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Research report

Supramodal agnosia for oblique mirror orientation in patients with periventricular leukomalacia

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ABSTRACT

Periventricular leukomalacia (PVL) is characterized by focal necrosis at the level of the periventricular white matter, often observed in preterm infants. PVL is frequently associated with motor impairment and with visual deficits affecting primary stages of visual processes as well as higher visual cognitive abilities. Here we describe six PVL subjects, with normal verbal IQ, showing orientation perception deficits in both the haptic and visual domains. Subjects were asked to compare the orientation of two stimuli presented simultaneously or sequentially, using both a two alternative forced choice (2AFC) orientation-discrimination and a matching procedure. Visual stimuli were oriented gratings or bars or collinear short lines embedded within a random pattern. Haptic stimuli comprised two rotatable wooden sticks. PVL patients performed at chance in discriminating the oblique orientation, both for visual and haptic stimuli. Moreover when asked to reproduce the oblique orientation, they often oriented the stimulus along the symmetric mirror orientation. The deficit generalized to stimuli varying in many low level features, was invariant for spatiotopic object orientation, and also occurred for sequential presentations. The deficit was specific to oblique orientations, and not for horizontal or vertical stimuli. These findings show that PVL can affect a specific network involved with the supramodal perception of mirror symmetry orientation.

1. Introduction

It is well established that the visual processes mediating object recognition can be dissociated from those implicated in object orientation perception. According to the dual visual pathway theory, the ventral cortical areas are involved in object recognition independently from orientation, while the perception of object position in the space and in relation to the observer's viewpoint are mediated by the dorsal stream to support action guidance (Goodale 2011, 2014; Goodale & Milner, 1992; Milner and Goodale 1993, 2008; Mishkin & Ungerleider, 1982; Mishkin et al., 1983; Ungerleider &

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Mishkin, 1982, pp. 549–586; Whitwell, Milner, & Goodale, 2014).

The description of orientation agnosia, the inability to perceive object orientation in space despite preserved object recognition supports this theory (Turnbull, Beschin & Della Sala, 1995; Turnbull, Beschin & Della Sala, 1997, Cooper & Humphreys, 2000, Karnath, Ferber, & Bulthoff, 2000, Harris et al., 2001, McCloskey, 2004, Riddoch et al., 2004, Fujinaga, Muramatsu, Ogano, & Kato, 2005, Robinson, Cohen, & Goebel, 2011). Some rare patients with lesions along the dorsal pathway selectively incurred in symmetry confusion, exhibiting mirror writing and reading or orientation agnosia for symmetric stimuli (Buxbaum, Coslett, Schall, McNally, & Goldberg, 1993; Davidoff & Warrington, 1999; Davidoff & Warrington, 2001; Harris et al., 2001; Lambon-ralph, Jarvis, & Ellis, 1997; Martinaud et al., 2014; Priftis, Rusconi, Umilta, & Zorzi, 2003; Riddoch & Humphrey, 1988; Rodriguez, Aguilar, & Gonzalez, 1989; Schott, 2007; Turnbull and McCarthy 1996; Valtonen, Dilks, & McCloskey, 2008; Vinckier et al., 2006).

The deficit selectivity of these rare patients suggests that mirror orientations are analyzed by at least partially independent networks with respect to the other orientations. Indeed a recent voxel-based lesion-symptom mapping on a cohort of patients suffering from stroke reported only partial overlap of the lesioned sites along the dorsal pathway in patients with orientation agnosia or agnosia for mirror stimuli (Martinaud et al., 2016).

Imaging studies on healthy volunteer have identified an extensive cortical network underlying symmetry and orientation perception. Interestingly this system is activated also by multisensory visuo-tactile signals (Bauer et al., 2015; Bona, Herbert, Toneatto, Silvanto, & Cattaneo, 2014; Kohler, Clarke, Yakovleva, Liu, & Norcia, 2016; Sasaki, Vanduffel, Knutsen, Tyler, & Tootell, 2005; Sathian & Zangaladze, 2002; Sathian, Zangaladze, Hoffman, & Grafton, 1997; Tyler et al., 2005). Similar bilateral occipito-parietal activation during visual and tactile orientation judgments as well as during symmetry perception suggests the existence of amodal neural substrates for these tasks.

