Electrical stimulation of the peripheral and central vestibular system

Christophe Lopez, Kathleen E Cullen

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Christophe Lopez[a] *and Kathleen E. Cullen*[b,c,d,e]

Purpose of review
Electrical stimulation of the peripheral and central vestibular system using noninvasive (galvanic vestibular stimulation, GVS) or invasive (intracranial electrical brain stimulation, iEBS) approaches have a long history of use in studying self-motion perception and balance control. The aim of this review is to summarize recent electrophysiological studies of the effects of GVS, and functional mapping of the central vestibular system using iEBS in awake patients.

Recent findings
The use of GVS has become increasingly common in the assessment and treatment of a wide range of clinical disorders including vestibulopathy and Parkinson's disease. The results of recent single unit recording studies have provided new insight into the neural mechanisms underlying GVS-evoked improvements in perceptual and motor responses. Furthermore, the application of iEBS in patients with epilepsy or during awake brain surgery has provided causal evidence of vestibular information processing in mostly the middle cingulate cortex, posterior insula, inferior parietal lobule, amygdala, precuneus, and superior temporal gyrus.

Summary
Recent studies have established that GVS evokes robust and parallel activation of both canal and otolith afferents that is significantly different from that evoked by natural head motion stimulation. Furthermore, there is evidence that GVS can induce beneficial neural plasticity in the central pathways of patients with vestibular loss. In addition, iEBS studies highlighted an underestimated contribution of areas in the medial part of the cerebral hemispheres to the cortical vestibular network.

Keywords
electrical brain stimulation, epilepsy, galvanic vestibular stimulation, vestibular cortex, vestibular system

INTRODUCTION

Noninvasive (galvanic vestibular stimulation, GVS) and invasive (intracranial electrical brain stimulation, iEBS) electrical stimulation of the peripheral and central vestibular system have a long history of use in studying self-motion perception and balance control [1,2].

Over the past two decades, GVS has increasingly been used to probe the vestibular contributions to several components of perception, cognition, and emotions (reviewed in [3,4]). However, until recently there was a paucity of data about the neural mechanisms of GVS and its oculomotor, postural, and perceptual effects in nonhuman primates and humans.

As GVS is compatible with functional MRI (fMRI) and PET, it has been used to describe the human equivalent of nonhuman primate's cortical vestibular network in neurotypical participants [5,6,7▪▪]. A complementary way to delineate central vestibular pathways and structures is iEBS, a gold standard for mapping brain functions in neurology [8]. Pioneering work in patients with epilepsy or during brain tumor resection in awake patients [9] has demonstrated that iEBS can provide new insights into the neural substrate of vestibular representations within the cerebral cortex.

[a]Laboratory of Cognitive Neuroscience (LNC), CNRS, Aix Marseille Univ, FR3C, Marseille, France, [b]Department of Biomedical Engineering, [c]Department of Otolaryngology-Head and Neck Surgery, [d]Department of Neuroscience and [e]Kavli Neuroscience Discovery Institute, Johns Hopkins University, Baltimore, Maryland, USA

Correspondence to Dr Christophe Lopez, Laboratoire de Neurosciences Cognitives – UMR 7291, Aix Marseille Univ & Centre National de la Recherche Scientifique (CNRS), Centre Saint-Charles, Fédération de Recherche 3C – Case B. 3, Place Victor Hugo. 13331 Marseille Cedex 03, France. Tel: +33 4 13 55 08 41; fax: +33 4 13 55 08 44; e-mail: christophe.lopez@univ-amu.fr

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KEY POINTS

- GVS produces robust and parallel activation of both canal and otolith afferents that significantly differ from those evoked by natural head motion stimulation.
- GVS evokes highly asymmetric responses in irregular afferents for cathodal versus anodal currents, leading to a directional bias in the net population central response.
- Recent studies suggest that GVS induces beneficial neural plasticity in the central pathways of patients with vestibular loss.
- iEBS has provided novel causal evidence of vestibular representations in medial brain areas (middle cingulate cortex and precuneus) and subcortical structures (basal ganglia, amygdala).
- GVS can contribute to the assessment and treatment of vestibulopathy and Parkinson's disease, whereas iEBS can help understand cingulate and precuneal epilepsies.

Electrical stimulation of both the peripheral and central vestibular systems are now common and their underlying mechanisms need to be understood, especially, given the growing evidence of potential therapeutic effects of various forms of GVS and iEBS [10–12].

This review summarizes a selection of recent studies that have used GVS and iEBS. We focus on single unit recordings to understand the effects of GVS on vestibular afferents and central structures, and the effects of iEBS to identify the cortical and subcortical structures processing vestibular signals.

GALVANIC VESTIBULAR STIMULATION

GVS is commonly used to noninvasively probe and perturb vestibular function in humans. The use of GVS involves stimulating the peripheral vestibular system via the application of current to external electrodes placed on the mastoid processes. In addition to its use in basic research, GVS is also now increasingly used in the assessment and treatment of a wide range of clinical disorders including vestibulopathy and Parkinson's disease [13,14].

Method of activation, and basic/clinical findings

In contrast to natural motion, GVS bypasses the mechanotransduction of both canal and otolith vestibular sensory organs to directly activate the vestibular afferents of the VIII nerve (and potentially hair cells themselves). The resulting afferent activation in turn, evokes eye movements via central vestibulo-ocular reflex (VOR) pathways [13], postural response via central vestibulospinal pathways [15], as well as virtual sensations of self-motion (e.g. [16–18]).

