Functional evaluation using magnetic resonance imaging of the visual cortex in patients with retrochiasmatic lesions

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Object. The goal of this study was to evaluate the clinical potential of combining functional magnetic resonance (fMR) imaging with conventional morphological MR imaging and to assess its usefulness for objective evaluation of visual function as part of treatment planning in patients harboring space-occupying lesions involving the posterior afferent visual system.

Methods. It was hypothesized that regional activation of the visual cortex during visual stimulation would show an asymmetric response consistent with the well-known retinotopical organization of the human visual cortex. To test this hypothesis, the pattern of regional cortical activity detected by fMR imaging during binocular repetitive photic stimulation (10 Hz) was compared with the findings of conventional visual field testing. Functional mapping of the visual cortex was performed using a noninvasive blood oxygen level–dependent MR technique in 10 patients with intraxial and two with extraxial lesions. Experiments involving two of the patients were unsuccessful because of motion artifacts. In all the remaining patients functional activity was demonstrated in the primary visual area that corresponded to the anatomical location of the calcarine cortex. In nine patients, the identified patterns of activation in the visual cortex were consistent with the visual field deficits (seven homonymous hemianopsias, one homonymous central scotoma, and one inferior quadrantanopsia) and with the traditional teaching of retinotopical representation. Discordance between fMR imaging and perimetric findings was observed in one case.

Conclusions. These results demonstrate that fMR imaging can be performed routinely and successfully in patients with visual abnormalities as part of a conventional neuroradiological evaluation. The technique provides essential information about the function–structure relationship specific to an individual patient and holds promise not only for diagnosis and therapy planning, but also for understanding the topography and functional specialization of the human visual cortex.

Key Words • occipital cortex • visual physiology • retinotopy • functional magnetic resonance imaging • brain neoplasm • perimetric examination
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Similar to that achieved in the most elaborate invasive animal studies,9–11,39,40,44 these studies of retinotopy, performed in normal volunteers by using widely available conventional MR imaging equipment, have provided significant new information about the organization of visual areas in the human cortex and have suggested the potential usefulness of the technique for routine clinical applications. In the present study, our rationale was to evaluate the clinical potential of combining fMR imaging with conventional morphological MR imaging and to assess its usefulness for objective evaluation of visual function as part of treatment planning for patients harboring space-occupying lesions involving the posterior afferent visual system. We hypothesized that regional activation of the visual cortex in patients with visual field defects identified by fMR imaging during visual stimulation would show an asymmetric response that is consistent with the well-known retinotopical organization of the human visual cortex. To test this hypothesis, the pattern of regional activity within the visual cortex detected by fMR imaging was compared with the findings of perimetric visual field testing.

Clinical Material and Methods

Patient Population

During a 1-year period, eight men and four women, ranging in age from 41 to 75 years, who had CT-documented space-occupying lesions lying posterior to the optic chiasm were included in this prospective study. The patients were referred to the neurosurgical department of our hospital for further assessment, and the selection criterion for participation in the study was the presence of a single lesion with evidence of involvement of the posterior afferent visual system. All patients underwent conventional spin-echo MR imaging, fMR imaging examination, and visual field testing before undergoing invasive investigation or surgery. In all patients, the specific histopathological diagnoses of a primary (seven patients) or metastatic (four patients) tumor and an intracranial abscess (one patient) were established by surgery (11 patients) or biopsy (one patient). Of these patients only five presented with visual symptoms. The patient characteristics, clinical presentation, histological diagnoses, and type of operation performed are summarized in Table 1.

Imaging Data Acquisition

Morphological and fMR examinations were performed during the same imaging session by using a 1.5-tesla (T) whole-body MR imaging system (Signa Horizon, Echospeed; General Electric Medical Systems, Milwaukee, WI) equipped with an ultrafast, three-axes gradient system characterized by a maximum amplitude of 22 mT/m, a rise time of 184 msec, and a slew rate of 120 mT/m/msec. A standard product whole-head transmit–receive coil and foam cushions and straps were used to immobilize the head comfortably. After anatomical localizer images were obtained in the sagittal plane, conventional T$_1$-weighted spin-echo sequences with a TR of 600 msec and an TE of 20 msec, and proton density– and T$_2$-weighted (TR 3500 msec; TE 17/102 msec) fast spin–echo sequences were acquired over the whole brain according to a routine presurgical imaging protocol.

