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Auditory-visual localization in hemianopia

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Abstract

Objective: Beyond visual field defects, patients with hemianopia have been suggested to perceive horizontal visual space in a distorted manner. However, the pattern of these distortions remained debatable. The aim of this study was to estimate the geometry of the visual representation of space in hemianopia using an auditory marker.

Method: Patients with pure left or right hemianopia (without neglect) were tested in tasks requiring them to bring a visual stimulus into spatial alignment with a target sound (Experiment 1) or *vice versa* (Experiment 2). In Experiment 1, patients adjusted the location of a light such that it was displaced towards the anopic side with reference to the physical sound position. In Experiment 2, patients adjusted the location of a sound such that it was displaced opposite to the anopic side with reference to the actual position of the visual target.

Results: Both these experiments consistently indicated that hemianopic patients perceived a sound and a light to be in spatial alignment when the physical position of the light deviated by several degrees from the sound toward the side of the anopic hemifield, that is, to the contralesional side.

Conclusions: Given that auditory localization in patients with hemianopia has been previously shown to be only slightly biased toward the anopic side, the observed distortion of visual space with reference to auditory space can be explained by assuming that visual positions were, in absolute terms, perceived as shifted toward the intact side. As a result, HA patients may perceive visual space as compressed on their ipsilesional (intact), in comparison with their contralesional (anopic) side.

Keywords: Hemianopia, Visual space perception, Sound localization, Visual cortex, Multisensory integration

Auditory-visual localization in hemianopia

Hemianopia (HA) is a visual field defect characterized by a loss of vision in one hemifield. The visual defect is caused by unilateral lesions in the cerebral hemisphere contralateral to the anopic side, either in post-chiasmatic optic tract, lateral geniculate nucleus, optic radiation, or occipital lobe. HA has a relatively common occurance affecting approximately 20% of stroke patients and severly affecting their quality of life (Schuett, Heywood, Kentridge, & Zihl, 2008). It has been suggested that patients with HA perceive horizontal visual space in a distorted manner. The primary experimental evidence for this conclusion comes from visual line bisection tasks. With these tasks, HA patients displace the bisection mark toward the anopic side, which has been interpreted as a bias of visual space toward the blind field (e.g. Axenfeld, 1894; Liepmann & Kalmus, 1900; Best, 1910, 1917; Strebel, 1924; Barton & Black, 1998; Hausmann, Waldie, Allison, & Corballis, 2003a). In approaches employing visual pointing or adjustment tasks, the visual straight-ahead of HA patients was shown to be displaced toward the anopic side (Zihl & Von Cramon, 1986; Ferber & Karnath, 1999; Lewald, Peters, Tegenthoff, & Hausmann, 2009a). The exact topography of the visual space in HA is, however, still a matter of debate. In two studies, the horizontal angular distance between visual stimuli (Zihl & Von Cramon, 1986) and the horizontal size of rectangles (Ferber & Karnath, 2001a) was perceived as smaller on the anopic side than on the intact side, thus suggesting a compression of visual space on the anopic side. Another study (Doricchi, Onida, & Guariglia, 2002) obtained the opposite result: HA patients estimated size and distance in the anopic hemifield as being longer than equivalent sizes and distances in intact hemifield. In each case, the most established result, that visual straight ahead is displaced to the anopic side in HA, is geometrically compatible only with both a bias of visual localization to the intact side and a compression and expansion of visual space on the intact and anopic sides, respectively. The reasons for these inconsistencies between studies are still unclear, but might lie in the fact that previous approaches often did not disentangle a putative distortion of space from accounts based on spatial attention. In addition, paper/pencil tasks or tasks with presentation of visual stimuli on a computer screen, as are often employed in this field of research, might not permit unequivocal interpretations of the topography of visual space since stimuli are not seen in isolation, but in relation to a visual surround. Finally, compensatory strategies, utilizing proprioceptive and vestibular cues from the eyes, the head and the arms (Doricchi et al., 2002), may vary among individuals, in particular depending on whether patients were tested in the acute or chronic phase of brain injury. Thus, conclusions about the absolute localization of a visual stimulus in space are difficult to draw from these previous approaches.

The starting point of the present study was the growing evidence that spatial hearing performance remains relatively unaffected in HA. Zimmer, Lewald and Karnath (2003) did not find any significant bias of the auditory median plane in HA patients as measured by variation of interaural time differences. In a direct comparison, Lewald et al. (2009a) showed that subjective straight ahead deviates in hemianopia substantially for visual stimuli whereas it is veridical for auditory stimuli. In a more detailed study (Lewald, Peters, Tegenthoff, & Hausmann, 2009b) which focussed on the topography of auditory space in HA, there were statistically significant distortions of auditory space in HA patients which can be interpreted by both rotation and compression of auditory space toward the anopic side. However, the mean amplitude of these distortions measured with a task of manual pointing was only 1.5° in the auditory modality, which is relatively small compared with the visual distortions that have been recently reported (4-8°; Zihl & von Cramon, 1986; Ferber & Karnath, 1999; Lewald et al., 2009a, b).

In the present study, we thus asked subjects to match the location of a single visual target with an auditory marker or *vice versa* in totally dark surroundings. The rationale for our approach was that accounts in which the relative attentional salience of stimuli with different spatial locations determines spatial judgements in hemianopia cannot readily be applied to a task in which there is only a single visual stimulus. For example, an attentional gradient might affect the way in which patients with hemianopia scan complex visual stimuli. It should not, however, affect simple alignment judgements containing a single visual stimulus.

Using such simple alignment tasks, the present study sought to establish whether more general distortions in the visual representation of space accompany deviations in visual straight ahead. In other words, rather than asking participants to make judgements about the relative locations of many visual stimuli (as is the case of the visual line bisection task), the present experiment used an auditory marker to indicate the location of a single visual stimulus. From such judgements in HA patients and normal observers, we aimed to estimate the potential distortions in the representation of visual space accompanied by HA.

