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Extinction of auditory stimuli in hemineglect: Space versus ear

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Abstract

Unilateral extinction of auditory stimuli, a key feature of the neglect syndrome, was investigated in 15 patients with right (11), left (3) or bilateral (1) hemispheric lesions using a verbal dichotic condition, in which each ear received simultaneously one word, and a interaural-time-difference (ITD) diotic condition, in which both ears received both words lateralised by means of ITD. Additional investigations included sound localisation, visuo-spatial attention and general cognitive status. Five patients presented a significant asymmetry in the ITD diotic test, due to a decrease of left hemispace reporting but no asymmetry was found in dichotic listening. Six other patients presented a significant asymmetry in the dichotic test due to a significant decrease of left or right ear reporting, but no asymmetry in diotic listening. Ten of the above patients presented mild to severe deficits in sound localisation and eight signs of visuo-spatial neglect (three with selective asymmetry in the diotic and five in the dichotic task). Four other patients presented a significant asymmetry in both the diotic and dichotic listening tasks. Three of them presented moderate deficits in localisation and all four moderate visuo-spatial neglect. Thus, extinction for left ear and left hemispace can double dissociate, suggesting distinct underlying neural processes. Furthermore, the co-occurrence with sound localisation disturbance and with visuo-spatial hemineglect speaks in favour of the involvement of multisensory attentional representations.

Keywords: Auditory neglect; Auditory cortex; Lesion; Double dissociation; Sound localisation

1. Introduction

Auditory hemineglect is defined as disability to pay attention to auditory stimuli coming from one hemispace (Heilman & Valenstein, 1972) and/or systematic distortion of auditory spatial representation (Bisiach, Cornacchia, Sterzi, & Vallar, 1984); most frequently, auditory neglect concerns the left hemispace, following right-hemispheric lesions. In a clinical setting, it has been tested with a variety of tasks that involved either bilateral simultaneous stimulation (finger snapping on both sides; dichotic listening to different verbal material through right and left ear) or sound localisation (free-field, simulation with interaural time or intensity differences).

Spatial deficits associated with auditory neglect are of two types: (i) imprecision in localising sounds in the hemispace contralateral to the lesion (Pinek & Brouchon, 1992; Pinek, Duhamel, Cave, & Brouchon, 1989); (ii) imprecisions in the whole space, associated frequently with errors towards the side ipsilateral to the lesion or alloacusis across the midline (Altman, Balonov, & Deglin, 1979; Ruff, Hersh, & Pribram, 1981; Soroker, Calamaro, Glicksohn, & Myslobodsky, 1997). The latter were interpreted either as essentially spatial impairments (Ruff et al., 1981) or as part of auditory hemineglect syndrome (Sterzi, Piacentini, Polimeni, Liverani, & Bisiach, 1996). Sound localisation deficits have often been reported in association with visuo-spatial neglect (Kerkhoff, Artinger, & Ziegler, 1999; Pavani, Ladavas, & Driver, 2002; Pavani, Meneghello, & Ladavas, 2001; Tanaka, Hachisuka, & Ogata, 1999) and their co-occurrence has been interpreted as the result of damage to multisensory spatial representations within the right hemisphere (e.g. Pavani, Ladavas, & Driver, 2003).

The extinction of auditory stimuli in dichotic listening paradigms, defined as simultaneous presentation of different stimuli to the two ears (Kimura, 1967), has been interpreted in two ways. Several authors have considered it to be a part of an attentional disorder and hence a manifestation of the auditory neglect (e.g. Heilman & Valenstein, 1972; Hugdahl & Wester, 1994; Hugdahl, Wester, & Asbjornsen, 1991). Others interpreted

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it as a perceptive extinction of information coming from one ear (Beaton & McCarthy, 1993; De Renzi, Gentilini, & Pattacini, 1984; Ogden, 1985), not necessarily involving multisensory spatial and attentional representations. The latter view is supported by cases of double dissociation between extinction in dichotic listening and visuo-spatial neglect (Damasio, Damasio, & Chui, 1980; De Renzi, Gentilini, & Barbieri, 1989).

Because it confounds ear and side of entry, the dichotic listening task does not distinguish between spatial-attentional and structural-perceptive mechanisms (Beaton & McCarthy, 1993, 1995; Hugdahl & Wester, 1994). A diotic test based on interaural time differences (ITD) has been used in order to dissociate these two mechanisms. In this paradigm, bilateral simultaneous spatial presentation is simulated without the inconvenience of dichotic presentation: each ear receives the same content with the same interaural intensity, but the stimuli are each presented with interaural time differences that simulate positions within the left and right hemispace, respectively. In this way, omission to report items presented in one hemispace cannot be accounted for by perceptive extinction. Fusions of simultaneously presented words can occur if the subject cannot use the distinct spatial origin of the words for segregation. Using this approach we have identified two types of auditory neglect in right brain-damaged patients selected on the basis of left ear extinction in dichotic listening (Bellmann, Meuli, & Clarke, 2001; Clarke & Thiran, 2004). In one type the asymmetry in the dichotic test was associated with hemispatial asymmetry in the ITD diotic test, and without sound localisation deficit; this pattern was interpreted as imbalance in allocation of attention to the left hemispace and was associated with subcortical lesions including basal ganglia. In the other type, the asymmetry in the dichotic test was not accompanied by an asymmetry in the diotic task, but rather was associated with ipsilesional spatial bias in sound localisation. This pattern was interpreted, apart from left ear extinction, as a distortion of auditory spatial representation and was associated with fronto-parietal lesions.

The question arises how far spatial and ear-related aspects of extinction can be dissociated, and in particular whether extinction of spatially presented sounds can occur without unilateral extinction on dichotic listening. Previously reported studies did not address the latter issue (Deouell & Soroker, 2000; Soroker et al., 1997). We present here 11 cases which document a double dissociation between the extinction in the dichotic versus diotic paradigms, both for right-hemispheric lesions associated with visuo-spatial neglect or left or bilateral lesions with or without visuo-spatial neglect.