The fMR imaging procedure was started by identifying the oblique course of the calcarine sulcus on the sagittal localizer images. Spin-echo T$_1$-weighted (TR 600 msec; TE 20 msec) anatomical slices with an in-plane resolution of 0.8 × 1.2 mm and a section thickness of 5 mm were collected to demonstrate the structural anatomy of the selected region. Careful placement of five to six contiguous slices, parallel to the calcarine sulcus, allowed adequate coverage of the superior and inferior calcarine cortex and most of the supra- and infracalcarine occipital cortex. Regional changes in neuronal activity in the visual cortex were detected using the blood oxygen level–dependent MR technique.36 Brain images produced by this technique reflect local responses in cerebral blood oxygenation during neuronal activity. A subtle decrease in the concentration of deoxyhemoglobin results in local magnetic susceptibility changes that decrease the apparent transverse relaxation time (T$_2$*) and, hence, increase the signal intensity of the activated regions. Gradient-echo T$_2$*-weighted (TR 2000 msec, TE 40 msec, flip angle of 40°), single-shot, echo planar images of the same slice thickness and orientation as the T$_2$*-weighted anatomical images and an in-plane resolution of 3.1 × 3.1 mm were obtained. Forty images were acquired in an interleaved manner in each slice during five alternating periods of rest–stimulation (five, 10, 10, 10, and five images in each period, respectively) for a total of 200 (five slice experiments performed in one patient) or 240 (six slice experiments performed in the rest of the patients) images. In all cases the visual stimulation experiment was repeated two times to test its reproducibility. The imaging time for each functional image was 1 minute and 31 seconds, resulting in a prolongation of the routine presurgical planning protocol by approximately 9 minutes (including the anatomical series for subsequent overlays and the reconstruction time for the two functional experiments). After administration of intravenous gadolinium-chelating contrast material, conventional T$_1$-weighted images were obtained to complete the presurgical evaluation MR imaging session.

Stimulus Conditions

Visual activation was achieved using a commercial strobeoscope (Lichtreizgerät stroboskop I typ STRN BN 980; Knott Elektronik, Munich, Germany), which generated white-light flashing stimuli at a frequency of 10 Hz. Previous positron-emission tomography (PET) scanning investigations13 have demonstrated that a maximum hemodynamic response in human visual cortex occurs at a stimulus temporal frequency between 7.8 Hz and 15.5 Hz. Flash duration and intensity were constant throughout the stimulation cycles. The patients, who were lying supine in the gantry, looked up into an adjustable angled mirror that allowed them to view comfortably, in the direction of their feet, the strobeoscope, which was fixed at the line of sight. The visual angles of the stimulus were 30° horizontal and 27° vertical. During the visual stimulation periods, the patients were instructed to stare at the center of the light-emitting source. During the resting state, the patients were kept in the dark and were instructed to avoid eye movement as much as possible. Uncontrolled visual stimulation was eliminated by dimming room lights and surrounding any potential source of light within the room with dense
fabric drapes. Before the start of the imaging session, the stimulation procedure was explained to all patients and the type of stimulus was demonstrated.

