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Activation of human primary visual cortex during visual recall: A magnetic resonance imaging study

(blood flow/blood oxygenation/human cognition/functional neuroimaging/echo-planar imaging)

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ABSTRACT **The degree to which the processes involved in visual perception and visual imagery share a common neuroanatomical substrate is unclear. Physiological evidence for localization of visual imagery early in the visual pathways would have important bearing on current theories of visual processing. A magnetic resonance imaging technique sensitive to regional changes in blood oxygenation was used to obtain functional activation maps in the human visual cortex. During recall of a visual stimulus, focal increases in signal related to changes in blood flow were detected in V1 and V2 cortex in five of seven subjects. These experiments show that the same areas of the early visual cortex that are excited by visual stimulation are also activated during mental representation of the same stimulus. Some of the processes used in topographically mapped cortical areas during visual perception may also be utilized during visual recall.**

The role of the cortical visual system in the processes underlying mental imagery has long been debated. An issue of particular interest concerns the degree to which the processes that are operative in visual perception are the same processes involved in the generation of visual imagery and whether visual representations are shared between imagery and perceptual processes (1–3). The finding that brain activity in relation to mental imagery occurs in at least some of the same locations as those seen during perception would be strong evidence that these two mental experiences share some common physiological mechanisms. Previous clinical and experimental studies provide support for spatial colocalization of these processes (4, 5). The clinical evidence is the finding that lesions to the occipital lobe in the human that result in disorders of visual perception can also result in visual imagery deficits (6, 7). The most compelling experimental evidence comes from functional neuroimaging studies demonstrating concordance between the neuroanatomical regions in occipital cortex activated by visual perception and imagery tasks in the same individual. Although the details of the results differ among experiments, all have found extrastriate visual areas that have been activated both when the stimulus is perceived and when it is recalled (8–11). In contrast, activation in striate cortex related to visual recall has been more difficult to demonstrate. This may result from the limited spatial and temporal resolution inherent in these techniques, so that precise response localization has not been possible. The one previous positron emission tomography study that investigated visual recall using tomographic measurements at higher resolution demonstrated small but statistically nonsignificant activations in the calcarine fissure (12). Furthermore, techniques that involve ionizing radiation exposure to subjects preclude the sort of repetitive studies that would provide greater sensitivity. Recent advances in magnetic resonance imaging (MRI) have demonstrated the feasibility of functional neuroimaging at a temporal resolution of seconds and spatial resolution of millimeters (13–17). This completely noninvasive procedure provides a powerful means to reinvestigate the question of the role of primary visual cortex in the generation of mental imagery.

The biophysical basis for the measurements made with functional MRI differs from those underlying other neuroimaging techniques. Transient changes in regional cerebral blood flow and oxygen extraction produce differences in the balance between paramagnetic deoxyhemoglobin and diamagnetic oxyhemoglobin in red cells (18–20). Changes in this balance, closely related to oxygen saturation, result in transient magnetic-susceptibility contrast that may be monitored directly and noninvasively by using fast MRI acquisition schemes. This method has been employed in the human brain to visualize activation of primary visual cortex by external sensory stimuli and sensorimotor cortex during voluntary movement (14–17). Using this technique, we report clear evidence that the primary visual cortex in the calcarine fissure can be activated during both visual perception and visual recall.

METHODS

Brain activation maps calculated with actual photic stimulation were compared with those obtained when the subject was later asked to recall the same visual stimulus. Seven normal subjects (five men and two women) ranging in age from 26 to 46 years underwent dynamic MRI. Studies were performed on a clinical 1.5-T whole-body MRI scanner (General Electric Medical Systems, Milwaukee, WI). To increase signal-to-noise ratio a 7.5-cm radiofrequency surface coil placed under the back of the head was used for signal reception. Cushions placed around the subject's head were used to minimize subject movement between scans. Activation studies were performed first with echo-planar imaging (21, 22) using a home-designed head (27-cm diameter) z-gradient coil. Acquisition parameters were as follows: echo time = 40 ms, repetition rate of 20 images per minute with an in-plane resolution of 2.5 × 2.5 mm^2. Images were obtained in coronal orientation, approximately perpendicular to the calcarine fissures (Fig. 1). Later, a conventional gradient-echo sequence was used [spoiled gradient-echo acquisition sequence in the steady state (GRASS) sequence, repetition time = 71 ms, echo time = 40 ms, flip angle = 40°, 10 images per minute] in two of our responding subjects. This sequence, which allows an in-plane resolution of 1.5 × 0.8 mm^2 and

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Abbreviations: MRI, magnetic resonance imaging; GRASS, gradient-echo acquisition in the steady state.

