Evaluating the Rare Cases of Cortical Vertigo Using Disconnectome Mapping

Julian Conrad (✉ julian.conrad@med.uni-muenchen.de)

Ludwig-Maximilians-Universität München <https://orcid.org/0000-0001-7912-0571>

Rainer Bögle

Klinikum der Universität München Standort Grosshadern

Ria Maxine Ruehl

Klinikum der Universität München Standort Grosshadern

Marianne Dieterich

Klinikum der Universität München Standort Grosshadern

Research Article

Keywords:

Posted Date: March 3rd, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1370704/v1>

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Abstract

Objective In rare cases, cortical infarcts lead to vertigo. We evaluated structural and functional disconnection in patients with acute vertigo due to ischemic cortical infarcts compared to infarcts without vertigo in a similar location with a focus on the connectivity of the parieto-opercular (retro-)insular cortex (PIVC).

Methods Using lesion maps from the published case reports, we computed lesion functional connectivity networks (FCN) in a set of 100 healthy individuals from the human connectome project (HCP). The probability of lesion disconnection was evaluated by white-matter disconnectome mapping.

Results The lesion-FCN included vestibulo-cerebellar hubs (lobules IX, X), the vestibular nuclei, the PIVC (anterior and posterior long insular gyri, area OP2), the retroinsular and posterior insular cortex (area PIC), the multisensory vestibular ventral intraparietal area, motion-sensitive areas (temporal area MT+ and cingulate visual sulcus) as well as hubs for ocular motor control (lateral intraparietal area, cingulate and frontal eye fields). However, this was not sufficient to differentiate between lesions with and without vertigo. Disconnection of interhemispheric connections via the corpus callosum (CC) were present in all ten cases with rotational vertigo, but the CC was spared in lesions of the PIVC without vertigo. Further, the arcuate fascicle (AF) was affected in 90% of the lesions with vertigo and spared in lesions without vertigo.

Conclusion Disruption of interhemispheric connections of the PIVC via the corpus callosum and intra-hemispheric disconnection via the AF seem to be the distinguishing factor between vestibular cortical network lesions that manifest with vertigo compared to those without vertigo.

Introduction

The brain continuously receives interoceptive information about the current homeostatic state, such as the position of the head and body relative to gravity via the vestibular system.(Owens et al. 2018) The vestibular system is located at the crossroads between interoceptive monitoring and exteroceptive perception of the Self in an allocentric space.(Craig 2002; Nakul et al. 2020; Mellenthin et al. 2021) Its endorgans in both ears continuously monitor and update the position of the eyes and head relative to the body and to gravity during ego- and object-motion. To provide a unique and stable perception, bilateral vestibular inputs need to be integrated with somatosensory, proprioceptive, viscerosensitive and visual signals to form one common representation of the bodily Self.(Angelaki and Cullen 2008; Cullen 2012) If the sensory signals from both sides are in congruence and properly weighted, there is no conscious vestibular perception.(Day and Fitzpatrick 2005)

To forward vestibular information from the labyrinth, the central vestibular brainstem pathways are bilaterally organized and reach the thalamus and the cortical network hubs via multiple crossing and non-crossing ascending tracts.(Lang et al. 1979; Conrad et al. 2014; Kirsch et al. 2016) The ascending pathways of both sides mediate eye and head coordination in all spatial directions and the position of the head in space relative to the gravitational vector. Additionally, vestibular signals are integrated with other sensory qualities as early as on the level of the vestibular nuclei. This integrated nature ensures that bilateral multisensory signals reach the cortical vestibular network in both hemispheres.(zu Eulenburg et al. 2012; Lopez et al. 2012; Raiser et al. 2020)

