EJN fens EUROPEAN JOURNAL OF NEUROSCIENCE

European Journal of Neuroscience, Vol. 30, pp. 1141–1150, 2009 doi:10.1111/j.1460-9568.2009.06910.x

COGNITIVE NEUROSCIENCE

Visual recalibration of auditory spatial perception: two separate neural circuits for perceptual learning

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Keywords: hemianopia, neglect, plasticity, ventriloquism after effect, visual awareness

Abstract

A remarkable example of rapid perceptual learning is the visual recalibration of auditory spatial perception, which can result in either a bias (ventriloquism after-effect) or an improvement (multisensory enhancement) in auditory localization. Here, we examine the possibility that these after-effects might depend on two distinct neural pathways (geniculostriate vs. collicular–extrastriate). To this end, patients with a lesion of the striate cortex (hemianopic patients) or temporoparietal cortex (neglect patients) were asked to localize weak sounds, before and after a brief exposure to repetitive auditory–visual stimulation which was given either in the normal or in the affected field. Adaptation comprised spatially disparate (Experiment 1) or spatially coincident (Experiment 2) auditory–visual stimuli. After exposure to spatially disparate stimuli in the normal field, all patients exhibited the usual shifts toward the visual attractor, at each sound location. In contrast, when the same kind of adaptation was given in the affected field, a consistent shift was still evident in neglect patients but not in patients with hemianopia. After adaptation to spatially coincident stimuli, and regardless of the adaptation hemifield, all patients exhibited a significant improvement in auditory localization, which was largest for sounds presented at the adapted location. The findings suggest the presence of two distinct recalibration mechanisms. Adapting to spatially conflicting stimuli invokes a corrective mechanism implemented within the geniculostriate circuit, which tries to reduce the registered discrepancy. Adapting to spatially aligned inputs invokes a mechanism implemented along a collicular–extrastriate circuit, which tries to reduce the localization error.

Introduction

The ability to localize an auditory stimulus in space is a highly complex computational process, one which is less accurate and reliable than visual localization. As a consequence, a visual cue is able to either bias (often referred to as the ventriloquism effect; Howard & Templeton, 1966) or reduce (i.e., multisensory enhancement) auditory localization errors. The ventriloquism effect is observed when the visual and the auditory stimuli are spatially disparate (Bertelson & Radeau, 1981; Howard & Templeton, 1966; Slutsky & Recanzone, 2001), while multisensory enhancement results from the integration of spatially coincident auditory–visual stimuli (Stein *et al.*, 1988; Frassinetti *et al.*, 2002, 2005; Bolognini *et al.*, 2007).

Neuropsychological studies have brought to light some of the neural mechanisms underlying these phenomena. Bertelson *et al.* (2000) investigated the occurrence of the ventriloquism effect in patients with a lesion of frontoparietal network (i.e., patients with visual neglect), demonstrating that visual stimuli, although not explicitly detected, could bias auditory localization. A recent study on patients with damage to the striate cortex (i.e., patients with hemianopia; Leo *et al.*, 2008) showed that the lesion prevents any visual bias, suggesting a crucial role of primary visual areas for this phenomenon. At the same time, multisensory enhancement was evident in these patients when the visual and the auditory stimuli were presented simultaneously in the same location. These findings suggest that visual bias and multisensory enhancement might be mediated by different circuits, with the former dependent on geniculostriate circuits and the latter dependent on collicular–extrastriate circuits.

Taken together, these two studies have demonstrated that visual stimuli, although not explicitly detected, can exert some effects on auditory spatial processing. It is worth pointing out that they studied the immediate or on-line effects of auditory–visual stimulation. However, we do not know whether cross-modal stimulation under the same circumstances can also induce off-line changes in spatial processing (i.e. perceptual learning). For instance, in healthy subjects, prolonged exposure to a ventriloquism-like situation leads to a remapping of auditory localization (i.e., the ventriloquism after-effect; AE); the apparent location of sounds, presented unimodally after a period of exposure to spatially incongruent sound–flash pairs, is

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Received 16 March 2009, revised 14 July 2009, accepted 16 July 2009

displaced in the direction of the preceding visual stimulus (Canon, 1970; Radeau & Bertelson, 1974; Recanzone, 1998; Lewald, 2002; Frissen *et al.*, 2003). It is generally agreed that AEs to such discrepant sensory inputs reflect a visually-driven recalibration process that results in a short-term reduction in the perceived discrepancy. This kind of perceptual learning is thought to play an important role in achieving and maintaining a coherent intersensory representation of space (Held, 1965; Welch, 1978).

The neural correlates of such AEs are still debated. Sensitivity to visual stimulation has been widely demonstrated in the auditory cortex of humans (Giard & Peronnet, 1999; Molholm *et al.*, 2002). Neuroimaging studies (Calvert *et al.*, 1999; Bernstein *et al.*, 2002; Calvert & Campbell, 2003; Pekkola *et al.*, 2005; van Wassenhove *et al.*, 2005; Lehmann *et al.*, 2006; Martuzzi *et al.*, 2006) promoted the notion that auditory–visual interactions occur in early auditory areas, possibly even in the primary auditory cortex. Recordings of local field potentials in auditory regions revealed a widespread influence of visual stimuli on acoustic responses (Schroeder & Foxe, 2002; Schroeder *et al.*, 2003; Ghazanfar *et al.*, 2005, 2008; Lakatos *et al.*, 2007). The visual inputs to the auditory cortex arise from a number of sources; in addition to multisensory inputs from association areas and the thalamic nuclei, there are direct connections from both the primary and the non-primary visual cortex (Rockland & Ojima, 2003; Budinger *et al.*, 2006; Bizley *et al.*, 2007; Hackett *et al.*, 2007). There is also extensive evidence that neural response properties of the auditory cortex can be shaped by learning and by other changes in sensory inputs (for a review, see Ohl & Scheich, 2005).