Method

Subjects

Results from ten patients with brain lesions were included in this study. All patients had received the diagnosis of persistent homonymous hemianopia (HA) confined to one hemifield, as confirmed by visual perimetry tests (see below). HA was left-sided (LHA) in seven patients (LHA1-LHA7) and right-sided (RHA) in three patients (RHA1-RHA3). Details on age, sex, visual field defects, and lesion sites are reported in Table 1 and Suppl. Table 1. All patients were congenitally right-handed, as assessed by a German adaptation of Coren's (1993) inventory (Siefer, Ehrenstein, Arnold-Schulz-Gahmen, Sökeland, & Luttmann, 2003), with a criterion of an individual score of ≥ 2 (range from -4 to 4) in the handedness section of this questionnaire. However, hemiparesis prevented two patients (LHA5, RHA2) from use of their contralesional hand, and one other patient showed mild (LHA7) impairment with use of the contralesional hand due to hemiparesis. In addition to these ten participants with HA, two further patients (one LHA and one RHA patient) were also tested, but were excluded from the study since they were unable to adequately perform the acoustic pointing task, in particular when visual targets were presented on the anopic side. For these two subjects, linear regression analyses of the pointing responses to targets on the anopic side resulted in rather poor coefficients of determination (R^2 of .06 and .17), which were more than four standard deviations below the R^2 values of the ten subjects included (range from .65 to .92, mean .78, SD .10; see 2.).

All HA patients had circumscribed brain lesions as a result of ischemic stroke or hemorrhage, demonstrated by magnetic resonance imaging (MRI) or computed tomography (CT). In all patients, lesions were unilateral (i.e., on the side contralateral to the anopic hemifield), with the exception of patient RHA3 who showed some minor involvement of right-hemispheric regions in addition to the predominant left-hemispheric lesion. Lesion sites of all patients are summarized in detail in Suppl. Table 1 and Suppl. Figure 1.

To test whether HA patients suffer from spatial neglect a neglect-test battery (Ferber & Karnath, 2001a) was applied, which consisted of the following tests: *(a)* Letter Cancellation task (Weintraub & Mesulam, 1985), which requires the patient to cancel 60 target letters 'A' distributed amid distractors on a horizontally oriented standard page (DIN A4). Responses were coded and the Center of Cancellation (CoC) index was measured using the software (www.mricro.com/cancel/) by Rorden and Karnath (2010). Patients are classified as suffering from spatial neglect when they show a CoC index > .09 (Rorden & Karnath, 2010). *(b)* Bells Test (Gauthier, Dehaut, & Joanette, 1998), which requires the patient to identify 35 bell symbols distributed on a horizontally oriented standard page with 40 distractor symbols.

Responses were analysed by calculating the CoC index (Rorden & Karnath, 2010) as with the Letter Cancellation Task, using the same cutoff threshold (> .09) for the patient's classification as suffering from spatial neglect. *(c)* Baking Tray Test (Tham & Tegnér, 1996), which requires the patient to place 16 identical items as evenly as possible on a blank standard page (8 on the left, and 8 on the right side). Any distribution more skewed than seven items on the left side and nine items on the right side are considered as a sign of spatial neglect. *(d)* Copying task (Ferber & Karnath, 2001a; Johannsen & Karnath, 2004), in which patients are asked to copy a complex multi-object scene consisting of four figures on a standard page (two on the left, and two on the right side). Omission of one left sided feature of each figure is scored as 1, and omission of each whole figure is scored as 2, resulting in a maximum score of 8. A score higher than 1 (i.e. > 12.5% omissions) is considered as a sign of spatial neglect. None of the HA patients exceeded the limit values in at least two of these four tests, which has been regarded as the criterion for presence of spatial neglect (Karnath, Himmelbach, & Rorden, 2002).

In addition, we applied a line-bisection task which comprised 17 horizontal black lines of 1 mm width on a horizontally-oriented white standard page. The lines ranged from 100 to 260 mm long, in steps of 20 mm. The mean length was 183.5 mm. Patients were asked to bisect all lines into two parts of equal length by marking the subjective midpoint of each line with a fine pencil (for details, see e.g. Hausmann et al., 2003a; Hausmann, Corballis, & Fabri, 2003b). The majority of neglect patients shows a large bisection bias towards the right, although about 30% of patients with acute neglect do not show any significant bias in line-bisection tasks (Ferber & Karnath, 2001b). Here, HA patients showed a significant mean bisection bias of 4.77% (SE 1.67, range from -2.15% to 11.32%), $t(9) = 2.85$, $p = .019$, toward the side of the anopic hemifield (LHA: mean leftward bias -6.58%, SE 1.96; RHA: mean rightward bias .53%, SE 1.47). This conforms with previous findings of a contralesional bias in patients with HA (e.g., Barton & Black, 1998; Hausmann et al., 2003a,b).

Prior to experimentation, the presence of homonymous HA was confirmed by visual static perimetry tests in all patients included in this study. In addition, after completion of the experiments the azimuthal dimensions of the visual field, and in particular the position of the binocular vertical visual field border (Table 1) was measured in more detail using visual stimulation by the experimental apparatus, as was already described in preceeding studing (Lewald et al., 2009b; Lewald, Tegenthoff, Peters, & Hausmann, 2012). For this purpose, white light flashes (duration 50 ms), delivered by light-emitting diodes (LEDs; see below), were presented in total darkness at random locations in the azimuthal plane over a range from -90° on the left to 90° on the right, in steps of 2°. Patients were instructed to fixate on a central red light emitting diode, that was permanent on, and to press a response button as soon as they perceived a white light flash. Stimuli were presented with a randomly varied time interval between 1 s and 3 s (steps of .5 s) after the patients' response. In one block, each stimulus position was presented three times, resulting in 273 trials. Data of four identical blocks (2 blocks conducted on one day and 2 blocks on a separate day) were pooled. For computation of the visual field border, the number of correct responses was plotted as a function of stimulus azimuth (θ) within the range of -46° on the left to 46° on the right, and fitted to the sigmoid equation:

$$f = 100 / (1 + e^{-k(\theta - \mathrm{VFB})})$$

where f is the frequency of responses, given as percentage; VFB (visual field border) is that θ where f is 50%; k is the slope of the function at 50%; e the base of the natural logarithm (Lewald et al., 2009b, 2012). The mean coefficient of determination (R^2) of the fit was .93 (range from .67 to 1.00; all $p < .0001$), indicating a sharp boundary of the visual field for all patients. Patients detected the vast majority of stimuli in the intact hemifield (mean

85.7%, SE 3.6) and only few in the anopic hemifield (7.7%, SE 2.2; measured over the range from 90° to 2° eccentricity on the respective side). Across all patients, the VFB was only slightly shifted toward the side of the anopic field (mean 3.38°, SE 1.28). One of the patients (LHA7) showed incomplete left HA, with a small peripheral area of vision lying to the left of the anopic field.

Ten healthy right-handed subjects (4 females and 6 males), ranging in age from 39 to 66 years (mean 49.9 years, SE 3.4), participated in the study as normal controls. Each control subject was matched with one of the 10 HA patients for sex and age (±3 years).