GVS is typically applied in a binaural manner that activates afferents from all five vestibular sensory end organs on one side with concurrent inhibition of those on the contralateral side. The resulting activation is thus unnatural as the pattern of combined otolith and semicircular canal afferent activation has no physiological motion equivalent. At the population level, the net effect of GVS has been modeled as a vector of the summed canal activation with an overall net cancellation of the otolithic signals [1,19], where asymmetries in afferent responses induces a directional bias in the net population response [20▪].

To date, three primary classes of wave forms have been utilized in basic and clinical GVS human studies: currents steps, sinusoids, and band-limited noise (also termed stochastic GVS or noisy GVS [13]). Most current work is focused on the use of stochastic GVS because of its efficiency of application and improved subject comfort. *Supra*threshold noisy GVS has been applied to probe vestibulomotor responses of both the eyes and different axial and appendicular muscles. Leg and trunk muscles show response over a limited frequency range (<15–25 Hz) that modulate with standing posture [21,22], postural transitions [23], and gait cycle [24,25]. In contrast, neck muscles show GVS responses for frequencies up to 150 Hz [26]) that are task-independent [1]. This latter result suggests that the vestibulocollic reflex is largely hardwired (reviewed by [1]).

Moreover, there has been much recent discussion regarding the use of *subt*hreshold noisy GVS to improve balance function. Although a number of studies have reported positive outcomes (healthy [11,27] and patients [27–29]), the mechanisms by which improvements occur remain unknown. On the one hand, it has been proposed that *subt*hreshold induces stochastic resonance (see, e.g. [30,31]). However, several recent investigations have failed to provide consistent support for this view (e.g. [32▪▪,33], reviewed in [34–36]). Importantly, an open question is whether the stimuli used in studies demonstrating positive outcomes have employed suprathreshold rather than subthreshold stimuli.

Effects of galvanic vestibular stimulation on the peripheral vestibular system

Single unit recording studies are required to understand how GVS actually activates the central neural pathways underlying perception and behavior. In turn, this fundamental knowledge has significant

implications for advancing the development of more accurate stimulation techniques to selectively probe and perturb vestibular function. A series of recent experiments conducted on macaque monkeys used a setup comparable to that commonly used in humans to explicitly establish how GVS activates vestibular afferents [20▪,26,37]. GVS was applied to surface electrodes placed behind the monkeys' ears (Fig. 1a) and induced torsional eye movements similar to those observed in humans [37]. Single unit recording experiments then established that GVS evokes robust and comparable responses in canal and otolith afferents and that these responses differ from those evoked by natural head motion stimulation. This latter finding is not unexpected given that GVS activates afferents by bypassing the biomechanics of both the semicircular canals and otolith organs, which contribute to the dynamics of responses to rotation and translation, respectively.

More specifically, in response to GVS canal and otolith afferents both demonstrate a similar increase in gain with increasing stimulation frequency.