Thus, one of the questions addressed in the present study is whether the ventriloquism AE is due to the influence of the striate cortex on the auditory cortex or whether it is the result of the activation of multisensory association areas. To this aim, we studied patients with impairment of visual awareness due to a lesion of either the striate cortex (i.e., hemianopic patients) or temporoparietal cortex (i.e., neglect patients). If the geniculostriate circuit, which is spared in neglect but not in hemianopic patients, is a crucial pathway for the occurrence of the ventriloquism AE, then such effect should be absent after adapting the contralesional field of hemianopic patients. In contrast, the ventriloquism AE should be evident after adapting the contralesional field of neglect patients, due to their spared striate cortex. These results would prove that striate areas have a crucial role in driving a plastic change in auditory spatial processing. To test this hypothesis, in Experiment 1, patients with visual neglect or hemianopia were adapted to auditory–visual stimuli that were spatially disparate.

However, a different kind of AE could be still possible after a lesion of the striate area. As already mentioned, visual information can exert an on-line enhancement of auditory localization through the collicular–extrastriate circuit (Leo *et al.*, 2008). To date, however, no AEs of multisensory enhancement have been demonstrated. In other words, it is unknown whether passive exposure to spatially coincident auditory–visual stimulation results in an improvement in auditory localization. Thus, in Experiment 2, adaptation was carried out with sound and light that were spatially coincident. We hypothesize that AEs of multisensory enhancement should be observed in both neglect and hemianopic patients because spatially coincident auditory–visual stimuli facilitate the activation of the collicular–extrastriate circuit, which is spared in both patient groups (Stein & Meredith, 1993; Bolognini *et al.*, 2007; Leo *et al.*, 2008).

Another aim was to evaluate how adaptation to consciously and unconsciously processed visual stimuli differently affect plasticity in the auditory localization system. The comparison between adaptation in the ipsilesional and contralesional hemifields will allow us to assess the role of visual awareness in the recalibration mechanisms.

The last aim of the present study was to assess the generalization of AEs across space, that is, whether perceptual learning, if any occurred, transfers to nonadapted locations (Zwiers *et al.*, 2003; Bertelson *et al.*, 2006; Sarlat *et al.*, 2006). In the current work, generalization of AEs to untrained spatial positions would indicate that adaptation reached a high level of processing. Such generalization is expected in Experiment 1, due to the presumed involvement of the geniculostriate circuit in this type of perceptual learning. Conversely, AEs limited to the trained location would suggest that adaptation was constrained to a lower level with a point-to-point representation of acoustic space (Stecker *et al.*, 2005). We expect to find such a spatially-specific effect in Experiment 2, due to the presumed involvement of collicular–extrastriate circuit.

Materials and methods

Experimental setup

The apparatus (see Fig. 1) consisted of a 110-cm-radius perimeter covering an azimuthal range of 180°, containing an array of red light-emitting diodes (LEDs) separated by 2.5° and loudspeakers separated by 10°. Seven speakers were used in the current study. They were positioned at 0° (i.e., straight ahead) and at 10, 20 and 30° to the left and to the right of straight ahead. An adjustable chin-mount was positioned at the centre of the perimeter. Offset 15 cm from the centre of the semicircle was a joystick-style yoke comprised of handles, two buttons and a laser pointer. The beam of the pointer fell on a black cardboard strip, and could be moved horizontally by turning the yoke. The spatial resolution of the laser pointer was better than 0.05°. The entire apparatus was set in a dark, sound-attenuated room. The experiment was controlled via a Pentium-class personal computer.

The auditory stimulus was a single 100-ms white-noise burst. Prior to the experiment, the stimulus was calibrated for each patient so as to be difficult to localize. The criterion for stimulus selection was an error of > 5°on at least 50% of the trials; otherwise, uncertainty was added by decreasing the sound intensity (range 78.5–68.5 dB; Leo *et al.*, 2008). The visual stimulus also lasted 100 ms with the luminance set at 3.5 cd/m^2; this stimulus was used in a unimodal visual detection task, a forced-choice task and in cross-modal adaptation trials.

Patients

Nine patients with hemianopia and six patients with left hemifield neglect were tested, according to the guidelines set out in the Declaration of Helsinki and with the approval of the Ethical Committee of the Department of Psychology of the University of Bologna. All patients were naïve to the purpose of the present experiment and none of them had participated in previous studies. They gave informed consent to participate. Details concerning sex, age, length of illness, lesion sites and side of the affected visual field are reported in Table 1. All patients participated in Experiment 1 and Experiment 2; seven of the 15 patients (P2, P4, P6, P8, P10, P12 and P14) started with Experiment 2 and then took part in Experiment 1.

All patients had normal hearing thresholds and normal visual acuity. Patients with hemianopia were selected based on their performance on a visual perimetry test and a neuropsychological examination, which also involved a test for visuospatial deficits typically used with neglect patients (i.e. Bell's test; Gauthier *et al.*, 1989). Their performance in this task was normal (see Table 2), as expected by the side and the site of patients' lesion (see Fig. 2). All of them showed a complete homonymous hemianopia with a visual field sparing of < 5°, and no other cognitive impairment. They were recruited at least 5 months

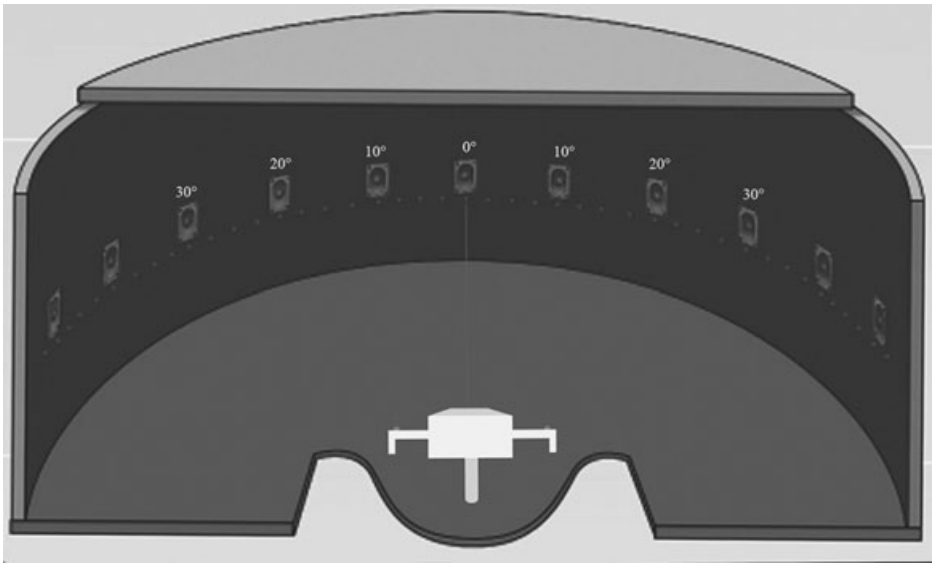

FIG. 1. Schematic view of the experimental setup. The laser beam depicted in the figure was used for the auditory localization task. Only the labelled loudspeakers were used in the experiment. In the detection task and in the two-alternatives forced-choice task, the patient used the two response buttons mounted on the joystick.