That mirror images are somewhat special with respect to the other orientations is also suggested by developmental studies. Habituation paradigms showed that four-month old infants confuse mirror symmetric stimuli, despite can discriminate oblique orientations (Bornstein, Gross, & Wolf, 1978). Symmetric oblique orientations in particular seem to pose the biggest challenge. Gregory & McCloskey (2011) analyzed the frequency of errors made during forced choice tasks in 4–5 years old children. Children were able to choose the correct orientation in 63% of the trials for the oblique orientation and 74% for the cardinals, when there was no memory load. The error-distribution analysis showed that children often confused mirror stimuli around the object principal axis of elongation (OPA, i.e., with respect to the object) and around the extrinsic vertical axis (EVA, i.e., with respect to the vertical external axis), performing left-right reflection. Correct categorization of left-right oblique orientations mature by the age of 6 years in normal children, while 90° errors are rare for cardinal orientations since very early in life (Palomares, Landau, & Egeth, 2009). These results suggest that an important difference should be made between perception of diagonal and cardinal orientations, the former being much more difficult to categorize than the latter for healthy children. At adult age almost no left-right errors are made, although decisions can still take longer for mirror symmetry (Gregory & McCloskey, 2010; Sekuler & Houlihan, 1968). This late development is probably linked to the written language and reading acquisition, known to refine human ability to distinguish between left-right mirror images (Kolinsky et al., 2011; Pegado and Comerlato, 2014; Pegado, Comerlato, Ventura, Jobert, Nakamura & Buiatti, M, 2014; Pegado, Nakamura & Hannagan, 2014). Q3

Mirror visual symmetry deficit is rarely observed in developmental disorders, with the exception of Williams syndrome. These children fail to report correctly mirror symmetry images particularly for the left-right reversal, suggesting that mirror symmetry visual perception is mediated by dorsal pathways that is strongly affected in this pathology (Atkinson & Braddick, 2011; Atkinson et al., 2003).

In the present experiment we describe a group of six subjects with periventricular leukomalacia (PVL) with supramodal agnosia for oblique mirror orientations, providing evidence that perception of oblique object orientations is dissociated from cardinal orientation and that the underlying network is shared between different modalities.

PVL refers to lesions to the cerebral white matter, usually occurring between the 24th and 36th week of gestational age (Volpe, 2009). Depending on the size and location of the PVL necrosis, a wide spectrum of clinical symptoms can be observed, from severe visual impairment, combined with cerebral palsy and mental retardation to mild visuo-motor impairments and normal intelligence (for a review see: Jacobson & Dutton, 2000). Previous studies have described visual-perceptual impairment in these subjects, such as restriction of visual field, deficit in crowding, visual integration (identification of whole figures from incomplete visual information), object recognition and motion perception (Cioni et al., 1997; Fazzi et al., 2004; Guzzetta et al., 2009; Jacobson, Ek, Fernell, Flodmark, & Broberger, 1996; Morrone et al., 2008; Stiers, De Cock, & Vandenbussche, 1998). Here we show that few of these children can also have mirror orientation agnosia that can greatly impact on their everyday life. The deficit can create difficulties in a wide range of contexts: from simple games with dolls (that were often dressed the other way around) to more complex learning activities at school, such as drawing and understanding the properties of geometrical shapes.

2. Methods

2.1. Subjects

Sixty patients with a neuroradiological diagnosis of PVL that referred to the Stella Maris Scientific Institute in Pisa were evaluated with a symmetry test assessing pictures orientation discrimination (see below). Six patients (four females and two males, aged between 12 and 23 years old) demonstrated a specific difficulty in discriminating between mirror images and were included in the present study. Three younger or age matched subjects with no neurological disorder were also

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