**Imaging Data Analysis**

All imaging data obtained from the conventional and functional imaging acquisitions were transferred to a workstation (Sun Microsystems, Inc., Palo Alto, CA) with commercially available software (Advantage Windows; GE Medical Systems) for further postprocessing and photographing. The imaging data from the functional experiments were screened for motion by viewing animations of the 40 images in each slice. Parametric maps of brain activity were generated by applying a pixel-by-pixel temporal correlation analysis based on a correlation coefficient algorithm. This algorithm correlates the time course data sets with generic reference functions that have a periodic “boxcar” wave form. Cross-correlating a pixel’s time series with a reference wave form can effectively remove artificial signals such as cerebrospinal fluid or brain pulsatility, which are randomly timed with respect to the stimulation paradigm. As a time reference, we applied a boxcar wave form, which was shifted by 2 to 6 seconds (one to three images) in the second sequence to account for the temporal low-pass filtering that occurs as a result of a hemodynamic response. Those pixels in which the mean of the MR signal in activation images significantly exceeded the mean of the resting images, with a probability value of less than 0.01, were used for viewing the functional maps. Generated functional maps of regional brain activity were displayed in pseudocolor, scaled according to statistical significance, and overlaid directly on the gray-scale high-resolution T₁-weighted anatomical MR images allowed the detection of the activated areas in each slice. Parametric maps of brain activity were generated by applying a pixel-by-pixel temporal correlation analysis based on a correlation coefficient algorithm. This algorithm correlates the time course data sets with generic reference functions that have a periodic “boxcar” wave form. Cross-correlating a pixel’s time series with a reference wave form can effectively remove artificial signals such as cerebrospinal fluid or brain pulsatility, which are randomly timed with respect to the stimulation paradigm. As a time reference, we applied a boxcar wave form, which was shifted by 2 to 6 seconds (one to three images) in the second sequence to account for the temporal low-pass filtering that occurs as a result of a hemodynamic response. Those pixels in which the mean of the MR signal in activation images significantly exceeded the mean of the resting images, with a probability value of less than 0.01, were used for viewing the functional maps. Generated functional maps of regional brain activity were displayed in pseudocolor, scaled according to statistical significance, and overlaid directly on the gray-scale high-resolution T₁-weighted images obtained at the same anatomical location. The exact location of activated areas in each slice was estimated for the anteroposterior and inferosuperior occipital regions relative to the calcarine fissure by cross-referencing the functional slices with the sagittal localizer images. The anatomical and functional changes were compared with the patient’s visual fields according to Holmes’ retinotopical map of the striate cortex, which was revised by Horton and Hoyt. The entire postprocessing procedure required approximately 15 to 20 minutes and the functional maps generated were printed and available, together with the rest of the structural MR imaging acquisitions, for discussion with neurosurgery colleagues prior to any intervention procedure. With the evolution of the study a motion correction algorithm was installed in a workstation (DEC-Alpha; Digital Equipment Corp., Maynard, MA) and selected cases have been additionally postprocessed retrospectively after motion correction. The same postprocessing algorithm and probability threshold was used in the motion-corrected images. The mean percentage of activation and the mean correlation coefficient were determined automatically by the algorithm.

**Ophthalmological Examination**

All patients were referred for neuroophthalmological examination within 3 days before fMR imaging. Visual fields in most patients were evaluated using the kinetic method developed by Hans Goldmann with the advantages of involvement of the peripheral visual field and the possibility to adjust the examination procedure to the performance of the patient. Selected cooperative patients were studied using the more sensitive method of computerized static perimetry either solely or in combination with kinetic testing. In these cases, the Octopus N1 program (Interzeag AG, Schlieren, Switzerland) was chosen, which is specifically designed for patients with suspected neurological visual field defects. One patient was only able to perform visual field testing in which the confrontation method was used, comparing the visual field of the examiner with that of the patient.

**Results**

**Analysis of Morphological MR Imaging Data**

Conventional T₁- and T₂-weighted and contrast-enhanced T₁-weighted anatomical MR images allowed the following: exclusion of associated lesions; differentiation between extra- and intraaxial disease; precise localization of the pathological site to specific gyri; appreciation of the extent of involvement of occipital cortical and white matter areas; rough discrimination between lesion infiltration and presence of edema; identification of blood-brain barrier disruption; and estimation of the degree of anatomical distortion produced by the pathological process. The locations of the lesions relative to the calcarine sulcus and the posterior afferent visual system are summarized in Table 1. In eight cases, MR imaging demonstrated clear involvement of the occipital lobe by an intraaxial (seven patients) or extraaxial (one patient) space-occupying lesion. Three of these lesions showed supra- and infracalcarine extension, two were confined to the supracalcarine region, one completely replaced the brain parenchyma of the occipital lobe, and one lesion was predominantly infracalcarine with associated edema extending supracalcarine. The extraxial lesion was located at the occipital apex and compressed the occipital pole anteriorly. In the other four cases the lesions were primarily located in the parietal lobe (two cases), temporal lobe (one case), or thalamus (one case) at a distance from the calcarine cortex; however, there was MR imaging evidence for involvement of the lateral geniculate body and/or the optic radiations. Although the location of the calcarine sulcus relative to the lesion was identified on morphological images in most cases, the presence of edema and/or tumor infiltration did not allow distinction between the calcarine cortical ribbon and the adjacent white matter in five cases (Fig. 1).

