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Active Tool Use with the Contralesional Hand Can Reduce Cross-modal Extinction of Touch on that Hand

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Abstract

After a unilateral brain lesion, patients may show cross-modal, visual–tactile extinction. Such patients may fail to report tactile stimuli on the contralesional hand when presented together with competing visual stimuli near the ipsilesional hand. In this work we tested the hypothesis that this cross-modal extinction may be reduced when a patient has used a tool with the contralesional hand to reach for objects in the ipsilesional visual field. Consistent with previous work, we hypothesize that active use of a tool may extend cross-modal interactions between visual stimuli at the tip of the tool and tactile stimuli on the hand wielding the tool. In the new situation of a tool connecting the contralesional hand with ipsilesional visual space, competition between stimuli on these opposite sides may be reduced, so that extinction decreases. We studied patient BV, who showed reliable cross-modal, visual–tactile extinction after right-hemisphere stroke. In two separate sessions we showed that prolonged tool use (10–20 min) with the contralesional hand in ipsilesional space reduced cross-modal extinction for up to 60–90 min post-training. We propose that an actively used tool may be effective in linking cross-modal stimuli presented along its extension. This can then overcome competition between stimuli presented on opposite sides of the body midline, thus modulating extinction.

Introduction

Patients with extinction after unilateral brain injury can typically detect isolated stimuli on the contralesional side, but are unaware of these when presented concurrently with ipsilesional stimuli (Bender, 1945; Driver *et al.*, 1997; Marzi *et al.*, 2001). This can manifest as one among several components of the unilateral neglect syndrome (Bisiach and Vallar, 2000), following cortical and/or subcortical lesions in different areas of the brain (Vallar *et al.*, 1994). The fact that contralesional stimuli only go undetected in the presence of simultaneous ipsilesional stimuli fits well with explanations of extinction in terms of competitive models of spatial attention (Duncan, 1980, 1984; Bundesen, 1990). According to such models, stimuli compete for limited attentional resources. In the presence of unilateral brain damage, an ipsilesional stimulus can then prevail in such competition over a contralesional one.

Although extinction is often studied between stimuli within the same sensory modality, there is an increasing interest in the occurrence of extinction between different sensory modalities, as one window on the nature of multimodal integration in the human brain. Early clinical evidence for cross-modal extinction between touch, vision and audition comes from the seminal work of Bender (e.g. Bender, 1970). While Inhoff and colleagues subsequently failed to elicit cross-modal extinction in patients with unimodal extinction (Inhoff *et al.*, 1992), more recent data show that extinction can be observed cross-modally, between vision and touch (e.g. di Pellegrino *et al.*, 1997; Mattingley *et al.*, 1997) or touch and audition (Làdavas *et al.*, 2001). In particular, a visual stimulus on the ipsilesional side can induce extinction of touch on the contralesional hand, and this is usually much stronger if the competing visual stimulus appears near the ipsilesional hand (di Pellegrino *et al.*, 1997; Làdavas *et al.*, 1998). This evidence has been related to data on multimodal single neurones in the monkey brain. Neurones in pre-motor (Rizzolatti *et al.*, 1981; Gentilucci *et al.*, 1988; Graziano *et al.*, 1994), as well as parietal cortex (Leinonen *et al.*, 1979; Colby *et al.*, 1993; Graziano and Gross, 1995) respond to tactile stimuli as well as visual stimuli presented near the tactile receptive field (within peripersonal space). Importantly, the visual response of such bimodal neurones coding for peripersonal space does not appear to be retinotopic, but remains anchored to the tactile receptive field (Gentilucci *et al.*, 1983; Graziano *et al.*, 1994; Graziano and Gross, 1995; Fogassi *et al.*, 1996) even when that particular body part is moved.

