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LETTER TO THE EDITORS

Vestibular and visual cortex activity during room tilt illusion

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Dear Sirs,

A sudden attack of transient upside-down inversion of vision is called a room tilt illusion (RTI), a rare clinical syndrome caused by false cortical integration of vestibular and visual cues for the perception of verticality. Usually, this mismatch of the cortical visual and vestibular 3D coordinate maps is caused by an acute vestibular tone imbalance [1–3]. The patient experiences either paroxysmal 90° tilts of the visual scene or 180° ("upside-down") vision without any alteration of the object's color, shape, or size [1, 4]. RTI occurs in various peripheral (bilateral vestibular failure, Méniere's disease) and central vestibular disorders, most notably in patients with lower brainstem infarctions [4–6], cortical lesions [7], or vestibular epilepsy [8]. The particular role that the visual and vestibular cortices and their intrahemispheric and transhemispheric interactions play in the pathophysiological mechanism remains unclear. We investigated this question in a patient who could voluntarily elicit repetitive, clockwise 90° tilts (perceived image tilted to the right) while lying in a magnetic resonance (MR) scanner.

The 61-year-old right-handed male patient had perceived an RTI once or twice a year for 8 years, mostly when he absentmindedly lay down on his back on the bed. RTIs did not occur when he was upright. The patient also reported having had paroxysmal attacks of rotational vertigo and trigeminal pain on the left side over the last 18 years after making quick head movements to the left. This was due to a megadolicho-basilar artery with fusiform dilatation and direct contact to the left 5th, 7th, and 8th cranial nerves (including the root entry zones) and to a displacement of the brainstem structure to the right (Fig. 1a). RTIs occurred whenever the patient lays supine, resting on the back of his head. Caloric irrigation showed that horizontal semicircular canal function was preserved, but there was a side difference of 23% left < right; adjustment of the subjective visual vertical was normal.

The aim of this study was to investigate both the chronic structural and acute functional correlates of RTI using a bimodal approach to image the main vestibular and visual cortical areas of the patient who experienced continuous RTI during measurement in the MR-scanner and to compare these findings with those of a group of 20 healthy subjects (right-handed, 10 males; age range 47–71 years, mean age 58.4 ± 7.8 years; normal video-head impulse test and subjective visual vertical).

The structure [9] was investigated with white and gray matter voxel-based morphometry (VBM_{wm}, VBM_{gm}), and

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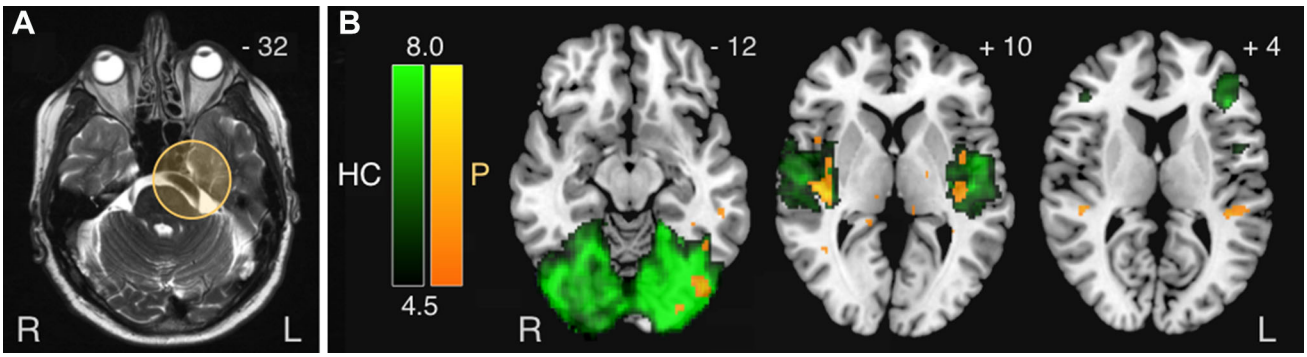