TABLE 1. Summary of clinical data

Patient	Age (years)	Sex	Etiology	Time from illness onset (months)	Lesion site	Deficit
Hemianopia						
P1	37	F	Vascular	54	T-O	Right hemianopia
P2	60	M	Vascular	18	T-P-O	Left hemianopia
P3	64	M	Vascular	5	O	Right hemianopia
P4	42	M	Vascular	8	O	Right hemianopia
P5	23	M	Trauma	60	F-T-O	Right hemianopia
P6	40	M	Vascular	108	O	Right hemianopia
P7	52	M	Vascular	54	T-O	Left hemianopia
P8	56	M	Vascular	18	O	Left hemianopia
P9	75	M	Vascular	5	O	Right hemianopia
Neglect						
P10	57	M	Vascular	18	T-P	Left hemineglect
P11	66	M	Meningioma	48	F-T	Left hemineglect
P12	60	F	Vascular	39	T-P	Left hemineglect
P13	34	F	Vascular	42	T-P	Left hemineglect
P14	70	F	Vascular	36	T-P	Left hemineglect
P15	72	F	Vascular	8	T-P	Left hemineglect

F, female; M, male; T, temporal; O, occipital; F, frontal.

TABLE 2. Scores in the cancellation test (Bell's test) and the behavioural inattention test (BIT)

	Bell's test (%)		BIT
	Left	Right	Score
Hemianopia			
P1	100	100	–
P2	100	100	–
P3	100	100	–
P4	100	100	–
P5	100	100	–
P6	100	100	–
P7	100	100	–
P8	100	100	–
P9	100	100	–
Neglect			
P10	56*	81	107*
P11	73*	93	105*
P12	67*	100	124*
P13	67*	100	121*
P14	67*	88	124*
P15	7*	93	107*

Bell's test, percentages of stimuli correctly cancelled; asterisks denote a pathological performance. BIT, asterisks denote a pathological performance (cutoff, 129). Asterisks indicate a pathological performance in both tasks. In the BIT, asterisks indicate a score < 129 (=cutoff).

after the onset of their hemianopia, when their visual field defects were stable. Eight patients had cerebral infarctions and one had traumatic brain injury. CT and MRI scans of these patients revealed that lesions mainly involved the occipital lobe, with a complete damage or deafferentation of striate cortex (see Fig. 2).

Patients with neglect were selected based on their defective performance in a standardized battery of tests for visuospatial deficits, i.e. the Bell's test (Gauthier *et al.*, 1989) and the Behavioural Inattention test (Wilson *et al.*, 1987; see also Table 2). They were recruited at least 8 months after their injury. None of them had a concomitant visual field defect, as documented by a clinical visual field test and as expected by the lesion site. Five of them suffered from cerebral infarctions, one had a meningioma. Structural images confirmed that lesions mainly involved the parietal and the temporal lobe, with the exception of one patient (P11) who showed a lesion also including frontal areas. It is worth noting, however, that both the striate areas and the optic radiations were spared in all patients with neglect (see Fig. 2).

Inclusion in the study was also based on performance on a unimodal visual detection task and a two-alternative forced-choice task, which directly assessed patients' capacity to detect the visual stimulus used during adaptation.

Assessment of visual processing

Unimodal visual detection task

A visual target was presented for 100 ms in each of four spatial positions, (7.5 and 20° left and right of the fixation point). Eighty trials