Following such evidence from the monkey brain, it has been suggested that, even in cases with brain damage, visual

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stimuli near a body part on the ipsilesional side may activate some multimodal (visual–tactile) representation of that body part (e.g. the ipsilesional hand). Activating a representation of the ipsilesional hand, in this way, could then compete with activation due to touch on the contralesional hand, resulting in cross-modal extinction. The findings that such cross-modal extinction is particularly pronounced from peripersonal visual stimuli (di Pellegrino *et al.*, 1997) may then suggest that, in humans as well as monkeys, there is an integrated visual–tactile representation of peripersonal space (Làdavas, 2002).

Recently it has been shown (Iriki *et al.*, 1996) that multimodal visual–tactile neurones in the intraparietal sulcus can plastically change their visual response if the animal wields a long tool, with visual stimuli near the end of the tool now activating multimodal neurones that previously responded only to visual stimuli much closer to the hand. It has been proposed (Iriki *et al.*, 1996) that active use of the tool might plastically modulate representations of the so-called 'body schema' (Head and Holmes, 1911), by changing the integration of visual, tactile and proprioceptive information in relation to the effector which wields the tool.

Moreover, in a recent report on the same patient described here (Maravita *et al.*, 2001), as well as in a group study by Farné and Làdavas (2000), it has been shown that when extinction patients use a long tool with the ipsilesional hand to reach for far visual stimuli in ipsilesional visual space, cross-modal extinction of contralesional touch can now be induced by more distant visual stimuli (that fall within the extended reaching space afforded by the tool, but were beyond reach without it).

In this study, we tested, for the first time, whether such tool-induced plasticity can be exploited to ameliorate rather than increase extinction. Specifically, we trained a right-hemisphere patient with cross-modal extinction of touch on the left hand (Maravita *et al.*, 2001) to use a tool with his contralesional hand in order to manipulate visual objects in the ipsilesional hemispace (with the tool thus held in a crossed position). We hypothesized that experience in this active tool use should come to link the left hand and right visual hemispace within a common, integrated visual–tactile space representation. In this way, either stimulus should now activate common multimodal neurones rather than different neural structures that would otherwise compete to produce extinction. If so, extinction of left touch by a right visual event should now be reduced following the training in crossed use of the tool by the left hand.

Methods and results

Patient BV is a 67-year-old right-handed male. After a right cortical occipitotemporal and subcortical parietal stroke (Fig. 1) he presented with left homonymous hemianopia, left hemiparesis (a score of 4 according to the Medical Research Council scale for grading muscle strength) and slight left proprioceptive deficits. He showed residual signs of left unilateral neglect in activities of daily living (e.g. bumping into items on his left side while walking, or ignoring items on the left side of the table when eating), as well as in visual search tasks [three left-sided items undetected in the star cancellation test (Wilson *et al.*, 1987) and seven in the Mesulam random shape cancellation test (Mesulam, 1985)]. BV also showed evident underuse of the non-paretic left arm. On visual field examination, a left homonymous hemianopia was found. Visual extinction, as tested by manual confrontation with single and double stimuli both within the right hemifield, was absent. BV was selected for a detailed study because he showed consistent cross-modal extinction, yet had sufficient strength in his contralesional arm to wield the tool (see below). In order to test formally somatosensory perception as well as perception of cross-modal visual–tactile stimuli, a computerized procedure was adopted. The tactile stimuli were single 85 ms taps delivered via electromagnetic tactors (Trans Dimension International Corporation, Riverside, CA, USA), while the visual stimuli were 85 ms flashes produced by 80 cd/m^2 LEDs. Perception was intact for unilateral stimuli on the right (100% correct) and left (98% correct) hands. On bilateral stimulations, BV showed extinction of left tactile stimuli when presented with concurrent ipsilateral touches (38%) or, critically, with concurrent ipsilateral flashes (41%).

In the experimental sessions (which were performed after BV gave his written, informed consent), we tested extinction for BV by using the same visual and tactile stimuli as those described above. BV held a tool (a rake) with the left hand so as to contact statically the LED, placed in the right hemispace just in front of his right hand (Fig. 2a). Tests were performed before (baseline) and then at four successive points after a training period (1, 30, 60 or 90 min post-training), during which BV had actively used the rake with his contralesional hand, moving it to sort small pieces of cardboard within ipsilesional visual space according to their visible size (Fig. 2b). Two testing sessions were performed on separate days: training in tool use lasted 20 min for the first session and 10 min for the second session.

