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SHORT COMMUNICATION

Vestibular compensation of otolith graviceptive dysfunction in stroke patients

Bernhard Baier[1,2] | Hannah Cuvenhaus[3] | Notger Müller[4] | Frank Birklein[2] | Marianne Dieterich[5,6,7]

[1]Edith-Stein-Fachklinik, Bad Bergzabern, Germany

[2]Department of Neurology, University of Mainz, Mainz, Germany

[3]Median Klinik NRZ,, Wiesbaden, Germany

[4]German Center for Neurodegenerative Diseases, Magdeburg, Germany

[5]Department of Neurology, University Hospital, Ludwig-Maximilians-University, Munich, Germany

[6]German Center for Vertigo and Balance Disorders—DSGZ, University Hospital, Ludwig-Maximilians-University, Munich, Germany

[7]SyNergy—Cluster for Systems Neurology, Munich, Germany

Correspondence
Bernhard Baier, Department of Neurology, Edith-Stein-Fachklinik, Wiesenstr. 25, 76887 Bad Bergzabern, Germany.
Email: baierb@uni-mainz.de

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Abstract

Background and purpose: A sensitive and frequent clinical sign of a vestibular tone imbalance is the tilt of the perceived subjective visual vertical (SVV). There are no data yet focusing on lesion location at the cortical level as a factor for predicting compensation from the tilt of the SVV.

Methods: With modern voxelwise lesion behavior mapping analysis, the present study determines whether lesion location in 23 right-hemispheric cortical stroke patients with an otolith dysfunction could predict the compensation of a vestibular tone imbalance in the chronic stage.

Results: Our statistical anatomical lesion analysis revealed that lesions of the posterior insular cortex are involved in vestibular otolith compensation.

Conclusion: The insular cortex appears to be a critical anatomical region for predicting a tilt of the SVV as a chronic disorder in stroke patients.

KEYWORDS
compensation, insular cortex, stroke, subjective visual vertical

INTRODUCTION

One frequent clinical sign of an acute vestibular lesion is a tilt of the perceived subjective visual vertical (SVV), indicating a tone imbalance in the roll plane due to an acute dysfunction of graviceptive pathways. This tone imbalance is caused by unilateral lesions of either the peripheral vestibular end organ or the pathways from the vestibular nuclei in the medullary brainstem via the thalamus to vestibular areas at the cortical level. Previous animal studies in macaque monkeys have shown that the parieto-insular vestibular cortex seems to be the "core" region within the vestibular cortical network [1]. The human homologue of this core region was assigned to an area including the posterior insular cortex (IC), retroinsular cortex and parietal operculum [2]. Unilateral lesions of the IC within this

cortical network indeed lead to deficits of vertical perception, that is, tilts of the SVV [3–5]. These SVV tilts from cortical lesions are transient, of a mild extent (4°–6°) and can deviate to the ipsilateral or contralateral side [3–5].

With respect to vestibular compensation of SVV tilts, it is known that patients with medullary brainstem infarctions show a normalization within 14–30 days [6,7] similar to that in patients with cerebellar infarctions within 12 days [8]. Concerning lesion location as a factor for predicting vestibular compensation in patients with cerebellar infarctions, mainly lesions of the cerebellar hemispheres (lobules V, VI, VIIa) were able to hinder vestibular compensation [9]. To date, there are no data focusing on lesion location at the cortical level as a factor for predicting compensation of a tilt of the SVV. Hence, our aim was to examine which lesion location in 23 right-hemispheric cortical stroke patients with an otolith graviceptive dysfunction could predict the compensation of a vestibular tone imbalance in the chronic stage.

METHODS

Subjects

Twenty-three patients (12 female; mean age 67.6 ± 11.1 years) with first-ever right-hemisphere acute ischaemic lesions as demonstrated by magnetic resonance imaging (MRI) and initially tested with pathological tilts of the SVV [3] participated in the study (see Table 1). Because lesions of the left middle cerebral artery territory are often associated with aphasia, making testing difficult, patients with left-hemispheric infarctions were not tested. The initial clinical testing of the acute/subacute stroke patients was carried out at a mean of 7.4 days post-stroke (initial phase), whereas the second clinical testing was done at a mean of 47.0 days post-stroke (chronic phase). Handedness was scored according to the Edinburgh Handedness Inventory (score >18/20) [10].

