Effect of prism adaptation on left dichotic listening deficit in neglect patients: glasses to hear better?


Unilateral neglect is a disabling syndrome frequently observed following right hemisphere brain damage. Symptoms range from visuo-motor impairments through to deficient visuo-spatial imagery, but impairment can also affect the auditory modality. A short period of adaptation to a rightward prismatic shift of the visual field is known to improve a wide range of hemispatial neglect symptoms, including visuo-manual tasks, mental imagery, postural imbalance, visuo-verbal measures and number bisection. The aim of the present study was to assess whether the beneficial effects of prism adaptation may generalize to auditory manifestations of neglect. Auditory extinction, whose clinical manifestations are independent of the sensory modalities engaged in visuo-motor adaptation, was examined in neglect patients before and after prism adaptation. Two separate groups of neglect patients (all of whom exhibited left auditory extinction) underwent prism adaptation: one group (n = 6) received a classical prism treatment (‘Prism’ group), the other group (n = 6) was submitted to the same procedure, but wore neutral glasses creating no optical shift (placebo ‘Control’ group). Auditory extinction was assessed by means of a dichotic listening task performed three times: prior to prism exposure (pre-test), upon prism removal (0 h post-test) and 2 h later (2 h post-test). The total number of correct responses, the lateralization index (detection asymmetry between the two ears) and the number of left-right fusion errors were analysed. Our results demonstrate that prism adaptation can improve left auditory extinction, thus revealing transfer of benefit to a sensory modality that is orthogonal to the visual, proprioceptive and motor modalities directly implicated in the visuo-motor adaptive process. The observed benefit was specific to the detection asymmetry between the two ears and did not affect the total number of responses. This indicates a specific effect of prism adaptation on lateralized processes rather than on general arousal. Our results suggest that the effects of prism adaptation can extend to unexposed sensory systems. The bottom-up approach of visuo-motor adaptation appears to interact with higher order brain functions related to multisensory integration and can have beneficial effects on sensory processing in different modalities. These findings should stimulate the development of therapeutic approaches aimed at bypassing the affected sensory processing modality by adapting other sensory modalities.

Keywords: neglect; auditory; prism; adaptation; crossmodal
Introduction

Unilateral neglect is frequently observed in right-handed patients following right hemisphere brain damage. It is a debilitating neurological disorder characterized by complex deficits in attention and spatial processing. The syndrome has been defined as a loss of awareness for stimuli, contra-lateral to the lesion and despite residual implicit processing (Driver and Mattingley, 1998; Marshall and Halligan, 1988). Typically, the patient fails to report, to orient towards left-sided stimuli (Heilman et al., 1985; Cappa et al., 1987), or tends to underestimate them on various perceptual dimensions (Halligan and Marshall, 1991; Milner et al., 1993). Neglect symptoms range from deficits in sensori-motor processing (Heilman et al., 1985; Mattingley et al., 1992, 1998) through to impairments in the mental representation of space (Bisiach and Luzzatti, 1978; Rode et al., 1995; Guariglia et al., 2005). In everyday life, neglect patients may omit to read the left part of a journal or a book, omit to eat food from the left half of a plate, forget to shave the left half of the face or hit obstacles on the left when moving in the environment.

In addition to these heterogeneous symptoms and reflecting the complexity of this multifaceted syndrome, it is now increasingly acknowledged that unilateral neglect is not just restricted to the visual modality, but can often affect different sensory modalities concurrently (for review see Brozzoli et al., 2006). In particular, numerous studies of patients with visuo-spatial neglect found concomitant deficits in auditory attention and spatial processing (Bisiach et al., 1984; Soroker et al., 1997; Pavani et al., 2004). Bisiach et al. (1984) first described impairments in auditory spatial processing in patients with spatial neglect, i.e. auditory localizations errors, particularly when pointing to contra-lesional sounds. They emphasized the importance of investigations in other sensory modalities in neglect and not just vision. In more recent years, auditory manifestations of unilateral neglect have been more frequently studied (Pavani et al., 2003, 2004). There is now some evidence that visual neglect patients can manifest contra-lesional deficits in a variety of auditory tasks (detection, identification and localization).

Impaired detection of contra-lesional sounds in visual neglect patients has been observed when targets were presented together with other competing sounds (De Renzi et al., 1989; Beaton and MacCarthy, 1993, 1995). In such a situation of auditory bilateral presentation, an auditory deficit has been reported for free-fields sounds (Bender and Diamond, 1965; Heilman and Valenstein, 1972) as well as for sounds presented dichotically over headphones (De Renzi et al., 1984, 1989).

Just as for simple auditory detection tasks, deficits in auditory identification tasks in neglect have more often been observed under bilateral simultaneous stimulation, with competition thus arising between different concurrent auditory targets. Deficits for contra-lesional sounds have been demonstrated for both free-field stimulation (Calamaro et al., 1995; Soroker et al., 1995, 1997; Deouell and Soroker, 2000) and dichotic presentation over headphones (Hugdahl et al., 1991; Bellmann et al., 2001; Pavani et al., 2005). These auditory deficits were typically more pronounced in visual neglect patients than in healthy controls and, more importantly, were more severe than in right-brain damaged patients without neglect (Calamaro et al., 1995; Pavani et al., 2005). The interpretation of this phenomenon was initially equivocal about whether deficits in neglect patients reflect suppression of auditory input from the contra-lesional ear or higher order deficits in spatial processing (Beaton and MacCarthy, 1993, 1995; Bellmann et al., 2001). More recent contributions (Pavani et al., 2005; Spierer et al., 2007) strongly suggest a role for higher level spatial factors in some of these auditory deficits. In combination, the available evidence converges to support the interpretation of neglect as a disturbance of multisensory spatial processing.