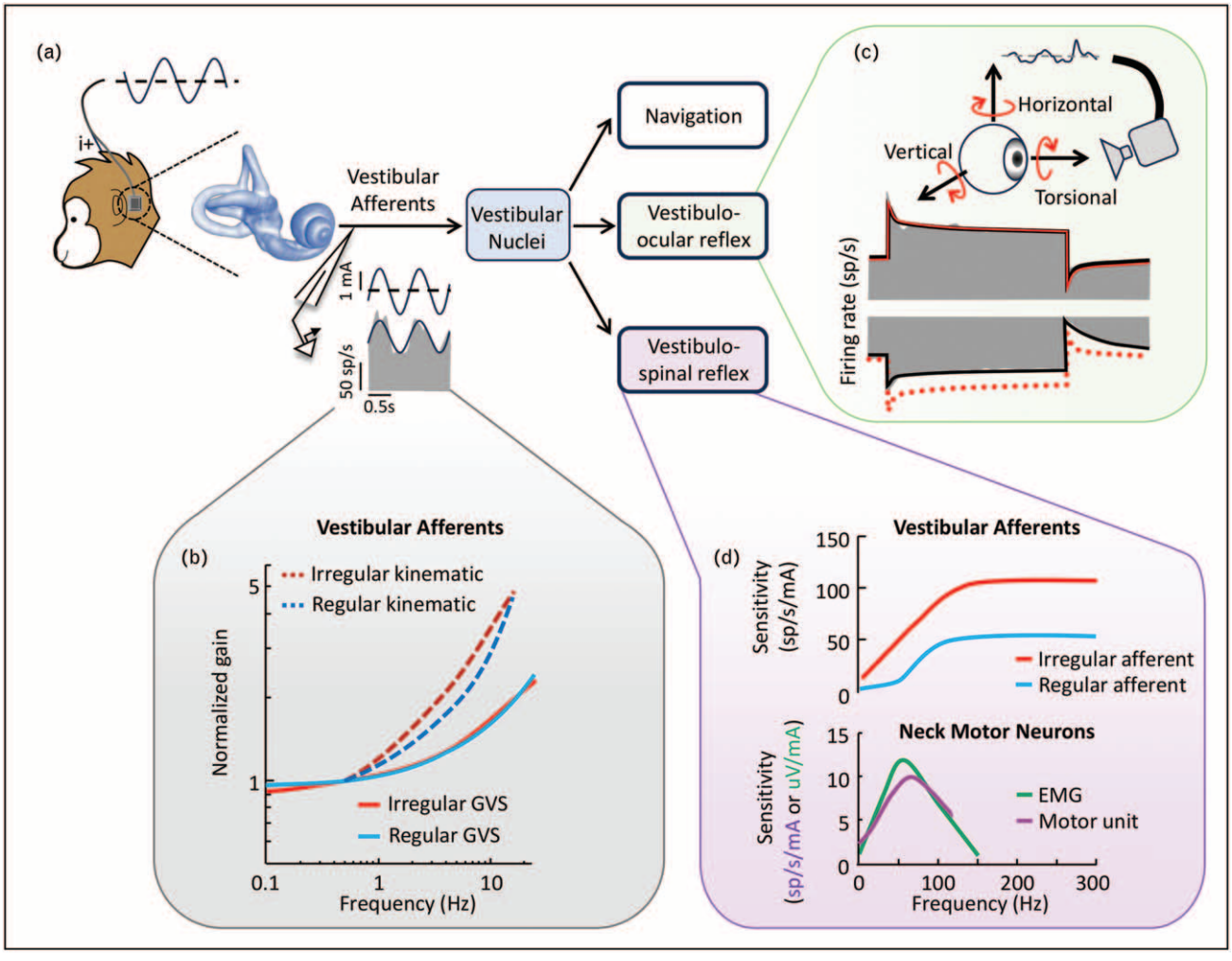

FIGURE 1. Effects of galvanic vestibular stimulation on the peripheral vestibular system. (a) Schematic of the setup used to apply GVS in the nonhuman primate model. Stimulation is applied between surface electrodes placed on the mastoid processes behind the ears, while the animal's eye movements and neural activity are recorded. (b) Response dynamics of vestibular canal afferents to sinusoidal GVS where the population averaged gain is shown for regular and irregular (blue and red, respectively) canal afferents. Dashed lines illustrating the corresponding responses to actual rotational motion are shown for comparison. (c) Constant current GVS evokes asymmetric changes in afferent firing rates during stimuli of opposing polarity, primarily for irregular afferents. Schematic of the asymmetric responses (gray) of an irregular afferent is shown for cathodal (top) versus anodal (bottom) stimulation. The red traces show the response fit to cathodal stimulation (solid), and the mirrored fit superimposed on the anodal response. (d) Response dynamics of monkey vestibular afferents and neck motor neurons to high-frequency (0–300 Hz) GVS. Population responses are shown for irregular versus regular canal afferents (top, red and blue, respectively) versus neck single unit versus EMG activity (bottom, purple and green, respectively). Data from Kwan *et al.* [85▪▪], Forbes *et al.* [26] and [20▪], with permission from the authors. GVS, galvanic vestibular stimulation.

Further, more irregular afferents demonstrate larger firing sensitivity compared with their regular counterparts. However, this gain increase is less than that observed for natural head motion (Fig. 1b). GVS evoked-afferent responses also became more phasically dynamic with increasing frequency, contrasting with reports based on internal stimulation of the inner ear [38,39]. Overall, the dynamics of GVS-induced afferent responses cannot be predicted by a simple stochastic model of repetitive afferent activity [40], suggesting that other key factors (e.g. hair-cell-mediated activity, nonquantal transmission, and the dynamics of vestibular afferent conductances) also shape afferent responses to GVS. The development of a mechanistic GVS model (e.g. [41▪]) is an important direction for future work.

Recent experimental findings in monkey have also challenged the prevailing view that GVS linearly activates the vestibular system. In response to cathodal versus anodal GVS currents, canal and otolith afferents both display significant response asymmetries, which also manifest in asymmetric eye movement responses via vestibulo-ocular pathways (Fig. 1c). For example, the onset of a cathodal versus anodal current step induces more pronounced changes in afferent responses [20▪]. These nonlinearities are more pronounced in irregular afferents relative to their regular counterparts. Simulations combining these experimental results with a well established computational model of the net effect of GVS [1], has led to the unexpected (and not yet tested) prediction that GVS induces directional biases in centrally integrated head motion signals [20▪].

Finally, it is noteworthy that recent GVS studies in macaque monkeys have directly compared the activation of afferents versus the neck musculature via vestibulospinal pathways, specifically the vestibulocollic reflex. The vestibulocollic reflex stabilizes head position in space by activating the neck musculature in response to unexpected self-motion across the natural range of head motion ([42]; Fig. 1d). Strikingly, both neck motoneurons and primary vestibular afferents respond to sinusoidal GVS stimulation up to 300 Hz, peaking around 70–80 Hz ([26]; Fig. 1d). Taken together, these findings suggest that that the high-frequency information encoded by afferents is indeed transmitted through the vestibular system to stabilize the head during unexpected head transients.

Effects of galvanic vestibular stimulation on the central vestibular system

Despite the recent progress made in understanding GVS's impact on individual vestibular afferents, our understanding of its effect on central vestibular pathways remains quite limited. Vestibular afferents directly target central neurons in the vestibular nuclei [43]. In-vitro studies using vestibular nuclei slices have long been used to investigate electrophysiological properties of individual neurons [44]. More recent experiments [34] have further shown that stochastic versus sinusoidal current waveforms – comparable with those used in the clinic – induce differential changes in neuronal membrane potential, neuronal regularity, and response gain across neurons. To date, however, only a handful of in-vivo studies have investigated how GVS alters signal transmission in central vestibular pathways. One 2020 study assessing how vestibular nuclei neurons encode combined GVS and motion stimulation [45] reported that sub additive responses similar to those reported for the integration of semicircular canal and otolith afferents in these cells [46]. This same group also reported that repeated GVS reduces vestibular nuclei neuronal potentials [45]. Notably, this reduction was accompanied by a decrease in AMPA and NMDA receptors, leading to proposal that GVS induces a reduction in the number of glutamate receptors that in turn modifies neuronal potentials in the vestibular nucleus.