2. Case reports

Fifteen patients with a first unilateral or bilateral hemispheric lesion were tested for diotic listening, ITD diotic listening and sound localisation and had a comprehensive neuropsychological evaluation (Table 1). They corresponded to consecutive cases recruited from outpatients treated in the Division of Neuropsychology or from inpatients in the Neurorehabilitation unit of the University Hospital of Lausanne, who met the following criteria: (i) no prior neurological or psychiatric illness; (ii) absence

Table 1
Patients who participated in this study and their performance in ITD diotic listening, dichotic listening, sound localisation and visual cancellation task

Case	Sex	Age (y)	Etiology	Lesion site	Lesion side	Post lesion delay (d)	Diotic listening				Dichotic listening				Sound Localisation					Cancellation task
							Lateralisation index	L	R	Fusions	Lateralisation index	L	R	Fusions	Relative localisation	Alloacusis		Center	Center coherence	
																R → L	L → R			
OF	M	49	Haemorrhage	par., occ., ins.	B	63	**16**	21	29	0%	1.7	29	30	0%	−1.2	**1**	**2**	**−2.1**	**2.6**	0
UF	M	40	TBI	fr., tp., par.	R	52	**17.6**	21	30	0%	8.0	**23**	27	0%	−0.6	0	0	**−5**	**2.2**	0.2
CC	F	57	Stroke	fr., tp.	R	82	**35.5**	**10**	21	**38%**	5.5	26	29	**10%**	−1.2	0	**1**	**8**	1.0	0.4
PJ	M	57	Stroke	tp.	R	41	**15.8**	16	22	**10%**	3.4	28	30	0%	**−7.3**	**1**	**11**	0.7	0.4	0
LC	M	62	Stroke	tp., par., occ.	L	93	**16.3**	18	25	0%	1.8	28	29	0%	0.5	0	**1**	**9.6**	0.7	0
LL	M	31	Stroke	tp., par., fr.	R	79	14.3	21	28	**10%**	**87.5**	**2**	30	**20%**	−0.1	0	1	**−8.5**	0.3	0.1
LK	M	36	Stroke	occ., thal.	R	54	1.9	26	27	**3%**	**15.4**	**22**	30	**3%**	1.0	0	0	**4.7**	**2.3**	0
AG	F	27	Stroke	tp.	R	40	5.7	25	28	**7%**	**13.2**	**23**	30	0%	**−3.4**	**4**	0	**−18**	0.1	0.9
RB	M	34	Cyst extraction	bg.	R	16	4.3	22	24	**10%**	**15.4**	**22**	30	**3%**	**−2.9**	0	0	**−7.8**	1.8	0.3
ES	F	64	Stroke	tp., lent.	L	116	6.4	22	25	**3%**	**13.2**	**23**	30	**3%**	−0.1	0	0	−0.6	−0.3	0
SD	F	45	Tumour resect.	fr.	L	14	−6.7	16	**14**	**7%**	**−100**	27	**0**	0%	1.0	0	0	**−4.2**	−0.2	0
CS	F	31	Tumour resect.	tp.	R	52	**24.4**	17	28	0%	**16**	**21**	29	**3%**	1.0	0	0	**2.8**	**3.4**	0.1
TC	F	49	Stroke	tp.	R	28	**73.3**	**2**	**13**	**50%**	**100**	**0**	26	**10%**	−1.2	0	**1**	**−5.4**	**3.8**	0.3
BA	M	50	Haemorrhage	tp., lent.	R	18	**16.3**	18	25	**10%**	**33.3**	**15**	30	**3%**	1.0	0	0	0	−0.3	0.2
HB	M	56	Stroke	bg., tp.	R	48	**23.5**	**13**	21	**25%**	**93.5**	**1**	30	0%	−1.2	0	**4**	−1.4	−0.1	0.2

Scores outside the normal range are in bold (excepted for the cancellation task). All patients were right handed (except PJ who was ambidextrous). For ITD diotic and dichotic listening test, lateralisation index corresponds to: $100 \times (R_{tot} - L_{tot})/(R_{tot} + L_{tot})$; 'L/R' = total number of correct responses to either the right/left side of space. The maximal asymmetry corresponds to 100. For evaluation of sound localisation, deficient performance was defined by *z*-scores ≤ -2 or $\geq +2$ relative to control population (see Section 3). For the cancellation task, the *z*-score corresponds to (right omissions–left omissions)/(right omissions–left omissions). B, bilateral; bg, basal ganglia; d, days; fr., frontal; ins., insular; L, left; lent., lenticular nucleus; par., parietal; occ., occipital; R, right; TBI, traumatic brain injury; tp., temporal; VSP negl., visuo-spatial neglect; y, years.

of brain stem lesion; (iii) normal hearing thresholds in tonal audiometry (see Section 3); (iv) absence of major behavioural and comprehension deficits; (v) availability to perform the whole auditory testing battery; and (vi) presence of auditory neglect symptomatology as assessed by dichotic listening and ITD diotic listening. The study was approved by the Ethics Committee of the Faculty of Biology and Medicine, University of Lausanne.

OF was a 49-year-old truck-driver, who sustained large right insular and parieto-occipital, and left parieto-occipital intraparenchymal haemorrhage. Two months after stroke, at the time of auditory testing reported in the results, he presented signs of left visuo-spatial hemineglect characterized by significantly slowed reaction times for visual stimuli presented in the left hemifield, whereas line bisection and cancellation tasks were within normal limits. Executive functions and anterograde visuo-spatial memory were moderately deficient. Language, constructional praxias and memory were within normal range. No hemianopia was present.

UF was a 40-year-old furrier, who sustained severe traumatic brain injury with a right frontal haemorrhage. At the time of auditory testing reported here, 1 month and a half after the trauma, he had a mild hemispatial neglect, which was present at cancellation tasks and in the spatial arrangement of a non-verbal production test, while line bisection, spatial aspect of writing as well as performance during double simultaneous stimulation in visual and tactile modalities were within normal limits. Verbal and visuo-spatial memory and executive functions were moderately deficient; language, calculation, constructional and ideomotor praxias and reasoning were within the range of normal performance. No hemianopia was present.

CC was a 57-year-old office employee, who sustained a right fronto-temporal ischemic stroke. Three months after stroke, at the time of auditory testing reported in the results, she presented moderate left visuo-spatial neglect characterized by left omissions at the cancellation task and a rightward shift in the line bisection test. Constructional praxias, perceptual and associative visual gnosias, executive functions, calculation and reasoning were deficient and left homonymous hemianopia was present. Language, ideomotor praxias and memory were preserved.

PJ was a 57-year-old storekeeper, who sustained a right sylvian ischemic stroke. One month after stroke, 10 days before the auditory testing reported in the results, he presented left hemianopia, verbal fluency and working memory deficits. Visual gnosias, verbal and visuo-spatial short-term memory, executive functions and reasoning were within normal range. No signs of visuo-spatial neglect nor hemianopia were noted.

LC was a 62-year-old civil servant, who sustained a left temporo-parieto-occipital ischemic stroke. Two months after stroke, 1 month before the testing reported in the results, he presented right homonymous hemianopia, severe naming deficits, pure alexia, associative visual agnosia and deficits in verbal episodic memory. Constructional and ideomotor praxias and executive functions were preserved and no signs of visuo-spatial neglect were present.

LL was a 31-year-old cook, who sustained a right temporo-parietal and frontal ischemic stroke. Two months before the auditory testing reported in the results, 2 weeks after stroke, he presented left visuo-spatial neglect characterized by left omission at cancellation task and in the copy of the Rey complex figure. Left extinction was present in visual and tactile double stimulation. Language, calculation, praxia and memory were preserved. Executive functions were deficient and he presented left homonymous hemianopia.