The patients gave their informed consent to participate in the study, which was approved by the ethics committee of the Rhineland-Palatinate Medical Association and carried out in accordance with the ethical standards outlined in the 1962 Declaration of Helsinki.

Clinical examination

The degree of hemiparesis, tilt of the SVV, and visual field defects were assessed as reported previously [4]. Patients with SVV tilts larger than 2.5° were defined as having a "pathological tilt," that is, a vestibular dysfunction in the roll plane of the vestibulo-ocular reflex [3]. Absolute tilt values were taken for voxel-based lesion behavioral mapping (VLBM) analyses. The tilts of the SVV were analyzed using the absolute values independent of the direction of the tilt, since no different pathomechanisms for contralesional and ipsilesional tilts of the SVV were reported [11].

TABLE 1 Demographic and clinical data of all 23 patients with right-brain lesions due to acute ischaemic infarctions

	M (SD)	*n* (%)
Sex		
Female		12 (52.2)
Male		11 (47.8)
Handedness		
Right		21 (91.3)
Left		2 (8.7)
Age	67.6 (11.1)	
Time since lesion (days)		
Imaging	5.6 (2.0)	
First clinical testing	7.4 (3.8)	
Second clinical testing	47.0 (6.4)	
Lesion volume (cm^3)	43.7 (40.3)	
Visus (% visual acuity)	79 (22.0)	
Contralesional paresis		23 (100)
Contralesional somatosensory deficit (touch)		16 (60)
Mini-Mental State Examination	25.3 (2.6)	
Tilt of SVV (°) (first testing) ($n = 23$)	6.0 (2.9)	
Tilt of SVV (°) (second testing) ($n = 23$)	2.7 (2.0)	
Pathological tilt of SVV (°) (≥2.5°) (first testing)		23 (100)
Ipsilateral		12 (52.2)
Contralateral		11 (57.8)
Pathological tilt of SVV (°) (≥2.5°) (second testing)		8 (34.7)
Ipsilateral		4 (17.4)
Contralateral		4 (17.4)
Neglect		17 (73.9)

Abbreviations: *M*, mean; *n*, subsample size; SVV, subjective visual vertical.

Imaging and lesion analysis

All patients had lesions due to an ischaemic stroke. Lesion mapping plots were carefully examined for possible edema, which is also visible in the MRI scan and might distort the lesion mapping. None of the patients showed substantial edema. MRI scans and VLBM were conducted as reported previously [4]. To evaluate the relationship in the chronic phase between lesion location and absolute values of tilt of the SVV a VLBM analysis was performed using first a subtraction analysis comparing the lesion plot subgroup of the patients in the second testing with a tilt of the SVV (>2.5°) versus the patients without a tilt of the SVV (tilt of the SVV <2.5°). In a second step, a VLBM analysis was applied using the *t* test statistic (https://people.cas.sc.edu/rorden/mricron/install.html) [12] allowing statistical inferences for the SVV tilts in the acute and chronic phase. This algorithm

