Unilateral vestibular failure suppresses cortical visual motion processing

Angela Deutschländer,1 Katharina Hütner,1 Roger Kalla,1 Thomas Stephan,1 Thomas Dera,1 Stefan Glasauer,1,2 Martin Wiesmann,3 Michael Strupp1 and Thomas Brandt1,2

1Department of Neurology, 2Bernstein Center for Computational Neuroscience and 3Department of Neuroradiology, Klinikum Grosshadern, Ludwig-Maximilians University, Marchioninistr. 15, 81377 Munich, Germany

Correspondence to: Angela Deutschländer, MD, Department of Neurology, Klinikum Grosshadern, Ludwig-Maximilians University, Marchioninistrasse 15, 81377 Munich, Germany
E-mail: angela.deutschlaender@med.uni-muenchen.de

Patients with unilateral vestibular failure (UVF) experience oscillopsia (apparent motion of the visual scene) during rapid head movements due to increased retinal slip caused by vestibulo-ocular reflex impairment. Oscillopsia is always smaller than the net retinal slip and decreases over time in patients with acquired vestibular loss; this correlates with increased thresholds for visual motion detection and increased tolerance to retinal slip. We investigated the underlying cortical adaptive processes using visual motion stimulation during blood oxygen level-dependent (BOLD) fMRI. Optokinetic nystagmus was elicited in seven patients with right-sided and seven patients with left-sided unilateral vestibular neurectomy and in seven age- and gender-matched healthy controls. Patients showed diminished activation of bilateral visual cortex areas (including the motion-sensitive area MT/V5, cuneus, middle occipital, fusiform and lingual areas) and ocular motor regions compared to their controls during visual motion stimulation. Concurrent BOLD signal decreases of temporo-parietal and insular multisensory cortical areas occurred in controls and patients. The diminished activation of visual motion processing areas plausibly reflects an adaptive mechanism that suppresses distressing oscillopsia in patients with UVF and thereby stabilizes the perceived visual surroundings. This study provides for the first time neuroimaging evidence of suppressed cortical visual motion processing in patients with vestibulopathy.

Keywords: functional magnetic resonance imaging; optokinetic; motion perception

Abbreviations: BOLD = blood oxygen level-dependent; OKN = optokinetic nystagmus; UVF = unilateral vestibular failure; VOR = vestibulo-ocular reflex


Introduction

Two ocular motor reflexes stabilize the image of the surroundings on the retina during self-motion (vestibulo-ocular reflex, VOR) or movement of the visual scene (optokinetic nystagmus, OKN). The VOR stabilizes gaze during head and body movements by generating compensatory eye movements in the opposite direction to head motion with a short latency of approximately 7–10 ms (Crane and Demer, 1998). Patients with chronic unilateral vestibular failure (UVF) suffer from impairment of the ipsilesional horizontal (head motion in the yaw plane) and vertical VOR (pitch plane; Aw et al., 1994). This VOR impairment leads to involuntary excess motion of visual images on the retina (retinal slip) during head movements, which is associated with oscillopsia, i.e. illusory movement of the visual scene, and blurred vision.

A dissociation between retinal slip and oscillopsia has been reported in patients with impaired eye–head coordination due to subacute eye muscle pareses, vestibular loss or nystagmus which overrides fixation. The magnitude of oscillopsia was always smaller than the calculated net retinal slip in patients with subacute eye muscle pareses (Wist et al., 1983) or downbeat nystagmus (Büchele et al., 1983), which was attributed to a central suppression mechanism. Similarly, in spite of the permanent VOR impairment, oscillopsia decreased over time in patients with bilateral vestibular failure (BVF) due to largely unknown compensatory mechanisms (Grunfeld et al., 2000). Visual-perceptual changes have been proposed to participate in this recovery process, e.g. modulations in visual motion processing. A normal physiological mechanism is known to impair visual motion processing during eye movements, e.g. smooth pursuit (Wertheim, 1981), and during...
self-motion (Probst et al., 1984), thus contributing to suppression of oscillopsia in healthy subjects. The existence of an additional adaptive impairment of central visual motion processing has been proposed in patients with impaired eye-head coordination, like downbeat nystagmus, congenital nystagmus and subacute eye muscle pareses (Büchele et al., 1983; Brandt and Dieterich, 1986; Dieterich and Brandt, 1987; Shallo-Hoffmann et al., 1998). This hypothesis was corroborated by psychophysical studies, which reported elevated latencies for the detection of visual motion in patients with BVF, even with the head stationary (Grünbauer et al., 1998; Shallo-Hoffmann and Bronstein, 2003). A reduction in sensitivity to visual motion has also been reported in other psychophysical studies on patients with BVF (Mesland et al., 2008).