LK was a 36-year-old record dealer, who sustained a right occipito-thalamic stroke following the dissection of the right internal carotid artery. At the time of the auditory testing presented in the results, almost 2 months after stroke, he presented left hemianopia and mild left visuo-spatial hemineglect characterized by a rightward shift in writing, in spatial arrangement of non-verbal production and in the line bisection test. Visuo-spatial anterograde memory, executive function and reasoning were deficient. Language, calculation, constructional and ideomotor praxias were within the normal range.

AG was a 27-year-old manual worker, who sustained a large right-hemispheric ischemic stroke following the dissection of the right internal carotid artery. At the time of auditory testing reported in the results, 1 month and a half after stroke, she presented severe left multimodal hemineglect characterized by left hemi-extinction in tactile or visual double stimulation, left omissions at cancellation task and left omissions in reading and calculation, as well as constructional apraxia, and deficits in visuo-spatial anterograde memory, non-verbal reasoning and executive functions. Language evaluation was within normal range. No hemianopia was present.

RB was a 34-year-old airport employee, who developed a colloidal cyst of the third ventricle, which was removed surgically. Postoperative MRI showed an ischemic lesion of the right caudate nucleus and striatum. Two weeks post-surgery, at the time of the testing reported in the results, the patient presented moderate left hemineglect characterized by left omissions at cancellation tasks and figure copy and under use of left half of the sheet on non-verbal fluency (Regard, Strauss, & Knapp, 1982), as well as moderates deficits in constructional praxia, visuo-spatial reasoning, anterograde memory and executive functions. No hemianopia was present.

ES was a 64-year-old commercial, who sustained a left sylvian ischemic stroke including lenticular nucleus. At the time of the auditory testing reported in the results, 4 month after stroke, she presented moderate right hemineglect in behavioural appreciations (Bergego et al., 1995) as well as severe language impairment (Broca aphasia), executive function, praxic and semantic memory deficits. Calculation and short-term memory were preserved. No hemianopia was present.

SD was a 45-year-old accountant, who developed left frontal tumour with infiltration of the genu of corpus callosum. Two weeks after the surgical removal of the tumour, at the time of the testing reported in the results, she presented mild language impairment (anomia), anterograde verbal short- and long-term memory and verbal working memory deficits. Numeric transcoding was impaired. Praxias, oral and written comprehension, reading and visuo-spatial anterograde memory were preserved and no signs of visuo-spatial neglect nor hemianopia were present.

CS was a 31-year-old saleswoman, who sustained right partial temporal lobectomy for right temporal anaplastic astrocytoma. At the time of auditory testing reported in the results, almost 2 months after surgery, she presented left visuo-spatial hemineglect characterized by left omissions at cancellation task and a bias toward the right at line bisection test. She also had mental calculation and constructional praxias deficits. Language, anterograde episodic verbal memory and executive functions were preserved. No hemianopia was present.

TC was a 49-year-old nurse, who sustained a cortico-subcortical right ischemic stroke. At the time of auditory testing reported in the results, 1 month after stroke, she presented a moderate left hemineglect characterized by left omissions at cancellation task and right to left description of a picture. She presented moderate language impairment (interpreted as crossed aphasia), verbal and visuo-spatial anterograde memory as well as executive, visuo-constructional, visuo-cognitive praxias, non-verbal reasoning and calculation deficits. No hemianopia was present.

BA was a 51-year-old post-office employee, who sustained a right lenticular haemorrhage. At the time of auditory testing reported in the results, 18 days after stroke, he presented left inferior homonymous quadrianopia and mild left hemineglect characterized by left omissions at cancellation task and a shift toward the right at line bisection test. Language, constructional and ideomotor praxias, verbal and visuo-spatial anterograde memory and executive functions were preserved.

HB was a 56-year-old farmer, who sustained an ischemic stroke in the territory of the right middle cerebral artery centred on the head of the caudate nucleus with a secondary haemorrhagic transformation within the posterior temporal region. One month after stroke, 2 weeks before the auditory testing reported in the results, he presented visuo-spatial neglect characterized by left omissions at cancellation task. Non-verbal reasoning, reaction time, reading and executive function were deficient. Constructional and ideomotor praxias, visual gnosia and memory were within normal range. No hemianopia was present.

3. Methods

The three auditory tests that were used in this study were digitally constructed on a Power Macintosh 8100 equipped with an audio-media card and the software Protools Powermix and Sound Designer II. The patients sat in a quiet room in front of the examiner. The stimuli were played through earphones (Sony MDR-CD480) linked to a CD player, and set at the volume judged comfortable by the patients.

3.1. ITD diotic task

For this task, pairs of disyllabic words (selected from a set of 30 words) were presented binaurally and simultaneously at the same intensity level through earphones. However, by introducing a 1 ms interaural time difference (ITD) we were able to simulate the presentation of each word to different lateralised positions in left and right hemispaces (see Morais & Bertelson, 1975 for a similar procedure). This procedure gives the subjective perception of two words being simultaneously presented to different locations, as in the below-mentioned dichotic task, and the control subjects we tested reported the two tasks as perceptually indistinguishable. Participants were informed that two words would be simultaneously presented on each trial and were instructed to concentrate equally on both words and to repeat both of them to the experimenter (if possible). Performance was scored as the number of correctly repeated words presented to each hemispace. We likewise calculated a laterality index, which was the difference between right and left side scores and multiplied by 100, divided by the sum of these scores. Each word was presented once to each hemispace. Likewise, following the dichotic condition, 10 words were presented to each side to verify that subjects could indeed correctly repeat words presented to each side. Sixty healthy subjects aged 20–65 years were tested as controls, their average scores (±S.D.) were 26.15 ± 4.63 and 24.87 ± 5.02 for right-sided and left-sided diotic presentations, respectively (Bellmann, 2001; Bellmann et al., 2001). Performance was significantly higher for right-sided presentations ($p < 0.0001$), and the average (±S.D.) lateralisation index was $3.52 \pm 5.96\%$. The limits of normal performance were defined as the mean ± 2S.D. Patients, but not normal subjects, presented occasionally fusions, i.d., reported chimeric (non)-words which mixed phonemes from items presented on the right and left side (e.g.,"souris" and "cheval" reported as "soural" or "seral").

3.2. Dichotic listening task

This task entailed the simultaneous and synchronous presentation of the same words from the diotic task, one of which was presented exclusively to the left ear and the other to the right ear (via earphones as above). As in the diotic task, subjects were instructed to repeat both words presented on each trial (30 total). Performance was scored as the number of correctly repeated words presented to the right and to the left ear. A laterality index, as above, was also calculated. Average score (±S.D.) from the 60 subjects of the control population aged 20–65 years was 29.2 ± 1.69 and 28.85 ± 2.74 for right and left ear presentations, respectively (Bellmann et al., 2001). The limits of normal performance were defined as the mean ± 2S.D. There was no evidence of a significant difference between the ears of presentation ($p = 0.1004$), and the average (±S.D.) lateralisation index was $0.99 \pm 4.45\%$.

