for regulating hormonal secretion, especially cortisol. The development of explicit or declarative memory functions appeared later, probably as a predictive evolution process of the primitive intero and exteroceptive memory activity [42]. The hippocampus is also essential for spatial memory, where vestibular afferents coming from vestibular nuclei modulate the hippocampal activity, giving important cues for constructing memories and allowing the creation of conceptual maps of outer space. Dr Milner made one of the first descriptions of that in a patient, who has difficulties in returning home after a hippocampal lesion. In sum, the hippocampal formation registers the internal and the external environmental conditions and memorizes the hormonal and autonomic answers to maintain homeostasis.

Vestibular System and Hippocampal Function in Animals

Evidence shows that the vestibular system modulates the hippocampal areas and requires vestibular input for acquiring memories [43], as well as vestibular indemnity for normal hippocampal activity [44]. In this regard, Zheng reported a diminution of hippocampal nitric oxide synthase (NOS) and less hippocampal volumes after bilateral vestibular lesions and mainly ipsilateral diminution of nitric oxide (NO) in the dentate gyrus of the hippocampus after unilateral ablation of the vestibular peripheric system in rats [45]. Impairment of the spatial memory during vestibular activity inhibition [46] and the finding of interrupted theta rhythm in hippocampal areas in rats while spatial tasks performing [47] also reinforce the influence of vestibular activity in hippocampal functioning. In addition, bilateral vestibular lessoned rats cannot recover the spatial ability, contrary to unilateral vestibular damage that recovers the capacity at five months [48]. In this context, Kim *et al*. [49] demonstrated that unilateral vestibular lesions in rats induce ipsilateral diminution of cFOS expression in the hippocampus and dentate areas. Smith [50] suggested that the thalamus transmits vestibular information to the hippocampus via the parietal cortex. However, he proposes that more direct pathways are likely possible. Liu *et al*. [51, 52] showed ipsilateral diminished hippocampal NO and NMDA receptor changes after vestibular lesions in rats.

In summary, animal studies demonstrate the vestibular system's modulation of hippocampal activity and evidence of ipsilateral neuronal pathways between the vestibular and the hippocampus.

Vestibular Modulation of Hippocampal Function in Humans

Human studies show similar findings. fMRI [53] and PET studies [54] demonstrated hippocampal activation during vestibular stimulation in healthy subjects. As was first demonstrated in rats, bilateral vestibular lesions evidenced bilateral atrophy of the hippocampus and impaired spatial memory [55]. Also, vestibular lessoned patients show spatial memory failure [56] and impaired navigation skills in chronic vestibular hypofunction without vertigo [57].

Although patients with right vestibular failure exhibit spatial and navigation impairments, no such impairments are observed in patients with left vestibular lesions [58]. In this regard, developing specific lateralized brain functions in humans is an important matter of attention, showing right side preponderance at list in spatial abilities. Shipman *et al*. [59] demonstrated right hippocampal activation during spatial tasks using fMRI in humans, and Weniger *et al*. [60] showed that right posterior parahippocampal girus lessoned patients failed in virtual maze acquisition.

In conclusion, normal vestibular activity is essential for allowing the physiologic function of the hippocampus. The right side of the hippocampus has been proven to have a primordial role in spatial and cognitive abilities. Finally, vestibular hippocampal modulation is mainly ipsilateral, which makes it possible to hypothesize that in cognitively impaired patients, the stimulation of right-side vestibular nuclei would enhance these functions.

Abnormal Hippocampal Asymmetry in Depression?

There is some evidence of diminution of the hippocampal volume in depression patients [61]. Even though the difference between the right and left hippocampus is still controversial, some studies have shown a diminution of the right side's volume [62]. Cognitive tests regarding spatial abilities and short memory tasks also show diminished hippocampal function in depression [63].

In sum, hippocampal brain areas are involved in memory and spatial functions. The right hippocampus is predominant for memory and spatial abilities. There are lateralized dysfunction of the hippocampus in mental disorders like depression. The vestibular system affects the hippocampus mainly through ipsilateral pathways.