OKN consists of a slow phase, which serves to keep an image steady on the retina, and a quick phase, which resets the eye in the opposite direction. It can be elicited by visual pattern motion in a stationary observer or by self-motion while observing a stationary environment (Büttner and Kremmyda, 2007, for review). OKN-related activation and deactivation patterns have been investigated in a number of functional brain imaging studies in healthy volunteers. These studies applied coherent visual pattern motion stimuli to induce OKN. Bilateral activations were consistently found in an assembly of visual cortex areas including the primary visual cortex, tempo-occipital visual motion-sensitive areas, adjacent parieto-occipital areas, as well as oculomotor areas, such as the frontal, supplementary and parietal eye fields (FEF, SEF, PEF, respectively) (Bucher et al., 1997; Dieterich et al., 1998a; Galati et al., 1999; Dieterich et al., 2003a; Konen et al., 2005; Bense et al., 2005, 2006). Furthermore, concurrent blood oxygen level-dependent (BOLD) signal decreases (deactivations) have been consistently detected in the posterior insula, retinocular regions and adjacent temporoparietal sites during OKN (Dieterich et al., 2003a; Konen et al., 2005; Bense et al., 2005, 2006) and during coherent visual motion stimulation in roll (Brandt et al., 1998; Kleinschmidt et al., 2002; Deutschländer et al., 2004). Since these sites corresponded best to the human homologue of the parieto-insular vestibular cortex (PIVC) defined in non-human primates (Grüsser et al., 1990), these findings were interpreted to be a correlate of an inhibitory visuo-vestibular interaction (Brandt et al., 1998; Dieterich et al., 2003a).

In the current fMRI study we addressed two major questions: Do patients with UVF show differential BOLD activity levels in cortical visual motion-sensitive areas (MT/V5) during visual motion stimulation, when compared to normals? Does OKN cause a concurrent deactivation of the vestibular cortex in patients with UVF, as it does in healthy volunteers?

**Materials and Methods**

**Subjects**

Seven patients with right-sided unilateral vestibular neurectomy (UVN) (age range: 47–62 years; mean age: 53.7 years; three females) and seven patients with left-sided UVN (age range: 49–62 years; mean age: 57.6 years; three females) participated in the study. Complete UVN for acoustic neuma removal was performed 5–13 years before the experiment at the Department of Neurosurgery, Ludwig-Maximilians University, Munich, Germany. All patients underwent complete neurological, neuro-otological and neuro-ophthalmological examination before the experiment. The Halmagyi–Curthoys head thrust test was pathological on the operated side in all patients. All patients had pronounced hypacusis or anacusis on the operated side following surgery. Six patients had left-sided, four patients right-sided peripheral facial palsy due to the surgery. Binocular visual acuity was normal in all patients. Patients had no history or symptoms of further neurological or neuro-otological disorders. DC-electronystagmography with bithermal caloric irrigation and yaw rotation in the dark was performed prior to the fMRI experiment in all patients; it confirmed complete UVF on the side of neurectomy in all patients and showed normal vestibular function on the other side.

Seven healthy volunteers (age range: 49–60 years; mean age: 54.0 years; three females) without any history or symptoms of neurological or neuro-otological disorders and normal binocular visual acuity served as the pairwise age- and gender-matched control group.

All participants were right-handed and had a laterality quotient for handedness of +100 according to the 10-item inventory of the Edinburgh test (Oldfield, 1971). No drugs known to act on the central nervous system, vestibular or ocular motor functions were being taken.

The study was approved by the local Ethics Committee of the Ludwig-Maximilians University, Munich, Germany. In accordance with the Declaration of Helsinki, all subjects gave their informed written consent to participate in the study after the experimental procedure had been explained.

