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*J. Neurol. Neurosurg. Psychiatry* 2007;78;74-81; originally published online 15 Sep 2006;
doi:10.1136/jnnp.2006.099374

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Training-induced cortical representation of a hemianopic hemifield

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Background: Patients with homonymous hemianopia often have some residual sensitivity for visual stimuli in their blind hemifield. Previous imaging studies suggest an important role for extrastriate cortical areas in such residual vision, but results of training to improve vision in patients with hemianopia are conflicting.

Objective: To show that intensive training with flicker stimulation in the chronic stage of stroke can reorganise visual cortices of an adult patient.

Methods: A 61-year-old patient with homonymous hemianopia was trained with flicker stimulation, starting 22 months after stroke. Changes in functioning during training were documented with magnetoencephalography, and the cortical organisation after training was examined with functional magnetic resonance imaging (fMRI).

Results: Both imaging methods showed that, after training, visual information from both hemifields was processed mainly in the intact hemisphere. The fMRI mapping results showed the representations of both the blind and the normal hemifield in the same set of cortical areas in the intact hemisphere, more specifically in the visual motion-sensitive area V5, in a region around the superior temporal sulcus and in retinotopic visual areas V1 (primary visual cortex), V2, V3 and V3a.

Conclusions: Intensive training of a blind hemifield can induce cortical reorganisation in an adult patient, and this case shows an ipsilateral representation of the trained visual hemifield in several cortical areas, including the primary visual cortex.

METHODS

Patient

The patient (IT) was a 61-year-old man who developed homonymous hemianopia after cerebral infarction. The lesion covered medial parts of the left occipital lobe, involved the calcarine cortex and extended anteriorly towards the left ventricle. Training started 22 months after the stroke, in December 2002. Training was intensive, taking place on average twice a week. After 5 months, flicker detection and sensitivity to recognise flickering letters in the blind hemifield were already comparable to the sensitivity of the normal hemifield.

During the follow-up period, he received no drugs affecting the central nervous system.

We followed the effect of training with fully non-invasive magnetoencephalography (MEG), and proceeded to map the cortical reorganisation with functional magnetic resonance imaging (fMRI). IT participated altogether in 13 MEG and 8 fMRI/MRI measurement sessions. Here, we show MEG results from measurements before (November 2002) and after 2 years of training (November 2004), and results from fMRI/MRI sessions measured as follows: anatomical images in September 2003, location of V5 in February 2004, MEG stimulus in fMRI in November 2004, phase-encoded retinotopic mapping in January 2005 and multifocal fMRI in April 2005. The training continued along with the fMRI measurements.

In addition, two of the authors (LH and SV) participated in a control experiment where we mapped changes in multifocal fMRI results during voluntary eccentric fixation and saccadic eye movements (details are available online at http://www.jnnpbmjjournals.com/supplemental).

