

## Clinical study

# Reorganisation of the visual cortex in callosal agenesis and colpocephaly

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**Summary** Structural defects involving eloquent regions of the cerebral cortex may be accompanied by abnormal localisation of function. Using functional magnetic resonance imaging (fMRI), we studied the organisation of the visual cortex in a patient with callosal agenesis and colpocephaly, whose visual acuity and binocular visual fields were normal. The stimulus used was a moving grating confined to one hemifield, on a background of moving dots. In addition to activation patterns elicited by stimulation of each hemifield in the patient, the activation pattern was compared to that seen in six normal volunteers. fMRI demonstrated large scale reorganisation of visual cortical areas in the left hemisphere, and fewer activation foci were observed in both occipital lobes when compared with normal subjects. © 2000 Harcourt Publishers Ltd

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## INTRODUCTION

An exciting application of non-invasive functional brain mapping techniques such as functional magnetic resonance imaging (fMRI) is the study of cortical sensory and motor reorganisation following central nervous system insults and developmental abnormalities. Studies in immature humans and animals have demonstrated that when the brain undergoes abnormal development or sustains widespread damage, the individual retains the capacity to demonstrate substantial function normally subserved by the damaged or abnormal cortex, often with only subtle discernible deficit.<sup>1,2</sup> Previous investigations of patients with callosal agenesis and colpocephaly (congenital dilatation of the occipital horns of the lateral ventricles) have demonstrated abnormalities in the structure of the cerebral cortex, particularly in the occipital region.<sup>3,4</sup> These abnormalities include a radial disposition of sulci and gyri on the medial hemispheric surface, and the failure of the calcarine and parieto-occipital sulci to intersect. Despite these findings, conventional neuro-ophthalmological examination in humans with callosal agenesis usually shows relatively normal visual abilities. This evidence of normal function in the presence of abnormal structure led us to examine the visual functional organisation in a human with this condition.

## SUBJECTS AND METHODS

### Subjects

The patient was a 16-year-old female with a 5 year history of predominantly nocturnal seizures, consisting of clonic movements of the left arm, leg and face. These seizures occurred approximately once per week and were refractory to anti-epileptic medications. She was the product of an uncomplicated pregnancy, was born at term by spontaneous vaginal delivery, and achieved her development milestones normally. Neurological examination was unremarkable; EEG

showed interictal slow wave activity throughout the right hemisphere and seizures with onset in the right temporo-frontal region. Ictal Tc99m HMPAO single photon emission computed tomography (SPECT) revealed a diffuse increase in perfusion within the right cerebral hemisphere. Neuropsychological evaluation demonstrated a low average intelligence (full scale IQ 84); fine motor coordination which was slightly impaired in the right hand and significantly impaired in the left, and mild impairment on tasks of visuo-spatial organisation. Testing of memory functions yielded adequate scores for the recall of verbal and simple visuospatial material. MRI showed complete callosal agenesis and colpocephaly. The enlargement of the posterior lateral ventricles was greater on the left than on the right, and there was thinning of the overlying occipital cortical mantle. Neuro-ophthalmological examination confirmed normal funduscopy, extraocular movements, visual acuity and full visual fields on Goldmann perimetry. In order to compare the pattern of visual cortical activation with that in normal individuals, we studied six volunteers (four female, two male; age range 19–44 years) with no known medical, neurological or ophthalmological abnormalities.

### Functional magnetic resonance imaging (fMRI)

Blood oxygen level-dependent (BOLD) fMRI was used to examine the pattern of activation in each occipital lobe upon stimulation of the contralateral visual hemifield. Multislice T2\*-weighted gradient recalled echo (GRE) echo-planar imaging (EPI) images (TR/TE=4 s/45 ms, flip angle 90°) were acquired with a Siemens Magnetom Vision 1.5T MRI scanner (Iselin, NJ, USA) in planes through the occipital cortex, parallel to the calcarine sulcus (10–12 contiguous 6 mm slices). These studies were conducted with the subjects laying on their back with a circularly polarised receive-only surface coil centred over the occipital poles. The visual stimulus was projected onto a rear-projection viewing screen placed at the end of the bore of the magnet, and the projection screen was viewed by means of a mirror mounted above the eyes at an angle of approximately 45°. Head position was fixed by a foam headrest and a combination of immobilising hearing protectors and a bar pressing on the bridge of the nose. The visual stimulus was generated on a MacIntosh Powerbook 160 using a modified program from the Vision Shell (Quebec, Canada). The baseline condition comprised viewing randomly moving dots