Vestibular-Hypothalamic Modulation

Effect on Circadian Rhythms, and Visceral-Metabolic Regulation

Hypothalamic centers control visceral and metabolic functions of the body, including autonomic and endocrine activity, thermoregulation, satiety and hunger, sleep, and weak states. All of those functions are highly rhythmic and synchronized in healthy subjects. The Suprachiasmatic Nuclei (SCN), also in the hypothalamus, seem to play a protagonist role in synchronizing that activity.

Vestibular System and Hypothalamic Activity

The influence of the vestibular system on hypothalamic activity hasn't been sufficiently studied in humans, but experimental animal models have demonstrated that there are modulatory nervous pathways from the vestibular nuclei to the hypothalamus. Experiments using hamsters show that vestibular activity can regulate eating behavior, sleep-wake cycles, and rhythms of hormonal secretion. The information about the quantity and kind of body movements probably modulates the metabolic cell function and the visceral autonomic activity in order to achieve the best performance according to the corporal physic activity. The accuracy of the autonomic response during rapid changes of position and body acceleration, sensed by the vestibular system, allows for maintaining homeostatic conditions, especially in blood irrigation.

The influence of the vestibular activity over the Suprachiasmatic Nucleus, which governs circadian functions, has been studied in hamsters by Fuller [64, 65], demonstrating that the vestibular system can modify the circadian rhythms [66]. The main neural pathways coming from the vestibular system to the hypothalamus are serotoninergic fibers coming from the Raphe Nuclei [67].

Hipothalamic Disorders in Mental Illness

Despite mental, cognitive, and mood disabilities are characteristic of psychiatric diseases, different kinds of autonomic and metabolic disorders depending on hypothalamic function deal with a significant amount of the invalidating symptoms of mental disorders. The prevalence of sympathetic activity in depression has been demonstrated by many authors [68-74]; meanwhile, other researchers have not [75]. Bär *et al*. [76] suggest that the reported findings are secondary to the use of antidepressants. Recently, Koschke *et al*. [77] showed exacerbation of sympathetic symptoms with serotonin-selective reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors in depressive patients. Coen *et al*. [78] and Quick *et al*. [79] published an enhancement of gastric motility (sympathetic response) in depression patients that is exacerbated with the use of antidepressants.

Lateralized brain activity has been linked to sympathetic or parasympathetic activity. In this regard, right PIVC lesions induce significantly more cardiac arrhythmic complications than left ones [80]. Also, Sukuki *et al*. [81] showed increased sympathetic activity in the right insula in humans during painful stimuli. Critchley *et al*. [82] demonstrated proarrhythmic changes and simultaneous right hypothalamic activation in human stress conditions. Complementing the last, an exciting study in fibromyalgia patients showed abnormal asymmetries of autonomic activity regarding diminished sympathetic activity at the right side of the body, evidenced by reduced skin conductance and temperature in the dominant side [83].

Animal studies also demonstrate, different lateralization; a study assessed by Min *et al*. [84] shows cardiac dysfunction proportional to elevated levels of noradrenalin in the heart after left, but not in right insular lessoned rats. Meanwhile, Xavier *et al*. [85] demonstrate midbrain lateralized control of autonomic activity, with an increased activity of right hypothalamic areas during sympathetic responses in rats. In addition Sullivan and Gratton [86] demonstrate the role of right prefrontal structures in enhancing the sympathetic response.

In summary, hypothalamic brain areas control sleep-weak cycles, autonomic and viscero-metabolic activity. There is evidence of lateralized regulation of autonomic activity in humans and of abnormal lateralization in mental disorders. There is evidence of vestibule hypothalamic regulation in experimental animals. No studies have been conducted on the neural pathways between the vestibular system and the hypothalamus in humans.