An acute vestibular tone imbalance due to a unilateral peripheral or lower brainstem lesion causes severe disabling rotatory vertigo or dizziness with nausea, gait unsteadiness and falls. If lesions affect the upper parts of the central vestibular circuitry in the rostral midbrain, thalamus and cortical vestibular areas, in most instances no rotational vertigo is reported. (Anagnostou et al. 2010; Dieterich and Brandt 2015; Baier et al. 2016; Conrad et al. 2022a) This is independent of a psychophysically measurable vestibular tone imbalance that can occur such as tilts of the subjective perception of verticality.(Brandt et al. 1994; Baier et al. 2016; Conrad et al. 2022a) These perceptual tilts in cortical lesions have been attributed to the higher level of sensory integration. The change of the vestibular perception in acute lesions from rotational vertigo in labyrinthine and pontomedullary lesions to a swaying dizziness or diffuse gait imbalance can be explained by

different types of vestibular neurons at brainstem and cortical level with a shift from a velocity to a position signal in the upper midbrain, thalamus and cortex.(Taube 2007; Angelaki and Cullen 2008; Dieterich et al. 2018)

Whereas symptom recovery in peripheral and brainstem lesions lasts several weeks due to sensory substitution and vestibular compensation(Bronstein and Dieterich 2019; Conrad et al. 2020, 2022b), symptoms in thalamic and cortical vestibular lesions are often mild and short-lasting. One reason could be, that the contralesional hemisphere - where vestibular, somatosensory and visual signals are in congruence - might be able to compensate quickly for the acute vestibular cortical dysfunction suppressing the disturbing symptoms of an acute vestibular tone imbalance.(Dieterich and Brandt 2015) Alternatively, the sensory weighting in cortical processing could be shifted to the unaffected sensory qualities. This could be the explanation for the results of a systematic evaluation of cortical vestibular symptoms in patients with acute ischemic hemispheric stroke that did not find vestibular signs.(Anagnostou et al. 2010)

However, in rare instances, patients with cortical infarcts suffer from cortical vertigo or dizziness mostly when a circumscribed lesion affects the parietal-opercular (retro-)insular vestibular cortex (PIVC).(Dieterich and Brandt 2015) This is also true for some instances of direct electrical stimulation of the posterior parts of the insula in patients with focal epilepsy. (Penfield 1957; Mazzola et al. 2014) On the other hand, in a highly selective group of patients with small isolated infarcts restricted to the posterior insula only, no vertigo or deficits of verticality perception were reported.(Baier et al. 2013) This prompted the question why in some rare cases of cortical lesions, the vestibular imbalance reaches conscious perception while in the vast majority of patients this is not the case. Could it be due to connectivity and disturbance of functional connectivity in the vestibular cortical network? Therefore, in the current study we analysed the pattern of disconnection in the published case reports on cortical vertigo.(Dieterich and Brandt 2015) These results were compared with the lesions from the ten published patients with isolated insular infarcts without vertigo, dizziness or tilts of the SVV.(Baier et al. 2013) Our hypothesis was that infarcts that lead to vertigo or dizziness are more densely connected to multiple hubs within the cortical vestibular network and that especially a disconnection of interhemispheric projections might lead to cortical vertigo.

Methods

Case selection and lesion segmentation

We used the lesion figures provided in the original publications to create lesion overlap images of all ten infarcts that caused cortical vertigo provided by Dieterich and Brandt, 2015.(Brandt et al. 1995; Cereda et al. 2002; Debette et al. 2003; Naganuma et al. 2006; Ahn et al. 2010; Nakajima et al. 2012; von Brevern et al. 2014; Dieterich and Brandt 2015) The infarcts were manually delineated in MNI152 space using neighbouring relationships with anatomical landmarks (anterior and posterior commissures, ventricles, distal fornix, internal capsule, thalamus, and the basal ganglia).(Dieterich and Brandt 2015) Lesions were extended 2 mm from the location reported in the literature.(Boes et al. 2015) For comparison, we used the lesion overlap of the ten patients with insular infarcts without vestibular deficits from Baier and colleagues.(Baier et al. 2013) All lesion maps were cross-checked by three experienced raters (JC, RB, RMR).