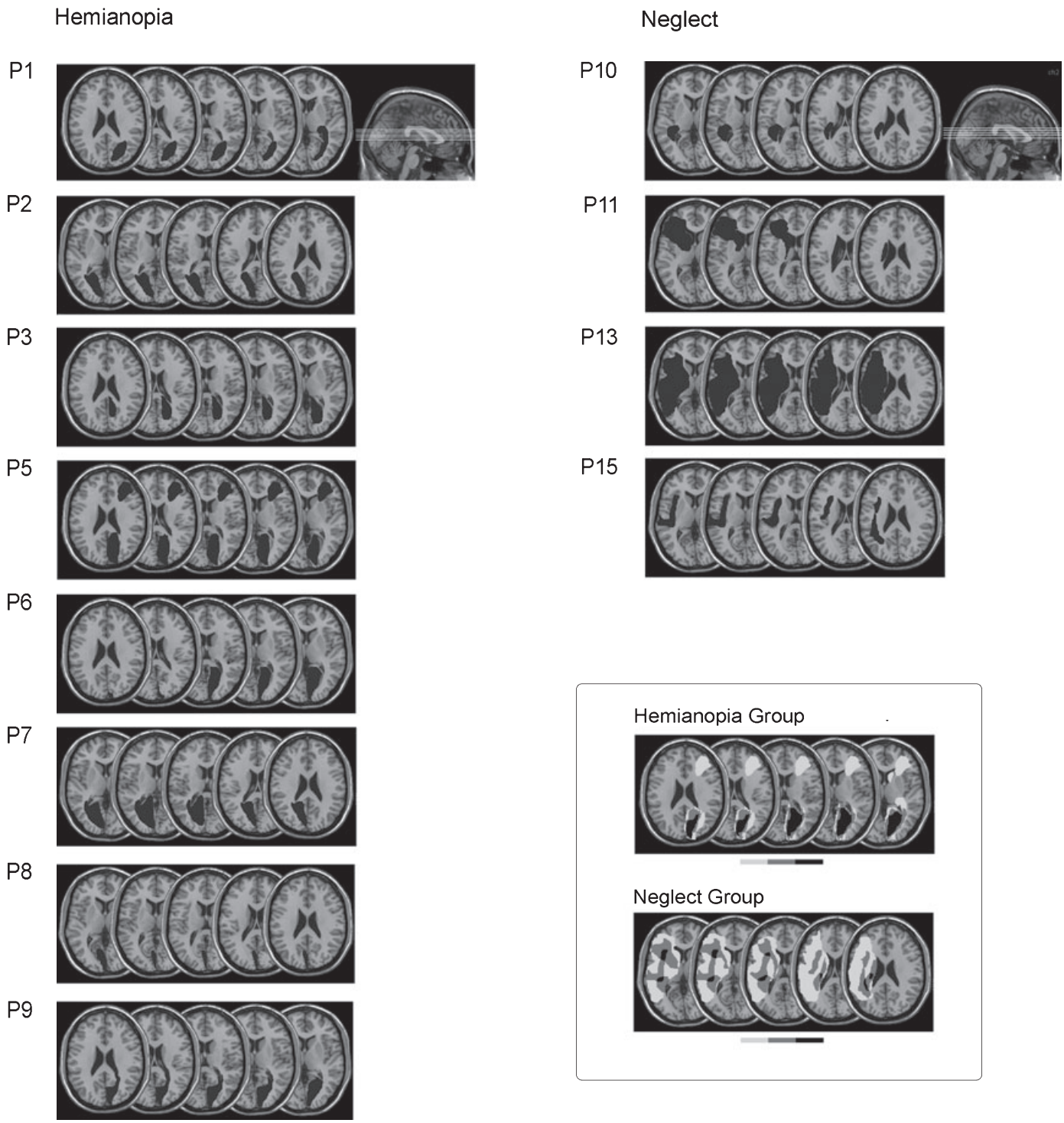

FIG. 2. Lesion reconstruction images from CT and MRI, superimposed on the normalized MNI template (http://www.bic.mni.mcgill.ca/cgi/icbm_view). Images from patients P4, P12 and P14 were not available. Note that the lesion site has to be referred to the opposite hemisphere, as shown in the original scans (i.e., a right lesion is viewed on the left hemisphere). Lesion overlapping for each group of patients is displayed in the box at the bottom right. Different intensity levels of the greyscale correspond to different levels of overlapping, with the dark colour indicating the higher level of overlapping.

were presented: 10 trials at each location and 40 trials in which no visual stimulus was presented (i.e. 'catch trials'). Patients were instructed to press a response button to indicate the presence of a visual target while fixating on a centrally located LED. To check fixation patients had to monitor the LED and verbally report occasional changes in light intensity. The results showed that patients were able to detect the presence of all ipsilesional visual stimuli (mean correct detection: neglect, 100%; hemianopia, 100%) but were severely impaired in detecting contralesional visual stimuli (mean percentage of correct detections: neglect, 18%; hemianopia, 2%; mean false alarms: neglect, 0%; hemianopia, 0%; see Table 3). All patients were able to maintain adequate gaze fixation during this task as

TABLE 3. Scores in the unimodal visual detection task and two-alternatives forced-choice task

	Scores in UVD task task (%)*				Scores in the 2AFC task (%)*			
	Left		Right		Target present		Target absent	
	20°	7.5°	7.5°	20°	20°	7.5°	7.5°	20°
Hemianopia								
P1	100	100	0	0	45	50	45	55
P2	0	0	100	100	60	45	40	45
P3	100	100	20	0	45	40	55	55
P4	100	100	0	0	50	55	60	50
P5	100	100	0	0	50	45	40	45
P6	100	100	0	0	55	55	50	45
P7	0	0	100	100	50	45	50	45
P8	0	0	100	100	55	45	45	60
P9	100	100	20	0	45	40	45	50
Neglect								
P10	0	0	100	100	50	40	55	40
P11	0	0	100	100	40	50	45	55
P12	0	0	100	100	45	55	50	55
P13	20	30	100	100	55	65	40	45
P14	30	50	100	100	55	65	45	40
P15	40	50	100	100	55	65	40	40

2AFC, two-alternatives forced-choice (task); UVD, unimodal visual detection (task). *In the unimodal visual detection task, percentages represent correct visual detection for each patient, and in the 2AFC task, percentages represent the target-present responses for each patient when target was present (Target-present condition) and absent (Target-absent condition).

documented by the mean detection changes in the intensity of the central light (98% accuracy). The reliability of patients' gaze behaviour was further confirmed by eye-movements recordings made during the clinical assessment (Passamonti *et al.*, 2009).

Forced-choice task

A total of 80 trials were presented in affected field; on half the trials a visual target was present (20 trials in each of two spatial locations 7.5 and 20°), and in the other half it was absent. Patients were asked to press one of two response buttons to indicate the presence or absence of the visual target. Also in this case patients were required to constantly look at the fixation point to detect occasional change in light intensity (accuracy was 100%). As expected, the patients' responses in the forced-choice task were at chance-level (two-tailed Fisher test, all $P > 0.1$; see Table 3).

Experimental procedure

Auditory localization task

This task was performed before (i.e. baseline) and after each adaptation phase (i.e. post adaptation) and consisted of 105 auditory trials, 15 from each of the seven loudspeakers, presented in randomized order. At the start of each trial the patient aligned the laser pointer with the central fixation point. After a random delay (between 250 and 750 ms) the auditory target was presented. The patients then indicated the perceived sound location as accurately as possible by turning the laser pointer. The trial ended when the subject approved his or her pointer setting by pushing a button.

Audiovisual adaptation

After the auditory localization task (baseline) patients were submitted to two different kinds of auditory–visual adaptation. In Experiment 1 the adapting stimuli were spatially disparate, and consisted of a sound coming from straight ahead (0°) and a discordant visual stimulus presented at 7.5° from the midline in either the normal or the affected field, in two separate blocks. In Experiment 2 the adapting stimuli were spatially coincident, and consisted of an auditory–visual stimulus pair presented at 20° from the midline in either the normal or the affected field, in two separate blocks.

In both the experiments the visual and the auditory stimuli were presented simultaneously. Each block of adaptation involved 240 cross-modal exposure trials; they lasted 100 ms and followed each other at 900-ms intervals, so that each exposure phase lasted exactly 4 min. Patients were told to look at the central fixation point for the entire duration of exposure, and monitor for occasional changes in light intensity.

