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Verbal memory and verbal fluency tasks used for language localization and lateralization during magnetoencephalography

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ABSTRACT

Objective: The aim of this study was to develop a presurgical magnetoencephalography (MEG) protocol to localize and lateralize expressive and receptive language function as well as verbal memory in patients with epilepsy. Two simple language tasks and a different analytical procedure were developed.
Methods: Ten healthy participants and 13 epileptic patients completed two language tasks during MEG recording: a verbal memory task and a verbal fluency task. As a first step, principal component analyses (PCA) were performed on source data from the group of healthy participants to identify spatiotemporal factors that were relevant to these paradigms. Averaged source data were used to localize areas activated during each task and a laterality index (LI) was computed on an individual basis for both groups, healthy participants and patients, using sensor data.
Results: PCA revealed activation in the left temporal lobe (300 ms) during the verbal memory task, and from the frontal lobe (210 ms) to the temporal lobe (500 ms) during the verbal fluency task in healthy participants. Averaged source data showed activity in the left hemisphere (250–750 ms), in Wernicke's area, for all participants. Left hemisphere dominance was demonstrated better using the verbal memory task than the verbal fluency task ($F_{1,19} = 4.41$, $p = 0.049$). Cohen's kappa statistic revealed 93% agreement ($k = 0.67$, $p = 0.002$) between LIs obtained from MEG sensor data and fMRI, the IAT, electrical cortical stimulation or handedness with the verbal memory task for all participants. At 74%, agreement results for the verbal fluency task did not reach statistical significance.
Significance: Analysis procedures yielded interesting findings with both tasks and localized language-related activation. However, based on source localization and laterality indices, the verbal memory task yielded better results in the context of the presurgical evaluation of epileptic patients. The verbal fluency task did not add any further information to the verbal memory task as regards language localization and lateralization for most patients and healthy participants that would facilitate decision making prior to surgery.

Abbreviations: ANOVA, analysis of variance; ECG, electrocardiogram; ECS, electrical cortical stimulation; EEG, electroencephalography; EOG, electrooculogram; fMRI, functional magnetic resonance imaging; IAT, intracarotid amobarbital test; LI, laterality index; MEG, magnetoencephalography; PCA, principal component analysis; ROI, region of interest; SF, spatial factor; sPCA, spatial principal component analysis; SSP, signal space projection; TF, temporal factor; tPCA, temporal principal component analysis; tsPCA, temporo-spatial principal component analysis; wMNE, weighted minimum norm estimate.

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1. Introduction

The first line of treatment for epilepsy is pharmacotherapy (Killgore et al., 1999). However, about 30% of patients have medically intractable epilepsy (Kwan and Brodie, 2000), in which case surgery is often considered to remove the epileptogenic zone. Surgery can eliminate or significantly decrease seizures in 50% to 90% of cases (Smith, 2001) and is most often performed in the temporal and frontal lobes.

Epileptic patients show greater variability as regards language dominance than neurologically healthy individuals (Berl et al., 2005). In 94% to 96% of healthy right-handers and 74% of left-handers, the left hemisphere is dominant for language (Pujol et al., 1999; Springer et al., 1999). In comparison, 4% to 37% of right-handed epileptic patients and 25% to 52% of left-handed or ambidextrous patients with epilepsy show right hemisphere language dominance (Helmstaedter et al., 1997; Springer et al., 1999). Prior to some epilepsy surgeries, it is important to determine the language-dominant hemisphere and to localize language functions in order to reduce postsurgical language impairments.

The medical standard for determining the language-dominant hemisphere prior to surgical resection is the intracarotid amobarbital test (IAT) or Wada test (Wada and Rasmussen, 2007). A major drawback of this method is that it only determines lateralization of language function and not its specific localization. Most importantly, the IAT is invasive and thus associated with risks of stroke, infection and haemorrhage (English and Davis, 2010). Finally, alternative methods are being investigated due to the shortage of sodium amobarbital across the world (Baxendale, 2009; Jones-Gotman and Smith, 2006).