Fig. 1 **a** Depiction of the patient's megadolicho-basilar artery with pronounced fusiform dilatation to the left side of the brainstem (view *yellow circle*); direct contact to the left 5th, 7th, and 8th cranial nerves (including the root entry zones) and a displacement of the brainstem to the right. **b** Seed-based fcMRI average ($p < 3.4e{-}06$ uncorrected; $z = 4.5$) for the patient (P) during a 90° clockwise room tilt illusion (RTI; *yellow*) in comparison to the healthy control group (HC; *green*) without RTI. The three sections represent three seed regions: primary visual cortex V1 (**b** *left*), parieto-insular vestibular cortex (PIVC; **b** *middle*), and V5 (**b** *right*). Note that PIVC and V1 were downregulated and lateralized (to the right Ig2 for PIVC and the left V5 for V1) when compared to HCs (see Table 1), whereas for the seed V5, the left OP1 and right Ig1 were activated in the patient, whereas in the HCs, the anterior intra-parietal sulcus (hIP1) and frontal lobe (BA45) were merely activated bilaterally

function [10] with seed-based functional connectivity magnetic resonance imaging (fcMRI). Data acquisition parameters were published in a previous study [11]. Participants had no other requirement than to keep their eyes open and fixate on one point, to remain still, and not to fall asleep. Institutional Review Board (IRB) approval was obtained prior to beginning the study. Participants provided their informed oral and written consent in accordance with the Declaration of Helsinki. Data processing was done in FSL (v5.0.9), AFNI (http://afni.nimh.nih.gov/afni), and in-house scripts as previously described [12]. Regions of interest (ROI) was extracted from the probabilistic Juelich histological (cyto- and myelo-architectonic) atlas and included the core area of the vestibular cortical network, the parieto-insular vestibular cortex (PIVC; Ig1 and OP2), the primary visual area V1, and the main vestibulo-visual area for movement perception V5. Statistical analyses were performed with R (version 3.23) and IBM SPSS Statistics software package (Version 20). The analyses included a proportion correction method [13] for determining the intracranial volume (ICV) to correct for variations in ICV between the patient (P) and the healthy control group (HC).

As a structural correlate (in mm^3), no pronounced differences between P and HC were found in gray or white matters in the regions of the PIVC (P_{gm} 124, HC_{gm} 126 ± 23; P_{wm} 147 mm^3, HC_{wm} 109 ± 8), V1 (P_{gm} 4590, HC_{gm} 4773 ± 570; P_{wm} 6738, HC_{wm} 4993 ± 960), or V5 (P_{gm} 456, HC_{gm}352 ± 35 mm^3; P_{wm}472 mm^3, HC_{wm}493 ± 49). For the functional correlate, the seed-based fcMRI average comparison showed on a descriptive level ($z \geq 4.5$; $p < 3.4e{-}06$ uncorrected) fewer and more lateralized activations for the seed PIVC and V1 (to the right Ig2 for the PIVC and the left V5 for V1) when compared to the HCs (Table 1; Fig. 1b). Notably, the patient's V5 activated more in the left OP1 and right Ig1 when compared to the HCs, who activated bilaterally in the anterior intra-parietal sulcus (hIP1) and frontal lobe (BA45).

These results, especially the localization of the vestibular and visual networks, are in line with the previous PET and fMRI studies, e.g., on patients with peripheral and central vestibular disorders [14, 15]. This case of RTI allows some hypothetical explanations of both the direction of the visual tilts (perception) and the pattern of fcMRI (pathomechanism) within the vestibular and visual cortex areas in both hemispheres:

(i) When the patient was in the supine position, the left 8th nerve was compressed by the megadolicho-basilar artery. This could cause excitation of the vestibular nerve fibers by ectopic discharges [16]. The patient would perceive either a counterclockwise body rotation (not reported) or a relative clockwise tilt of the visual scene (reported). Thus, vestibular excitation of the left 8th nerve was perceived as a visual tilt. This interpretation agrees with the view of a RTI as a disorder of visual-vestibular integration.

(ii) Seed-based fcMRI detected bilateral changes of vestibular and visual cortex activity in the patient during RTI. Compared to the activity in controls, the activity of the patient's vestibular insular cortex was downregulated, maintaining more activity in the (vestibular) dominant right hemisphere; the same was true for the primary visual cortex activity, which, however, was more