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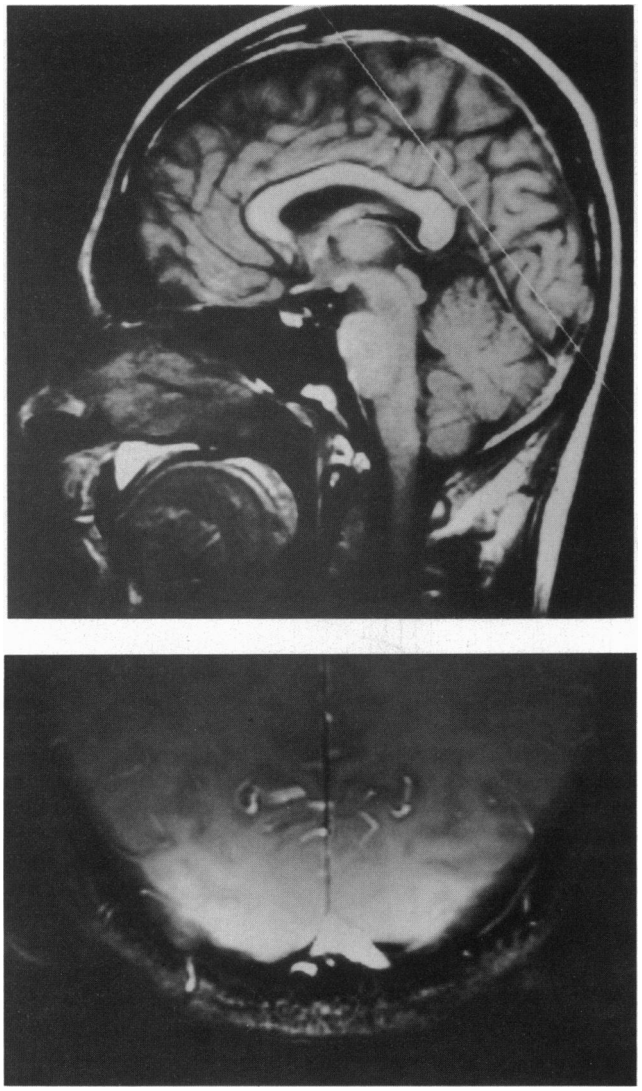

FIG. 1. (*Upper*) Sagittal T1-weighted MRI image. Such images were acquired for localization and selection of coronal (echo-planar imaging) and oblique-transverse (spoiled GRASS) slices. The obliquity of the transverse slices (line in *Upper*) was chosen to include a large part of the calcarine fissure. (*Lower*) This oblique slice is shown with high-resolution and T1-weighted contrast.

acquisition of images in an axial-oblique orientation, following the calcarine fissures (Fig. 1), gave a better identification of striate cortex. The visual stimulation was provided by light-proof binocular goggles (model S10VS, Grass Instruments, Quincy, MA) fitted with red light-emitting diodes geometrically arranged as two square patterns flashing at 16 Hz (23). With these goggles, the stimulus was diffuse and excited both visual fields within a large angle. The task sequence consisted of a single prestimulation of the visual cortex for 30 s during which time the subjects were asked to memorize the stimulus. The stimulus was then switched alternately on and off twice for periods of 24 s. Between these two actual photic stimulation episodes, the subjects were asked instead to recall the previously seen stimulus for 24 s, controlled by vocal command. The subjects were in complete darkness during the experiment and were asked to keep their eyes open for the duration of data acquisition.