Sound localization tasks have also revealed predominantly contra-lesional deficits, even for single unilateral stimuli. Different sound-localization paradigms have been used, such as pointing to sounds (Ruff et al., 1981; Bisiach et al., 1984) and auditory midline perception (Vallar et al., 1995; Kerkhoff et al., 1999; Tanaka et al., 1999). Pavani et al. (2001) demonstrated a deficit in auditory localization for contra-lesional space processing in visual neglect patients. In combination, these results support the existence of some impairment in detecting changes in sound position in visual neglect patients.

In addition, evidence suggests that non-spatial auditory deficits may also be observed. Using an auditory test of sustained attention, Robertson et al. (1997) reported a non-spatial auditory deficit in right brain-damaged patients with neglect compared to non-neglect patients, with a correlation between impairment in this task and severity of visual neglect. Attentional limits have been evoked to explain a deficit arising during a task of comparisons between brief successive sounds presented centrally (Cusack et al., 2000). Pavani et al. (2005) reported difficulties in a task in which words were presented bilaterally and diotically, this deficit affecting ‘left’ and ‘right’ sounds equally on double stimulation, suggesting a general capacity limitation in neglect patients in addition to their lateralized spatial biases.

Finally, recent studies concerning multimodal representation have provided empirical evidence indicating that parietal cortex and other brain structures commonly associated with neglect (superior temporal lobe: Karnath et al., 2001; premotor and frontal cortices: Husain and Kennard, 1996) may play a fundamental role in multisensory processing of space.

Hence, auditory deficits occur frequently in right brain-damaged patients with neglect. Although it is well established that the presence of post-stroke neglect is a poor prognostic factor for recovery (e.g. Denes et al., 1982; Jehkonen et al., 2000), the specific consequences for recovery and rehabilitation of the multisensory aspects of neglect have yet to be explored. For instance, it can be speculated that the debilitating outcome of the neglect syndrome may be compounded when neglect-related disorders affect different sensory modalities simultaneously. A rehabilitation protocol that proves to be simultaneously effective on the different clinical manifestations of the neglect syndrome would thus have a greater impact on clinical outcome. In this respect, prism adaptation, a rehabilitative procedure introduced 11 years ago (Rossetti et al., 1998) appears particularly promising (Milner and MacIntosh, 2005; Luauté et al., 2006a), since it has been shown to produce improvement in a wide range of neglect symptoms in the visual
domain (for review see Rossetti and Rode, 2002; Rode et al., 2003, 2006a, 2007; Pisella et al., 2006; Revol et al., 2007), and has recently shown rehabilitative efficacy for neglect-related disorders in the tactile domain (Maravita et al., 2003; Dijkerman et al., 2004).

Previous studies have demonstrated that a short period of visuo-motor adaptation to a rightward prismatic shift of the visual field can improve symptoms of hemispatial neglect in a wide range of visuo-motor tasks such as line-bisection, line-cancellation or copy drawing (Rossetti et al., 1998), but also in mental imagery (Rode et al., 1998), postural imbalance (Tilkete et al., 2001), wheelchair driving (Jacquin-Courtois et al., 2008), visuo-verbal measures (Farnè et al., 2002), neglect dysgraphia (Rode et al., 2006b) and number bisection (Rossetti et al., 2004). This suggests that visuo-manual adaptation can modify spatial representations at a higher level than at a simply sensory level, suggesting a possible link between sensori-motor plasticity and space representation. Prominently, while in the first study (Rossetti et al., 1998) patients’ improvement was fully maintained 2 h later, in further case studies the effects of a single session of prism adaptation have been reported to last up to 4 days (e.g. Maclntosh et al., 2002; Pisella et al., 2002). Repeated sessions of prism adaptation over several weeks have been shown to induce a long-lasting improvement of neglect patients’ performance, not only in standard clinical tests of neglect but also in more ecological assessment (Frassinetti et al., 2002; Humphreys et al., 2006; Shiraishi et al., 2008; Serino et al., 2009). The improvement found after prism adaptation in a wide variety of visuo-spatial tasks indicates that prism adaptation may affect the organization of higher levels of spatial representation, such as those impaired in neglect patients.

Although tactile effects of prism adaptation have been described (Maravita et al., 2003; Dijkerman et al., 2004), it is possible that such effects can be ascribed to cross-talk within the somato-sensory system between proprioception (which is directly modified by adaptation) and the tactile modality. However, if visuo-manual prism adaptation improves auditory manifestations of neglect, this would imply that adaptation alters higher level representations of space in such a way that it can modify the processing of sensory input that has not been directly altered by prism exposure.

The aim of the present study was to test whether prism adaptation effects generalize to neglect symptoms that are independent of any of the components directly linked to visuo-manual adaptation. To this end, a common auditory manifestation of neglect, auditory extinction, was quantified by a dichotic listening task. Amelioration of auditory extinction by prism adaptation would be particularly remarkable, because this neglect-related deficit emerges from a different sensory modality (audition) than those involved in the adaptation procedure (i.e. vision and proprioception), and it is assessed by a non-manual response (i.e. verbal report). Hence, auditory extinction is tested by a task that is fully independent from the sensory and motor components intrinsic to the prism adaptation procedure.

In our study, auditory extinction was examined in neglect patients before and after prism adaptation. Patients were randomly assigned to two groups to assess the effect of prism adaptation: one group received a classical prism treatment and the other group underwent the same procedure but wore neutral glasses that do not create any optical shift.