3.3. Sound localisation

The task and stimuli have been described in detail in our previous work (Clarke, Bellmann, Meuli, Assal, & Steck, 2000), and it is the normative data from 60 control subjects reported therein that were used here. Subjects were presented with broadband noises (frequency range: 20–16000 Hz; 44.1 KHz sampling rate); resembling a 'bumblebee'; 2 s duration; 100 ms rising and falling times that were presented binaurally through earphones. On each trial, subjects were required to indicate the perceived position on their head with their ipsilesional hand (see also Altman et al., 1979; Bisiach et al., 1984 for the same procedure). This position was recorded by the experimenter from a graduated semicircle (ranging from 0° to ±90°) affixed to the headband of the earphones worn by participants. A central azimuthal position and two positions in each hemispace were simulated by varying ITD (0, ±300, or ±1000 μs). We selected these values based on prior evidence indicating that fused acoustic images were perceived for ITDs of up to 2 or 2.5 ms, with the most lateral positions reported for ITDs between 800 μs and 1 ms (Jones, Pitman, & Halliday, 1991; Walsh, 1957). The 60 control subjects who performed this task all reported single sound sources with the ITD values used and provided normative data for comparison with the patients described here. These normative data indicate that the average (±S.D.) perceived angular positions (relative to the vertical meridian) were $60.1 \pm 13.0°$ to the left and $62.9 \pm 12.5°$ to the right for a 1000 μs ITD, $37.8 \pm 13.8°$ to the left and $40.5° \pm 14.2°$ to the right for a 300 μs ITD, and $0.09 \pm 4.5°$ to the left for a 0 μs ITD.

As a measure of overall performance, the relative positions attributed to two consecutive stimuli were compared; a response was counted as correct when a stimulus was correctly placed to the left or the right of the previous stimulus in correspondence with the difference in ITD or within ±10° of the previous location for identical ITDs. The 60 normal subjects achieved on average 57.15 (S.D. = 1.79) correct responses for the global score. Three other measures were used to quantify potential deficits: (i) directional bias was estimated using the deviation of the midline position, i.e. the difference between the theoretical 0° and the actual mean angular response given for the stimuli with no ITD; and (ii) the number of alloacusis, i.e. the number of right side presented stimuli reported left and the reverse. Control subjects located the central stimuli (no ITD) at 0.09° to the left (S.D. = 4.5°) and alloacusis never occurred. (iii) Center coherence was assessed by the standard deviation of the responses to the midline stimulus. Control subjects achieved on average a center coherence of 5.69° (S.D. = 6.48).

In addition to the above tests, all patients had a tonal audiometry evaluation. Perception threshold were tested for eight frequencies (250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz). Pure tones were first presented at 60 dB and the intensity was progressively decreased by steps of 5 dB. Perception threshold was determined as the value of the last intensity that the patient perceived for each frequency. Patients with asymmetric and/or abnormal loss of acuity (as compared to age-matched normal population) were excluded from this study.

The cancellation task used (Figs. 1–3) was the bells test, where target bells were mixed with distractors (Gauthier, Dehaut, & Joanette, 1989) or the line cancellation task (Albert, 1973). The items were equally distributed on a horizontally placed A4 sheet; for analysis of performance, the sheet was subdivided into seven equally wide vertical columns, each of which contained five items. A lateralisation was calculated as the difference of correctly cancelled items in the three right-most versus the three left most columns, divided by the sum of both (Fig. 4; same procedure as Pavani, Hussain, Ladavas, & Driver, 2004). Visuo-constructional abilities were evaluated with the copy of the Rey–Osterrieth figure (Osterrieth, 1944) and/or the copy of a cube or a house.

4. Results

4.1. Extinction of stimuli lateralised with ITD without asymmetry in dichotic listening

Five of our patients presented this profile. OF, who sustained bilateral lesion and presented discrete signs of left visuo-spatial neglect, had a significant bias on diotic listening with a disadvantage for left hemispace (Table 1; Fig. 1). No fusion of words occurred in the diotic test. No significant asymmetry was present on dichotic listening. In sound localisation, he presented two left-to-right alloacusis for the extreme left position. Furthermore, he indicated the position of the centrally presented stimuli with great variability and a significant tendency to the left.

UF, who sustained a right lesion with a mild left visuo-spatial neglect, had a significant bias in diotic listening with a disadvantage for left hemispace (Table 1; Fig. 1). No fusion of words occurred in the diotic condition. No significant asymmetry was present on dichotic listening. When indicating positions of sounds lateralised with ITD, he placed the centrally presented stimuli with great variability and with a significant bias to the left.

CC, who sustained a right lesion associated with left visuo-spatial neglect and visuo-constructive deficits, reported asymmetrically diotic items with a disadvantage for left hemispace (Table 1; Fig. 1); numerous fusions occurred in the diotic test. No significant asymmetry was present in dichotic listening. In sound localisation, she misplaced the centrally presented stimuli to the right. One left-to-right alloacusis was observed associated with a great variability for the left position.

PJ, who sustained a right lesion without signs of visuo-spatial neglect, reported asymmetrically diotic items with a disadvantage for left hemispace (Table 1; Fig. 1); three fusions of words occurred. No significant asymmetry was present on dichotic listening. In sound localisation, he tended to misplace the centrally presented stimuli into the right hemispace; he also presented numerous left-to-right alloacusis.

LC, who sustained a left lesion without signs of visuo-spatial neglect, reported asymmetrically items presented in the ITD diotic listening with a disadvantage for left hemispace (Table 1; Fig. 1); no fusion of words occurred. No significant asymmetry was present on dichotic listening. When indicating positions of sounds lateralised with ITD, he misplaced the centrally presented stimuli into the right hemispace.

In summary, unilateral extinction of stimuli lateralised with ITD without asymmetry in dichotic listening following a right or bilateral hemispheric lesion was found in association with impaired sound localisation. All but two of these patients presented signs of mild to severe left visuo-spatial neglect.

4.2. Extinction of dichotically presented stimuli without asymmetry in ITD diotic listening

Six other patients presented this opposite profile. LL, who sustained a right lesion with left visuo-spatial neglect, presented an almost complete extinction items presented dichotically to the right ear (Table 1; Fig. 2); numerous fusions occurred. No significant asymmetry was present on diotic listening, but several fusions occurred. In sound localisation, he shifted the centrally presented stimuli toward the left hemispace and presented one right-to-left alloacusis.

LK, who sustained a right lesion with left visuo-spatial neglect, reported asymmetrically items presented in dichotic listening with a disadvantage for the left ear (Table 1; Fig. 2). No significant asymmetry was present on ITD diotic listening. In sound localisation, he shifted the centrally presented stimuli toward the right hemispace and tended to attribute locations with great variability.