**Analysis of the fMR Imaging Data**

In the 12 patients a total of 24 separate fMR activation studies were performed. Two patients (one with a large parietal glioblastoma multiforme (GBM), and one with a temporoooccipital metastatic lesion from a primary bronchus carcinoma) could not cooperate in the functional experiment and both fMR imaging data sets were degraded by gross motion. The remaining patients were cooperative enough to remain motionless for the functional procedure and, as best we could ascertain, no significant head movement was identified in any of the 20 separate fMR imaging experiments. These activation studies were retained for further examination and image processing.
these patients, a stimulus-related, statistically significant activation was demonstrated within the expected regions of the primary visual cortex. Focal MR signal intensity changes in areas of maximum correlation varied from patient to patient, but were generally in the range of 1.3 to 5.2% over baseline. The signal rise and fall corresponded with the beginning and end of stimulation and was typically delayed by two to three images (4–6 seconds). The qualitative activation patterns and their locations, as well as the overall range of magnitude of activation, were reproducible in repeated experiments.

Anatomical Localization of Activation

In the unaffected hemispheres, activation was distributed over the anterior and posterior regions of the medial occipital lobe corresponding to the anatomical location of the calcarine fissure. In each patient, these responses were identified in the most inferior imaging planes and extended across one or two adjacent sections that included the calcarine cortex. The location and shape of these primary responses varied slightly across patients but always corresponded to individual variations in the location and shape of the calcarine fissure. For instance, the activated regions were oriented perpendicular or oblique to the medial occipital surface extending laterally at a variable distance depending on the orientation and extent of the calcarine fissure. We considered that these responses originated in large part from the striate cortex (V1 or Brodmann’s Area 17). Additional regions of activation were detected superior and dorsolateral to the primary responses in eight of the 10 patients and in cortical areas close to the occipitotemporal region ventrolateral to the primary responses in six of the 10 patients. These were typically smaller in size and considered to represent extrastriate visual responses. The pattern of activation elicited in the unaffected hemispheres of the patient population was consistent with those we have observed in normal healthy volunteers in whom fMR imaging and similar stimulation conditions were used.24

The hemispheres ipsilateral to the lesion exhibited variable patterns of activation. In seven patients (Cases 1–7), activation of the primary visual cortex ranged from completely absent to significantly diminished as compared with the contralateral hemisphere (Fig. 1). In one patient (Case 8) there was absence of activity in the posterior portion of the calcarine cortex, but significant activation was detected in the area of the primary cortex close to the junction of the calcarine fissure with the parietooccipital sulcus (Fig. 2). In the last two patients (Cases 9 and 10), significant activation was observed on the most inferior slices, which included the primary visual cortex, but clearly diminished activity was present in the more superior imaging planes through the supracalcarine extrastriate occipital cortex (Fig. 3). Although small focal areas of residual activity were identified within the infiltrated striate cortex in two patients with tumors extending both supracalcarine, no activation was detected within the tumor outside the region of the calcarine cortex in any case.

Comparison by visual inspection of the patterns of activation in the two hemispheres showed that visual stimuli induced a marked right-to-left side asymmetric response in the primary visual cortex, which was related to the hemispheric location of the lesion in eight patients. In the other two patients, bilateral symmetric activity was detect-
ed in the primary visual cortex, but prominent right-to-left side asymmetry was found in the dorsal extrastriate cortical areas.

Correlation of Activation Patterns With Perimetric Examination

Nine of the patients were cooperative enough to undergo a complete neuroophthalmological examination. One patient (Case 5), who had a parietal lesion infiltrating the thalamus, lateral geniculate nucleus, and optic radiations, was unable to cooperate with the perimetric examination and a complete homonymous hemianopsia was diagnosed by the confrontation method. In the other patients, kinetic and/or static perimetry revealed the following patterns: complete or near-complete homonymous hemianopsia in four patients; relative homonymous hemianopsia in two