Abbreviations: fMRI, functional magnetic resonance imaging; MCE, minimum current estimate; MEG, magnetoencephalography.
MEG responses were measured for contrast checkerboard patterns on both sides of the fixation, starting at pic mapping with rotating wedge-shaped stimulus disclosed comprised four 6-min runs/hemifield. Phase-encoded retinotopy to about 26˚ in diameter. The fMRI series because the narrow magnet bore and head coil limited the 10.0 s. The only difference in the checkerboard stimulus in interstimulus interval within a hemifield varied from 0.9 to 1.1 s between the contrast reversals of checkerboards on either side of the fixation. Interstimulus interval was 0.9–1.1 s between the contrast reversals of checkerboards on either side of the fixation. The stimulus in MEG consisted of two 10˚-wide and 35˚-high checkerboard pattern within the wedge reversed contrast at 8 Hz. The field patterns during stimulation of the normal hemifield. L, left hemisphere; R, right hemisphere. Figure 1 shows the change in the MEG field patterns during training. Before training, stimulation of the blind hemifield evoked no measurable responses. The responses appeared over the right hemisphere and increased to reach the same amplitude as responses after stimulation of the normal hemifield.12 In the recording after 2 years of training, there were robust field patterns for the stimulation of the blind (right) hemifield over the right hemisphere, emerging over the medial occipital regions and then moving to more temporal regions (fig 1A). Figure 1B shows the MEG field patterns after stimulation of the normal hemifield. These evoked fields were clearly affected during the training of the blind hemifield. As ipsilateral visual processing is exceptional, we examined the reactivity of spontaneous oscillations for further support. Typically, spontaneous oscillations close to sensory cortices attenuate transiently after sensory stimulation.14 Figure 2 shows time–frequency representations of oscillatory activity time locked to stimulation of the blind hemifield, averaged over a set of channels over the occipital lobes. Before training, left-side channels showed strong oscillations in the frequency range of 8–13 Hz with minor reactivity to stimulation (fig 2A), whereas the...
channels over the right occipital lobe showed the strongest oscillations in the frequency range of 13–17 Hz without any reactivity (fig 2B). After 2 years of training, the oscillations showed almost no suppression on the left side (fig 2C), but oscillatory activity on the right side was clearly suppressed at 150 ms after stimulus presentation (fig 2D, arrow). Strong oscillations may hide minor reactivity on the left, but obviously, training has mainly affected the behaviour of the intact (right) hemisphere. While the right occipital lobe has gained reactivity for stimulation of the blind (right) hemifield, the strong non-reactive oscillations on the left suggested functional disconnection of the left occipital cortex from visual input.

To identify major source regions and their dynamics, MCE analysis was applied to the MEG data acquired after training. Figure 3A shows the mean estimated brain activity between 100 and 200 ms after stimulations of the blind and normal hemifields. The MCEs show single maxima, which can be explained with active brain areas shown with ellipsoids over the magnetic resonance image. The activity is presumably emerging from several visual areas. The mean location of the source after stimulation of the blind hemifield is in the same hemisphere but located more posteriorly than the source activated by stimulation of the normal hemifield. Time courses of the selected regions of interest show how the response after stimulation of the blind hemifield peaks later than the steep response after stimulation of the normal hemifield. Figure 3B shows MCEs between 275 and 320 ms after stimulation of the blind hemifield and between 160 and 180 ms after stimulation of the normal hemifield. The lateral activities can be localised close to the visual motion-sensitive area V5. Compared with the normal hemifield, the V5 activation is delayed after stimulation of the blind hemifield stimulation.
In fMRI, we first localised the visual motion-sensitive area V5 with a low-contrast circularly symmetrical moving stimulus, and found a strong asymmetry between the hemispheres (fig 4A). In the intact hemisphere, V5 and a more dorsal and anterior satellite area around the superior temporal sulcus were strongly activated, whereas in the lesioned hemisphere only a marginal response was visible around a typical V5 location (arrow). To explore the functional reorganisation after training, the pattern-reversal checkerboard stimulus evoking clear signals in MEG (fig 1) was transferred to fMRI. Figure 4B shows activations for both the stimulation of the normal and blind hemifields. Consistent with the MEG field patterns,
In retinotopic areas, eccentricity is coded as in the normal hemifield using a rotating wedge-shaped localised with mapping of the meridional position (polar angle) (fig 5). The borders between retinotopic visual areas were reconstructed cortical surface of the intact occipital lobe. During one frame, half of the regions are on and the other half off, and the set of active regions changes every 10.9 s. In fig 6B the activation for stimulation of the blind hemifield is assigned to IT’s reconstructed and unfolded cortical surface of the intact (right) occipital lobe. In addition, V5 and the dorsal satellite region in both hemispheres were active for this stimulation (data not shown). This was the last measurement, and the first time we recorded good signals from IT’s V5 in the left hemisphere. Bilateral activity in V5 without responsiveness of early visual cortical areas has been reported previously. We assume that continuing training was changing the functional organisation even after >2 years of training. Figure 6C shows the normal retinotopic organisation of responses as a function of eccentricity mapped with multifocal stimulation of the normal (left) hemifield. The unfolded view shows overlapping representations of the hemifields (arrow). Figure 6D confirms the accuracy between the retinotopic maps obtained with the multifocal method and the phase-encoded approach. The polar angle map of the normal hemifield (multifocal data) and the borders between retinotopic areas (phase-encoded data) are in register as expected (see online material available at http://www.jnnpbmjournals.com/supplemental).