AG, who sustained a right lesion associated with severe left visuo-spatial neglect and visuo-constructive apraxia, presented a significant bias on dichotic listening, with disadvantage for the left ear (Table 1; Fig. 2). No significant asymmetry was present on diotic listening, but few fusions occurred. In sound localisation, she tended not to discriminate the left-sided positions and she presented four right-to-left alloacusis. Furthermore, centrally presented sounds were misplaced in the left hemispace.

RB, who sustained a right lesion with mild left visuo-spatial neglect, presented a significant bias on dichotic listening, with a disadvantage for the left ear (Table 1; Fig. 2). No significant asymmetry was present on diotic listening, but three fused words were reported. In sound localisation, he shifted the centrally presented stimuli toward the left hemispace and tended not to discriminate the relative positions of consecutively presented stimuli.

ES, who sustained a left lesion associated with mild signs of right visuo-spatial neglect and visuo-constructional disturbances, presented a significant asymmetry with disadvantage for left ear in dichotic listening (Table 1; Fig. 2). No significant asymmetry was observed in diotic listening. In sound localisation, she tended to be inconsistent for sounds-presented within the left and right hemispace.

SD, who developed a left lesion without signs of visuo-spatial neglect, presented a complete extinction of items presented dichotically to the right ear (Table 1; Fig. 2). No significant asymmetry was present on diotic listening, but two pairs of words presented simultaneously in the left and right hemispace, respectively, were rendered in a fused fashion. In sound localisa-

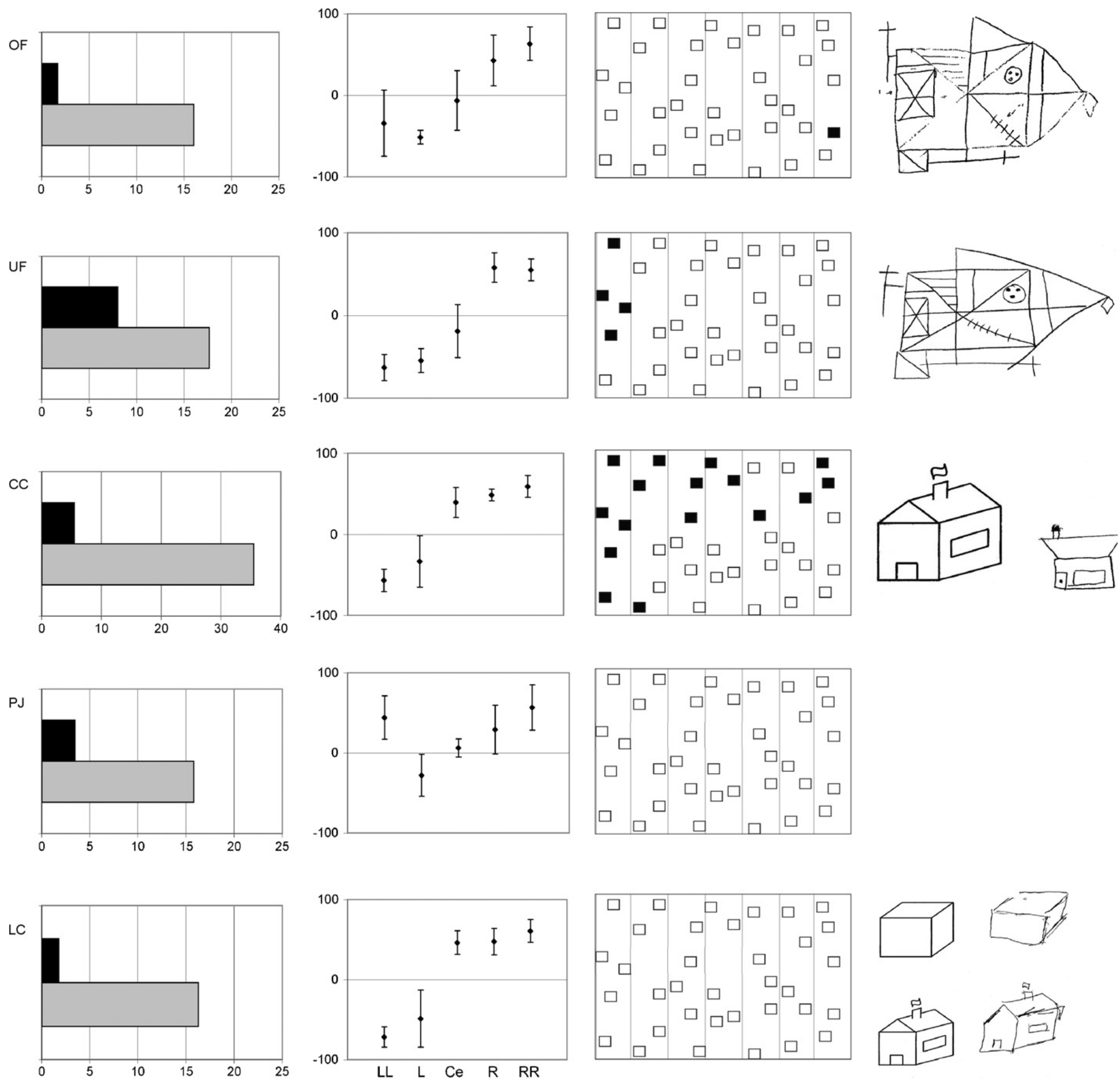

Fig. 1. Performance of patients with a significant asymmetry in diotic but not in dichotic listening. First column shows lateralisation index of ITD diotic (grey) and dichotic (black) listening; second column performance in sound localisation (mean angular values and standard deviations of pointing responses for distinct ITD values; negative for left; LL and RR correspond to ITD of 1 ms favouring the left and right ear, respectively, L and R to ITD of 0.3 ms and Ce to ITD of zero); third column performance in cancellation task (black squares correspond to non-cancelled items); and fourth column the copy of the Rey–Osterrieth figure, a cube or a house (the latter two are shown with the corresponding examples).

tion, she presented a shift of centrally presented sounds toward the left hemispace and variable responses for sounds-presented within the left and right hemispace.

In summary, unilateral left extinction in dichotic but not in diotic listening following a right-hemispheric lesion was found in association with impaired (patients LL, LK, AG, RB and SD); see also Bellmann et al. (2001), or with preserved sound localisation (patient ES). In four cases left visuo-spatial neglect was present.