DISCUSSION

The vestibular system, a key player in corporal balance, also holds significant sway in regulating mental states, including mood, attention, cognition, and visceral functions. This article delves into the evidence surrounding abnormal functional asymmetries in mental disorders and the impact of lateralized vestibular stimulation on three pivotal cerebral centers: the parieto-insular cortex (PIVC), the hippocampus, and the hypothalamus. Lateralized modulatory stimulation could potentially restore healthy mental states. The aim of this article is to unravel the limited and often confusing evidence available about the brain asymmetries involved in mental disorders and to outline the vestibular pathways that influence and regulate those centers. We detail the effect of various modalities of vestibular stimuli, such as caloric, galvanic, rotatory, and optokinetic, on brain activity, and propose their potential use in restoring normal brain lateralization. The selection of the appropriate technique and stimulation side is crucial to successfully achieve our therapeutic target. In conclusion, vestibular stimulation could potentially treat mental disorders by reinstating the functional symmetry of the brain.

This article offers a unique perspective on mental disorder physiopathology, honing in on the functional asymmetries of three neuronal centers that are crucial in mental disorders and are intricately linked to the vestibular system.

CONFLICTS OF INTEREST

I declare no conflict of interest.

REFERENCES

[1] Petigrew JD. (2001) Searching for the switch: neural bases for perceptual rivalry alternations. Brain and Mind 2, 85-118. https://doi.org/10.1023/A:1017929617197

[2] Miller SM, Liu GB, Ngo TT, Hooper G, Riek S, Carson RG, Petigrew JD. Interhemispheric switching mediates perceptual rivalry. Curr Biol 10, 383-92. https://doi.org/10.1016/S0960-9822(00)00416-4

[3] Carson AJ, Siobhan M, Allen K, *et al*. (2000) Depression after stroke and lesion location: A Systematic review. Lancet 356, 122-126. https://doi.org/10.1016/S0140-6736(00)02448-X

[4] Dodson MJ (2004)" Vestibular stimulation in mania: a case report." J Neurol Neurosurg Psychiatry 75, 168-169

[5] Bruder GE, Stewart JW, Schaller JD, Mc Grath PJ (2007) Predicting therapeutic response to secondary treatment with bupropion: a dichotic listening tests of functional brain asymmetry. Psychiatry Res 31, 137-143. https://doi.org/10.1016/j.psychres.2007.04.011

[6] Bruder GE, Stewart JW, Mc Grath PJ, Delyllanides D, Quitkin FM (2004) Dichotic lestening tests of functional brain asymmetry predict response to fluoxetine in depressed woman and men. Neuropsychopharmacology, 29, 1752-61. https://doi.org/10.1038/sj.npp.1300519

[7] Soza Ried AM, Aviles M. (2007) Asymmetries of vestibular dysfunction in major depression. Neuroscience 144, 128-34. https://doi.org/10.1016/j.neuroscience.2006.09.023

[8] Goldberg JM, Smith CE,and Fernandez C. (1984) Relation between discharge regularity and responses to externally applied galvanic currents in vestibular nerve of squirrel monkey. J Neurophysiol 51, 1236-1256. https://doi.org/10.1152/jn.1984.51.6.1236

[9] Petit L, Beauchamp MS (2002) Neural basis of visually guided head movements studied with fMRI. J Neurophysiol 89, 2516-2527. https://doi.org/10.1152/jn.00988.2002

[10] Craig, A. D. (2009). How do you feel - now? The anterior insula and human awareness. Nature Reviews Neuroscience, 10(1), 59-70. https://doi.org/10.1038/nrn2555

[11] Lopez, C., & Blanke, O. (2011). The parieto-insular vestibular cortex: A multisensory hub for the integration of bodily signals. Nature Reviews Neuroscience, 12(6), 432-441.

[12] Bremmer, F., *et al*. (2002). Multisensory processing in the superior temporal sulcus. Philosophical Transactions of the Royal Society B: Biological Sciences, 357(1424), 1325-1332.

[13] Critchley, H. D., *et al*. (2004). Neural activity in the human brain related to both emotion and attention. Nature, 429(6993), 358-362.

[14] Naqvi, N., & Bechara, A. (2009). The insula and decision-making. Frontiers in Neuroscience, 3(1), 52-62.

[15] Macey, P. M., *et al*. (2004). Brain activity during the Valsalva maneuver. Journal of Applied Physiology, 97(3), 1242-1251.

