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Common and distinct neural mechanisms of visual and tactile extinction: A large scale VBM study in sub-acute stroke

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ABSTRACT

Extinction is diagnosed when patients respond to a single contralesional item but fail to detect this item when an ipsilesional item is present concurrently. Extinction has been studied mainly in the visual modality but it occurs also in other sensory modalities (touch, audition) and hence can be considered a multisensory phenomenon. The functional and neuroanatomical relations between extinction in different modalities are poorly understood. Here, we used voxel-based mophometry (VBM) to examine the neuronal substrates of visual versus tactile extinction in a large group of sub-acute patients ($n = 454$) with strokes affecting different vascular territories. We found that extinction deficits in tactile and visual modalities were significantly correlated ($r = 0.341$; $p < 0.01$). Several lesions within the right hemisphere were linked to extinction including the inferior parietal lobule, the superior parietal lobule, the middle frontal and occipital gyri, while lesions involving the superior temporal gyrus, inferior temporal gyrus and putamen were associated with tactile extinction. Damage within the middle temporal gyrus and superior temporal sulcus was linked to both deficits. We conclude that extinction in different modalities emerges after damage to both common (supra-modal) and distinct (modality specific) brain regions, and that contrasting sites emerge after damage to different vascular territories. We discuss the implications for understanding extinction as a multisensory disorder.

1. Introduction

Extinction is a common cognitive disorder following unilateral brain damage, diagnosed when patients who can respond to a single contralesional item fail to detect this item when an ipsilesional item is present concurrently (Bender and Teuber, 1946; Wortis et al., 1948; Critchley, 1953). It can be considered to be a disorder of attention characterized by a striking bias for the ipsilesional stimulus at the expense of a contralesional item, due to the brain lesion unbalancing the competition for selection from the stimuli on each side of space (Duncan et al., 1997; Driver and Vuilleumier, 2001). Similarly to other spatial attention disorders such as unilateral neglect, extinction has been mainly reported following right hemisphere strokes and is usually thought to be asymmetrically associated with the damage within the right hemisphere (e.g., Becker and Karnath, 2007; Stone et al., 1993; though see Ogden, 1985, for an opposite finding). The higher incidence of both extinction and neglect after damage to the right hemisphere suggests that the right hemisphere is dominant for the distribution of attention within extrapersonal space (Kinsbourne, 1977, 1987; Weintraub and Mesulam, 1988).

Extinction has been studied most extensively in the visual modality but it occurs also in other sensory modalities (touch, audition, and olfaction) and hence can be considered a multisensory phenomenon (e.g. Bellas et al., 1988a,b; De Renzi et al., 1984; Deouell and Soroker, 2000; Hillis et al., 2006; Ladavas et al., 2001; Maravita et al., 2000; Vaishnavi et al., 2001). Not surprisingly extinction has been also reported cross-modally, for example between vision and touch (e.g., Maravita et al., 2000; Sarri et al., 2006). Taking these different aspects together, the syndrome provides a unique opportunity to study the neural substrates of multisensory perception and spatial awareness. However, the functional and neuroanatomical relations between extinction in different modalities are poorly understood. It may be hypothesized that extinction emerges in different modalities after damage to both common (attention specific) and distinct (modality specific) brain regions, each of which may be modulated by competition between stimuli for selection (see Duncan et al.,

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1997). The overlapping spatial deficits across modalities could represent a number of factors. For example it could mean that: i) space is represented at the multi-modal level (see Driver and Spence, 1998a,b), ii) that there is a generalized cross-hemisphere competition and mutual inhibition (see Kinsbourne, 1977; Vallar et al., 1994) and/or iii) an important role of a central system that selects for subsequent action between contra- and ipsilateral stimuli irrespective of their original modality (see Bickerton et al., 2011; Chechlacz et al., in press). These hypotheses are not mutually exclusive. To date there have been relatively few studies that have attempted to systematically assess the neuroanatomical basis of extinction within and across modalities (though see Chechlacz et al., in press; Hillis et al., 2006; Vallar et al., 1994) and thus there is a lack of understanding about which neural regions support modality-specific and which modality-general cognitive processes. Furthermore, there are some discrepancies across the reported results. In cases of tactile extinction, for example, deficits have been linked to damage to posterior frontal cortex and the middle temporal gyrus (Kaplan et al., 1995), to the inferior parietal cortex (Hillis et al., 2006) and the post-central gyrus and putamen (Chechlacz et al., in press). Visual extinction has been linked to visual association cortex (BA19, Hillis et al., 2006), the angular gyrus (Vossel et al., 2011), the temporo-parietal junction (TPJ; Karnath et al., 2003; Ticini et al., 2010), and to the superior temporal sulcus, middle occipital gyrus and insula (Chechlacz et al., in press). Cross-modal deficits have been associated with damage to the inferior parietal cortex (Hillis et al., 2006; Kaplan et al., 1995) and the temporo-parietal junction (TPJ; Chechlacz et al., in press).

