

REVIEW | *Sensory Processing*

The parieto-insular vestibular cortex in humans: more than a single area?

Sebastian M. Frank^{1,2,3} and  Mark W. Greenlee¹

¹*Institute for Experimental Psychology, University of Regensburg, Regensburg, Germany;* ²*Department of Psychological and Brain Sciences, Dartmouth College, Hanover, New Hampshire;* and ³*Department of Cognitive, Linguistic, and Psychological Sciences, Brown University, Providence, Rhode Island*

Submitted 19 December 2017; accepted in final form 3 July 2018

Frank SM, Greenlee MW. The parieto-insular vestibular cortex in humans: more than a single area? *J Neurophysiol* 120: 1438–1450, 2018. First published July 11, 2018; doi:10.1152/jn.00907.2017.—Here, we review the structure and function of a core region in the vestibular cortex of humans that is located in the midposterior Sylvian fissure and referred to as the parieto-insular vestibular cortex (PIVC). Previous studies have investigated PIVC by using vestibular or visual motion stimuli and have observed activations that were distributed across multiple anatomical structures, including the temporo-parietal junction, retroinsula, parietal operculum, and posterior insula. However, it has remained unclear whether all of these anatomical areas correspond to PIVC and whether PIVC responds to both vestibular and visual stimuli. Recent results suggest that the region that has been referred to as PIVC in previous studies consists of multiple areas with different anatomical correlates and different functional specializations. Specifically, a vestibular but not visual area is located in the parietal operculum, close to the posterior insula, and likely corresponds to the nonhuman primate PIVC, while a visual-vestibular area is located in the retroinsular cortex and is referred to, for historical reasons, as the posterior insular cortex area (PIC). In this article, we review the anatomy, connectivity, and function of PIVC and PIC and propose that the core of the human vestibular cortex consists of at least two separate areas, which we refer to together as PIVC+. We also review the organization in the nonhuman primate brain and show that there are parallels to the proposed organization in humans.

area PIC; area PIVC; self-motion perception; vestibular cortex; visual-vestibular network

INTRODUCTION

The vestibular sensors are located in the inner ear, neighboring the sensors of the auditory system, and consist of the semicircular canals that signal angular accelerations and the otoliths that signal linear accelerations, including effects of gravity (Angelaki and Cullen 2008; Bárány 1907; Day and Fitzpatrick 2005; Fernández and Goldberg 1976; Goldberg and Fernández 1971). Traditionally, the vestibular system has been conceived of as the balance system of the brain — its sensors detect movements of the head and this information supports the reflexive control of posture, gait, and gaze (Brandt and Dieterich 2017; Bronstein et al. 2015; Day and Fitzpatrick 2005; Dieterich and Brandt 1995, 2015; Fetter 2007; Gimmon et al. 2017; Horak 2006; Khan and Chang 2013; Mergner 2010; Mergner et al. 2009). However, in addition to these established functions, it has become clear that vestibular cues also influ-

ence a wide range of other processes, which may not be immediately thought of as “vestibular.” This includes basic autonomic functions (Yates et al. 2014; Yates and Miller 1998) but also higher-level processes such as spatial navigation, learning, and memory (Brandt et al. 2005; Cullen and Taube 2017; Gurvich et al. 2013; Smith and Zheng 2013; Taube 2007; Taube et al. 1996), perceptual and motor decision making (Medendorp and Selen 2017), mental imagery and mental rotation (Falconer and Mast 2012; Mast et al. 2006, 2014), or bodily self-consciousness (Lopez 2015, 2016). The vestibular system does not operate in isolation but strongly interacts with other sensory systems, in particular with the visual system (Angelaki and Cullen 2008; Cullen 2012; Greenlee et al. 2016; Gu 2018; Smith et al. 2017). Such interactions are helpful to resolve ambiguities in sensory signals. For example, when an object is getting closer, the brain has to determine whether that is because the object is moving independently or because the observer is moving or a combination of both. Vestibular signals can help to resolve this ambiguity inherent in visual signals (Bremmer 2011; Britten 2008; DeAngelis and Angelaki

Address for reprint requests and other correspondence: M. W. Greenlee, Institute for Experimental Psychology, University of Regensburg, Universitätsstrasse 31, Regensburg 93053, Germany (e-mail: mark.greenlee@psychologie.uni-regensburg.de).

2012; Greenlee 2000; Greenlee et al. 2016; Lappe et al. 1999; Smith et al. 2017).

Vestibular cues are projected from the semicircular canals and the otoliths via the vestibular portion of the VIII cranial nerve to the vestibular nuclei in the brain stem (Barmack 2003; Büttner-Ennever 1992; Highstein and Holstein 2006; Korte 1979). Further projections are sent to the cerebellum (Hitier et al. 2014; Korte and Mugnaini 1979). The vestibular nuclei integrate vestibular, cerebellar, visual, and somatosensory signals (Barmack 2003; Büttner-Ennever 1992; Carleton and Carpenter 1983; Cullen 2012; Goldberg et al. 2013; Shinder and Taube 2010; Waespe and Henn 1977) and are critically involved in several reflexes that stabilize our perception and position in space (Barmack 2003), such as the vestibulo-ocular reflex (Bronstein et al. 2015; Dieterich and Brandt 1995; Fetter 2007) or the vestibulocervical and vestibulospinal reflexes (Cullen 2012; Goldberg and Cullen 2011; Goldberg et al. 2013; Wilson and Peterson 1978). Moreover, the vestibular nuclei participate in orthostatic reflex functions of the autonomic nervous system that adjust blood pressure, heart rate, and respiration (Yates et al. 2014; Yates and Miller 1998). Finally, it should be noted that voluntary head movements are preceded by an anticipatory (so-called efference copy) signal, which the cerebellum uses to compute a forward model for the expected vestibular feedback resulting from the movement (Cullen 2012). The prediction is then matched with the incoming vestibular signals and, if there is a match, the responses of the brain stem nuclei to the vestibular cues are suppressed (Brooks et al. 2015; Brooks and Cullen 2014; Cullen and Brooks 2015), thus enabling a distinction between externally caused motion and self-generated head/body motion already at an early subcortical level (Cullen and Taube 2017).

The brain stem nuclei send projections to multiple thalamic nuclei, including the ventral posterior, ventral lateral, ventral anterior, intralaminar, and even geniculate nuclei (Büttner and Henn 1976; Hitier et al. 2014; Kirsch et al. 2016; Lang et al. 1979; Lopez and Blanke 2011; Meng et al. 2007; Wijesinghe et al. 2015; Wirth et al. 2018). The anterior nuclear group in the thalamus, including the anterodorsal and anteroventral nuclei, also receives strong indirect vestibular-related projections through multiple subcortical connections (see Taube 2007 for review). From the thalamus, two pathways emerge that send these vestibular signals to the cortex (Cullen and Taube 2017; Hitier et al. 2014; Shinder and Taube 2010): The anterior pathway, via the anterior nuclear group, plays an important role for navigational processes and sends vestibular-related information to the retrosplenial and entorhinal cortices. The posterior pathway originates from the ventral posterior thalamus and projects to the vestibular cortex (Akbarian et al. 1992). Further projections to the vestibular cortex originate from the pulvinar (for a detailed overview of the thalamic vestibular projection patterns, see Hitier et al. 2014; Lopez and Blanke 2011; Shinder and Taube 2010; Wijesinghe et al. 2015). The transmission of vestibular signals to the cerebral cortex is very fast, with a latency as short as 6 ms (de Waele et al. 2001).

Early neurophysiological recordings in the cerebral cortex of cats (Ödkvist et al. 1975; Walzl and Mountcastle 1949), rhesus monkeys (Büttner and Büttner 1978; Fredrickson et al. 1966), and squirrel monkeys (Ödkvist et al. 1974), as well as results from cortical stimulation in human subjects (Penfield 1957; Penfield and Rasmussen 1950) suggested the existence of

multiple sites in the cortex where vestibular signals are represented, including regions located at the junction of the intraparietal sulcus (IPS) with the postcentral sulcus (referred to as area 2v), the fundus of the central sulcus (referred to as area 3av), and the Sylvian fissure with the surrounding peri-Sylvian cortex. Given the diverse functions that have been attributed to the vestibular system, one might expect to find such a distributed network of areas in the cerebral cortex that is, at least to some degree, “vestibular” and overlaps with other sensory and cognitive networks.

Indeed, detailed investigations in nonhuman primates in the past decades have revealed an even more extended vestibular network in the neocortex than was originally expected (Angelaki and Cullen 2008; Gu 2018; Guldin and Grüsser 1998; Lopez and Blanke 2011; Shinder and Taube 2010; Smith et al. 2017; Ventre-Dominey 2014). Results from human imaging studies point to a similarly distributed cortical vestibular network, including regions in the parietal, somatosensory, cingulate, frontal, and insular cortices (Dieterich and Brandt 2015; Lopez and Blanke 2011; Smith et al. 2017; Ventre-Dominey 2014). Figure 1 shows an overview of the vestibular network in the cerebral cortex of nonhuman primates and humans. Some attempts have been made to combine vestibular areas into separate clusters that may support different functions (see Lopez and Blanke 2011; Shinder and Taube 2010). However, to date it is not clear how these different cortical areas interact and how computations within each area relate to an overall vestibular sensation of self-motion, although some progress has been made for certain regions [e.g., the medial superior temporal area (MST); see Bremmer et al. 1999; Duffy 1998; Gu et al. 2006, 2008].

Based on the organization of other sensory cortices, such as the visual or auditory cortical systems (Felleman and Van Essen 1991; Kaas and Hackett 2000), one may wonder whether there is a center or core region within the vestibular cortex. Indeed, there is one region that appears to be of critical importance to vestibular processing. Studies in humans (e.g., Bense et al. 2001; Dieterich et al. 2003; Eickhoff et al. 2006; Fasold et al. 2002; Frank et al. 2016b; Kahane et al. 2003; Lobel et al. 1998; Mazzola et al. 2014; Penfield 1957; Penfield and Rasmussen 1950) and nonhuman primates (Akbarian et al. 1988; Chen et al. 2010, 2011, 2016; Grüsser et al. 1990a, 1990b; Guldin and Grüsser 1998) point to the midposterior Sylvian fissure as a site of robust vestibular responses across studies and vestibular stimulation techniques (Lopez et al. 2012; zu Eulenburg et al. 2012). Based on its location and in analogy to the nomenclature used in research on nonhuman primates, this region has been referred to as the parieto-insular vestibular cortex (PIVC) in humans (Dieterich and Brandt 2008, 2015, 2018; Lopez and Blanke 2011; Lopez et al. 2012; zu Eulenburg et al. 2012).

Although there is general agreement that the region described as PIVC in humans is critical to vestibular processing, there is no firm agreement about the exact location and spatial extent of PIVC (Dieterich and Brandt 2015, 2018; Eickhoff et al. 2006; Lopez and Blanke 2011; Lopez et al. 2012; zu Eulenburg et al. 2012), such that activations spanning from the temporo-parietal junction (TPJ) down to the retroinsula, parietal operculum, and posterior insula have been referred to as PIVC in different studies.