Disconnectome mapping

Structural disconnection

We used the tractography-based method implemented in the BCB toolkit (<http://toolkit.bcbi-lab.com/>) to calculate the probability of disconnection of specific white matter tracts for each lesion.(Foulon et al. 2018) High resolution (7T) tractography data of 170 healthy participants from the Human Connectome Project (HCP) was used to track fibers that pass through each individual lesion. The patients' lesions in MNI space are registered to the native space of each healthy participant's tractography data using affine and deomorphic deformations.(Klein et al. 2009; Avants et al. 2011) This seed is then used to perform the tractography in TrackVis (<http://www.trackvis.org/>). The results are transformed to visitation maps, binarized and registered to MNI152 space. From these maps, the percentage of overlap of each voxel in the normalized subject visitation maps is depicted as the voxel-wise probability of disconnection for each lesion. The number of voxels

within the individual disconnectome map was thresholded at 0.5 (50% or higher probability of disconnection). In addition, we quantified the probability of disconnection using Tractotron.(Thiebaut de Schotten et al. 2014).

Functional connectivity

In analogy to the structural dis-connectivity, we aimed to determine which functional network connectivities were disrupted by the lesions. While structural connectivity might be more appropriate to study local connectivity of the lesion, the functional imaging approach could be more suitable for bottom-up interoceptive processes that influence multiple distant functional networks. Therefore, distant networks which include the lesion sites could also be important for the lost function and occurrence of vertigo.

We used the human connectome project (HCP) “100 unrelated subjects” pre-processed resting-state fMRI dataset from the Human Connectome Project (HCP, <https://www.humanconnectome.org/>), Release Q3. These data contained fMRI resting-state acquisitions from 100 unrelated subjects (54 females, 46 males, mean age = 29.1 ± 3.7 years, 2 runs of 14 minutes 33 seconds each, one with phase encoding left to right and the other in the opposite direction) of the HCP 900 data release.(Van Essen et al. 2012)

Data were processed following the HCP functional pre-processing guidelines.(Glasser et al. 2013; Smith et al. 2013) Briefly, processing steps included artifact removal, motion correction, and registration to standard Montreal Neurological Institute space in volumetric format, with weak high pass temporal filtering ($> 2,000$ s full width at half maximum), for slow drift removal.(Smith et al. 2013) MELODIC ICA was applied to volumetric data, and artifact components were subsequently identified using FSL-FIX.(Jenkinson et al. 2012; Salimi-Khorshidi et al. 2014) Artifacts and motion-related time courses (i.e., the six rigid-body parameter time series, their backward-looking temporal derivatives, plus all 12 resulting regressors squared) were then regressed out of volumetric data.(Smith et al. 2013)

Individual Lesion - Functional Connectivity Networks (Fcn)

Each lesion map was used as the starting point for a whole brain correlation analysis. Each lesion mask is used to create the mean time course of the region and this time course is then used for correlation with the time courses of all other voxels in the brain.

Contrasts were created to determine the differences in connectivity that distinguish the lesion sites that produce vertigo from the lesion sites that do not produce vertigo using SPM12.

Results

Lesion localization

The ischemic lesions were centered around the insula, involving mainly the posterior parts (anterior long insular gyrus (IV) and posterior long insular gyrus (V)), and extended to the anterior insula. Representative slices for each case and the lesion overlap from(Baier et al. 2013) are depicted in Fig. 1. One lesion also covered the parietal opercular vestibular region OP2(Brandt et al. 1995) and another one was located in the left intraparietal sulcus encompassing the vestibular multisensory area VIP (ventral intraparietal area).(Naganuma et al. 2006) Furthermore, one lesion extended towards the temporal lobe and included the motion sensitive area MT+.(von Brevern et al. 2014) Putative cortical vestibular structures affected by the lesions are shown in Fig. 2.

Structural disconnection

Disconnectome maps for all individual lesions were calculated using a threshold of 0.5 ($> 50\%$ probability of a tract being disconnected by the lesion). Common disconnection of all lesions (with vertigo: lesions 1–10, without vertigo: lesion overlaps

11, 12) involved the posterior parts of the fronto-insular tracts (mainly fronto-insular tracts 4 and 5) which connect the parietal operculum with the posterior parts of the insula and the inferior fronto-occipital fascicle (IFOF). The third branch of the superior longitudinal fascicle (SLF III) was also preferentially affected. Interestingly, two white matter tracts were disconnected in the lesions with vertigo but were spared in the lesions without vertigo (posterior segments of the arcuate fascicle 9/10 and fibers of the corpus callosum 10/10 in with vertigo cases). **Table 1** shows the probability of specific white matter tracts being disconnected. The two white matter tracts that were disconnected in the cases with vertigo but spared in the lesions without vertigo are highlighted in bold print. Disconnection with two distinct brainstem pathways was detected connecting the pontomedullary brainstem (vestibular nuclei region) with the PIVC, one of these seemingly bypassing the thalamus while the other enters the lateral thalamic nuclei. In addition, disconnection was observed with the superior cerebellar peduncle. (Fig. 3, lesion-disconnection of vertigo associated lesions only). Individual disconnectome maps for each lesion are shown in the online supplement (**supplementary Fig. 1**).

