International Congress Series 1278 (2005) 397–400

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Interareal connectivity in the human language system: a cortico-cortical evoked potential study

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Abstract. *Objective*: To investigate functional connectivity in the human language system in vivo by means of a cortico-cortical evoked potential (CCEP) study. *Methods*: Eight epilepsy patients underwent chronic subdural electrode implantation in the language dominant hemisphere for epilepsy surgery. Single pulse electrical stimuli were delivered to the anterior language (eight patients), posterior language (four) or face motor (two) area, and CCEPs were obtained by averaging electrocorticograms recorded from the perisylvian and extrasylvian basal temporal language areas time locked to the stimulus. *Results*: Stimulation at the anterior language area elicited CCEPs (7/8 patients at 3–21 electrodes) in the middle and posterior part of the superior temporal gyrus, the adjacent part of the middle temporal gyrus and the supramarginal gyrus. CCEPs occurred at and/or around the core language area identified by conventional electrical stimulation. Similar early and late CCEPs were obtained from the basal temporal area by stimulating the anterior language area (3/3). In contrast, stimulation of the adjacent face motor area did not elicit CCEPs in language areas but rather in the postcentral gyrus. Stimulation of the posterior language area produced CCEPs in the anterior language (3/4) as well as in the basal temporal area (1/2). *Conclusion*: This study, for the first time, demonstrated that perisylvian and extrasylvian language areas participate in the language system as components of a network by means of feed-forward and feed-back projections. Judging from the CCEP distribution in the posterior language area, a rather broad neuronal network seems to surround the previously recognized core region of this area. © 2004 Elsevier B.V. All rights reserved.

Keywords: Language areas; Functional connectivity; Cortical stimulation; Evoked potential; Epilepsy

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doi:10.1016/j.ics.2004.11.128

1. Introduction

A better understanding of the workings of brain systems requires a detailed knowledge of neuronal connectivity between functional cortical regions. Because the invasive tracer techniques cannot be used for studying neuronal connectivity of the human brain, almost all of the research on connectivity has been conducted in nonhuman primates. As it relates to higher cognitive functions, such as language, studies performed in nonhuman primates are largely not relevant. We recently reported a new method we developed for stimulating and recording from subdural grids to track the cortico-cortical connections in vivo in humans, and we termed 'cortico-cortical evoked potentials' (CCEPs) [1]. A single electrical stimulus is applied on the cortex to look at the evoked potentials that emanate from an adjacent or distant region of the cortex, attempting to analyse interareal connectivity of the two cortical regions. By electrically stimulating one language area and recording neuronal responses from others, we studied the interareal or cortico-cortical connections within the perisylvian language area, as well as between the perisylvian and extrasylvian language areas. This study has been reported elsewhere as a full paper [2].

2. Methods

2.1. Subjects

Eight patients who underwent chronic subdural electrode placement for the presurgical evaluation of medically intractable partial epilepsy were studied (age 13–42, 2 FLE and 6 TLE patients). Six patients had subdural electrodes placed in the hemisphere dominant for language, and two had bilateral language representation. All the patients underwent functional mapping with conventional (50 Hz) electrical stimulation as a part of the evaluation. We refer to the site of the electrode which produced language impairment on electrical stimulation as the 'language electrode' herein. The present study was approved by the Institutional Review Board Committee at The Cleveland Clinic Foundation, and informed consent was obtained from all subjects (IRB #4513).

2.2. Stimulus condition and data acquisition of CCEP

The electrical stimulus used for this purpose consisted of a constant-current square wave pulse of 0.3 ms duration, which was given in alternating polarity at a frequency of 1 Hz through adjacent two electrodes. The current was given at 80% of the intensity that produced clinical signs or afterdischarges during the standard cortical stimulation. The intensity was set at 10–12 mA if no clinical sign or after discharges were present at 15 mA. Single pulse electrical stimuli were delivered to the anterior language (eight patients), posterior language (four) or face motor (two) area, and CCEPs were obtained by averaging electrocorticograms recorded from the perisylvian and extrasylvian basal temporal language areas time locked to the stimulus (bandpass 1–800~1000 Hz). In each session, at least two trials of 20–100 responses were averaged separately to confirm the reproducibility of the responses. The subjects were not asked to perform any tasks during the experiment. Subdural electrodes were coregistered with 3D MRI to identify their surface locations [3]. The detail of this methodology has been described elsewhere [1,2].

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