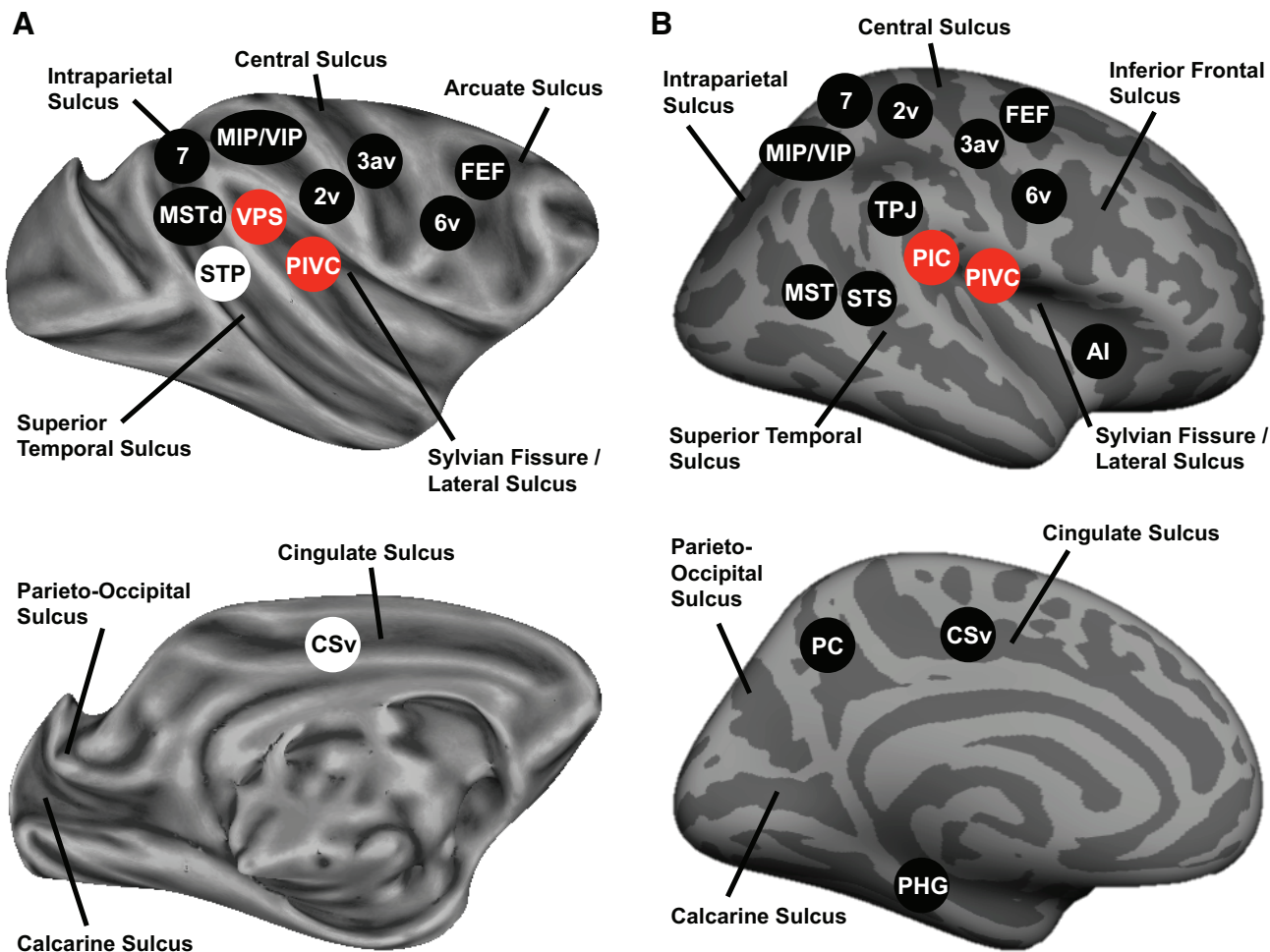


Fig. 1. The cortical vestibular network in nonhuman primates (A) and humans (B). Regions where vestibular responses have been observed are shown on the inflated left (medial view) and right hemispheres (lateral view) of an average MRI macaque brain (Seidlitz et al. 2018) and an average MRI human brain (Dale et al. 1999; Fischl et al. 1999) (light gray, gyri; dark gray, sulci). The depicted areas have been gathered and combined from previous articles reviewing the vestibular network (Dieterich and Brandt 2008; Gu 2018; Guldin and Grüsser 1998; Lopez and Blanke 2011; Shinder and Taube 2010; Smith et al. 2017; Sugiuchi et al. 2005; Ventre-Dominey 2014). The core of the vestibular cortex (shown in red) is located in the midposterior Sylvian fissure and consists of the parieto-insular vestibular cortex area (PIVC) and the posterior insular cortex area [PIC; visual posterior Sylvian area (VPS) in nonhuman primates]. The presence of vestibular signals in areas shown in white is indicated (Cottereau et al. 2017) but requires further investigation. Areas 3av and 7 in the nonhuman primate brain may be further separated into two portions each (3aNv and 3aHv; 7a and 7b) (Guldin and Grüsser 1998). Areas 3aNv and 3aHv are located in the somatosensory neck/trunk and hand/arm representations of the central sulcus, respectively. Some studies have noticed activations in the inferior frontal cortex during vestibular stimulation (see Lopez and Blanke 2011; Ventre-Dominey 2014), but since the evidence for the existence of vestibular responses in these areas is still sparse, we did not include them in our overview of the vestibular network. In addition to the parahippocampal gyrus (PHG), vestibular signals have been found also in the human hippocampus (e.g., Vitte et al. 1996; Dieterich et al. 2003; Suzuki et al. 2001). In the rodent brain a larger circuit of structures including the hippocampus, the entorhinal cortex, and the retrosplenial cortex uses vestibular cues to generate spatial signals related to heading direction and location in space (Cullen and Taube 2017; Shinder and Taube 2010; Taube 2007). AI, anterior insula; CSv, cingulate sulcus visual area; FEF, frontal eye fields (in particular the portion that controls smooth pursuit eye movements); MIP/VIP, medial/ventral intraparietal area; MST, medial superior temporal area; MSTd, dorsal portion of the MST; PC, precuneus; STP/STS, polysensory area of the superior temporal sulcus; TPJ, portion of the temporo-parietal junction bordering the posterior Sylvian fissure.

In this review article, we want to bring forth a new idea to resolve this ambiguity about the location and spatial extent of PIVC: rather than a single area, the region that has been referred to as PIVC may consist of at least two anatomically and functionally separate areas (Frank et al. 2016b; Wirth et al. 2018), similar to the organization that is found in the nonhuman primate brain (Chen et al. 2010, 2011, 2016; Gu 2018; Guldin and Grüsser 1998).

Our discussion is based on recent functional and structural brain-imaging studies (Billington and Smith 2015; Frank et al. 2014, 2016a, 2016b; Schindler and Bartels 2018; Wirth et al. 2018) that have brought forth evidence for

the existence of at least one additional, visual-vestibular area in close proximity to and immediately posterior to PIVC. This region has been named the posterior insular cortex area (PIC; Sunaert et al. 1999), although it is located in the retroinsular cortex (Fig. 2). Overall, the results suggest that PIC differs from PIVC in anatomical location (Frank et al. 2016b), anatomical connectivity (Wirth et al. 2018), and responses to visual motion cues (Billington and Smith 2015; Frank et al. 2014, 2016a, 2016b; Schindler and Bartels 2018), suggesting a separation between PIVC and PIC. This proposed separation parallels the architecture of the vestibular cortex in nonhuman primates (Gu 2018; Smith et al. 2017), where a visual-vestibular asso-

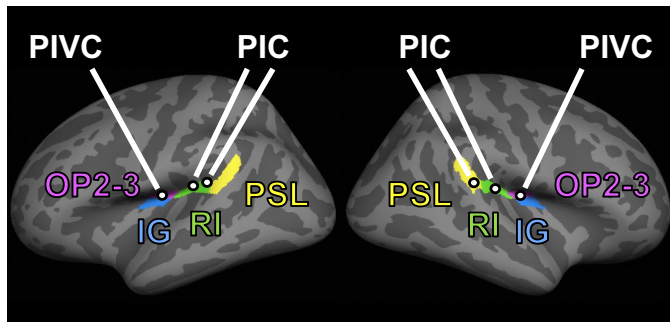


Fig. 2. Anatomical locations of areas PIVC and PIC on the inflated cortical surfaces of an average MRI human brain. Small white dots depict the average centroids of PIVC and PIC as identified in group analyses (Frank et al. 2016b). Based on the recent multimodal anatomical parcellation of the cerebral cortex by Glasser and colleagues (2016), area PIVC is located in a subdivision of the parietal operculum (referred to as “OP2-3” by Glasser et al., color-coded as magenta) and it borders with the insular gyrus (IG, color-coded as blue). PIC is located primarily in the retroinsular cortex (RI, color-coded as green) and may consist of two separate clusters. The anterior cluster is located in the retroinsula, while the posterior cluster is located at the border between the retroinsula and the posterior end of the Sylvian fissure (referred to as PSL in the classification by Glasser et al. 2016, color-coded as yellow). PIC, posterior insular cortex; PIVC, parieto-insular vestibular cortex.

ciation area (referred to as the visual posterior Sylvian area, VPS) is located posterior to PIVC (Chen et al. 2010, 2011, 2016; Guldin and Grüsser 1998).

In the following, we will review evidence concerning the structural and functional relationship of areas PIVC and PIC in the human brain. We will start our discussion with an introduction to the structure and function of the vestibular cortex in the Sylvian fissure of nonhuman primates.

VESTIBULAR AREAS IN THE SYLVIAN FISSURE OF NONHUMAN PRIMATES

Grüsser, Guldin, and colleagues have performed pioneering work on the organization of the vestibular cortex in Java (*Macaca fascicularis*) and squirrel (*Saimiri sciureus*) monkeys. The results of these studies suggest that at least two separate areas exist in the midposterior Sylvian fissure (Guldin and Grüsser 1998). These two areas are PIVC and, posterior to PIVC, an area that was originally described as area T3 (Akbarian et al. 1992, 1994; Guldin et al. 1992; Jones and Burton 1976) but is now referred to as VPS (Chen et al. 2011; Gu 2018; Guldin and Grüsser 1998). Later studies by Angelaki, DeAngelis, and colleagues in rhesus monkeys (*Macaca mulatta*) have confirmed and extended the separation between PIVC and VPS (see below). In the following, we will review the location, connectivity, and function of these two areas in the vestibular cortex of nonhuman primates.

First described based on evidence from cytoarchitectonics by Pandya and Sanides (1973), area PIVC is located in the depth of the Sylvian fissure, in a region spanning from the posterior end of the insula to the posterior parietal operculum and the retroinsula (Akbarian et al. 1988, 1994; Grüsser et al. 1990a; Guldin et al. 1992; Guldin and Grüsser 1998). In contrast, VPS is located more posterior in the Sylvian fissure than PIVC and extends from the posterior end of the retroinsula to the more posterior area T3 (Akbarian et al. 1994; Guldin et al. 1992; Guldin and Grüsser 1998). Tracer studies have shown that PIVC is connected with other key regions of the cortical

vestibular network, including areas 3aNv, 3aHv, 2v, 7a and 7b, 6v, VPS, retroinsular and posterior insular cortices, 8a (a region referred to as the frontal eye fields in Fig. 1A), SII (corresponding to the secondary somatosensory cortex), and the cingular sulcus (Guldin et al. 1992; Guldin and Grüsser 1998). With some exceptions, the cortical connectivity of VPS largely overlaps with that of PIVC, but VPS is also connected with the superior temporal sulcus and with temporo-occipital and parieto-occipital regions (Guldin et al. 1992; Guldin and Grüsser 1998). On the subcortical level, PIVC is connected with the ventral posterior thalamus (specifically the posterior parts) and the medial pulvinar (Akbarian et al. 1992). VPS also exhibits connections with the ventral posterior thalamus, but its connectivity is more pronounced with the pulvinar, specifically with the medial, lateral, and inferior pulvinar (Akbarian et al. 1992). Both PIVC and VPS have direct efferent projections to the vestibular nuclei in the brain stem, suggesting a cortical influence on brain stem-dependent vestibular reflexes (Akbarian et al. 1994; Guldin and Grüsser 1998).

Recent studies in rhesus monkeys suggest that neurons in both PIVC (Chen et al. 2010; Liu et al. 2011) and VPS (Chen et al. 2011) respond to translational and rotational head or full body movements, extending previous reports for Java and squirrel monkeys (Akbarian et al. 1988; Grüsser et al. 1990a; Guldin et al. 1992; Guldin and Grüsser 1998). In VPS, neurons are also tuned to optic flow cues, which combine with the vestibular cues either in a congruent or an incongruent fashion in different neurons (Chen et al. 2011). Contrary to other visual-vestibular areas such as MST or the ventral intraparietal area (VIP), the majority of cells in VPS appear to prefer visual and vestibular cues in incongruent directions (Chen et al. 2011), the reason for this is currently unclear (Gu 2018). The visual input may reach VPS by means of a retino-collicular-pulvinar pathway (Akbarian et al. 1992) and through connections with other extrastriate visual areas, including the superior temporal sulcus (Guldin et al. 1992).

Originally, Guldin and Grüsser (1998, p. 255) summarized the functional differences between PIVC and VPS as such: “The PIVC is a vestibular region with optokinetic input whereas the VPS is an optokinetic region with vestibular input.” However, more recent results in rhesus macaques by Chen, DeAngelis, and Angelaki (2010) could find no evidence for visual responses in PIVC, whereas such responses were clearly present in VPS (Chen et al. 2011). Moreover, the results by Chen et al. (2011) suggest that more neurons in VPS of rhesus monkeys may be tuned to vestibular stimuli than previously reported for squirrel monkeys (Guldin and Grüsser 1998).