All subjects, HA patients and normal controls, were tested for general hearing loss. For this purpose, white-noise bursts with a duration of 1 s were presented monaurally *via* headphones (K271, AKG Acoustics, Vienna, Austria) at various sound-pressure levels (SPLs, range 10-80 dB re 20 µPa, steps of 10 dB; onset/offset time 50 ms), and subjects pressed a button as soon as they heard a sound. A two-factor ANOVA with Ear (ipsilateral, contralateral) as within-subject factor and Group (LHA patients, RHA patients, controls) as three-level between-subjects factor revealed neither a main effect nor interaction, all $F \leq 2.77$, $p > .09$. Most importantly, HA patients did not show any superiority of the ear on the side of the intact (contralateral) or the anopic (ipsilateral) hemifield, $t(9) = .00$, $p = 1.00$.

A subsequent hearing test was focussed on the symmetry in loudness perception of the subjects' left and right ears, which is more relevant to the experiments conducted here than thresholds. For this purpose, incoherent white-noise signals (preventing binaural fusion) were presented binaurally *via* headphones (as above). Interaural SPL (average root mean square) differences for these stimuli were varied between trials following a quasi-random order over a range from 20 dB (higher SPL at the left ear) to 20 dB (higher SPL at the right ear), in steps of 4 dB (duration 1 s; onset/offset time 50 ms; mean SPL 70 dB). Subjects were instructed to make a two-alternative forced choice as to which of the two sounds was louder, the one on the left or the one on the right. The test was composed of 110 trials (10 presentations of each level difference) and lasted about 5 min. The point of subjective equality measured in HA patients (LHA: mean .05 dB, SE 1.33; RHA: mean -1.12 dB, SE 1.60) and controls (mean -0.73 dB, SE .58) did not differ, $F(2,17) = .45$, $p = .64$, nor was there any bias to the side of the intact or the anopic hemifield in HA patients, $t(9) = .37$, $p = .72$. Taken together, with respect to these basic auditory tests, the HA patients' auditory performance of both ears was symmetrical and normal.

This study conformed to the Code of Ethics of the World Medical Association (Declaration of Helsinki), printed in the British Medical Journal (18 July 1964). All subjects gave their informed consent to participate in the study, which was approved by the Ethical Committee of the Medical Faculty of the Ruhr University Bochum.

Apparatus

The experiments took place in a sound-proof and anechoic room ($5.4 \times 4.4 \times 2.1$ m^3), which was insulated by 40 cm (height) × 40 cm (depth) × 15 cm (width at base) fiberglass wedges on each of the six sides. A suspended mat of steel wires served as the floor. The ambient background noise level was below 20 dB(A) SPL. All experiments were conducted in total darkness.

The acoustic stimulus was band-pass-filtered noise (lower cut-off frequency .8 kHz; upper cut-off frequency 3 kHz) with a maximum duration of 12 s (rise/fall time 100 ms). Sound stimuli were generated digitally and converted to analog form *via* a computer-controlled external soundcard (Sound Blaster Audigy 2 NX, Creative Labs, Singapore) at a sampling rate of 96 kHz. Sound stimuli were delivered via a semicircular loudspeaker system, with an SPL of 75 dB. The subject sat on a comfortable chair. In front of the subject at a constant distance of 1.5 m from the centre of the head, 91 broad-band loudspeakers (5 × 9 cm^2, Visaton SC 5.9, Visaton, Haan, Germany) were mounted in the subject's horizontal plane. The azimuth of the loudspeakers ranged from -90° (left) to 90° (right), in steps of 2°, with the centre loudspeaker at 0°. For visual stimulation at corresponding azimuthal positions, at the lower edge of the chassis of each loudspeaker a white LED was mounted in a central position. The LED (diameter 10 mm; luminance about 100 cd/m^2) was mounted in a small housing impermeable to light, with a central circular aperture of 2 mm diameter immediately in front of the LED.

Procedure for Experiment 1: Visual pointing to acoustic targets

The subject's head was fixed by a custom-made framework with stabilizing rests for the chin, forehead, and occiput (see Lewald, 1997). In Experiment 1, subjects had to bring a visual stimulus into spatial alignment with a target sound. This task is a modification of the method originally described in Lewald and Ehrenstein (1998). In each trial, a stationary target sound was presented. Acoustic stimuli were presented from 21 loudspeaker positions: straight ahead of the subject (0°), 10 positions on the left and 10 positions on the right with constant angular separation of 4°, thus covering an angular range from 40° to the left to 40° to the right. Each trial began with the onset of the sound stimulus at one of the 21 positions. The stimulus position changed in a quasi-random order between trials. At the moment of sound onset, a continuous light stimulus, delivered from an LED, was presented simultaneously at one out of nine locations (from -24° to 24° azimuth, with angular separation of 6°). The initial position of the light was varied following a quasi-random order. The subject controlled the azimuthal position of the light (over a total range of 180°, in steps of 2°) by adjusting the knob of a potentiometer. The potentiometer was mounted in a small case, so that the subject held it in one hand while turning the knob with the other hand (see Fig. 2 in Lewald et al., 2009a). Subjects were instructed to direct their gaze to the light and, while maintaining fixation on it, to adjust its position (by turning the knob of the potentiometer) toward the position of the sound until the locations of both these stimuli were perceived to be in exact alignment. HA patients were explicitly encouraged to search for the visual stimulus by eye movements, as it could start in their anopic field. The subjects were instructed to press a button (mounted beside the potentiometer knob on the case) as soon as the adjustment was completed. At the moment the key was pressed, both the light and the sound disappeared and the final position of the visual stimulus was recorded. Each of the 21 loudspeaker positions was presented in combination with each of the nine starting positions of the LED, thus resulting in a total number of 189 trials plus repetitions. Two seconds after key pressing, the next trial began. The sound and light stimuli had a maximum duration of 12 s. After about 40 practice trials, all subjects were able to perform the task within about 5-8 s. In cases in which the key was not pressed before the stimulus ended automatically (that is, within 12 s), the trial was repeated at the end of the experiment. Each experiment comprised 168 trials plus repetitions (eight presentations of each stimulus position). The timing of the stimuli and the recording of the subject's responses were controlled by custom-written software.