**Experimental procedure**

Subjects lay supine in the MRI scanner in a completely darkened room. Computer-generated visual stimulus patterns were presented to the participants by means of MR-compatible video goggles (Resonance Technology, Northridge, USA), that were also used for continuous registration of eye movements by infrared video-oculography (VOG). The visual field of view (FOV) was restricted to 30° (horizontal) × 20° (vertical). The subject’s head was fixed by a head-holder and taped to the head coil to reduce movement artefacts. Subjects wore ear protection. Subjects were instructed to lie in a relaxed position and avoid any movements during data acquisition.

VOG was performed in all participants throughout the whole scanning procedure. Calibration was performed immediately before the scanning, using fixation targets that appeared at defined gaze angles. Performance of OKN and vigilance were monitored continuously by inspecting the VOG recordings during...
the whole acquisition period. Two-dimensional eye movement analyses were performed offline.

**Experimental conditions**

Subjects were instructed to look straight ahead at the visual stimulus without fixing any dots during all conditions. Small-field (SF) visual stimuli were presented using two different visual field sizes: SF1 (10° horizontal × 10° vertical; round) and SF2 (30° horizontal × 20° vertical; quadrangular). Four different experimental conditions were applied during the fMRI session: (i) STAT(SF1): SF1 stationary visual stimulus, a random dot pattern that consisted of 24 white dots (diameter: 0.5–1.1°) on a black background was presented. (ii) OKN(SF1): SF1 optokinetic stimulation, the random dot pattern of STAT(SF1) moved horizontally to the right from the subject’s point of view at a constant velocity of 13.5°/s. (iii) STAT(SF2): SF2 stationary visual stimulus, a random dot pattern that consisted of 120 white dots (diameter: 0.5–1.1°) on a black background was presented. (iv) OKN(SF2): SF2 optokinetic stimulation, the random dot pattern of STAT(SF2) moved horizontally to the right from the subject’s point of view at a constant velocity of 13.5°/s.

After fMRI data acquisition, subjects were asked to evaluate the perception of apparent self-motion (vection) during visual motion stimulation. All subjects reported that they had not experienced vection during optokinetic stimulation.

**Functional MRI: data acquisition and analysis**

Functional images were acquired on a 1.5T standard clinical MRI scanner (Siemens Vision, Erlangen, Germany) using echoplanar imaging with a T2*-weighted gradient-echo multislice sequence (TE = 60 ms, voxel size: 3.75 × 3.75 × 3.75 mm³, matrix 64 × 64, FOV = 240 mm, TR: 3.5 s). Twenty-eight transversal slices covering the whole cerebrum and upper parts of the cerebellum were acquired. Images were collected parallel to the AC–PC line.

Each scanning session consisted of two runs. One run lasted 14.23 min. Experimental conditions were applied as blocks of six images. Each block lasted 21 s. Each condition was applied 10 times per run in a pseudo-randomized order. A dynamic visual condition was invariably followed by a static condition. Data processing was performed using SPM2 (http://www.fil.ion.ucl.ac.uk/spm/). The first four images of each run were discarded to eliminate spin saturation effects. Data sets were realigned, normalized to the standard anatomical space defined by the Montreal Neurological Institute (MNI) template and smoothed with a 12 mm Gaussian kernel. All stereotactic coordinates given in this paper refer to the MNI space. During normalization, image data were resampled to a resolution of 2 × 2 × 2 mm³. Due to technical problems with the scanner two runs in the group of patients with UVN-left had to be discarded.

Functional imaging data were collapsed into one representative image per contrast of interest per subject. The resulting condition images were compared among subjects, yielding a second-level random effects model (one sample t-test for group analyses; two sample t-test for intergroup comparisons). Intergroup comparisons and group analyses were performed for the following contrasts: OKN(SF1) — STAT(SF1); OKN(SF2) — STAT(SF2); OKN — STAT. To compute the contrast OKN versus STAT, OKN(SF2) and OKN(SF1) data were pooled, as were STAT(SF2) and STAT(SF1) data. Activations and deactivations exceeding a threshold of P < 0.001 were considered significant. The nomenclature of anatomical structures follows Talairach and Tournoux (1988) for the supratentorial brain and Schmahmann et al. (2000) for the cerebellum. Additionally, region of interest (ROI) analyses were performed using MNI coordinates of MT (x, y, z = 45, 76, 3) bilaterally (Tootell et al., 1995) as centre of a sphere (radius: 20 mm) and applying a significance threshold of P < 0.05 (FDR-corrected). ROIs were created using WFU PickAtlas, Version 2.1 (Maldjian et al., 2003).