Some of the above discrepancies may arise because (i) relatively small numbers of patients have been studied (e.g., Kaplan et al., 1995; Ticini et al., 2010), (ii) some studies have assessed patients at an acute stage (e.g., Hillis et al., 2006) while others have tested chronic patients (e.g., Chechlacz et al., in press), (iii) some studies have used all-or-none (e.g., Karnath et al., 2003; Ticini et al., 2010) and others continuous measures of extinction (e.g., Chechlacz et al., in press; Vossel et al., 2011), and (iv) some studies fail to control for the neglect symptoms that frequently coincide with extinction (e.g., Hillis et al., 2006). An additional important factor contributing to these inconsistencies may be the difference in the general vascular territories affected by the stroke in the patients examined, as this determines the location of the lesion. This highlights a weakness of uni-mass voxel-based approaches, which assume a one-to-one mapping between function and lesion tested through correlations. A problem is that, if there is only a relatively small number of one type of patients in the sample (e.g., in a stroke sample patients with lesions around the posterior cerebral artery [PCA] will typically be lower in number than patients with a lesion in the territory of the middle cerebral artery [MCA]), then an overall VBM analysis will typically fail to reliably detect an association. Strikingly, Mort et al. (2003) reported differences in the critical lesions associated with neglect following MCA and PCA strokes (linked respectively to the inferior parietal lobe and the parahippocampal region), but this has not been attempted yet in patients with extinction (Mort et al., 2003). By separating out patients with damage to different stroke territories, we may gain a finer-grained analysis of lesion-symptom mapping. To address these points the current study examined extinction symptoms in an unselected group of patients with damage affecting different vascular territories. We first report results across the overall sample to give a general overview of lesion-symptom relations before examining variations in the relations according to the stroke territory.

The neuronal substrates of visual and tactile extinction were assessed on the data from a large group of sub-acute stroke patients (n = 454). Our analysis concentrated on the effects of grey matter lesions, which provided a clear delineation of the relations between extinction in the two modalities. We acknowledge, however, that visuospatial deficits may also arise as a consequence of white matter disconnections (Bartolomeo et al., 2007; Chechlacz et al., 2010, in press; Doricchi and Tomaiuolo, 2003; He et al., 2007; Karnath et al., 2009; Thiebaut de Schotten et al., 2008). Interestingly our previous work using MRI data has demonstrated that white matter disconnections arising from damage along the superior longitudinal fasciculus were associated with both visual and tactile extinction, while the cortical substrates varied with the stimulus modality (Chechlacz et al., in press). This last conclusion was tested further here.

To assess visual and tactile extinction we used matched procedures, minimizing the chances that non-specific task effects confounded the results. As the data were collected as a part of a large clinical trial, we used a relatively simple measure of extinction (with a relatively low number of event repetitions) and we assessed brain integrity from CT scans routinely used in clinical practice. In a previous analysis of visual neglect we have shown that VBM analyses of CT scans, based on large patient numbers, can yield highly reliable and interpretable results replicating previous findings observed using MRI scans (Chechlacz et al., 2012). We employed here whole brain statistical analyses using voxel-based morphometry (VBM; Ashburner and Friston, 2000) to evaluate common structure–function relationships. The analyses treated the behavioural measurements as continuous variables rather than as categorical scores, which increases both the ability to tease apart the neural substrates of extinction in different modalities (visual vs. tactile) and the overall sensitivity for detecting brain–behaviour associations. All analyses controlled for potential confounding factors including the aetiology (the type of stroke: ischaemia or haemorrhage), lesion size, age, gender, handedness, time from stroke to scan, patient overall orientation, anosognosia and presence of neglect symptoms. The analyses included the entire patient sample independently of lesion location or specific symptoms, thus providing an internal control for non-specific stroke effects and non-specific attentional deficits, not linked to extinction. This also enabled us to avoid biasing the results based on a-priori neuroanatomical or behavioural assumptions and therefore enabling us to generalize the observed findings to the entire sampled population. Finally, we evaluated how the lesion-symptom mapping may vary depending on the vascular territory affected by the stroke.

Our results highlight both common (attention specific) and distinct (modality specific) neural mechanisms of extinction and are discussed in relation to the organization of brain networks for spatial attention.

2. Methods

2.1. Participants

All patients were recruited as part of a large clinical study, the BUCS project (Birmingham University Cognitive Screen, http://www.bucs.bham.ac.uk), drawn from participating stroke units across the West Midlands of the United Kingdom. We used visual inspection of individual scans, blind to the category of patients, to exclude data from patients who either had enlarged ventricles or poor quality CT scans, to prevent artifacts in the neuroimaging analyses. A total of 454 sub-acute stroke patients (240 males and 214 females; average age of 69.9 years, range 30 to 93 years; see Table 1 for full demographic and clinical data) were included. Within this group 215 patients had middle cerebral artery (MCA) stroke and 47 posterior cerebral artery (PCA) stroke. The remaining 192 patients had other types of strokes including the anterior cerebral artery (ACA) area, basal ganglia and thalamus (LSA and AChA territories strokes) as well as the cerebellum. The study included both patients who suffered ischaemic stroke (417 patients) and haemorrhagic stroke (37 patients). Behavioural data were only collected from patients who were physically stable, willing to perform the task and had a concentration span of at least 60 min (judged clinically). Clinical and demographic data were obtained from the patients' clinical files. All participants provided written informed consent in agreement with ethics protocols approved by the National NHS ethic committee and local NHS trusts.