Procedure for Experiment 2: Acoustic pointing to visual targets

In Experiment 2, subjects were asked to bring an acoustic stimulus into spatial alignment with a visual target. The task was conducted analog to that described for Experiment 1, with the only difference that visual and auditory stimuli were interchanged. Stationary visual target stimuli were presented from 21 LED positions: straight ahead of the subject (0°), 10 positions on the left and 10 positions on the right with constant angular separation of 4° (from -40 to 40° azimuth). The light and sound stimuli had a maximum duration of 12 s. The position of the target light changed in quasi-random order between trials. In each trial, at the moment of light onset a continuous sound stimulus (as described above) was simultaneously delivered from a loudspeaker at one out of nine locations (from -24° to 24° azimuth, with angular separation of 6°). The initial position of the sound was varied following a quasi-random order. The subject controlled the azimuthal position of the sound (over a total range of 180°, in steps of 2°) by adjusting the knob of the potentiometer in an identical manner as described above for adjustment of light stimuli (see 2.3.). Subjects were instructed to direct their gaze to the light and, while maintaining fixation on it, to adjust the sound position (by turning the knob of the potentiometer) toward the position of the light until the locations of both these stimuli were perceived to be in exact alignment. The subjects pressed the button as soon as the adjustment was completed. HA patients were able to perform this task with similar ease as that in Experiment 1. At the moment the key was pressed, both the light and the sound disappeared and the final position of the auditory stimulus was recorded automatically. Each of the 21 LED positions was presented in combination with each of the nine starting positions of the sound, thus resulting in a total number of 189 trials plus repetitions. All other parameters and conditions were identical to those in Experiment 1.

Data analysis

For analysis of the data obtained in Experiments 1-2, the subject's individual pointing responses were determined as a function of target position, and were fitted to a regression line. Data obtained for stimuli presented in the left and right hemispaces were analysed separately. Responses were normalized such that positive angles indicate pointing toward the hemispace within which the stimulus was presented, and negative angles indicate pointing responses to the opposite hemispace (cf., e.g., Fig. 1). Three parameters, derived from the fit, were used to describe different aspects of the subject's individual performance. *(1)* The y-intercept of the regression line was taken as a measure of the subject's constant error in pointing to either side. *(2)* The slope of the regression line (a) was taken as a measure of the subject's general tendency to underestimate ($a < 1$) or overestimate ($a > 1$) the distances between target positions. *(3)* The coefficient of determination (R^2) was taken as a measure of the subject's precision in pointing.

For statistical comparisons, results of LHA and RHA patients, obtained in Experiments 1-2, were normalized and pooled. For this purpose, data were classified according to whether they had been obtained within the hemispace of the patient's anopic or intact field. As already mentioned, each HA patient was assigned to a healthy control subject matched for age and sex. Each data set of the control subject was treated in exactly the same way as the data of the related patient. That is, as data obtained for the left (right) hemispace in LHA patients and data obtained for the right (left) hemispace in RHA patients were pooled, the data obtained for the left (right) hemispace of the matched LHA controls and the data obtained for the right (left) hemispace of matched RHA controls were also pooled. This was mainly done in order to account for effects of handedness on analyses of the normalized data.

Furthermore, *y*-intercepts resulting from analyses were normalized such that positive values indicate a bias in pointing toward the anopic side and negative values a bias toward the intact side. Finally, to adequately compare the *y*-intercepts obtained in Experiment 1 with those of Experiment 2, these values were normalized such that in both experiments positive values indicate final deviations of the visual stimulus from the auditory stimulus toward the anopic side, irrespective of whether the visual stimulus was aligned with the auditory target (Experiment 1) or the auditory stimulus was aligned with the visual target (Experiment 2).

At the first stage of statistical analysis, multi-factor analyses of variance (ANOVAs) were conducted in order to compare performances of HA patients and controls. In subsequent stages of analysis, one-factor ANOVAs were used to reveal differences between the performances measured in the intact hemispace and in the anopic hemispace of HA patients. For all computations, F-statistics were based on ε-corrected degrees of freedom

(Greenhouse-Geisser correction). Bonferroni-corrected p-values were used for multiple comparisons.

Results

Although HA patients had some difficulties in performing these tasks, linear regression of the pointing responses as a function of target azimuth was significant ($p < .0001$) for all participants, both in Experiment 1 (HA patients: mean $R^2 = .87$, range from .48 to .96; controls: mean $R^2 = .93$, range from .82 to .97) and in Experiment 2 (HA patients: mean $R^2 = .80$, range from .65 to .94; controls: mean $R^2 = .87$, range from .71 to .95).

A 2 × 2 × 2 mixed ANOVA with Task [visual pointing, acoustic pointing] and Hemispace [anopic, intact] as within-subject factors and Group [HA, controls] as between-subjects factor was conducted for the coefficient of determination (R^2) of the linear regression. The ANOVA revealed a main effect of Task, $F(1,18) = 12.32$, $p = .003$, $\eta_p^2 = .41$, indicating a generally higher precision with light pointing than with acoustic pointing (Fig. 1, 2). No further main effect or interaction was significant (all $F \leq 3.71$).

For the normalized y-intercept resulting from the linear regression, an analogous ANOVA was conducted. The ANOVA revealed a main effect of the factor Group, indicating the general bias in adjustments with visual stimuli shifted, with reference to auditory stimuli, to the side of the anopic hemifield, $F(1,18) = 12.39$, $p = .002$, $\eta_p^2 = .41$. Furthermore, a main effect of Hemispace, $F(1,18) = 6.19$, $p = .023$, $\eta_p^2 = .26$, was in alignment with the general asymmetry in displacements. Finally, a three-way interaction of Task × Hemispace × Group, $F(1,18) = 5.08$, $p = .037$, $\eta_p^2 = .22$, was found. Taken together, the findings of this ANOVA confirmed the obvious influence of HA on cross-modal constant error, as obtained concordantly in both tasks: Stimulus pairs were adjusted such that visual stimuli were shifted toward the anopic side with reference to the auditory stimuli. As confirmed by the three-way interaction, this bias was stronger in the patients' anopic hemispace than on the intact side, and the bilateral asymmetry was more prominent with the light-pointing task than with acoustic pointing (Figs. 1-3).

Finally, an ANOVA, computed for the slope of the regression line, revealed a main effect of the factor Task, $F(1,18) = 31.33$, $p < .0001$, $\eta_p^2 = .64$, confirming that in the acoustic pointing task (Experiment 2) lateral target positions were increasingly underestimated with increasing eccentricity, whereas in the light pointing task (Experiment 1) the lateral target positions were increasingly overestimated with increasing eccentricity (cf. Figs. 1, 2). In addition, a Task × Hemispace × Group threefold interaction, $F(1,18) = 13.74$, $p = .002$, $\eta_p^2 = .43$, indicated a differential influence of HA on the slope in both tasks: The slope obtained with light pointing was decreased in the patients' anopic hemifield and increased in the intact hemifield with reference to healthy controls, whereas the opposite pattern was found with acoustic pointing (Fig. 3 C, D).

