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Research report

Prism adaptation enhances activity of intact fronto-parietal areas in both hemispheres in neglect patients

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ABSTRACT

Unilateral spatial neglect involves a failure to report or orient to stimuli in the contralesional (left) space due to right brain damage, with severe handicap in everyday activities and poor rehabilitation outcome. Because behavioral studies suggest that prism adaptation may reduce spatial neglect, we investigated the neural mechanisms underlying prism effects on visuo-spatial processing in neglect patients. We used functional magnetic resonance imaging (fMRI) to examine the effect of (right-deviating) prisms on seven patients with left neglect, by comparing brain activity while they performed three different spatial tasks on the same visual stimuli (bisection, search, and memory), before and after a single prism-adaptation session. Following prism adaptation, fMRI data showed increased activation in bilateral parietal, frontal, and occipital cortex during bisection and visual search, but not during the memory task. These increases were associated with significant behavioral improvement in the same two tasks. Changes in neural activity and behavior were seen only after prism adaptation, but not attributable to mere task repetition. These results show for the first time the neural substrates underlying the therapeutic benefits of prism adaptation, and demonstrate that visuo-motor adaptation induced by prism exposure can restore activation in bilateral brain networks controlling spatial attention and awareness. This bilateral recruitment of fronto-parietal networks may counteract the pathological biases produced by unilateral right hemisphere damage, consistent with recent proposals that neglect may reflect lateralized deficits induced by bilateral hemispheric dysfunction.

1. Introduction

Unilateral spatial neglect is a frequent disorder after right brain lesion, resulting in a failure to report or orient to stimuli in the contralesional (left) space (Heilman and Valenstein, 1979), with severe handicap in everyday activities and poor rehabilitation outcome. Both behavioral and anatomical studies have indicated that neglect is produced by lesions

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affecting fronto-parietal networks involved in spatial attention and spatial cognition (Corbetta et al., 2005; Thiebaut de Schotten et al., 2005; Verdon et al., 2010), which can in turn lead to secondary functional abnormalities in structurally intact brain areas including visual cortices (Corbetta et al., 2005; Rees et al., 2000; Vuilleumier et al., 2001). Many therapeutic approaches have been proposed to treat this disorder (e.g., visual scanning training, limb activation, eye-patching, etc.), but improvements are generally modest and limited to the trained situations (Luauté et al., 2006a).

A pioneer study by Rossetti et al. (1998) was the first to suggest that prism adaptation can produce long-lasting and widespread effects on spatial neglect. This approach was motivated by classic findings that, in healthy people, repetitive pointing to visual targets seen with optical prisms (shifting the perceived target locations) does not only bias pointing in the opposite direction following prism removal (so-called after-effect), but also shifts the subjective body midline in this direction. Furthermore, neglect patients typically show a rightward bias when asked to point straight-ahead (Heilman et al., 1983; Saj and Vuilleumier, 2007), although this deviation is not found in all cases (Bartolomeo and Chokron, 1999; Chokron and Bartolomeo, 1997; Farnè et al., 1998) or sometimes even occurs in the opposite (leftward) direction (Honoré et al., 2009). Motivated by these findings, Rossetti et al. (1998) exposed neglect patients to right-deviating prisms to induce a subsequent visuo-motor deviation toward their pathological left-side. Following prism adaptation, patients showed greater accuracy for body-midline judgments and reduced neglect symptoms in several clinical tests (including line bisection, drawing, reading, and search). In the past 12 years, these results have been extended by many studies examining various behavioral measures of neglect or daily situations such as wheelchair navigation (Fortis et al., 2010; Luauté et al., 2006a). These beneficial effects may last 2 h up to 1 week after a single session of prism adaptation, and even up to 6 weeks following repetitive adaptation (Luauté et al., 2006a; Rossetti et al., 1998). The generalization and persistence of these effects make prism adaptation a treatment of choice, but the underlying neural mechanisms still remain to be established.

Neuroimaging studies of prism adaptation in healthy volunteers have implicated a distributed network including posterior parietal, temporal, and cerebellar regions (Clower et al., 1996; Danckert et al., 2008; Luauté et al., 2006b, 2009), but some of these regions and their connections are frequently damaged in neglect patients (Doricchi et al., 2008; He et al., 2007; Verdon et al., 2010). Similarly, a positron emission tomography (PET) study in five neglect patients after prism adaptation showed increased perfusion in the right cerebellum, as well as temporo-occipital and subcortical areas of the left (intact) hemisphere (Luauté et al., 2006b), but it remains unclear whether such changes differ from non-specific learning effect, and how they relate to dysfunction within the fronto-parietal networks mediating spatial attention. In addition, only a few functional magnetic resonance imaging (fMRI) studies (Corbetta et al., 2005; Thimm et al., 2008) have investigated changes in brain activity correlating with spontaneous recovery of neglect after stroke. Their results suggest initial increases in intact left parietal areas followed by restoration of right-side activity after recovery, consistent with a functional imbalance between the two hemispheres that may underlie abnormal spatial biases in the patients (Corbetta et al., 2008; Kinsbourne, 1970; Vuilleumier et al., 1996). However, these studies also revealed significant changes in both hemispheres which may reflect a more global compensatory reorganization (Corbetta et al., 2005; Vuilleumier et al., 2001). Other fMRI studies in neglect patients have observed functional changes in intact sensory areas subsequent to parietal damage, which could underlie perceptual impairments of the patients in visual (Vuilleumier et al., 2001, 2008) or tactile tasks (Maravita et al., 2003; Valenza et al., 2001).

Here we used fMRI to study the effects of prism adaptation on cortical brain activity in patients with unilateral spatial neglect. Our aim was to clarify the neural substrates underlying behavioral improvements induced by this technique, and determine how prism-induced changes would generalize across different visuo-spatial tasks that are frequently impaired in these patients. As this study is the first attempt to address this issue, we selected a group of rare patients who (i) were able to participate to three scanning sessions in the same day, (ii) showed consistent signs of neglect on repeated testing, and (iii) had relatively small, focal damage in the right hemisphere allowing us to obtain reliable fMRI data from spared regions and perform efficient whole-brain group analysis.

2. Methods

2.1. Patients

Seven patients [mean age = 68, standard deviation (SD) = 15; min–max = 45–84 years] were recruited consecutively among stroke patients admitted to the Neurology Department, with a first right-hemisphere stroke (haemorrhagic or ischemic). All lesions were confirmed by MRI or CT scan (Fig. 1). Neglect and other neuropsychological deficits were assessed using a standard battery of clinical tests (Azouvi et al., 2002). The presence and severity of spatial neglect (Table 1) were determined by failures on three sensitive tests, namely, Bell Cancellation (Gauthier et al., 1989), Figure Copy (Gainotti et al., 1972), and Line Bisection (Schenkenberg et al., 1980). All patients were also examined using a routine battery of standardized clinical tests, including mini-mental state examination, to exclude dementia and any other major cognitive disorder that would impact on task performance and collaboration. Because participation in the fMRI study required normal vigilance and ability to cooperate, we excluded patients with large hemispheric stroke (affecting more than two lobes) and/or reduced alertness. Selecting patients with well-circumscribed lesions also ensured sufficient overlap of spared brain regions for subsequent group-based statistics of fMRI data. The scanning took place on average 19 days post-stroke onset (SD = 9; min–max: 10–32), when neglect symptoms were still present, as confirmed by testing on the same day prior to scanning.

To identify brain networks normally recruited in these tasks, a group of 26 healthy participants (29.6 + 3.44-year-old, range 25–39; 11 women and 18 men) also underwent fMRI without prism adaptation (three sessions). These controls