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Functional organisation of visual pathways in a patient with no optic chiasm

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ABSTRACT

Congenital achiasma offers a rare opportunity to study reorganization and inter-hemispheric communication in the face of anomalous inputs to striate cortex. We report neuroimaging studies of a patient with seesaw nystagmus, achiasma, and full visual fields. The subject underwent structural magnetic resonance imaging (MRI), diffusion tensor imaging (DTI) studies, and functional MRI (fMRI) using monocular stimulation with checkerboards, motion, objects and faces, as well as retinotopic quadrantic mapping. Structural MRI confirmed the absence of an optic chiasm, which was corroborated by DTI tractography. Lack of a functioning decussation was confirmed by fMRI that showed activation of only ipsilateral medial occipital cortex by monocular stimulation. The corpus callosum was normal in size and anterior and posterior commissures were identifiable. In terms of the hierarchy of visual areas, V5 was the lowest level region to be activated binocularly, as were regions in the fusiform gyri responding to faces and objects. The retinotopic organization of striate cortex was studied with quadrantic stimulation. This showed that, in support of recent findings, rather than projecting to an ectopic location contiguous with the normal retinotopic map of the ipsilateral temporal hemi-retina, the nasal hemi-retina's representation overlapped that of the temporal hemi-retina. These findings show that congenital achiasma can be an isolated midline crossing defect, that information transfer does not occur in early occipital cortex but at intermediate and higher levels of the visual hierarchy, and that the functional reorganisation of striate cortex in this condition is consistent with normal axon guidance by a chemoaffinity gradient.

1. Introduction

Congenital absence of the optic chiasm (achiasma; (Apkarian, Bour, & Barth, 1994) is a rare syndrome. While achiasma can be associated with vertebral, cardiac, renal, and limb defects in the VACTERL syndrome (Prakash, Dumoulin, Fischbein, Wandell, & Liao, 2010), in most cases it is an apparently isolated finding (Korff et al., 2003). In Belgian sheepdogs, a canine model of achiasma, the defect is inherited in autosomal recessive fashion (Dell'Osso, Williams, Jacobs, & Erchul, 1998; Williams & Garraghty, 1994). Achiasma is often suspected by the presence of congenital seesaw nystagmus (Apkarian & Bour, 2001; Korff et al., 2003; Prakash et al., 2010).

While patients with acquired lesions of the optic chiasm have bitemporal hemianopia (Adler, Austin, & Grant, 1948), subjects with achiasma have full visual fields. Rather, both the right and left visual hemifields of one eye project to the striate cortex ipsilateral to that eye (Apkarian, 1996). Because of this, the disorder has sometimes also been called the 'non-decussating retinal-fugal fibre syndrome' (Apkarian & Bour, 2001; Apkarian, Bour, Barth, Wenniger-Prick, & Verbeeten, 1995). Thus achiasma presents a counterpart to the situation in albinism, in which there is an excessive decussation of fibres at the optic chiasm (Apkarian, 1996).

Visual evoked potentials have previously been used to confirm the functional consequences of failure of decussation: that is, monocular input to ipsilateral striate cortex (Apkarian et al., 1994, 1995; Hertle et al., 2002; Jansonius, Van Der Vliet, Cornelissen, Pott, & Kooijman, 2001; Korff et al., 2003; Prakash et al., 2010). The absence of the optic chiasm can also be clearly shown on high-resolution structural MRI (Apkarian et al., 1995; Korff et al., 2003). In some patients, damage to the optic chiasm can result in the nasal optic nerves being no longer able to project information to visual cortex, resulting in bitemporal hemianopia (see for example, (Hassan, Crompton, & Sandhu, 2002). However, patients with achiasma have completely intact visual fields, suggesting a rerouting of information. Three studies have also used functional MRI (fMRI) to show that striate cortex receives

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inputs from the ipsilateral eye only (Hoffmann et al., 2012; Prakash et al., 2010; Victor et al., 2000).

A number of important questions remain about the nature and implications of congenital achiasma. First, is achiasma an isolated problem of decussation or it is accompanied by other midline crossing problems? In animals, some knockout models result in not only achiasma but also anomalies of the anterior commissures and corpus callosum (Bertuzzi, Hindges, Mui, O'Leary, & Lemke, 1999). Establishing whether or not similar anomalies are seen in humans with congenital achiasma may help narrow down the possible origins of this syndrome.