If the ANOVAs for all three dependent variables were restricted to HA patients with left hemispheric lesions (together with corresponding control subjects), the significance of the results (not shown here) remained essentially unchanged (the 3-way interaction for the *y*-intercept dependent variable only approached significance, $F(1,12) = 4.43$, $p = .057$).

If the three patients with lesions involving parietal areas and their respective controls were excluded and the analyses were restricted to patients with temporal and/or occipital lesions, all main effects and interactions with Group as a factor remained the same when analysing the slope and R^2. The only difference occurred for the *y*-intercept, for which the three-way interaction of Task × Hemispace × Group only approached significance, $F(1,12) = 3.50$, $p = .086$, $\eta_p^2 = .23$.

These results, and in particular the three-way interaction are complicated by the fact that the slope for the auditory pointing task is in terms of degrees of auditory pointing location *per* degree of change in visual location whilst the slopes for the visual pointing task are in the inverse units. One means of clarifying the results for slope is to recast the analysis so that, for both tasks, the dependent variable slope is always the change in position of the auditory stimulus obtained for a given change in location of the visual stimulus (i.e., as in Fig. 3C and 3D). When we did this, the analysis revealed a significant effect of Task, $F(1,18) = 15.64$, $p < .001$, and an interaction between Group and Hemispace, $F(1,18) = 15.08$, $p < .001$. The three-way interaction (which in the original analysis merely reflected the fact that the auditory location and visual location axes were interchanged in the two tasks) disappeared. These results clarified the finding from the untransformed data insofar as visual space relative to the auditory representation of space was compressed more strongly on the intact, than on the anopic, side in HA patients, while normal controls performed essentially symmetrically.

Subsequent analyses for the group of HA patients were conducted for the three parameters resulting from the linear regression, using one-factor ANOVAs with Hemispace as factor. The analysis for the coefficient of determination did not provide significant differences between hemispaces, thus suggesting equal precision in pointing in both hemispaces (Experiment 1: $F(1,9) = 2.20$, $p = .17$, $\eta_p^2 = .20$; Experiment 2: $F(1,9) = 2.70$, $p = .14$, $\eta_p^2 = .23$). However, an analogous ANOVA revealed a significant difference in the position of the *y*-intercept between hemispaces for Experiment 1, $F(1,9) = 7.29$, $p = .024$, $\eta_p^2 = .45$: The bias of visual pointing, with reference to auditory targets, toward the anopic side was stronger within anopic hemispace (mean 6.72°, SE 1.15) than within intact hemispace (mean 2.96°, SE .98; Fig. 3). In Experiment 2, the bias of acoustic pointing was almost equal in anopic (mean 4.39°, SE .83) and intact hemispaces (mean 3.83°, SE .70), $F(1,9) = .64$, $p = .44$, $\eta_p^2 = .07$ (Fig. 3). Finally, an analogous one-factor ANOVA with Hemispace as factor indicated a significantly steeper slope of the regression line in anopic (mean .86, SE .06), than in intact, hemispace (mean .77; SE .05) in Experiment 2, $F(1,9) = 14.25$, $p = .004$, $\eta_p^2 = .61$, thus suggesting that the effects of HA partially counteracted the normally observed pattern of increasing underestimation with increasing target eccentricity (see above). For Experiment 1, this approached significance, $F(1,9) = 3.81$, $p = .08$, $\eta_p^2 = .30$, suggested that the normally observed increase in overestimation with increasing target eccentricity was partially reduced in anopic hemispace (see above).

It is important to note that these results describe divergences between visual and auditory spatial representations, but not deviations of perceptual from physical spatial coordinates. As a consequence, these findings, if considered in isolation, did not allow any conclusions of whether HA patients showed perceptual anomalies in audition or vision, or in both of these modalities. To clarify this problem, data obtained in one modality are needed in addition. In our preceeding study (Lewald et al., 2009b), all HA patients included here had been tested for auditory localization by using a task of hand pointing to acoustic targets. In that study, these ten individuals showed a constant error in pointing toward the anopic side, that was, however, relatively small in amplitude (anopic side: mean 2.63°, SE 1.54; intact side:mean .42°, SE 1.81). A statistical comparison of the intermodal divergence between visual and auditory locations (mean normalized *y*-intercepts from Experiments 1 and 2; Fig 3A, B) and the unimodal auditory *y*-intercepts taken from Lewald et al. (2009) for both hemispaces revealed a significantly larger bias in the present study (mean 4.47°, SE .67) than in the preceeding study (mean 1.52°, SE .50), $t(9) = 4.00$, $p = .003$. Also, the slope obtained by Lewald et al. (2009b) for the regression line of hand pointing responses as a function of auditory target position (mean .94, SE .05) was significantly flatter than the mean slope obtained here after conversion of data such that visual positions were always plotted as a function of sound position (mean 1.18, SE .06), $t(9) = 3.93$, $p = .003$. Thus, given the previous unimodal auditory results from the same HA patients (Lewald et al., 2009b), the already known distortion of their auditory space significantly differed from the intermodal distortion found here.

Discussion

These results demonstrated a significant distortion of visual space with reference to auditory space in patients with pure HA. First, HA patients generally perceived visual locations to be displaced toward their intact hemifield. Secondly, HA patients perceived visual space relative to the auditory representation of space as more compressed in their intact, than in their anopic, hemifield.

The interpretation of these findings is complicated by the fact that HA patients might potentially exhibit distortions not only in their visual representations of space (Zihl & von Cramon, 1986; Ferber & Karnath, 1999) but also in the auditory modality (Lewald et al., 2009a, b), although these latter anomalies seemed to be relatively slight. Nevertheless, unimodal auditory distortions of space perception cannot explain the intermodal divergences found here. The same patients, who were participants in the current study have also been tested in hand pointing to auditory targets (Lewald et al., 2009b). The extent of the unimodal distortion found in that previous study cannot account for the intermodal distortion found here. Lewald et al. (2009b) reported constant errors that were about half the values obtained here for intermodal bias. This suggests that the results obtained in the current study had their origin primarily in the anomalies of visual spatial perception, rather than in the auditory domain. Lewald et al. (2009a) found the auditory straight ahead of HA patients not to differ from that of normal controls. It may therefore be reasonable to conclude that constant errors in auditory localization, although statistically significant, are small in magnitude compared with the distortions of visual space in HA. If one assumes that auditory space perception is only subject to relatively small errors, the pointing bias obtained in both experiments is consistent with a distortion of visual space in which visual positions were mislocalized toward the unimpaired hemifield (Fig. 3A, B), suggesting visual space was perceived as compressed on the intact, compared with the anopic, hemifield (Fig. 3C, D).