To test for laterality effects, subject-specific contrast images were flipped across the midline, and on a second level flipped and non-flipped images were compared using a paired t-test; voxels exceeding a threshold of P < 0.001 were considered significant.

To test whether BOLD activity levels in ocular motor and visual cortical areas including MT/V5 during OKN correlated with OKN intensity, a correlation analysis was computed by entering each subject’s mean slow phase velocity (MSPV) during OKN as correlation factors into a simple regression model using SPM2. Both whole brain analyses (P < 0.001) and ROI analyses of MT/V5 (P < 0.05; FDR-corrected) were performed.

To account for possible differential effects due to the motion aftereffect (MAE) or optokinetic afternystagmus (OKAN), we computed comparisons of the first half of the static condition (STAT1) with the second half of the static condition (STAT2) for patients with right-sided UVN, left-sided UVN, and controls (n = 7; one sample t-test; P < 0.001) as well as intergroup comparisons (n = 14; two sample t-test; P < 0.001).

**VOG: data analysis**

MSPV over conditions (OKN, STAT) and subject groups were compared using a repeated measures ANOVA (within subjects factors: OKN versus STAT). For each subject, 5 min of eye movement recordings by were analysed. Data from one patient with left-sided UVN could not be analysed due to image quality. Raw VOG data were calibrated using data from the calibration run (nine targets at a regular ± 8.75° grid) to yield eye positions (Schneider et al., 2002). Only horizontal eye positions were used for analysis. Fast phases and saccades were detected automatically using a velocity criterion and were deleted. From the remaining periods, the MSPV for each condition (STAT, OKN) and each subject was computed. Separate one-way ANOVA over subject groups were calculated for MSPV (P < 0.05). The average frequency of saccades was determined by counting the number of detected saccades in STAT and OKN and dividing it by the duration of the paradigm.

**Results**

**VOG**

Eye movement recordings during the fMRI session showed that OKN was elicited in all subjects over the entire visual motion stimulation period. Subjects gazed straight ahead during the static conditions, performing only a few small-amplitude saccades. All subjects performed the tasks accurately over the whole scanning procedure.

A separate one-way ANOVA over subject groups showed that MSPV was not different during STAT [F(2,17) = 2.66; P = 0.099], but was during OKN [F(2,17) = 3.93; P = 0.040]. Patients had a slightly reduced MSPV during OKN (controls: 10.79 ± 0.82°/s; patients with right-sided
UVN: 10.10 ± 1.3°/s; patients with left-sided UVN: 9.05 ± 1.20°/s). There was no significant difference between subject groups as regards saccade frequencies during OKN (controls: 2.64 ± 0.21/s; patients with right-sided UVN: 2.55 ± 0.26/s; patients with left-sided UVN: 2.65 ± 0.38/s). The time course of the minimal spontaneous nystagmus during STAT (MSPV during STAT: controls: −0.06 ± 0.25°/s; UVN-right: −0.13 ± 0.47°/s; UVN-left: 0.25 ± 0.28°/s) was analysed to identify a possible OKAN. No OKAN beating in the direction of the OKN was observed in either group.

**Functional MRI**

**Group analyses: activations and deactivations in the contrast OKN-STAT**

Healthy controls activated an assembly of visual and ocular motor cortical areas during OKN (Fig. 1; Supplementary Table 1). Widespread activations were found in the visual cortex bilaterally (cuneus, superior, middle and inferior occipital gyri), covering Brodmann areas (BA) 17, 18 and 19 and merging into the motion-sensitive temporo-occipital cortex bilaterally (MT/V5) as well as into adjacent parieto-occipital areas (right precuneus). Bilateral activations along the intraparietal sulcus (IPS; BA 7, 40) corresponded best to the PEF. Bilateral activations in the precentral gyri bordering the middle frontal gyri (BA 4, 6) corresponded best to the inferior and superior subregion of the FEF. This activation cluster extended into the medial frontal gyri bilaterally (SEF). An activation cluster in the right middle and inferior frontal gyri (BA 9, 44) corresponded well to another inferior subregion of the FEF, which was previously proposed to be related to OKN (Dieterich et al., 2003a).

Deactivations were found in the posterior insula bilaterally, in the superior and middle temporal gyri bilaterally, in the right anterior cingulate, right angular and right superior frontal gyri, as well as in the precuneus bilaterally.