Second, how does the striate cortex of an achiasmatic subject represent a full 360° of direction (polar angle)? Typical striate cortex has a retinotopic map of 180° of vision, in which there is an orderly dorso-ventral progression of the polar angle of the visual field, from the horizontal meridian in the calcarine fissure to the upper vertical meridian on the lower bank and the lower vertical meridian on the upper bank. If this orderly progression merely continues in this fashion in the achiasmatic subject, then one would predict a map in which the lower temporal hemifield is represented dorsal to the lower nasal hemifield, and the upper temporal hemifield ventral to the upper nasal hemifield. Such a map could result from a development of retinotopy in which axon guidance is governed mainly by adhesion molecules that bind axons that receive input from adjacent areas of the visual map (Huberman, Feller, & Chapman, 2008). A second possibility is that the temporal and nasal hemifield maps overlap, so that locations that are mirror-symmetric across the vertical meridian occupy the same position. In this map the aberrant projections from the ipsilateral nasal hemiretina would simply take up the positions that would have been occupied by the contralateral eye's nasal hemiretina. Such a map would result if axon guidance during retinotopic map formation is based on chemoaffinity mechanisms involving molecular gradients (McLaughlin & O'Leary, 2005). Indeed, such an overlapping map might be expected, given findings that the lateral geniculate nucleus of achiasmatic Belgian sheepdogs shows overlapping representations of mirror-symmetric locations in the nasal and temporal hemifields (Williams & Garraghty, 1994). In albinism, an excessive decussation at the chiasm results in regions of the temporal hemiretina projecting to contralateral rather than ipsilateral striate cortex. Previous studies have suggested different possible retinotopic outcomes in which either the anomalous visual input of the nasal hemi-retina has an ectopic cortical representation contiguous with the normal retinotopic map of the temporal hemi-retina (the 'Boston' Siamese cat; (Hubel & Wiesel, 1971), the input from the temporal hemi-retinal map is suppressed (the 'Midwestern' Siamese cat; (Kaas & Guillery, 1973), or the nasal and temporal hemi-retinal maps are superimposed (the 'true albino pattern' observed in monkeys; (Guillery et al., 1984). Previous fMRI studies have shown the latter outcome in human achiasmatic individuals, in which left and right hemifields show overlapping representations in visual cortex (Hoffmann et al., 2012; Victor et al., 2000). However, given the differences observed in animals, one question is whether similar differences in outcomes may also exist in humans with congenital achiasma.

Finally, if striate cortex is monocular innervated, at what point does callosal transfer occur so that visual information from both eyes is represented, to allow the possibility of binocular inputs and/or interactions? In healthy subjects, in whom striate cortex represents the contralateral hemifield of both eyes, callosal transfer serves a different purpose, to provide input from not only the contralateral but also the ipsilateral hemifield. Neurophysiologic studies of monkeys show that receptive fields of neurons overlap the ipsilateral field in middle temporal areas, with progressively larger receptive fields that span both hemifields as one moves higher in the hierarchy (Raiguel et al., 1997); however, the earliest level in the visual system in which this occurs remains unclear. In humans, fMRI studies of retinotopy suggest that ipsilateral hemifield responses may occur earliest in intermediate levels of visual cortex, such as the V5 complex (Tootell, Mendola, Hadjikhani, Liu, & Dale, 1998). If callosal projections between visual areas are similar in patients with congenital achiasma, this suggests that binocular innervation in these subjects would be expected at the level of intermediate visual cortex.

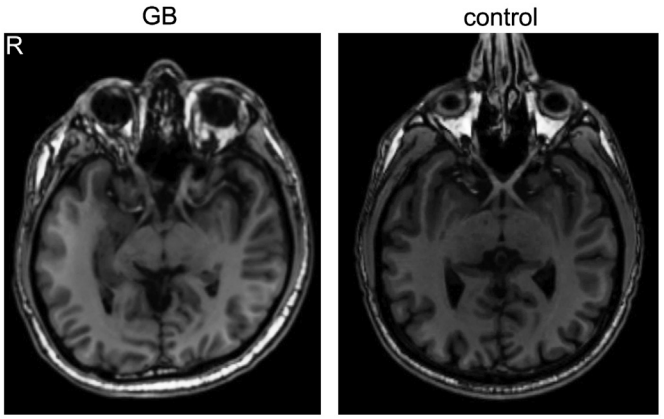

Fig. 1. Structural T1-weighted MRI scan shows the optic chiasm in a control subject but not in GB.

In this report, we describe neuroimaging studies with structural MRI, DTI, and functional MRI of a patient with congenital achiasma (non-decussating retinal-fugal fibre syndrome) that were aimed at determining: (1) whether achiasma is an isolated problem of decussation or if it is accompanied by other midline crossing problems; (2) how the striate cortex of an achiasmatic subject represents a full visual field; and (3) at what point in the visual system callosal transfer occurs.

2. Material and methods

2.1. Case description

GB is a 28-year-old right-handed man with nystagmus first noted by his mother a few weeks after birth. He had had strabismus surgery at ages 2 and 5 years. He denied oscillopsia. He has been otherwise healthy, He has one sister, but there is no family history of visual or neurological problems. His best-corrected Snellen visual acuity is 20/70 in the right eye and 20/80 in the left eye. He scored normally on pseudo-isochromatic plates for colour vision, and Goldmann perimetry showed full visual fields in both eyes. Fundoscopy showed normal optic discs. In primary position he had an exotropia with a small right hypertropia. He had a complex congenital nystagmus, with left-beating horizontal nystagmus in primary and left gaze, reversing to right-beating in right gaze, upon which there was superimposed a pendular seesaw component, most prominent in down-gaze (a video of the patients' eye-movements is available here: http://www.neuroophthalmology.ca/cases/case94/case94.html). His neurological exam was otherwise normal, without macular hypoplasia, and without mirror movements or limb anomalies. T1 structural scans suggested absence of the optic chiasm (Fig. 1).

2.2. Subjects

GB participated in all studies below. One 27-year-old right-handed male control subject had similar structural, functional, and DTI scans. In addition to the control subject, T1 anatomical scans of 9 other subjects (3 males, mean age=26, range=20–29 years), who took part in a separate study, were included in the structural analysis, one of whom also took part in the DTI analysis (27-year-old male). All subjects were right-handed, with corrected visual acuity of 20/20, and were healthy with no history of neurological dysfunction, vascular disease or cognitive complaints. The protocol was approved by the institutional review boards of the University of British Columbia and Vancouver General Hospital, and written informed consent was obtained for all subjects in accordance with The Code of Ethics of the World Medical Association, Declaration of Helsinki.