It is difficult to reconcile these contradictory results on visual responses in PIVC. Some of the differences might be accounted for by the visual stimuli and by the occurrence of tracking eye movements during the visual stimulation. Studies that reported visual activity in PIVC either used large field optokinetic stimuli by rotating a drum with visual patterns around the monkey (Akbarian et al. 1988; Grüsser et al. 1990a; Guldin et al. 1992) or a single moving visual target (Shinder and Newlands 2014). In contrast, Chen et al. (2010) used 3D optic flow cues. Moreover, visual tracking eye movements following the moving visual targets might have influenced the activity in PIVC (Akbarian et al. 1988; Grüsser et al. 1990a; Guldin et al. 1992; Shinder and Newlands 2014). In contrast,

such ocular responses were suppressed in the study by Chen et al. (2010), who trained the monkeys to maintain central fixation. Therefore, the existence of visual responses in area PIVC in nonhuman primates remains to be clarified. The results from human imaging studies on this matter (see ARE PIVC AND PIC SEPARATE REGIONS?) are less controversial and suggest a robust effect of activity suppression in PIVC when visual (motion) cues are presented (Brandt et al. 1998; Deutschländer et al. 2002; Frank et al. 2016b; Kleinschmidt et al. 2002; Laurienti et al. 2002; Shulman et al. 1997) and specifically when the visual stimuli are processed attentively (Frank et al. 2016a). Moreover, functional imaging studies in humans indicate that both tracking eye movements (Konen et al. 2005; Nagel et al. 2006) and fixation suppression of optokinetic or caloric nystagmus (Dieterich et al. 1998; Naito et al. 2003) are both correlated with a suppression of activity in PIVC.

The work of Grüsser, Guldin, and their colleagues has shown that the region they refer to as PIVC is a multisensory region, where neurons are responsive not only to vestibular cues, but also to somatosensory stimuli. In particular, stimulation of the neck and shoulder receptors (induced by movements of the trunk while the head is stationary) evoked activation in neurons that exhibit vestibular tuning (Akbarian et al. 1988; Grüsser et al. 1990a, 1990b). In humans, vibratory stimuli applied at the neck lead to activation in the posterior Sylvian fissure (Bottini et al. 2001; Fasold et al. 2008). Therefore, these studies suggest that while neurons in PIVC are primarily driven by vestibular stimulation, some of these neurons can also be driven by somatosensory stimulation of cervical mechanoreceptors. In agreement with these results vestibular signals in PIVC appear to be represented in a reference frame that is intermediate between a head-centered and body-centered coordinate system (Chen et al. 2013). Moreover, some neurons in the PIVC region are also activated by somatosensory cues that are unrelated to head/body movements, such as touch of the skin (Akbarian et al. 1988; Grüsser et al. 1990a, 1990b), again emphasizing the multisensory nature of PIVC.

To summarize, the results from nonhuman primate studies suggest that vestibular responses in the Sylvian fissure may be clustered into at least two separate regions, referred to as PIVC and VPS. Both of these areas also respond to other sensory cues such as somatosensory stimuli, but recent results suggest that the response patterns of PIVC and VPS might differ dramatically during visual processing: whereas VPS clearly responds to visual motion cues (Chen et al. 2011), PIVC may show only weak or negligible responses (Chen et al. 2010). This functional dissociation is supported by anatomical differences in the connectivity of PIVC and VPS, where VPS may receive visual signals from the pulvinar and the superior temporal sulcus. We will now compare these results to evidence obtained in human subjects and begin with a brief introduction to prominent vestibular stimulation techniques in humans during functional brain imaging.

IDENTIFICATION OF PIVC AND PIC USING FUNCTIONAL BRAIN IMAGING IN HUMANS

The optimal stimuli required to activate the vestibular sensory system would be active or passive head movements. Such stimuli can be combined easily with neuronal recording techniques that do not necessitate the immobilization of the sub-

ject's head and body (for example, single cell recordings in nonhuman primates or electroencephalographic recordings in human participants, e.g., Gale et al. 2016; Gutteling et al. 2015). However, the constraints imposed by functional brain imaging techniques in humans such as functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) do not easily allow for such movements, since they require the immobilization of the participant's head. Although there have been some attempts to induce controlled head motion during fMRI recordings (see Petit and Beauchamp 2003; Schindler and Bartels 2018), brain imaging studies in humans using head movements for vestibular stimulation have remained an exception.

Therefore, rather than direct vestibular cues, artificial stimulation techniques have been used to activate the vestibular system (Dieterich and Brandt 2008, 2015; Lopez and Blanke 2011; Lopez et al. 2012; zu Eulenburg et al. 2012). Two prominent methods are caloric vestibular stimulation (CVS) and galvanic vestibular stimulation (GVS). Both techniques activate the vestibular system artificially. In CVS the external auditory canal is stimulated with a tempered medium such as water or gas. Typically, hot or cold is used and the change in temperature relative to body temperature in the middle ear induces convection currents in the endolymph of (primarily) the nearby horizontal semicircular canals in the inner ear. This depolarizes (hot) or hyperpolarizes (cold) the vestibular hair cells and in turn increases or decreases the firing rate of the vestibular nerve afferents (Bárány 1907; Barnes 1995; Lopez and Blanke 2014; Shepard and Jacobson 2016). In GVS, electrical stimulation is applied noninvasively to the skin over the mastoid processes (with an anode and a cathode on opposite body sides), which galvanically activates the nerve afferents of both the otoliths and the semicircular canals on the side of the cathode, while the firing rate decreases on the side of the anode (Cohen et al. 2012; Curthoys and MacDougall 2012; Fitzpatrick and Day 2004; Goldberg et al. 1984; Wardman et al. 2003). In both CVS and GVS the artificially evoked vestibular signals are propagated to the cortex and activate key regions of the vestibular network (Lopez et al. 2012). The cortical activations with both techniques overlap in the mid-posterior Sylvian fissure (Lopez et al. 2012; zu Eulenburg et al. 2012), although some differences in the specific activation patterns in other regions have been noticed (Lopez et al. 2012). Moreover, both CVS and GVS may evoke compensatory eye movements (for CVS, those are referred to as caloric nystagmus, e.g., Bronstein et al. 2015; Naito et al. 2003) and may induce illusory sensations of self-motion, which are usually experienced as rotations in the yaw and roll planes for CVS (Frank and Greenlee 2014; Frank et al. 2016b), whereas the movement sensation is more complex for GVS due to the stimulation of both semicircular canal and otolith nerve afferents (Cohen et al. 2012; Fitzpatrick and Day 2004; Lobel et al. 1998; Stephan et al. 2005; Wardman et al. 2003).

In our own experiments we have used MRI-safe CVS (Frank and Greenlee 2014) to identify the average location of PIVC across participants. Figure 2 shows the results of a group analysis (based on data from Frank et al. 2016b). The location of PIVC coincides with the parietal operculum, specifically with the subregion labeled as OP2–3 in the recent multimodal anatomical segmentation of the cerebral cortex by Glasser et al.

(2016). PIVC also borders on the posterior extent of the insular gyrus.

To identify PIC, we have used visual object-motion cues. Although it was recently reported that PIC also responds to CVS (Frank et al. 2014, 2016b; see also Roberts et al. 2017), GVS (Billington and Smith 2015), and natural head movements (Schindler and Bartels 2018), we have used a visual motion localizer consisting of 100% coherent dot fields to define PIC, since one of our goals was to relate our results to original descriptions of PIC that employed visual motion stimuli (e.g., Claeys et al. 2003; Orban et al. 2003; Sunaert et al. 1999). Compared with PIVC, area PIC is located at a more posterior site in the Sylvian fissure (Fig. 2), primarily in the retroinsular cortex, partially extending into the posterior end of the Sylvian fissure in a region referred to as PSL by Glasser and colleagues (2016).

The locations we report here for PIVC and PIC agree with results of previous imaging studies of the vestibular system, which concluded that these sites represent the core of the vestibular cortex in humans (Lopez et al. 2012; zu Eulenburg et al. 2012). However, these earlier studies did not consider the possibility that a visually responsive area, PIC, could also be located posterior to PIVC. In the following, we will review recent evidence suggesting that PIVC and PIC are indeed different areas rather than two parts of the same region.

ARE PIVC AND PIC SEPARATE REGIONS?

Anatomical Differences

PIVC and PIC are located at different anatomical sites in the Sylvian fissure (see Fig. 2) and also differ in their anatomical connectivity patterns. In a recent human imaging study, Wirth et al. (2018) defined PIVC and PIC by means of their functional responses to vestibular and visual motion cues and investigated their anatomical connections with diffusion weighted imaging (DWI) and tractography analysis. The results of this study suggest that PIC is more strongly connected with the supramarginal gyrus and the superior temporal sulcus compared with PIVC (Wirth et al. 2018). The supramarginal gyrus is part of a larger region that is referred to as the temporo-parietal junction. Other studies using the DWI approach (Smith et al. 2018) suggest that connections exist between PIC and the cingulate sulcus visual area (CSv), which is another key region in the network of areas that processes visual cues related to self-motion (Smith et al. 2017). Area CSv also responds to GVS (Smith et al. 2012). Furthermore, other visual optic flow-sensitive areas in the parietal cortex (e.g., VIP, the precuneus motion area, and area 2v) have anatomical connections that terminate in the region where PIC is located (Uesaki et al. 2018). Compared with PIC, area PIVC has more pronounced connections to the anterior insula, Heschl's gyrus, the precuneus, the IPS, and the posterior callosum (Wirth et al. 2018). This study also showed that PIVC and PIC are strongly interconnected and that both areas have connections with the insula, other portions of the Sylvian fissure, the parietal cortex, the superior temporal cortex, and the inferior frontal gyrus. Subcortically, both PIVC and PIC are connected with the lateral nuclei of the thalamus (including the ventral posterior lateral, lateral posterior, ventral lateral, and ventral anterior nuclei), the pulvinar, and the basal ganglia (in particular the

putamen) (Wirth et al. 2018). Another recent connectivity study in humans reported that the posterolateral thalamic region connects the vestibular nuclei in the brain stem with PIVC (Kirsch et al. 2016).

Taken together, the evidence from DWI and tractography indicates that PIVC and PIC exhibit different anatomical connectivity fingerprints. Specifically, the connections between PIC and other visual regions in the superior temporal, parietal, and cingulate cortices, support the existence of visual responses in PIC. Moreover, both PIVC and PIC share connectivity with other key structures of the cortical and subcortical vestibular network.

Functional Differences

The most robust evidence for functional differences between PIVC and PIC is their opposite response patterns during visual processing. Whereas PIC is strongly activated by various types of visual motion cues (Antal et al. 2008; Beer et al. 2009; Claeys et al. 2003; Dupont et al. 1994, 1997; Ferri et al. 2016; Frank et al. 2014, 2016b; Indovina et al. 2005; Maffei et al. 2010; Miller et al. 2008; Orban et al. 2003; Sunaert et al. 1999), PIVC is suppressed during dynamic visual stimulation (e.g., Brandt et al. 1998; Deutschländer et al. 2002; Frank et al. 2016a, 2016b; Kleinschmidt et al. 2002; Laurienti et al. 2002; Shulman et al. 1997). This suppression of PIVC can already be observed a few weeks after birth (Biagi et al. 2015). In the following we will use the term “suppression” to refer to lower activity in one condition relative to a control or baseline condition.

Brandt and colleagues (1998) reported in a PET-imaging study that visually induced sensations of self-motion (referred to as “vection”; see Bremmer 2011; Britten 2008; DeAngelis and Angelaki 2012; Gibson 1950; Greenlee 2000; Greenlee et al. 2016; Lappe et al. 1999; Smith et al. 2017) were correlated with suppressed activity in PIVC. They proposed a theory of reciprocal inhibitory visual-vestibular interactions, where visual stimulation inhibits the vestibular system, and vice versa, thereby avoiding visual-vestibular conflicts (Brandt et al. 1998; Dieterich and Brandt 2015). An important question for the theory of inhibitory visual-vestibular interactions is whether the proposed suppression of PIVC is specific to visual stimuli that induce vection or whether the inhibition can be induced under other conditions as well. Moreover, it is unclear whether inhibitory visual-vestibular interactions are also found in PIC.

Previous studies have reported evidence that visual processing that does not induce vection already suppresses PIVC (e.g., Laurienti et al. 2002; Shulman et al. 1997) and that simultaneous vestibular cues cannot completely abolish this visually induced suppression (Della-Justina et al. 2015; Deutschländer et al. 2002). However, visual stimuli that induce vection appear to evoke a stronger suppression of PIVC (Kleinschmidt et al. 2002).