Vestibular stimulation also activates higher level areas of central vestibular processing. The vestibular input to the hippocampus is thought to play an essential role in spatial navigation and for updating brain representations of spatial information [43]. A recent study in rats demonstrated that GVS altered hippocampal cell proliferation and neurogenesis; high amplitude GVS causes a marked decrease in cell proliferation, and corresponding decrease in neurogenesis [47]. Surprisingly, however, these changes were not linked to functional impairments in spatial memory. Human imaging studies have likewise shown that GVS activates the hippocampus [48,49]. In addition, imaging studies have shown that GVS activates regions of the cerebellum, thalamus, and cortical areas (i.e. PIVC, 3aV, and 2v) associated with self-motion processing [7▪▪,50▪,51,52▪,53]. Interestingly, bilateral vestibulopathy patients demonstrate reduced resting state brain activity in several of these core cortical vestibular regions, that can be increased via GVS (Fig. 2a; [54,55]). Moreover, these GVS-induced changes were linked to better patient outcomes, suggesting that GVS might induce beneficial neural plasticity. A recent comparison of noisy versus conventional (current step) GVS indicated that the former resulted in greater increase in brain activity in vestibular cortical areas [56]. Although this result led the authors to suggest that noisy GVS evokes stochastic resonance, further investigation will be required to understand the actual neural mechanisms responsible