**Methods**

**Subjects**

Twelve right brain-damaged patients were included in this study, according to the following criteria: (i) unilateral right hemisphere damage with no history of previous neurological illness; (ii) left unilateral visual neglect on admission to the rehabilitation unit, as assessed by classical neuropsychological tests [line cancellation test (Albert, 1973), line bisection task (Schenkenberg et al., 1980) and a copy-drawing task (Gainotti et al., 1972)]; (iii) left ear extinction on the dichotic listening task (see ‘Methods’ section) (preliminary clinical evaluation of auditory extinction was performed with the sound of snapping fingers being delivered to both ears; left auditory extinction represented repeated neglect of applied sound stimulus to left ear); (iv) adequate hearing threshold as measured by pure tone audiometry (determined over a range of frequencies between 256 and 8192 Hz) and no asymmetric loss (<10 dB difference in mean threshold between left and right ear); and (v) right-handedness. In addition, 10 healthy control subjects (4 male, 6 female) aged between 23 and 58 years (mean = 37; SD = 12.60) were recruited to obtain normative data for the dichotic listening task.

At the time of clinical examination, there was neither confusion nor temporal or spatial disorientation. Informed consent was obtained from all patients prior to testing; the procedure, approved by French law on patients’ rights (4 March 2002), was in accordance with the Declaration of Helsinki. Patients were randomly assigned to the two groups. A finding commonly observed and reported in the literature is that neglect patients do not overtly (neither spontaneously nor following direct questioning) detect the visual perturbation caused by prisms, which normally induce a spontaneous surprise reaction in healthy subjects (Michel et al., 2007). Further, neglect patients do not show any changes in skin conductance when prisms are unexpectedly introduced in the course of a pointing task (Calabria et al., 2004). This evidence suggests that neglect patients are not aware of the visual perturbation, but nevertheless they adapt to it. Accordingly, our patients did not report that the goggles produced any visual shift, even when specifically questioned.

Clinical and paraclinical data, lesion topography and co-morbid disorders are summarized for each patient in Table 1. All patients had a CT or MRI scan to define the lesion topography (Fig. 1). As shown in Table 1, the implication of the global fronto-parieto-temporal network was more frequent in the ‘Control’ group. However, Fig. 1 shows that lesion size tended to be larger in the ‘Prism’ group. Patients’ lesions depicted in Fig. 1 have been quantified by a computerized imaging system (Leica imaging system and Quantimet 500 software). This system quantified each area marked in black on Fig. 1 and provided a total area value for each patient in arbitrary pixel unit. A t-test performed on the total lesion surface showed that the ‘Prism’ group (mean = 13 933, SEM = 6278) does not differ significantly (t(10) = 1.44; P > 0.17) from the ‘Control’ group (mean = 9333, SEM = 4640) (t(10) = 1.44; P > 0.17). In addition, both groups are comparable in terms of paraventricular fibre lesion corresponding to the auditory inter-hemispheric pathway (two patients in the ‘Control’ group, three patients in the ‘Prism’ group) and no patient exhibited callosal disconnection at the mid-sagittal plane. Visual and tactile extinction
were assessed by confrontation testing. At the time of testing, 7/12 patients still showed left unilateral neglect. ‘Prism’ group (n = 6) refers to patients who underwent prism adaptation, ‘Control’ group (n = 6) refers to patients who wore neutral glasses. There was no difference between the groups in scores on the visual neglect tests performed prior to the experimental intervention [Albert test: t(10) = −1.43, P > 0.18; Schenkenberg test: t(10) = 0.33, P > 0.74]. The two groups also did not differ significantly in age (‘Prism’ group: mean age = 59.7 years, SEM = 6.5 and ‘Control’ group: mean age = 56.7 years, SEM = 4.7) or in their post-stroke onset delay prior to experimental intervention.

Table 1 Clinical and paraclinical data for all patients (‘Prism’ and ‘Control’ groups)

<table>
<thead>
<tr>
<th>Group</th>
<th>Patient</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Lesion (right hemisphere)</th>
<th>Delay (days)</th>
<th>L. visual neglect</th>
<th>Left visual extinction</th>
<th>Left somesthetic extinction</th>
<th>Left auditory extinction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prism</td>
<td>D.M.</td>
<td>M</td>
<td>72</td>
<td>Parietal</td>
<td>73</td>
<td>No</td>
<td>Not determined</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Prism</td>
<td>B.E.</td>
<td>F</td>
<td>42</td>
<td>Temporo-parietal</td>
<td>566</td>
<td>No</td>
<td>Left hemianopia</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Prism</td>
<td>A.E.</td>
<td>F</td>
<td>75</td>
<td>Parieto-occipital</td>
<td>80</td>
<td>Yes</td>
<td>Left hemianopia</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Prism</td>
<td>G.C.</td>
<td>F</td>
<td>38</td>
<td>Fronto-parietal</td>
<td>124</td>
<td>Yes</td>
<td>Left hemianopia</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Prism</td>
<td>L.A.</td>
<td>M</td>
<td>62</td>
<td>Temporo-occipital</td>
<td>515</td>
<td>Yes</td>
<td>Left hemianopia</td>
<td>Not determined</td>
<td>Yes</td>
</tr>
<tr>
<td>Prism</td>
<td>M.J.</td>
<td>M</td>
<td>69</td>
<td>Thalamic</td>
<td>60</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Control</td>
<td>B.B.</td>
<td>F</td>
<td>50</td>
<td>Parietal</td>
<td>30</td>
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<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Control</td>
<td>N.G.</td>
<td>M</td>
<td>70</td>
<td>Parieto-occipital</td>
<td>35</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Control</td>
<td>B.C.</td>
<td>F</td>
<td>71</td>
<td>Parietal</td>
<td>109</td>
<td>No</td>
<td>Not determined</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Control</td>
<td>D.J.</td>
<td>M</td>
<td>45</td>
<td>Capsulolenticular</td>
<td>41</td>
<td>Yes</td>
<td>Left hemianopia</td>
<td>Not determined</td>
<td>Yes</td>
</tr>
<tr>
<td>Control</td>
<td>G.M.</td>
<td>F</td>
<td>47</td>
<td>Fronto-temporo-parietal</td>
<td>53</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Control</td>
<td>F.J.Y.</td>
<td>M</td>
<td>57</td>
<td>Fronto-temporo-parietal</td>
<td>146</td>
<td>Yes</td>
<td>Left hemianopia</td>
<td>Not determined</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Figure 1 Brain lesions in patients. The figure shows the location of brain damage in each patient, for both groups (‘Prism’ and ‘Control’), according to the standard template provided by Damasio and Damasio (1989). The lesion areas depicted in black were subjected to quantitative analysis by a computerized imaging system.
Neglect was defined by a deficit in at least two of these tests. Neglect was assessed by three classical neuropsychological tests: line cancellation (Albert, 1973), line bisection (Schenkenberg et al., 1980) and a copy-drawing task (Gainotti et al., 1972). The presence of neglect was defined by a deficit in at least two of these tests.