Fig. 1. Case 1. Findings obtained in a 52-year-old man with GBM. Upper Left: Coronal contrast-enhanced T1-weighted MR image demonstrating extension of tumor above and below the parietooccipital sulcus and involvement of the right medial occipital lobe. Upper Right: Functional MR maps obtained during binocular visual stimulation, overlaid on the corresponding anatomical images, clearly demonstrating diminished activation of the right calcarine cortex, which is indistinguishable from infiltrating GBM. Lower: Goldmann perimetry showing an almost complete left-sided homonymous hemianopsia with sparing of some of the upper central field on the left side.
patients, homonymous central scotoma in one patient; inferior homonymous quadrantanopsia in one patient; and normal visual fields in one patient. Correlation of the findings of the perimetric examination with the areas of activation detected in fMR images showed consistent results with both methods in nine patients. In the seven cooperative hemianoptic patients, qualitative estimation of the activation in the visual cortex showed markedly reduced activity in the hemisphere contralateral to the visual field loss (Fig. 1). The patient with the central homonymous scotoma showed a clear activation area in the anterior portion of the contralateral calcarine cortex with absent activity in the posterior region close to the occipital pole (Fig. 2). The patient with the inferior homonymous quadrantanopsia demonstrated bilateral activity in the primary V1 cortex, but a strikingly reduced activity in the superior V2 and V3 extrastriate cortical areas of the affected hemisphere (Fig. 3). In the last patient who had normal visual fields, bilateral symmetric activation was observed in the primary striate cortex, but there was clearly diminished

Fig. 2. Case 8. Findings obtained in a 47-year-old woman with occipital lobe meningioma. **Upper Left:** Sagittal T_{1}-weighted MR image revealing extraaxial tumor compressing the posterior portion of the left calcarine sulcus. The anterior portion of the calcarine sulcus is identified at its junction with the parietooccipital sulcus. **Upper Right:** Functional MR mapping of the visual cortex, overlaid on anatomical images obtained at the tilted axial orientation plane that is indicated in the **upper left** panel, demonstrating significant activation in the anterior portion of the calcarine cortex on both sides and clear right-to-left side asymmetry with diminished response on the left side in the posterior portion of the calcarine cortex that is compressed by tumor. **Lower:** Goldmann perimetry showing normal-looking isopters with a right homonymous scotoma in the central 8° of vision.
Fig. 3. Case 9. Findings obtained in a 44-year-old man with occipital abscess. Upper Left: Sagittal T1-weighted MR image demonstrating the abscess with moderate perilesional edema located between the calcarine sulcus inferiorly and the parietooccipital sulcus superiorly. Upper Center: Anatomical T1-weighted MR images revealing predominant involvement by the lesion of the left occipital visual cortical areas located superior to the primary calcarine cortex. Upper Right: Functional MR imaging data at the corresponding anatomical sections demonstrating significant bilateral activation in the most inferior section through the primary calcarine cortex and diminished activity on the left side in the more superior sections through the supracalcarine V2 and V3 cortical areas. Lower: Goldmann perimetry showing a right-sided inferior quadrantanopsia with perfectly aligned margins along both the horizontal and vertical meridians.
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activity in the more superior extrastriate areas ipsilateral to the lesion.

Discussion

In the human brain most of the primary visual cortex is located in the occipital lobe within and surrounding the calcarine fissure. Clinical studies of soldiers who received missile injuries early in this century demonstrated that neurons within this area are retinotopically organized with the horizontal meridian occupying the base of the calcarine fissure, the vertical meridian demarcating the outer perimeter of the striate cortex, the central retina projecting caudally in the occipital pole, and the peripheral retina projecting rostrally in the anterior portion of the calcarine cortex. With the introduction of tomographic neuroradiological imaging, this broad retinotopical schema was confirmed and further refined by clinicoradiological correlation. Although these lesion–deficit correlations provided a general schema of striate organization, relating the anatomical extent of a lesion observed on MR or CT imaging to the functional perimetric finding has inherent limitations. Conventional neuroradiological imaging simply outlines lesion location and its gross extent, but it is often difficult to differentiate between lesion infiltration and the presence of edema or to determine whether lesions involve cortex only or both cortex and white matter. Furthermore, structural alterations of local anatomy do not necessarily imply neuronal death. On the other hand, perimetric examination provides a subjective determination of variation in function at one point in time and lacks direct anatomical information. A major advance in function–structure correlation of striate organization has been provided by functional PET imaging studies in normal volunteers. However, the gross spatial resolution of this technique, the associated radiation exposure, and the limited availability of PET units have restricted its application for routine evaluation of patients with visual field defects to a few clinical reports.