To rule out any non-specific effects due to prolonged active use of the left hand rather than specific use of the long crossed tool with that hand, in the second session a 20 min period of control training (hand training) was also first implemented. For this, the sorting task was performed directly with the left hand in right space, without using the rake. For each of the above conditions, extinction testing consisted of 32 bilateral cross-modal stimuli (16 double stimulations with right flash plus left touch and 16 triple stimulations with right flash plus right and left touch, which were introduced with the aim of increasing extinction rate still further), and eight each of the following unilateral trials: right touch, left touch, right flash, right touch plus right flash. In every trial, BV was asked to fixate a central cross on the table and to report verbally any stimulation perceived.

The overall response to unilateral trials was good with no trend observed across different sessions for any of the

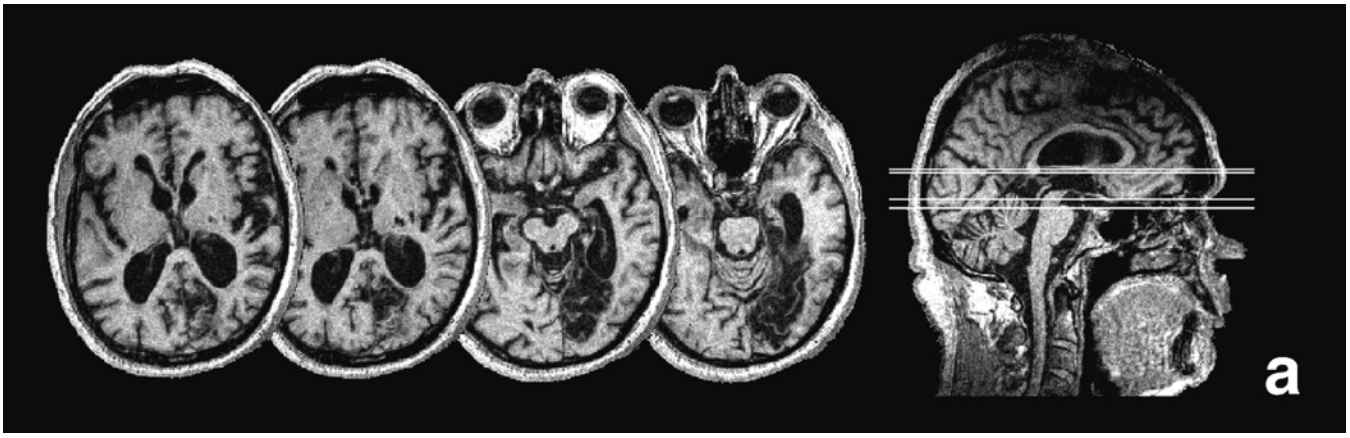

Fig. 1. T1-weighted magnetic resonance images of patient BV's brain lesion, as reconstructed with MRIcro software by Chris Rorden (http://www.psychology.nottingham.ac.uk/staff/cr1/mricro.htm). The damage involves the calcarine area, the cuneus, fusiform, lingual, parahippocampal gyri and the pulvinar, plus parietal white matter in the right hemisphere.

