FUNCTIONAL MR imaging is now widely used for the mapping of sensorimotor cortex areas in presurgical examination of patients with rolandic lesions.\textsuperscript{1,16,17,19} This method of localization relies on the indirect effect of neuronal activity on local blood flow. Increased neuronal activity produces an increase in local blood flow that exceeds the oxygen utilization, thereby decreasing paramagnetic deoxyhemoglobin in favor of diamagnetic oxyhemoglobin. This induces changes in the magnetic susceptibility of blood that produce the BOLD contrast observed in fMR imaging.\textsuperscript{1,16} One of the crucial limitations encountered in fMR imaging–based brain mapping is the inability to localize with high reliability the cortical area involved in the sensory task. The difficulty in interpreting an fMR imaging signal stems from the fact that although the hemodynamic response originates primarily in the microvasculature of the activated cortical area, the signal is continuously transported into the venous network.\textsuperscript{3,8,14}

It seems obvious that signals from the microvasculature are highly specific to activated areas, whereas BOLD contrast from the venous network arises not only from the activated area but from the whole territory drained by the veins. Evidence has been found that BOLD contrast intensity is dependent on vessel diameter, suggesting that it might be possible to distinguish microvasculature and venous drainage fMR imaging signals by using activation ratios for a given stimulation.\textsuperscript{4,9,12} However, because the microvasculature and venous network constitute a continuous structure, the determination of the threshold for fMR imaging signals useful for the attribution of a function to an evoked area is in practice empirical. Nevertheless, different kinds of sensory stimulation such as those used for fMR imaging\textsuperscript{6,10,14,16,18,19,21,22} (brushing, scraping, or vibrating stimulation) or for magnetoencephalography or elec-

Role of the mode of sensory stimulation in presurgical brain mapping in which functional magnetic resonance imaging is used

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Object. The aim of this study was to evaluate different types of sensory stimulation used to distinguish between microvasculature and venous drainage on functional magnetic resonance (fMR) images with blood oxygen level–dependent (BOLD) contrast.

Methods. Seven volunteers received three sensory stimulations. One consisted of small discontinuous automated pokes to the ventral aspect of the right thumb. The other two were delivered by the investigator, who vigorously brushed the ventral aspect of the right thumb either alone or in combination with the thenar region. Seven contiguous axial slices of the head were acquired using echoplanar fMR imaging during each mode of stimulation. Boxcar analysis and Student’s t-test were performed. Cluster analysis was used to determine significant differences between rest and activation phases.

The major findings were 1) that a discontinuous sensory stimulation involving a small skin area was able to evoke a limited activated area in the postcentral gyrus with a low activation index (AI [2%]); 2) that this limited activated area was included in the activated area elicited by the continuous sensory stimulations; and 3) that this also evoked multiple activated areas exhibiting AIs of either approximately 2% or greater than 5%. This indicated that the limited discontinuous tactile stimulation evoked a BOLD-contrast fMR image essentially of microvasculature, whereas the more extensive continuous stimulations evoked a BOLD-contrast fMR image in both microvasculature and venous drainage.

Conclusions. Different sensory stimulations are necessary to differentiate primary sensory cortex from venous drainage for presurgical brain mapping.

KEY WORDS • sensory stimulation • functional magnetic resonance imaging • brain mapping • activation index
troencephalography\textsuperscript{5,7,11,20} (discontinuous vibrating, electrical, or mechanical stimulation) might generate a range of hemodynamic local responses leading to more or less migration of BOLD contrast out of the microvasculature of the activated cortical area. Thus there may exist optimum experimental conditions that induce only limited propagation of BOLD contrast to venous drainage.

The aim of our study was to compare various types of sensory stimulation for their tendency to elicit BOLD-contrast fMR imaging conditions that allow distinction between microvasculature and venous drainage. For this purpose, we analyzed cortical activation in healthy volunteers who received three different sensory stimulations, a discontinuous one and two continuous stimulations that consisted of brushing two different-sized areas of skin.

**Clinical Material and Methods**

Healthy adult volunteers (three women and four men) ranging in age from 25 to 46 years were studied. Informed consent was obtained from all participants before the study.