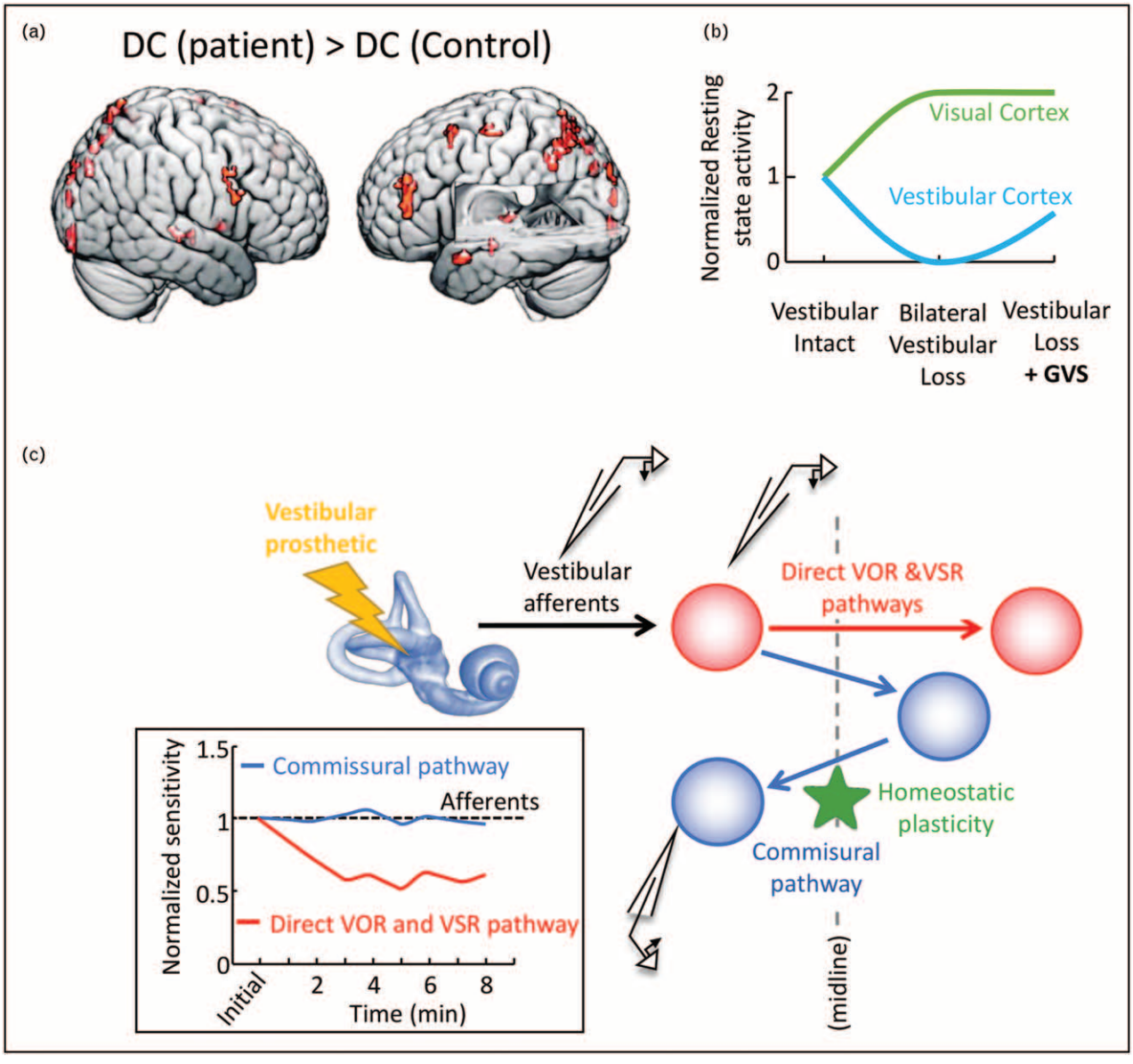

FIGURE 2. Effects of galvanic vestibular stimulation and vestibular implant stimulation on the central vestibular system. (a) Compared with healthy control subjects, resting state brain activity of bilateral loss patients was smaller in vestibular core regions but larger in several frontoparietal and occipital brain areas associated with visual processing. (b) GVS increased resting state in vestibular core regions in both groups, as well as in visual regions in patients that was associated with lower dizziness. Helmchen *et al.* [55]. (c) Schematic diagram of the direct versus commissural pathways mediating the VOR and vestibulospinal reflexes. Inset: normalized sensitivity of direct versus commissural pathway neurons in the vestibular nuclei over a 10 min period following activation of the vestibular nerve. The black dashed line is showing, for comparison, the lack of adaption in vestibular afferents. Adapted with permission from Mitchell *et al.* [98].

for the observed enhancements and to further optimize the application of GVS as a noninvasive therapeutic approach to improve patient outcomes. Correspondingly, the development of new methods for internal peripheral stimulation using a vestibular implant (Fig. 2c, see 'Future Directions') provides another promising approach for improving patient outcomes.

INTRACRANIAL ELECTRICAL BRAIN STIMULATION

The central vestibular network described above [7▪▪,50▪,51,52▪,53] has been revealed by neuroimaging studies contrasting BOLD signal during GVS with various control conditions. Complementary to this approach, iEBS can disrupt neural activity within specific nodes of the central vestibular

pathways. iEBS can provide causal evidence [8] of the specific contribution of cortical and subcortical structures in the neural network processing vestibular information. iEBS consists of delivering an electrical current through electrodes directly at the surface of the cortex, in deep structures, or subcortical fibers. iEBS can evoke from simple perceptions, such as vestibular illusions, to complex hallucinations, and behaviors.

Cortical networks underpinning vestibular representations as revealed by intracranial electrical brain stimulation

One part of the cortex that has long been related to vestibular information processing in nonhuman primates is the posterior insula (with adjacent parietal operculum and retroinsular cortex) [57–59]. Surprisingly, Penfield and Faulk [60] had originally reported that iEBS in the insula evoked no vestibular sensation during surgery for focal epilepsy. However, a retrospective analysis of 219 patients with epilepsy revealed that vestibular sensations (illusory body rotation or translation, vertigo, dizziness) in fact represents ~8% of all responses evoked by iEBS through implanted electrodes in the insula [61]. Notably, vestibular sensations were mostly elicited by iEBS in the posterior insula, and rotatory and translational self-motion illusions were evoked by iEBS more posterior than vertigo and dizziness [61]. Following up on this, Yu *et al.* [62] analyzed the effect of operculo-insular iEBS in patients with epilepsy, and found that dizziness was evoked by stimulation of the superior part of the left posterior long gyrus (i.e. posterior insula). Other functional mapping of the insula with iEBS revealed that its posterior part, while eliciting some vestibular sensations, was more involved in somatosensory and pain perception, whereas the anterior insula was more involved in visceral functions [63].

The parietal cortex has also long been associated with vestibular information processing in animal models, as evidenced by vestibular-sensitive neurons in the primary somatosensory cortex, intraparietal sulcus, retroinsular cortex, and parietal operculum [64]. Consistent with these findings, iEBS in epileptic patients demonstrated vestibular sensations in both the lateral and medial parts of the parietal cortex [65]. Operculo-insular stimulation in patients with epilepsy revealed that vertigo and the feeling of body elevation or movement to one side were evoked by iEBS of the bilateral parietal operculum, and by no other opercular region [62]. A recent retrospective analysis in a large patient cohort with epilepsy ($n = 165$) revealed that ~21% of iEBS evoking vertigo were in the posterior insula or parietal operculum (area OP2) [66▪▪]. This data provides causal evidence that stimulation in this core area within the vestibular cortical network [7▪▪,67,68▪,69] produces a vestibular sign. Balestrini *et al.* [70] retrospectively analyzed data from iEBS in the parietal cortex in 172 patients with epilepsy. Vertigo was observed during iEBS in the precuneus, inferior parietal lobule, posterior cingulum, superior parietal lobule, intraparietal sulcus, and postcentral gyrus. In contrast, no such responses were evoked by iEBS in the primary somatosensory cortex in two retrospective studies [71,72], despite evidence of vestibular projections to the primary somatosensory cortex in several animal species [73,74].

Interestingly, the precuneus, which was until recently not considered a main vestibular area, is the parietal area where most vestibular responses have been elicited [70]. A recent study emphasized vestibular illusions in the anterior precuneus [75▪▪], with iEBS in the left precuneus evoking mostly sensations of dropping, slipping, falling, and dizziness, whereas iEBS in the right precuneus evoked mostly sensations of floating and elevation. This finding is consistent with those of recent fMRI studies identifying an egomotion selective area in the anterior precuneus, referred to as Pcm (precuneus motion area), that responded to both GVS and optic flow [7▪▪]. Yet, other studies described area Pcm as only sensitive to optic flow [76▪▪].

Taken together, these studies suggest that the medial part of the cerebral hemispheres may play a more substantive role in shaping vestibular representations than has been assumed based on early studies in nonhuman primates [57,77]. In fact, in the last few years, evidence of vestibular responses in the cingulate cortex were provided by electrophysiological recordings in the macaque posterior cingulate cortex [78], fMRI in rats during optogenetic activation of the vestibular nuclei [79], and fMRI in humans using GVS or caloric vestibular stimulation [7▪▪,76▪▪,80].

