Clinical Neurophysiology 126 (2015) 39–46

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

# Mapping mental calculation systems with electrocorticography

Keisuke Ueda [a], Erik C. Brown [c], Katsuaki Kojima [a], Csaba Juhász [a,b], Eishi Asano [a,b,*]

[a] Department of Pediatrics, Children's Hospital of Michigan, Wayne State University, Detroit Medical Center, Detroit, MI 48201, USA
[b] Department of Neurology, Children's Hospital of Michigan, Wayne State University, Detroit Medical Center, Detroit, MI 48201, USA
[c] Psychiatry and Behavioral Neurosciences and MD–PhD Program, Wayne State University, School of Medicine, Detroit, MI 48201, USA

ARTICLE INFO

*Article history:*
Accepted 26 April 2014
Available online 9 May 2014

*Keywords:*
Pediatric epilepsy surgery
Intracranial ECoG recording
Subdural EEG
Ripples
Physiological high-frequency oscillations (HFOs)
Event-related synchronization
Time-frequency analysis
Spatio-temporal-dynamics
Functional brain mapping
Number
Numeral
Auditory
Speech
Language
Cognition
Angular gyrus

HIGHLIGHTS

- Calculation and naming tasks differentially elicited augmentation of gamma activity.
- Calculation-specific gamma activity involved the left parietal, temporal and frontal lobes.
- The timing of calculation-specific gamma activity differed across the regions.

ABSTRACT

*Objective:* We investigated intracranially-recorded gamma activity during calculation tasks to better understand the cortical dynamics of calculation.
*Methods:* We studied 11 patients with focal epilepsy (age range: 9–28 years) who underwent measurement of calculation- and naming-related gamma-augmentation during extraoperative electrocorticography (ECoG). The patients were instructed to overtly verbalize a one-word answer in response to auditorily-delivered calculation and naming questions. The assigned calculation tasks were addition and subtraction involving integers between 1 and 17.
*Results:* Out of the 1001 analyzed cortical electrode sites, 63 showed gamma-augmentation at 50–120 Hz elicited by both tasks, 88 specifically during naming, and 7 specifically during calculation. Common gamma-augmentation mainly took place in the Rolandic regions. Calculation-specific gamma-augmentation, involving the period between the question-offset and response-onset, was noted in the middle-temporal, inferior-parietal, inferior post-central, middle-frontal, and premotor regions of the left hemisphere. Calculation-specific gamma-augmentation in the middle-temporal, inferior-parietal, and inferior post-central regions peaked around the question offset, while that in the frontal lobe peaked after the question offset and before the response onset. This study failed to detect a significant difference in calculation-specific gamma amplitude between easy trials and difficult ones requiring multi-digit operations.
*Conclusions:* Auditorily-delivered stimuli can elicit calculation-specific gamma-augmentation in multiple regions of the left hemisphere including the parietal region. However, the additive diagnostic value of measurement of gamma-augmentation related to a simple calculation task appears modest.
*Significance:* Further studies are warranted to determine the functional significance of calculation-specific gamma-augmentation in each site, and to establish the optimal protocol for mapping mental calculation.


## 1. Introduction

Mental calculation, performed in mind without the help of a pen, paper, or fingers, is an essential skill in our daily activities. Mental calculation relies on a highly complex set of processes, many of which are not strictly specific to the number domain (Ashcraft, 1992; Dehaene et al., 2003). For example, the verbal processing required to answer 'Thirteen' for an audible task 'Four plus nine' includes (1) phonological and semantic analyses of each word and (2) syntactic analysis of a given equation. Such phonological, semantic, and syntactic analyses are needed not only during calculation but also during object naming. Conversely, retrieval of memorized arithmetic facts is a central calculation-specific

* Corresponding author. Address: Division of Pediatric Neurology, Children's Hospital of Michigan, Wayne State University, 3901 Beaubien St., Detroit, MI 48201, USA. Tel.: +1 313 745 5547; fax: +1 313 745 0955.
*E-mail address:* eishi@pet.wayne.edu (E. Asano).

http://dx.doi.org/10.1016/j.clinph.2014.04.015
1388-2457/

process for solving addition and subtraction problems involving single-digit or teen integers (McCloskey et al., 1991; Ashcraft, 1992; Dehaene et al., 2003; Klein et al., 2010). By the fourth grade, children generally secure a memory retrieval strategy for simple problems, while very young children still heavily rely on overt or covert counting strategy (Ashcraft and Fierman, 1982). Older children and adults can effortlessly retrieve a correct answer for easy problems (such as 'Three plus two'). Conversely, more difficult and less familiar problems involving multi-digit operations (such as 'Four plus nine') might require some additional strategies such as counting or referring to related operations (Campbell and Xue, 2001; Grabner et al., 2009).

We believe that mapping of the cortical sites involved in mental calculation including arithmetic fact retrieval is highly justified in epilepsy surgery. Yet, not many investigators have incorporated a calculation task in functional cortical mapping using direct cortical stimulation or measurement of task-related signal changes on electrocorticography (ECoG). In the present study, thus, we attempted to explore if intracranial measurement of event-related gamma activity would reveal the spatial–temporal characteristics of cortical activation specific to mental calculation and not to object naming. Augmentation of gamma activity at 50–120 Hz is an excellent summary measure of *in situ* cortical activation (Lachaux et al., 2012; Kojima et al., 2013a,c). Since equation stimuli were presented auditorily in the present study, we expected that calculation-specific gamma-augmentation would involve the period between the offset of auditory stimuli and the onset of overt responses and that such delayed gamma augmentation cannot be simply explained by difference in the physical property of auditory stimuli. We also tested the hypothesis that relatively difficult calculation problems, compared to easy ones, would elicit larger calculation-specific gamma augmentation.