[16] Augustine, J. R. (1996). Circuitry and functional aspects of the insular lobe in primates. Brain Research Reviews, 22(3), 229-244. https://doi.org/10.1016/S0165-0173(96)00011-2

[17] Cauda, F., *et al*. (2012). Functional connectivity of the insular cortex. PLOS ONE, 7(4), e30346.

[18] Stephan T, Deutschlander A *et al*. (2005) Functional MRI of galvanic vestibular stimulation with alterning currents at different frequencies. Neuroimage 26: 721-732. https://doi.org/10.1016/j.neuroimage.2005.02.049

[19] Dieterich M, Bense S, Lutz S, Drzezga A, Stephan T, Bartenstein P and Brandt T. (2003) Dominance for VestibularCortical Function in the Non-dominan Hemisphere. Cerebral Cortex 13, 994-1007. https://doi.org/10.1093/cercor/13.9.994

[20] Dieterich M, Bartenstein P, Spiegel S, Bense S, Schwaiger M, Brandt T. (2005) Thalamic infarctions cause side-specific suppression of vestibular cortex activations Brain; 128, 2052-67. https://doi.org/10.1093/brain/awh551

[21] Marcelli V, Esposito F, Aragri A, Furia T, Riccardi P, Tosetti M, Biagi L, Marciano E, Di Salle F. (2008) Spatio-temporal pattern of vestibular information processing after brief caloric stimulation. European Journal of Radiology 70, 312-316. https://doi.org/10.1016/j.ejrad.2008.01.042

[22] Naito Y, Tateya I, Hirano S, Inoue M, Funabiki K, Toyoda H, Ueno M, Ishizu K, Nagahama Y, Fukuyama H and Ito J. (2003) Cortical correlates of vestibulo-ocular reflex modulation: a PET study. Brain 126, 1562-1578. https://doi.org/10.1093/brain/awg165

[23] Grüsser OJ, Pause M and Schreiter U. (1989) Localization and responses of neurons in the parieto-insular vestibular cortex of awake monkeys(macaca fascicularis)Journal of Physiology 430: 537-557. https://doi.org/10.1113/jphysiol.1990.sp018306

[24] Konen CS, Kleiser R, Seitz RJ, Bremmer F. (2005) An fMRI study of optokinetic nystagmus and smooth-pursuit eye movements in humans. Exp Brain Res.165, 203-16. https://doi.org/10.1007/s00221-005-2289-7

[25] Bense S, Janusch B, Schlindwein P, Bauermann T, Vucurevic G, Brandt T, Stoeter P and Dieterich M. (2006) Direction-dependent visual cortex activation during horizontal

optokinetic stimulation (fMRI study) Hum Brain Mapp. 27, 296-305.
https://doi.org/10.1002/hbm.20185

[26] Dieterich M, Bucher SF, Seelos KC and Brandt T. (1998) Horizontal or vertical optokinetic stimulation activates visual motion-sensitive, ocular motor and vestibular cortexareas with right hemispheric dominance. An fMRI study. Brain 121, 1479-1495.
https://doi.org/10.1093/brain/121.8.1479

[27] Bucher SF, Dieterich M, Seelos KC and Brandt T. (1997) Sensorimotor cerebral activation during optokinetic nystagmus. Afunctional MRI study. Neurology 49, 1370-1377.
https://doi.org/10.1212/WNL.49.5.1370

[28] Dieterich M, Müller-Schunk S, Stephan T, Bense S, Seelos K and Yousry TA. (2009) Functional magnetic resonance imaging activations of cortical eye fields during saccades, smooth pursuit, and optokinetic nystagmus. Ann N Y Acad Sci. 1164, 282-292.
https://doi.org/10.1111/j.1749-6632.2008.03718.x

[29] Galati G, Pappata S, Pantano P, Lenzi GL, Samson Y and Pizzamiglio L. (1999) Cortical control of optokinetic nystagmus in humans: a positron emission tomography study. Exp Brain Res. 126, 149-159.
https://doi.org/10.1007/s002210050725