One possibility is that the suppression of PIVC during visual processing without vection may be augmented when the visual stimuli are actively attended rather than merely perceived (Frank et al. 2016a). We examined this possibility by using an attentional tracking paradigm (Pylyshyn and Storm 1988), where the amount of attentional load can be varied parametrically while the amount of visual information remains constant (see Culham et al. 2001) (Fig. 3A).

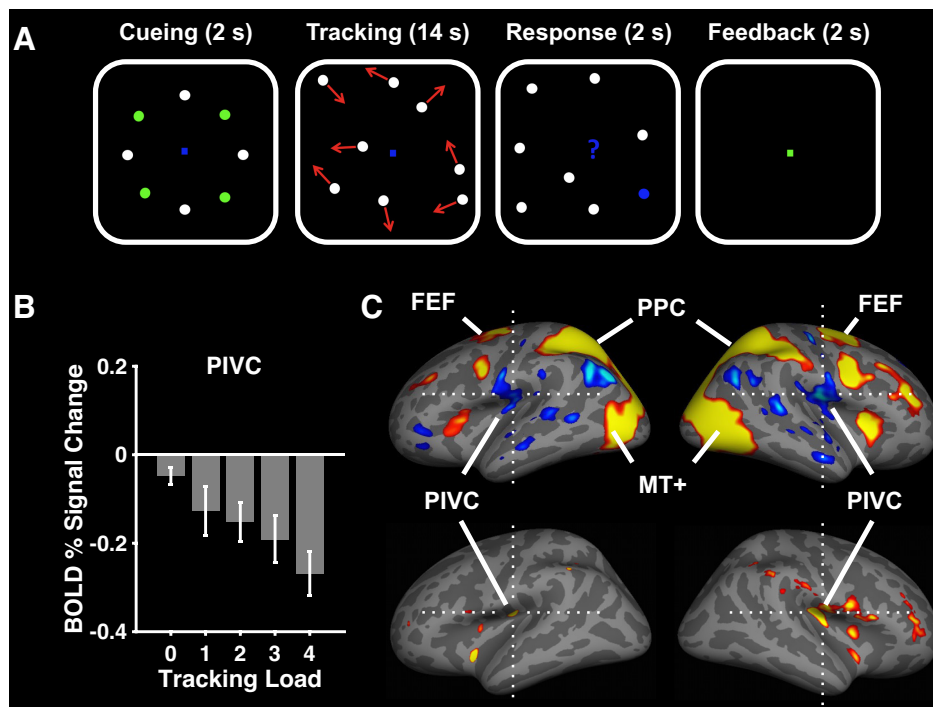


Fig. 3. Cross-modal suppression of activity in PIVC by visual attention (see Frank et al. 2016a). *A*: attentional tracking task. At the beginning of each trial a subset of disks was designated targets and presented in green color. After cueing the target disks turned white and were physically undistinguishable from the distractor disks. Then, all disks moved randomly across the screen for a period of 14 s and participants attentively tracked the targets while maintaining central fixation. At the end of each trial one disk was highlighted in blue and participants indicated whether this disk was a target or a distractor by pressing one of two buttons. Participants received feedback about the correctness of their response. *B*: a detailed analysis of activation in PIVC (for a subset of $n = 8$ participants with individual caloric localizer scans) suggested that the suppression in PIVC was a true suppression of activity below baseline (corresponding to activation during a dark blank screen, “0” on y -axis). Moreover, the suppression scaled with the visual attentional load: There was a moderate suppression of activity in PIVC during passive viewing of the moving disks (corresponding to “Tracking Load 0” on the x -axis), which increased dramatically once visual attention became involved during tracking (see the linear increase in suppression for tracking 1–4 disks on the x -axis). *C, top*: whole brain activity during attentional tracking ($n = 25$ participants). Activity in the fronto-parietal attention network (frontal eye fields, FEF, and posterior parietal cortex, PPC) and in the visual motion sensitive area MT+ increased when the attentional load on the visual system increased (color coded as red-yellow). In striking contrast to these effects, the ongoing activity in PIVC (shown by crosshairs) became increasingly suppressed with increasing attentional loads (color-coded as blue-white). Other regions with suppressed activity correspond to the default mode network, which PIVC is not part of (see Raichle 2015). *Bottom*: the average location of PIVC (shown by crosshairs) in a sample of $n = 25$ different participants who performed caloric vestibular localizer scans (unpublished data), as described previously (see Frank et al. 2016b). Please note that a conservative statistical threshold ($P < 0.001$, false discovery rate corrected) was chosen for the definition of caloric vestibular activity corresponding to PIVC, which removed less significant activations in other regions of the cortical vestibular network. PIVC, parieto-insular vestibular cortex.

The results of this fMRI-study (Frank et al. 2016a) suggested that there was only minor suppression of PIVC when participants passively viewed the moving stimuli, confirming previous reports (Frank et al. 2016b; Kleinschmidt et al. 2002). However, the magnitude of suppression increased dramatically once attention was directed to visual processing (Fig. 3, *B* and *C*).¹ Different effects were found in PIC, where visual attention increased activity (Frank et al. 2016a; see also Luks and Simpson 2004).

¹ A new interpretation of the theory of inhibitory visual-vestibular interactions has to take into account the role of visual attention. For example, periods of visual stimulation during which participants sense vection may be associated with increased levels of attention. Therefore, the amount of suppression induced by the sensation of vection has to be dissociated from the suppression that is due to increased attention to the visual stimulus during vection. Moreover, the origin of the inhibition should be investigated. If the inhibition of PIVC is primarily caused by visual attention, area IPS, a key structure of the fronto-parietal attention network, might trigger the suppression of PIVC. This hypothesis is supported by recent findings that show anatomical connections between IPS and PIVC (Wirth et al. 2018). Finally, possible behavioral effects of visual attention on the vestibular system (e.g., an alternation of vestibular thresholds during periods of attentive visual processing) should be investigated in future studies.

These results suggest that the suppression of PIVC during visual processing is strongly influenced by attention and that attentive visual processing activates PIC rather than suppressing it. However, do visual motion cues such as optic flow that induce vection evoke a response in PIC that is different from the response to mere object motion? Several studies have addressed this question and found that PIC — in addition to other areas of the visual motion network such as MST, VIP, or CSv (Smith et al. 2017) — responds stronger during periods of vection, which could suggest that PIC processes visual cues related to self-motion² (Cardin and Smith 2010, 2011; Huang et al. 2015; Kirolos et al. 2017; Nishiike et al. 2002; Uesaki and Ashida 2015; Wada et al. 2016). However, in many of these studies brain activity in the posterior Sylvian fissure during visual self-motion has been interpreted as corresponding to PIVC (Cardin and Smith 2010, 2011; Huang et al. 2015; Nishiike et al. 2002; Riccelli et al. 2017; Uesaki and Ashida 2015; Wada et al. 2016), whereas more recent discussions have

² Future studies should try to dissociate the amount of activation in PIC that is due to increased attention during vection from the activity that is due to the sensation of vection.

reinterpreted these activations as corresponding to PIC (Kirolos et al. 2017; Smith et al. 2017, 2018; Uesaki et al. 2018). The strong suppression of PIVC during visual processing as well as the location of PIC in the retroinsula and more posterior parietal regions where activity during vection or self-motion-related visual processing is usually observed (Cardin and Smith 2010, 2011; Huang et al. 2015; Nishiike et al. 2002; Riccelli et al. 2017; Uesaki and Ashida 2015; Wada et al. 2016) suggest that these earlier studies have observed activation that corresponds to PIC rather than PIVC.

Finally, if PIC is to be considered a vestibular area, it should also respond to vestibular cues induced by CVS/GVS or head movements. Early imaging studies have observed such activations in the retroinsular cortex (e.g., Bense et al. 2001; Bottini et al. 2001; Deutschländer et al. 2002; Dieterich et al. 2003; Fink et al. 2003; Indovina et al. 2005; Lobel et al. 1998; Petit and Beauchamp 2003; Smith et al. 2012; Stephan et al. 2005) but did not conduct independent visual motion localizers for PIC. The location of PIC in the retroinsula coincides with the location of a distinct activation cluster reported in a meta-analysis of functional imaging studies of the vestibular cortex (Lopez et al. 2012). In this meta-analysis, the retroinsular cortex was the only region besides the parietal operculum and the posterior insula where strong vestibular activations across studies were observed. We speculate that this common activation in the retroinsular cortex may correspond to, or overlap with, area PIC. More recently, vestibular responses have been confirmed in PIC during CVS (Frank et al. 2014, 2016b; see also Roberts et al. 2017), GVS (Billington and Smith 2015), and active head movements (Schindler and Bartels 2018). Some studies have also reported evidence for integrated visual-vestibular signals in PIC (Billington and Smith 2015; Schindler and Bartels 2018; see also Roberts et al. 2017). Area PIC in humans may thus show similarities with other regions of the vestibular cortex (e.g., areas MST or VIP), which do not only respond to visual and vestibular stimuli but also appear to integrate them for an accurate representation of heading direction (Gu 2018; Lopez and Blanke 2011; Smith et al. 2017).

In summary, PIVC and PIC are similar because they both process vestibular cues. However, they are strikingly dissimilar in their responses to visual stimulation: PIC is activated, while PIVC is suppressed. These effects are dramatically augmented by visual attention. The differential activity patterns in PIVC and PIC suggest that both areas are not only anatomically but also functionally distinct.

COMPARISON OF RESULTS IN NONHUMAN PRIMATES AND HUMANS

To summarize, the anatomical location and cortical/subcortical connectivity of PIVC and VPS in nonhuman primates shows parallels to that of PIVC and PIC in humans (see also Smith et al. 2017). Specifically, the location of neurons with vestibular tuning in a region ranging from the posterior insula to the parietal operculum, the retroinsula, and posterior sections of the Sylvian fissure is similar to the location of areas PIVC and PIC in humans. Comparing the structural connectivity between species is more difficult since different techniques (*ex vivo* tracer studies vs. *in vivo* MRI-based DWI) were used. However, structural connections between PIVC/PIC/VPS and the pulvinar and between PIC/VPS and the

superior temporal sulcus were found with the respective methods in both species. Moreover, the functional response characteristics of PIVC and VPS, except the controversial results concerning activation in PIVC for optokinetic vs. optic flow cues, show parallels to the human PIVC and PIC.

Although it is tempting to infer that there is a similar organization of the vestibular cortex in humans and nonhuman primates, it is difficult to draw such conclusions without further evidence. For instance, it would be important to show that CVS/GVS in monkeys activates both PIVC and VPS, whereas visual stimulation/visual attention suppresses activity in PIVC but not in VPS. First results using functional MRI in nonhuman primates are promising and suggest that VPS in rhesus macaques prefers optic flow cues that simulate self-motion, similar to PIC in human observers (Cottreau et al. 2017).

A CONCEPT FOR THE ORGANIZATION OF THE CORE OF THE VESTIBULAR CORTEX

Recent studies have referred to activation in the midposterior Sylvian fissure as “PIVC/PIC” (Biagi et al. 2015; Billington and Smith 2015) or “PIC+” (Uesaki et al. 2018), implying an organization that is similar to the so-called “MT+ complex,” a region of extrastriate visual cortex that consists of two anatomically and functionally separate areas (areas MST and MT), which are commonly referred to as “MT+” (Born and Bradley 2005; Huk et al. 2002). Given what is known about areas PIVC and PIC, is it justified to suggest a similar “PIVC+” in the vestibular cortex of humans? We believe that the reviewed studies in this article suggest that two separate areas do exist in the midposterior Sylvian fissure. These two areas, PIVC and PIC, are similar in some regards (both respond to vestibular stimuli) but dissimilar in others (PIVC is suppressed during visual processing whereas PIC is strongly activated). Based on these results, we propose the following tentative organization of the core of the vestibular cortex (see Fig. 4).

We assume that visual and vestibular signals reach PIC and PIVC from several subcortical structures, including the lateral thalamic nuclei (specifically the ventral posterior nuclei) and the pulvinar (Wirth et al. 2018). The pulvinar as well as the superior temporal sulcus and other cortical regions of the visual self-motion network (e.g., MST, VIP, CSv, see Smith et al. 2017) may exchange visual signals with PIC (Smith et al. 2018; Uesaki et al. 2018; Wirth et al. 2018). Furthermore, we hypothesize that the suppression of PIVC during attentive visual processing is triggered by the IPS, a key structure of the attention network and anatomically connected with PIVC (Wirth et al. 2018). Based on nonhuman primate results (Guldin and Grüsser 1998) and indications in recent DWI studies (Smith et al. 2018; Uesaki et al. 2018; Wirth et al. 2018) we predict that both PIVC and PIC have connections with several other structures of the cortical vestibular network such as areas 7, 3av, and 2v, although this has to be confirmed in future studies.