Recently developed fMR imaging technologies have significantly expanded the possibilities for noninvasive study of human cerebral function and disease. In the past few years, fMR imaging studies have provided new and valuable information in understanding the organization and functional properties of visual areas in the human cortex as a result of the enhanced spatial and temporal resolution of this technique in comparison to PET scanning and the ability to study activations in single patients and to study patients longitudinally in repeated scan sessions. Moreover, the ability to map brain areas quickly using a conventional fMR imaging system suggests that the technique should be useful clinically for diagnosis, surgical planning, and studies of recovery of function.

Applications of fMR Imaging Mapping in Patients With Visual Abnormalities

To date, few fMR imaging studies investigating abnormalities of the retinogenicoculocarinate system have been reported. Preliminary data obtained in patients with congenous homonymous hemianopsia caused by retrochiasmatic disease and in those with visual loss caused by lesions of the optic nerves and the chiasm have displayed a good agreement between the findings of fMR imaging and those of perimetric examination. Another study of three individuals with albinism showed asymmetric activation of the primary visual cortex during monocular visual stimulation, a finding consistent with known crossing abnormalities of the visual pathways in albinism, confirming the potential of fMR imaging for evaluation of the visual pathways in pathological conditions.

In the present study we attempted to bring this technique into the clinical setting by examining patients harboring intracranial space-occupying lesions affecting the posterior afferent visual system. Our results demonstrate that fMR imaging can be performed successfully and, in a qualitative sense, reproducibly in patients with visual field defects as part of the routine preoperative neuroradiological imaging in the clinical environment. Binocular photic stimulation yielded statistically significant activation of the occipital cortex in 10 (83%) of the 12 patients examined. The two patients who were unable to remain motionless for the experiment had large infiltrative lesions involving the temporal and parietal lobes. Patients with parietal lobe disorders may be so impersistent and distractable and have such difficulty maintaining fixation that despite their willingness to cooperate and follow instructions, visual examination may prove impossible. These individuals present a special problem not only for fMR imaging examination but also for perimetric examination. Moreover, extensive damage of the parietal lobe may cause anosognosia and, thus, denial of the visual field defect by the patient who provides the examiner with a misleading report. This might have been the case in one of the two uncooperative patients with normal visual fields on perimetric examination.

The parenchymal responses observed in the unaffected hemispheres of the cooperative patients were located in the medial portions of the occipital lobes and corresponded to the territory of the calcarine sulcus extending in the adjacent cortical lips of the fissure. These parenchymal areas predominantly represented activation of the primary visual cortex. However, due to the 5-mm slice thickness used in this study and the great variability in the location of human cortical areas, it is possible that portions of associated visual cortex (V2 or Brodmann’s Area 18) also contributed to these primary responses. Area V2 shares a common border with V1; the former concentrically surrounds the latter and appears to be activated by all multimodalities of vision similarly to area V1. Activation was additionally detected in cortical areas distant from the V1 and V2, presumably representing extrastriate responses. More than 30 visual areas have been identified in the monkey brain, each of which analyzes information corresponding to particular features, such as shape, color, or movement. By using noninvasive fMR imaging techniques and retinotopically specific stimuli, the location and functional specialization of several of these areas have been recently documented in humans. Because of the simplicity of the stimulus used in the present study, the significance of activation or lack thereof and the relationship between these areas and the lesions were not further analyzed.

Correlation of fMR Imaging Maps With Visual Field Defects

As predicted, a comparison of the fMR imaging activa-
tion maps in affected versus nonaffected hemispheres showed asymmetry that correlated well with the patterns of visual field loss mapped using conventional subjective perimetry. In seven patients with homonymous hemianopsia, fMR imaging demonstrated clearly reduced activation in the occipital cortex that was always contralateral to the field defect. In four of these cases obvious damage to the primary visual cortex was demonstrated on structural images; however, in three patients (Cases 4, 5, and 7) the lesions predominantly involved the optic radiations and the lateral geniculate nucleus, whereas the occipital cortex was apparently intact. These cases demonstrate that fMR imaging can detect visual field defects that are caused not only by lesions that produce destruction of the primary visual cortex, but also by lesions that interrupt the visual pathway, creating a lack of sensory input. Although the usefulness of fMR images to demonstrate the function–structure relationship and to be used as a reliable tool for preoperative planning in patients with tumors seems unquestionable, the sensitivity of the technique to be used for objective evaluation of visual deficits will eventually be determined by the ability of the method to detect field defects produced by lesions that cause denervation of the occipital cortex by remote interruption of the visual pathways, without destruction of the occipital cortex.