**DISCUSSION**

Training induced functional reorganisation in the intact hemisphere in visual areas V1, V2, V3, V3a and V5, and in the putative human superior temporal polysensory area around the superior temporal sulcus. The representation of the blind hemifield is distributed to the same functionally defined cortical areas with the normal hemifield representation. In accordance with this reorganisation, the fields evoked by stimulation of the normal hemifield appear to have shifted during the training (fig 1). Our results, showing the strongest responsiveness to the stimulation of the blind hemifield in V5, V3a and the superior temporal polysensory area, are in line with studies on macaque monkeys with inactivated primary visual cortex, but extend the previous findings by indicating strong involvement of low-level retinotopic areas. The reorganisation of low-level retinotopic areas could be due to the combination of long rehabilitation, repeated difficult tasks in the training and ipsilateral processing—that is, processing in a healthy part of the brain, where these retinotopic areas are available. Ipsilateral processing of residual vision, including areas V3a and V5, has been shown in patients who have undergone hemispherectomy. In healthy people, much more limited ipsilateral responses are found. The probable explanation for why training enhanced ipsilateral instead of contralateral processing of residual vision is the possible partial functional disconnection of the left occipital regions from the visual processing, as suggested by the strong poorly reacting oscillations (fig 2).

Unsteady fixation has been suspected to be the main cause of enlargement of the visual field. If a patient is looking, perhaps unconsciously, toward the stimulus in the blind hemifield instead of fixating steadily at the fixation cross, stimulation of the blind hemifield could be seen by the normal hemifield. Here we list five major proofs against fixation inaccuracies in our data.
Consistent results in follow-up imaging data and successful training are found independently in MEG and psychophysical experiments, where several different control measures for eye position were used.

Our patient was experienced. In the few fMRI sessions where fixation was unstable, activation in the retinotopic areas was strongly attenuated (two sessions before video control, data not shown). Experienced subjects, on average, move their eyes only about 10 arcmin and patients with homonymous hemianopia keep their fixation comparable before and after training of visual functions.

In some experiments, the eye position was followed online on a video display, and fixation instabilities exceeding the proximal edge of the peripheral stimulus would have been detected.

In Fig 5, the activations in response to stimulations of the right and left hemifield in the right V2d, V3 and V3a are at approximately the same distance from the foveal confluence. If activation during stimulation of the blind hemifield was derived from eccentric fixation, the patient should have fixated far outside the display on the right, instead of fixation cross on the left.
IT’s ability to fixate was controlled with multifocal fMRI, where regions in the visual field are stimulated in parallel.

If the subject cannot keep fixation, retinotopy breaks down (no signals emerge); and if the subject has stable eccentric fixation, retinotopy shows unusual organisation of the responses. Figure 6 shows the retinotopic map of responses during multifocal stimulation of the normal (left) hemifield. The activation is strongest in the primary visual cortex and extends to neighbouring retinotopic areas, which is a typical distribution of responses expected for a normal visual field in a multifocal fMRI experiment. If IT had had stable eccentric fixation on the right side of the fixation point, the activation coded in colour in fig 6C should be more distant from the foveal confluence than the activation shown by white lines, and the activation patterns coded in red and purple in fig 6D should be inside V1 and not at the border between visual areas V1 and V2, where the vertical meridian is represented (more details are available online at http://jnnpbmjournals.com/supplemental).

Owing to parallel stimulation of the hemifields, findings from the multifocal data can only be explained by activation of retinotopic areas of the intact hemisphere by stimuli in either hemifield.