A 1.5-tesla MR imager (Signa; General Electric Medical Systems, Milwaukee, WI) with echoplanar gradients was used. Each volunteer was positioned supine in the machine and wore earplugs. Sagittal T\textsubscript{1}-weighted MR images were acquired for anatomical localization. For fMR image acquisition, seven contiguous axial slices (5 mm thick) 35 mm above and parallel to the anterior commissure–posterior commissure line were used. Acquisition parameters for echoplanar single-shot images were as follows: pulse angle 90\degree, TE 50 msec, TR 3000 msec, field of view 28 × 21 cm, matrix 96 × 64. Image acquisition started with Slice 1, followed by Slices 3, 5, 7, 2, 4, and 6; 70 images were obtained in this manner for each of the seven slices in each of the three series corresponding to the different stimulations. For each of these series 490 images were acquired in 3 minutes and 30 seconds. Fast spin-echo images were then acquired at the same site with TR 400 msec, TE 20 msec, field of view 28 × 21, matrix 256 × 256 for high-resolution anatomical localization.

**Paradigm and Tactile Stimulation**

For each volunteer, three fMR imaging series of 490

![Fig. 1. Functional MR imaging activation maps evoked by ST1, ST2, and ST3 in one representative volunteer for Slices 1 through 7. The first slice is situated 35 mm above and parallel to the anterior commissure–posterior commissure line. Each slice is 5 mm thick. Arrows indicate the location of ROIs with the same coordinates in the three stimulation series.](image-url)
Sensory stimulation for presurgical brain mapping

**TABLE 1**

<table>
<thead>
<tr>
<th>Vol No.</th>
<th>ST1</th>
<th>ST2</th>
<th>ST3</th>
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<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>none</td>
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</tr>
<tr>
<td>2</td>
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<td>7</td>
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Activated Area (mm\(^2\)) for Slices 1–7

- ST1
- ST2
- ST3

Data Analysis

The echoplanar images were analyzed using commercially available software (Functool, version 2.0.18; General Electric Medical Systems). The matrix size was zero-filled to 128 × 128 before analysis. First, the series were viewed in cine mode to eliminate motion artifacts. Using a box-car model, a cross-correlation analysis between signal time course and the paradigm was performed. The first two images of each series were eliminated. Then for each slice, the images obtained during the averaged resting period (38) and those obtained during the averaged activation period (30) were compared using Student’s t-test on a pixel-by-pixel basis (p < 0.001). The cross-correlation coefficient threshold was set at 0.45 and a minimum number of four pixels per ROI (< 19.1 mm\(^2\)) was selected for cluster analysis. Time courses were analyzed to ensure that activation followed and did not precede the stimulus, and to calculate the mean signal change between conditions. For further analysis, we used the ROI area (square millimeters) and an AI, which was calculated by averaging the last seven of 10 values for each phase, subtracting the corresponding average resting phase value from the average activation phase value, and dividing the result by the resting value (expressed as a percentage).

Functional results were superimposed on the fast spin-echo images acquired in the same plane as the echoplanar images.

**Results**

Figure 1 shows activation maps yielded by the three different kinds of stimulation in a representative volunteer. In the postcentral gyrus (Fig. 1, arrows), ST1 evoked activated areas in five of seven volunteers, whereas ST2 and ST3 evoked activated areas in all volunteers (Table 1). Moreover, ST2 and ST3 evoked activated areas with an AI higher than 5%, which was never observed with ST1 (Table 2), indicating venous drainage involvement in upper slices after ST2 and ST3. Figure 2 shows that total activated areas per slice, with an AI less than 5%, were greatly increased for both ST2 and ST3 with respect to ST1, especially in Slices 2 to 4, the only sections in which ST1 activation occurred. The total activated area was also significantly increased for ST3 with respect to ST2 in Slices 4 to 7 (Fig. 2). However, with the number of ROIs classified in four categories according to the AI (Table 2), it was noted that not only activated areas with an AI greater than 5% but also with an AI between 3.75% and 5% were evoked by ST2 and ST3 but not by ST1.

In the five volunteers who exhibited activation areas evoked by ST1 in the postcentral gyrus, activated areas located images were obtained with a common paradigm and three different stimulation types. The paradigm consisted of seven alternating rest and activation phases of 30 seconds beginning with a rest phase (four resting phases and three activation phases), which were studied on seven slices by obtaining 10 images per slice per phase. Each volunteer underwent three types of tactile stimulation in one session. The ST1 was a pulsed poke delivered to the ventral side of the patient’s right thumbtip by using a circular plunger 6 mm in diameter driven by 40-msec pulses of air pressure (80 psi) delivered from outside the MR imaging room through a pneumatic tube and held by an adjustable clamp with foam cushioning to keep pressure constant (BTi; Biomagnetic Technologies Magnes, Aachen, Germany). The rhythm of stimulation was 1 Hz. The ST2 was performed by the investigator, who scraped the ventral surface of the right thumbtip with a small brush by using vigorous back-and-forth strokes parallel to the thumb. The ST3 was also performed by the investigator, who scraped the ventral surface of the patient’s right thumbtip with a small brush by using vigorous back-and-forth strokes parallel to the thumb. The ST3 between 350 and 450 mm\(^2\), and by ST3 between 1000 and 1500 mm\(^2\).

