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Research report

Functional reorganization of the attentional networks in low-grade glioma patients: A longitudinal study

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ABSTRACT

Right brain damage often provokes deficits of visuospatial attention. Although the spatial attention networks have been widely investigated in stroke patients as well as in the healthy brain, little is known about the impact of slow growing lesions in the right hemisphere. We here present a longitudinal study of 20 patients who have been undergoing awake brain surgery with per-operative line bisection testing. Our aim was to investigate the impact of tumour presence and of tumour resection on the functional (re) organization of the attention networks. We assessed patients' performance on lateralized target detection, visual exploration and line bisection before surgery, and in the acute and post-acute operative phases after surgery. Clear evidence for transient neglect signs was observed in the acute post-operative phase, although full recovery had invariably occurred in all patients. The resection of the right angular gyrus was associated with transient neglect-like symptoms in all tasks, whereas resection of more anterior regions correlated with transient deficits only in visual exploration or detection (but not in line bisection). The attentional networks showed substantial functional recovery. This impressive pattern of

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recovery is discussed in terms of involvement of the contralateral left hemisphere and of preservation of long-range white matter pathways within the right hemisphere.

1. Introduction

Visuospatial attention allows us to efficiently interact with objects in the environment by selecting important items on the basis of their perceptual salience as well as on our goals. Anatomically, visuospatial attention relies on two large fronto-parietal networks (Bartolomeo, Thiebaut de Schotten, & Chica, 2012; Corbetta & Shulman, 2002, 2011), linked by three branches of the superior longitudinal fasciculus (SLF) (Thiebaut de Schotten et al., 2011). A dorsal attentional network includes the intraparietal sulcus/superior parietal lobule and the frontal eye field/dorsolateral prefrontal cortex (Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Hopfinger, Buonocore, & Mangun, 2000; Kastner, Pinsk, De Weerd, Desimone, & Ungerleider, 1999). Evidence from neuroimaging studies in healthy subjects indicates that the dorsal network is recruited for control of the spatial orienting of attention (Corbetta & Shulman, 2002; Macaluso, Frith, & Driver, 2002; Sereno, Pitzalis, & Martinez, 2001; Silver, Ress, & Heeger, 2005). An additional more ventral attentional network which includes the temporo-parietal junction and the ventral frontal cortex (inferior and middle frontal gyri), and is lateralized to the right hemisphere (Corbetta & Shulman, 2002), seems to be crucial for several non-lateralized attentional functions, such as visual and temporal capacity (Husain & Rorden, 2003; Peers, Ludwig, Rorden, Cusack, & Bonfiglioli, et al., 2005; Shapiro, Hillstrom, & Husain, 2002), arousal and vigilance (Coull, Frackowiak, & Frith, 1998; Pardo, Fox, & Raichle, 1991; Rueckert & Grafman, 1996; Wilkins, Shallice, & McCarthy, 1987), saliency detection (Downar, Crawley, Mikulis, & Davis, 2000; Serences, Yantis, Culberson, & Awh, 2004; Shulman et al., 2010), and the reorienting of attention (Arrington, Carr, Mayer, & Rao, 2000; Corbetta et al., 2000; He et al., 2007; Macaluso et al., 2002; Rengachary, He, Shulman, & Corbetta, 2011); it may also be important in the case of late consequences of exogenous orienting of attention, such as inhibition of return (Chica, Bartolomeo, & Valero-Cabré, 2011).

Patients with damage to right-sided attentional networks often suffer from a disabling condition known as left visual neglect. They behave as if the left part of the world no longer existed, and have poor functional outcome (Denes, Semenza, Stoppa, & Lis, 1982). Although neglect often spontaneously improves with time, residual signs of spatial bias, such as slowed response times (RTs) to left-sided targets (Bartolomeo, 1997), may persist and put the patient at risk in rapidly changing situations (e.g., during driving).

The localisation in the right hemisphere of lesions producing neglect is currently debated. Most lesion overlapping studies in patients with vascular strokes indicate the inferior parietal lobule to be a crucial cortical site of lesion (Mort et al., 2003; Vallar & Perani, 1986), while others negate the role of parietal lesions and stress the importance of damage to the temporal lobe (Karnath, Ferber, & Himmelbach, 2001). Further lesion overlapping studies suggest an important role for white matter damage along the course of the SLF (Leibovitch et al., 1998), in a likely disconnection of frontal and parietal regions (Doricchi & Tomaiuolo, 2003). Additional evidence from stroke patients also confirmed the role of SLF disconnection in the most severe forms of neglect assessed by several tests (Verdon, Schwartz, Lovblad, Hauert, & Vuilleumier, 2010), to be found also in a patient with an ischemic infarct limited to the white matter (Ciaraffa, Castelli, Parati, Bartolomeo, & Bizzi, 2013). A further study identified disconnection of the intermediate branch of the SLF as a reliable anatomical predictor of persistent neglect in stroke patients (Thiebaut de Schotten et al., 2012).

The study of low-grade glioma patients has confirmed the importance of SLF disconnection in neglect. Intra-operative stimulation directly demonstrated the occurrence of temporary signs of visual neglect (rightwards shifts on line bisection) upon transitory inactivation of the intermediate branch of the SLF (Thiebaut de Schotten et al., 2005), which connects the caudal node of the ventral attentional network to the rostral node of the dorsal network (Thiebaut de Schotten et al., 2011). This result led to the proposal of intra-operative assessment of line bisection as a tool to prevent post-operative neglect in low-grade glioma patients (Bartolomeo, Thiebaut de Schotten, & Doricchi, 2007). These findings were subsequently confirmed (Vallar et al., 2013), although with some inter-subject variability (Roux et al., 2011). Moreover post-operative assessment in two low-grade glioma patients supports the importance of SLF damage in neglect, by uncovering new or worsened signs of left neglect after surgical section of the SLF (Shinoura et al., 2009). Thus, rather than resulting from focal cortical damage, signs of neglect seem to depend on a dysfunction of large-scale fronto-parietal networks in the right hemisphere (Bartolomeo, 2006; Bartolomeo et al., 2007; Corbetta & Shulman, 2011; Bartolomeo et al., 2012). In agreement with this idea, Shallice and collaborators recently published a study in which they tested the sensitivity of parieto-occipitally loaded tests (optic ataxia; fragmented letters and cube analysis; star cancellation) in a large sample of brain tumour patients harbouring either a high or low grade glioma in the left or right hemisphere. Regardless of tumour localization within the right hemisphere, low grade glioma patients showed a deterioration in visual exploration (e.g., Star cancellation task) after operation, thus supporting the involvement of right-sided fronto-parietal networks in neglect (Bartolomeo, 2006; Bartolomeo et al., 2007; Corbetta & Shulman, 2011; Bartolomeo et al., 2012). Nevertheless, the role of tumour localization on the type of deficits is challenged