Patients with right-sided UVN activated bilateral visual areas including MT/V5 bilaterally during OKN (Fig. 1; Supplementary Table 1). However, activation clusters were smaller compared to healthy controls and did not extend into the precuneus and superior occipital gyrus. A small activation was seen along the left IPS, which corresponded best to the left PEF. Activations corresponding to the SEF were not seen.
Deactivations were seen in the right superior frontal gyrus and bilaterally in the posterior insula, superior and middle temporal gyri, posterior cingulate gyrus, hippocampus and precuneus.

Patients with left-sided UVN activated bilateral visual areas including MT/V5 bilaterally during OKN (Fig. 1; Supplementary Table 1). However, activation clusters were smaller compared to those of healthy controls and did not extend into the precuneus and superior occipital gyrus. Activations along the IPS corresponding to the PEF were seen bilaterally as well as bilateral activations in the precentral gyri bordering the superior and middle frontal gyri (BA 4, 6; superior portion of FEF). No activations corresponding to the SEF were seen.

Deactivations were seen bilaterally in the posterior insula, in the right superior temporal gyrus, and in the right hippocampus.

A correlation analysis over all subjects showed a trend toward a positive correlation between the magnitude of MSPV during OKN and OKN-induced BOLD signal increases in visual (including MT/V5 and the superior cuneus) and ocular motor areas. However, this trend did not reach significance for any BOLD signal changes in visual and ocular motor areas.

**Intergroup comparisons: patients versus controls**

Intergroup comparisons showing differential BOLD activity levels during OKN (versus STAT) were computed for ‘controls versus patients with UVN-right’ and for ‘controls versus patients with UVN-left’.

**Visual cortex.** Differential BOLD signal increases were prominent in early and higher visual cortex areas (Fig. 2; Table 1). Controls showed more pronounced activations than patients in MT/V5 bilaterally, in the cuneus bilaterally extending into the middle occipital gyrus (presumably including V3A), in the left middle occipital gyrus extending to the calcarine sulcus (V1, V2), and in the precuneus. Furthermore, controls showed stronger activations than patients with left-sided UVN in ventral visual areas (fusiform and lingual gyri). Clusters in superior and middle occipital areas with differential BOLD activity levels were larger (higher number of activated voxels) in the left hemisphere, whereas clusters in MT/V5 and ventral visual areas with differential activity levels were larger in the right hemisphere (Table 1). No areas in the visual cortex showed stronger activations in the patients than in the controls.

ROI analyses of MT/V5 also showed that BOLD activity levels in MT/V5 were bilaterally higher in the control group than in the patients (Table 2). With respect to cluster sizes, differential MT/V5 activation was more pronounced in the right hemisphere. No areas within the ROI showed stronger activations in the patients than in the controls.

**Ocular motor regions.** Differential signal changes that could be attributed best to ocular motor areas were seen in the right precentral gyrus bordering the middle frontal gyrus (BA 4, 6), corresponding best to the right FEF (Table 1). This region exhibited higher activity levels in the controls than in the patients during OKN. Similarly, the left PEF (BA 7, 40) showed more pronounced BOLD increases in the controls than in the patients with right-sided UVN, and the right SEF (BA 6) showed more pronounced activation in the controls than in the patients with left-sided UVN.

**Multisensory vestibular cortex.** Differential activity levels corresponding best to multisensory vestibular areas were limited to temporo-parietal areas of the right hemisphere. The patients showed diminished deactivation in the right inferior parietal lobule bordering the occipital cortex and in the right superior and middle temporal gyri during OKN (Table 1).

To evaluate potential differential effects due to intergroup differences in the MAE, the first half of the static condition (STAT1) was compared with the second half of the static condition (STAT2). The contrast STAT1–STAT2
showed large activations in widespread visual cortex areas including MT/V5 in both the patients and controls (group analyses), indicating a strong MAE in all groups. The intergroup comparisons (patients versus controls) did not produce any significant differential signal changes in visual cortical areas. Thus, we found no evidence of differential MAE-associated BOLD activity levels comparing patients versus controls.