Functional disconnection

The overlap of all individual lesion functional connectivity network (FCN) maps was calculated to evaluate the common network structure for cortical lesions that caused vertigo. Figure 5 shows the overlap of eight or more FCNs in the group with vertigo. The individual lesion FCNs are shown in **supplementary Fig. 2**. The common subcortical components of the FCNs include the vestibular nuclei (VN), the cerebellar vestibular and ocular motor representations in lobules IX (nodulus, uvula) and X (flocculus / paraflocculus). Cortical network hubs included the PIVC, posterior insular cortex (PIC) and adjacent superior temporal gyrus but also more distant vestibular multisensory areas such as the ventral intraparietal area (VIP), motion-sensitive areas MT + in the temporal lobe and cingulate visual sulcus (CSv) and ocular motor areas of the parietal (lateral parietal area - LIP) and frontal lobes (frontal eye fields, FEF, and dorsolateral prefrontal cortex, DLPFC). Additional connectivity was also seen with primary somatosensory and visual cortex. However, when the seed of the lesion without vertigo overlaps were considered individually (lesions 11,12), a strikingly similar network emerged. (**Fig. 6**)

Discussion

The main findings of this lesion disconnectome study were as follows: i) Lesions that caused vertigo compared to those without vertigo disconnected parts of the cortical vestibular network and interhemispheric connections via the corpus callosum and the posterior parts of the arcuate fascicle. ii) A common lesion-FCN involved cerebellar lobules IX, X, the vestibular nuclei, the thalamus, the PIVC (anterior / posterior long gyrus, retroinsular cortex, OP2), posterior insular cortex (area PIC), parietal multisensory vestibular area VIP, the parietal, frontal and cingulate eye-fields (area LIP, FEF, CEF), and motion-sensitive areas of the temporal lobe (MT+) and cingulate cortex (CSv). However, this did not seem sufficient to explain cortical vertigo as these structures were also part of the lesion-FCN of patients without vertigo.

Lesion functional connectivity mapping

The individual lesion-FCNs emphasized the network aspect of the cortical vestibular system. (Bense et al. 2001; Dieterich et al. 2003; Raiser et al. 2020) The functional connectivity showed involvement of the VN, the cerebellar vestibular lobules IX, X and the cortical vestibular and multisensory areas (PIVC (insular gyri IV, V, OP2, Ri), area PIC, area VIP, MT+, CSv). (Raiser et al. 2020) Fittingly, we found functional connectivity with components of the cortical ocular motor centers in the cerebellum, parietal, cingulate and frontal lobes (ocular motor vermis (OMV), areas LIP, CEF, FEF). A close interaction of the vestibular and ocular motor system is known, as demonstrated in existing imaging evidence. (Dieterich et al. 2009; zu Eulenburg et al. 2012)

Interestingly, the patterns of the established FCNs did not substantially differ between the lesions that led to cortical vertigo compared to those that did not. Therefore, a lesion-FCN difference based only on the location and extent of the lesions was not sufficient to explain the differences between lesions with vertigo and those without vertigo.

White matter disconnection

Using disconnectome mapping we identified two distinct white matter structures that were lesioned in 9/10 (AF) and 10/10 (CC) with vertigo cases but were spared in the lesion overlaps of cases without vertigo.

Posterior segment of the arcuate fascicle

The arcuate fascicle is part of the superior longitudinal fiber system that comprises the SLF (I-III) and the arcuate fascicle. (Vavassori et al. 2021) It connects the inferior, middle and superior temporal gyri and the supramarginal gyrus with the frontal operculum (pars opercularis, pars triangularis), middle frontal gyrus (MFG) and the ventral premotor cortex and is left-lateralized. (Fernández-Miranda et al. 2015) Its posterior portion connects the temporal parts with the supramarginal gyrus (SMG) and angular gyrus (AG) of the inferior parietal lobule (IPL).