RESULTS

Regions of interest (pixel-by-pixel irregular regions) were placed on the areas of maximum response during actual stimulation on the medial surface of the occipital lobe in the bank of the calcarine fissure. These areas of maximum response lay within 1–2 cm of the occipital pole, 0–2 cm from midline, which includes cortex within V1 and V2 regions (24, 25). This position may result from the diffusiveness of the stimulus. Moreover, the positron emission tomography study of retinotopic organization of V1 by Fox *et al.* (26) shows a similar localization of response using visual stimuli similar to our own. The exact position and shape of each region of interest were defined for each individual from the activation map calculated during actual stimulation. Typical size for regions of interest was 10–20 mm^2. The same regions of interest were used to determine the amplitude of the response during the recalled stimulus as well.

Fig. 2 displays the measured MRI signal changes in a region of interest in the striate cortex in one of our subjects during visual stimulation conditions and rest (this blank trial was given as a control without the instruction to imagine) (Fig. 2*A*) and when asked to recall the stimulus between the two actual stimulation episodes (Fig. 2*B*). During actual photic stimulation, each of our seven subjects showed a significant increase in MRI signal occurring bilaterally within the calcarine fissure (unpaired Mann–Whitney test, $P < 0.004$, with an average increase of 2.8 ± 1.1% (Table 1).

More interestingly, significant signal increases were also observed in five of our seven subjects in the same regions when the subject was recalling the stimulus (unpaired Mann–Whitney test, $P < 0.01$) (Table 1). However, the amplitude of the response to the recalled stimulus, when present, was not as large as the response to the actual stimulus (1.5 ± 0.6%, $n = 5$). In two of our subjects, otherwise unremarkable, no significant signal increase from baseline could be demonstrated during the recall condition, although a brief signal increase could be seen. However, we had no way to screen for attention and quality of the visual recall performance. Measurements within the visual cortex, but beyond V1 and probably V2, showed no significant response and very stable signal intensity over the acquisition period (variations of <0.2% of the mean signal intensity).

Activation maps, $A(x, y)$, were calculated on a voxel-by-voxel basis as the normal deviate statistical variable Z,

$$A(x, y) = \left[\sum_{j=1}^{n} J_j(x, y)/n - \sum_{i=1}^{m} I_i(x, y)/m\right]/\mathrm{SD}, \qquad [1]$$

in which the mean of n images (typically 5) acquired in actual or imagined stimulation state, $J(x, y)$, was compared with the mean of m "baseline" images, $I(x, y)$ (typically 5). SD is the standard deviation of the measurements. Functional activation images from one subject are shown in Fig. 3. Regions in the primary visual cortex showed highly localized changes of intensity during actual stimulation (Fig. 3*A*), in agreement with previous studies (13–17). The recalled stimulus activation map (Fig. 3*B*) clearly shows that primary visual cortex is also activated, but with less intensity, when the subject is asked to recall the stimulus.

DISCUSSION

These variations in MRI intensity directly reflect changes in the amount of intravascular deoxyhemoglobin. The overall increase in signal intensity during actual or recalled stimulation is believed to originate from the increase in blood flow and blood volume leading to an increase in oxygen supply (18–20) which overcomes the increase in oxygen extraction (27). In all subjects, the rise time of the response to activation patterns was several seconds, in agreement with optical imaging measurements of cortical signal changes associated with hemodynamic perturbations (28). In all cases, during the