In recent years, noninvasive neuroimaging methods have been developed to evaluate language presurgically. Functional magnetic resonance imaging (fMRI) has received the most attention as a possible replacement or alternative for the IAT, followed by magnetoencephalography (MEG). fMRI offers excellent spatial resolution and its results correlate highly with the IAT (86% in a group of 229 patients) (Janecek et al., 2013). MEG has been found to complement fMRI findings with its temporal resolution of less than a millisecond (Frye et al., 2009; Hari et al., 2010; Stefan et al., 2011). Moreover, MEG is completely noninvasive and can be used with children (Bowyer et al., 2005b; Breier et al., 1999, 2001; Papanicolaou et al., 2004).

MEG studies investigating receptive language and verbal memory using a word recognition task reported high concordance between MEG and the IAT (86–92%) (Breier et al., 1999, 2001; Doss et al., 2009; Maestu et al., 2002; Papanicolaou et al., 2004) and revealed, in most healthy individuals, strong left temporoparietal activation. Although fewer MEG studies have looked at expressive language tasks, high concordance between MEG and the IAT (82%) (Bowyer et al., 2005b) was found using a verb generation task that generated activations in both frontal (Breier and Papanicolaou, 2008; Fisher et al., 2008; Kamada et al., 2006) and temporal (Bowyer et al., 2005a) lobes. Thus, the word recognition task has been replicated and provides good results in the presurgical evaluation of epileptic patients. The verb generation task shows the best laterality results with regards to expressive language but can be too complex for younger children, particularly those showing cognitive difficulties associated with epilepsy. To date, there is no consensus on a battery of tests including localization of both receptive and expressive language function that can be used in the presurgical evaluation of patients.

The aim of this study was to develop a simple presurgical MEG language protocol allowing to localize and lateralize expressive and receptive language function as well as verbal memory in patients with epilepsy. To this end, two tasks were first validated in a group of healthy participants and subsequently used in a group of patients with epilepsy. A simple word recognition task (verbal memory task) provides information on receptive language, as participants have to analyze verbal information, and verbal memory, since words are committed to memory and recognized on subsequent trials. The verbal fluency task, using simple semantic categories, allows expressive language to be evaluated.

Table 1
Gender, age, seizure location and age of onset of seizures.

Subject	Gender	Age (yr)	Seizure location	Age at onset of seizures (yr)
C1	F	22	N/A	N/A
C2	F	24	N/A	N/A
C3	F	24	N/A	N/A
C4	F	23	N/A	N/A
C5	M	28	N/A	N/A
C6	M	29	N/A	N/A
C7	F	26	N/A	N/A
C8	M	23	N/A	N/A
C9	M	26	N/A	N/A
C10	M	24	N/A	N/A
P1	M	35	Right frontal	12
P2	M	37	Left temporal	5
P3	F	31	Left insula	4
P5	M	55	Right mesiotemporal	37
P6	F	38	Left operculoinsular	5
P7	F	22	Left insula	5
P9	M	60	Right frontal	14
P10	M	26	Left temporal	3
P11	M	35	Left mesiotemporal	10
P12	F	46	Right frontal	12–13
P13	F	26	Left mesiotemporal	17

M: male. F: female. yr: years. N/A: non-applicable.

2. Methods

2.1. Participants

Ten healthy participants (average age: 24.9 ± 1.8; five men and five women) and 13 patients with refractory epilepsy who were surgical candidates (average age: 40.2 ± 11.1; eight men and five women) completed a language protocol during MEG recording (see Table 1 for detailed demographic and clinical data). Two patients (P4 and P8) were excluded due to significant artifacts in the MEG signal, giving a total of 11 patients included in the analyses. All participants were native French speakers. All healthy subjects were right-handed as revealed by the Edinburgh Handedness Inventory (Oldfield, 1971). Epileptic patients showed variability with respect to handedness (eight right-handed, two left-handed, one ambidextrous) and location of epilepsy foci (eight in the temporal lobe, three in the frontal lobe; seven in the left hemisphere, four in the right hemisphere).

2.2. Language paradigms

Both tasks were carefully explained to the participants prior to the MEG data acquisition and completed during MEG recording in a randomized order.

For the verbal fluency task, participants completed a practice round to ensure they understood the instructions, since answers were to be given subvocally in the MEG. During MEG recording, participants were asked to generate one word in a given auditorily presented semantic category. A total of ten categories (body parts, animals, fruits, vegetables, colors, boys' first names, girls' first names, clothing, toys and desserts) were each presented ten times in a random order (100 trials). The duration of these stimuli varied between 0.520 and 1.390 s and a variable interstimulus interval was used (between 1.8 and 2.2 s).