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Combining fMRI and MEG increases the reliability of presurgical language localization: A clinical study on the difference between and congruence of both modalities

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To avoid neurological impairment during surgery near language-related eloquent brain areas, we performed presurgical functional brain mapping with functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG) in 172 patients using language tasks. For MEG localizations, we used either a moving equivalent-current dipole fit or a current–density reconstruction using a minimum variance beamformer with a spatial filter algorithm. We localized the Wernicke and Broca language areas for every patient. We integrated the results into a frameless stereotaxy system. To visualize the results in the navigation microscope during surgery, we superimposed the fMRI and MEG findings on the brain surface. MEG and fMRI results differed in 4% of cases, and in 19%, one modality showed activation but not the other. In the vicinity of large gliomas, the BOLD (blood oxygenation level-dependent) effect was suppressed in 53% of our patients. Of the 124 patients who had surgery, only 7 patients (5.6%) experienced a transient language deterioration, which resolved in all cases. We used MEG and fMRI to show different aspects of brain activity and to establish validation between MEG and fMRI. We conclude that measurement by both MEG and fMRI increases the degree of reliability of language area localization and that the combination of fMRI and MEG is useful for presurgical localization of language-related eloquent cortex.

Keywords: Magnetoencephalography; Functional magnetic resonance imaging; Language; Neuronavigation; Wernicke; Broca

Introduction

During surgery near eloquent brain areas, a detailed knowledge about the topographic relation of the lesion to the functional brain area is crucial to avoid causing postoperative neurological deficits. Unlike the primary sensorimotor cortex, the cortex subserving language comprehension in the human brain shows high interindividual variability (Ojemann et al., 1989). Language-specific areas may also shift from their original positions because of lesions (Duffau et al., 2002; Grummich et al., 2005). Furthermore, normal sulcal anatomy is often not recognizable because of tumor growth. These situations require methods for localizing language-specific areas before surgery to avoid disastrous postoperative results.

The classical procedure for language localization is intraoperative electrical stimulation mapping in awake patients (Penfield, 1959; Berger and Rostomily, 1997; Duffau et al., 2003b; Reulen et al., 1997). In recent years, however, two noninvasive techniques have been found for presurgical language localization: magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI). Studies using either fMRI or MEG successfully lateralize and even localize language activity (Hinke et al., 1993; Salmelin et al., 1994; Cuenod et al., 1995; Desmond et al., 1995; Binder et al., 1996; Simos et al., 1998; Papanicolaou et al., 1999; Kober et al., 2001; Grummich et al., 1994).

MEG- and fMRI-derived information about the extent of cortical involvement in language function can also be used in conjunction with image-guided surgery during resection of lesions adjacent to eloquent brain areas under general anesthesia (Ganslandt et al., 2004). The use of preoperative functional brain mapping with image-guided surgery provides important information for (1) indicating hemispheric dominance; (2) showing the risk of a surgical procedure; and (3) planning the surgical approach.

In this study, we present our experience with localization of the language-related cortex in a large series of patients who underwent

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preoperative language mapping with MEG and fMRI. We compare the language localizations from both methods and discuss the differences between the MEG and fMRI results.

Methods

We performed MEG measurements simultaneously over both hemispheres with a dual-sensor 74-channel (2 × 37 channels) biomagnetometer system (Magnes II, 4-D Neuroimaging, San Diego, CA, USA) in a magnetically shielded room. To minimize movement artifacts, we fixed the patient's position with a vacuum body cushion and stabilized the head comfortably between the two MEG sensors. We recorded a single-channel electrocardiogram (ECG) simultaneously. For each stimulation paradigm, we recorded 15–30 min of data at a sampling rate of 520.8 Hz, with an online high-pass filter of 0.1 Hz and antialiasing filter of 200 Hz. We also filtered the data with a high-pass filter having a 6-dB edge-frequency between 0.3 and 1 Hz to eliminate breathing artifacts or other slow wave disturbances. We manually discarded motion and eye movement artifacts during visual inspection of the raw epochs after data acquisition. If the MEG signal was contaminated by the magnetocardiogram, we subtracted the appropriate amount from the raw data using the ECG channel as a template.