This conclusion is in line with previous findings on the position of the visual straight ahead in pure HA. Several studies consistently demonstrated a bias of the visual straight ahead toward the anopic side (Zihl & von Cramon, 1986; Ferber & Karnath, 1999; Lewald et al., 2009a). That is, if a visual stimulus is physically located straight ahead, it will be mislocalized toward the intact side. The amplitude of the shift in visual straight ahead was reported to be about 4-8°, which is compatible with the average bias of 4.47° obtained here given a substraction of the mean unimodal auditory bias of 1.52° measured by Lewald et al. (2009b). These earlier results are, however, based on estimates of visual locations with reference to the subjective coordinates of the body. They could be confounded by a proprioceptive bias that might occur in addition to visual anomalies with HA (Lewald et al., 2009a). Such proprioceptive factors cannot account for the results obtained in the current study.

Unlike the previous findings on visual straight ahead, which were restricted to one central point in space only, the present results provide information on a broader topography of visual space in HA patients. Taken together, our data indicate that the rotation of the visual space along the horizontal axis results in a perceptual expansion in the contralesional (blind) hemifield and a compression in the ipsilesional (intact) hemifield. There is a conflict in the literature about the nature of visual space distortion in HA. Our conclusion is consistent with findings of Doricchi et al. (2002), showing that HA patients estimated lengths and distances in the contralesional space as being larger than their equivalents in the ipsilesional space. Our results are not consistent with studies showing that the horizontal angular distances between visual stimuli (Zihl & Von Cramon, 1986) or sizes of rectangles along the horizontal axis

(Ferber & Karnath, 2001a) were perceived as smaller on the anopic hemifield than on the intact side. The reasons for this inconsistency between previous studies are not entirely clear (see discussion in Ferber & Karnath, 2001a; Doricchi et al., 2002).

From a methodological point of view, it is important to emphasize that in our experiments patients fixated a single light spot in total darkness. In the studies of Zihl & Von Cramon (1986), Ferber & Karnath (2001a), and Doricchi et al. (2002) patients had to judge distances between simultaneously presented visual stimuli or the size of visual objects in space. In the present study, subjects were presented with single punctiform visual stimulus in otherwise empty space. Their pointing responses (whether with a visual pointer or with a visual target) are more likely to reflect absolute judgements of localization than judgements of the relatiave locations of pairs of points. Relative spatial judgement may enage processes above and beyond those required to make a simple localization. Our results may therefore provide a more direct estimate of space distortion in HA.

Several methodological issues have to be considered given our use of two complementary tasks, The analyses of the coefficient of determination (R^2) showed that the acoustic-pointing responses were more variable than light-pointing responses. This may reflect greater uncertainty in the localization of the acoustic pointer compared with the light pointer and the fact that subjects were, doubtlessly, more familiar with pointing to objects visually in everyday life. Critically, however, there were no significant differences in variability between groups, suggesting that these task differences did not have a differentially strong effect on HA patients. These differences in task difficulty may have contributed to the task-related differences in slope as found in both normal controls and HA patients. While light pointing was nearly veridical, with acoustic pointing subjects generally underestimated the eccentricity of the target, resulting in flatter slope of regression lines (Fig. 1, 2). Most likely, the acoustic marker was not moved far enough due to the greater uncertainty in this task. In the acoustic pointing task, the stationary visual target, which may have been in a location initially invisible to HA patients, had to be localized at the start of a trial. This imposed a visual search demand that was not present in the light pointing task. There was, however, no time pressure to respond and the opportunity to repeat the trial if the target was not perceived in time. The results (see Fig. 2) suggest that HA patients did not have specific problems in acoustic pointing (Experiment 2), compared with visual pointing (Experiment 1).

There is another potential problem with using two modalities simultaneously. In the so-called ventriloquism effect the location of an auditory stimulus is captured by a simultaneously presented visual stimulus. This effects is, however, unlikely to have affected results in the current study because it is critically dependent on synchronized transient or modulated signals in the auditory and visual modalities (see, e.g., Lewald, Ehrenstein, & Guski, 2001). In our experiment, visual and auditory stimuli were present continously and so no such synchronized transients occurred.

The patients' perceptual anomalies found here provide direct evidence for substantial differences in the distortions of sensory space between auditory and visual modalities. There is already a large body of evidence showing significant differences between uni-modal and cross-modal processing in brain-damaged patients, including those with visual field defects. In fact, although HA patients may exhibit distortions in their visual representations of space as well as in the auditory modality, their cross-modal abilities might be preserved (e.g., Bolognini, Rasi, Coccia, & Làdavas, 2005; Leo, Bolognini, Passamonti, Stein, & Làdavas, 2008; Passamonti, Frissen, & Làdavas, 2009). However, had the distortions of auditory and visual space been essentially similar, then in our bimodal approach they would have cancelled each other out. Pointing responses would appear to be veridical as the coordinates in the distorted auditory and visual spaces would nevertheless be congruent with one another. Our finding that these space distortions cannot be similar matches the direct comparison by

Lewald et al. (2009a) who showed a considerable divergence between the subjective straight-ahead directions of HA patients in the visual and auditory modalities. Based on the earlier literature on distortions of visual space in HA (see above), Lewald et al. (2009b) originally assumed that processes of cross-modal spatial adaptation induced a visual miscalibration of auditory space, such that its coordinates would be slightly shifted toward the point of alignment with the distorted visual coordinates. Although the present experiments were not intended to test this hypothesis, the results shed doubts on its validity. It seems reasonable to conclude that the auditory space of patients with pure HA remained largely unaffected by the consistent auditory-visual disparity. If HA patients retain an undistorted representation of auditory space, then it should be possible to exploit the auditory system in rehabilitation of visual field disorders, even when very severe impairment of visual abilities limits the effectiveness of purely visual approaches (Lewald et al., 2012).

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Table 1. Summary of clinical data and visual field defects of patients with hemianopia.

