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Topographical representations of mental images in primary visual cortex

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We report here the use of positron emission tomography (PET) to reveal that the primary visual cortex is activated when subjects close their eyes and visualize objects. The size of the image is systematically related to the location of maximal activity, which is as expected because the earliest visual areas are spatially organized[1–5]. These results were only evident, however, when imagery conditions were compared to a non-imagery baseline in which the same auditory cues were presented (and hence the stimuli were controlled); when a resting baseline was used (and hence brain activation was uncontrolled), imagery activation was obscured because of activation in visual cortex during the baseline condition. These findings resolve a debate in the literature about whether imagery activates early visual cortex[6–11] and indicate that visual mental imagery involves 'depictive' representations, not solely language-like descriptions[12–14]. Moreover, the fact that stored visual information can affect processing in even the earliest visual areas suggests that knowledge can fundamentally bias what one sees.

We tested 12 right-handed male volunteers in five conditions while local cerebral blood flow was monitored using PET. The resting baseline task followed the procedure and instructions of ref. 10. Subjects were blindfolded with a dark cloth, and told to close their eyes, relax and to 'have it black in front of their mind's eye'. Such an uncontrolled rest state probably corresponds to many states that do not preclude some form of imagery. The other four conditions used the same type of auditory stimuli, which either were listened to passively or used as prompts to form images of previously memorized pictures (Fig. 1). Subjects received three imagery conditions, each of which consisted of four practice trials and 24 experimental trials. The imagery conditions differed only in the size at which images were formed, at 0.25, 4.0 or 16.0 degrees of visual angle. We compared activation in the three imagery conditions with each of the two baselines.

Here we focus entirely on activation in the medial occipital region. First, when activation in the resting baseline was subtracted from the imagery conditions the only occipital activation was in area 19 (only for medium-sized images), including the parieto-occipital sulcus and precuneus. This is very similar to the region reported previously with this baseline condition[15]; the *X Y Z* Talairach coordinates were −20 −68 28. Second, Fig. 2 and Table 1 present the results of subtracting activation in the listening baseline from the three imagery conditions; we focus here on activation within 15 mm of the midline (the smoothness parameter used in analysis was 14 mm) in the occipital lobe, and consider only activations that had *Z* scores greater than 3.0. Locations are specified using the stereotactic coordinate system[16]. As is evident, we find very posterior activation only for the small images, and very anterior activation only for the