Consistent with these findings, three recent retrospective analyses in patients with epilepsy reported vestibular responses during iEBS in the cingulate cortex [81,82,83▪]. Vestibular responses represented 4.3% [83▪] to 8.3% [81] of all responses evoked by cingulate cortex stimulation. The two studies with the largest samples ($n = 329$ [81] and $n = 124$ [83▪]) identified most vestibular responses in the middle cingulate cortex (right posterior middle cingulate cortex, as well as to a smaller extent the ventral anterior middle cingulate cortex) and the posterior cingulate cortex (dorsal part [81]). By contrast, the study with the smallest sample ($n = 47$ [82]) reported that vestibular sensations were evoked by iEBS in the left anterior and posterior cingulate

cortex. Altogether, the data suggest predominant vestibular representations at the junction between the middle and posterior cingulate cortex [83▪]. Although data in animals are rare, it was also in the posterior cingulate cortex that neurons responded to whole-body translations and rotations, and to a lesser extent to optic flow [78]. Altogether, results from recent iEBS studies confirm the existence of a vestibular and visual area, referred to as the cingulate sulcus visual area (CSv), in the posterior part of the middle cingulate cortex [7▪▪,76▪▪,80,84▪].

A recent systematic review of the literature by Dary *et al.* [85▪▪] summarized cases of illusory whole-body translations and rotations (excluding vertigo/dizziness) evoked by iEBS. Across the different studies (Fig. 3a–c), most iEBS-evoking vestibular sensations were in the middle cingulate cortex, posterior insula, inferior parietal lobule, amygdala, precuneus and superior temporal gyrus, whereas vestibular sensations were very rare after occipital and frontal cortex stimulation (Fig. 3b) [85▪▪]. In addition, the proportion of vestibular sensations after iEBS in the right hemisphere was significantly higher than it

