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Electrocorticographic correlates of overt articulation of 44 English phonemes: intracranial recording in children with focal epilepsy

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Abstract

Objective—We determined the temporal-spatial patterns of electrocorticography (ECoG) signal modulation during overt articulation of 44 American English phonemes.

Methods—We studied two children with focal epilepsy who underwent extraoperative ECoG recording. Using animation movies, we delineated ‘when’ and ‘where’ gamma- (70–110 Hz) and low-frequency-band activities (10–30 Hz) were modulated during self-paced articulation.

Results—Regardless of the classes of phoneme articulated, gamma-augmentation initially involved a common site within the left inferior Rolandic area. Subsequently, gamma-augmentation and/or attenuation involved distinct sites within the left oral-sensorimotor area with a timing variable across phonemes. Finally, gamma-augmentation in a larynx-sensorimotor area took place uniformly at the onset of sound generation, and effectively distinguished voiced and voiceless phonemes. Gamma-attenuation involved the left inferior-frontal and superior-temporal regions simultaneously during articulation. Low-frequency band attenuation involved widespread regions including the frontal, temporal, and parietal regions.

Conclusions—Our preliminary results support the notion that articulation of distinct phonemes recruits specific sensori-motor activation and deactivation. Gamma attenuation in the left inferior-

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frontal and superior-temporal regions may reflect transient functional suppression in these cortical regions during automatic, self-paced vocalization of phonemes containing no semantic or syntactic information.

Significance—Further studies are warranted to determine if measurement of event-related modulations of gamma-band activity, compared to that of the low-frequency-band, is more useful for decoding the underlying articulatory functions.

Keywords

Speech; Language; Vocalization; Phonetics; Intracranial ECoG recording; Ripples; Physiological high-frequency oscillations (HFOs); Pediatric epilepsy surgery; In-vivo animation of event-related gamma activity

1. INTRODUCTION

Most spoken words in American English consist of combinations of several phonemes out of 24 consonants and 20 vowels (International Phonetic Association, 1999; Ladefoged and Johnson, 2010). Articulation involves phoneme-specific sequential changes in shape and position of oral structures, while air passes through the vocal tract (Greenberg, 1969). Previous neuroimaging studies using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have reported that articulation-related cortical circuits include the inferior portion of Rolandic areas (i.e. pre- and post-central gyri) with larger intensity in the left hemisphere (Brown et al., 2009; Pulvermüller et al., 2006; Zatorre et al., 1992). An fMRI study reported that tongue- and lip-related phonemes were associated with distinct hemodynamic activation patterns (Pulvermüller et al., 2006). The temporal dynamics of cortical activity during overt phoneme articulation have been relatively understudied, partly due to the slow profile of hemodynamic responses on fMRI.

Intracranial electrocorticography (ECoG) recording in patients with focal epilepsy has recently received growing attention among neuroscientists. ECoG can monitor cortical processing with (i) a temporal resolution on the order of tens of milliseconds (ms), (ii) a spatial resolution of 1 cm or below, (iii) signal-to-noise ratio 20 to >100 times better than that of scalp EEG, and (iv) minimal electromyographic artifacts associated with overt articulation (Ball et al., 2009; Lachaux et al., 2012). Augmentation of gamma activity at >50 Hz elicited by sensory-motor and cognitive tasks, is generally considered to reflect cortical activation (Cervenka et al., 2013; Kojima et al., 2013a; 2013b; Niessing et al., 2005; Ray et al., 2008), while event-related gamma-attenuation reflecting deactivation (Shmuel et al., 2006). Previous ECoG studies of overt articulation of 4 to 22 phonemes have shown that articulation of different phonemes elicited augmentation of gamma activity at >50 Hz in distinct Rolandic sites (Bouchard et al., 2013; Fukuda et al., 2010b). An ECoG study of three adults with focal epilepsy demonstrated somatotopic superior-to-inferior arrangement of articulator representations within the Rolandic area in the following sequence: larynx, lips, jaw, tongue and larynx (Bouchard et al., 2013).

In the present study, we delineated how cortical processing took place during self-paced, overt articulation of 44 American English phonemes, using animation movies of event-

related ECoG amplitude modulations (Brown et al., 2008a). We specifically determined how each phoneme was characterized by augmentation and attenuation of gamma activity_{70–110 Hz} in oral sensorimotor sites. We also determined if gamma-augmentation_{70–110 Hz} involved the left inferior frontal gyrus before involving the Rolandic area. We finally determined if articulation-related gamma-augmentation_{70–110 Hz} involved the Rolandic sites more selectively compared to low-frequency band attenuation_{10–30 Hz}. Previous ECoG studies reported that motor and somatosensory tasks elicited gamma-augmentation and low-frequency band attenuation in the contralateral Rolandic area (Crone et al., 1998a; 1998b; Miller et al., 2007; Fukuda et al., 2008; 2010a).