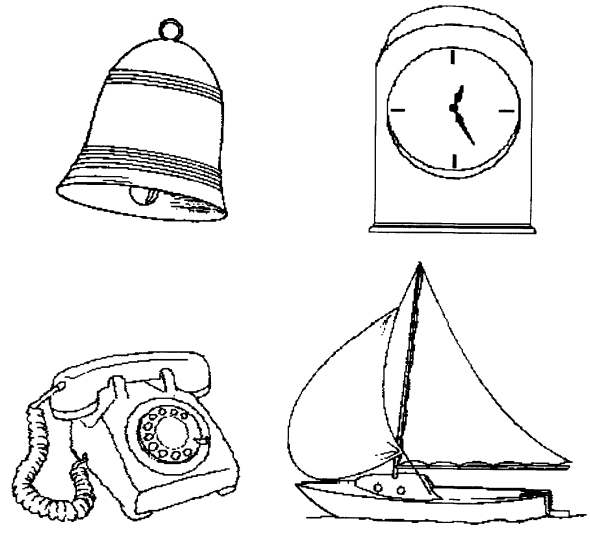

FIG. 1 Stimuli used in four of the five conditions. In the listening baseline condition, subjects received trials of the following sort. First they heard the name of a common object (such as 'anchor'), and 4 s later heard a spatial comparison term (such as 'right higher'), and then responded. One second later, another trial was presented. Subjects were told to close their eyes and respond as quickly as possible on hearing the comparison terms, alternating feet from trial to trial; they were told not to visualize anything during these 28 trials. The order of this baseline and the resting baseline was counterbalanced. Half of the subjects received the resting baseline at the beginning of the experiment, and half received it at the end of the experiment; in both cases, the listening baseline always preceded the first imagery condition (this was necessary because once subjects knew the meanings of the cues, they would be unlikely to listen passively). Immediately before the imagery conditions, subjects studied 28 pictures, adapted from ref. 19, as illustrated here. Each picture appeared on the screen when its name was read aloud by the computer. After memorizing the pictures, four spatial judgements were defined; for example, 'right higher' required them to decide whether the rightmost point was higher than the leftmost point. Pictures of objects (not used in the actual experiment) illustrated 'yes' and 'no' judgements. At the beginning of each set of imagery trials, subjects memorized the size of a square piece of cardboard taped to the screen. Subjects heard the same type of stimuli used in the listening baseline condition, but now closed their eyes and visualized each named picture at the size of the square. Subjects were urged to visualize each object at the correct size and to maintain the image at this size. When they heard the spatial comparison term, they evaluated the imaged picture as quickly and accurately as possible. Four different sets of 28 pictures were used, and counterbalancing ensured that the names and associated spatial comparison terms occurred equally often in the listening baseline and in each imagery condition in each order, and that the spatial comparison terms and yes/no responses appeared equally often in each condition.

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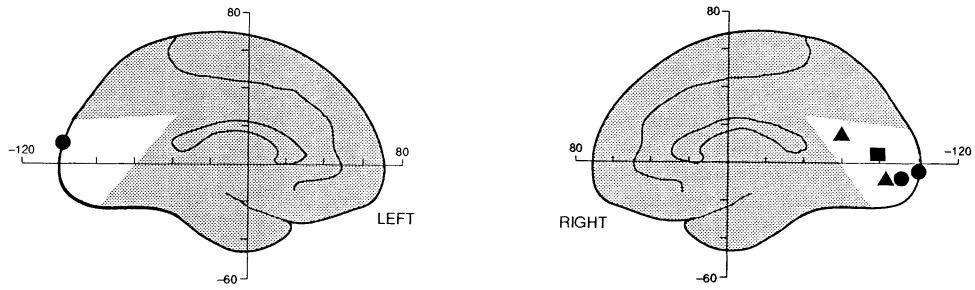

FIG. 2 Left and right PET results in medial occipital cortex; points indicate the most activated pixel using statistical parametric mapping[20] with $Z>3.0$. Small imagery (●), medium imagery (■), and large imagery (▲), all minus listening baseline. Activation for the smallest images was very posterior, −102 mm from the anterior commissure for left- and right-hemisphere area 18, which included area 17 in the right hemisphere, as well as −88 mm in a more medial portion of area 18. Activation for medium images was −79 mm in area 17 in the right hemisphere. Finally, activation for the largest images was −60 mm in a region that includes area 17 and the precuneus, and −83 mm in another part of area 17 and 18, which may have been activated by internal details of the images. The PET machine was a GE Scanditronix PC4096 15-slice whole-body tomograph in its stationary mode (see ref. 21). Contiguous slices were 6.5 mm apart (centre-to-centre; the axial field was 97.5 mm); the axial resolution was 6.0 mm full width at half maximum. Each subject was fitted with a custom moulded face mask (TRUE SCAN, Annapolis, MD), and his head was aligned relative to the CM (cantho-meatal) line. Nasal cannulae were connected to a radiolabelled gas inflow, and a face mask, attached to a vacuum, was placed over the subject's nose. On each PET run, 20 measurements were taken: the first 3 were 10 s and the remaining 17 were 5 s long. The PET protocol was as follows: (1) the camera acquisition program was started (which measured residual background from past studies); (2) stimulus presentation began 15 s later, and the subject began the task; (3) ^{15}O-CO_2 gas was administered 15 s after this; and (4) 60 s later, scanning ended and the gas was stopped (for additional details, see experiment 2 of ref. 7).

largest images, with medium images activating intermediate regions. Inspection of the scans from each individual indicated that activation was in fact in the primary visual cortex.

We next compared the two baselines by subtracting blood flow during the listening baseline from that during the resting baseline. We found more blood flow during the resting baseline in area 17 (primary visual cortex), $t(11)=3.94$, $P=0.002$ (two-tailed) (Fig. 3). To examine the possible effects of practice in both baselines, we compared only the first condition for each subject, and found greater activation in area 17 during the resting baseline, $F(1, 10)=5.65$, $P=0.039$; we also compared only the second baseline condition for each subject, and again found more activation in area 17 during the resting baseline, $F(1, 10)=7.06$, $P=0.024$. Moreover, when baseline and order were considered in a single analysis of variance, there was no interaction between the two factors, $F<1$.