What are the functions of areas PIVC and PIC? The answer, at this point, must remain speculative, but based on the available evidence in humans and nonhuman primates we propose that PIVC encodes head and full body movements (Akbarian et al. 1988; Grüsser et al. 1990a) and is involved in estimating heading direction by means of such movements (Chen et al.

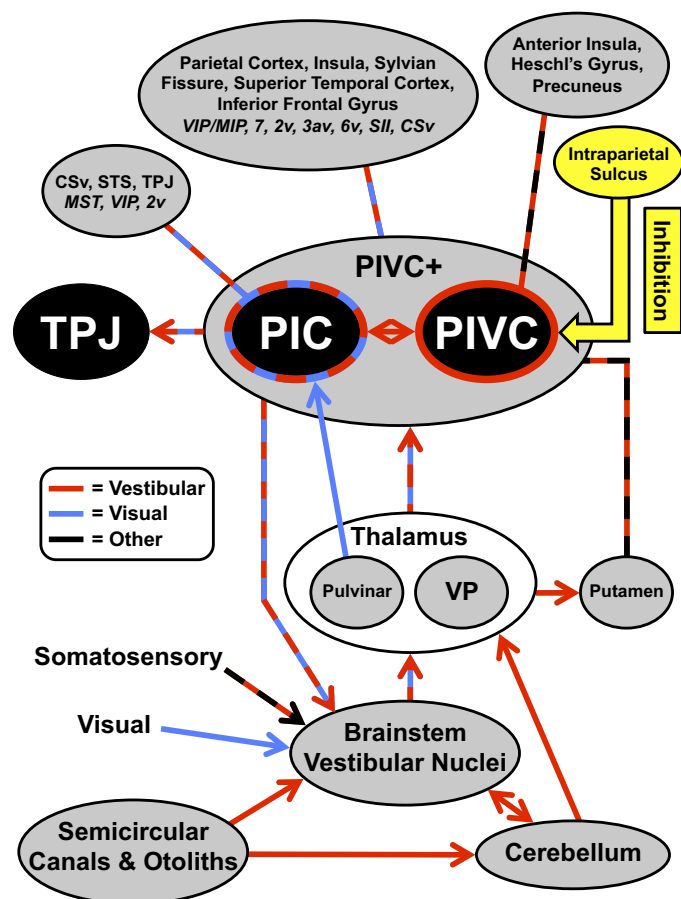


Fig. 4. Schematic illustration of possible projections of subcortical and cortical vestibular and visual signals to and from PIVC and PIC (referred to together as PIVC+). Connectivity results were derived from recent studies in humans using diffusion weighted imaging (DWI) techniques (Kirsch et al. 2016; Smith et al. 2018; Uesaki et al. 2018; Wirth et al. 2018). Please note that no inference about the direction of connectivity can be obtained from DWI. Directions shown by arrowhead are either based on nonhuman primate results or they are theoretically inferred (see the direction included for the connection between the intraparietal sulcus and PIVC). Specific areas of the vestibular cortex that are potentially connected with PIVC and PIC are italicized. Please note that vestibular projections from the thalamus also terminate in other parts of the vestibular cortex (e.g., area 3av or areas in the superior parietal cortex, see Fig. 1 and Hittier et al. 2014; Lopez and Blanke 2011). Since our focus in this review is on areas PIVC and PIC we do not show these additional projections. CSv, cingulate sulcus visual area; MST, medial superior temporal area; PIC, posterior insular cortex; PIVC, parieto-insular vestibular cortex; SII, secondary somatosensory cortex; STS, superior temporal sulcus; TPJ, portion of the temporo-parietal junction bordering the posterior Sylvian fissure; VIP/ MIP, ventral/medial intraparietal area; VP, ventral posterior thalamic nuclei.

2010, 2016). In contrast to PIVC, PIC may serve two functions. One function could be the estimation of heading direction by combining visual and vestibular cues (Billington and Smith 2015; Frank et al. 2014, 2016b; Roberts et al. 2017; Schindler and Bartels 2018; VPS in nonhuman primates: Chen et al. 2011, 2016), while the other function could be the distinction between visual self-motion and visual object motion, potentially supported by neurons with incongruent visual-vestibular tuning (Gu 2018). In that regard, it is our observation that the sensory weight in PIC appears to be more on visual cues, since visual stimuli immediately evoke activation in PIC (Claeys et al. 2003; Frank et al. 2014, 2016b; Orban et al. 2003; Sunaert et al. 1999). We hypothesize that the output of visual-vestibular

processing from PIVC+ is sent to the TPJ, where visual-vestibular signals related to self-motion and heading direction are integrated into an egocentric representation of the self in space (Blanke 2012; Falconer and Mast 2012; Ionta et al. 2011; Lopez 2015, 2016; Pfeiffer et al. 2014).

Future theories of PIVC and PIC will also have to consider the roles of other sensory cues (e.g., somatosensory signals), which activate neurons in PIVC (Akbarian et al. 1988; Grüsser et al. 1990a, 1990b) and potentially also in PIC (Bottini et al. 2001; Fasold et al. 2008; Gentile et al. 2011; Martin et al. 2004).

OPEN QUESTIONS

Even though the understanding of the human vestibular cortex has been advanced in the past decades, a lot of questions remain to be answered. Some of these questions that are specifically related to PIVC and PIC are

- How do PIVC and PIC interact with other areas of the vestibular cortex (e.g., areas 2v, 3av) and how do computations in each area relate to an overall sensation of self-motion?
- Is there a hemispheric dominance effect in PIC? A dominance of the right hemisphere of right-handed subjects in the cortical vestibular network has been suggested (Dieterich et al. 2003; zu Eulenburg et al. 2012), but it remains to be clarified whether there is dominance of right over left PIC in vestibular processing.
- What are the functional consequences of suppressing PIVC by visual attention? Since we strongly depend on our visual senses, one may assume that PIVC is suppressed permanently. Does such a sustained suppression have any consequences for the sensation of head movements or the estimation of heading direction, specifically when attention is focused on visual processing?
- Are central vestibular disorders (see Brandt and Dieterich 2017) associated with dysfunctions of areas PIVC and PIC, and if so, do the symptoms differ when the dysfunction affects primarily PIVC or PIC? Lesions in the region where PIVC and PIC are located result in tilts of the subjective visual vertical (Brandt et al. 1994), but more specific deficits in visual-vestibular processing such as impaired perception of visual gravitational motion (Maffei et al. 2016) could have their origin in lesions that affect primarily PIC rather than PIVC.

CONCLUSION

Traditionally, only a single region, PIVC, has been assumed to exist at the core of the vestibular cortex in humans. However, recent advances suggest that another area, referred to as PIC, is located in the retroinsular cortex posterior to PIVC. Area PIC has been identified in human imaging studies almost 20 years ago but has not been included in the vestibular network until recently. Overall, the results suggest that the core of the vestibular cortex in humans consists of at least two anatomically and functionally separate areas, which we refer to together as PIVC+.

ACKNOWLEDGMENTS

We thank Alexandra Otto and Katharina Hense for help with data collection and our participants for their time. We are grateful to Christian Renner for

constructing and maintaining the caloric vestibular stimulation device. We thank Jeffrey Taube (Dartmouth College) for helpful comments on a previous version of the manuscript.

GRANTS

This research was funded in part by support from the German Research Council (Deutsche Forschungsgemeinschaft, project GR 988 25-1, core facility grant number INST 89/393-1) and from the University of Regensburg.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

S.M.F. and M.W.G. conceived and designed research; S.M.F. and M.W.G. performed experiments; S.M.F. analyzed data; S.M.F. and M.W.G. interpreted results of experiments; S.M.F. and M.W.G. prepared figures; S.M.F. and M.W.G. drafted manuscript; S.M.F. and M.W.G. edited and revised manuscript; S.M.F. and M.W.G. approved final version of manuscript.