### Experimental procedures

#### Evaluation of left visuospatial neglect at time of testing

Neglect was assessed by three classical neuropsychological tests: line cancellation (Albert, 1973), line bisection (Schenkenberg et al., 1980) and a copy-drawing task (Gainotti et al., 1972). The presence of neglect was defined by a deficit in at least two of these tests.

#### Evaluation of left auditory extinction

The patients sat in a quiet room in front of the examiner. Stimuli were played through earphones, at the volume judged most comfortable by each patient, in order to study extinction in its everyday clinically relevant form.

The dichotic listening task was a verbal dichotic listening test, including 60 pairs of stimuli (total across all categories). The two stimuli of each word pair were simultaneously presented, one to the left and the other to the right ear, through the earphones. There were four categories of stimuli: pairs of phonologically similar disyllabic words (e.g. blague/blag (joke); claquette/klak (slap)), pairs of single words (e.g. couleur/ku.lœ (colour); lundi/le.de (monday)), pairs of numbers (e.g. deux/da (two); cinq/Ss ˆk (five)) and meaningful short groups of words (e.g. un bon repas/αr/αp (a good meal); un gros gâteau/ɡa.to (a big cake)). Patients were instructed to concentrate equally on both stimuli and to repeat them. To familiarize patients with the procedure, this evaluation was preceded by a brief period of practice with right and left presentations of eight items (four single words to the right and four single words to the left).

Individual responses were first scored as the percentage of correctly repeated words presented to the right and left ear (Table 2). Performance was then assessed using two main parameters. First, a quantitative measure was used to assess the patient’s global performance. This global quantitative measure was simply the total number of auditory stimuli correctly reported by the patients, pooled over the four stimulus categories. Second, we computed a lateralization index for each patient, a sensitive means of detecting and quantifying asymmetry in the detection of stimuli presented to the two ears (Bellmann et al., 2001). The lateralization index = 100 × \((R – L)/(R + L)\), where \(R\) and \(L\) are the total number of correctly reported stimuli from the right ear and left ear, respectively. The lateralization index metric represents the proportionally greater number of right than left ear stimuli detected, with the difference expressed as a percentage of the total number of stimuli detected. In addition, incorrect responses were examined for fusion errors. Fusion errors are verbal responses where one phoneme from words presented on the left is combined with words presented on the right to produce a novel combination that was not actually presented to the patient, though each constituent part was. Fusion errors imply some degree of processing of the left ear (Gainotti et al., 2003).
stimulus rather than total extinction. The number of fusions was also analysed as an additional variable.

**Prism adaptation**

Subjects in the ‘Prism’ group were exposed to a rightward optical shift of the visual field produced by the prismatic lenses. Glacier goggles (Julbo®) were fitted with wide-field, point-to-point wedge lenses creating an optical shift of 10° (OptiquePierre.com, Lyon) affording wide binocular vision. The total visual field was 110° and the one-eye visual field was 80° (including a 50° binocular field). With these goggles on, the visual field was uniformly displaced to the right with minimal visual distortion. The exposure period consisted of 50 pointing responses to visual targets presented 10° to the right or to the left of the objective body midline. During the prism exposure, each patient was asked to point at a fast but comfortable speed; he/she could see the target, the second half of the pointing trajectory and the terminal error. His/her head was kept aligned with the body’s sagittal axis by a chin-rest and controlled by an investigator throughout the adaptation procedure. The total duration of this exposure was ~8 min.

The dichotic listening task was presented three times: once in the pre-test (prior to prism exposure) and twice as post-tests (after prism adaptation): upon prism removal (0 h post-test) and 2 h later (2 h post-test).

Subjects from the ‘Control’ group underwent the same procedure except that the goggles were fitted with neutral sham glasses (the weight of these sham goggles was matched to the real prisms by having two pairs of 5° prisms for each eye; the bases of these two prisms were oriented left and right in front of each eye, such that the two deviations cancelled out, yielding no net optical shift).

**Statistical analyses**

Simple comparisons (e.g. age, delay post-stroke) were performed with t-tests. All other multiple comparisons of means (e.g. Group, Session and/or Category) were performed with ANOVAs. Further planned comparisons of the means were used when appropriate (least-square method). All analyses were realized in the Statistica version 8.0 (StatSoft France, 2008). Threshold for statistical significance was set at 0.05.

**Results**

None of the patients complained about discomfort or the auditory task’s difficulty and all testing was completed without interruption. All patients heard and reported 100% of stimuli during the preliminary monaural presentation (used as a familiarization practice) for both right and left monaural stimuli. As validated by preliminary testing, the 5 s interval between auditory stimuli allowed patients to perform the test at a comfortable pace, such that no data were lost due to time constraints. To validate the occurrence of substantial prism adaptation in the ‘Prism’ group, a simple clinical procedure was used. Two open-loop pointing trials (i.e. without visual feedback) were performed by each patient at the end of prism exposure (goggles were removed). We checked that performance on these pointing trials was shifted by at least 5° with respect to the visual target. Using this procedure, we confirmed that all patients in the ‘Prism’ group showed a sufficient amount of prism adaptation.