Results

Experiment 1: adaptation to spatial disparity

In order to verify the effects of adaptation on auditory localization accuracy, the absolute localization error at each sound location was measured before and after adaptation. Error means were submitted to a four-way ANOVA, with Group (Hemianopia vs. Neglect) as between-subjects factor, Side of adaptation (Normal Field vs. Affected Field), Session (Baseline vs. Post adaptation) and Sound Location (seven locations: 0, 10, 20 and 30° left and right) as within-subjects factors. A significant interaction between Side of adaptation and Session emerged [$F_{1,364} = 3.77$, $P < 0.05$]. *Post hoc* comparisons revealed a trend towards a decreased auditory localization accuracy (i.e., a greater error) after adapting the normal field (pre, 7.84°; post, 9.03°; $P < 0.1$), but not the affected one (pre, 7.79°; post, 6.70°; $P > 0.1$).

We then calculated AEs by subtracting mean reported locations pre-adaptation from those post-adaptation. AEs were counted as positive when they went in the direction of the visual discrepancy and negative when they went in the opposite direction. The AEs were then submitted to a three-way ANOVA, with Group (Hemianopia vs. Neglect) as between-subjects factor, Side of adaptation (Normal Field vs. Affected Field) and Sound Location (seven locations: 0, 10, 20 and 30° on adapted side and 10, 20 and 30° on nonadapted side) as within-subjects factors. The Newman–Keuls test was used for *post hoc* comparisons. The ANOVA revealed a significant main effect of Group [$F_{1,182} = 30.52$, $P < 0.0001$] and Side of Adaptation [$F_{1,182} = 11.52$, $P < 0.0001$]. Crucially, a significant interaction was found between Group and Side of Adaptation [$F_{1,182} = 18.35$, $P < 0.0001$]. Hemianopic patients showed a greater shift in sound localization after adaptation in the normal field (3.43°) than in the affected field (−1.24°, $P < 0.0001$; see Fig. 3A). In contrast, the shift found in neglect patients after adaptation in the normal field (4.18°) was not different from that observed after adaptation in the affected field (4.72°, $P = 0.53$; see Fig. 3A). The Interaction Group × Side of Adaptation × Sound Location was not significant ($P = 0.38$). Thus, the magnitude of the observed shift did not vary across sound locations in a significant way, either when the normal field (see Fig. 3B) or the affected field (see Fig. 3C) were adapted. Looking at each data point in Fig. 3B, the shift observed in the normal field at 20° appears to be greater for neglect patients. However, this result was strongly driven by two patients with neglect (P10 and P11), who showed a large shift (i.e., a rightward bias) at this location; this is a well-known effect in neglect patients (Heilman & Valenstein, 1979). In addition, by looking at each data point in Fig. 3C, a shift opposite to the expected direction was observed within the normal field of hemianopic patients for the sound located at 10°. However, looking at the individuals, this result