REFERENCES

- Akbarian S, Berndt K, Grüsser OJ, Guldin W, Pause M, Schreier U. Responses of single neurons in the parietoinsular vestibular cortex of primates. *Ann N Y Acad Sci* 545: 187–202, 1988. doi:10.1111/j.1749-6632.1988.tb19564.x.
- Akbarian S, Grüsser OJ, Guldin WO. Thalamic connections of the vestibular cortical fields in the squirrel monkey (*Saimiri sciureus*). *J Comp Neurol* 326: 423–441, 1992. doi:10.1002/cne.903260308.
- Akbarian S, Grüsser OJ, Guldin WO. Corticofugal connections between the cerebral cortex and brainstem vestibular nuclei in the macaque monkey. *J Comp Neurol* 339: 421–437, 1994. doi:10.1002/cne.903390309.
- Angelaki DE, Cullen KE. Vestibular system: the many facets of a multimodal sense. *Annu Rev Neurosci* 31: 125–150, 2008. doi:10.1146/annurev.neuro.31.060407.125555.
- Antal A, Baudewig J, Paulus W, Dechent P. The posterior cingulate cortex and planum temporale/parietal operculum are activated by coherent visual motion. *Vis Neurosci* 25: 17–26, 2008. doi:10.1017/S0952523808080024.
- Bárány R. *Physiologie und Pathologie (Funktions-Prüfung) des Bogengang-Apparates beim Menschen. Klinische Studien*. Leipzig, Germany: Franz Deuticke, 1907.
- Barmack NH. Central vestibular system: vestibular nuclei and posterior cerebellum. *Brain Res Bull* 60: 511–541, 2003. doi:10.1016/S0361-9230(03)00055-8.
- Barnes G. Adaptation in the oculomotor response to caloric irrigation and the merits of bithermal stimulation. *Br J Audiol* 29: 95–106, 1995. doi:10.3109/03005369509086586.
- Beer AL, Watanabe T, Ni R, Sasaki Y, Andersen GJ. 3D surface perception from motion involves a temporal-parietal network. *Eur J Neurosci* 30: 703–713, 2009. doi:10.1111/j.1460-9568.2009.06857.x.
- Bense S, Stephan T, Yousry TA, Brandt T, Dieterich M. Multisensory cortical signal increases and decreases during vestibular galvanic stimulation (fMRI). *J Neurophysiol* 85: 886–899, 2001. doi:10.1152/jn.2001.85.2.886.
- Biagi L, Crespi SA, Tosetti M, Morrone MC. BOLD response selective to flow-motion in very young infants. *PLoS Biol* 13: e1002260, 2015. doi:10.1371/journal.pbio.1002260.
- Billington J, Smith AT. Neural mechanisms for discounting head-roll-induced retinal motion. *J Neurosci* 35: 4851–4856, 2015. doi:10.1523/JNEUROSCI.3640-14.2015.
- Blanke O. Multisensory brain mechanisms of bodily self-consciousness. *Nat Rev Neurosci* 13: 556–571, 2012. doi:10.1038/nrn3292.
- Born RT, Bradley DC. Structure and function of visual area MT. *Annu Rev Neurosci* 28: 157–189, 2005. doi:10.1146/annurev.neuro.26.041002.131052.
- Bottini G, Karnath HO, Vallar G, Sterzi R, Frith CD, Frackowiak RS, Paulesu E. Cerebral representations for egocentric space: Functional-anatomical evidence from caloric vestibular stimulation and neck vibration. *Brain* 124: 1182–1196, 2001. doi:10.1093/brain/124.6.1182.
- Brandt T, Bartenstein P, Janek A, Dieterich M. Reciprocal inhibitory visual-vestibular interaction. Visual motion stimulation deactivates the parieto-insular vestibular cortex. *Brain* 121: 1749–1758, 1998. doi:10.1093/brain/121.9.1749.
- Brandt T, Dieterich M. The dizzy patient: don't forget disorders of the central vestibular system. *Nat Rev Neurol* 13: 352–362, 2017. doi:10.1038/nrneurol.2017.58.
- Brandt T, Dieterich M, Danek A. Vestibular cortex lesions affect the perception of verticality. *Ann Neurol* 35: 403–412, 1994. doi:10.1002/ana.410350406.
- Brandt T, Schautzer F, Hamilton DA, Brüning R, Markowitsch HJ, Kalla R, Darlington C, Smith P, Strupp M. Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. *Brain* 128: 2732–2741, 2005. doi:10.1093/brain/awh617.
- Bremmer F. Multisensory space: from eye-movements to self-motion. *J Physiol* 589: 815–823, 2011. doi:10.1113/jphysiol.2010.195537.
- Bremmer F, Kubischik M, Pekel M, Lappe M, Hoffmann KP. Linear vestibular self-motion signals in monkey medial superior temporal area. *Ann N Y Acad Sci* 871: 272–281, 1999. doi:10.1111/j.1749-6632.1999.tb09191.x.
- Britten KH. Mechanisms of self-motion perception. *Annu Rev Neurosci* 31: 389–410, 2008. doi:10.1146/annurev.neuro.29.051605.112953.
- Bronstein AM, Patel M, Arshad Q. A brief review of the clinical anatomy of the vestibular-ocular connections—how much do we know? *Eye (Lond)* 29: 163–170, 2015. doi:10.1038/eye.2014.262.
- Brooks JX, Carriot J, Cullen KE. Learning to expect the unexpected: rapid updating in primate cerebellum during voluntary self-motion. *Nat Neurosci* 18: 1310–1317, 2015. doi:10.1038/nn.4077.
- Brooks JX, Cullen KE. Early vestibular processing does not discriminate active from passive self-motion if there is a discrepancy between predicted and actual proprioceptive feedback. *J Neurophysiol* 111: 2465–2478, 2014. doi:10.1152/jn.00600.2013.
- Büttner U, Büttner UW. Parietal cortex (2v) neuronal activity in the alert monkey during natural vestibular and optokinetic stimulation. *Brain Res* 153: 392–397, 1978. doi:10.1016/0006-8993(78)90421-3.
- Büttner U, Henn V. Thalamic unit activity in the alert monkey during natural vestibular stimulation. *Brain Res* 103: 127–132, 1976. doi:10.1016/0006-8993(76)90692-2.
- Büttner-Ennever JA. Patterns of connectivity in the vestibular nuclei. *Ann N Y Acad Sci* 656: 363–378, 1992. doi:10.1111/j.1749-6632.1992.tb25222.x.
- Cardin V, Smith AT. Sensitivity of human visual and vestibular cortical regions to egomotion-compatible visual stimulation. *Cereb Cortex* 20: 1964–1973, 2010. doi:10.1093/cercor/bhp268.
- Cardin V, Smith AT. Sensitivity of human visual cortical area V6 to stereoscopic depth gradients associated with self-motion. *J Neurophysiol* 106: 1240–1249, 2011. doi:10.1152/jn.01120.2010.
- Carleton SC, Carpenter MB. Afferent and efferent connections of the medial, inferior and lateral vestibular nuclei in the cat and monkey. *Brain Res* 278: 29–51, 1983. doi:10.1016/0006-8993(83)90223-8.
- Chen A, DeAngelis GC, Angelaki DE. Macaque parieto-insular vestibular cortex: responses to self-motion and optic flow. *J Neurosci* 30: 3022–3042, 2010. doi:10.1523/JNEUROSCI.4029-09.2010.
- Chen A, DeAngelis GC, Angelaki DE. Convergence of vestibular and visual self-motion signals in an area of the posterior sylvian fissure. *J Neurosci* 31: 11617–11627, 2011. doi:10.1523/JNEUROSCI.1266-11.2011.
- Chen A, Gu Y, Liu S, DeAngelis GC, Angelaki DE. Evidence for a causal contribution of macaque vestibular, but not intraparietal, cortex to heading perception. *J Neurosci* 36: 3789–3798, 2016. doi:10.1523/JNEUROSCI.2485-15.2016.
- Chen X, DeAngelis GC, Angelaki DE. Diverse spatial reference frames of vestibular signals in parietal cortex. *Neuron* 80: 1310–1321, 2013. doi:10.1016/j.neuron.2013.09.006.
- Claeys KG, Lindsey DT, De Schutter E, Orban GA. A higher order motion region in human inferior parietal lobule: evidence from fMRI. *Neuron* 40: 631–642, 2003. doi:10.1016/S0896-6273(03)00590-7.
- Cohen B, Yakushin SB, Holstein GR. What does galvanic vestibular stimulation actually activate? *Front Neurol* 2: 90, 2012. doi:10.3389/fneur.2011.00090.
- Cottureau BR, Smith AT, Rima S, Fize D, Héjja-Brichard Y, Renaud L, Lejards C, Vayssière N, Trotter Y, Durand JB. Processing of egomotion-consistent optic flow in the rhesus macaque cortex. *Cereb Cortex* 27: 330–343, 2017. doi:10.1093/cercor/bhw412.
- Culham JC, Cavanagh P, Kanwisher NG. Attention response functions: characterizing brain areas using fMRI activation during parametric variations of attentional load. *Neuron* 32: 737–745, 2001. doi:10.1016/S0896-6273(01)00499-8.

- Cullen KE.** The vestibular system: multimodal integration and encoding of self-motion for motor control. *Trends Neurosci* 35: 185–196, 2012. doi:10.1016/j.tins.2011.12.001.
- Cullen KE, Brooks JX.** Neural correlates of sensory prediction errors in monkeys: evidence for internal models of voluntary self-motion in the cerebellum. *Cerebellum* 14: 31–34, 2015. doi:10.1007/s12311-014-0608-x.
- Cullen KE, Taube JS.** Our sense of direction: progress, controversies and challenges. *Nat Neurosci* 20: 1465–1473, 2017. doi:10.1038/nn.4658.
- Curthoys IS, MacDougall HG.** What galvanic vestibular stimulation actually activates. *Front Neurol* 3: 117, 2012. doi:10.3389/fneur.2012.00117.
- Dale AM, Fischl B, Sereno MI.** Cortical surface-based analysis. I. Segmentation and surface reconstruction. *Neuroimage* 9: 179–194, 1999. doi:10.1006/nimg.1998.0395.
- Day BL, Fitzpatrick RC.** The vestibular system. *Curr Biol* 15: R583–R586, 2005. doi:10.1016/j.cub.2005.07.053.
- de Waele C, Baudonnière PM, Lepceq JC, Tran Ba Huy P, Vidal PP.** Vestibular projections in the human cortex. *Exp Brain Res* 141: 541–551, 2001. doi:10.1007/s00221-001-0894-7.
- DeAngelis GC, Angelaki DE.** Visual-vestibular integration for self-motion perception. In: *The Neural Bases of Multisensory Processes*, edited by Murray MM, Wallace MT. Boca Raton, FL: CRC, 2012, chapt 31. https://www.ncbi.nlm.nih.gov/books/NBK92839/.
- Della-Justina HM, Gamba HR, Lukasova K, Nucci-da-Silva MP, Winkler AM, Amaro E Jr.** Interaction of brain areas of visual and vestibular simultaneous activity with fMRI. *Exp Brain Res* 233: 237–252, 2015. doi:10.1007/s00221-014-4107-6.
- Deutschländer A, Bense S, Stephan T, Schwaiger M, Brandt T, Dieterich M.** Sensory system interactions during simultaneous vestibular and visual stimulation in PET. *Hum Brain Mapp* 16: 92–103, 2002. doi:10.1002/hbm.10030.
- Dieterich M, Bense S, Lutz S, Drzezga A, Stephan T, Bartenstein P, Brandt T.** Dominance for vestibular cortical function in the non-dominant hemisphere. *Cereb Cortex* 13: 994–1007, 2003. doi:10.1093/cercor/13.9.994.
- Dieterich M, Brandt T.** Vestibulo-ocular reflex. *Curr Opin Neurol* 8: 83–88, 1995. doi:10.1097/00019052-199502000-00014.
- Dieterich M, Brandt T.** Functional brain imaging of peripheral and central vestibular disorders. *Brain* 131: 2538–2552, 2008. doi:10.1093/brain/awn042.
- Dieterich M, Brandt T.** The bilateral central vestibular system: its pathways, functions, and disorders. *Ann NY Acad Sci* 1343: 10–26, 2015. doi:10.1111/nyas.12585.
- Dieterich M, Brandt T.** The parietal lobe and the vestibular system. *Handb Clin Neurol* 151: 119–140, 2018. doi:10.1016/B978-0-444-63622-5.00006-1.
- Dieterich M, Bucher SF, Seelos KC, Brandt T.** Horizontal or vertical optokinetic stimulation activates visual motion-sensitive, ocular motor and vestibular cortex areas with right hemispheric dominance. An fMRI study. *Brain* 121: 1479–1495, 1998. doi:10.1093/brain/121.8.1479.
- Duffy CJ.** MST neurons respond to optic flow and translational movement. *J Neurophysiol* 80: 1816–1827, 1998. doi:10.1152/jn.1998.80.4.1816.
- Dupont P, De Bruyn B, Vandenberghe R, Rosier AM, Michiels J, Marchal G, Mortelmans L, Orban GA.** The kinetic occipital region in human visual cortex. *Cereb Cortex* 7: 283–292, 1997. doi:10.1093/cercor/7.3.283.
- Dupont P, Orban GA, De Bruyn B, Verbruggen A, Mortelmans L.** Many areas in the human brain respond to visual motion. *J Neurophysiol* 72: 1420–1424, 1994. doi:10.1152/jn.1994.72.3.1420.
- Eickhoff SB, Weiss PH, Amunts K, Fink GR, Zilles K.** Identifying human parieto-insular vestibular cortex using fMRI and cytoarchitectonic mapping. *Hum Brain Mapp* 27: 611–621, 2006. doi:10.1002/hbm.20205.
- Falconer CJ, Mast FW.** Balancing the mind: vestibular induced facilitation of egocentric mental transformations. *Exp Psychol* 59: 332–339, 2012. doi:10.1027/1618-3169/a000161.
- Fasold O, Heinau J, Trenner MU, Villringer A, Wenzel R.** Proprioceptive head posture-related processing in human polysensory cortical areas. *Neuroimage* 40: 1232–1242, 2008. doi:10.1016/j.neuroimage.2007.12.060.
- Fasold O, von Brevern M, Kuhberg M, Ploner CJ, Villringer A, Lempert T, Wenzel R.** Human vestibular cortex as identified with caloric stimulation in functional magnetic resonance imaging. *Neuroimage* 17: 1384–1393, 2002. doi:10.1006/nimg.2002.1241.
- Felleman DJ, Van Essen DC.** Distributed hierarchical processing in the primate cerebral cortex. *Cereb Cortex* 1: 1–47, 1991. doi:10.1093/cercor/1.1.1.
- Fernández C, Goldberg JM.** Physiology of peripheral neurons innervating otolith organs of the squirrel monkey. I. Response to static tilts and to long-duration centrifugal force. *J Neurophysiol* 39: 970–984, 1976. doi:10.1152/jn.1976.39.5.970.
- Ferri S, Pauwels K, Rizzolatti G, Orban GA.** Stereoscopically observing manipulative actions. *Cereb Cortex* 26: 3591–3610, 2016. doi:10.1093/cercor/bhw133.
- Fetter M.** Vestibulo-ocular reflex. In: *Neuro-Ophthalmology*, edited by Straube A, Büttner U. Basel, Switzerland: Karger, 2007, vol. 40, p. 35–51. doi:10.1159/000100348.
- Fink GR, Marshall JC, Weiss PH, Stephan T, Grefkes C, Shah NJ, Zilles K, Dieterich M.** Performing allocentric visuospatial judgments with induced distortion of the egocentric reference frame: an fMRI study with clinical implications. *Neuroimage* 20: 1505–1517, 2003. doi:10.1016/j.neuroimage.2003.07.006.
- Fischl B, Sereno MI, Dale AM.** Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system. *Neuroimage* 9: 195–207, 1999. doi:10.1006/nimg.1998.0396.
- Fitzpatrick RC, Day BL.** Probing the human vestibular system with galvanic stimulation. *J Appl Physiol* (1985) 96: 2301–2316, 2004. doi:10.1152/jappphysiol.00008.2004.
- Frank SM, Baumann O, Mattingley JB, Greenlee MW.** Vestibular and visual responses in human posterior insular cortex. *J Neurophysiol* 112: 2481–2491, 2014. doi:10.1152/jn.00078.2014.
- Frank SM, Greenlee MW.** An MRI-compatible caloric stimulation device for the investigation of human vestibular cortex. *J Neurosci Methods* 235: 208–218, 2014. doi:10.1016/j.jneumeth.2014.07.008.
- Frank SM, Sun L, Forster L, Tse PU, Greenlee MW.** Cross-modal attention effects in the vestibular cortex during attentive tracking of moving objects. *J Neurosci* 36: 12720–12728, 2016a. doi:10.1523/JNEUROSCI.2480-16.2016.
- Frank SM, Wirth AM, Greenlee MW.** Visual-vestibular processing in the human Sylvian fissure. *J Neurophysiol* 116: 263–271, 2016b. doi:10.1152/jn.00009.2016.
- Fredrickson JM, Figge U, Scheid P, Kornhuber HH.** Vestibular nerve projection to the cerebral cortex of the rhesus monkey. *Exp Brain Res* 2: 318–327, 1966. doi:10.1007/BF00234777.
- Gale S, Prsa M, Schurger A, Gay A, Paillard A, Herbelin B, Guyot JP, Lopez C, Blanke O.** Oscillatory neural responses evoked by natural vestibular stimuli in humans. *J Neurophysiol* 115: 1228–1242, 2016. doi:10.1152/jn.00153.2015.
- Gentile G, Petkova VI, Ehrsson HH.** Integration of visual and tactile signals from the hand in the human brain: an fMRI study. *J Neurophysiol* 105: 910–922, 2011. doi:10.1152/jn.00840.2010.
- Gibson JJ.** *Perception of the Visual World*. Boston, MA: Houghton-Mifflin, 1950.
- Gimmon Y, Millar J, Pak R, Liu E, Schubert MC.** Central not peripheral vestibular processing impairs gait coordination. *Exp Brain Res* 235: 3345–3355, 2017. doi:10.1007/s00221-017-5061-x.
- Glasser MF, Coalson TS, Robinson EC, Hacker CD, Harwell J, Yacoub E, Ugurbil K, Andersson J, Beckmann CF, Jenkinson M, Smith SM, Van Essen DC.** A multi-modal parcellation of human cerebral cortex. *Nature* 536: 171–178, 2016. doi:10.1038/nature18933.
- Goldberg JM, Cullen KE.** Vestibular control of the head: possible functions of the vestibuloocollic reflex. *Exp Brain Res* 210: 331–345, 2011. doi:10.1007/s00221-011-2611-5.
- Goldberg JM, Fernández C.** Physiology of peripheral neurons innervating semicircular canals of the squirrel monkey. I. Resting discharge and response to constant angular accelerations. *J Neurophysiol* 34: 635–660, 1971. doi:10.1152/jn.1971.34.4.635.
- Goldberg JM, Smith CE, Fernández C.** Relation between discharge regularity and responses to externally applied galvanic currents in vestibular nerve afferents of the squirrel monkey. *J Neurophysiol* 51: 1236–1256, 1984. doi:10.1152/jn.1984.51.6.1236.
- Goldberg ME, Walker MF, Hudspeth AJ.** The vestibular system. In: *Principles of Neural Science*, edited by Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ. New York McGraw-Hill, 2013, chapt 40, p. 917–934.
- Greenlee MW.** Human cortical areas underlying the perception of optic flow: brain imaging studies. *Int Rev Neurobiol* 44: 269–292, 2000. doi:10.1016/S0074-7742(08)60746-1.
- Greenlee MW, Frank SM, Kaliuzhna M, Blanke O, Bremmer F, Churan J, Cuturi LF, MacNeilage PR, Smith AT.** Multisensory integration in

