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Reorganization of posterior language area in temporal lobe epilepsy: A cortico-cortical evoked potential study

Rei Enatsu [a], Yuichi Kubota [a,d], Yosuke Kakisaka [a,e], Juan Bulacio [a], Zhe Piao [a], Timothy O'Connor [a], Karl Horning [a], John Mosher [a], Richard C. Burgess [a,b], William Bingaman [a,c], Dileep R. Nair [a,b,*]

[a] *Epilepsy Center, Cleveland Clinic Foundation, Cleveland, OH, USA*
[b] *Department of Neurology, Cleveland Clinic, Cleveland, OH, USA*
[c] *Department of Neurosurgery, Cleveland Clinic, Cleveland, OH, USA*
[d] *Department of Neurosurgery, Tokyo Women's Medical University, Tokyo, Japan*
[e] *Department of Pediatrics, Tohoku University School of Medicine, Sendai, Japan*

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Summary
Objective: To investigate the connectivity associated with the reorganized language network in patients with temporal lobe epilepsy (TLE) using cortico-cortical evoked potential (CCEP), which reveals the brain networks.
Methods: Six patients with intractable TLE who underwent chronic intracranial electrode placement and revealed an atypical distribution of posterior language areas (Wernicke's areas) were studied. Alternating 1 Hz electrical stimuli were delivered to the anterior language areas (Broca's areas). CCEPs were recorded by averaging electrocorticograms time-locked to stimuli from the subdural electrodes. Thereafter, the posterior language areas identified by the electrical cortical mapping and CCEP distributions were compared by calculating the root mean square of CCEP responses.
Results: CCEP responses were observed in various areas within the temporal, temporo-parietal or temporo-occipital area. The correlation between CCEP distributions and posterior language areas revealed two patterns. In two patients, the posterior language areas were located within CCEP distribution, but out of the maximum responses in the temporal lobe. On the other hand, parts of the language areas were outside CCEP-positive areas in four patients.

* Corresponding author at: Epilepsy Center, Desk S51, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, USA. Tel.: +1 216 444 2560; fax: +1 216 445 4378.
E-mail address: naird@ccf.org (D.R. Nair).

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Conclusion: Our results suggest that language reorganization might be associated with a functional shift from the termination of anterior—posterior language connection to the surrounding cortices. It should be noted that language areas can be identified outside the anterior—posterior language connection.

Introduction

Two specific cortical areas are essential for language function. Broca's area (anterior language area: ALA) is located just in front of the cortical region that contains the motor representation and is responsible for a speech output (Geschwind, 1970). Wernicke's area (posterior language area: PLA) lies next to the auditory cortex and is involved in recognition of the spoken language. Wernicke and then later Geschwind postulated that these perirolandic language areas were connected via the arcuate fasciculus and destruction of this connection would produce conduction aphasia (Geschwind, 1970).

It is well known that epilepsy is likely to cause atypical language organization (Hamberger and Cole, 2011). Unlike the sudden disruption of established language circuits following stroke or traumatic brain injury, slowly progressive disease such as chronic epileptic activity might shift language from the left to the right hemisphere (Liegeois et al., 2004; Brazdil et al., 2005; Janszky et al., 2006; Gaillard et al., 2007; Powell et al., 2007), or relocate language areas from traditional to non-traditional sites within the dominant hemisphere (Duchowny et al., 1996; Brazdil et al., 2005; Federico, 2011; Hamberger and Cole, 2011). Mbwana et al. (2009) reported several subgroups of language reorganization in left-sided seizure disorders which includes intra-hemispheric reorganization (i.e., compensation by ipsilateral adjacent regions) and inter-hemispheric reorganization (i.e., shift to contralateral homologous regions). This phenomenon is clinically relevant, particularly in the context of epilepsy surgery for the treatment of pharmacologically refractory seizures, because it is necessary to localize and to spare the language function before resecting the epileptogenic cortex.

In vivo human language network studies have begun using non-invasive methods, such as diffusion tensor imaging (DTI) (Powell et al., 2007; Frey et al., 2008; Glasser and Rilling, 2008; Upadhyay et al., 2008; Ellmore et al., 2010) and invasive cortical/subcortical electrical stimulation mapping (Schaffler et al., 1996; Duffau et al., 2008b). Although the combination of these techniques provides approximate information about the relationship between the cortical language area and subcortical network (Duffau et al., 2008c; Duffau, 2008a; Ellmore et al., 2009), these techniques cannot provide a direct locational correlation between language areas and termination of the subcortical fibers among cortical regions. It would be optimal if both functional cortical regions and the termination of white matter connections could be mapped, so as to be able to track exact neuronal connections. Electrical stimulation in vivo was recently introduced in humans to track the various brain networks (Wilson et al., 1990, 1991; Greenlee et al., 2007; Lacruz et al., 2007, 2010; Oya et al., 2007; Rosenberg et al., 2009; Keller et al., 2011) and evaluate the cortical excitability (Valentin et al., 2002, 2005a, b; Flanagan et al., 2009). Cortico-cortical evoked potentials (CCEPs) are an electrical stimulation method, which was developed by averaging responses time-locked to electrical stimuli. This method provides an opportunity to track connectivity among various functional areas that can be defined by cortical electrical stimulation (Matsumoto et al., 2004b, 2007, 2011; Terada et al., 2008, 2012; Umeoka et al., 2009; Kikuchi et al., 2012; Koubeissi et al., 2011).

Previous CCEP studies elucidated the physiological language network and revealed the well-correlated CCEP responses with cortical language areas (Matsumoto et al., 2004a; Conner et al., 2011). We revealed a bidirectional connection between ALAs and PLAs in the patients with typical language distribution, and the PLAs were identified within CCEP responses elicited by the electrical ALA stmulation (Matsumoto et al., 2004a). However, the reorganized language area was not analyzed in these previous reports and the connectivity associated with the reorganized language network is still unclear.

By means of CCEP, we report here the connectivity pattern of ''reorganized'' PLAs from the ALAs in patients with intractable temporal lobe epilepsy, and discuss the mechanism of language reorganization and the utility of CCEP in these patients.

Methods

Patients

Six patients with epileptogenicity including the temporal lobe (temporal, temporo-parietal or temporo-occipital lobe epilepsy) who showed atypical distribution of the PLA (described in the next section) were studied. All patients had undergone chronic intracranial electrode placement over the lateral convexity of the frontal and temporal lobe for presurgical evaluation of medically intractable partial epilepsy between 2006 and 2011 (Table 1). The subdural electrodes were made of platinum and measured 3.97 mm in diameter with a center—center inter-electrode distance of 1 cm (custom-made at Cleveland Clinic Foundation, OH). Depth electrodes were made of platinum 2.5 mm contacts with a 2.5 mm gap and a diameter of 1.25 mm (Integra, Plainsboro, NJ).

The study was performed extraoperatively after the standard presurgical evaluation and restarting antiepileptic medications. The relationship of the electrode position to major cerebral sulci was identified on a pre-surgical three-dimensionally reconstructed MRI image coordinated with post-operative high resolution volumetric CT (1 mm slice thickness).

After the intracranial electrode evaluation, all patients underwent resective surgery. The resected cortical area