TABLE 1 Data showing blood flow under experimental conditions

	X	Y	Z	Z-score
(*a*) Small-sized images − listening baseline				
Left hemisphere regions				
Area 18	−13	−102	8	3.20
Right hemisphere regions				
Area 18/17	15	−102	−4	3.40
Area 18	6	−88	−8	3.42
(*b*) Medium-sized images − listening baseline				
Right hemisphere regions				
Area 17	8	−79	4	3.00
(*c*) Large-sized images − listening baseline				
Midline				
Area 17*	2	−83	0	3.25
Area 18*	−4	−83	−8	3.30
Precuneus/17	−2	−60	16	3.09
(*d*) Resting baseline − listening baseline				
Left hemisphere regions				
Area 18/Cuneus	−7	−102	8	3.79
Area 17*	−11	−69	8	3.21
Area 18*	−6	−67	4	3.39
Right hemisphere regions				
Area 19/18	12	−92	24	3.65
Area 18	6	−81	0	3.60

Blood flow in the listening baseline condition was subtracted from blood flow in the small (*a*), medium (*b*), and large (*c*) visual mental imagery conditions and from blood flow in the resting baseline condition (*d*; $Z>3.0$).

*Part of the same continuous area of activation.

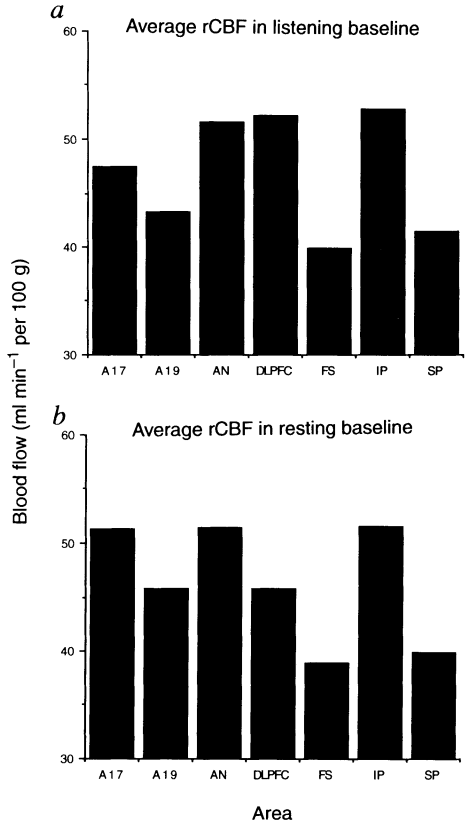

FIG. 3 Blood flow relative to the global mean for different brain areas during the two baseline conditions. Each brain was normalized to the same value, 50 ml min^{-1} per 100 g, and the relative flows in area 17 and other cortical areas were analysed relative to the mean. Activation in area 17 (A17) was average in the listening baseline (*a*), but above average in the resting baseline (*b*). The activation in area 17 was compared to the mean blood flow in the previously activated regions[7] of area (A19), the angular gyrus (AN), dorsolateral prefrontal cortex (DLPFC), the fusiform gyrus (FS), the inferior parietal lobe (IP), and the superior parietal lobe (SP), not the normalized value of 50 ml min^{-1} per 100 g; thus, the mean blood flow in A17 (47.4) is not different ($F<1$) from the mean blood flow in those other brain areas (46.8) during the listening baseline, whereas the mean blood flow in A17 (51.3) is higher than that in the other brain areas (45.6) during the resting baseline ($F=59.8$; $P=0.0001$). Most of the same extrastriate regions were activated during each of the three sizes, but not all such areas were activated in common.

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We also considered the variability associated with each baseline, and found comparable variances (5.91 and 7.65 for the listening and resting baselines, respectively). Moreover, we found more blood flow in area 17, relative to the global mean, than in the average of the other cortical areas we examined in the resting baseline condition (consistent with ref. 17), but not in the listening baseline condition, (see Fig. 3).