[30] Kikuchi M, Naito Y, Senda M, Okada T, Shinohara S, Fujiwara K, Hori SY, Tona Y, Yamazaki H. (2009) Cortical activation during optokinetic stimulation - an fMRI study. Acta Otolaryngol. 129, 440-3.
https://doi.org/10.1080/00016480802610226

[31] De Ridder D, Van Laere K, Dupont P, Menovsky T, Van de Heyning P. 2007Visualizing out-of-body experience in the brain. N Engl J Med. 357, 1829-33.
https://doi.org/10.1056/NEJMoa070010

[32] Le Chapelain L, Beis JM, Paysant J, André JM. (2001) Vestibular caloric stimulation evokes phantom limb illusions in patients with paraplegia. Spinal Cord. 39, 85-7.
https://doi.org/10.1038/sj.sc.3101093

[33] Plaze M, Marie- Paillère-Martinot L. (2009). "Where Do Auditory Hallucinations Come From?"-A Brain Morphometry Study of Schizophrenia Patients With Inner or Outer Space Hallucinations. Schizophrenia Bulletin 7.
https://doi.org/10.1093/schbul/sbp081

[34] Craig AD. 2003 Interoception: the sense of the physiological condition of the body. Curr Opin Neurobiol. 4, 500-5.
https://doi.org/10.1016/S0959-4388(03)00090-4

[35] Lopez C, Halje P, Blanke O. (2008) Body ownership and embodiment: vestibular and multisensory mechanisms Neurophysiol Clin. 38, 149-61.
https://doi.org/10.1016/j.neucli.2007.12.006

[36] Ursini, T., Di Forti, M., & Cavedo, E. (2011). Structural and functional neuroimaging findings in major depression. Current Psychiatry Reviews, 7(3), 153-160.

[37] Kross, E., Davidson, M., & Wager, T. D. (2013). Social rejection shares somatosensory representations with physical pain. Proceedings of the National Academy of Sciences, 110(14), 6960-6965.

[38] Wang, X., Li, Z., & Zhang, X. (2011). Insula dysfunction in schizophrenia: Implications for emotional processing and self-awareness. NeuroImage, 56(4), 1775-1784.

[39] Paulus, M. P., & Stein, M. B. (2006). An insular view of anxiety. Biological Psychiatry, 60(4), 383-387.
https://doi.org/10.1016/j.biopsych.2006.03.042

[40] Ursini, T., Di Forti, M., & Cavedo, E. (2011). Structural and functional neuroimaging findings in major depression. Current Psychiatry Reviews, 7(3), 153-160.

[41] Hamilton, J. P., Etkin, A., & Furman, D. J. (2012). Functional neuroimaging of emotional processing in mood and anxiety disorders. Trends in Cognitive Sciences, 16(11), 557-565.

[42] Lathe R. (2001) Hormones and the hippocampus.Journal of Endocrinology 169, 205-231.
https://doi.org/10.1677/joe.0.1690205

[43] Russell NA, Horii A, Smith PF, Darlington CL, Bilkey DK. (2003) Bilateral peripheral vestibular lesions produce long-term changes in spatial learning in the rat. J Vestib Res. 13, 9-16.
https://doi.org/10.3233/VES-2003-13102

[44] Horii A, Takeda N, Mochizuki T, Okakura-Mochizuki K, Yamamoto Y, Yamatodani A, Kubo T. (1995) Vestibular modulation of the septo-hippocampal cholinergic system of rats. Acta Otolaryngol Suppl. 2: 395-8.
https://doi.org/10.3109/00016489509125280

[45] Zheng Y, A. Horii, I. Appleton, C. L. Darlington and P. F. Smith. (2001). Damage to the vestibular inner ear causes long-term changes in neuronal nitric oxide synthase expression in the rat hippocampus Neuroscience, 105: 1-5.
https://doi.org/10.1016/S0306-4522(01)00217-2

[46] Stackman RW, Clark AS, Taube JS (2002). Hippocampal spatial representations require vestibular input hippocampus; 12: 291-303
https://doi.org/10.1002/hipo.1112

