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Observation of unaveraged giant MEG activity from language areas during speech tasks in patients harboring brain lesions very close to essential language areas: expression of brain plasticity in language processing networks?

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Abstract

We describe a series of 12 patients who suffered from lesions adjacent to the classic Broca and Wernicke areas and were examined by magnetoencephalography (MEG) for presurgical language localization while performing a protocol of different language tasks. In these patients very large MEG activity of up to 5 pT was observed, which was located not only in the adjacent language processing brain areas but also in more distant areas, which are part of the language processing neuronal network. The high amplitude and the focal spatial extent of this activity allowed MEG source localization from the unaveraged data. In nine patients sources of this high amplitude activity were even found in the homologous language areas on the contralateral, the nondominant side of the brain. The physiological interrelationship of these large MEG changes needs to be investigated in more detail in further studies especially in the context of possible mechanisms for brain plasticity to overcome inhibitory activity of the impaired language area.

Keywords: Magnetoencephalography; Language; Wernicke; Broca; Unaveraged; Laterality; Brain plasticity

Magnetoencephalography (MEG) is an important tool for the precise localization of language processing brain areas for presurgical functional imaging [19,28]. MEG has the advantage of both a high temporal and spatial resolution and is able to depict the temporal interrelationship of language related brain areas during stimulation tasks [35].

The observation of high amplitude activity following external stimuli is not frequently reported. Penfield, Jasper and Forster described [9,30] a girl with a capillary hemangioma, who showed very large evoked potentials both in electrocorticography and EEG, which were induced by tapping the left shoulder. In their book they also mention similar cases like exaggerated auditory evoked responses. Other observations of enlarged brain activities (increased somatosensory potentials) are reported by Miwa and Mizuno [25] and by Kofler et al. [21] in a case of progressive supranuclear palsy and by Ugawa et al. [41] in cases of galactosialidosis and cortical reflex myoclonus.

In this study we describe for the first time several cases, which show high amplitude changes of the magnetic field within the unaveraged MEG-data during language stimulation. Clearly these signals were different from the common artifacts (e.g. eye movement, pulse, breathing movement). When localizing these activities the origin of the signals was found within Broca's and Wernicke's area. The signals were originating not only from the language area which was situated directly adjacent to the tumor, but large activations originated also from the other language area. The high amplitude activity was propagated through the whole network of language and cognitive processing brain areas. These are known

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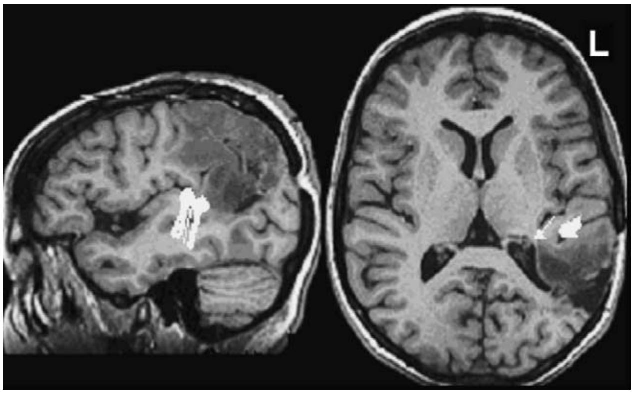

Fig. 1. MEG language localization of Wernicke's area in a patient with an astrocytoma (WHO III) about 500 ms after stimulus onset. Localizations of 270 ms interval of the averaged measurement with language stimulation (adding up displayed numbers; correlation 0.97; confidence volume $<2.0\,cm^3$) in close relation to tumor (patient 8).

from previous studies applying electrical stimulation, from lesion location studies, from fMRI and PET examinations, and MEG [3,6,8,15,19,29,31,37,45,47].

During the last year we examined 38 patients for the presurgical assessment of language related brain areas. Out of these we were able to find giant MEG language activity in 12 patients. These 12 patients had in common that their lesions were closer than 3 mm to Broca's or Wernicke's area (Fig. 1).