### Table 1 BOLD signal changes in the contrast OKN–STAT (controls–patients)

<table>
<thead>
<tr>
<th>Brain regions</th>
<th>BA</th>
<th>Voxels</th>
<th>T</th>
<th>x, y, z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls–patients with UVN-right</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signal increases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MT/V5</td>
<td>19, 37</td>
<td>189</td>
<td>6.39</td>
<td>-46, -84, 0</td>
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<td>Cu</td>
<td>19</td>
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<td>18</td>
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<tr>
<td>GPrC, GFM</td>
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<tr>
<td>Lp, PCu</td>
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<td>Signal increases</td>
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<td>519</td>
<td>8.11</td>
<td>18, 48, 18</td>
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### Table 2 Differential activations in MT/V5 during OKN (controls–patients)

<table>
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<tr>
<th>MT/V5 right</th>
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<th>Voxels</th>
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<td>UVN-right</td>
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<td>UVN right</td>
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<td>44, -84, 2</td>
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<td>UVN-left</td>
<td>1417</td>
<td>44, -84, 2</td>
</tr>
</tbody>
</table>

Healthy controls showed more pronounced activations in MT/V5 compared to patients with UVN (region of interest analyses for MT/V5; n = 14; two sample t-test; P < 0.05; FDR-corrected) under all stimulation conditions [OKN-STAT; OKN(SF1)-STAT(SF1); OKN(SF2)-STAT(SF2)].

### Intergroup comparison: patients with UVN-right versus UVN-left

The intergroup comparison ‘patients with UVN-right versus patients with UVN-left’ showed three clusters, all of them representing less-pronounced deactivation in the patients with UVN-left during OKN. They were located in the right superior frontal gyrus (BA 8; x, y, z = 24, 36, 34; T = 5.05; 29 voxels), left middle temporal gyrus (BA 21; x, y, z = -66, -10, -10; T = 4.89; 29 voxels) and left posterior insula (x, y, z = -44, -8, -14; T = 4.87; 41 voxels). No differential BOLD responses were seen in visual or ocular motor cortical areas.

### Laterality effects in multisensory vestibular, visual and ocular motor cortical areas

To test for laterality effects, flipped and non-flipped subjects-specific contrast images were compared using a paired t-test. Temporo-parietal areas, insular and retroinsular regions and the cingulate cortex are well recognized to be a part of the multisensory vestibular cortex. Healthy controls showed a right-hemispheric predominance of deactivations in the superior posterior insula (x, y, z = -18, 18, 24; T = 5.65; 4 voxels) and superior temporal gyrus (BA 22; x, y, z = -52, 2, -8; T = 8.26; 9 voxels). In patients with left-sided or right-sided UVN, no significant laterality effects in areas that may have corresponded to multisensory vestibular areas were observed.
Healthy controls and patients showed more pronounced activation of the right than the left visual areas (superior cuneus, MT/V5, middle occipital, fusiform and lingual gyri), which was consistent with earlier reports of a right-hemispheric dominance for OKN processing in visual cortex areas (Dieterich et al., 1998a).

Laterality effects of cortical ocular motor areas (FEF, SEF, PEF) were restricted to a predominance of the left FEF in patients with right-sided UVN \(x, y, z = -28, -6, 46; T = 9.47; 42\) voxels).

**Discussion**

The major finding of this fMRI study was that patients with right-sided or left-sided UVN showed reduced visual cortex activation during visual motion stimulation compared to their healthy controls. Reduced visual cortex activation was widespread and affected an assembly of early and higher visual areas of the dorsal and ventral streams. It was most prominent in MT/V5, in the cuneus, and in the middle occipital gyri bilaterally. Further findings of this study were: (i) Ocular motor regions showed reduced activation during OKN in the patients (right FEF, right SEF and left PEF). (ii) Deactivations in the posterior insula and in the superior and middle temporal gyrus (BA 21, 22, 39) were found in the controls as well as in patients during the performance of OKN. These regions corresponded best to multisensory vestibular areas (human homologue of the PIVC). Thus, the inhibitory visuo-vestibular interaction was preserved in patients with UVF. (iii) Deactivations in multisensory vestibular cortex areas showed laterality effects only in the controls with a right-hemispheric predominance (posterior insula and superior temporal gyrus). Evidence of a right-hemispheric dominance for vestibular cortical function has been reported earlier in healthy subjects (Dieterich et al., 2003b). (iv) Patients showed a slightly reduced MSPV during OKN. Since OKN is associated with BOLD signal changes in the visual cortex including motion-sensitive areas and in ocular motor regions (Dieterich et al., 1998a, 2003a), its reduction may lead to reduced ocular motor as well as altered visual cortical activations. However, there was no significant correlation between the MSPV of OKN and OKN-induced BOLD signal changes in visual and ocular motor cortical areas in the respective correlation analysis.