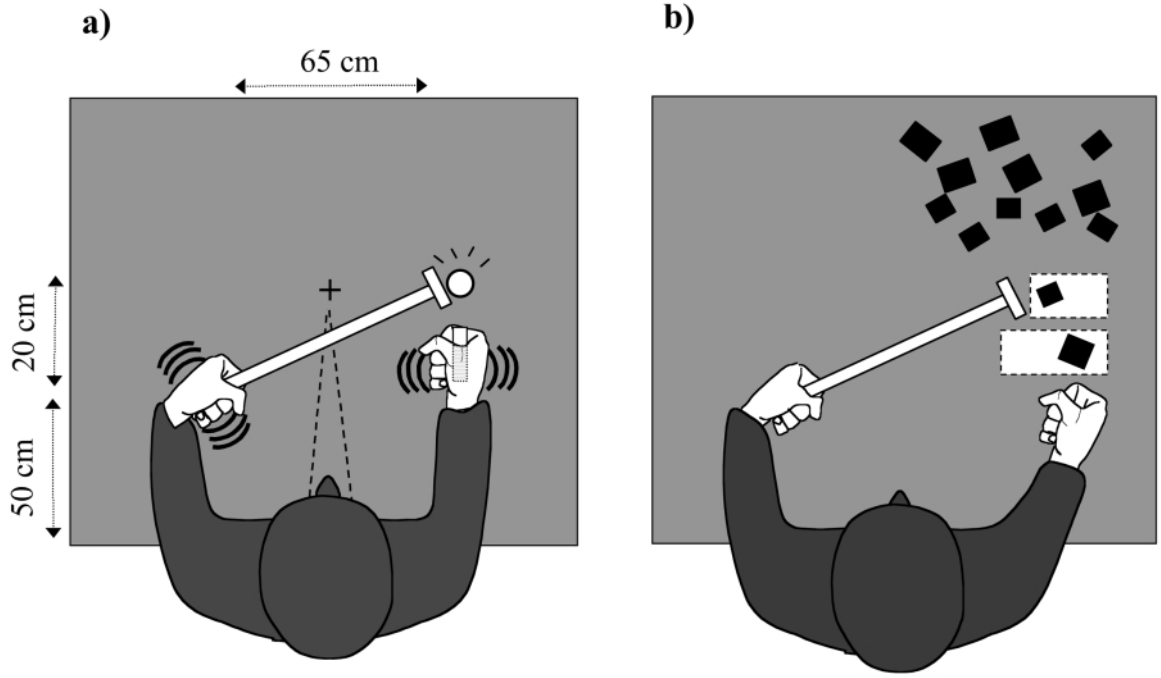

Fig. 2. (a) Experimental set-up. BV rested his hands on the table and fixated (indicated by white dotted lines) a central cross throughout. Tactile stimulators (represented schematically by the dark curves indicating vibration) were placed externally on small plastic tubes (7 cm long, 3 cm wide) held in each hand, taped to ensure stable contact with the palm. The sound emitted by the vibrators was masked with continuous white noise. The 70 cm long rake was joined on to the short tube held in the left hand. A visual stimulator (an LED pair) was placed in front of the right hand (indicated by a white circle). (b) Training procedure. BV was required to sort small pieces of cardboard (represented here by black patches) according to their visible size, dragging them with the rake into either of two size-appropriate areas marked on the table (here represented as white areas on the table surface). This sorting task was performed continuously for 20 min in the first session and for 10 min in the second session.

unilateral conditions. Left touch trials were missed in 6% of such trials; right flash or right flash plus touch trials were missed in 4% each. Right unilateral touches were never missed when presented alone. Figure 3 shows the critical results from trials with bilateral stimulation. An analysis was performed on the number of correct detections on bilateral cross-modal trials (with double and triple stimulations pooled, as they showed a similar pattern). In both sessions, extinction of left touch was significantly reduced after training in active use of the tool by the contralesional hand to manipulate ipsilesional visual objects (first session $\chi^2_{(1)} = 13.7$, $P < 0.01$; second session $\chi^2_{(1)} = 9.5$, $P < 0.05$). This improvement lasted for at least 60 min in the first session (after 20 min of tool use) and for 30 min in the second session (after 10 min of tool use). No improvement was found after the manual training without the long tool (i.e. for hand training), for which performance was identical to the baseline.