[47] Russell NA, Horii A, Smith PF, Darlington CL, Bilkey DK. (2006) Lesions of the vestibular system disrupt hippocampal theta rhythm in the rat. J Neurophysiol. 96, 4-14.
https://doi.org/10.1152/jn.00953.2005

[48] Zheng YW, Goddard M, Darlington CL, Smith PF. (2009) Long-Term Deficits on a Foraging Task After Bilateral Vestibular Deafferentation in Rats Hippocampus 19: 480-486.
https://doi.org/10.1002/hipo.20533

[49] Kim MS, Choi MA, Choi DO, Cho BG, Jin YZ, Kim JH, Kry D, Park BR. (2002). Effect of vestibular end-organs on expression of cFos and FosB injury in the hippocampal formation of rats. J Korean Bal Soc. 1: 223-234.

[50] Smith PF. (1997) Vestibular -hippocampal interactions. Hippocampus 7, 465-471.
https://doi.org/10.1002/(SICI)1098-1063(1997)7:5<465::AID-HIPO3>3.0.CO;2-G

[51] Liu Ping, Zheng Y, King J, Darlington C L., Smith P.F. (2003) Nitric oxide synthase and arginase expression in the vestibular nucleus and hippocampus following unilateral vestibular deafferentation in the rat Brain Research, 966, 19-25.
https://doi.org/10.1016/S0006-8993(02)04146-X

[52] Liu, Y. Zheng, J. King, C. L. Darlington, P. F. Smith. (2003) Long-term changes in hippocampal n-methyl- -aspartate receptor subunits following unilateral vestibular damage in rat. Neuroscience, 117, 965-970.
https://doi.org/10.1016/S0306-4522(02)00878-3

[53] Suzuki M, Kitano H, Ito R, Kitanishi T, Yazawa Y, Ogawa T, Shiino A, Kitajima K. (2001) Cortical and subcortical vestibular response to caloric stimulation detected by functional magnetic resonance imaging.Brain Res Cogn Brain Res 12,441-9.
https://doi.org/10.1016/S0926-6410(01)00080-5

[54] Kisely M, Tóth A, Emri M, Lengyel Z, Kálvin B, Horváth G, Trón L, Bogner B, Sziklai I. (2001). Processing vestibular impulses in the central nervous system. Study based on positron emission tomography. HNO 49: 347-54.
https://doi.org/10.1007/s001060050761

[55] Brandt T, Schautzer F, Hamilton DA, Brüning R, Markowitsch HJ, Kalla R, Darlington C, Smith P, Strupp M. (2005). Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans Brain. 128, 2732-41.
https://doi.org/10.1093/brain/awh617

[56] Schautzer F, Hamilton D, Kalla R, Strupp M, Brandt T. (2003). Spatial memory deficits in patients with chronic bilateral vestibular failure. Ann N Y Acad Sci.1004, 316-24.
https://doi.org/10.1196/annals.1303.029

[57] Hamann KF, Weiss U, Ruile A. (2009) Effects of acute vestibular lesions on visual orientation and spatial memory, shown for the visual straight ahead. Ann N Y Acad Sci. 1164: 305-8.
https://doi.org/10.1111/j.1749-6632.2009.03867.x

[58] Guidetti G, Monzani D, Trebbi M, Rovatti V. (2008) Impaired navigation skills in patients with psychological distress and chronic peripheral vestibular hypofunction without vertigo Acta Otorhinolaryngol Ital. 28, 21-5.

[59] Shipman SL, Astur RS. (2008) Factors affecting the hippocampal BOLD response during spatial memory Behav Brain Res.187, 433-41.
https://doi.org/10.1016/j.bbr.2007.10.014

[60] Weniger G, Lange C, Sachsse U, Irle E. Amygdala and hippocampal volumes and cognition in adult survivors of childhood abuse with dissociative disorders. Acta Psychiatr Scand. 2008 Oct 118(4): 281-90. Epub 2008 Aug 27. PMID: 18759808.
https://doi.org/10.1111/j.1600-0447.2008.01246.x

[61] Elker C, Gonul AS. (2010) Volumetric MRI studies of the hippocampus in major depressive disorder: Meanings of inconsistency and directions for future research World J Biol Psychiatry11: 19-35.
https://doi.org/10.3109/15622970902737998

