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Cortical activation in hemianopia after stroke

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Abstract

Changes in neuronal activity of the visual cortex have been described in patients with hemianopia. The anatomical areas that are involved in neuroplastic changes have not been studied in a larger group of stroke patients with a homogenous structural pathology of the visual cortex. Brain activation was measured in 13 patients with a single ischemic lesion of the striate cortex and partially recovered hemianopia and in 13 age-matched control subjects using blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI). Differences in activation between rest and visual hemifield stimulation were assessed with statistical parametric mapping using group and multi-group studies. In normal subjects, the most significant activation was found in the contralateral primary visual cortex (area 17) and bilaterally in the extrastriate cortex (areas 18 and 19). In patients, these areas were also activated when the intact hemifield was stimulated. During stimulation of the hemianopic side, bilateral activation was seen within the extrastriate cortex, stronger in the ipsilateral (contralesional) hemisphere. Stimulation of the hemianopic visual field is associated with ipsilateral activation of the extrastriate visual cortex. This pattern of activation suggests extensive neuronal plasticity within the visual cortex after postgeniculate ischemic lesions and may have implications for therapeutic interventions.

Keywords: Stroke outcome; Magnetic resonance imaging; Visual cortex; Hemianopia; Plasticity

Hemianopia is a reduction of vision in one half of the visual field due to damage of the postgeniculate optic pathways and a common finding after infarction of the posterior cerebral artery. Patients with hemianopia may be severely disabled in performing activities of daily living (ADL). Functional brain reorganization has been proposed to explain recovery of impaired function after peri-infarct edema has resolved and the ischemic penumbra has resumed its function. Several aspects of cortical organization are thought to remain plastic into adulthood, allowing cortical maps to be modified continuously by experience. This dynamic nature of cortical circuitry is important for learning, as well as for repair after injury to the nervous system. Plasticity in the visual cortex has been described in several primate studies [7]. Recovery from visual field defects occurs to varying degrees [21] and there is an ongoing debate on the capacity of the human primary visual cortex to undergo long-term functional reorganization. Recently, neuroimaging studies have indicated residual responsiveness to blind hemifield stimulation in the extrastriate cortex of the unaffected hemisphere in patients with vascular or surgical lesions [12,2]. These data, however, are mostly derived from smaller case series or case reports. To date, the anatomical areas that may be involved in plasticity of patients with post-stroke visual field defects have not been systematically studied in a population with a homogenous structural pathology of the visual cortex. The aim of this study was to investigate patterns of brain activation in a larger group of patients with post-stroke visual field defects after a single occipital cortex stroke.

Thirteen stroke patients were studied (median age 60, range 39–75 years, three females, median time post-stroke 10 months). Inclusion criteria were a first single ischemic lesion of the primary visual cortex, minimum interval from stroke onset to study of 2 months, lesion in the striate cortex causing homonymous

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hemianopia, and the ability to maintain fixation for at least 6 min. In all subjects the vascular lesion involved the striate cortex causing dense contralateral homonymous, macula-sparing hemianopia at the time of stroke. Patients with neglect, any other visuospatial impairment, or those with contraindication for MRI were excluded. Visuospatial neglect was excluded using line bisection test [11], line cancellation test [1] and drawing of clock [8]. MRI of the brain and computed perimetry were performed in all patients prior to fMRI. Thirteen healthy age-matched control subjects (median age 61, range 51–70 years, six females) were recruited through local advertisements. Prior to each fMRI, a full neurological exam was obtained for each subject. All patients gave written informed consent. This study was approved by the Review Board of Ethics Committee of the University of Essen.

Visual stimuli were projected with a laptop computer onto a 154 cm × 115 cm screen. During rest, the screen remained gray. During activation, a black-and-white checkerboard pattern reversal was used to stimulate each hemifield separately. Subjects were given clear instructions to fixate a red point in the center of the screen during both conditions. All subjects were experienced in performing the fixation task during hemifield stimulation and had practiced repetitively in the laboratory. Prior to fMRI, all subjects were acclimated to the scanner and the fixation task in a prescan session. Fixation was not monitored in the scanner, but presumed to be similar to behavioral performance measured in the laboratory, as in precedent studies of functional imaging of the visual system [12]. The light intensity of the gray screen during baseline and of the contralateral hemifield during stimulation was adjusted to be equal to the average light intensity of the black-and-white checkerboard in order to avoid unintentional stimulation caused by changes in brightness of the environment.