In two patients (Cases 6 and 7) with relative homonymous hemianopsia, small foci of activation were identified in occipital cortical areas that on structural MR images seemed involved by high-grade tumors. Although this may be interpreted as function in hemodynamic response, it does not necessarily imply function in retained vision. It was recently demonstrated using intraoperative electrical stimulation mapping during tumor resection that functioning motor, sensory, or language tissue can be located within the boundaries of infiltrative gliomas or surrounding infiltrated brain. Further correlative studies are needed to determine whether fMR imaging can be used preoperatively to map these areas and, therefore, be used for planning the extent of tumor resection and deciding whether to proceed with stereotactic biopsy or radical resection.

In one patient (Case 8), a complete congruous central homonymous hemianopsia corresponded to markedly reduced activation of the posterior portion of the contralateral primary visual cortex, which was compressed by an occipital pole meningioma. Sparing of the striate cortex adjacent to the parietooccipital–calcarine fissure junction corresponded to preservation of the peripheral fields in the same case. Representation of the central visual field at the striate cortex has created much discussion since the original publications of Inouye and Holmes and Lister, in which 25% of the surface area of the striate cortex was allocated to the central 15° of vision. Based on MR imaging studies in patients with occipital lesions, Horton and Hoyt expanded the area subserving central vision and reduced the area devoted to peripheral vision; these changes were in agreement with microelectrode recording studies in closely related nonhuman primate species. Functional MR imaging studies provided further spatial resolution of the central visual field representation, suggesting that the central 2° in the human area V1 extends over 30 mm of cortical distance. Although compression of the occipital pole does not necessarily imply dysfunctional cortical tissue, the extraaxial lesion in our patient extended deep into the occipital lobe, approximately 23 mm as measured on sagittal T1-weighted images. The posterior portion of the calcarine cortex corresponding to this distance was compressed anteriorly and did not show any functional response on fMR imaging, suggesting the expanded representation of central vision. The only functioning area was located anteriorly, close to the parietooccipital–calcarine junction and measuring approximately 14 mm on sagittal images.

Another interesting case in this series is that of a patient (Case 9) who presented with a congruous inferior quadrantanopia, with margins perfectly aligned on both the vertical and the horizontal meridians. Several explanations have been proposed for the quadrantic nature of visual field defects. They may be caused by a unilateral lesion involving either the upper or lower calcarine banks that does not extend beyond the projection line of the horizontal meridian along the base of the calcarine fissure. However, to create a perfect quadrantic field defect, this line needs to be accurately respected, which is quite improbable considering its winding shape and the infiltrative nature of most lesions in this location. Another theory proposed that localized lesions of the optic radiations corresponding to the upper or lower halves of the retina can cause selective injury to the upper or lower field quadrants. This possibility was questioned by Horton and Hoyt because of the spatial spread of visual fibers throughout the optic radiations and the fact that involvement of these structures typically produces field defects that have sloping borders, are not aligned along the horizontal meridian, and are often incongruous. Instead these researchers proposed that a lesion involving extrastriate cortical areas V2 and V3 is sufficient to create such field defects. This hypothesis was based on structural MR imaging evidence obtained in two patients with inferior quadrantanopsia and lesions involving the contralateral upper peristriate cortex, although the primary striate cortex was apparently spared. The explanation offered was that, because of the topographic arrangement of Areas V2 and V3, which concentrically surround Area V1, and the representation of the extrastriate horizontal meridian, which is shared by Areas V2 and V3 along their common border, a lesion in the extrastriate cortex crossing the V2–V3 border will damage tissue sharing common retinotopic coordinates. This would produce a sharp horizontal edge in quadrantic field defects as long as the lesion does not reach the representation of the horizontal meridian in V1. Our case provides functional evidence of this hypothesis and suggests that fMR imaging can objectively document such quadrantic field defects. The sharp homonymous lower quadrantanopsia of the patient corresponded to clearly diminished activation in the contralateral extrastriate areas involved by the lesion, whereas the primary calcarine cortex showed bilateral symmetric activation.