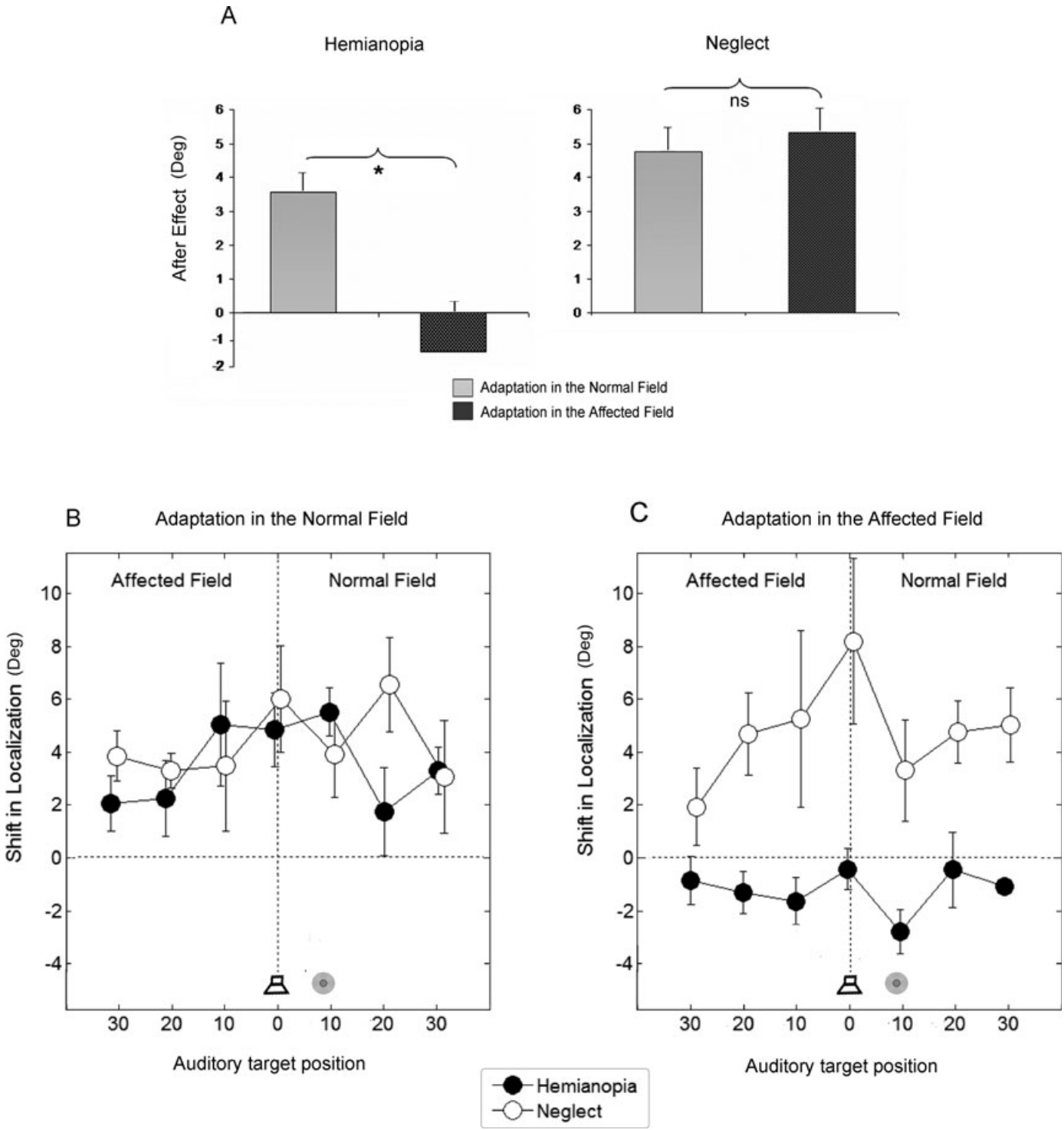

FIG. 3. Results from Experiment 1 (adaptation to spatial disparity). The upper panel (A) represents the mean + SEM AE across all seven sound locations for each group of patients (hemianopia vs. neglect), following adaptation in the normal field (light grey bar) and in the affected field (dark grey bar). A positive value of AE (displayed on the *y*-axis) indicates that the perceived location of the auditory target was shifted in the direction of the adapting visual stimulus, while a negative value indicates a shift in the opposite direction. $*P < 0.05$; ns, not significant. The two lower panels represent the mean ± SEM degrees of AEs at each sound location, when the visual stimulus was presented in (B) the normal field and in (C) the affected field during adaptation. The values on the *x*-axis indicate locations of the auditory target within the affected field and the normal field. The two symbols on the *x*-axis indicate the location of the auditory stimulus (loudspeaker at 0°) and the visual stimulus (LED at 7.5°) during adaptation. The values on the *y*-axis indicate the amount of AE, i.e. the shift of auditory localization after adaptation (positive values indicate a shift in the direction of the adapting visual stimulus). Different curves correspond to patients with hemianopia (black dots) and patients with neglect (white dots). AE was not significantly different across locations.

appears to be strongly driven by one patient (P1) and it does not reflect a common trend. A further analysis comparing left and right hemianopic patients revealed no significant differences between these groups ($P = 0.28$).

Experiment 2: adaptation to spatial coincidence

The results are shown in Fig. 4. In order to verify the effects of adaptation on auditory localization accuracy, mean auditory localization errors were submitted to a four-way ANOVA with Group (Hemianopia vs. Neglect) as between-subjects factor, Side of adaptation (Normal Field vs. Affected Field), Session (Baseline vs. Post-adaptation) and Sound Location (seven locations) as within-subjects factors. Only the main effect of Session [$F_{1,364} = 11.23$, $P < 0.001$] was significant. Thus, both groups of patients gained a clear reduction in auditory localization error post-adaptation (5.80°) compared to baseline (7.44°, $P < 0.001$), regardless of the adapted hemifield.

We then calculated the amounts of error reduction (i.e., AEs) for each sound location by subtracting mean auditory localization errors pre-adaptation (i.e., baseline) from those post-adaptation. These values were submitted to a three-way ANOVA with Group (Hemianopia vs. Neglect) as between-subjects factor, Side of adaptation (Normal Field vs. Affected Field) and Sound Location (seven locations) as within-subjects factors. The Interaction Group × Side of Adaptation was not significant ($P = 0.22$). Thus, both neglect and hemianopic patients exhibited AEs after adaptation in the normal field (hemianopia, 2.38°; neglect, 3.12°) and in the affected field (hemianopia, 2.64°; neglect, 2.94°; see Fig. 4A). Only the main effect of Sound Location was significant [$F_{6,182} = 3.56$, $P < 0.003$]: *post hoc* comparisons showed a greater error reduction for sounds presented at the adapted location (20°, mean of error reduction = 4.17°) compared to each untrained location (locations in the same hemifield of the adapted sound: 0°, 1.85°; 10°, 1.75°; 30°, 2.32°; all $P < 0.05$; locations in the opposite hemifield: 10°, 0.67°; 20°, 0.73°; 30°, 0.11°; all $P < 0.05$) either when the normal field (see Fig. 4B) or the affected field (see Fig. 4C) were adapted. Again, no significant differences were observed between left and right hemianopic patients ($P = 0.61$).

Discussion

AEs of visual influence on auditory localization are remarkable examples of rapid adaptive changes in auditory spatial localization caused by visual stimuli (Canon, 1970; Radeau & Bertelson, 1974). In the present study we explored AEs of cross-modal adaptation in patients with impairment of visual awareness due to a lesion of the striate cortex (i.e., hemianopic patients) or parietotemporal cortex (i.e., neglect patients). The comparison between the two different groups of patients provided the opportunity to address the contribution of different neural circuits in cross-modal recalibration of auditory spatial perception, in particular the relevance of the geniculostriate and collicular–extrastriate circuits. In addition, comparing AEs between the affected and the normal field allowed us to evaluate how adaptation to consciously (within the ipsilesional hemifield) and unconsciously (within the contralesional hemifield) processed visual stimuli differently affect plasticity in the auditory localization system. An additional aim was to verify whether AE generalized to untrained sound locations or not (e.g., Bertelson *et al.*, 2006), and whether the pattern of spatial generalization differed with respect to the type of adaptation employed.

In order to explore these issues, we asked our patients to localize weak sounds before and after a brief session (4 min) of auditory–visual adaptation; stimuli could be presented in spatially disparate locations (Experiment 1) or spatially coincident locations (Experiment 2). We found that after exposure to spatially disparate stimuli (Experiment 1) presented in the normal field, all patients exhibited the usual shifts in sound localization toward the visual attractor. The magnitude of the shift was around half of the actual spatial disparity between sound and light, which is in accordance with previous studies on normal subjects (Recanzone, 1998; Lewald, 2002; Frissen *et al.*, 2003). In contrast, when the same kind of adaptation was given within the affected field, a consistent shift was still evident in neglect patients but not in patients with hemianopia. The absence of AEs in the hemianopic field supports the key role of the geniculostriate circuit for such an effect; when the striate cortex has been damaged no ventriloquism AEs are observed. Our findings show that striate cortex plays a crucial role for visual recalibration of auditory spatial perception when that recalibration involves correcting for apparent sensory conflicts between the visual and auditory localization systems. These results are in line with a recent neuroimaging study which suggests that the ventriloquism illusion is directly related to the visual influences on the response of the auditory cortex to sound (Bonath *et al.*, 2007), i.e. the visual influence of auditory spatial processing is mediated by pathways from visual cortex to multimodal association areas and then to the planum temporale of auditory cortex.