Here we propose that reduced visual cortex activation of motion-sensitive areas like MT/V5 during optokinetic stimulation in patients with UVN may reflect decreased sensitivity to visual motion in patients with impaired eye-head coordination, which was demonstrated in psychophysical studies even with the head still (Grunfeld et al., 1998; Shallo-Hoffmann and Bronstein, 2003). Decreased sensitivity to visual motion may serve as an adaptive strategy to alleviate oscillopsia during head and body movements. At the same time, the absence of vestibular input, which leads to impaired self-motion perception, may be substituted by increasing the weight of the input of other sensory modalities, like the visual or the somatosensory. These two strategies are diametrical opposites. In the following, we will first provide support for the suppression of visual motion perception as the possible mechanism to reduce oscillopsia in patients with VOR impairment. Then we will discuss the relevance of substitution for missing vestibular input by increasing the sensitivity of other sensory modalities.

**Reduction of oscillopsia by decreasing the sensitivity of visual motion perception**

The reduced VOR gain in subjects with BVF or UVF induces a persisting increase in retinal slip during head motion toward the lesioned side and in pitch (Aw et al., 1994). The severity of oscillopsia decreases over time due to largely unknown mechanisms (Bronstein and Hood, 1987). Grünbauer et al. (1998) found that four of eight patients with BVF had increased latencies for visual motion detection in the horizontal and in the vertical direction even with the head still, i.e. in a position that does not require VOR activation. This finding of impaired visual motion perception was interpreted as evidence for a central mechanism to reduce oscillopsia during head movements, which is not or not fully switched off when the head is stationary. Similarly, motion detection thresholds were found to be raised with the head still as well as during whole-body oscillations in both the horizontal and vertical directions in a group of 12 patients with BVF (Shallo-Hoffmann and Bronstein, 2003). Patients with BVF showed abnormalities in visual velocity discrimination (Morland et al., 1995; Mesland et al., 1996; Morland et al., 1998) and deteriorated spatial vision during self-motion (Morland et al., 1998). Grunfeld et al. (2000) showed that the greater the retinal slip during visual stimulation on a moving chair, the less patients with BVF suffered from oscillopsia. They attributed their seemingly paradoxical finding to increased tolerance toward retinal slip, which underlies the reduction of oscillopsia. Similarly, dynamic visual acuity during active head movements in pitch correlated negatively with the experience of oscillopsia in patients with UVF or BVF, i.e. subjects with poor visual acuity during head movements experienced less oscillopsia and blurring while walking (Schubert et al., 2002).

All these findings were interpreted to indicate an impairment of visual motion perception as a strategy to reduce oscillopsia and blurring in subjects with UVF or BVF. We propose that the reduction in the sensitivity to visual motion is reflected by decreased visual cortex activation, which we detected in early and higher visual cortex areas, including the motion-sensitive area MT/V5 bilaterally. A functional interpretation of the asymmetry of the sizes of clusters with differential BOLD activity levels in MT/V5 (larger clusters in the right hemisphere) as well as in the cuneus and middle occipital gyri (larger clusters in the left hemisphere) remains speculative. We found no differential
BOLD signal changes in visual cortex areas of patients with right-sided versus patients with left-sided UVN. Although retinal slip during head movements is unidirectional in patients with UVN, it affects both visual hemifields. Thus, a decrease of visual motion sensitivity in the visual cortices of both hemispheres appears to be required for increased tolerance toward retinal slip.

Like patients with UVF or BVF, patients with oculomotor disorders (acquired infranuclear ocular motor palsy, congenital nystagmus, upbeat and downbeat nystagmus, downgaze palsy) experience increased retinal slip. Parallelizing the interpretation in subjects with BVF, it was proposed that these patients rarely report oscillopsia due to suppressed visual motion perception, which was also demonstrated in several psychophysical studies (Dieterich and Brandt 1987; Brandt and Dieterich 1986, 1988; Heide et al., 1990; Dieterich et al., 1998b; Shallo-Hoffmann et al., 1998).