All patients but one were right handed. Handedness was evaluated before MEG measurement with the Edinburgh Handedness Inventory [26]. The dominant hemisphere in each patient was determined by WADA-testing in three patients (patient numbers: 1, 2, and 5). In the remaining patients laterality was determined using both fMRI and MEG in conjunction with the Edinburgh handedness inventory. The convergence of these methods together with the clinical symptoms allowed the determination of the laterality. For further details see Table 1. Though patients showed occasionally language dysfunctions, language disorders were not observed during measurement with the exception of one patient, who showed permanent problems when naming objects. All other patients were able to read and name objects without difficulty. Six of the12 patients had occasional seizures in their medical history (patient numbers: 1, 2, 3, 5, 7, and 8). Patients 1, 2, and 5 showed epileptic EEG activity in a former EEG recording. However, during our MEG recording we did not observe spike activity.

MEG measurements were performed simultaneously over both hemispheres with a 2×37 channel biomagnetic system (Magnes II, 4D Neuroimaging, San Diego, CA, USA) in a magnetically shielded room. Simultaneously we recorded the electrocardiogram (ECG) signal.

The total acquisition time was 15–30 min for each stimulation paradigm with a data sampling rate of 520.8 Hz and an online high-pass filter of 0.1 Hz. In cases of breathing artifacts or other slow wave disturbances the data were filtered with a highpass filter adapted to reject these disturbances (6 dB edge frequency of highpass was 0.3 Hz).

Motion and eye movement artifacts were manually discarded during the visual inspection of the raw epochs after the data acquisition. If the MEG signal was contaminated by the magnetocardiogram we automatically subtracted the appropriate amount of the ECG from the raw dataset.

During the MEG measurement all patients were asked to perform language tasks. We used several paradigms to obtain language related brain activity: silent-naming of pictures, silent reading of words or words with spelling or grammatical mistakes, and a calculation task. During calculation task the patient had to read and understand numbers, remember the last sum, add the new number, and memorize the new sum. This engages language areas [5], the calculation area (in the intra parietal sulcus), and the hippocampus.

Experiences of our stimulation paradigms have been described previously [19]. About 800 stimuli were presented. The interstimulus interval ranged from 1400 to 2100 ms. The length of the interstimulus interval was adjusted to the patient's abilities. For all paradigms we used visual stimulation to avoid interference from the primary auditory cortex.

For source localization we used a single dipole fitting algorithm based on a least square search [36] and a current density localization approach based on a spatial filter beamformer (CLSF: current localization by spatial filtering).

Table 1
Patients characteristic

Number	Sex, age	Diagnosis	Language dysfunction	Location of lesion	Dominance
1	M, 52	cavernoma	Naming difficulties, semantic paraphrasia	Broca left	Left
2	M, 23	Scar tissue after tumor surgery	Naming difficulties	Broca left	Left
3	M, 40	Scar tissue after tumor surgery	Postictal speaking and understanding problems	Wernicke right	Bilat
4	F, 48	Ganglioglioma	Speaking, writing, reading problems	Wernicke left	Left
5	F, 66	Astrocytoma (WHO III)	Anomic aphasia, stuttering, speech arrest	Broca right	Bilat
6	M, 60	Glioblastoma (WHO IV)	Semantic paraphrasia	Wernicke/hippoc. left	Left
7	M, 32	Pilocytic astrocytoma (WHO I)	Postictal sensory aphasia	Wernicke/ hippoc. left	Left
8	F, 33	Oligoastrocytoma (WHO III)	Dyslexia, acalculia, anomia swapping letters	Wernicke/parietal l. left	Right
9	M, 42	Glioblastoma (WHO IV)	Anomia	Wernicke left	Left
10	F, 79	Glioblastoma (WHO IV)	Mild motor aphasia	Broca right	Bilat
11	F, 49	Cavernoma	Anomia, speech arrest	Wernicke left	Left
12	M, 38	Astrocytoma (WHO III)	Anomia	Wernicke left	Left