For fMRI, we used a 1.5-T MR scanner with echo planar imaging (Magnetom Sonata, Siemens Medical Solutions, Erlangen, Germany). Measurements were done with 25 slices of 3 mm thickness and resolution TR = 2470, TE = 60. Stimulation was done in a block paradigm ("boxcar") with 180 measurements in 6 blocks. We performed 30 measurements in an activation condition during which the patient was instructed to perform a language task; we alternated these with 30 measurements in a resting condition. By means of a mirror attached to the head coil, the patient observed words or pictures projected onto a screen. For motion correction, we applied an image-based prospective acquisition correction applying interpolation in the k-space (Thesen et al., 2000). We constructed activation maps by analyzing the correlation between signal intensity and a square wave reference function for each pixel according to the paradigm. Pixels exceeding a significance threshold (typical correlations above a threshold of 0.3 with $P < 0.000045$) were displayed if at least 6 contiguous voxels built a cluster to eliminate isolated voxels. We aligned the functional slices to MPRAGE (magnetization prepared rapid acquisition gradient echo) images using 160 slices of 1-mm slice thickness and resolution obtained from the same patient position.

Stimulation paradigm

For all patients, we used visual stimulation. The primary visual cortex is more distant from most relevant cognitive areas than is the primary auditory cortex, and thus recordings over the Broca and Wernicke language areas are less disturbed by activity from the primary visual cortex than would be the case for auditory stimulation. Therefore, with visual stimulation, a better signal-to-noise ratio can be achieved. For comparison, we studied three patients using acoustic stimulation, where subjects listened to a story.

We developed several stimulation paradigms for localizing the Broca and Wernicke areas. Each patient participated in two different stimulation paradigms during MEG measurements and in 3 or 4 different paradigms during fMRI measurements. The paradigms were selected according to tumor location and adapted to the individual mental abilities of each patient. For each paradigm, about 800 stimuli were presented. The length of the interstimulus interval was adjusted according to the patient's abilities, varying between 1200 ms and 2300 ms for MEG measurements and between 900 ms and 2000 ms for fMRI measurements. The duration of the stimulus presentation was between 600 and 2000 ms (300 ms less then the interstimulus interval) to avoid overlap of the stimulus off-response with the late language activation. We asked the patients to perform the tasks as quickly as possible immediately upon stimulus presentation and to perform the task silently to avoid artifacts from mouth movement.

Our stimulation tasks have been described previously (Kober et al., 2001). In the reading task, we presented 300 mixed nouns (concrete or abstract) and asked the patients to read them and to understand the meaning. In the sentence-reading task, we presented 61 sentences with 4–7 words displayed and asked the patients to read and understand the meaning. During the naming task, we presented 75 simple black-and-white line drawings of common objects and asked the patients to correctly name them. During the verb generation task, we presented nouns, and the patients had to form a sentence from these with a semantically related verb. During an arithmetic task, we presented numbers, which the patients were asked to add.

Our principal requirement was to receive presurgical localizations as precise as possible in patients with interindividual mental and intellectual abilities which are additionally constricted by their disease. Therefore, we chose to use paradigms according to the individual abilities of each patient. All tasks engaged Broca as well as Wernicke areas.

Paradigms were chosen on the basis of (a) tumor location, (b) patient abilities and (c) measurement modality:

(a) For that reason in case of tumor location in the inferior parietal area close to the intraparietal sulcus, we used an arithmetic task so that besides Wernicke's area (activated by reading the number and formulating the result) the cortex for calculation in the intraparietal sulcus was activated and regarded during surgery.

In case of tumor location close to Broca's area, we selected language tasks, which are not only receptive, but are also expressive and demand grammatical abilities, because these may increase activity in the Broca area. This happens during the verb generation task but also the sentence-reading task gives suitable Broca activations.

(b) For patients with constricted abilities rather simple tasks were selected to receive stable results. Especially in patients who suffered from word finding disorders, we avoided the picture naming task. In the case of short-sighted patients, we could not use the tasks with sentences, because these could not be recognized by those patients. For patients with better cognitive performance, we selected one or more complex tasks like verb generation task, because these are reported to show a better accentuated lateralization. Whereas in patients who have difficulties in this complex task, the activation is worse, than with a simple paradigm.

(c) Measurement modality also influenced the choice of paradigm: In MEG sessions verb generation and arithmetic tasks result in unsatisfactory average data in patients who were not able to perform these tasks regularly.

In the following, it is listed in which instances a certain task was selected:

The Naming task was used in short-sighted patients or in patients whose intellectual capabilities allowed only simple tasks.