While these tracts run in close proximity to the insular and parietal opercular cortex, terminations in these regions seem not to exist. In terms of function, the left AF is recognized as part of the language network (Forkel et al. 2011, 2020). The function of the right AF is far less well-defined but has been implicated in the ability to recognize the mental state of others. (Herbet et al. 2014) A role of the AF in vestibular processing has not been proposed up to now; therefore, a theoretical framework to explain the affection of the AF does not exist yet. In our opinion, this might be an epiphenomenon of lesions that affect the PIVC and underlying white matter.

Corpus callosum

The CC is the largest white matter tract of the human brain and is the main interhemispheric connection in humans. Parcellations of the CC have been proposed on anatomical landmarks, histology, structural connectivity, functional connectivity gradients and simple geometry. (Witelson 1989; Aboitiz and Montiel 2003; Hofer and Frahm 2006; Friedrich et al. 2020) The anterior and mid-portions project to the prefrontal and motor cortex, while the more posterior regions connect the temporal, parietal and occipital lobes. An interhemispheric connection of the PIVC has been described by DTI via the posterior parts of the CC. (Kirsch et al. 2016; Wirth et al. 2018). Indeed, in patients with subcortical ischemic strokes presenting with vestibular symptoms, vestibular recovery / compensation took place over time and was accompanied by volumetric changes in the posterior portions of the CC using voxel-based morphometry. (Conrad et al. 2022a, b). In addition, volumetric increases were also seen in the white matter around the PIVC after recovery of perceptual deficits, i.e., tilts of the SVV. (Conrad et al. 2022b) These volumetric increases of the CC also map to the interhemispheric connection between the PIVCs of both hemispheres.

Interhemispheric connectivity of the PIVC

Based on the current data, we provide evidence for the theory that interhemispheric inhibitory connections from the contra-lesional (intact) PIVC can suppress the perception of vertigo. (Dieterich and Brandt 2015) Visual and vestibular inputs have to be matched for the proper detection of the position of head and body in space relative to the gravitational vector to provide a congruent perception of position and motion in space. In healthy individuals, there are no diverging visual and vestibular perceptions. (Brandt 1997) In the case of lesions to the PIVC, the mismatch between vestibular and visual inputs could be detected by a central predictor via a feedback loop connecting both hemispheres where the predicted input is compared with the actual sensory input. (Brandt et al. 2005) The visual-vestibular signal which best matches the predicted input then is further processed while the input from the lesioned hemisphere is suppressed. In contrast, if the interhemispheric connection between the PIVC is disturbed, the intra-hemispheric visual-vestibular mismatch and / or the interhemispheric mismatch is perceived as cortical vertigo.

Limitations

The current study was based on case reports of rare patients with cortical infarcts that led to vertigo. In these publications, single slices depicting the lesions are presented. Therefore, the constructed lesion maps are approximations of these lesions. Here, an approach was chosen that has been previously reported to provide reliable results. (Boes et al. 2015; Darby et al.

2018; Cohen et al. 2019) In our opinion, the current results provide the most accurate evidence for interhemispheric disconnection in these patients with cortical infarcts to date. Because of the rarity of cortical vertigo, a systematic prospective evaluation of cortical vertigo was not helpful to answer this particular research question.(Anagnostou et al. 2010)

We used the lesion maps of the individual lesions with vertigo and the lesion overlap of the lesions without vertigo for the fc analysis. However, it is possible that subcomponents of the lesion FCN between lesions with and without vertigo might differ. A more fine-grained voxel-by-voxel analysis of connectivity differences might decipher subtle FCN differences both groups. (Kirsch et al. 2018)

Conclusions

Lesions that cause vertigo are part of FCN that connects the vestibulo-cerebellum, the vestibular nuclei, the PIVC, area PIC, vestibular multisensory area VIP, temporal (MT+) and cingulate motion-sensitive areas (CSv) as well as parietal, cingulate and frontal ocular motor areas (LIP, CEF, FEF). However, a lesion-FCN does not explain the occurrence of cortical vertigo in rare cases, as the same lesion-FCN also emerged when small infarcts of the posterior insula were considered that did not cause vertigo. A structural disconnection of the posterior parts of the CC and the arcuate fascicle was found to be the distinguishing factor between lesions that caused vertigo (structural interhemispheric disconnection) and lesions that did not (CC and AF spared).