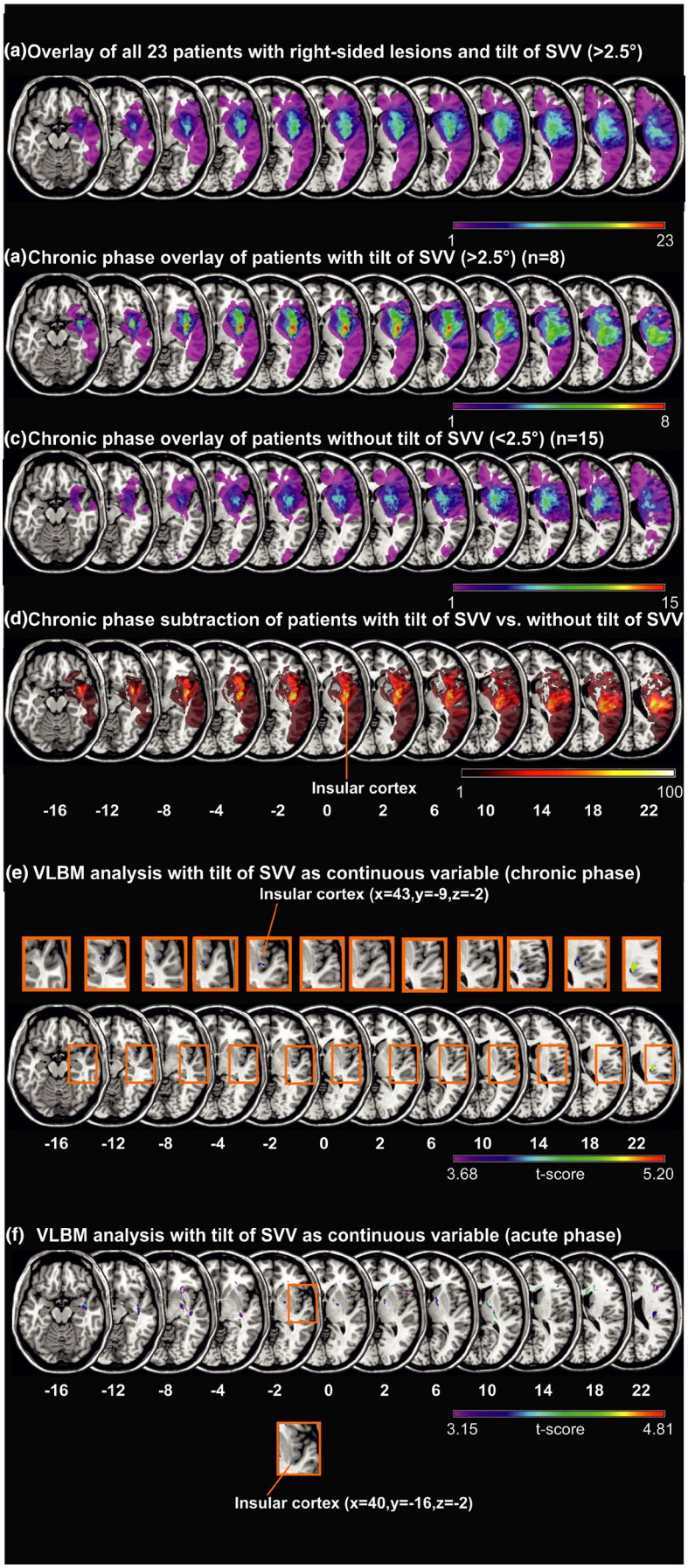

FIGURE 1 (a) The overlay of all 23 patients. (b) The overlay of the eight patients in the second testing (chronic phase) with a pathological tilt of the SVV (>2.5°) that was not completely compensated and (c) the overlay of the 15 patients in the chronic phase without a tilt of the SVV (<2.5°). (d) The subtraction plot of the eight patients with a tilt of the SVV versus the plot of the 15 patients without a tilt of the SVV (<2.5°). Values 1–100 show the relative frequency of damage, that is, the voxels more often damaged in the group with a tilt of the SVV than in the group without a tilt of the SVV. (e) VLBM analysis comparing the 23 patients with respect to absolute SVV tilt of the chronic phase (*t* test statistic). (f) VLBM analysis comparing the 23 patients with respect to absolute SVV tilt of the acute phase (*t* test statistic) [Colour figure can be viewed at wileyonlinelibrary.com]

uses the deviations of the SVV as a continuous, independent variable and separates those subjects on the voxel level who have a lesion of a specific voxel versus subjects who do not. A control for multiple comparisons was made by using a 5% false discovery rate correction. To relate the statistical map to gray matter structures, it was overlaid with the automated anatomical labeling atlas [13]. In addition, the fiber tract maps from the human probabilistic cytoarchitectonic atlas were used to identify white matter tracts that overlapped with the resulting statistical map [14].