[62] Abe O, Yamasue H, Kasai K, Yamada H, Aoki S, Inoue H, Takei K, Suga M, Matsuo K, Kato T, Masutani Y, Ohtomo K. Voxel-based analyses of gray/white matter volume and diffusion tensor data in major depression. Psychiatry Res. 2010 Jan 30; 181(1): 64-70. PMID: 19959342.
https://doi.org/10.1016/j.pscychresns.2009.07.007

[63] Preiss M, Kucerova H, Lukavsky J, Stepankova H, Sos P, Kawaciukova R. (2009) Cognitive deficits in the euthymic phase of unipolar depression. Psychiatry Res. 30; 169: 235-9.
https://doi.org/10.1016/j.psychres.2008.06.042

[64] Fuller *et al*. in "Neurovestibular modulation of circadian and homeostatic regulation: vestibulohypothalamic connection? Proceedings of the National Academy of Sciences 99: 24 15723-15728.
https://doi.org/10.1073/pnas.242251499

[65] Fuller and Fuller (2006)" Genetic evidence for a neurovestibular influence on the mamalian circadian pacemaker" Journal of Biological Rhythms 21: 177-184.
https://doi.org/10.1177/0748730406288148

[66] Alpini D, Cesarani A, Fraschini F, Kohen-Raz R, Capobianco S, Cornelio F "Aging and vestibular system: specific tests and role of melatonin in cognitive involvement."Arch Gerontol Geriatr Suppl. (2004); 9: 13-25.
https://doi.org/10.1016/j.archger.2004.04.005

[67] Horowitz SS, Blanchard JH, Morin LP). (2004). "Intergeniculate leaflet and ventral lateral geniculate nucleus afferent connections: An anatomical substrate for functional input from the vestibulo-visuomotor system." J Comp Neurol. 21: 227-45.
https://doi.org/10.1002/cne.20125

[68] Barnes RF, Veith RC, Borson S, Verhey J, Raskind MA, Halter JB. (1983) High levels of plasma catecholamines in dexamethasone-resistant depressed patients. Am J Psychiatry; 140: 1623-5.
https://doi.org/10.1176/ajp.140.12.1623

[69] Esler M, Turbott J, Schwarz R, Leonard P, Bobik A, Skews H, Jackman G. (1982) The peripheral kinetics of norepiniphrine in depressive illness. Arch Gen Psychiatry; 39: 285-300.
https://doi.org/10.1001/archpsyc.1982.04290030035006

[70] Lake CR, Pickar D, Ziegler MG, Lipper S, Slater S, Murphy DL. (1982) High plasma NE levels in patients with major affective disorder. Am J Psychiatry; 139: 1315-8.
https://doi.org/10.1176/ajp.139.10.1315

[71] Roy A, Pickar D, De Jong, J, Karoum F, Linnoila M. (1988) NE and its metabolites in cerebrospinal fluid, plasma, and urine. Arch Gen Psychiatry 5, 849-57.
https://doi.org/10.1001/archpsyc.1988.01800330081010

[72] Wyatt RJ, Portnoy B, Kupfer DJ, Snyder F, Engelman K. (1971) Resting plasma catecholamine concentrations in patients with depression and anxiety. Arch Gen Psychiatry.24, 65-70.
https://doi.org/10.1001/archpsyc.1971.01750070067009

[73] Siever L, Davis K.(1985)Overview: toward a dysregulation hypothesis of depression. Am J Psychiatry.142: 1017-31.
https://doi.org/10.1176/ajp.142.9.1017

[74] Veith RC, Lewis N, Linares OA, Barnes RF, Raskind MA, Villacres EC, Murburg MM, Ashleigh EA, Castillo S, Peskind ER, Pascualy M, Halter JB. Sympathetic nervous system activity in major depression. Arch Gen Psychiatry 1994; 51: 411-22. [Abstract/Free Full Text].
https://doi.org/10.1001/archpsyc.1994.03950050071008