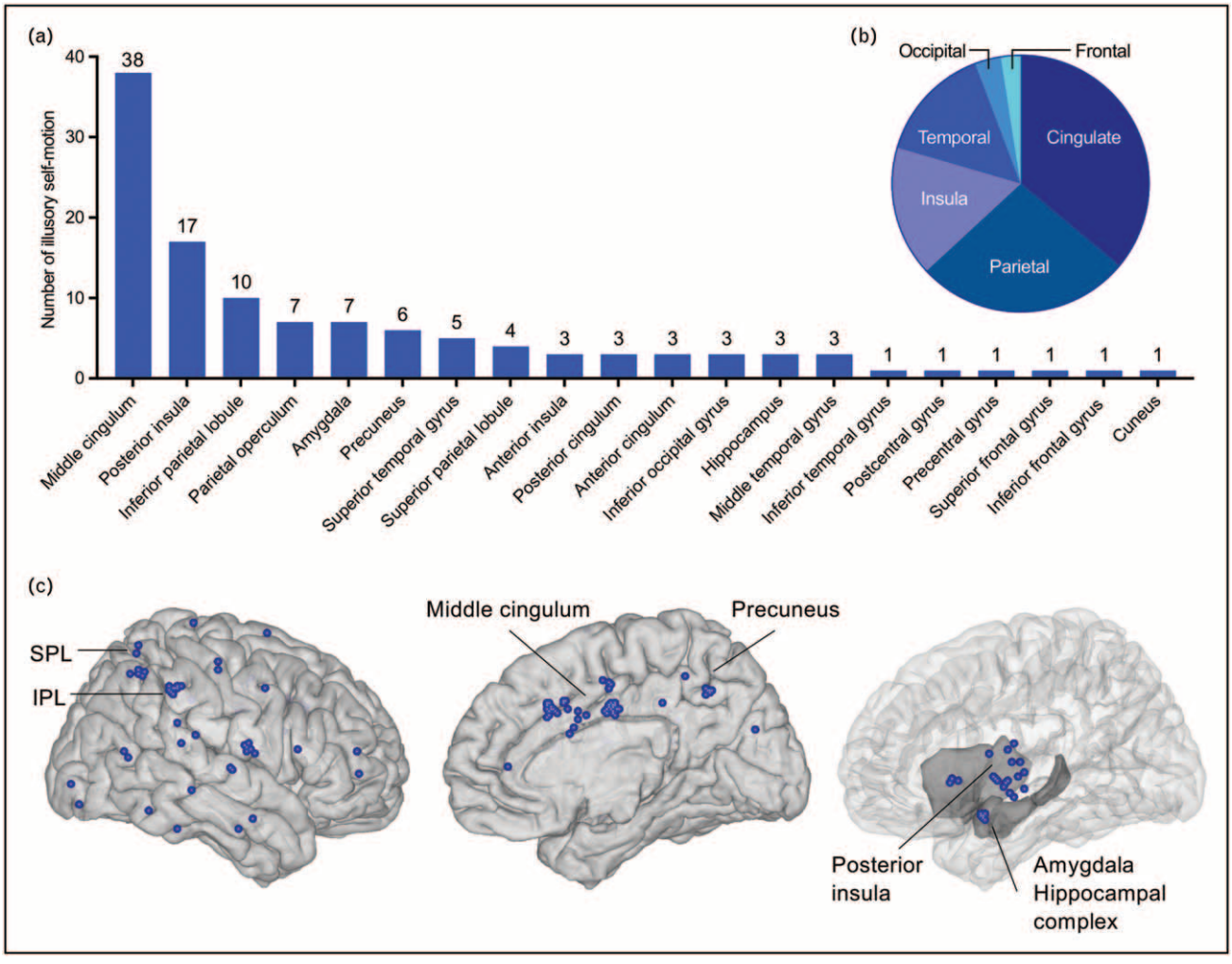

FIGURE 3. Localization of intracranial electrical brain stimulation evoking vestibular illusions reported in a systematic review of the literature. The review identified 131 cases of illusory self-motion perception (excluding vertigo and dizziness) evoked by iEBS reported in the literature between 1937 and 2022. Most of the electrode contacts where vestibular illusions were evoked by iEBS could be located retrospectively according to published electrode coordinates, or with the best approximation possible considering the published MRI, implantation schema, or the original description of iEBS in terms of gyrus, sulcus, and Brodmann area. The number of illusory self-motion perception evoked by iEBS is showed for different brain areas (a), and as a function of iEBS in the different lobes and cingulate cortex (b). (c) iEBS sites evoking illusory self-motion perception are displayed on 3D views of a right cerebral hemisphere. The rightmost part shows iEBS in the insula and mesiotemporal region. IPL, inferior parietal lobule; SPL, superior parietal lobule. Adapted from Dary *et al.* [85▪▪], with permission from the authors. IEBS, intracranial electrical brain stimulation.

was in the left hemisphere, a finding coherent with the right-sided dominance of vestibular pathways to the cerebral cortex in neurotypical individuals [86].

Effects of intracranial electrical brain stimulation on subcortical structures

Evidence for vestibular representations in subcortical structures has recently been investigated during presurgical evaluation of epilepsy [87▪▪,88▪▪] and in Parkinson's disease. Here we focus on the former, as the latter has been reviewed in detail elsewhere [2,12,89▪▪].

Recently, Qi *et al.* [87▪▪] reviewed the effects of iEBS in the basal ganglia in 35 patients with epilepsy. Vestibular sensations were the second most frequent responses after sensorimotor responses. They were elicited by iEBS in the putamen and external globus pallidus, mostly on the right side (Fig. 4a). No vestibular response was found in the dorsal caudate nucleus, internal globus pallidus and subthalamic nucleus. This causal demonstration of vestibular representations in the basal ganglia helps disambiguate heterogenous results about the basal ganglia involvement in vestibular networks [90]. Indeed, recent studies in rats identified very few striatal neurons responding to electrical stimulation applied to the round window [91]. However, in response to the same type of stimulation, local field potentials were recorded in the tail of the rat striatum [92▪▪] and neurochemical changes were found in the striatum [93]. Vestibular pathways to the striatum may involve the perifascicular nucleus in the thalamus and direct projections from the cortex [90] (Fig. 4b).

Furthermore, vestibular responses evoked by iEBS of the amygdala have recently been described in patients with epilepsy [88▪▪]. Out of 250 responses evoked by iEBS in the amygdala, vestibular sensations represented ~6% of all reports. Sites at which iEBS evoked vestibular responses were in the laterobasal and superficial groups of the amygdala. It is unclear how vestibular information reaches the amygdala. Yet, the parabrachial nucleus, which responds to vestibular stimulation, is reciprocally connected with the vestibular nuclei, amygdala, hypothalamus and prefrontal cortex [94].