2. METHODS

2.1. Patients

This study has been approved by the Institutional Review Board at Wayne State University, and written informed consent was obtained from the guardians of patients. The inclusion criteria consisted of (i) patients with focal epilepsy who underwent extraoperative ECoG recording as a part of presurgical evaluation in Children's Hospital of Michigan in Detroit from 2010 to 2013; (ii) ECoG sampling involving the Rolandic area from 0 to 4 cm above the sylvian fissure (Fukuda et al., 2008; 2010b); (iii) measurement of ECoG amplitude modulations elicited by overt articulation of 44 American English phonemes. The exclusion criteria consisted of (i) presence of structural lesion, seizure onset zone, or interictal spike discharges originating from the Rolandic area, inferior frontal gyrus or superior temporal gyrus; (ii) history of previous epilepsy surgery; (iii) history of hearing impairment; and (iv) evidence of language delays based on the standard neuropsychological assessment. Such strict criteria were employed in this study, partly because interictal spike discharges may contaminate measurement of the amplitude of gamma activity on ECoG (Jacobs et al., 2011; Zijlmans et al., 2011). Two right-handed native English speakers (Patient 1: 12 year old girl, and Patient 2: 9 year old girl) were studied. Patient 1 was on lamotrigine and lacosamide, while Patient 2 was on phenytoin and oxcarbamazepine.

2.2. ECoG Data Acquisition

For ECoG recording, platinum grid and strip electrodes (10 mm intercontact distance, 4 mm diameter) were surgically implanted (Asano et al, 2009; Figures 1 and 2), and the location of each subdural electrode was co-registered to each individual's three-dimensional surface MR image (Alkonyi et al., 2009; Muzik et al., 2007; von Stockhausen et al., 1997). Extraoperative video-ECoG recordings were obtained using a 192-channel Nihon Kohden Neurofax 1100A Digital System (Nihon Kohden America Inc, Foothill Ranch, CA, USA). The sampling frequency was set at 1000 Hz with the amplifier band pass at 0.08–300 Hz. The averaged voltage of ECoG signals derived from the fifth and sixth (or third and fourth) intracranial electrodes of the ECoG amplifier was used as the original reference. ECoG signals were then re-montaged to a common average reference (Korzeniewska et al., 2008; Wu et al., 2011); channels contaminated with large interictal spike discharges or artifacts were excluded from the common average reference. No notch filter was used.

Functional cortical mapping using electrical stimulation was performed (Figure 2) (Kumar et al., 2012; Kojima et al., 2013b). Extraoperative ECoG recording revealed that all ictal discharges arose from the left medial temporal region. Left anterior temporal lobe resection resulted in seizure freedom in both patients.

2.3. Articulation Task

None of the patients had a seizure within two hours prior to the task. Both patients were unsedated and comfortably lying on the bed in a quiet room. To avoid potential hand movements synchronized with articulation, patients were asked to put hands still on a stuffed animal on the thigh during the task. Patients were instructed to repeatedly articulate a given phoneme distinguishably at their own pace (about 1 per second) until an examiner found that a given phoneme was repeated 30 times. Initially, 20 vowels were assigned, followed by 24 consonants (Supplementary Video S1). Because of technical problems, phonemes /w/, /s/ and /ʃ/ were not recorded clearly in Patient 2; thus, we could not analyze ECoG changes during articulation of these three phonemes in this patient. In order to rule out the effect of ordering, each patient articulated the first-assigned phoneme /æ/ after completing the articulation of all 44 phonemes. The audible session was recorded, via hands-free microphone, on a Digital Voice Recorder (Sampling frequency: 44.1 kHz; WS-300M, Olympus America Inc, Hauppauge, NY, USA) concurrently with ECoG recording, and the amplified audio waveform was integrated into the Digital ECoG Recording System (Brown et al., 2008a; Fukuda et al., 2010b).

2.4. Time-Frequency Analysis

We determined 'when' and 'where' the amplitudes of gamma activity_{70–110 Hz} and low-frequency-band activity_{10–30 Hz} were augmented or attenuated (Figure 3). In short, the primary measures of interest were the percent change in amplitude of gamma activity_{70–110 Hz} relative to that during the reference period (i.e. the resting baseline) as well as statistical significance of task-related modulation of gamma activity. We previously reported that electrical stimulation of sites showing event-related gamma-augmentation according to our analytic approach resulted in relevant sensory, motor, and language symptoms with statistically-significant accuracy (Fukuda et al., 2008; Nagasawa et al., 2010a; 2010b; Kojima et al., 2012). We also reported that resection of sites showing such gamma-augmentation resulted in postoperative functional impairment (Kojima et al., 2013a; 2013b).