Patient	Age	Sex	Side of HA	VF border	Time since onset	Ethiology	Lesion site
LHA1	38	F	L	-1.2°	7 months	AVM, ICH	R temporo-parieto-occipital
LHA2	60	M	L	-2.9°	7 years	ICH	R temporal
LHA3	64	M	L	-1.7°	6 months	CI	R temporo-occipital
LHA4	64	M	L	-4.6°	5 years	CI	R occipital
LHA5	42	F	L	-0.3°	35 months	CI	R temporal
LHA6	54	F	L	-0.2°	19 months	CI	R temporo-parieto-occipital
LHA7	39	M	L	-1.8°	5 years	CI	R occipital
RHA1	44	M	R	12.5°	5 months	CI	L temporo-occipital
RHA2	48	M	R	0.4°	33 months	CI	L temporo-occipital
RHA3	37	F	R	8.2°	6 months	CI	L parieto-occipital, R occipital

Abbreviations AVM, cerebral arteriovenous malformation; CI, cerebral ischemia; F, female; ICH, intracerebral hemorrhage; HA, hemianopia; L, left; M, male; R, right; VF, visual field. Negative angles are to the left, positive angles to the right.

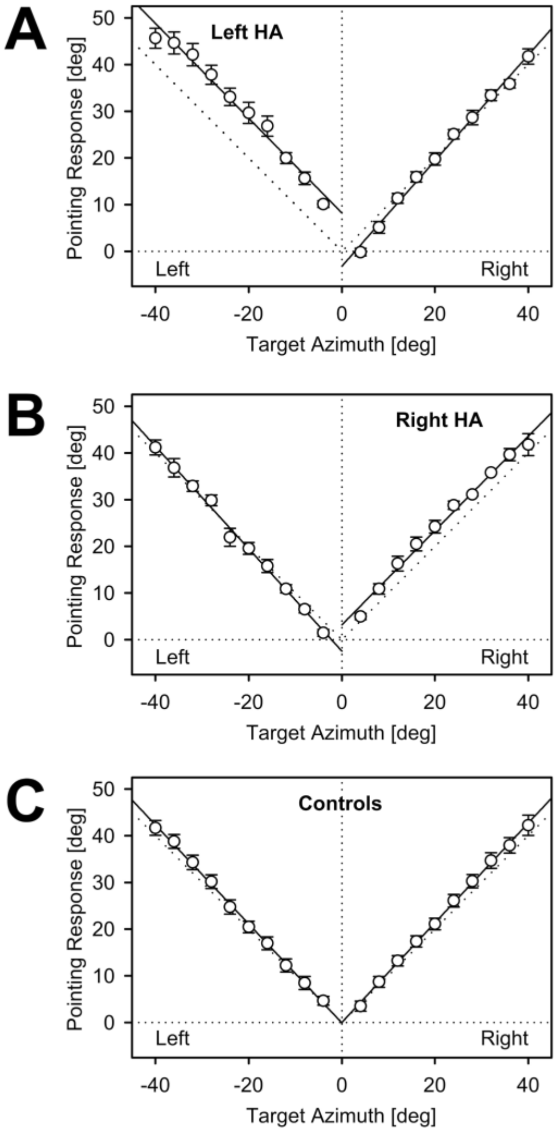


Figure 1. Results of Experiment 1 (visual pointing to acoustic targets). Final pointing eccentricities (mean values ±SE) are plotted as a function of target azimuth for patients with left (A) and right HA (B), and for matched controls (C). Data obtained for stimuli presented in the left and right hemispaces were analysed separately. Responses were normalized such that positive angles indicate pointing toward the hemispace within which the stimulus was presented, and negative angles indicate pointing responses to the opposite hemispace. Continuous lines indicate regression lines, dotted lines indicate ideal performance.

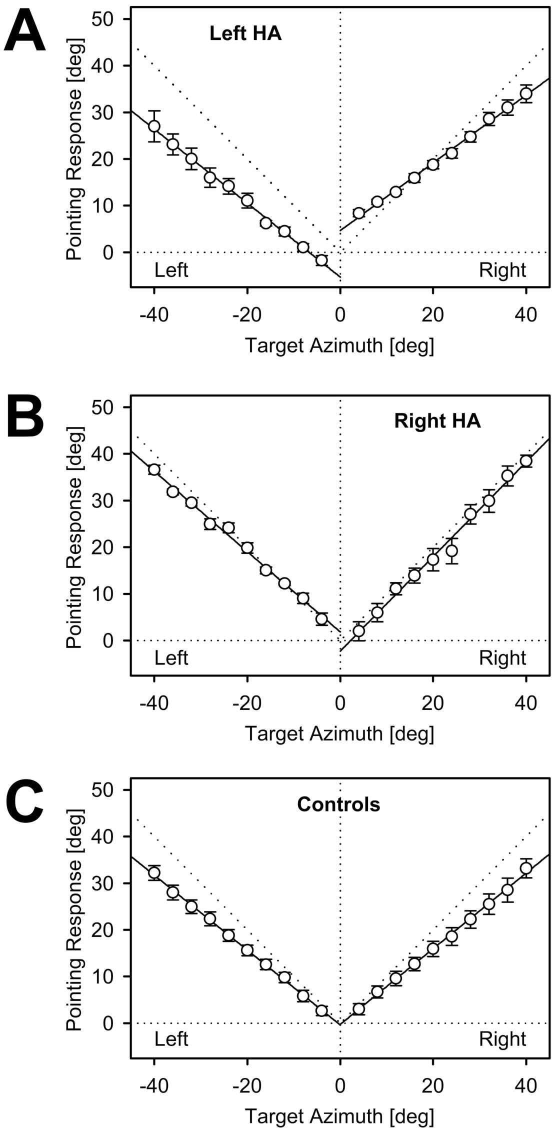


Figure 2. Results of Experiment 2 (acoustic pointing to visual targets). Final pointing eccentricities (mean values ±SE) are plotted as a function of target azimuth for patients with left (A) and right HA (B), and for matched controls (C). Conventions are as in Fig. 1.