The present results also show that the neural network subserving visual spatial attention, i.e., the parietotemporal network, has no crucial role in the present phenomenon because neglect patients exhibited the same AEs after adaptation in both ipsilesional and contralesional sides. This finding is in line with a previous study which demonstrated on-line visual biases in the neglected field (Bertelson *et al.*, 2000), and it suggests that AEs are generated in processing stages which are not consciously accessible (Radeau & Bertelson, 1974; Radeau, 1992, 1994). It is interesting to note that the neglect patients' AEs were much stronger than the on-line bias reported by Bertelson and colleagues. Thus, whereas we found AEs of ∼60% of the auditory–visual spatial conflict, they found effects of ∼25%. Although it is difficult to compare these values directly across such different methods and paradigms, they might indicate that the adaptation paradigm is the more sensitive measure for studying residual visual processing and its effects on auditory spatial perception.

When adaptation comprised spatially coincident stimuli (Experiment 2), both neglect and hemianopic patients exhibited significant reductions in auditory localization error, regardless of the adapted hemifield. In other words, auditory localization performance was significantly enhanced after adaptation, even when visual stimuli were not overtly processed. Moreover, the quantitative change was virtually identical in the two groups of patients. This can be considered as further (indirect) evidence that the lesioned brain areas in either group of patients are not involved in this particular form of perceptual learning. Thus, even without the involvement of striate and parietotemporal areas, visual information is capable of calibrating auditory space as long as visual and auditory information are spatially aligned. The AE of multisensory enhancement found in the present study might be attributed to the spared collicular–extrastriate pathway, as previously shown for on-line effects (Leo *et al.*, 2008). Studies of multisensory integration in cat's superior colliculus (SC) have shown that spatially and temporally congruent stimuli tend to result in response enhancement, whereas spatially discordant stimuli give rise to suppressive interactions (e.g. Meredith & Stein, 1986). It is generally assumed that these changes in firing rate contribute to the relative accuracy with which animals orient toward unisensory and bisensory stimuli (Stein *et al.*, 1988), an assumption supported by the