4.3. Extinction of dichotically and diotically presented stimuli

Four patients presented significant extinction on both the diotic and dichotic tasks. CS, who sustained a right lesion associated with left visuo-spatial hemineglect and visuo-constructional apraxia, presented a significant asymmetry on diotic and dichotic listening with a disadvantage for left hemispace and left ear (Table 1; Fig. 3). In the dichotic task, she

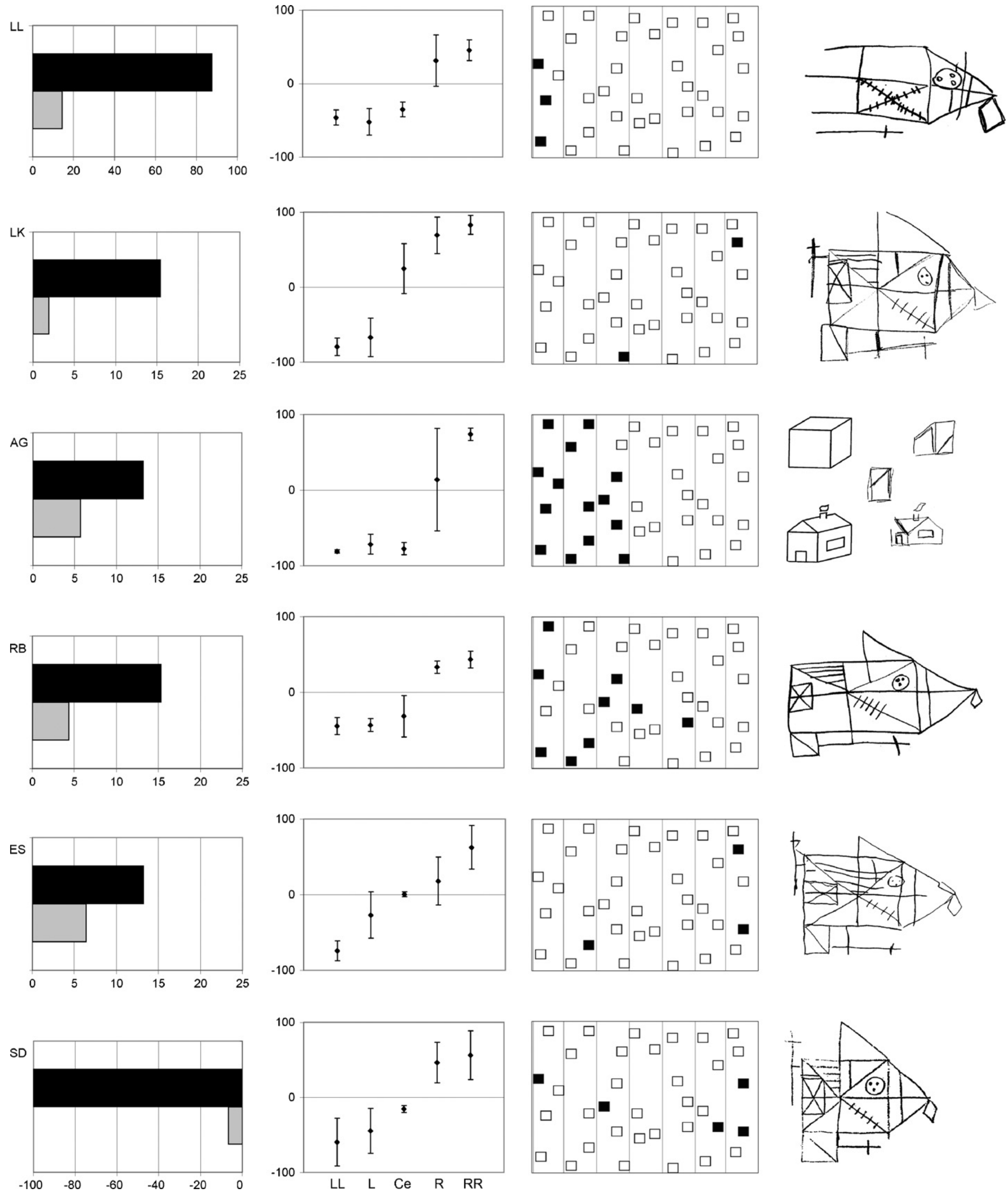

Fig. 2. Performance of patients with a significant asymmetry in dichotic but not in diotic listening. Same conventions as in Fig. 1.

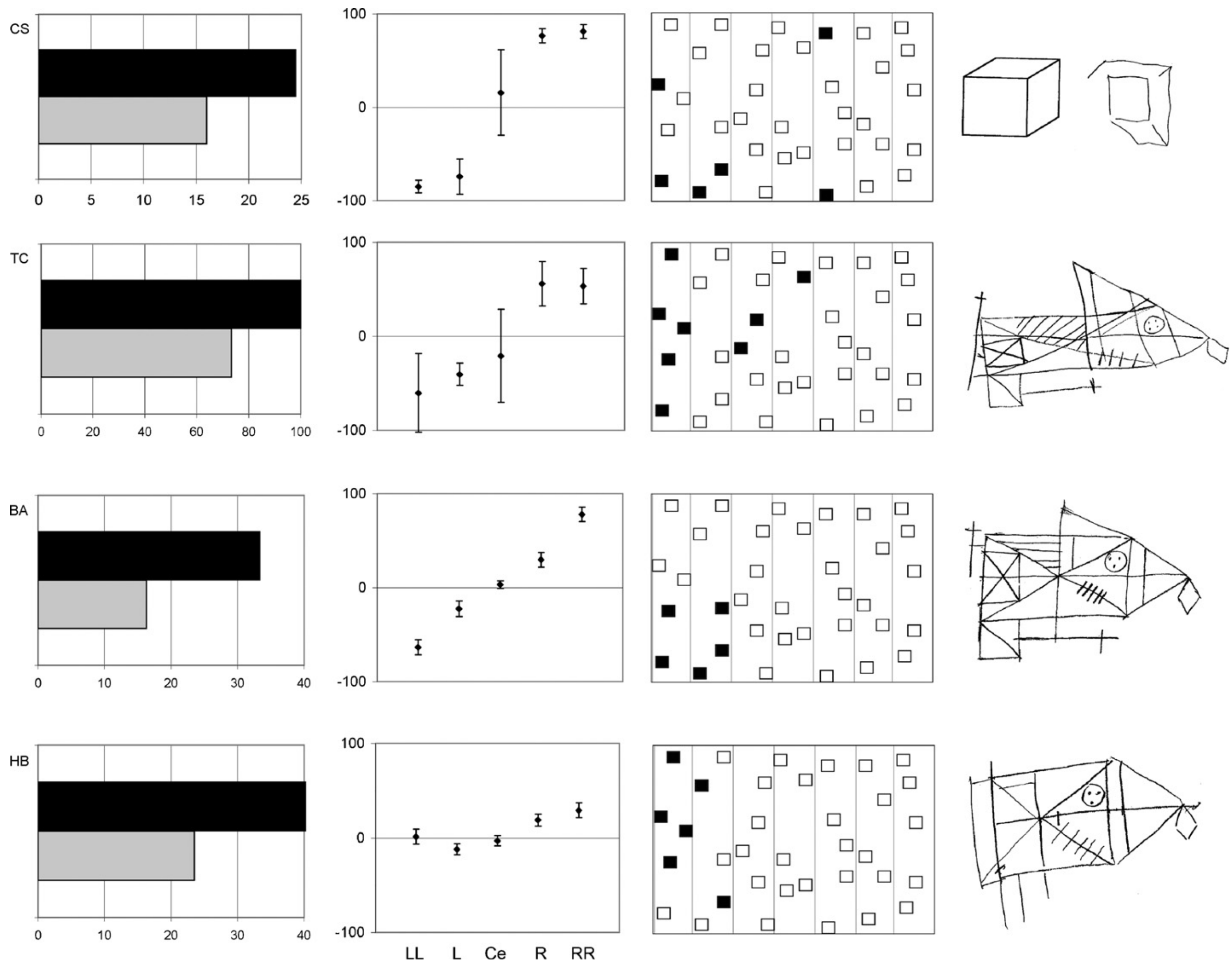

Fig. 3. Performance of patients with a significant asymmetry in diotic and dichotic listening. Same conventions as in Fig. 1.