We expected that calculation-specific gamma-augmentation would at least involve the left parietal region. Previous lesion studies suggested that the left parietal lobe may be crucial for calculation (Gerstmann, 1940; Grafman et al., 1982; Dehaene and Cohen, 1991). A more recent study reported patients with isolated acalculia resulting from strokes involving the left intraparietal sulcus (Takayama et al., 1994). A study using functional MRI (fMRI) and transcranial magnetic stimulation (TMS) showed that the left and right parietal lobes were hemodynamically activated during a calculation task and that stimulation of the activated areas increased the response time (Andres et al., 2011). A recent ECoG study of three adult patients with focal epilepsy showed augmentation of gamma activity in the left or right parietal lobe (Dastjerdi et al., 2013). While the aforementioned fMRI, TMS, and ECoG studies with equation stimuli presented visually, the uniqueness of the present study was that both calculation and naming questions were delivered auditorily. Replication of parietal gamma augmentation in a calculation task with stimuli of a different modality would further clarify the causal role of parietal lobe in mental calculation.

## 2. Methods

### 2.1. Patients

We studied 11 native English-speaking patients with focal epilepsy (age range: 9–28 years; 3 males, 8 females; Table 1) who satisfied the following inclusion and exclusion criteria. The inclusion criteria included: (i) history of focal epilepsy scheduled for extraoperative ECoG recording as part of the presurgical evaluation at Children's Hospital of Michigan or Harper University Hospital, Detroit, between August 2009 and November 2013, and (ii) completion of both calculation and naming tasks during extraoperative ECoG recording. The exclusion criteria consisted of: (i) presence of massive brain malformations (such as perisylvian polymicrogyria or megalencephaly) altering the major anatomical landmarks, (ii) severe cognitive dysfunction reflected by verbal comprehension index or verbal IQ of <70, and (iii) diagnosis of acalculia. This study has been approved by the Institutional Review Board at Wayne State University, and written informed consent was obtained from each adult patient or the legal guardian of each pediatric patient. Written assent was obtained from children above 13.

### 2.2. Subdural electrode placement

Subdural platinum grid and strip electrodes (10-mm intercontact distance; 4-mm diameter) were surgically placed on the presumed epileptogenic hemisphere (left-sided in eight and right-sided in three patients). Placement of subdural electrodes was clinically guided by the results of Phase-I presurgical evaluation including: scalp video-EEG recording, MRI, and 2-deoxy-2-[$^{18}$F] fluoro-D-glucose positron emission tomography (FDG PET) (Asano et al., 2009). The total number of analyzed electrodes per patient ranged from 86 to 138. All electrode plates were stitched to adjacent plates or the edge of dura mater, to avoid movement of subdural electrodes after placement. In all patients, intraoperative photographs were taken with a digital camera before dural closure as well as after re-opening during the second stage of surgery. All electrodes were displayed on the three-dimensional brain surface reconstructed from high-resolution MRI (Alkonyi et al., 2009; Wu et al., 2011). We confirmed the spatial accuracy of electrode display on the three-dimensional brain surface by comparison to the intraoperative digital photographs.

### 2.3. Extraoperative video-ECoG recording

Extraoperative video-ECoG recordings were obtained for 3–5 days, using a 192-channel Nihon Kohden Neurofax 1100A Digital System (Nihon Kohden America Inc., Foothill Ranch, CA, USA) at a sampling frequency of 1000 Hz and an amplifier band pass of 0.08–300 Hz. The averaged voltage of ECoG signals derived from the fifth and sixth subdural electrodes of the ECoG amplifier was used as the original reference (Wu et al., 2011). ECoG signals were then re-montaged to a common average reference. Channels contaminated with artifacts or large interictal epileptiform discharges were excluded from the common average reference to minimize their influence on the results (Fukuda et al., 2008). Surface electromyography electrodes were placed on the left and right deltoid muscles, and electrooculography electrodes were placed 2.5 cm below and 2.5 cm lateral to the left and right outer canthi. ECoG traces were visually inspected with a time-constant of 0.003 s and a sensitivity of 20 μV/mm; thereby, irregular broadband signals synchronized with facial and ocular muscle activities seen on electrooculography electrodes were treated as artifacts (Otsubo et al., 2008; Jerbi et al., 2009; Kovach et al., 2011; Kojima et al., 2013c). Seizure onset sites were clinically determined (Asano et al., 2009) and excluded from further analysis.

### 2.4. Mental calculation task

During extraoperative ECoG recording, patients were assigned a series of 96 calculation trials, each of which was either simple addition or subtraction. All questions were delivered via playback of an audio recording of a native English speaking researcher's (E.C.B.) voice using Presentation version 9.81 software (Neurobehavioral Systems Inc., Albany, CA, USA). Integers between 1 and