[75] Baumert M, Lambert GW, Dawood T, Lambert EA, Esler MD, McGrane M, Barton D,Sanders P, Nalivaiko E. (2009)Short-term heart rate variability and cardiac norepinephrine spillover in patients with depression and panic disorder. Am J Physiol Heart Circ Physiol. 297, H674-9.
https://doi.org/10.1152/ajpheart.00236.2009

[76] Bär KJ, Greiner W, Jochum T, Friedrich M, Wagner G, Sauer H. (2004) The influence of major depression and its treatment on heart rate variability and pupillary light reflex parameters. J Affect Disord. 82, 245-52.
https://doi.org/10.1016/j.jad.2003.12.016

[77] Koschke M, Boettger MK, Schulz S, Berger S, Terhaar J, Voss A, Yeragani VK, BärKJ. (2009) Autonomy of autonomic dysfunction in major depression. Psychosom Med. 71, 852-60.
https://doi.org/10.1097/PSY.0b013e3181b8bb7a

[78] Coen SJ, Yágüez L, Aziz Q, Mitterschiffthaler MT, Brammer M, Williams SC, Gregory LJ. (2009)Negative mood affects brain processing of visceral sensation Gastroenterology. 137,253-61.
https://doi.org/10.1053/j.gastro.2009.02.052

[79] Quick C, Kliem A, Berger S, Hocke M, Tancer M, Juckel G, Yeragani VK, Bär KJ. Gastric dysmotility in major depression. Prog Neuropsychopharmacol Biol Psychiatry. 2010 Feb 1; 34(1): 92-7. PMID: 19819283.
https://doi.org/10.1016/j.pnpbp.2009.10.003

[80] Christensen H, Boysen G, Christensen AF, Johannesen HH. (2005) Insular lesions, ECG abnormalities, and outcome in acute stroke J Neurol Neurosurg Psychiatry. 76, 269-71
https://doi.org/10.1136/jnnp.2004.037531

[81] Suzuki H, Watanabe S, Hamaguchi T, Mine H, Terui T, Kanazawa M, Oohisa N, Maruyama M, Yambe T, Itoh M, Fukudo S. (2009) Brain activation associated with changes in heart rate, heart rate variability, and plasma catecholamines during rectal distention Psychosom Med. 71, 619-26.
https://doi.org/10.1097/PSY.0b013e31819b69ca

[82] Critchley HD, Taggart P, Sutton PM, Holdright DR, Batchvarov V, Hnatkova K, Malik M, Dolan RJ. (2005) Mental stress and sudden cardiac death: asymmetric midbrain activity as a linking mechanism. Brain. 128, 75-85.
https://doi.org/10.1093/brain/awh324

[83] Mitani Y, Fukunaga M, Kanbara K, Takebayashi N, Ishino S, Nakai Y. (2006) Evaluation of psychophysiological asymmetry in patients with fibromyalgia syndrome. Appl Psychophysiol Biofeedback. 31, 217-25
https://doi.org/10.1007/s10484-006-9020-8

[84] Min J, Farooq MU, Greenberg E, Aloka F, Bhatt A, Kassab M, Morgan JP, Majid A. (2009) Cardiac dysfunction after left permanent cerebral focal ischemia: the brain and heart connection. Stroke. 40, 2560-3.
https://doi.org/10.1161/STROKEAHA.108.536086

[85] Xavier CH, Nalivaiko E, Beig MI, Menezes GB, Cara DC, Campagnole-Santos MJ, Fontes MA. (2009) Functional asymmetry in the descending cardiovascular pathways from dorsomedial hypothalamic nucleus. Neuroscience. 164, 1360-8. https://doi.org/10.1016/j.neuroscience.2009.09.018

[86] Sullivan RM, Gratton AJ. (1999) Lateralized effects of medial prefrontal cortex lesions on neuroendocrine and autonomic stress responses in rats. Neurosci. 19, 2834-40. https://doi.org/10.1523/JNEUROSCI.19-07-02834.1999

Received on 23-10-2024 Accepted on 23-11-2024 Published on 26-11-2024

https://doi.org/10.12974/2313-1047.2024.11.07