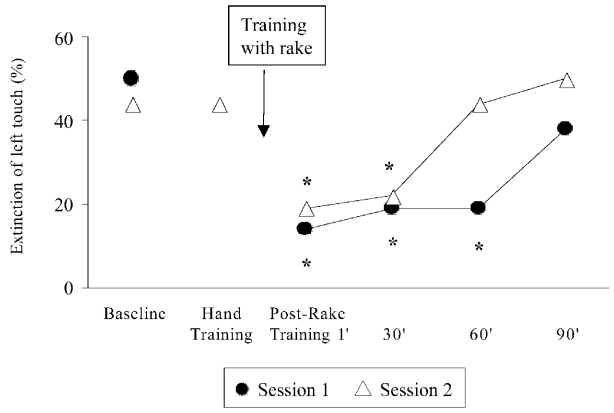

Fig. 3. Extinction results. Percentage extinction of left touches on bilateral cross-modal stimulation (total of 32 such trials per point), for the two sessions. 'Baseline' was before training; also shown are measures at 1, 30, 60 and 90 min post-training. In the second session (dotted line), training in using the left hand to sort directly in right visual hemispace, without the rake, was shown to have no effect on the extinction observed (see 'hand training' data point). Asterisks indicate a significant reduction in extinction, relative to baseline, at $P < 0.01$ by χ^2.

Discussion

These results show that experience in using a long tool with the contralesional hand to touch visual objects in ipsilesional space can beneficially alter the pattern of cross-modal extinction between ipsilesional visual stimuli and contralesional tactile stimuli, reducing such extinction.

We interpret these results in the light of recent data from electrophysiology and neuropsychology.

In monkeys trained to use tools (Ishibashi *et al.*, 2000), cross-modal neurones in the intraparietal sulcus have been shown to extend their visual receptive field into the space reached by the far end of a tool, when this tool is actively wielded by the body part on which the tactile receptive field lies (e.g. the hand) (Iriki *et al.*, 1996, 2001). After training with the tool, the visual response from these neurones was stronger for visual stimuli far from the body, which were previously unable to elicit any response before training. A similar increase in visual response for stimuli at the far end of a wielded tool, and the integration of this with any somatosensory afference received from the tool-wielding effector, could presumably facilitate control of action in their working space.

Previous neuropsychological work has shown that cross-modal extinction of a left contralesional touch by a right ipsilesional visual stimulus can be reduced when a concurrent contralesional visual stimulus is added to the bilateral stimulation, near the contralesional hand (Làdavas *et al.*, 1998). In other words, the congruent activation by vision and touch of a representation of space surrounding the contralesional hand can increase the chances of detecting a touch on that hand, when a competing ipsilesional tactile stimulus is also presented. Here we extend this to show that, when a visual stimulus far from the contralesional hand (indeed, located within the ipsilesional hemifield) becomes linked by the tool to the contralesional hand, then extinction of touch on that hand is analogously reduced. The novelty of this result is that it was obtained by linking the contralesional hand with an ipsilesional visual stimulus, thus showing an influence on the nature of the spatial competition (Duncan, 1980, 1984; Bundesen, 1990) which may lie at the core of the extinction phenomenon.

From a neuronal point of view, our results might potentially relate to the activity of cross-modal neurones whose visual response is typically anchored to a particular point of the skin corresponding to their tactile receptive field (Gentilucci *et al.*, 1983; Graziano *et al.*, 1994; Graziano and Gross, 1995; Fogassi *et al.*, 1996), even when such a body part is moved in visual space. In the present situation, we can speculate that following active use of the rake, analogous neural structures may have enlarged their visual receptive field to include the whole length of the tool (Ishibashi *et al.*, 2000), so that their visual response to stimuli at the tip of the tool can remain strong even when this is displaced into the visual field contralateral to the hand that wields the tool [cf. Maravita *et al.* (2002) for related results in normal human observers]. In principle, a logically similar result might also be obtained by linking the contralesional hand with a concurrent contralesional visual stimulus via an uncrossed tool during bilateral tactile stimulation. This particular situation could not be tested in the present case, due to hemianopia.

Our results corroborate and extend a previous demonstration that active tool use can plastically alter the spatial nature of cross-modal extinction (Farné and Làdavas, 2000). Whereas that study showed that experience in wielding a tool with the ipsilesional hand could increase cross-modal extinction from an ipsilesional visual stimulus, we show conversely for the first time that wielding a tool with the contralesional hand (crossed over into ipsilesional visual space) can instead decrease such extinction, by forging a new link between right visual space and the left hand.