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

RESULTS

See Table 1 for the patients' clinical data. As indicated and as a criterion to participate in the study, all 23 patients presented with a pathological tilt of the SVV during the first clinical testing. During the second testing only eight patients showed a pathological tilt of the SVV (≥2.5°) [3] (see Table 1). A difference of the absolute tilts of the SVV was seen between the first and the second clinical assessment (paired *t* test df = 22; $T = 8.894$, $p \leq 0.01$) (see also Table 1). Figure 1a illustrates the simple overlap of all 23 patients with tilts of the SVV. The IC was damaged more frequently in the group with tilts of the SVV than in the group without (Figure 1d). Using the VLBM *t* test statistics and allowing for statistical inferences, the posterior IC ($x = 43$, $y = -9$, $z = -2$; $x = 40$, $y = -10$, $z = -1$; $x = 34$, $y = -21$, $z = 16$) as well as the border region to the Rolandic operculum ($x = 38$, $y = -20$, $z = 23$) were associated with tilts of the SVV in the chronic phase (Figure 1e). The posterior IC ($x = 40$, $y = -16$, $z = -2$) was also damaged in the acute phase (Figure 1f).

DISCUSSION

The present results indicate that lesions of the posterior IC are involved in vestibular compensation of lesions affecting graviceptive function. Our anatomical assignments demonstrate—in line with previous data—that the posterior IC represents an important structure for perceptual tasks in a three-dimensional space such as perception of verticality [4,5]. Furthermore, the posterior IC appears to be a critical anatomical region for predicting a tilt of the SVV as a chronic disorder (6–7 weeks after stroke onset). In other words, an acute lesion of the temporo-parietal lobe affecting the IC may hinder the vestibular compensation of a disturbed perception of verticality. Interestingly, it appears that small, circumscribed lesions restricted to the posterior IC alone do not suffice to cause a disturbed perception of verticality [15]. One possible explanation could be that lesions restricted to the IC might immediately be compensated by neighboring areas within the neural vestibular network [4] or by regions (e.g., somatosensory) within the broad network for spatial orientation that exceeds the multisensory vestibular network [2]. Brain regions associated with graviceptive function not only include the vestibular insular-opercular cortex (as shown here) but also have a bihemispheric distribution along the somatosensory cortex and intraparietal sulcus representing multisensory integration [2]. According to our previous results, none of the current stroke patients presented with an isolated lesion of the IC. With respect to the acute phase the posterior IC was also involved amongst other regions (Figure 1f). Thus, it cannot be entirely excluded that higher SVV values in the chronic phase might be attributed to higher SVV values in the acute phase. Therefore, another VLBM analysis was in addition calculated using an absolute difference of SVV tilts in the acute versus chronic phase. However, no significance was reached on the *t* test statistics.

In conclusion, the present data underline the importance of the posterior IC as a key region within the multisensory vestibular network, pointing towards a special role in the post-stroke compensation of perceptual deficits of graviceptive function in three-dimensional space. Concerning the practical relevance the present study emphasizes that patients with tilts of the SVV and lesions of the posterior IC should be included in intensive vestibular rehabilitation programs.

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CONFLICT OF INTEREST

The authors report no conflicts of interest.

AUTHOR CONTRIBUTIONS

Bernhard Baier: Conceptualization (lead); formal analysis (equal); investigation (lead); methodology (lead); writing—original draft (lead). Hannah Cuvenhaus: Data curation (equal); formal analysis (equal); project administration (equal). Notger Müller: Conceptualization (equal); methodology (equal); validation (equal). Frank Birklein: Funding acquisition (equal); validation (equal); writing—original draft (equal); writing—review and editing (equal). Marianne Dieterich: Conceptualization (lead); funding acquisition (equal); investigation (equal); resources (equal); validation (equal); writing—original draft (equal).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

ORCID

Bernhard Baier https://orcid.org/0000-0003-0793-0350

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