The present findings do not imply that visual images are stored in primary visual cortex. About 32 cortical areas have now been shown to process visual information in the macaque monkey brain, and the spatially organized early areas not only send information to areas later in the processing stream, but also receive information from those later areas[18]; indeed, the feedback connections are of comparable size to the feedforward connections[4]. Thus, it is possible that higher-level areas that actually store visual information can evoke activity in earlier areas.

The fact that the size of the image systematically affected the locus of activation rules out the possibility that hypometabolism in visual cortex artefactually produced the appearance of imagery activation when the listening baseline was used. Moreover, the use of three sizes eliminates the possibility that different sizes activated different brain areas (as could have occurred in ref. 7, in which two sizes were examined, and which also did not include any baseline conditions but rather examined activation only relative to the other size, and thereby did not allow precise localization of activity). Finally, the relatively high occipital activation during the resting baseline explains why previous researchers using this baseline failed to find evidence that imagery activates area 17. By using three sizes of pictures of common objects, comparing them to a baseline that had the same physical stimuli (but different, non-imagery, mental processing), and showing that the three sizes induce activation along a continuum (but only when we compare them to the listening baseline), we circumvent the problems inherent in the earlier designs, thereby convincingly demonstrating that visual imagery activates primary visual cortex. □

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Recovery from spinal cord injury mediated by antibodies to neurite growth inhibitors

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THERE is little axonal growth after central nervous system (CNS) injury in adult mammals. The administration of antibodies (IN-1) to neutralize the myelin-associated neurite growth inhibitory proteins leads to long-distance regrowth of a proportion of CNS axons after injury[1–5]. Our aim was: to determine if spinal cord lesion in adult rats, followed by treatment with antibodies to neurite growth inhibitors, can lead to regeneration and anatomical plasticity of other spinally projecting pathways; to determine if the anatomical projections persist at long survival intervals; and to determine whether this fibre growth is associated with recovery of function. We report here that brain stem–spinal as well as corticospinal axons undergo regeneration and anatomical plasticity after application of IN-1 antibodies. There is a recovery of specific reflex and locomotor functions after spinal cord injury in these adult rats. Removal of the sensorimotor cortex in IN-1-treated rats 2–3 months later abolished the recovered contact-placing responses, suggesting that the recovery was dependent upon the regrowth of these pathways.

Young adult (6–8 weeks of age, 150–200 g) Lewis rats (N=45) received a mid-thoracic microsurgical spinal cord lesion (over hemisection, HX) interrupting the dorsal columns and corticospinal axons bilaterally and the lateral and ventral funiculi and intervening grey matter unilaterally as described previously[6–8]. At the time of spinal cord surgery, hybridoma cells secreting IN-1 antibody (N=23) or secreting control (horseradish peroxidase, HRP) antibodies (N=22) were placed into the parietal cortex[1,2]. Small slowly growing tumours formed under immune suppressive treatment (cyclosporin A) and secreted antibodies that reached the spinal cord through the cerebrospinal fluid[1,2]. Cyclosporin A was discontinued after two weeks; this led to the resorption of the hybridoma tumours within about a week. Additional rats received the spinal cord lesion without any further treatment (N=16, HX). Unlesioned age-matched rats (N=16) served as controls. Spinal cord lesions and IN-1 treatment were performed in Zurich, rats were number coded and randomly mixed groups were shipped to Washington and analysed without knowledge of treatment history. Rats were allowed to recover for 4–6 weeks before behavioural training and qualitative and quantitative analysis of reflex and locomotor function[6,7,9,10]. At the completion of the behavioural analysis (3–4 weeks later), regeneration of corticospinal axons was assessed using anterograde tracing with horseradish peroxidase[1–3,11]. Serotonergic and noradrenergic pathways were visualized immunocytochemically[10,12,13]. The spinal cord lesion site was reconstructed serially for each of the animals. Animals in which the transverse extent of the lesion was smaller or larger than intended were excluded from the analysis. In order to determine the extent to which the regrowth of corticospinal axons contributed to the recovery of function in IN-1 treated animals, we removed the sensorimotor cortex bilaterally in a group of animals 3 months after the initial spinal cord injury (HX+IN-1, N=5;

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