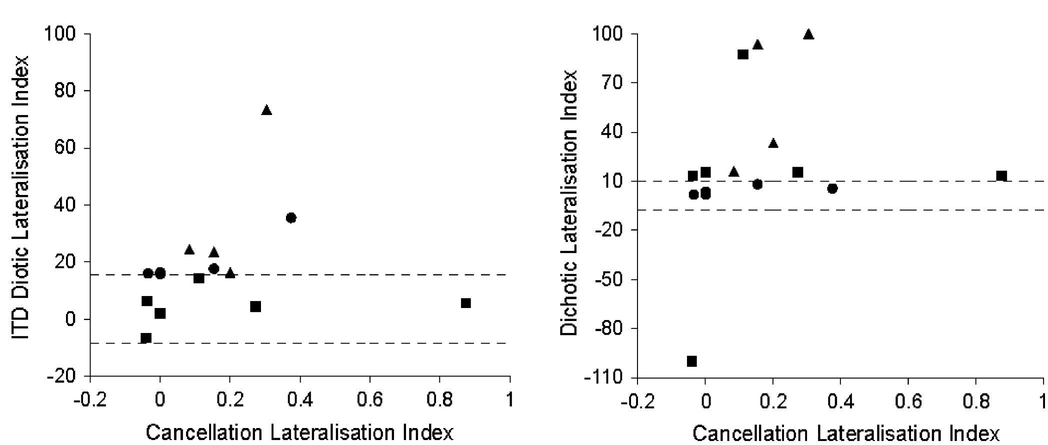

Fig. 4. Correlation between performance in diotic (A) or dichotic listening (B) and cancellation task. The performance on cancellation is expressed by a lateralisation index; high positive values indicate strong visuo-spatial neglect. Dotted line indicates the limits of normal performance in the diotic or dichotic tasks (controls' mean ± 2S.D.). Triangles, patients with significant asymmetry in the diotic and dichotic task; dots, patients with significant asymmetry in the diotic (but not dichotic) task; squares, patients with significant asymmetry in the dichotic (but not diotic) task.

reported one pair of words in a fused fashion. In sound localisation, she indicated the centrally presented sounds with great variability and, on average with a significant shift towards the right.

TC, who sustained a right lesion with left visuo-spatial hemineglect and visuo-constructional disturbances, had complete or almost complete left extinction of dichotically or diotically presented words (Table 1; Fig. 3). In the diotic condition, half of the pair of words were reported in a fused fashion. In sound localisation, she presented a shift of the centrally presented sounds toward the left and one left-to-right alloacusis.

BA, who sustained a right lesion with left visuo-spatial hemineglect, had significant asymmetry on diotic and dichotic listening with a disadvantage for the left hemispace and the left ear (Table 1; Fig. 3). On diotic listening three fusions occurred. In sound localisation, his performance was within normal limits.

HB, who sustained a right lesion with visuo-spatial neglect, presented a significant asymmetry on diotic and dichotic listening with a disadvantage for the left hemispace and the left ear (Table 1; Fig. 3). Numerous fusions occurred in diotic listening. In sound localisation, he presented four left-to-right alloacusis.

In summary, unilateral left extinction in dichotic and diotic listening was found in the absence of sound localisation deficits (patients BA and HB), as already described in our previous paper (Bellmann et al., 2001) or associated with sound localisation deficits (patients CS and TC). In all four cases the combined dichotic and diotic extinction was associated with visuo-spatial hemineglect.

4.4. Auditory extinction and visuo-spatial neglect

In the 12 cases with damage to the right or bilateral hemisphere the severity of auditory extinction and of visuo-spatial neglect were compared. The latter was assessed by a lateralisation index in the cancellation tasks (Table 1; Fig. 4).

In cases with significant asymmetry in diotic (but not dichotic) listening, i.e., patients OF, UF, CC, PJ, a greater left-sided extinction was associated with worse performance on cancellation tasks (see dots in Fig. 4A; $r(2) = 0.95$, $p < 0.05$). In cases of right-hemispheric lesions with significant asymmetry in dichotic (but not diotic) listening, i.e., patients LL, LK, AG, RB, (see squares in Fig. 4B) no such relationship was apparent. In cases of significant asymmetry of both the diotic and dichotic listening, i.e., patients CS, TC, BA, HB greater left extinction tended to be associated with worse performance on cancellation tasks, however without reaching the 0.05 significance level (see triangles in Fig. 4A and B).

5. Discussion

5.1. Auditory extinction for space but not for ear

We have demonstrated for the first time that an attentional auditory deficit for the left hemispace can occur in the absence of a left ear extinction on dichotic listening test. In cases with right-hemispheric lesions, we found this pattern with (OF, UF, CC) or without left visuo-spatial neglect (PJ); in one case visuo-spatial neglect was associated with major visuo-constructive disturbances (CC). Thus, in the context of the neglect syndrome, auditory inattention for one hemispace can be clearly dissociated from monaural suppression, suggesting differences in the underlying processing.

Although this dissociation appears to be clear, it has to be considered that the dichotic test represents also an extreme case of auditory space representation by means of interaural intensity differences. Our finding suggests that the spatial representations based on interaural time and intensity differences contribute separately to the auditory attentional system. This is at least partially the case at the preattentional level, where electrophysiological evidence demonstrated segregated treatment of these cues at the cortical level (Tardif, Murray, Meylan, Spierer, & Clarke, 2006; Ungan, Yagcioglu, & Goksoy, 2001). Data from brain-damaged patients further support a segregation between spatial representations based on ITD or IID cue (Yamada, Kaga, Uno, & Shindo, 1996).

