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Research report

Blindsight in children with congenital and acquired cerebral lesions

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ABSTRACT

It has been shown that unconscious visual function can survive lesions to optical radiations and/or primary visual cortex (V1), a phenomenon termed "blindsight". Studies on animal models (cat and monkey) show that the age when the lesion occurs determines the extent of residual visual capacities. Much less is known about the functional and underlying neuronal repercussions of early cortical damage in humans. We measured sensitivity to several visual tasks in four children with congenital unilateral brain lesions that severely affected optic radiations, and in another group of three children with similar lesions, acquired in childhood. In two of the congenital patients, we measured blood oxygenation level dependent (BOLD) activity in response to stimulation of each visual field quadrants. Results show clear evidence of residual unconscious processing of position, orientation and motion of visual stimuli displayed in the scotoma of congenitally lesioned children, but not in the children with acquired lesions. The calcarine cortical BOLD responses were abnormally elicited by stimulation of the ipsilateral visual field and in the scotoma region, demonstrating a profound neuronal reorganization. In conclusion, our data suggest that congenital lesions can trigger massive reorganization of the visual system to alleviate functional effects of early brain insults.

1. Introduction

Although the primary visual cortex (V1) is a fundamental stage for visual information processing, subjects with lesions of V1 often have substantially spared visual function (Poppel et al., 1973; Weiskrantz et al., 1974; Barbur et al., 1980; Stoerig and Cowey, 1997; Radoeva et al., 2008). Consistent with a key role of V1 in visual awareness, residual vision for these patients is associated with a lack of consciousness, a condition termed *blindsight* (Weiskrantz et al., 1974). Subjects with blindsight are able to direct their eyes toward visual stimuli presented within the scotoma (Poppel et al., 1973;

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Weiskrantz et al., 1974), to point toward it (Danckert et al., 2003) and in many cases to discriminate the orientation (Morland et al., 1996), the direction of motion (Barbur et al., 1980), the spatial distribution (Sanders et al., 1974) and the wavelength (for a review see: Stoerig and Cowey, 1997) of the stimuli. In the literature a distinction has been drawn between blindsight without visual awareness (Type I) and blindsight associated with awareness of the presence of the stimulus, without perceiving it (Type II) (Weiskrantz, 1997; Sahraie et al., 2010). However, the behavioral discriminations with forced-choice testing are similar for the two types of blindsight (Sahraie et al., 2010). Although many functional aspects of blindsight have been extensively studied, the neural correlates underlying this phenomenon are as yet poorly understood (Cowey, 2010). Some evidence points to major anatomical and functional reorganization of neuronal circuitry. In a recent study on subject GY, an hemianopic subject whose right V1 is lesioned, Bridge et al. (2008) show abnormal contralateral connections between the right lateral geniculate nucleus (LGN) and the left MT+/V5, as well as cortical connections between the two MT+/V5 areas that are absent on controls. Both these aberrant connections bypass calcarine cortex. Abnormal contralateral projections from superior colliculus (SC) to associative, parietal and primary visual areas have also been observed (Leh et al., 2006). Taken together, these data indicate that SC and LGN may have a key role in the reorganization of neuronal structures subserving blindsight (Tomaiuolo et al., 1997; Leh et al., 2010; Tamietto et al., 2010) supporting earlier evidence from monkey and cat lesion studies (Payne et al., 1996; Sorenson and Rodman, 1999; Lyon et al., 2010; Das et al., 2012). However, a contribution associated with a plastic reorganization of primary visual cortical circuitries cannot be excluded. A recent study showed that the spared V1 can respond to ipsilateral stimuli in the hemianopic visual field, but only after prolonged visual training (Henriksson et al., 2007) that also restores perceptual awareness.

Both in cat and monkey, early cortical lesions yield more extensive residual capabilities than those occurring in adulthood, including near-normal shape discrimination (Cornwell et al., 1989; Cornwell and Payne, 1989), motion discrimination (Moore et al., 2001) and visual orienting oculomotor behaviors (Moore et al., 1996). Interestingly, one of the factors that makes blindsight more likely is the age at lesion (Ptito and Leh, 2007) and blindsight subjects who acquired the damage during childhood (e.g., the extensively studied subject GY by the age of 8) are those that show a more profound neural reorganization (Leh et al., 2006; Bridge et al., 2008). A study on a large group of subjects with occipital lesions acquired between late teens and around 30 years reported a solid correlation between age at lesion and the probability that the scotoma shrinks during the years following brain injury (Teuber, 1975). Similarly, recovery of visual capabilities was greater in patients who underwent hemispherectomy at the age of 7, compared with cases where the surgery occurred later in life (Perenin, 1978; Perenin and Jeannerod, 1978). Of particular interest are the clinical cases in which brain lesions occur very early, around birth, when the visual system is highly plastic and susceptible to massive neurophysiological reorganization and capable of compensating for functions normally attributed to the damaged structures (Kiper et al., 2002; Knyazeva et al., 2002). Werth (2006) reported the case of a child who underwent hemispherectomy at 4 months of age, but later developed a normal visual field comparable to age-matched controls. Recently, Muckli et al. (2009) reported V1 blood oxygenation level dependent (BOLD) activation with a retinotopic map to ipsilateral stimuli in a patient born with only one hemisphere.

In this study we measured residual perceptual capacities in children with homonymous hemianopia caused by unilateral lesions involving the posterior cortico-subcortical visual pathways caused by medial cerebral artery stroke occurring around the time of birth, which usually affects the optic tract or optic radiations (Jacobson et al., 2010). We compared hemianopic patients with congenital optic radiation lesions with those who acquired similar lesions during childhood to reveal the functional and anatomical reorganization potential of the human visual system in response to an early (perinatal) brain lesion.

2. Subjects and methods

2.1. *Clinical description*

This study was conducted under ethical approval from the Stella Maris Scientific Institute Ethics Committee. Subjects and parents gave informed consent in accordance with the Declaration of Helsinki. Subjects belonged to two different groups: "congenital" and "acquired" brain lesions children. All subjects in the first group had experienced neonatal arterial infarction around term whilst children of the second group suffered similar arterial damages from vascular insult occurring later in childhood (see Table 1). Brain lesions of all subjects were documented by MRI-scans. For all subjects vascular trauma resulted in complete or severe unilateral damage of optic radiation (see Figs. 1 and 6 for anatomical MRI of S2) that in turn causes a scotoma in the hemifield contralateral to the lesion. The visual field of each patient was assessed by means of an automated perimetry system (KOWA AP 340: similar to the Humphrey perimeter). Each eye was tested at full strength and full field (237 points), monitoring fixation. No subject showed peripheral or refractive errors, except for a mild (.5 diopter) astigmatism in S4. All have a normal intelligence quotient as measured by Wechsler scales. They all have a motor disability classified as hemiplegia (Hagberg et al., 1975) due to the brain lesion. Age at testing ranged from 11 to 17 years. Table 1 reports a detailed clinical history of each subject.

Subjects with congenital lesions all have very extensive unilateral damage to the left or the right temporal–parietal cortex, extending to occipital and frontal cortex. Importantly, all had damage to the optic radiations, but only S2 (see also Fig. 6) had a lesion of the calcarine cortex in the affected hemisphere. All subjects have major visual field defects contralateral to the side of the brain lesion, and S2 showed a complete hemianopia in the right hemifield with no central sparing.

The acquired lesion group comprised two children who had experienced a rupture of a cerebral artery between