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The role of prestimulus activity in visual extinction ☆

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ABSTRACT

Patients with visual extinction following right-hemisphere damage sometimes see and sometimes miss stimuli in the left visual field, particularly when stimuli are presented simultaneously to both visual fields. Awareness of left visual field stimuli is associated with increased activity in bilateral parietal and frontal cortex. However, it is unknown why patients see or miss these stimuli. Previous neuroimaging studies in healthy adults show that prestimulus activity biases perceptual decisions, and biases in visual perception can be attributed to fluctuations in prestimulus activity in task relevant brain regions. Here, we used functional MRI to investigate whether prestimulus activity affected perception in the context of visual extinction following stroke. We measured prestimulus activity in stimulus-responsive cortical areas during an extinction paradigm in a patient with unilateral right parietal damage and visual extinction. This allowed us to compare prestimulus activity on physically identical bilateral trials that either did or did not lead to visual extinction. We found significantly increased activity prior to stimulus presentation in two areas that were also activated by visual stimulation: the left calcarine sulcus and right occipital inferior cortex. Using dynamic causal modelling (DCM) we found that both these differences in prestimulus activity and stimulus evoked responses could be explained by enhanced effective connectivity within and between visual areas, prior to stimulus presentation. Thus, we provide evidence for the idea that differences in ongoing neural activity in visually responsive areas prior to stimulus onset affect awareness in visual extinction, and that these differences are mediated by fluctuations in extrinsic and intrinsic connectivity.

1. Introduction

1.1. The phenomenon of visual extinction

Visual extinction is commonly observed after right parietal damage. Patients with visual extinction perceive unilateral stimuli presented either in the left *or* the right visual field, but sometimes miss a stimulus in the left visual field during bilateral simultaneous presentation. Awareness of these left visual field stimuli is effectively "extinguished" by the stimulus in the right visual field. Visual extinction therefore offers a rare opportunity to study the neural correlates of perceptual awareness and unconscious processing.

1.2. How does visual extinction relate to spatial neglect?

The nosology of visual extinction is not clear. It could either represent a component, or mild form, of the classical visuospatial neglect syndrome (Heilman, Watson, & Valenstein, 1994; Rafal, 1994; Vallar, 1993) or a completely different type of visuospatial attention deficit (Umarova et al., 2011). Some data suggest a dissociation between the two syndromes (Hillis et al., 2006; Vallar, Rusconi, Bignamini, Geminiani, & Perani, 1994; Vossel et al., 2011), whereas others emphasise the similarity, especially when the lesions are clustered in the inferior parietal lobule (Posner, Walker, Friedrich, & Rafal, 1984; Rees et al., 2000, Vallar et al., 1994; Vuilleumier & Rafal, 2000). Umarova et al. (2011) compared the activation patterns of acute stroke patients with neglect and visual extinction during visuospatial processing and

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found an increased activation in the left prefrontal cortex only for patients with extinction. These results suggest that visual extinction and neglect are separate syndromes. However, this study used only unilateral stimuli and did not identify the areas involved in the extinction of the left stimulus during bilateral stimulation. Interestingly, the right inferior parietal cortex has been implicated in the simultaneous processing of bilateral targets (in animal studies (Lynch & Mclaren, 1989) and healthy participants (Çiçek, Gitelman, Hurley, Nobre, & Mesulam, 2007).

1.3. Mechanisms of visual extinction

Several previous studies have investigated the neural mechanisms of visual extinction, using bilateral and unilateral stimuli. Essentially, two different approaches have been employed. The first approach investigates residual cortical processing of the extinguished stimulus by comparing responses in bilateral extinguished trials with responses in unilateral right trials; i.e., trials with different physical properties that lead to the same behavioural response. Contrasting these experimental conditions using functional MRI shows that the extinguished stimulus in the left visual field activates early visual cortex, as well as the extrastriate visual cortex in the damaged right hemisphere, e.g. (Driver, Vuilleumier, Eimer, & Rees, 2001; Rees et al., 2000, 2002b; Rees, Kreiman, & Koch, 2002a; Vuilleumier et al., 2002; Vuilleumier et al., 2010). A cross modal study using the same paradigm with tactile information reported activation of primary sensory cortex (S1) in response to extinguished stimuli (Sarri, Kalra, Greenwood, & Driver, 2006). These results provide a potential explanation for the unconscious processing assessed using indirect measures such as priming, e.g. (Baylis, Driver, & Rafal, 1984; Berti, Rizzolatti, & Umana, 1987; Driver et al., 2001; Ladavas, Paladini, & Cubellli, 1993; Vuilleumier et al., 2002, 2010).