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(1 Hz; 128 luminance grey levels). The activation condition consisted of a black and white semicircular ring (inner radius 8°, outer radius 11°) with two embedded gratings (each 1.5°) moving vertically in opposite directions (8 Hz), presented unilaterally on the background of randomly moving dots. The purpose of the background of random dots was to minimise light diffusion into the surrounding visual field. During the activation and baseline conditions, the subject fixated on a small black circle in the centre of the screen.

### Anatomical MRI scanning

T1-weighted anatomical MRI images were acquired with the surface-coil in place, prior to the commencement of the functional scans. This utilised a three-dimensional GRE sequence (TR=18 ms; TE=10 ms; flip angle 30°) and yielded approximately 80 256 × 256 sagittal images. In all subjects, T1-weighted (TR=18 ms; TE=10 ms; flip angle 30°) global MRI images were acquired with a circularly polarised transmit-and-receive head-coil, also using a three-dimensional GRE sequence, yielding approximately 170 256 × 256 sagittal images comprising 1 mm<sup>3</sup> voxels. All studies were performed with the informed consent of the subjects and were approved by the Montreal Neurological Institute Research Ethics Committee.

### Image analysis

The images were analysed on SGI workstations using purpose-built software developed in the Neuroimaging Laboratory at the Montreal Neurological Institute. The anatomical MRI scans were corrected for intensity non-uniformity and mapped into the common standard (stereotactic) space of Talairach and Tournoux.<sup>5,6</sup> The surface-coil anatomical scans were aligned with the head-coil anatomical scans using an automated script combining correction for the intensity gradient and intra-subject registration.<sup>6</sup> The functional data were blurred with a 6 mm full-width-at-half-maximum Gaussian filter and analysed using a Spearman rank order statistical test. An activation minus baseline subtraction was performed, and the acquired *t*-statistic map transformed into the stereotactic coordinate space of Talairach and Tournoux<sup>5</sup> by combining the transformation files from the previous two image registration steps. *t*-values corresponding to *P*-values smaller than 0.05 were considered significant. For the controls, individual activation patterns were examined, and the results for all subjects were averaged for group analysis.