Substitution for vestibular loss by other sensory modalities

While decreased visual motion sensitivity has been proposed to reduce oscillopsia in patients with BVF, the opposite mechanism of increased sensitivity of other sensory modalities has been suggested to substitute for absent vestibular input (vicarious functioning; Smith and Curthoys, 1989, for review). In the current fMRI study, however, no evidence of increased sensitivity of other sensory modalities was found.

As regards increased sensitivity of the visual system, circularvection induced by large moving visual scenes had a shorter latency in six patients with BVF compared to healthy controls and patients with UVF (Johnson et al., 1999). Thus, BVF was associated with increased sensitivity to optic flow for self-motion perception. Visual input or potentiation of visual information was proposed to improve dynamic properties of impaired vestibular reflexes (Courjon et al., 1977; Precht and Dieringer, 1985, for review; Fetter et al., 1988).

Regarding increased sensitivity of the somatosensory system, decreased thresholds for somatosensory circularvection induced by apparent stepping around were reported in patients with BVF (Bles et al., 1984; Bles and De Jong, 1986). However, no alteration in podokinetic intensity during podokinetic after-rotation and thus no evidence of increased somatosensory sensitivity were found in these patients in another study (Earhart et al., 2004). During unilateral stimulation of the posterior neck muscles by vibration patients with UVF had higher ocular displacements than controls, which was interpreted as evidence of somatosensory substitution (Strupp et al., 1998). Similarly, the sensorimotor weight and the gain of the cervico-ocular reflex (COR) were reported to be enhanced in patients with BVF (Kasai and Zee, 1978; Bles et al., 1983; Bronstein and Hood, 1986) and in labyrinthectomized animals (Goldberg and Marsh, 1988; Rioul-Pedotti and Dieringer, 1988). One patient showed a negligible COR immediately after the acute onset of BVF, an increased COR gain 1 month after the lesion, and a normal gain after recovery of labyrinthine function (Bronstein et al., 1995). Thus, these studies provided evidence of increased sensitivity of the visual and somatosensory modalities, particularly in BVF, which is associated with profound impairment of self-motion perception.

A recent fMRI study reported that patients with BVF due to various aetiologies had increased BOLD activations in MT/V5 during OKN compared to healthy controls. Increased activation of MT/V5 was suggested to reflect increased visual sensitivity and interpreted as evidence of visual substitution in these patients (Dieterich et al., 2007). These findings appear to be contradictory to our results, which showed no evidence of increased visual sensitivity, especially since oscillopsia and involuntary retinal slip are even greater in patients with BVF than UVF. However, the fMRI study of Dieterich et al. (2007) differed in a number of aspects from our study. Most importantly, the patients had bilateral vestibulopathy, and they suffered from incomplete vestibular loss as opposed to the patients in our study, who had complete UVF (eighth cranial nerve cut). Patients with BVF furthermore had a shorter duration of their disease (mean duration: 32 months) than patients with UVF (5–13 years). We propose that the seemingly contradictory findings of the two fMRI studies can be best attributed to the perceptual consequences implied by bilateral as opposed to unilateral VOR impairment. Two directly opposed mechanisms, increase and decrease of visual sensitivity, appear to exist in parallel in patients with vestibular loss. Depending on the task and deficit, one mechanism may prevail. Patients with BVF experience profound impairment of the perception of self-motion during locomotion or head movements, which is generally thought to be substituted by other sensory modalities, like the visual system (Johnson et al., 1999). This may underlie the finding of increased MT/V5 activation in the study by Dieterich et al. (2007). In patients with UVF, however, the remaining labyrinth still senses self-motion during locomotion and head movements, thus reducing the need for substitution of missing vestibular input by other sensory modalities. In patients with UVF the mechanism of suppressed perceptual sensitivity to visual motion prevailed, which serves to reduce oscillopsia and blurred vision even with the head still (Grünbauer et al., 1998; Shallo-Hoffmann and Bronstein, 2003).

In conclusion, the suppressed activation of bilateral visual cortex areas including visual motion processing areas like MT/V5 during visual motion stimulation plausibly reflects an adaptive strategy of patients with UVF for experiencing less oscillopsia despite increased retinal slip. Earlier psychophysical experiments have provided examples of an association of vestibular loss with suppression of functional sensitivity in the visual system, which persists with the head still. This study provides for the first time neuroimaging...
Vestibular loss suppresses visual processing

evidence of reduced visual motion sensitivity in patients with UVF.

Supplementary material
Supplementary material is available at Brain online.

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References