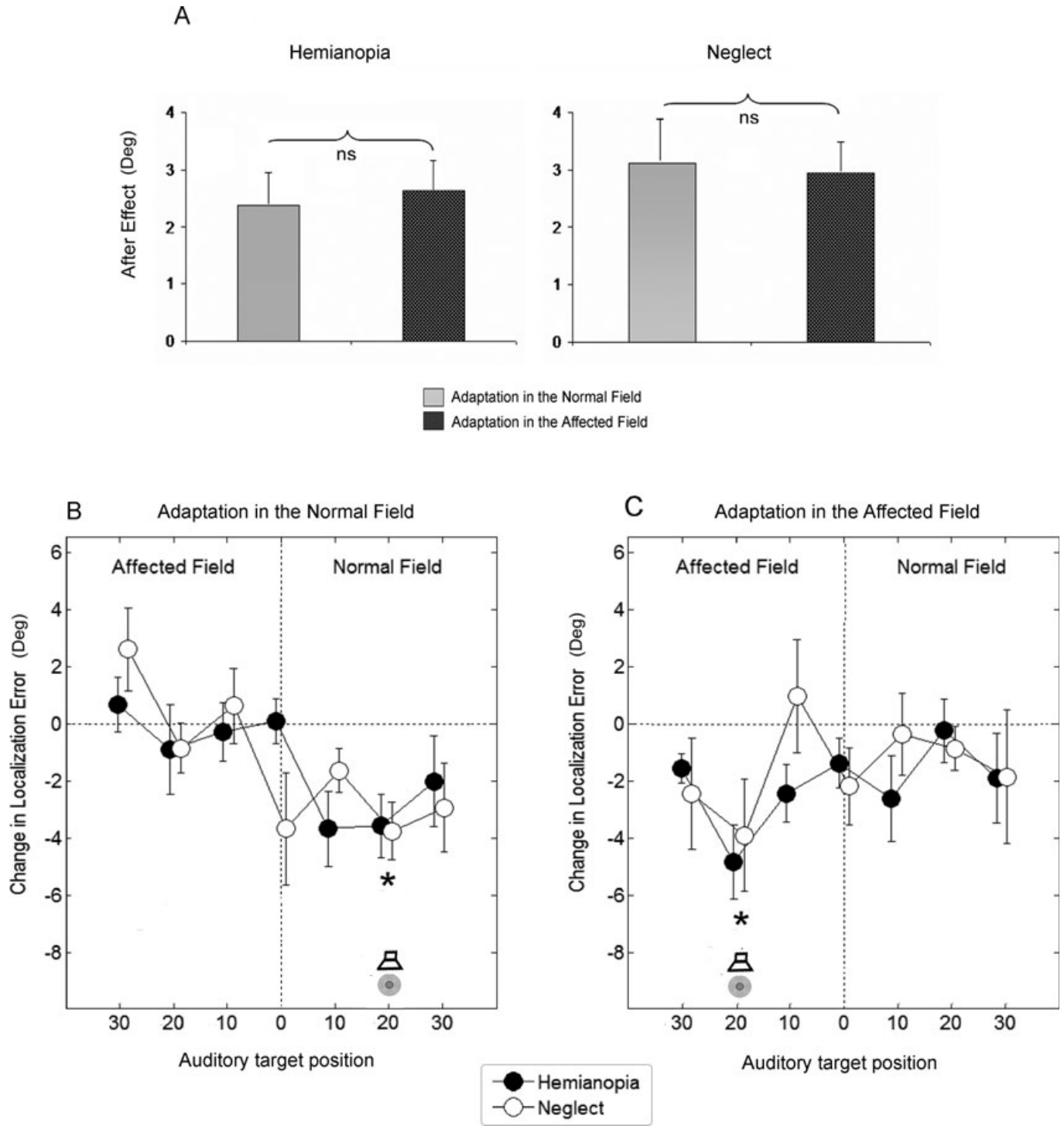

FIG. 4. Results from Experiment 2 (adaptation to spatial coincidence). (A) Mean + SEM AE across locations for each group of patients (hemianopia vs. neglect), following adaptation in the normal field (light grey bar) and in the affected field (dark grey bar). The *y*-axes indicates the magnitude of error reduction after adaptation (ns, not significant). (B and C) Mean ± SEM degrees of AEs at each sound location, in patients with hemianopia (black dots) and patients with neglect (white dots), when the auditory–visual stimulus was presented in (B) the normal field and in (C) the affected field during adaptation. The values on the *x*-axis indicate locations of the auditory target within the affected field and the normal field. The values on the *y*-axis indicate the amount of AE, i.e. the magnitude of error reduction after adaptation. The two symbols on the *x*-axis indicates the location of the auditory stimulus (loudspeaker at 20°) and the visual stimulus (LED at 20°) during adaptation. Note that, in these two graphs, negative values indicates a reduction in auditory localization error after adaptation while positive values indicates an increase in auditory localization error. Error reduction was largest (*) for sounds presented at the adapted location.

behavioural deficits observed following collicular lesions (Burnett *et al.*, 2004). However, the SC is part of a larger network of cortical and subcortical regions that jointly contribute to the formation of integrated multisensory percepts (Stein & Stanford, 2008). The ability of SC neurons to integrate cross-modal inputs is known to involve descending inputs from specific regions of association cortex and not

from primary or secondary cortices (Wallace & Stein, 1994). This suggests the possibility that extrastriate areas in humans might have a key-role in driving AEs of multisensory enhancement. Multisensory effects for audiovisual stimuli have also been reported in heteromodal cortical regions such as the superior temporal sulcus (Stevenson *et al.*, 2007). However, while extrastriate areas are spared in both neglect and hemianopic patients, temporal and parietal areas are largely damaged in patients with neglect. Thus, it is unlikely that any cortical site within these regions would have a crucial role in mediating multisensory effects in the present experiment.

The involvement of two different neural routes is further suggested by the emergence of two distinct patterns of spatial generalization of AEs, depending on the spatial constraint of adapting stimuli. Exposure to spatially disparate stimuli (Experiment 1) led to a generalized remapping of auditory space to nontrained locations. This indicates that auditory spatial processing is not strictly dependent on a region of space, otherwise perception in the nonadapted locations would not have been modified (Canon, 1970; Sarlat *et al.*, 2006). This is consistent with the notion that auditory space is represented in a distributed manner across cortical populations, probably in the superior temporal gyrus (STG; Zatorre *et al.*, 2002). The STG, which contains the auditory cortex, including the planum temporale, has been shown to be influenced by the visual information from striate areas (Bonath *et al.*, 2007).

Adaptation to spatially coincident stimuli (Experiment 2), on the other hand, induced an improvement that was largest at the adaptation location and diminished for more distant locations. This is consistent with the activation of a topographic representation of auditory space under conditions of spatial coincidence of auditory and visual events. One probable candidate site for this cross-modal recalibration is the inferior colliculus (IC), which contains a population of spatially selective neurons (Konishi, 1986). Further evidence for this comes from studies in the barn owl, which show a topographical representation of auditory space in the inferior colliculus that can be calibrated by a visual instructional signal, originating in the visual map of the optic tectum, which in turn arises from topographic projections from the retina (Brainard & Knudsen, 1993; Knudsen, 1999; Luksch *et al.*, 2000). One might speculate that an analogous mechanism is involved in the human brain. Auditory location is initially encoded at very early levels of the auditory pathway, even in the brainstem. The ascending parallel auditory pathways converge in the IC of the midbrain before continuing to the auditory cortex (AC) via the thalamus. The IC also receives substantial corticofugal projections from the AC (Winer, 2006). It has been proposed that descending corticocollicular pathways might be involved in learning-induced plasticity (Suga & Ma, 2003). Studies on ferrets, in fact, have shown that the ablation of corticocollicular neurons impairs adaptation (Bajo *et al.*, 2006), suggesting that signals transmitted by descending cortical pathways are likely to mediate training-induced plasticity of auditory localization.

The present study sheds light on the possibility of inducing a short-term improvement in auditory localization even when visual information processing is impaired, a possibility that might have interesting clinical applications (Làdavas, 2008). Thus, it represents a real chance to exploit the innate ability of the brain to integrate multisensory events.

One important question not explored in the current work, and which needs to be addressed for such a regime to be of practical value, is the time course of such cross-modal recalibration. For instance, how fast does the recalibration dissipate, or decay? It is known generally that more exposure leads to longer retention of AEs (Welch, 1978). As for the ventriloquism AE, only one study (Frissen, 2005) looked at the dissipation functions and found substantial AEs after 90 s even with an adaptation period as short as 1 min. The opposite question is how fast does the recalibration 'build up'? Studies that looked explicitly at this (Radeau & Bertelson, 1976; Bertelson, 1993; Frissen, 2005) found very fast build-up indeed. The fastest was recorded by Frissen (2005), who found reliable aftereffects within as few as four discrete exposures to a discrepant auditory–visual pair, although this was very much dependent on the size of the discrepancy. As the present work is the first demonstration of an AE for spatially coincident stimuli, virtually nothing is known about its time course.

In summary, the present study provides a number of contributions to our understanding of cross-modal short-term plasticity in the auditory localization system. First, it reveals the presence of two distinct recalibration mechanisms, mediated by different neural routes. On the one hand, adapting to spatially conflicting stimuli invokes a corrective mechanism (Held, 1965; Welch, 1978) implemented within the geniculostriate circuits. On the other hand, adapting to spatially aligned inputs invokes a mechanism implemented along a collicular–extrastriate circuit. It is incidentally also the first demonstration of the latter AE. Second, it suggests that on-line and off-line effects of visual influence on auditory spatial perception are mediated by the same neural circuits. Third, it establishes the minimal role of conscious visual awareness in these recalibration mechanisms. Finally, it opens up potential avenues for relatively simple clinical interventions to relieve auditory spatial impairments due to brain damage.

Acknowledgements

This work was supported by grants from MURST to E.L.

Abbreviations

AE, after-effect; LED, light-emitting diode.

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