The second approach examines the neural correlates of awareness by comparing seen and unseen stimuli during bilateral presentation; i.e., trials with the same physical properties leading to different behavioural responses. Converging evidence from several studies supports the idea that the interplay between posterior visual areas and fronto-parietal circuits is crucial for a visual stimulus to reach awareness, e.g. (Driver et al., 2001; Rees et al., 2002a, 2002b). Thus, it has been suggested that a pathological bias in attention towards the ipsilesional visual field leads to the “extinction” of the contralesional stimulus from awareness during bilateral stimulation. This is in line with the observation that the colour and form of the extinguished stimulus can still be processed to a certain extent. In short, the parietal damage might compromise spatial awareness and responding, rather than disrupting early visual processing.

1.4. Prestimulus activity affects perception

It is well known that ongoing or intrinsic neuronal activity influences subsequent evoked responses. Furthermore, prestimulus activity has been related to systematic variations in behaviour and thus is functionally significant. For example, Fox, Snyder, Vincent, and Raichle (2007) found that 74% of spontaneous trial-to-trial variability in button press force can be accounted for by ongoing fluctuations in the intrinsic activity in somatosensory cortex. Similarly, correlations between ongoing fluctuations of brain activity and perception are observed across different paradigms and different species (Giesbrecht, Jongen, Smulders, & Merckelbach, 2006; Hesselmann, Kell, Eger, and Kleinschmidt, 2008a; Hesselmann, Kell, and Kleinschmidt, 2008b; Ress, Backus, & Heeger, 2000). Fluctuations in prestimulus activity in visual areas measured with EEG and MEG influences the detection of upcoming stimuli (Mathewson, Gratton, Fabiani, & Beck, 2009; Wyart & Tallon-Baudry, 2009). Specifically, alpha activity in somatosensory areas might play a crucial role in optimising neuronal processing, thereby influencing behaviour (Haegens, Händel, & Jensen, 2011). In addition, functional MRI results suggest that the BOLD signal in a cortical area preferentially responding to faces is higher preceding experimental trials that are perceived as faces compared to vases using an ambiguous figure (Hesselmann et al., 2008a). In motion coherence tasks, BOLD signals in motion-responsive brain areas are higher before trials that are perceived as showing coherent compared to random motion (Hesselmann et al., 2008b). Finally, a recent functional MRI study extended the investigation of fluctuations in ongoing brain activity to the domain of cognitive control: prestimulus activity in several task relevant regions – including higher cognitive areas – scales with the size of the Stroop effect (Coste, Sadaghiani, Friston, & Kleinschmidt, 2011). In sum, there is strong evidence that endogenous variations in prestimulus neuronal activity bias subsequent perceptual decisions.

1.5. Can we analyse visual extinction using prestimulus activity?

Here, we set out to answer the question *how* it is possible that patients with visual extinction sometimes see and sometimes miss the left stimulus during bilateral stimulation. Our strategy was to compare prestimulus BOLD signals before bilateral visual stimulus presentation depending on whether the trial was subsequently categorised as a “bilateral seen” or as a “bilateral unseen” trial; in other words, whether the patient failed to detect the stimulus in the left visual field. We focused on visually response areas and used a simple detection paradigm with bilateral and unilateral face stimuli. First, we identified visually responsive areas in a patient showing visual extinction. Second, we compared prestimulus activity in these regions during bilateral stimulation with and without extinction. Finally, we used dynamic causal modelling (DCM) (Friston, Harrison, & Penny, 2003) to examine whether changes in the coupling or excitability of these regions could explain both prestimulus activity and subsequent differences in stimulus bound responses. Specifically, we investigated whether extinction might be mediated by a difference in intrinsic (within area), or extrinsic (between areas), effective connectivity, i.e. the causal influences that neural units exert over one another (Friston, 1994), or sensitivity to neuronal afferents. DCM is the method of choice for our question because it tests hypotheses or models that are cast in terms of directed connections among neuronal populations. This contrasts with less informed approaches – such as functional connectivity – that simply measure (undirected) correlations between haemodynamic responses at different points in the brain.

2. Material and methods

2.1. Participant

One male patient (IPJ) aged 66 with left visual extinction (following a right parietal stroke, see Fig. 2) gave informed consent to participate in the study. The participant showed left visuospatial neglect on four standard clinical measures – see Section 2.2.1. Functional imaging was conducted 3 years and 4 months post-stroke. IPJ was suited for in-depth study as he had a structurally intact visual cortex in the right hemisphere, despite suffering from enduring visual extinction on clinical confrontation and formal computerised testing. However, he showed lower left quadrant visual field impairment. Therefore, all experimental stimuli were presented in the upper visual quadrants.

2.2. Design and procedure

The experiment was approved by the local ethics committee.

2.2.1. Neuropsychological testing

Prior to functional imaging, IPJ was tested for clinical signs of visual extinction by confrontation. In addition, he was presented with bilateral, unilateral left and