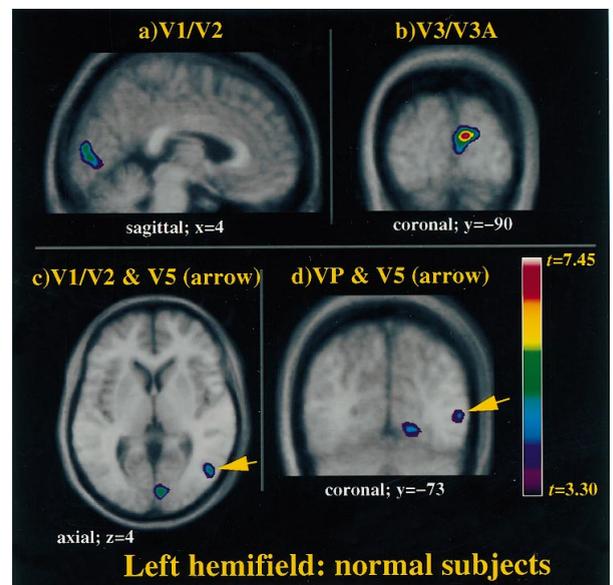
## RESULTS

### Controls

As expected, activation patterns were symmetrical and consistent across subjects, with statistically significant ( $P < 0.05$ ) activation in the contralateral areas V1/V2, V3/V3A, VP, and V5. Specifically, after the results of right hemifield activation were averaged, significant activation foci ( $P < 0.01$ ) were observed in V1/V2 (calcarine sulcus; Talairach coordinates -10, -86, 4.6), V3/V3A (occipital pole; -17, -93, 22), VP (lingual gyrus; -15, -77, -2.9), and V5 (parieto-temporo-occipital junction; -50, -72, 7.5). The statistically significant activation was produced in homologous regions of the right occipital lobe with left hemifield stimulation (Fig. 1). In all studies activation was observed exclusively in the cerebral hemisphere contralateral to the stimulated visual field.

### Case study

The corpus callosum in J R the patient was absent, and the sulci on the medial hemispheric surfaces were arranged in a radial pattern.



**Fig. 1** *t*-statistic maps of the average activation pattern following left hemifield stimulation in six normal volunteers.

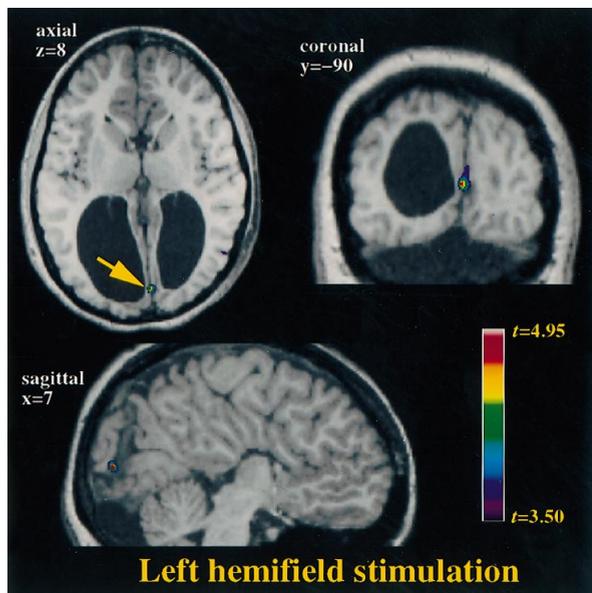
The calcarine fissure was not identified with certainty on the left, and failed to intersect with the parieto-occipital sulcus on the right. In contrast to activated regions seen in control subjects, strikingly asymmetrical activation resulted from stimulation of the two hemifields in the patient. From left hemifield stimulation statistically significant activation was observed in the right calcarine sulcus (V1/V2;  $t=4.95$ ;  $P < 0.05$ ; Talairach coordinates -7, -90, 8) (Fig. 2). A distinct peak was also observed at the right temporo-occipital junction, although this did not reach statistical significance (V5;  $t=4.12$ ; 55, -64, 9). In contrast, right hemifield stimulation produced statistically significant activation peaks in what appears to be a dorsally displaced calcarine sulcus (V1/V2;  $t=7.73$ ;  $P < 0.01$ ; 1, -96, 27) and the lingual gyrus (VP;  $t=6.76$ ;  $P < 0.01$ ; -7, -83, -12) (Fig. 3).

## DISCUSSION

Abnormal organisation of the occipital cortex is evident in this 16-year-old with colpocephaly and callosal agenesis. As the patient exhibited no apparent visual deficits, this represents an anatomical reorganisation in which the functionality of the visual cortex is preserved. Evidence of plasticity within the visual system has been furnished by studies in both animals and humans. Visual field reversal in normal monkeys results in large scale reorganisation,<sup>7</sup> and cross-modal plasticity in blind humans (activation of visual cortex by tactile stimulation) has also been documented.<sup>8</sup>

The stimulus used in this study was a moving stimulus confined to one hemifield. Previous positron emission tomography<sup>9</sup> and fMRI<sup>10</sup> studies in humans have demonstrated the presence of a cortical region (V5) specialised for the processing of visual motor information. Other areas, most recently V3A,<sup>11</sup> have been implicated in the processing of visual motion. The locations and borders of these areas (V1/V2, V3/V3A, VP and V5) have been previously determined in humans.<sup>12</sup> With the stimulus used in this study, we were able to obtain robust activation in these areas in our control group. In 10 of 11 hemifields stimulated in the control group, statistically significant activation was observed in all of these visuotopically organised regions. This was in stark contrast to the pattern of activation in the patient.