Declarations

Author contributions

All authors contributed to the study conception and design. Data collection and analysis were performed by Julian Conrad, Rainer Boegle, and Ria Maxine Ruehl. . All authors read and approved the final manuscript.

Funding

This work was supported by the Bundesministerium für Bildung und Forschung (BMBF, grant # E0091 to MD), the support program for research and education at LMU (FöFoLe-LMU, grant no 1065 to JC) and the German Foundation for Neurology (Deutsche Stiftung Neurologie to MD).

Acknowledgements

We thank Katie Goettlinger for copy-editing the manuscript.

Ethics approval

The study was performed in accordance with the 1964 Declaration of Helsinki (latest applicable revision Fortaleza 2013) and approved by the institutional review board of LMU Munich, Germany (no.094-10). All HCP scanning protocols were approved by the local Institutional Review Board at Washington University in St. Louis, and all healthy subjects gave written informed consent to the HCP consortium.

Data availability

The individual lesion and disconnectome maps will be publicly available upon publication (<https://osf.io/tr8x2/>).

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Tables

Table 1 Probability of white matter disconnection for each lesion with vertigo and the lesion overlap of lesions that did not cause vertigo (n=10).

	Left-sided lesions				Right-sided lesions						L	R
tract lesion	□	□	□	□	□	□	□	□	□	□	□	□
AC	0.232	0.071	0	0	0	0.288	0	0	0	0.464	0	0
Anterior thalamic projections	0	0	0.5	1	0	0.24	0	0	0.66	0	0	0
Arcuate fascicle												
Arcuate anterior segment	0.94	0.013	0.26	0.96	0.82	0.24	0.38	0.6	0	0.48	0	0.215
Arcuate long segment	0.48	0.291	0.48	0.9	0.74	0.2	0.3	0.5	0	0.92	0	0
Arcuate posterior segment	0.56	0.34	0.7	0.88	1	0.6	0.56	0.88	0.728	1	0	0
Corpus callosum	0.792	0.728	0.824	0.808	0.992	0.928	0.92	0.944	0.728	1	0.26	0.488
Cortico-spinal tract	0.352	0	0.488	0	0.528	0.64	0.28	1	1	0.48	0	0
Face-U tract	0.571	0	0	0	0	0	0	0	0	0.279	0	0
Fornix	0	0	0	0	0	0	0	0	0	0.344	0	0
Frontal Aslant	1	0.019	0	0	0	0	0.24	0.44	0	0	0.24	0
Frontal commissure	0.38	0	0	0	0	0	0	0	0	0	0	0
Fronto-insular tracts												
Fronto-insular tract 1	0.12	0	0	0	0	0	0	0	0	0	0.05	0.26
Fronto-insular tract 2	0.34	0	0	0	0	0	0.24	0.64	0	0	0	0.26
Fronto-insular tract 3	0.7	0.52	0	0	0	0.66	0.94	0.92	0	0	0.68	0.86
Fronto-insular tract 4	0.98	0.96	0.92	0	0.48	0.098	1	1	0	0	0.94	0.98
Fronto-insular tract 5	0.94	0.98	0.98	0	1	1	1	1	1	0.64	0.92	1
Fronto-striatal	0.94	0.88	0.9	0	0.56	0.66	0.56	1	0.94	0.4	0.56	0.24
Hand-inferior-U tract	0.388	0	0	0.5	0	0	0	0	0	0		
Hand-inferior-U tract	0	0	0	0	0	0	0	0	0	0		
IFOF	1	0.98	0.46	0	0.82	0.86	0	0.68	0.34	1	0.72	0.84
ILF	0.28	0	0	0	0.776	0.64	0	0.352	0	1	0.002	0.232
Optic radiation	0.36	0.26	0	0	0	0.376	0	0.24	0	0.864	0	0
Pons	0.22	0.223	0.92	0	0.46	0.46	0	1	1	0	0	0
Superior longitudinal fascicle (SLF)												
SLF I	0	0	0	0	0	0	0	0	0	0.656	0	0
SLF II	0.208	0	0	0.992	0.784	0	0	0	0	0.826	0	0
SLF III	0.928	0.336	0.488	1	1	0.704	1	0.992	0.336	1	0.32	0.63
Uncinate	0.78	0	0	0	0	0	0	0	0	0	0.76	0.07

