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The dynamics of language-related high-gamma activity assessed on a spatially-normalized brain

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HIGHLIGHTS

- We made spatial normalization of 1512 intracranial electrodes in 21 patients with intractable epilepsy to identify typical dynamics of semantic processing.
- Word interpretation task evoked high gamma activity (HGA) at 200 ms after stimulus onset on the posterior temporal language area and alternatively at 400 ms on the frontal language area, following the initial HGA of bilateral fusiform gyri.
- The novel ECoG-normalization technique evolved visualization of electrophysiological dynamics related to semantic processing among individual subjects.

ABSTRACT

Objective: We developed a novel technique of spatial normalization of subdural electrode positions across subjects and assessed the spatial–temporal dynamics of high-gamma activity (HGA) in the dominant hemisphere elicited by three distinct language tasks.
Methods: The normalization process was applied to 1512 subdural electrodes implanted in 21 patients with intractable epilepsy. We projected each task-related HGA profile onto a normalized brain.
Results: The word interpretation task initially elicited HGA augmentation in the bilateral fusiform gyri at 100 ms after stimulus onsets, subsequently in the left posterior middle temporal gyrus, in the left ventral premotor cortex at 200 ms and in the left middle and left inferior frontal gyri at 300 ms and after. The picture naming task elicited HGA augmentation in few sites in the left frontal lobe. The verb generation task elicited HGA in the left superior temporal gyrus at 100–600 ms. Common HGA augmentation elicited by all three tasks was noted in the left posterior-middle temporal and left ventral premotor cortices.
Conclusions: The spatial–temporal dynamics of language-related HGA were demonstrated on a spatially-normalized brain template.
Significance: This study externally validated the spatial and temporal dynamics of language processing suggested by previous neuroimaging and electrophysiological studies.

1. Introduction

Language functions are generated by complex neural networks. To obtain better understanding of language mechanisms, it is necessary to make detailed maps using functional imaging and electrophysiological techniques. In particular, fine-scale time series analysis of the whole brain has great potential for the elucidation of neural networks.

Numerous lesional and hemodynamic studies have provided information about language networks (Binder et al., 2009; Dronkers et al., 2004; Price, 2010; Vigneau et al., 2006). In addition to the classical Wernicke's and Broca's areas, recent studies have found several language-related epicenters throughout the whole brain. The regions that are activated depend on the cognitive function being performed, for example, various areas of the brain have been found to be associated with orthography (Binder et al., 2006; Cohen et al., 2002; Tsapkini and Rapp, 2010), phonology (Binder et al., 2000; Buchsbaum et al., 2001; Rauschecker, 1998),

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lexico-semantic memory (Martin et al., 1995, 1996; Moore and Price, 1999; Noppeney et al., 2005), semantic selection/decisions (Badre and Wagner, 2007; Noppeney et al., 2004; Thompson-Schill et al., 1999; Wagner et al., 2001), speech production/perception (D'Ausilio et al., 2009; Hickok, 2001; Hickok et al., 2003; Pulvermuller et al., 2006; Wilson et al., 2004), syntax and sentence level comprehension (Friederici et al., 2003; Hashimoto and Sakai, 2002; Homae et al., 2002, 2003; Humphries et al., 2001; Ni et al., 2000), and verbal working memory (Champod and Petrides, 2007, 2010; Hickok et al., 2003; Jonides et al., 1998; Ravizza et al., 2004; Tsukiura et al., 2001). Although multiple epicenters have been found, it is difficult to elucidate the time course of the brain activity of distributed language areas and the dynamics of the language network. This is due to the technical limitations of hemodynamic studies such as positron emission computed tomography (PET) and functional MRI (fMRI), which have insufficient temporal resolution to describe the dynamics of neural activity.

On the other hand, electroencephalography (EEG) and magnetoencephalography (MEG) have been used to record event-related responses at high time resolution; i.e., event-related potentials (ERP) and event-related fields (ERF), respectively. Using these techniques, previous groups have demonstrated semantic responses within 200 ms of letter presentation for primary perception and within about 400 ms for letter cognition (Dhond et al., 2007; Salmelin et al., 1994; Vartiainen et al., 2009). However, questions remain about how to solve inverse problems, which interfere with source localization. In fact, there have been considerable disagreements about the origins of certain components (e.g., N400) (Curran et al., 1993; Halgren et al., 2002; Helenius et al., 1998; Johnson and Hamm, 2000; Maess et al., 2006; Pylkkanen and McElree, 2007; Tse et al., 2007; Uusvuori et al., 2008).

In the last few years, increasing effort has been made to assess brain oscillatory activity such as event-related synchro/desynchronization (ERS/ERD) using intracranial electrodes. Event-related augmentation of the ongoing EEG has been referred to as ERS, and augmentation of high gamma activity (HGA) at >50 Hz is generally considered to reflect cortical activation (Crone et al., 1998; Pfurtscheller and Lopes da Silva 1999).