- self-motion perception. *Multisens Res* 29: 525–556, 2016. doi:10.1163/22134808-00002527.
- Grüsser OJ, Pause M, Schreiter U.** Localization and responses of neurones in the parieto-insular vestibular cortex of awake monkeys (*Macaca fascicularis*). *J Physiol* 430: 537–557, 1990a. doi:10.1113/jphysiol.1990.sp018306.
- Grüsser OJ, Pause M, Schreiter U.** Vestibular neurones in the parieto-insular cortex of monkeys (*Macaca fascicularis*): visual and neck receptor responses. *J Physiol* 430: 559–583, 1990b. doi:10.1113/jphysiol.1990.sp018307.
- Gu Y.** Vestibular signals in primate cortex for self-motion perception. *Curr Opin Neurobiol* 52: 10–17, 2018. doi:10.1016/j.conb.2018.04.004.
- Gu Y, Angelaki DE, DeAngelis GC.** Neural correlates of multisensory cue integration in macaque MSTd. *Nat Neurosci* 11: 1201–1210, 2008. doi:10.1038/nn.2191.
- Gu Y, Watkins PV, Angelaki DE, DeAngelis GC.** Visual and nonvisual contributions to three-dimensional heading selectivity in the medial superior temporal area. *J Neurosci* 26: 73–85, 2006. doi:10.1523/JNEUROSCI.2356-05.2006.
- Guldin WO, Akbarian S, Grüsser OJ.** Cortico-cortical connections and cytoarchitectonics of the primate vestibular cortex: a study in squirrel monkeys (*Saimiri sciureus*). *J Comp Neurol* 326: 375–401, 1992. doi:10.1002/cne.903260306.
- Guldin WO, Grüsser OJ.** Is there a vestibular cortex? *Trends Neurosci* 21: 254–259, 1998. doi:10.1016/S0166-2236(97)01211-3.
- Gurvich C, Maller JJ, Lithgow B, Haghgoie S, Kulkarni J.** Vestibular insights into cognition and psychiatry. *Brain Res* 1537: 244–259, 2013. doi:10.1016/j.brainres.2013.08.058.
- Gutteling TP, Selen LP, Medendorp WP.** Parallax-sensitive remapping of visual space in occipito-parietal alpha-band activity during whole-body motion. *J Neurophysiol* 113: 1574–1584, 2015. doi:10.1152/jn.00477.2014.
- Highstein SM, Holstein GR.** The anatomy of the vestibular nuclei. *Prog Brain Res* 151: 157–203, 2006. doi:10.1016/S0079-6123(05)51006-9.
- Hitler M, Besnard S, Smith PF.** Vestibular pathways involved in cognition. *Front Integr Neurosci* 8: 59, 2014. doi:10.3389/fnint.2014.00059.
- Horak FB.** Postural orientation and equilibrium: what do we need to know about neural control of balance to prevent falls? *Age Ageing* 35, Suppl 2: ii7–ii11, 2006. doi:10.1093/ageing/af077.
- Huang RS, Chen CF, Sereno MI.** Neural substrates underlying the passive observation and active control of translational egomotion. *J Neurosci* 35: 4258–4267, 2015. doi:10.1523/JNEUROSCI.2647-14.2015.
- Huk AC, Dougherty RF, Heeger DJ.** Retinotopy and functional subdivision of human areas MT and MST. *J Neurosci* 22: 7195–7205, 2002. doi:10.1523/JNEUROSCI.22-16-07195.2002.
- Indovina I, Maffei V, Bosco G, Zago M, Macaluso E, Lacquaniti F.** Representation of visual gravitational motion in the human vestibular cortex. *Science* 308: 416–419, 2005. doi:10.1126/science.1107961.
- Ionta S, Heydrich L, Lenggenhager B, Mouthon M, Fornari E, Chapuis D, Gassert R, Blanke O.** Multisensory mechanisms in temporo-parietal cortex support self-location and first-person perspective. *Neuron* 70: 363–374, 2011. doi:10.1016/j.neuron.2011.03.009.
- Jones EG, Burton H.** Areal differences in the laminar distribution of thalamic afferents in cortical fields of the insular, parietal and temporal regions of primates. *J Comp Neurol* 168: 197–247, 1976. doi:10.1002/cne.901680203.
- Kaas JH, Hackett TA.** Subdivisions of auditory cortex and processing streams in primates. *Proc Natl Acad Sci USA* 97: 11793–11799, 2000. doi:10.1073/pnas.97.22.11793.
- Kahane P, Hoffmann D, Minotti L, Berthoz A.** Reappraisal of the human vestibular cortex by cortical electrical stimulation study. *Ann Neurol* 54: 615–624, 2003. doi:10.1002/ana.10726.
- Khan S, Chang R.** Anatomy of the vestibular system: a review. *NeuroRehabilitation* 32: 437–443, 2013. doi:10.3233/NRE-130866.
- Kirrollos R, Allison RS, Palmisano S.** Cortical correlates of the simulated viewpoint oscillation advantage forvection. *Multisens Res* 30: 739–761, 2017. doi:10.1163/22134808-00002593.
- Kirsch V, Keeser D, Hergenroeder T, Erat O, Ertl-Wagner B, Brandt T, Dieterich M.** Structural and functional connectivity mapping of the vestibular circuitry from human brainstem to cortex. *Brain Struct Funct* 221: 1291–1308, 2016. doi:10.1007/s00429-014-0971-x.
- Kleinschmidt A, Thilo KV, Büchel C, Gresty MA, Bronstein AM, Frackowiak RS.** Neural correlates of visual-motion perception as object- or self-motion. *Neuroimage* 16: 873–882, 2002. doi:10.1006/nimg.2002.1181.
- Konen CS, Kleiser R, Seitz RJ, Bremmer F.** An fMRI study of optokinetic nystagmus and smooth-pursuit eye movements in humans. *Exp Brain Res* 165: 203–216, 2005. doi:10.1007/s00221-005-2289-7.
- Korte GE.** The brainstem projection of the vestibular nerve in the cat. *J Comp Neurol* 184: 279–292, 1979. doi:10.1002/cne.901840205.
- Korte GE, Mugnaini E.** The cerebellar projection of the vestibular nerve in the cat. *J Comp Neurol* 184: 265–277, 1979. doi:10.1002/cne.901840204.
- Lang W, Büttner-Ennever JA, Büttner U.** Vestibular projections to the monkey thalamus: an autoradiographic study. *Brain Res* 177: 3–17, 1979. doi:10.1016/0006-8993(79)90914-4.
- Lappe M, Bremmer F, Van den Berg AV.** Perception of self-motion from visual flow. *Trends Cogn Sci* 3: 329–336, 1999. doi:10.1016/S1364-6613(99)01364-9.
- Laurienti PJ, Burdette JH, Wallace MT, Yen YF, Field AS, Stein BE.** Deactivation of sensory-specific cortex by cross-modal stimuli. *J Cogn Neurosci* 14: 420–429, 2002. doi:10.1162/089892902317361930.
- Liu S, Dickman JD, Angelaki DE.** Response dynamics and tilt versus translation discrimination in parietoinsular vestibular cortex. *Cereb Cortex* 21: 563–573, 2011. doi:10.1093/cercor/bhq123.
- Lobel E, Kleine JF, Bihan DL, Leroy-Willig A, Berthoz A.** Functional MRI of galvanic vestibular stimulation. *J Neurophysiol* 80: 2699–2709, 1998. doi:10.1152/jn.1998.80.5.2699.
- Lopez C.** Making sense of the body: the role of vestibular signals. *Multisens Res* 28: 525–557, 2015. doi:10.1163/22134808-00002490.
- Lopez C.** The vestibular system: balancing more than just the body. *Curr Opin Neurol* 29: 74–83, 2016. doi:10.1097/WCO.0000000000000286.
- Lopez C, Blanke O.** The thalamocortical vestibular system in animals and humans. *Brain Res Brain Res Rev* 67: 119–146, 2011. doi:10.1016/j.brainresrev.2010.12.002.
- Lopez C, Blanke O.** Nobel Prize centenary: Robert Bárány and the vestibular system. *Curr Biol* 24: R1026–R1028, 2014. doi:10.1016/j.cub.2014.09.067.
- Lopez C, Blanke O, Mast FW.** The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis. *Neuroscience* 212: 159–179, 2012. doi:10.1016/j.neuroscience.2012.03.028.
- Luks TL, Simpson GV.** Preparatory deployment of attention to motion activates higher-order motion-processing brain regions. *Neuroimage* 22: 1515–1522, 2004. doi:10.1016/j.neuroimage.2004.04.008.
- Maffei V, Macaluso E, Indovina I, Orban G, Lacquaniti F.** Processing of targets in smooth or apparent motion along the vertical in the human brain: an fMRI study. *J Neurophysiol* 103: 360–370, 2010. doi:10.1152/jn.00892.2009.
- Maffei V, Mazzarella E, Piras F, Spalletta G, Caltagirone C, Lacquaniti F, Daprati E.** Processing of visual gravitational motion in the peri-sylvian cortex: Evidence from brain-damaged patients. *Cortex* 78: 55–69, 2016. doi:10.1016/j.cortex.2016.02.004.
- Martin RE, MacIntosh BJ, Smith RC, Barr AM, Stevens TK, Gati JS, Menon RS.** Cerebral areas processing swallowing and tongue movement are overlapping but distinct: a functional magnetic resonance imaging study. *J Neurophysiol* 92: 2428–2443, 2004. doi:10.1152/jn.01144.2003.
- Mast FW, Merfeld DM, Kosslyn SM.** Visual mental imagery during caloric vestibular stimulation. *Neuropsychologia* 44: 101–109, 2006. doi:10.1016/j.neuropsychologia.2005.04.005.
- Mast FW, Preuss N, Hartmann M, Grabherr L.** Spatial cognition, body representation and affective processes: the role of vestibular information beyond ocular reflexes and control of posture. *Front Integr Neurosci* 8: 44, 2014. doi:10.3389/fnint.2014.00044.
- Mazzola L, Lopez C, Faillenot I, Chouchou F, Mauguière F, Isnard J.** Vestibular responses to direct stimulation of the human insular cortex. *Ann Neurol* 76: 609–619, 2014. doi:10.1002/ana.24252.
- Medendorp WP, Selen LJP.** Vestibular contributions to high-level sensorimotor functions. *Neuropsychologia* 105: 144–152, 2017. doi:10.1016/j.neuropsychologia.2017.02.004.
- Meng H, May PJ, Dickman JD, Angelaki DE.** Vestibular signals in primate thalamus: properties and origins. *J Neurosci* 27: 13590–13602, 2007. doi:10.1523/JNEUROSCI.3931-07.2007.
- Mergner T.** A neurological view on reactive human stance control. *Annu Rev Contr* 34: 177–198, 2010. doi:10.1016/j.arcontrol.2010.08.001.
- Mergner T, Schweigart G, Fennell L.** Vestibular humanoid postural control. *J Physiol Paris* 103: 178–194, 2009. doi:10.1016/j.jphysparis.2009.08.002.
- Miller WL, Maffei V, Bosco G, Iosa M, Zago M, Macaluso E, Lacquaniti F.** Vestibular nuclei and cerebellum put visual gravitational motion in context. *J Neurophysiol* 99: 1969–1982, 2008. doi:10.1152/jn.00889.2007.
- Nagel M, Sprenger A, Zapf S, Erdmann C, Kömpf D, Heide W, Binkofski F, Lencer R.** Parametric modulation of cortical activation during smooth pursuit with and without target blanking: an fMRI study. *Neuroimage* 29: 1319–1325, 2006. doi:10.1016/j.neuroimage.2005.08.050.