The location of functional activation upon stimulation of the left hemifield was relatively normal in the patient, however, only the

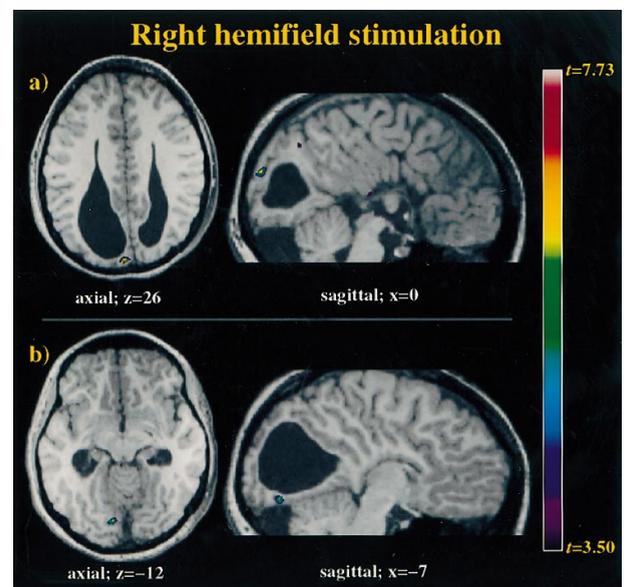


**Fig. 2** Stimulation of the left hemifield in the patient resulted in a statistically significant focus in right calcarine sulcus (V1/V2). Observe the absence of the corpus callosum and dilatation of the occipital horns of the lateral ventricles.

primary visual cortex and V5 were activated. Right hemifield stimulation produced a clearly abnormal pattern of activation in the left occipital cortex. The focus of activation in the dorsal region of the left occipital lobe appeared to correspond to a dorsally displaced calcarine sulcus, and, therefore, should represent the primary visual cortex; alternatively, it may represent an extra-calcarine V1/V2. A third possible explanation is that this region is V3/V3A and that V1/V2 was not activated on this side. This abnormal activation belies a normally functioning visual system. Failure to activate several of the visual cortical areas which were robustly activated in normal subjects occurred with stimulation of either hemifield and may be a consequence of either an absence or severe dysfunction of these regions in the patient, or the failure of true activation to reach statistically significant levels (as occurred in almost all normal subjects). Several structural anomalies in the posterior cerebral cortex have been documented in callosal agenesis, suggesting that the organisation of function within this region may also be altered. As in our patient, the sulcal pattern on the medial hemispheric surface is arranged characteristically in a radial manner and the calcarine and parieto-occipital sulci frequently do not intersect.<sup>3,4</sup> Agenesis of the corpus callosum is frequently associated with colpocephaly, a congenital dilatation of the occipital horns of the lateral ventricles,<sup>13</sup> a striking feature in the case reported here.

## CONCLUSION

In this case of callosal agenesis and colpocephaly, we demonstrate anatomical reorganisation of the visual cortex. The presence of normal visual function in the face of such substantial structural deformity probably reflects the fact that this condition was of early onset and that the visual pathways are able to successfully develop or compensate in the absence of 'normally' disposed anatomical substrates.



**Fig. 3** Stimulation of the right hemifield in the patient. (a) Sagittal and axial sections. The strongest activation peak ( $t=7.7$ ,  $P<0.001$ ) was found on the medial surface of the occipital lobe, in what appears to be a dorsally displaced calcarine sulcus. (b) Sagittal and axial views reveal an activation peak ( $t=6.76$ ,  $P<0.01$ ) in the left lingual gyrus. The radial disposition of sulci on the medial hemispheric surface are demonstrated in the sagittal section.

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