Using a block design, 250 volumes of 48 contiguous axial fMRI slices (3.3 mm × 3.3 mm × 3.0 mm spatial resolution) were acquired with echoplanar imaging (TR/TE 3000/60 ms, flip angle = 90°, Siemens Sonata 1.5-T, 40 mT gradients) covering the whole brain (60 volumes for each condition). The angle (along the horizontal meridian) between the fixation point and the lateral edge of stimulation with high-contrast checkerboards pattern was 40.5° for controls and patients (each square of 60 arc/min). The pattern reversed at 5 Hz. Raw data were processed and analyzed using statistical parametric mapping (SPM 1999, Wellcome Department of Cognitive Neurology, London, UK) [5]. Functional images were realigned with sinc interpolation and then normalized. No distortion due to the occipital infarction was noted on normalized images. Finally, x, y, and z spatial coordinates were transformed to the three-dimensional anatomical space according to Talairach and Tournoux [17]. Functional images were smoothed to accommodate intersubject variability of brain anatomy using an isotropic Gaussian kernel of 12 mm. Because seven patients had left-sided lesions, data of the remaining six patients with a right-sided lesion were flipped across the midsagittal plane. Thus, for the group analyses, the hemianopic side was always right.

Assessment of significant signal changes between rest and visual stimulation was performed using SPM'99. Statistical inferences were based on group effects using a random effects model [6]. A voxel × voxel comparison according to the general linear model and t statistics was used to calculate differences of activation between hemifield stimulation and rest in patients and normal subjects (group study). The same model was used for comparisons between patients and controls (multi-group study). The resulting statistical parametric map (SPM) was subsequently used to assign P-values (to voxels and also to clusters), which were corrected for multiple comparisons applied for the whole brain using a random effects model. Significant differences were defined at $P < 0.001$.

Table 1
Increases of rCBF during visual stimulation of control subjects

Region	BA	x, y, z	z-scores
(a) Left hemifield			
Contralateral activations			
Striate cortex	17	12, −84, 2	5.1
Extrastriate cortex	18/19	45, −75, −3	4.6
Ipsilateral activations			
Extrastriate cortex	19	−50, −73, 4	4.6
Region	BA	x, y, z	z-scores
(b) Right hemifield			
Contralateral activations			
Striate cortex	17	−9, −84, 4	5.6
Extrastriate cortex	19	−39, −64, 9	5.6
Ipsilateral activations			
Extrastriate cortex	19	33, −90, −3	5.1

BA: Brodmann area. Coordinates are according to Talairach and Tournoux [17]. Group study, $P < 0.001$.

At study time, all patients reported some recovery from hemianopia, but all had persisting partial visual field defects. During stimulation of either hemifield in control subjects maximum increase of rCBF was seen in the contralateral primary visual cortex (Table 1; Fig. 1). This area of maximum rCBF changes also extended to the peristriate and extrastriate cortex covering Brodmann areas 18 and 19. Weaker and much smaller activation was also found in the extrastriate cortex ipsilateral to the side of stimulation. During stimulation of the unaffected (left) hemifield in patients, an area of maximum activation was again observed in the contralateral primary visual cortex (Table 2a; Fig. 2b). As in normal subjects, activation also involved the peristriate and extrastriate cortex. During stimulation of the hemianopic (right) hemifield bilateral activation of the extrastriate cortex in areas 18 and 19 was found. The extrastriate activation of the ipsilateral hemisphere extended medially towards area 17, but the ipsilateral primary visual cortex did not show significant increases in blood flow. The contralateral primary visual cortex was not activated (Table 2b; Fig. 2b).

Areas that were significantly more activated in stroke patients compared to normal subjects during stimulation of the hemianopic (right) field were identified by subtracting increases of rCBF during right hemifield stimulation in normal subjects from those in patients. In this analysis, significant increases of rCBF were found in BA 18 of the ipsilateral extrastriate cortex (12, −90, 0; z-score = 3.9, Fig. 3a). Conversely, areas that were sig-