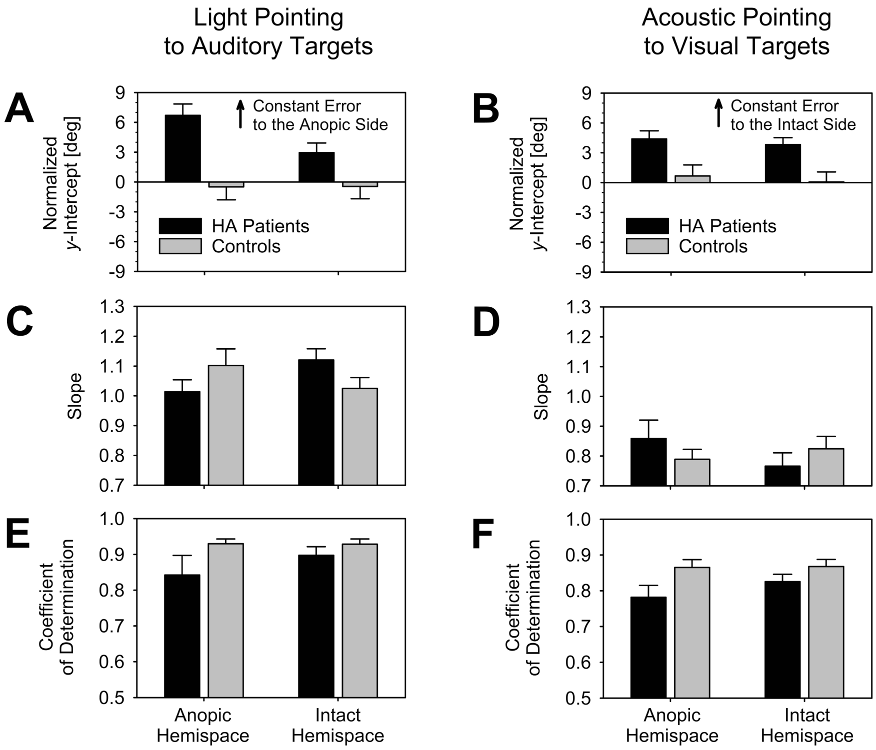
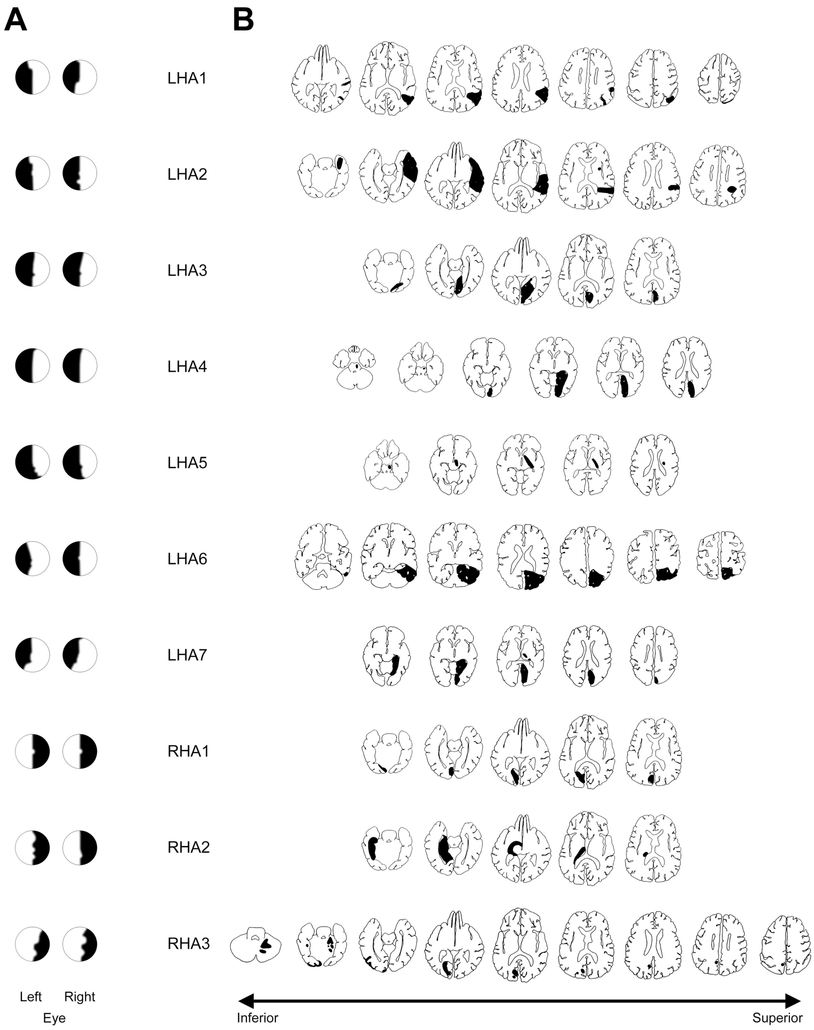


Figure 3. Linear regression analysis of the pointing responses for Experiments 1 and 2. Each panel shows data (mean values ± SEM) obtained in the anopic and intact hemispaces of patients with HA as well as data from matched controls. For the control subjects the 'anopic hemispaces' and 'intact hemispaces' were that hemispaces that were assigned as controls to the anopic and intact hemispaces of patients with HA (see Materials and Methods). (A and B) *y*-intercepts of the regression lines that were taken as a measure of constant error in pointing. Data were normalized such that positive values indicate final deviations of the visual stimulus from the auditory stimulus toward the anopic side, irrespective of whether the visual stimulus was aligned with the auditory target (A) or the auditory stimulus was aligned with the visual target (B). (C and D) Slopes of the regression lines that were taken as a measure of the subject's general tendency to underestimate (values < 1) or overestimate (values > 1) distances between target positions. (E and F) Coefficients of determination of the regression lines that were taken as a measure of precision in light pointing (E) and acoustic pointing (F).

Supplementary Material

Supplementary Table 1. Summary of lesion data. Areas involved by lesion are coded using the method of Damasio and Damasio (1989)

Patient	Frontal lobe	Temporal lobe	Parietal lobe	Occipital lobe	Central grey and adjoining white matter
LHA1		Right T6	Right P2	Right O4, O5	
LHA2		Right T3, T4, T 6, T 9, T12			
LHA3		Right T11		Right O1, O2, O3, O7	Right BG1
LHA4		Right T4		Right O1, O2, O4, O5	
LHA5		Right T10, T11, T12			Right Th1, Th3, IC2
LHA6	Right F2	Right T4, T6	Right P2, P4	Right O1, O2, O3, O4, O5	
LHA7				Right O1, O2	
RHA1	Left F2			Left O1, O2, O3, O6	
RHA2		Left T6, T10, T11		Left O3, O6	
RHA3	Left F2		Left P4	Left O1, O2, O3, O6 Right O4	



Supplementary Figure 1. Visual field defects and lesion sites of patients with left (LHA1-7) and right hemianopia (RHA1-3). (A) Reconstructions of the monocular central visual fields based on static perimetry (up to 30° eccentricity; black areas, anopic regions; white areas, intact regions). (B) Series of schematic brain slices along the superior-inferior direction for each of the ten patients are depicted using standardized templates from Damasio and Damasio (1989), with black areas indicating the lesioned sites. More inferior templates are to left, more superior templates to the right. Templates are in neurological orientation, i.e., the left side of the template refers to the left side of the brain.