In a previous report on the same patient (Maravita *et al.*, 2001) we observed an increase in cross-modal extinction when holding a long stick in the ipsilesional hand in static contact with a far visual stimulus in ipsilesional space. Interestingly, no specific training in active tool use was required to produce this particular effect [see also Berti and Frassinetti (2000) and Pegna *et al.* (2001) for related observations on line bisection by a tool held in the ipsilesional hand for neglect patients]. This differs from the present study, where statically holding a tool in the contralesional hand that contacted the location of any ipsilesional visual event (see Fig. 1a) was insufficient to modulate extinction, with active tool use being required instead. Indeed, the cross-modal extinction rate when statically holding the stick prior to the training in tool use, did not differ from that found in our initial testing without the stick (see the 41% cross-modal extinction rate described when giving the patient details above). There are several reasons why prolonged experience in active tool use might be required to modulate extinction by a tool held in the contralesional hand but not in the

ipsilesional hand. First, BV has complete left homonymous hemianopia, so that the tool would not be seen resting in the contralesional hand during central fixation (Fig. 2a). Second, he also has slight proprioceptive deficits, together with clinical signs of motor neglect (see Laplane and Degos, 1983) that are specific to his contralesional but not ipsilesional hand. Finally, when held in the contralesional hand, the tool was crossed over into ipsilesional space, whereas in previous studies of tools held in the ipsilesional hand, the tool was uncrossed.

Further studies using modifications of the present paradigm could disentangle the roles played by such potential factors. The effect of a similar procedure on unimodal tactile extinction or even on unilateral spatial neglect could also be tested in future studies. For now, the present data show for the first time that tool-related plastic cross-modal effects can arise laterally and across the midline, rather than only in the radial plane (cf. Berti and Frassinetti, 2000; Farné and Làdavas, 2000; Maravita *et al.*, 2001; Pegna *et al.*, 2001). Moreover, they show that their influence can be beneficial under these circumstances, substantially reducing pathological cross-modal extinction. Finally, our results show that this beneficial influence can be relatively long-lasting. This raises the possibility that such tool use might be of interest for rehabilitation.

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Active tool use with the contralesional hand can reduce cross-modal extinction of touch on that hand

A. Maravita, K. Clarke, M. Husain and **J. Driver**

Abstract

After a unilateral brain lesion, patients may show cross-modal, visual–tactile extinction. Such patients may fail to report tactile stimuli on the contralesional hand when presented together with competing visual stimuli near the ipsilesional hand. In this work we tested the hypothesis that this cross-modal extinction may be reduced when a patient has used a tool with the contralesional hand to reach for objects in the ipsilesional visual field. Consistent with previous work, we hypothesize that active use of a tool may extend cross-modal interactions between visual stimuli at the tip of the tool and tactile stimuli on the hand wielding the tool. In the new situation of a tool connecting the contralesional hand with ipsilesional visual space, competition between stimuli on these opposite sides may be reduced, so that extinction decreases. We studied patient BV, who showed reliable cross-modal, visual–tactile extinction after right-hemisphere stroke. In two separate sessions we showed that prolonged tool use (10–20 min) with the contralesional hand in ipsilesional space reduced cross-modal extinction for up to 60–90 min post-training. We propose that an actively used tool may be effective in linking cross-modal stimuli presented along its extension. This can then overcome competition between stimuli presented on opposite sides of the body midline, thus modulating extinction.

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O275

Primary diagnosis of interest

Cross-modal extinction

Author's designation of case

BV

Key theoretical issue

- Improving cross-modal extinction by linking ipsilesional and contralesional sides via an actively used tool

Key words: extinction; neglect; vision; touch; cross-modal integration; brain lesion; tool use; rehabilitation

Scan, EEG and related measures

Magnetic resonance imaging

Standardized assessment

Cancellation tasks, line bisection

Other assessment

Computerized visual and tactile extinction test

Lesion location

- Right cortical occipitotemporal and subcortical parietal stroke

Lesion type

Ischaemic stroke

Language

English