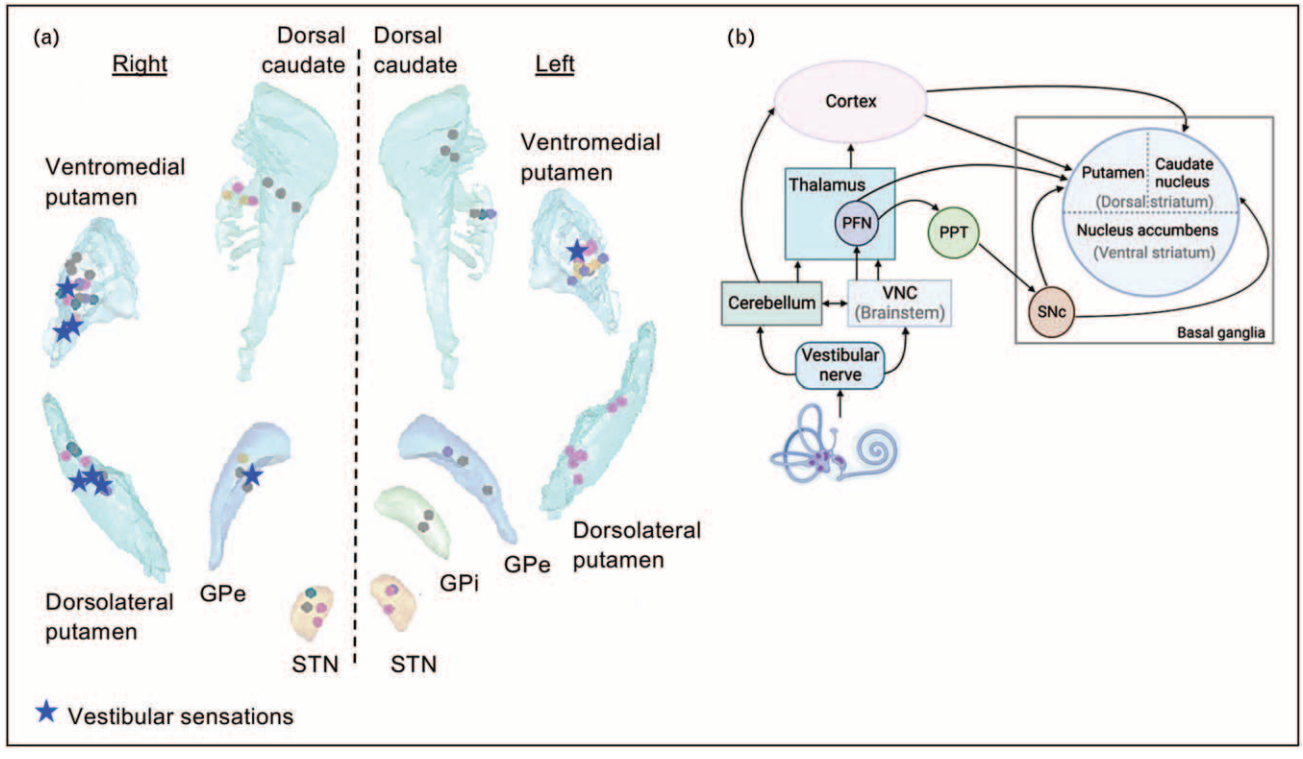

FIGURE 4. Vestibular representations in the basal ganglia. (a) Location of electrode contacts evoking vestibular sensations during iEBS. After sensorimotor responses ($n = 23$), vestibular sensations were the second most frequent responses evoked by iEBS ($n = 8$; dizziness, spinning, floating). Vestibular sensations were evoked by iEBS in the ventromedial putamen ($n = 4$), dorsolateral putamen ($n = 3$), and external globus pallidus ($n = 1$). Modified from Qi *et al.* [87▪▪] (images under Creative Commons Attribution 4.0 International License). (b) Probable pathways from the vestibular apparatus to the basal ganglia. iEBS, intracranial electrical brain stimulation; PFN, parafascicular nucleus; PPT, pedunculopontine tegmental nucleus; SNc, substantia nigra pars compacta; VNC, vestibular nuclei complex. Reproduced from Sabzevar *et al.* [92▪▪] (images under Creative Commons Attribution 4.0 International License).

Causal demonstration of vestibular representations in subcortical structures should motivate to study their contribution to spatially oriented behaviors and spatial cognition.

FUTURE DIRECTIONS

Above we have reviewed how the electrical stimulation of the peripheral and central vestibular systems has advanced our understanding of the neural mechanisms and networks underpinning vestibular processing and self-motion perception. These lines of research offer opportunities for developing novel therapeutic strategies in patients with vestibular disorders and have clinical relevance for neurology.

Internal peripheral stimulation and vestibular implants

Pulsatile stimulation of chronically implanted electrodes in animals has been an essential tool for probing the circuitry of vestibular pathways. Recent work based on this approach has led to the development of vestibular implants for patients with bilateral peripheral loss. These implants typically comprise electrodes implanted into or near the ampulla of the semicircular canals. Head motion information, sensed by gyroscopes, is first projected into the three canal planes, and then converted into a sequence of electrical pulses for each implanted electrode (reviewed in [10,13]). Ongoing clinical trials have reported improvements in postural control [95▪] and to a lesser extent gaze stability [96,97]. Significant challenges must still be overcome, including the reduction of central vestibular pathway efficacy because of stimulation-induced afferent synchrony (Fig. 2c; [98,99]) and expanding vestibular implants to restore otolith as well as canal function.

Advances in diagnosis and treatment of focal epilepsy

Epileptic seizures with prominent vertigo and dizziness have been related to epileptic foci in the temporal cortex and temporo-parieto-occipital junction [100]. Recent evidence of vestibular representations in the medial part of the cerebral hemispheres should help understand the complex semiology of seizures in patients with cingulate [101] or precuneal epilepsy [102], which are difficult to characterize by surface EEG. To better characterize seizures associated with vertigo and dizziness, it would be important to delineate the exact connectivity within the cortical vestibular network, using effective connectivity (e.g. corticocortical-evoked potentials) and functional connectivity (e.g. nonlinear correlation of EEG signals) from iEBS and stereo-electroencephalography in patients with epilepsy (for similar approaches, see [75▪▪,82]).

CONCLUSION

Studies summarized in this review help understand long-described effects of electrical stimulation of the peripheral and central vestibular system, which commonly evoke illusory self-motion perception and modulate multisensory integration properties to ensure balance and gaze stability. By modulating the functioning of large networks from the brainstem to the cerebral cortex, basal ganglia, and other subcortical structures, GVS offer avenues for the neuromodulation of vestibular functions using safe, accessible, and inexpensive procedures.

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Conflicts of interest

There are no conflicts of interest.

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- ▪▪ of outstanding interest

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A functional neuroimaging study that used binaural GVS in the to date largest cohort of right-handed participants ($n = 131$). Participants received local anesthesia of the postauricular region to control for unspecific effects of GVS. Some participants were shown an optic flow that was compatible or incompatible with egomotion (i.e. coherent/incoherent motion of dots). The conjunction of BOLD responses to vestibular stimulation and to egomotion-compatible visual stimulation was particularly evident in the uvula, cingulate sulcus [CSv (cingulate sulcus visual area) and Pcm/pCi (precuneus motion area)] and in the temporoparietal cortex [newly identified 'area h7a' in the supramarginal gyrus and area VPS (visual posterior Sylvian area)].

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