**Baseline pre-test evaluation of dichotic listening performance**

A range of measures were used to assess performance in dichotic listening: average total number of correct responses; lateralization index for overall task performance and for each Stimulus Category, lateralization index = 100 × (R – L)/(R + L), where R and L are the total number of correctly reported stimuli from the right ear and left ear, respectively; and fusion errors, verbal responses where one phoneme from words presented on the left is used to produce a new word that was not actually presented to the patient.

In healthy controls (n = 10), the average lateralization index was 1.02 (range from −5.26 to +4.89; SE = 0.99), coherent with the small right ear advantage that has been described in right-handed subjects (Michel et al., 1986).

Next, we tested for baseline differences in task performance between the two patient groups, the ‘Prism’ group and the ‘Control’ group. Global task performance was assessed using a one-way ANOVA. The average total number of correct responses obtained in the ‘Prism’ group (mean = 79.7; SE = 9.8) did not differ significantly [F(1, 10) = 0.66; P > 0.43] from that obtained in the ‘Control’ group (mean = 69.2; SE = 8.4). A significant left-right effect, however, was present [F(1, 10) = 73.23, P < 0.001], coherent with the left extinction observed in all patients (i.e. patients omit more left than right stimuli). Figure 2 shows the left and right scores (correct responses) obtained in the two groups, confirming that the global performance observed before prism adaptation was identical in the two groups.

The asymmetry of detection performance was quantified using the lateralization index. All patients presented major left auditory extinction with an average global lateralization index of +68.5 (SE = 10.7) in the ‘Prism’ group and of +66.4 (SE = 11) in the ‘Control’ group. Figure 3 presents lateralization index values for
each Stimulus Category. Lateralization index values were numerically smaller for phonologically similar words than the other stimulus categories (in particular as compared to short groups of words). We tested for any significant differences in performance between the groups across stimulus categories. An ANOVA with Group as a between-subject factor and Stimulus Category as a within-subject factor was performed on the lateralization index values obtained in the pre-test. There was no significant effect of Group \( F(1, 10) = 0.009, \quad P > 0.92 \) or Stimulus Category \( F(3, 30) = 2.11, \quad P > 0.12 \), nor was there an interaction.

Although the total number of fusion errors was low, the two groups were also compared for the raw number of fusion errors obtained during the pre-test. A marginally significant difference was found \( t(10) = -2.25, \quad P > 0.048 \), caused by the ‘Prism’ group (0.83) producing an average of two fewer fusion errors than the ‘Control’ group (2.83).

**Effect of prism adaptation on dichotic listening performance**

The following analyses compared the two groups of patients (‘Prism’ and ‘Control’) for their dichotic listening performance across the three evaluation sessions (pre-test, post-test 0 h and post-test 2 h, i.e. before and after prism adaptation).

First, a comparison of the two groups’ global performance (total number of correct responses) was performed over the three evaluation sessions with a two-way ANOVA (Fig. 4). No group effect was observed \( F(1, 10) = 1.28, \quad P > 0.28 \), but a significant Session effect was obtained \( F(2, 20) = 14.41, \quad P < 0.001 \). Planned comparisons showed a significant difference between pre-test and 0 h post-test for both groups \( F(1, 10) = 27.94, \quad P < 0.0005 \), as well as between pre-test and 2 h post-test \( F(1, 10) = 16.00, \quad P < 0.005 \). No difference was found between 0 h and 2 h post-test \( F(1, 10) = 0.21, \quad P > 0.6 \). There was no Group × Session interaction \( F(2, 20) = 1.43; \quad P > 0.26 \). Hence, both groups improved their performance across repeated task sessions, presumably owing to task practice effects. Although the improvement in the ‘Prism’ group was twice that of the ‘Control’ group (‘Prism’: pre-test = 79.7 ± 9.2, 0 h post-test = 93 ± 9.6, 2 h post-test = 93 ± 9.3; ‘Control’: pre-test = 69.2 ± 9.2, 0 h post-test = 75.3 ± 9.6, 2 h post-test = 77.2 ± 9.3), this difference was not significant. The absence of an interaction suggests that prism adaptation does not significantly improve global, non-lateralized aspects of auditory performance.

To assess our primary hypothesis, that prism adaptation would improve lateralized aspects of task performance (i.e. auditory extinction), we analysed the lateralization index data. An ANOVA with Group as the between-subject factor and Session (pre-test, 0 h post-test and 2 h post-test) and Stimulus Category as within-subject factors revealed a dramatic improvement of left auditory extinction after prism adaptation in the ‘Prism’ group compared to the ‘Control’ group (Fig. 5). There was no main effect of Group \( F(1, 10) = 0.39; \quad P > 0.54 \) or Session \( F(2, 20) = 1.09; \quad P > 0.35 \). A main effect of Stimulus Category \( F(3, 30) = 3.41; \quad P < 0.05 \) was observed, caused by a smaller lateralization index for phonologically similar words than for short groups of words. There was also a significant Category × Session interaction \( F(6, 60) = 2.49; \quad P < 0.05 \). The three-way interaction was not significant \( F(6, 60) = 0.19; \quad P > 0.97 \). Critically, however, there was a significant Group × Session interaction \( F(2, 20) = 3.64; \quad P < 0.05 \). This interaction was caused by a significant reduction of the lateralization index for the ‘Prism’ group immediately after the test (0 h post-test) \( F(1, 10) = 7.03; \quad P < 0.05 \). In addition, 2 h later, a trend towards a reduction of the lateralization index (that is towards improved performance) could still be detected \( F(1, 10) = 2.40; \quad P = 0.076 \) (see Fig. 5).