Figures

Figure 1

A Representative axial slices for each lesion of the published case reports on hemispheric lesions associated with (lesions 1-10) and without vertigo (lesion-overlap of 10 cases; 11-12). Left-sided lesions with vertigo are shown in the top row. Lesions

were manually delineated in MNI152 space using anatomical landmark neighbouring relationships.

Figure 2

A Overlap image of ischemic infarcts involving the insula (overlap of at least 2 lesions is depicted): The ischemic lesions were mainly located in the posterior parts of the insula (anterior long insular gyrus and posterior long insular gyrus - IV, V). **B** In rare cases, the lesions involved vestibular structures in the parietal operculum (OP2), the intraparietal sulcus (area VIP) and the temporal lobe (MT+). None of the lesions directly affected area PIC; however, lesion 5 is in close proximity to this structure.

OP2, parietal operculum 2; MT+, motion sensitive middle temporal area; VIP, ventral intraparietal area; PIC, posterior insular cortex, IV anterior insular long gyrus, V posterior insular long gyrus.

Figure 3

Disconnectome map of all ten lesions that manifested with vertigo. Disconnectome results are thresholded at 0.5 (> 50% probability of disconnection). Disconnection was observed for the posterior fronto-insular tracts (IV, V) that connect the posterior insula with the opercula. Intrahemispheric disconnection affected the arcuate fascicle and the superior longitudinal fascicle (SLF, mostly third branch). Interhemispheric disconnection was observed in the splenium of the corpus callosum. Additionally, disconnection was observed with the vestibular nuclei group in the pontomedullary brainstem (possibly via the medial longitudinal fascicle and medial lemniscus) and also with the cerebellum via the superior cerebellar peduncle.

Figure 4

Overlap of functional connectivity networks (FCN) of the individual lesions (positive correlations with the lesion site). The individual lesion-network maps are thresholded at $p < 0.001$, FWE corrected for multiple comparisons after calculating 10 000 permutations using TFCE. The figure shows an overlap of eight or more cases. Common vestibular network hubs to all lesions include the cerebellar vestibular and ocular motor representations in lobules IX (nodulus, uvula), lobule X (flocculus / paraflocculus), the vestibular nuclei (VN), the thalamus, the parieto-insular vestibular cortex (PIVC; includes insular gyri IV, V (anterior and posterior long insular gyri), area OP2, and retroinsular cortex), the posterior insular cortex (area PIC), motion-sensitive temporal and cingulate areas MT+ and CSv (cingulate visual area), ocular motor and vestibular intraparietal areas LIP and VIP (lateral and ventral intraparietal area), the frontal and cingulate eye fields (FEF, CEF). The color bar gives the number of overlapping lesion-FCNs.

Figure 5

Figure 5 shows the FCN of the right- and left-sided lesions of the posterior insula that did not lead to vertigo / dizziness (n=10 cases). The FCN observed in these lesions was remarkably similar, involving the vestibulo-cerebellum and the cortical vestibular and ocular motor networks. All results thresholded at $p < .001$, FWE corrected for multiple comparisons on the cluster level after 10 000 permutations using TFCE. The color bar shows t-score intensities. IX, X cerebellar lobules IX, X, MT+ motion-sensitive temporal area, PIVC parieto-opercular (retro-)insular vestibular cortex, PIC posterior insular cortex, FEF frontal eye field, CEF cingulate eye field, LIP / VIP lateral / ventral intraparietal area, CsV cingulate visual sulcus.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [IndividualDisconnectome.eps](#)

- IndividualFCN.eps