Attentional auditory deficits for left hemispace were also observed in the case of a left hemispheric lesion, accompanied by naming deficits, pure alexia and right hemianopia. This patient, LC, presented left-sided extinction in diotic listening and also other signs of auditory neglect, including the shift of the central position to the right hemispace and left-to-right alloacusis. In both aspects, this case resembled other patients with left neglect (CC, CS). This puzzling observation raises the question of a true "crossed neglect" where parts, but not necessary all symptoms of left hemineglect occur after a left hemispheric lesion. This symptomatology has not been described before; so-called crossed right-hemispheric syndromes were found in association with right visuo-spatial neglect (for review see e.g. Marchetti, Carey, & Della Sala, 2005). This observation calls for further studies, including systematic testing of large series of patients with left hemispheric lesions.

5.2. Auditory extinction for ear but not for space

Left ear extinction on dichotic listening is described here in the absence of attentional auditory deficits for left hemispace, i.e. with normal performance on the ITD diotic task. In five cases it has been found in association with sound localisation deficits following right or left lesions. Four cases corresponded to the previously described type of auditory neglect, characterized by distortions of auditory space representation in the absence of auditory attentional deficits for left hemispace after right-hemispheric lesions (Clarke & Thiran, 2004). All four patients presented signs of visuo-spatial neglect.

In another case we have found complete right ear extinction on dichotic listening in association with a left hemispheric lesion, without signs of hemineglect but with minor disturbances of sound localisation (SD). This right ear extinction is very similar to those reported previously after left hemispheric lesions (De Renzi et al., 1984; Kimura, 1967).

Another patient had a "paradoxical" left ear extinction following a left lesion (ES) as already reported previously (Damasio & Damasio, 1979; Poncet, Habib, & Robillard, 1987) and believed to result from an intra-hemispheric callosal disconnection.

Profiles which associate contralesional extinction in dichotic listening and preserved performance in diotic listening fit with the perceptive-structural interpretation to ear-extinction phenomena. This latter suggests that messages received by each ear are transmitted to the auditory cortex by a weak ipsilateral and a strong contralateral auditory pathway (Kimura, 1967). In the case of interaural competition as in dichotic listening, the ipsilateral pathway is proposed to be inhibited by the contralateral pathway at cortical and subcortical levels (Beaton & McCarthy, 1995; Sparks & Geschwind, 1968; Zaidel, 1976). Thus, unilateral hemispheric lesions may interfere with contralateral ear input processing and lead to contralesional extinction in dichotic listening. This hypothesis is supported by observations that contralesional ear extinction occurs as often after right as left hemispheric lesions (De Renzi et al., 1984).

The extinction of the contralesional ear on dichotic listening tasks in cases of hemispheric lesions can be also interpreted as cortico-subcortical diaschisis phenomenon. Two lines of evidence support this hypothesis. First, animal studies have demonstrated descending projections from the auditory cortex to the ipsilateral medial geniculate body (Winer, Diehl, & Larue, 2001), the inferior colliculus (for review see Winer, 1992), superior olivary complex (Coomes & Schofield, 2004), and the cochlear nucleus (Jacomme et al., 2003). Second, in our series fusions of simultaneously presented words in the ITD diotic condition were more frequently observed in cases with auditory extinction concerning the contralesional ear than the contralesional hemispace. Fusion phenomena can be due to deficient spatial segregation, i.e., when the patient perceives one fused word instead of the two spatially separated words (Yost, Mapes-Riordan, & Guzman, 1997). In several mammalian species, spatial positions derived from ITD were shown to be coded by the superior olivary complex, the nuclei of the lateral lemniscus and the inferior colliculus (for review see Moore, 1991). A disturbance of processing in these structures, which may occur in the context of a cortical lesion, may interfere with the processing of auditory spatial information, including sound object segregation.

In conclusion, auditory extinction of one ear or of one hemispace can occur independently of each other in the context of visuo-spatial neglect. This strengthens the hypothesis of neglect as the consequence of damage to multisensory spatial representations (Pavani et al., 2003), but suggests also the existence of distinct spatial-attentional processing modules.

5.3. Auditory extinction and visuo-spatial neglect

A previous meta-analysis reported a positive correlation between the severity of visuo-spatial neglect, as assessed with cancellation tasks, and signs of auditory neglect (Pavani et al., 2004). These authors supported the interpretation of neglect as disturbance of multisensory spatial processing. We have addressed this same issue in our population.

All but one (PJ) of our patients with damage to the right hemisphere presented signs of left visuo-spatial neglect, i.e., all patients with dichotic-but-not-diotic extinction; all patients with diotic-plus-dichotic extinction; and all but one with diotic-but-not-dichotic extinction. The correlation analysis between extinction and cancellation suggested a difference between the patients who presented a significant asymmetry in diotic listening and those who did not. A significant positive correlation was found for patients who had a significant extinction in diotic but not in dichotic listening and a (non-significant) tendency in patients with a combined extinction in diotic and dichotic tasks. No relationship was, however, present in cases of dichotic-but-not-diotic extinction. We would like to stress that meta-analysis of several studies would be necessary to clarify this point. Although the correlation between performance in diotic and cancellation tasks reached in our study the 0.05 significance level by the group with significant asymmetry in diotic (but not dichotic) listening, this result is based on relatively few data points and it appears to be driven by one extreme case. A previous study already demonstrated the co-occurrence of neglect symptomatology in auditory and visual domains (Pavani et al., 2004).

This observation confirms further a relationship between the severity of auditory and visual components of spatial neglect, but suggests that the multisensory aspects of neglect are better reflected by extinction on diotic than in dichotic listening.

5.4. Sound localisation, hemianopia and visuo-spatial hemineglect

Previous reports have indicated that hemianopia, in the absence of neglect, may influence the perception of sound locations and in particular be associated with a shift of auditory space representation towards the hemianopic field; this was reported for a left and a right-hemispheric lesion (Kerkhoff et al., 1999) and for a group of seven patients with right-hemispheric lesions (Zimmer, Lewald, & Karnath, 2003). One of our patients presented a right homonymous hemianopia of a visual hemifield without signs of visuo-spatial neglect (LC); he perceived the auditory central position and the left position with a shift towards the right, i.e., hemianopic field and presented left auditory extinction, in the diotic task, suggesting that the rightward shift in sound localisation was part of left auditory neglect.

Patients with left ear extinction on dichotic listening were found to present different types of disturbances in sound localisation. In a previous study (Bellmann et al., 2001) we reported two cases with right-hemispheric lesions, who presented a significant left-ear extinction in dichotic listening (but normal performance in diotic listening) associated with a severe spatial bias directed to right side in sound localisation. One patient (LK) in the present study had a similar profile, while two others (AG, RB) presented more profound sound localisation disturbances with a predominant bias towards the left hemispace. This heterogeneity in sound localisation deficits is very similar to that described by others in association with visuo-spatial neglect (Zimmer et al., 2003), where half of the patients showed a profound disturbance in sound localisaton and the other half a shift to the right.

Taken together, data from previous publications (Kerkhoff et al., 1999; Zimmer et al., 2003) and the present data suggest a complex relationship between hemianopia, auditory spatial representation and associated deficits and call for further investigations.

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