The only case without good agreement between findings on fMR imaging and those of perimetric examination was Case 10. Although bilateral symmetric activity was evident in the posterior calcarine cortex of this patient, clear asymmetry was detected in the imaging planes through the anterior calcarine cortex and the supracalcarine extrastriate cortical areas. According to this func-
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tional pattern, as well as the obvious involvement of optic radiations by prominent perilesional edema, an inferior incomplete field defect involving the peripheral vision would be expected in perimetric examination. However, the results on static perimetry of the central 26° were normal. This discrepancy could be explained by two reasons. First, it might be that residual visual function in the areas involved by the lesion was below the threshold of appearance as an area of activation in fMR imaging. Second, it is possible that a peripheral scotoma was insufficiently demonstrated on static perimetry due to the emphasis on evaluating the central visual fields in patients with retrochiasmatic lesions. The likelihood of the second possibility is enhanced by the fact that progressive visual loss was the presenting symptom of this patient.

Methodological Issues

Despite the increased number of fMR imaging studies in which the retinotopical organization and functional specialization of the visual cortex in normal volunteers has been explored, the scarcity of similar studies in patients does not yet allow estimation of the sensitivity of the method as an objective tool for diagnosis of visual field defects. Our results, as do those of others, show that this approach is promising, but evaluation of a larger population with various disorders of visual function is needed to establish the future role of fMR imaging in the diagnosis and clinical management of these patients. Several concerns regarding the relationship between neuronal activity and the fMR imaging signal remain to be elucidated. To what degree hemodynamic changes correlate spatially to regions of significant neuronal activity is still not known. A large proportion of the blood oxygen level–dependent signal has been attributed to draining veins at some distance from the site of activity that can potentially blur the borders between distinct regions corresponding to the projections of separate parts of the retina to visual cortex. Recent experiments indicate that vessels serving significantly less than 6 mm of visual cortex must contribute to the fMR imaging signal. Several groups using specially designed periodic visual stimuli and cortical unfolding algorithms realized localization of the fMR signal to within 1.1 mm in normal volunteers. Our experimental setting lacks the sophistication of these studies. We used a stimulus paradigm of great simplicity and required no volitional response from our patients in an effort to activate visual sensory systems solely and not increase the discomfort of the patients or lengthen the examination time. However, it is possible that more structured stimulus regimens aimed at smaller neuronal populations would result in more discrete areas of activation with better topographical correlation. Visual tasks can be performed more easily than other kinds of tasks when fMR imaging is used and the experimental condition is less demanding than conventional perimetry because the patients do not have to make decisions whether they can see the stimulus. However, reliable fixation is still essential and difficult to control when the patient is lying within the closed bore of the magnet. A method to be invented to control for eye movements and a more sophisticated stimulus delivery system has to be devised to present the stimulus accurately, irrespective of the patient’s ability to fixate. Similar systems are presently under development in our center.

For wide application of fMR imaging in the clinical setting, very rapid imaging is essential because patients with intracranial lesions are often limited in their ability to hold still during a long evaluation time. Furthermore, postprocessing techniques need to be not only reliable but also fast and easy to use so that functional information together with structural data are available to clinicians in time to make the correct diagnosis and to take the appropriate therapeutic course.

Conclusions

In this study we demonstrated that fMR imaging can be performed routinely, successfully, and reproducibly in patients who have visual abnormalities caused by intracranial space-occupying lesions. The identified patterns of activation in the visual cortex were consistent with the visual field deficits and with the traditional teaching of retinotopical representation. Thus, the technique provides essential information about the function–structure relationship specific to the individual patient and holds promise for diagnosis and therapy planning. Follow-up fMR imaging may also be useful in studies of recovery of function because it is noninvasive, provides good spatial resolution, and is potentially available at hundreds of facilities in which clinical MR imaging systems are used. Although the method is not being evaluated as a replacement for quantitative perimetry, validation of the fMR imaging data with those of perimetric examination suggests that it may provide an alternative diagnostic tool in the clinical assessment of visual function in patients who cannot undergo subjective perimetric examination. Further progress in image collection and processing techniques and use of more specific visual stimuli in selected patients with well-localized focal lesions promise to advance the understanding of the topography and functional specialization of the human visual cortex, both primary and of higher order.

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