Table 1 Overview of the seed-based fcMRI analyses

Seed of interest	Laterality	Cluster/brain area	Brodman's area	Number of voxels	MNI coordinates		
					x	*y*	*z*
(A) Seed-based analysis. Brain regions showing significant connectivity in the healthy control group (HC); cluster size ≥10 voxels							
PIVC	L	(1) OP2 L	–	11	−40	−22	20
		(2) OP2 R	–	10	36	−14	12
	R	OP2 R	–	11	40	−18	20
V1	L	V4 L	18	17	−30	−88	−10
	R	V5 R	37	12	48	−64	2
V5	L	(1) hIP1 L	40	17	−38	−52	40
		(2) FL L	45	11	−42	42	18
		(3) PMC	6	11	−28	2	58
	R	hIP1 R	7	11	38	−56	52
(B) Seed-based analysis. Brain regions showing significant connectivity in the patient (P) within the respective HC cluster with exception of V5, since the activation did not overlap; cluster size ≥4 voxels							
PIVC	L	(1) Ig2 L	22	8	−42	−22	2
		(2) Id2 R	–	7	40	−20	4
	R	(1) Ig2 R	–	8	40	−14	4
		(2) Ig2 L	–	8	−40	−16	2
V1	L	V5 L	–	6	−46	−76	−6
	R	–	–	–	–	–	–
V5	L	(1) OP1 L	–	5	−50	−32	−50
		(2) Ig2 R	–	4	38	−24	4
	R	(1) OP1 L	–	5	−50	−36	10
		(2) Ig1 R	–	4	36	−26	8

FL frontal lobe, *hIP* anterior intra-parietal sulcus, *I* insula, *L* left, *OP* parietal operculum, *PMC* premotor cortex, *R* right, *V* visual cortex

reduced in the right hemisphere. This is compatible with a functional suppression of the distressing visual-vestibular mismatch [15, 17].

(iii) A bilateral temporo-parietal region centering on the left OP1 and right Ig1 in the patient was activated during RTI attacks. With some reservations, one might suggest that this multisensory temporo-parietal region may be engaged in resolving the visual-vestibular mismatch to restore a reliable global perception of verticality.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no competing financial interests.

References

1. Brandt T (1997) Cortical matching of visual and vestibular 3D coordinate maps. Ann Neurol 42:983–984. doi:10.1002/ana.410420624
2. Brandt T, Strupp M, Dieterich M (2014) Towards a concept of disorders of "higher vestibular function". Front Integr Neurosci 8:47. doi:10.3389/fnint.2014.00047
3. Brandt T, Dieterich M (1999) The vestibular cortex: its locations, functions, and disorders. Ann N Y Acad Sci 871:293–312. doi:10.1111/j.1749-6632.1999.tb09193.x
4. Sierra-Hidalgo F, De Pablo-Fernández E, Martín AHS et al (2012) Clinical and imaging features of the room tilt illusion. J Neurol 259:2555–2564. doi:10.1007/s00415-012-6536-0
5. Ropper AH (1983) Illusion of tilting of the visual environment. Report of five cases. J Clin Neuroophthalmol 3:147–151
6. Tiliket C, Ventre-Dominey J, Vighetto A, Grochowicki M (1996) Room tilt illusion. A central otolith dysfunction. Arch Neurol 53:1259–1264
7. Solms M, Kaplan-Solms K, Saling M, Miller P (1988) Inverted vision after frontal lobe disease. Cortex 24:499–509
8. Smith BH (1960) Vestibular disturbances in epilepsy. Neurology 10:465–469
9. Ashburner J (2007) A fast diffeomorphic image registration algorithm. Neuroimage 38:95–113. doi:10.1016/j.neuroimage.2007.07.007

10. Biswal BB, Mennes M, Zuo X-N et al (2010) Toward discovery science of human brain function. Proc Natl Acad Sci 107:4734–4739. doi:10.1073/pnas.0911855107
11. Kirsch V, Keeser D, Hergenroeder T et al (2016) Structural and functional connectivity mapping of the vestibular circuitry from human brainstem to cortex. Brain Struct Funct 221:1291–1308. doi:10.1007/s00429-014-0971-x
12. Karch S, Keeser D, Hümmer S et al (2015) Modulation of craving related brain responses using real-time fMRI in patients with alcohol use disorder. PLoS One 10:e0133034. doi:10.1371/journal.pone.0133034
13. O'Brien LM, Ziegler DA, Deutsch CK et al (2011) Statistical adjustments for brain size in volumetric neuroimaging studies: some practical implications in methods. Psychiatry Res 193:113–122. doi:10.1016/j.pscychresns.2011.01.007
14. Lopez C, Blanke O (2011) The thalamocortical vestibular system in animals and humans. Brain Res Rev 67:119–146. doi:10.1016/j.brainresrev.2010.12.002
15. Dieterich M, Brandt T (2008) Functional brain imaging of peripheral and central vestibular disorders. Brain 131:2538–2552. doi:10.1093/brain/awn042
16. Arbusow V, Strupp M, Dieterich M et al (1998) Alternating episodes of vestibular nerve excitation and failure. Neurology 51:1480–1483
17. Bense S, Bartenstein P, Lochmann M et al (2004) Metabolic changes in vestibular and visual cortices in acute vestibular neuritis. Ann Neurol 56:624–630