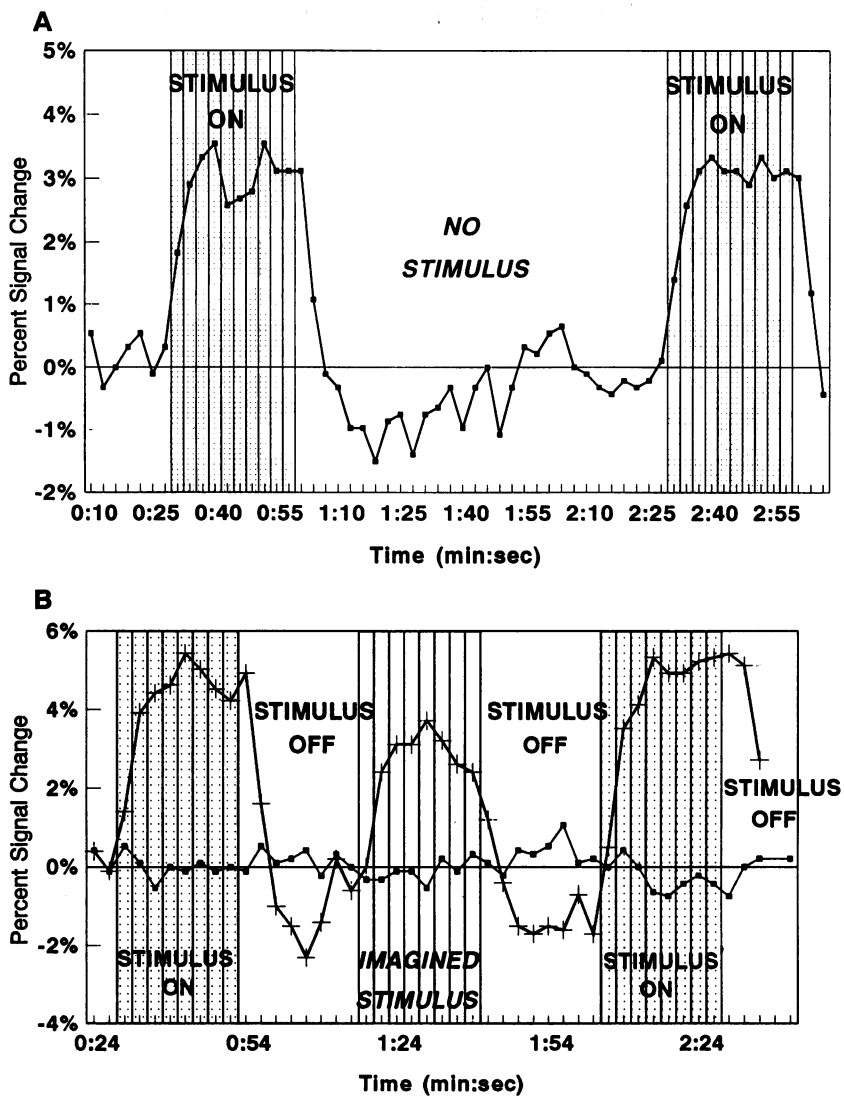

FIG. 2. Plot of MRI signal intensity relative changes versus time for primary visual cortex and a cortical region outside the striate cortex (echo-planar imaging data). In *A*, the subject was resting between the two actual stimuli (blank trial) (■, visual striate cortex). In *B*, the same subject was asked to recall the stimulus (+, visual striate cortex; ■, non-striate cortex).

period of rest immediately following actual and imagined stimulation the signal from the excited areas dropped below its resting value (Fig. 2). This origin of this drop in signal intensity below baseline level is still unclear but may represent the known undershoot in blood flow in the posterior cerebral artery following visual activation or continued higher metabolism and oxygen consumption by tissue after blood flow returns to baseline.

Table 1. Comparison of activation during actual and imagined stimulation

	Actual stimulation		Imagined stimulation	
Subject	% change from baseline	*P*	% change from baseline	*P*
1	3.6	0.004	1.4	0.004
2	1.1	0.004	0.5	0.01
3	1.9	0.0009	(0.04)	0.5 (NS)
4	2.5	0.0008	1.7	0.0008
5	4.1	0.0003	1.6	0.0007
6	2.4	0.002	(0.4)	0.1 (NS)
7	4.1	0.003	2.4	0.003
Mean	2.8 ± 1.1 (n = 7)		1.5 ± 0.6 (n = 5) 1.0 ± 0.9 (n = 7)	

We determined the regions of interest with the greatest change for the actual stimulus (coronal echo-planar imaging data). The activation ratios for the actual stimulation and the imagined stimulation were calculated according to Eq. 1. Statistical analysis was performed for each region of interest by using a Mann–Whitney test (unpaired, one-tailed) between the average signal in the baseline images and the average signal in the images acquired during actual or imagined stimulation. For comparison of response amplitudes, statistics for the recall condition are also given for the responding subjects only. NS, not significant.