To investigate whether this change in lateralization index was a robust effect measurable across all the different stimulus categories, we plotted data separately for Group, Session and
Category (Fig. 6). This confirmed that there was a systematic improvement in performance for the ‘Prism’ versus ‘Control’ groups across all four categories of stimulus (‘Prism’ group percent mean improvement at 0 h post-test for words = −21%, groups of words = −20%, phonologically similar words = −36%; ‘Control’ group % mean improvement at post-test 0 h for words = 1%, groups of words = 8%, phonologically similar words = 35%, numbers = −10%; for all individual patient effect sizes see Table 3).

The clinical relevance of the present results depends on observing not only a significant group effect, but also an effect size that leads to concrete individual benefit. To determine treatment efficacy at the individual level, we counted the number of patients in each group who exhibited a benefit across test sessions of at least 20%. These results are shown in Table 3 (0 h post-test/pre-test comparison, post-pre(%) at 0 h i.e. \([\text{LI } 0 \text{ h post-test}]/\text{LI pre-test}\)) in the ‘Prism’ group, all but one patient improved and three showed an improvement of >20%. In the ‘Control’ group, only one patient showed an improvement (16%). In the 2 h post-test/pre-test comparison [post-pre(%) at 2 h] [i.e. \((\text{LI } 2 \text{ h post-test})/\text{LI pre-test}\)] in the ‘Prism’ group, four of the six patients showed an improvement of at least 10%, with two of those improving by >20%.

As a supplementary analysis, we performed a repeated measure ANOVA on the number of fusion errors. There was no main effect of Group \([F(1, 10) = 1.44; P > 0.25]\) or Session \([F(2, 20) = 0.26; P > 0.77]\) but the interaction was marginally significant \([F(2, 20) = 3.42; P = 0.052]\). The planned comparison (between Group and pre-test versus post-test, with the post-test data pooled over 0 h and 2 h post-test) showed a significant increase in the number of fusion errors after prism adaptation \([F(1, 10) = 5.87; P < 0.04]\) (Fig. 7).

This secondary finding of an increase in the number of fusion responses, taken together with the improvement in lateralization index after prism adaptation, indicates that prism adaptation specifically benefits a lateralized component of patient deficit in auditory extinction. In the context of no baseline difference, and no global change over time in dichotic listening performance between the ‘Prism’ and ‘Control’ groups, the present results suggest that prism adaptation does not induce a general improvement in attentional capacity, but rather specifically redresses an imbalance in left–right attentional allocation.

As described in the ‘Subjects’ section, the time since stroke onset tended to be higher in the ‘Prism’ group than in the sham ‘Control’ group. This difference was not significant. There was also no difference in baseline task performance between the two groups (Fig. 5). In any case, such a difference in time since stroke onset would likely predict a more favourable spontaneous recovery rate in the ‘Control’ group than the ‘Prism’ group, so it cannot explain the specific improvement in the ‘Prism’ group that was observed. Alternatively, it could be argued that lesion–age difference might have contributed to the performance improvement in the ‘Prism’ group. The lesion–age difference was caused mainly by two patients (B.E. and L.A.) who suffered from their lesion over 500 days prior to the test. One of these patients (L.A.) was an outlier in the ‘Prism’ group, but in a direction that weakened the effect. This argues against the possibility that lesion–age difference between the groups caused the observed effect.

It is conceivable that some form of unconscious bias on the part of the experimenter might have contributed to the results observed. That is, this study was not blinded, so the potential for sources of bias need to be considered. To determine whether any such effect was likely to have contaminated the data, we performed an additional experiment. The responses of three new neglect patients were recorded in the same dichotic listening task, and the recording was analysed by ten independent hearers. Results showed remarkably low between-hearer variability in the assessments. The average standard error of the mean obtained across the three patients was 0.16 units and the greatest individual hearer’s deviation from the mean was 1.54 units. These values
## Table 3  Auditory extinction results in the two groups ('Prism' and 'Control') with absolute lateralization index score as a function of evaluation sessions and stimulus category

<table>
<thead>
<tr>
<th>Group</th>
<th>Patient</th>
<th>Words</th>
<th>Pre-test</th>
<th>0 h post-test</th>
<th>2 h post-test</th>
<th>0 h post-test</th>
<th>2 h post-test</th>
<th>0 h post-test</th>
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<th>0 h post-test</th>
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<th>0 h post-test</th>
<th>2 h post-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prism</td>
<td>D.M.</td>
<td>76</td>
<td>50</td>
<td>81</td>
<td>94</td>
<td>76</td>
<td>100</td>
<td>78</td>
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<td>57</td>
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<tr>
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<td>93</td>
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<td>53</td>
<td>54</td>
<td>75</td>
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<td>84</td>
<td>52</td>
<td>60</td>
<td>–38</td>
</tr>
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<td>33</td>
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<td>100</td>
<td>100</td>
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<td>77</td>
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<td>43</td>
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<td>–63</td>
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<td>45</td>
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<td>–9</td>
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<td>10</td>
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<td>89</td>
<td>75</td>
<td>72</td>
<td>–16</td>
</tr>
<tr>
<td>Mean (SEM)</td>
<td></td>
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<td>53 (12.8)</td>
<td>75 (11.9)</td>
<td>60 (13.4)</td>
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<td>37 (11.9)</td>
<td>68 (10.7)</td>
<td>53 (10.8)</td>
<td>56 (10.8)</td>
<td>–23% (11)</td>
</tr>
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</table>

Post-test (%)  

<table>
<thead>
<tr>
<th>Group</th>
<th>Patient</th>
<th>Words</th>
<th>Pre-test</th>
<th>0 h post-test</th>
<th>2 h post-test</th>
<th>0 h post-test</th>
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<th>0 h post-test</th>
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<th>0 h post-test</th>
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<th>0 h post-test</th>
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<td>Control</td>
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<td>–23% (11)</td>
<td>–18% (10)</td>
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</tr>
<tr>
<td>Control</td>
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<td>8</td>
<td>–20</td>
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<td>100</td>
<td>100</td>
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<td>100</td>
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<tr>
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<td>57 (16.1)</td>
<td>55 (17.5)</td>
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<td>70 (10.1)</td>
<td>65 (10.7)</td>
<td>8 (8)</td>
<td>2 (17)</td>
<td></td>
</tr>
</tbody>
</table>

Post-test (%)  

**Discussion**

The present experiment aimed to test the effect of a visuo-manual adaptation procedure (prism adaptation) on auditory extinction using dichotic listening tasks. The results clearly show that prism adaptation can improve the left-sided deficit typically found in neglect patients. The results support the hypothesis that adaptation of visuo-motor coordination can affect performance in a sensory modality (audition) that is not directly implicated in the visuo-motor adaptation process. This generalization further underscores the potential of prism adaptation as a clinically effective intervention for post-stroke rehabilitation.