Data Analysis

In the five volunteers who exhibited activation areas evoked by ST1 in the postcentral gyrus, activated areas located

**TABLE 2**

Number of ROIs observed in all slices for all volunteers, divided into four classes depending on AI

<table>
<thead>
<tr>
<th>AI (%)</th>
<th>ST1</th>
<th>ST2</th>
<th>ST3</th>
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<tbody>
<tr>
<td>≤2.5</td>
<td>6 (Slices 2–4)</td>
<td>25 (Slices 1–6)</td>
<td>19 (Slices 1–7)</td>
</tr>
<tr>
<td>&gt;2.5–≤3.75</td>
<td>1 (Slice 3)</td>
<td>13 (Slices 1–7)</td>
<td>14 (Slices 1–7)</td>
</tr>
<tr>
<td>&gt;3.75–≤5</td>
<td>none</td>
<td>4 (Slices 6 &amp; 7)</td>
<td>5 (Slices 1–7)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>none</td>
<td>1 (Slice 7)</td>
<td>5 (Slices 3–7)</td>
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* The slices in which the activated ROIs were observed are in parentheses.
AIs were in the same range for ST1 and ST2 (2.1 ± 0.2% for ST1 and 2.5 ± 0.3% for ST2). Values are expressed as the means ± standard error of the mean for the seven volunteers. * p < 0.05 for ST2 and ST3; # p < 0.05 for ST3.

The major findings of our work were 1) that a discontinuous sensory stimulation (ST1) involving a small skin area can evoke a limited activated cortical area in the postcentral gyrus with a low AI (2%); 2) that this limited activated area was included in the activated areas evoked by the continuous sensory stimulations ST2 and ST3; and 3) that this also evoked multiple activated areas in upper slices with an AI of approximately 2% or greater than 5%.12 This suggested that the discontinuous tactile stimulation evoked a BOLD-contrast fMR image essentially of large blood vessels.12 Thus, we used cluster size as an index of functional areas projecting to S-1, according to somatotopic maps.14,15 However, in addition to these differences between ST1 and ST2 in activated cortical area, with ST1 we were unable to evoke cortical BOLD contrast from large vessels. Two hypotheses could explain such results: 1) the difference in stimulated skin area; and 2) the discontinuous compared with the continuous sensory stimulation. In fact, we believe that both factors play a substantial role. A discontinuous stimulation pattern (1 Hz) could induce a less effective summation of the individual hemodynamic responses, thus lowering the effective block response of the active phase of 30 seconds. As we observed, this induces a smaller activated area, a lower AI, and less migration of BOLD contrast to the venous network.

The challenge for the development of fMR imaging in preoperative brain mapping depends on our capacity using fMR imaging to localize with high reliability functional areas in the vicinity of lesions. For the interpretation of activation maps, one should note that the fMR imaging signal originates from an essentially indirect indicator of neuronal activity, that is, the hemodynamic response.4,6,9,12 Indeed, the complexity of the venous network, added to the fact that multiple activated areas are generally evoked by stimulations, means that caution must be used when interpreting the functional involvement of activated areas.8,12 From a histological point of view, it is obvious that such functional information is provided by the capillaries in the vicinity of the stimulated neurons. Because BOLD contrast higher than 3.75% or 5% probably indicates draining veins rather than functional areas, it is essential to discriminate between these two types of signals. The most accurate MR imaging technique for determining areas of
Sensory stimulation for presurgical brain mapping

active cortex is probably to look at the initial early desaturation signal. However, this is not possible with our 1.5-tesla machine. In that context, our results indicate that the key to security in presurgical mapping could be the use of not only robust continuous sensory stimulation involving large skin areas but also discontinuous sensory stimulation of limited skin areas. The robust continuous stimulation gives access to the functional area as well as the venous network, whereas the restricted functional area is strongly delineated by the discontinuous sensory stimulation.

Conclusions

Although fMR imaging addresses the question of the delineation of functional areas before surgical procedures, it appears that different types of sensory stimulation are necessary to differentiate primary sensory cortex from the venous draining network.

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References


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