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# Partial recovery of visual extinction by pavlovian conditioning in a patient with hemispatial neglect

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ARTICLE INFO

*Article history:*
Received 10 July 2012
Reviewed 31 August 2012
Revised 14 September 2012
Accepted 13 November 2012
Action editor H. Branch Coslett
Published online 6 December 2012

*Keywords:*
Emotion
Attention
Neglect
Extinction
Pavlovian conditioning

ABSTRACT

Patients with parietal lesions and unilateral spatial neglect (USN) are unable to detect or respond to information in the contralesional side of space. However, some residual sensory processing may still occur and overcome inattention symptoms when contralesional stimuli are perceptually or biologically salient, as shown for emotional faces or voices. These effects have been attributed to enhanced neural responses of sensory regions to emotional stimuli, presumably driven by feedback signals from limbic regions such as the amygdala. However, because emotional faces and voices also differ from neutral stimuli in terms of physical features, the affective nature of these effects still remains to be confirmed. Here we report data from a right parietal patient in whom left visual extinction was reduced for contralesional visual stimuli following pavlovian aversive conditioning, relative to the same stimulus before conditioning, and relative to similar but non-conditioned stimuli. This reduction of visual extinction was thus mediated by the emotional meaning of stimuli acquired through implicit learning. Functional magnetic resonance imaging also showed that conditioned visual stimuli elicited greater activation in right visual cortex, relative to the non-conditioned stimuli, together with differential activations in amygdala. These results support the hypothesis that emotional appraisal, not only the processing of perceptual features, may partly restore attention to salient information in contralesional space. These findings open new perspectives to improve rehabilitation strategies in neglect, based on affective and motivational signals.



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0010-9452/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.cortex.2012.11.005

## 1. Introduction

Patients with unilateral spatial neglect (USN) are typically unable to detect or respond to stimuli in the contralesional side of space (Vuilleumier, 2007). However, neuropsychological evidence suggests that part of this information may still be processed, even without full awareness, due to a relative sparing of low-level sensory pathways (see Domínguez-Borràs et al., 2012 for a review; Vuilleumier et al., 2002b; Esterman et al., 2002). For instance, detection of contralesional targets is improved when the latter *pop out* due to salient physical features or form structured objects through visual grouping mechanisms (Domínguez-Borràs et al., 2012; Driver and Mattingley, 1998; Lucas and Vuilleumier, 2008; Vuilleumier et al., 2001b; Ward and Goodrich, 1996). Likewise, emotional stimuli such as faces with negative expressions, emotional visual scenes, or affective voice prosody, all tend to elicit less severe neglect and extinction symptoms when presented in the contralesional hemispace, as compared with similar neutral stimuli (Fox, 2002; Grabowska et al., 2011; Lucas and Vuilleumier, 2008; Tamietto et al., 2007; Vuilleumier and Schwartz, 2001; see also Marshall and Halligan, 1988). These emotional effects are paralleled with increased hemodynamic responses to emotional stimuli in sensory (e.g., visual) and limbic brain regions in neglect patients (Vuilleumier et al., 2002a), as observed in healthy subjects (Vuilleumier, 2005). Such increases have been attributed to "top–down" feedback signals from the amygdala (Pourtois et al., in press; Vuilleumier, 2005). However, it remains an open question whether these effects truly result from preserved affective appraisal (i.e., an evaluation of the emotional significance of a stimulus as being "aversive" or "appetitive", see Ellsworth and Scherer, 2003), or rather reflect purely perceptual discrimination responses due to the different physical features inherently associated with emotional stimuli. Both affective and perceptual saliency could be mediated by feature recognition systems in intact sensory areas, which could still act on visual inputs despite ipsilesional biases in spatial attention (see Domínguez-Borràs et al., 2012; Vuilleumier et al., 2002a).

To address this question, we tested whether contralesional visual extinction would be influenced by newly acquired emotional (aversive) meaning, as obtained with a classic pavlovian conditioning paradigm. Aversive conditioning provides a powerful and well-known paradigm that is known to rely on amygdala function (LeDoux, 2000) and to influence subsequent orientation of attention to conditioned stimuli (Armony and Dolan, 2002). A number of studies have shown an impact of affective appraisal on perception and attention through associative conditioning in healthy human volunteers (Gerritsen et al., 2008; Notebaert et al., 2011; Stolarova et al., 2006; Armony and Dolan, 2002). Here we examined a neglect patient who underwent visual extinction testing before and after aversive conditioning, and used functional magnetic resonance imaging (fMRI) to determine the neural impact of this procedure. This allowed us to compare neural responses to visual stimuli that varied in emotional significance but were physically similar.

## 2. Methods

Our patient was a 72-year-old, right-handed male who presented with spatial neglect and chronic visual extinction, but intact bilateral visual fields, following a focal hemorrhagic stroke in the superior right parietal lobe (see Table 1). The patient gave informed written consent to participate and the study was approved by the local ethics committee. At the time of testing, the patient bisected 21/40 lines in Albert cancellation test (Albert, 1973) and 15/30 letters on the Mesulam cancellation test (Weintraub and Mesulam, 1985), omitted numerous left-sided details in drawings, and showed a marked rightward deviation on line bisection (average 5.5 cm from midpoint for 20 cm long lines; Fig. 1A). He presented mild sensory and motor loss in the left hand (for more details on the neuropsychological procedure see Maravita et al., 2007). He also showed tactile and auditory extinction during clinical exam, but these modalities were not examined in this study. Other cognitive and neurological functions were preserved.

The patient underwent a behavioral conditioning experiment in three successive phases, 4 months after stroke onset. First, a baseline test was given to assess visual extinction (PRE-conditioning) with simple visual shapes (red, blue, or green triangles, approximately 5° of visual angle, 200-msec duration). These were presented in either the right visual field (RVF) alone, the left visual field (LVF) alone, or both sides, in pseudo-random order (Fig. 1B). Bilateral trials always included shapes of different colors. The task was to report aloud whether triangles appeared on the right or left side, and whether each was pointing upward or downward. There were 192 trials in total (stimulus-onset asynchrony -SOA- 8 sec). After a 2–3 min rest, a fear-conditioning phase (COND) started, where the same visual stimuli were presented, this time unilaterally (RVF or LVF, 50% each). Critically in this phase, 80% of red triangles were presented with a loud white-noise played binaurally through headphones (with volume rated by the subject as unpleasant but not painful, as in Armony and Dolan, 2002), irrespective of the target side, while the blue and green triangles always appeared with no sound. Thus, the white-noise operated as an unconditioned stimulus (US) and

**Table 1 – Regions affected by the lesion in the patient.**

| |
|---|
| Cortical regions (in decreasing order of importance) |
| Right angular gyrus |
| Right superior parietal lobe |
| Right inferior parietal lobe |
| Right middle temporal |
| Right superior occipital lobe |
| Right precuneus |
| Right cuneus |
| White matter structures |
| Right superior longitudinal fasciculus |
| Right posterior thalamic radiation |
| Right posterior corona radiate |

Patient lesions as identified with standard atlases (AAL, Tzourio-Mazoyer et al., 2002 and JHU-DTI-SS, Oishi et al., 2009).