These additional measurements confirm the reliability of the positive and negative charge in lateralization index values correspond to an aggravation or an improvement of extinction, respectively. Although task performance by the control group changes after the sham intervention as a function of Stimulus Category, the ‘Prism’ group maintains its advantage after prism adaptation, irrespective of Stimulus Category.
Prism adaptation effect on dichotic listening excludes a simple left ear sensory deficit

When using dichotic stimuli, one issue to address is whether extinction for left stimuli reflects poor or abolished processing of auditory information entering the contra-lesional ear, or higher level attentional disturbance involving contra-lesional space (Bellmann et al., 2001; Beaton and McCarthy, 1995). Several studies have aimed at specifying the characteristics of extinguished stimuli in order to localize the level at which the auditory processing deficit arises (Deouell and Soroker, 2000; Deouell et al., 2000; Shisler et al., 2004). The findings parallel previous studies of visual extinction, suggesting that auditory extinction may be due, in part, to a failure to bind together information about stimulus identity and stimulus location.

In assessing auditory attention deficits (as in extinction), it is important to rule out potential peripheral hearing deficits. This can be achieved by presenting auditory stimuli diotically. Diotic presentation involves that each stimulus reaches both ears, with an interaural time difference serving as the only lateralization cue (see Bellman et al., 2001; Spierer et al., 2007). In such cases, there is no difference of content because both ears receive both items of each pair at the same intensity level, allowing control for sensory deficits. In dichotic presentation two different stimuli are presented, one to the right ear and one to the left one, implying that different content reaches each ear. In the present study, we used dichotic presentation. However, the key finding in our study was a change in dichotic listening performance after prism adaptation. It does not seem plausible that prism adaptation could cause such a change in patients suffering from unilateral sensory hearing loss. The fact that five out of six patients in the ‘Prism’ group consistently showed an improvement after the adaptation procedure suggests that the auditory extinction deficit in these patients is a consequence of higher level deficits in contra-lesional spatial processing. The finding that prism adaptation improves auditory extinction suggests a locus of effect at a higher level of sensory integration; whereby adaptation shifts the spatial alignment between vision and proprioception, with apparent knock-on benefits for location processing in other sensory domains and for spatial cognition more generally.

Cross-modal effects of prism adaptation

Changes in visuo-motor (target pointing) performance following prism adaptation are believed to arise through changes in the mapping between visual, proprioceptive and motor processing (Redding et al., 2005). After-effects of these changes in visuo-motor performance have, however, been demonstrated to generalize over a range of tasks beyond the pointing procedure that is directly adapted. Benefits for unilateral neglect patients after prism adaptation have been shown on line bisection and cancellation tasks, postural imbalance, spatial judgement tasks, reading tasks and even wheel-chair driving (Rossetti et al., 1998; Tilikete et al., 2001; Farné et al., 2002; MacIntosh et al., 2002; Pisella et al., 2002; Jacquin-Courtois et al., 2008). Since each of these tasks involve some form of visual or motor processing, it is possible that performance improvements may arise directly from changes to visuo-motor processes that are to a greater or lesser extent directly altered by the prism adaptation procedure itself. Mental imagery (Rode et al., 1998, 2001, 2007) has also been found to be improved following adaptation, but visuo-spatial imagery tasks are known to recruit the visual system (Kosslyn et al., 1999). The amelioration of number bisection in neglect patients (Rossetti et al., 2004) may also result from an activation of visuo-spatial representations via spatial-numerical association (Hubbard et al., 2005; Lacour et al., 2005; Rode et al., 2007). A few reports have described an amelioration of somato-sensory processing in neglect patients following prism adaptation. First, the haptic circle centring task described by MacIntosh et al. (2002) involves a strong proprioceptive component, which might have been directly altered by prism adaptation. Second, Maravita et al. (2003) tested tactile extinction in four neglect patients and found an improvement of contra-lesional tactile perception in all patients after adaptation to a rightward prismatic shift. Third, Dijkerman et al. (2004) described a patient who, despite having recovered from visual neglect, still exhibited a somato-sensory deficit on the left side. After prism adaptation, the patient’s tactile and proprioceptive thresholds were significantly lowered. These last two studies are interesting because they demonstrate a beneficial effect of visuo-manual adaptation on tactile sensitivity, a modality that appears not to be directly modified by prism adaptation. However, it can be hypothesized that cross-talk between proprioceptive and tactile processes may explain these effects.

In contrast, in the present study, beneficial effects of prism adaptation were observed on auditory extinction, a modality that is independent from visual, somato-sensory and manual components. In addition, the semantic nature of the task (verbal reproduction of words) clearly distinguishes it from spatial tasks. These new results show that the effects of prism adaptation are not restricted to visuo-motor tasks but can also affect perception in a non-adapted sensory modality. Prism adaptation is believed to alter the mapping between proprioceptive and visual modalities directly, and both visual and somato-sensory processing are
intrinsically bound to the action system. This is clearly not the case for auditory verbal recognition. There is no obvious functional link between the adaptation of a visuo-manual pointing task to a lateral visual shift and the ability to identify verbal stimuli from the left ear. Therefore the present results demonstrate a striking cross-modal transfer of prismatic after-effects to the auditory domain.