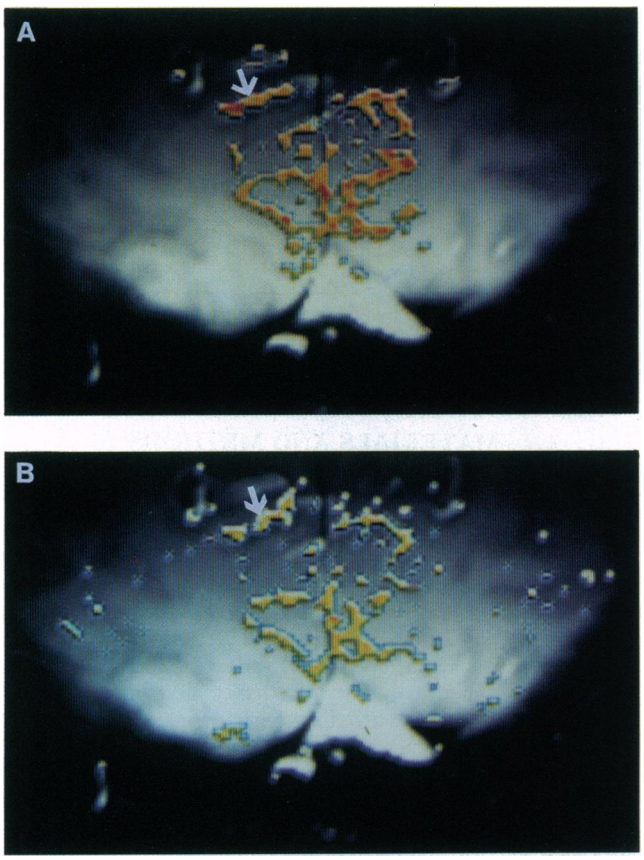

FIG. 3. Color activation maps of the brain during actual stimulation (*A*) and during imagined stimulation (*B*). These activation maps, $A(x, y)$, represent Z variable and are color coded (green for $1 < Z \leq 2$, yellow for $2 < Z \leq 3$, orange for $3 < Z \leq 4$, red for $Z > 4$) and overlaid on a gray-scale anatomical image (shown in Fig. 1*B*) for identification of activated structures. Images were obtained using the gradient-echo (spoiled GRASS) sequence with 0.8×1.5 mm^2 in-plane resolution. Slice thickness is 8 mm. Comparison of *A* and *B* shows that most of the structures activated by actual stimuli are also activated during recall of the stimuli. Note that pseudo-activation is also sometimes seen in accompanying feeding or draining large vessels (arrow).

Although there was little spatial variability among subjects in the response to stimulation, important differences in the magnitude of the response were observed (Table 1). However, repeated measurements indicated that intra-individual variations were also important for both the perceptual and the recall conditions. Such variations may reflect slightly different locations of the image slice and partial volume effects in different parts of the visual cortex. It is also worth noting that, in some of our subjects (data not shown here), the end of the measured response sometimes occurred too early or too late with respect to the expected end of the recall interval, as if the subject had difficulty in maintaining or terminating the recall task. The subject's attention may be an important factor to consider in the quality of the mental imagery. On the other hand, in recall responding subjects (Fig. 2), the blank control demonstrates that when the stimulus is omitted and the subject does not recall it, there is no activation of primary visual cortex due to afterimages or the subject's expectancy.

The present work demonstrates that changes associated with cognition, such as the mental representation of an imagined visual pattern, may be mapped completely noninvasively with unmatched combined spatial and temporal resolution by using MRI. Such high resolution has enabled us to demonstrate that some of the same cortical visual areas that are active during visual perception are also activated during short-term recall of the stimulus.

The ease and noninvasiveness of this technique, which can be repeated at will on the same subject, and the information about metabolism and hemodynamics which it may provide should significantly improve our understanding of the working brain during cognitive processes, in terms of both physiological research and clinical assessment.

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