Distributions of HGA augmentation display strong correlations with various functions, including motor (Crone et al., 1998; Leuthardt et al., 2007; Miller et al., 2007), auditory (Crone et al., 2001a; Edwards et al., 2005; Sinai et al., 2009; Trautner et al., 2006), visual (Lachaux et al., 2005; Tanji et al., 2005), language (Brown et al., 2008; Crone et al., 2001b; Sinai et al., 2005; Wu et al., 2011, 2010), episodic memory (Sederberg et al., 2007), working memory (Axmacher et al., 2007; Howard et al., 2003; Meltzer et al., 2008; van Vugt et al., 2010), and attention functions (Jung et al., 2008; Ray et al., 2008; Tallon-Baudry et al., 2005). Furthermore, studies of HGA can achieve both high spatial and temporal resolution. Therefore, analyzing HGA dynamics is one of the most powerful approaches for studying complex neural networks (Canolty et al., 2007; Edwards et al., 2010; Mainy et al., 2008).

One practical issue with this technique is the positioning of intracranial electrodes. Since it is impossible to control the electrode positions for research purposes from an ethical point of view, each patient is monitored with a different number of electrodes, and there are also inter-individual differences in their locations. As a result, consistent HGA dynamics are rarely obtained because of inter-individual variations in electrode positioning.

In order to overcome these limitations, we spatially normalized individual brains and the subdural electrodes of patients with intractable epilepsy and superimposed 1512 electrodes of the dominant hemisphere onto a normalized brain. We hypothesized that this novel method could allow us to demonstrate representative HGA patterns for various semantic tasks such as word interpretation, picture naming, and verb generation.

2. Subjects and methods

2.1. Subjects

We recorded ECoG in 34 patients with intractable epilepsy, who underwent subdural electrode implantation for diagnostic purposes at the University of Tokyo Hospital between May 2005 and November 2010. During the recording, we instructed the patients to perform 3 language tasks, word interpretation, picture naming, and verb generation. Thirteen patients were excluded because of a low intelligence quotient (<70) ($n = 9$), young age (<15) ($n = 1$), a lack of electrodes in the left hemisphere ($n = 1$), low signal quality ($n = 1$), or continuous epileptic activity ($n = 1$). As a result, we restricted this analysis to 21 patients (8 men, 13 women). Before the epilepsy surgery, we confirmed which hemisphere was dominant for language processes in each individual using the Wada test or a combination of fMRI and MEG, as described elsewhere (Kamada et al., 2007). There was no case in which the right hemisphere was dominant for language processes.

We used grid and strip type subdural electrodes, which consisted of silastic sheets embedded with platinum electrodes (3 mm in diameter), and a 10 mm inter-electrode interval (center to center) (Unique Medical, Tokyo, Japan). Since the purpose of this study was to elucidate the language dynamics in the dominant hemisphere, we excluded ECoG electrodes on the lateral surface of the right hemisphere.

This study was approved by the institutional review board of our institute. Written informed consent was obtained from each patient or their family after a detailed explanation of the ECoG and language evaluation procedures.

2.2. ECoG recording

2.2.1. Data acquisition

Each patient was seated on a bed with a reclining backrest in a quiet, electrically shielded room. A computer monitor was placed 100 cm from the patient. Stimuli were then presented using a Stimuli Output Sequencer (NoruPro Light Systems Inc., Tokyo, Japan).

The resultant ECoG were digitally recorded at a sampling rate of 400 Hz, using a 128 channel EEG system (BMSI 6000, Nicolet Biomedical Inc., Wisconsin). The band-pass filter for the data acquisition was set to 0.55–150 Hz. Electric triggers generated by the stimulus computer were simultaneously recorded by one of the channels.

A reference electrode was placed on the scalp at Cz (international 10–20 system).

2.2.2. Language tasks

Word interpretation (WI) task: The stimuli for the word interpretation task consisted of three-letter words. All letter strings were white with a black background and presented for 350 ms with a randomly variable inter-stimulus intervals, ranging between 2700 and 3300 ms. The words were displayed randomly, and each was presented once or twice, yielding 100 data epochs. The patients were instructed to covertly categorize the presented words into "abstract" or "concrete".

Picture naming (PN) task: The 100 stimuli used for the picture naming task consisted of 42 color illustrations of familiar objects. They were presented for 1000 ms with an inter-stimulus interval ranging between 2700 and 3300 ms. The patient was requested to silently name each presented object.

Verb generation (VG) task: Common concrete nouns spoken by a native Japanese speaker were presented by the computer. The twenty stimuli were presented in random order to generate 100