The present auditory effect suggests that the lateralized remapping of visuo-motor information induced by prism adaptation may subsequently alter the orientation of attention in other sensory modalities. Eye movement modulation could be one potential mechanism for such effects. However, it has been shown that the visuo-motor and cognitive effects of prism adaptation can be double-dissociated (Dijkerman et al., 2003; Ferber et al., 2003, but see Serino et al., 2006). Dijkerman et al. (2003) showed that prism adaptation can reduce ocular exploration asymmetry without affecting size under-estimation in a neglect patient. In addition, Ferber et al. (2003) reported on a neglect patient exposed to a prismatic deviation, who exhibited a shift in exploratory eye movements towards the left, but without a concomitant improvement of the deficit in stimulus identification on the left side. So far, no clear link has been demonstrated between modification of oculomotor patterns and clinical effects induced by prism adaptation.

A crucial feature of the present study is that the amelioration found in the ‘Prism’ group was specific to the lateralization index. No significant changes were obtained for the total number of responses. This suggests that prism adaptation did not act through a general arousal enhancement, but rather through a specific lateralized mechanism. However, several lines of argument suggest that the after-effects of prism adaptation produce widespread changes in spatial cognition that are not purely restricted to the lateralized spatial processing deficits observed in unilateral neglect. First, non-visuo-motor, cognitive effects of prism adaptation have been demonstrated in healthy control subjects (Coillet et al., 2000; Michel et al., 2003a, b, 2006; Loftus et al., 2008). Second, beneficial effects of prism adaptation have been reported for non-neglect symptoms and non-neglect patients (Tilikete et al., 2001; Striemer and Danckert, 2007; Sumitani et al., 2007). Tilikete et al. (2001) tested the effect of prism adaptation on postural imbalance in left-hemiparetic patients who did not have neglect at the time of testing. Postural imbalance was reduced following adaptation to the right (but not the left), suggesting a recalibration of the representational distortion in brain-damaged patients. Striemer and Danckert (2007) demonstrated that rightward prism adaptation can reduce both the rightward attentional bias and the disengagement deficit in right brain-damaged patients, irrespective of the presence of neglect. Finally, Sumitani et al. (2007) showed that adaptation to a prismatic displacement of the visual field toward the unaffected side can alleviate pathological pain in patients with complex regional pain syndrome, possibly through an attentional effect. The fact that prism adaptation after-effects generalize across such a wide range of functions suggests that adaptation may modify a common level of spatial representation important for multisensory integration (Rossetti et al., 1998). That adaptation can also improve higher order aspects of spatial cognition (e.g. mental imagery, constructional deficits; Rode et al., 1998), both by reducing lateralized bias and enlarging the represented space, further suggests that prism adaptation might be used to treat not only neglect, but a range of spatial cognition disorders and visuo-spatial dysfunctions (Rode et al., 2006a, 2007). The question arises about the possible neural substrates of this higher order representation. The current model of prism adaptation suggests that prism-induced cerebellar effects interact with contra-lateral posterior parietal cortex (Pisella et al., 2006). The implication of such a lateralized cerebello-cerebral network has been recently confirmed by a neuroimaging study in neglect patients (Luaute et al., 2006b). Interestingly, posterior parietal cortex is not only involved in visual attention and spatial domains, but could also mediate auditory attention (Shomstein and Yantis, 2006).

The present study focused on ameliorating neglect patients’ inability to report contra-lesional stimuli when a concurrent target is presented in ipsilesional space (auditory extinction). However, neglect patients have also been shown to have deficits for single auditory targets in terms of correctly localizing them in space (e.g. Bisiach et al., 1984; Pavani et al., 2001, 2005). Such deficits have been characterized as reflecting increased uncertainty for the spatial location of contra-lesional sounds, rather than mere mislocalization along the horizontal dimension (Pavani et al., 2002). Future studies should examine whether prism adaptation can also improve these neglect-related deficits for sound localization.

**Conclusion**

In this randomized controlled study, a beneficial effect of prism adaptation was observed on auditory extinction in a group of chronic stroke patients. The lateralization index (detection asymmetry on bilateral trials) was the specific variable improved after adaptation. The positive effect was significant immediately after prism adaptation and tended to be maintained over at least 2 h, as has been previously reported for several other tasks (Rossetti et al., 1998; Tilikete et al., 2001; Jacquin-Courtois et al., 2008; review in Rode et al., 2003, 2006a; Luaute et al., 2006a; Pisella et al., 2006). It is interesting, and largely unexpected, that prism adaptation produced such a marked and lasting beneficial effect in the auditory domain, and further indicates the potential value of prism adaptation for the amelioration of a variety of neglect-related deficits (not restricted to the visuo-motor domain). In addition, the beneficial effects of prisms for neglect and neglect-related symptoms appear to last longer than the positive consequences observed after other interventions such as vestibular stimulation or trunk rotation. Clinical efficacy could be further increased by use of repeated prism interventions, which might result in even longer lasting benefits (Shiraiashi et al., 2008; Serino et al., 2009).

The fact that prism adaptation after-effects generalize across tasks of various levels of complexity and/or several sensory modalities implies a restructuring of high-level spatial representations. This conclusion should open a new orientation of rehabilitation strategies and widen the potential scope of application of ‘bottom-up’ therapeutic approaches. Rather than to rehabilitate an injured process directly, prism adaptation suggests that using
plasticity may provide a new processing route for affected sensory information. It may activate brain functions related to multisensory integration necessary for spatial representations and gating the access of sensory information to the higher levels of spatial integration.

Acknowledgements

The authors would like to thank an anonymous referee for raising the issue that the study was not blinded and therefore potential for sources of bias needed to be considered.

Funding

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