- Naito Y, Tateya I, Hirano S, Inoue M, Funabiki K, Toyoda H, Ueno M, Ishizu K, Nagahama Y, Fukuyama H, Ito J. Cortical correlates of vestibulo-ocular reflex modulation: a PET study. *Brain* 126: 1562–1578, 2003. doi:10.1093/brain/awg165.
- Nishiike S, Nakagawa S, Nakagawa A, Uno A, Tonoike M, Takeda N, Kubo T. Magnetic cortical responses evoked by visual linear forward acceleration. *Neuroreport* 13: 1805–1808, 2002. doi:10.1097/00001756-200210070-00023.
- Ödkvist LM, Liedgreen SR, Larsby B, Jerlvald L. Vestibular and somatosensory inflow to the vestibular projection area in the post cruciate dimple region of the cat cerebral cortex. *Exp Brain Res* 22: 185–196, 1975. doi:10.1007/BF00237688.
- Ödkvist LM, Schwarz DWF, Fredrickson JM, Hassler R. Projection of the vestibular nerve to the area 3a arm field in the squirrel monkey (*saimiri sciureus*). *Exp Brain Res* 21: 97–105, 1974. doi:10.1007/BF00234260.
- Orban GA, Fize D, Peuskens H, Denys K, Nelissen K, Sunaert S, Todd J, Vanduffel W. Similarities and differences in motion processing between the human and macaque brain: evidence from fMRI. *Neuropsychologia* 41: 1757–1768, 2003. doi:10.1016/S0028-3932(03)00177-5.
- Pandya DN, Sanides F. Architectonic parcellation of the temporal operculum in rhesus monkey and its projection pattern. *Z Anat Entwicklungsgesch* 139: 127–161, 1973. doi:10.1007/BF00523634.
- Penfield W. Vestibular sensation and the cerebral cortex. *Ann Otol Rhinol Laryngol* 66: 691–698, 1957. doi:10.1177/000348945706600307.
- Penfield W, Rasmussen T. *The Cerebral Cortex of Man: A Clinical Study of Localization of Function*. Oxford, UK: Macmillan, 1950.
- Petit L, Beauchamp MS. Neural basis of visually guided head movements studied with fMRI. *J Neurophysiol* 89: 2516–2527, 2003. doi:10.1152/jn.00988.2002.
- Pfeiffer C, Serino A, Blanke O. The vestibular system: a spatial reference for bodily self-consciousness. *Front Integr Neurosci* 8: 31, 2014. doi:10.3389/fnint.2014.00031.
- Pylyshyn ZW, Storm RW. Tracking multiple independent targets: evidence for a parallel tracking mechanism. *Spat Vis* 3: 179–197, 1988. doi:10.1163/156856888X00122.
- Raichle ME. The brain's default mode network. *Annu Rev Neurosci* 38: 433–447, 2015. doi:10.1146/annurev-neuro-071013-014030.
- Riccelli R, Indovina I, Staab JP, Nigro S, Augimeri A, Lacquaniti F, Passamonti L. Neuroticism modulates brain visuo-vestibular and anxiety systems during a virtual rollercoaster task. *Hum Brain Mapp* 38: 715–726, 2017. doi:10.1002/hbm.23411.
- Roberts RE, Ahmad H, Arshad Q, Patel M, Dima D, Leech R, Seemungal BM, Sharp DJ, Bronstein AM. Functional neuroimaging of visuo-vestibular interaction. *Brain Struct Funct* 222: 2329–2343, 2017. doi:10.1007/s00429-016-1344-4.
- Schindler A, Bartels A. Integration of visual and non-visual self-motion cues during voluntary head movements in the human brain. *Neuroimage* 172: 597–607, 2018. doi:10.1016/j.neuroimage.2018.02.006.
- Seidlitz J, Sponheim C, Glen D, Ye FQ, Saleem KS, Leopold DA, Ungerleider L, Messinger A. A population MRI brain template and analysis tools for the macaque. *Neuroimage* 170: 121–131, 2018. doi:10.1016/j.neuroimage.2017.04.063.
- Shepard NT, Jacobson GP. The caloric irrigation test. *Handb Clin Neurol* 137: 119–131, 2016. doi:10.1016/B978-0-444-63437-5.00009-1.
- Shinder ME, Newlands SD. Sensory convergence in the parieto-insular vestibular cortex. *J Neurophysiol* 111: 2445–2464, 2014. doi:10.1152/jn.00731.2013.
- Shinder ME, Taube JS. Differentiating ascending vestibular pathways to the cortex involved in spatial cognition. *J Vestib Res* 20: 3–23, 2010. doi:10.3233/VES-2010-0344.
- Shulman GL, Corbetta M, Buckner RL, Raichle ME, Fiez JA, Miezin FM, Petersen SE. Top-down modulation of early sensory cortex. *Cereb Cortex* 7: 193–206, 1997. doi:10.1093/cercor/7.3.193.
- Smith AT, Beer AL, Furlan M, Mars RB. Connectivity of the cingulate sulcus visual area (CSv) in the human cerebral cortex. *Cereb Cortex* 28: 713–725, 2018.
- Smith AT, Greenlee MW, DeAngelis GC, Angelaki DE. Distributed visual-vestibular processing in the cerebral cortex of man and macaque. *Multisens Res* 30: 91–120, 2017. doi:10.1163/22134808-00002568.
- Smith AT, Wall MB, Thilo KV. Vestibular inputs to human motion-sensitive visual cortex. *Cereb Cortex* 22: 1068–1077, 2012. doi:10.1093/cercor/bhr179.
- Smith PF, Zheng Y. From ear to uncertainty: vestibular contributions to cognitive function. *Front Integr Neurosci* 7: 84, 2013. doi:10.3389/fnint.2013.00084.
- Stephan T, Deuschländer A, Nolte A, Schneider E, Wiesmann M, Brandt T, Dieterich M. Functional MRI of galvanic vestibular stimulation with alternating currents at different frequencies. *Neuroimage* 26: 721–732, 2005. doi:10.1016/j.neuroimage.2005.02.049.
- Sugiuchi Y, Izawa Y, Ebata S, Shinoda Y. Vestibular cortical area in the periacute cortex: its afferent and efferent projections. *Ann N Y Acad Sci* 1039: 111–123, 2005. doi:10.1196/annals.1325.011.
- Sunaert S, Van Hecke P, Marchal G, Orban GA. Motion-responsive regions of the human brain. *Exp Brain Res* 127: 355–370, 1999. doi:10.1007/s002210050804.
- Suzuki M, Kitano H, Ito R, Kitanishi T, Yazawa Y, Ogawa T, Shiino A, Kitajima K. Cortical and subcortical vestibular response to caloric stimulation detected by functional magnetic resonance imaging. *Brain Res Cogn Brain Res* 12: 441–449, 2001. doi:10.1016/S0926-6410(01)00080-5.
- Taube JS. The head direction signal: origins and sensory-motor integration. *Annu Rev Neurosci* 30: 181–207, 2007. doi:10.1146/annurev.neuro.29.051605.112854.
- Taube JS, Goodridge JP, Golob EJ, Dudchenko PA, Stackman RW. Processing the head direction cell signal: a review and commentary. *Brain Res Bull* 40: 477–484, 1996. doi:10.1016/0361-9230(96)00145-1.
- Uesaki M, Ashida H. Optic-flow selective cortical sensory regions associated with self-reported states of vection. *Front Psychol* 6: 775, 2015. doi:10.3389/fpsyg.2015.00775.
- Uesaki M, Takemura H, Ashida H. Computational neuroanatomy of human stratum proprium of interparietal sulcus. *Brain Struct Funct* 223: 489–507, 2018. doi:10.1007/s00429-017-1492-1.
- Ventre-Dominey J. Vestibular function in the temporal and parietal cortex: distinct velocity and inertial processing pathways. *Front Integr Neurosci* 8: 53, 2014. doi:10.3389/fnint.2014.00053.
- Vitte E, Derosier C, Caritu Y, Berthoz A, Hasboun D, Soulié D. Activation of the hippocampal formation by vestibular stimulation: a functional magnetic resonance imaging study. *Exp Brain Res* 112: 523–526, 1996. doi:10.1007/BF00227958.
- Wada A, Sakano Y, Ando H. Differential responses to a visual self-motion signal in human medial cortical regions revealed by wide-view stimulation. *Front Psychol* 7: 309, 2016. doi:10.3389/fpsyg.2016.00309.
- Waespe W, Henn V. Neuronal activity in the vestibular nuclei of the alert monkey during vestibular and optokinetic stimulation. *Exp Brain Res* 27: 523–538, 1977. doi:10.1007/BF00239041.
- Walzl EM, Mountcastle VB. Projection of vestibular nerve to cerebral cortex of the cat. *Am J Physiol* 159: 595, 1949.
- Wardman DL, Taylor JL, Fitzpatrick RC. Effects of galvanic vestibular stimulation on human posture and perception while standing. *J Physiol* 551: 1033–1042, 2003. doi:10.1113/jphysiol.2003.045971.
- Wijesinghe R, Protti DA, Camp AJ. Vestibular interactions in the thalamus. *Front Neural Circuits* 9: 79, 2015. doi:10.3389/fncir.2015.00079.
- Wilson VJ, Peterson BW. Peripheral and central substrates of vestibulospinal reflexes. *Physiol Rev* 58: 80–105, 1978. doi:10.1152/physrev.1978.58.1.80.
- Wirth AM, Frank SM, Greenlee MW, Beer AL. White matter connectivity of the visual-vestibular cortex examined by diffusion-weighted imaging. *Brain Connect* 8: 235–244, 2018. doi:10.1089/brain.2017.0544.
- Yates BJ, Bolton PS, Macefield VG. Vestibulo-sympathetic responses. *Compr Physiol* 4: 851–887, 2014. doi:10.1002/cphy.c130041.
- Yates BJ, Miller AD. Physiological evidence that the vestibular system participates in autonomic and respiratory control. *J Vestib Res* 8: 17–25, 1998. doi:10.1016/S0957-4271(97)00035-9.
- zu Eulenburg P, Caspers S, Roski C, Eickhoff SB. Meta-analytical definition and functional connectivity of the human vestibular cortex. *Neuroimage* 60: 162–169, 2012. doi:10.1016/j.neuroimage.2011.12.032.