During training, IT became conscious of his right hemifield, patches of form vision emerged, and the far periphery of the blind hemifield brightened. Restored function and the coinciding right hemisphere activation are due to therapeutic intervention, and not to spontaneous recovery. Spontaneous recovery occurs typically within the first 3 months after unilateral visual field loss, although single cases have continued improving without treatment for up to 2 years. In our patient, training was performed in the third and fourth year after the stroke. Before, IT showed a stable homonymous hemianopia, with no evoked neuromagnetic responses in response to the stimulation of his blind hemifield. At such a chronic stage after brain injury, the probability of any further spontaneous recovery is negligible, and restoration of function must result from intervention.

Callosal connections have been proposed to mediate ipsilateral extrastriate activations documented with healthy subjects, but the extent of ipsilateral processing differs between IT and healthy people. As only minor activation was detected in healthy subcortical pathways including IT’s left hemisphere (fig 4), callosal connections seem to be an unlikely explanation of the responses. Further extrastriate activations documented with healthy subjects in the chronic stage after brain injury, the probability of any further spontaneous recovery occurs typically within the first 3 months after unilateral visual field loss, although single cases have continued improving without treatment for up to 2 years. In our patient, training was performed in the third and fourth year after the stroke. Before, IT showed a stable homonymous hemianopia, with no evoked neuromagnetic responses in response to the stimulation of his blind hemifield. At such a chronic stage after brain injury, the probability of any further spontaneous recovery is negligible, and restoration of function must result from intervention.

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Cortical representation of a hemianopic hemifield

Figure 1 (A) Right external carotid arteriography shows the right internal maxillary, right ascending pharyngeal and right superficial temporal arteries feeding vessels to a cerebral arteriovenous malformation (AVM). (B) Common carotid arteriography shows branches of the external carotid artery feeding vessels to the AVM.

Figure 2 (A) Diffusion-weighted magnetic resonance imaging shows multiple hyperintense lesions in the right occipital and temporal lobes and right caudate nucleus. (B) Computed tomography shows a hypodense lesion in the right occipital lobe. Multiple hyperdense lesions are present in bilateral occipital lobes, showing evidence of embolic material.

NEUROLOGICAL PICTURE

A case of brain embolism during catheter embolisation of head arteriovenous malformation.

What is the mechanism of stroke?

A 52-year-old man presented with facial swelling owing to progression of arteriovenous malformation (AVM). Angiography under endotracheal anaesthesia showed the right internal maxillary, right ascending pharyngeal and right superficial temporal arteries feeding an AVM (fig 1A). Clear connections to the intracranial circulation were not found. Vessels were emboled using N-butyl-2-cyanoacrylate and iodinated oily x ray contrast medium comprising 40% iodine in poppy seed oil (Lipiodol; Terumo, Tokyo, Japan; fig 1B).

After AVM embolisation, disturbance of consciousness and left hemiparesis were present. Diffusion-weighted magnetic resonance imaging showed multiple hyperintense lesions of the right middle cerebral artery, right posterior cerebral artery and right posterior inferior cerebellar artery territories (fig 2A). Computed tomography showed low-density lesions with high-density spots (fig 2B). We confirmed a patent foramen ovale (PFO) using transcranial Doppler and transoesophageal echocardiography with saline contrast. No lesions contributing to cerebral embolism were present in the carotid artery or the aortic arch. We finally considered that paradoxical brain embolism occurred because of embolic material passing through the PFO.

Cerebral complications during catheter embolisation have rarely been described in detail. Firstly, embolic material would have had to pass from the artery to the vein through the cerebral AVM during catheter embolisation. Pulmonary embolism as a complication of transcatheter arterial embolisation with rays has indeed been documented. Secondly, mechanical ventilation may have contributed to an elevation of right atrial pressure. Increasing pressure in the right atrium would generate conditions such as a Valsalva manoeuvre. Therefore, embolic material could have passed from the right to the left atrium through the PFO, resulting in multiple brain infarctions.

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Competing interests: None declared.

References