Each ECoG trial containing a phoneme articulation was transformed into the time-frequency domain using a complex demodulation technique (Papp and Ktonas, 1977) incorporated in BESA® EEG V.5.1.8 software (BESA GmbH, Gräfelfing, German; Hoechstetter et al., 2004). The time-frequency transform was obtained by multiplication of the time-domain signal with a complex exponential, followed by a low-pass filter. The low-pass filter used here was a finite impulse response filter of Gaussian shape, making the complex demodulation effectively equivalent to a Gabor transform. The filter had a full width at half maximum of 2×15.8 ms in the temporal domain and 2×7.1 Hz in the frequency domain. A given ECoG signal was assigned an amplitude (a measure proportional to the square root of power) as a function of time and frequency at each trial. Time-frequency transformation was

performed, in steps of 5 Hz and 10 ms, between 10 and 150 Hz and latencies between -500 and +1000 ms relative to the onset of sounds generated by patients. At each time-frequency bin, we determined the mean percent change in ECoG amplitude (averaged across articulation trials) relative to the mean amplitude in sixty 1500-ms silent and resting periods between articulation tasks. Such a change in amplitude has been termed “temporal spectral evolution” (TSE) (Salmelin and Hari, 1994).

In order to better visualize ‘when’, ‘where’ and ‘how many fold’ gamma activity_{70–110 Hz} and low-frequency band activity_{10–30 Hz} were increased or decreased, the ECoG amplitude of interest was sequentially delineated on the individual three-dimensional MRI (Figure 4; Supplementary Video S2; Akiyama et al., 2006; Brown et al., 2008a; Nagasawa et al., 2010a). Previous ECoG studies have reported that naming-related gamma-augmentation most commonly involved a frequency band of 70–110 Hz, regardless of patient’s age (Kojima et al., 2013b; Pei et al., 2011; Ruescher et al., 2013; Towle et al., 2008).

2.5. Determination of significant amplitude modulation during articulation of each individual phoneme

To test for statistical significance for each TSE value, a studentized bootstrap statistic was applied to obtain an uncorrected p-value independently for each time-frequency bin. This test compared the amplitude in each time-frequency bin with the averaged amplitude in the reference time period. In a second step, a Bonferroni correction was performed for multiple testing at each frequency at each channel. The corrected significance level α was set to 0.05.

Finally, TSE values in a given site were declared significant only if, after the Bonferroni correction, a minimum of eight time-frequency bins contained within the gamma range from 70- to 110-Hz were arranged in a continuous array spanning (i) at least 20-Hz in width and (ii) at least 20-ms in duration. Likewise, a minimum of eight time-frequency bins contained within the low-frequency band from 10- to 30-Hz were arranged in a continuous array spanning (i) at least 10-Hz in width and (ii) at least 40-ms in duration. Different definitions of significance were applied (Fukuda et al., 2010a), since the time constant differs between gamma- and low-frequency-band activities.

2.6. Determination of phoneme-class-specific gamma-augmentation

To localize the sites of which gamma-augmentation can distinguish phoneme classes, we employed the following group-level statistics on each Rolandic site within 4 cm from the sylvian fissure. First, we compared the ‘peak’ and ‘peak-latency’ of gamma-augmentation between 20 vowels and 24 consonants (Mann–Whitney U test). Second, we compared the peak of gamma-augmentation between six lip-related and 14 tongue-related consonants (Mann–Whitney U test; Supplementary Video S1). Lip-related consonants included bilabials (/p/, /b/, /m/ and /w/) and labiodentals (/f/ and /v/), while tongue-related consonants included dentals (/θ/ and /ð/), alveolars (/t/, /d/, /s/, /z/, /n/, /l/ and /r/) and palate-alveolars (/ʃ/, /ʒ/, /tʃ/ and /dʒ/ and /j/). Statistical significance was defined as a two-sided p-value of 0.05. A Bonferroni correction was applied for multiple comparisons across sites.

3. RESULTS

3.1. General findings

In both patients, articulation was associated with significant gamma-augmentation in variable sites within the Rolandic region, but also associated with gamma-attenuation in smaller subsets of Rolandic sites as well as in many inferior-frontal and superior-temporal sites (Figure 4; Supplementary Video S2). Low-frequency band attenuation was noted not only in the Rolandic sites but also in other widespread regions including the frontal, temporal, and parietal lobes (Supplementary Video S2). A qualitatively-similar degree of amplitude modulations were elicited by the first and second sets of articulation of phoneme /æ/.

3.2. Different phonemes were commonly associated with gamma-augmentation in a Rolandic site

In both patients, significant gamma-augmentation most commonly involved the very bottom of the Rolandic region, which is also known as the subcentral gyrus (Bouchard et al., 2013). Electrical stimulation of a pair including the subcentral gyrus elicited sensorimotor symptoms involving the larynx, pharynx, or back portion of the tongue (Figure 2). In Patient 1, 97.7% of phonemes elicited significant gamma-augmentation in the subcentral gyrus (95% confidence interval [95%CI]: 88.2 to 99.6%), while 31.8% of phonemes (95%CI: 20.0 to 46.6%) in the second most commonly activated site (Supplementary Table S1). Likewise, in Patient 2, 68.3% of phonemes (95%CI: 53.0 to 80.4%) in the subcentral gyrus, while 9.8% (95%CI: 3.9 to 22.6%) in the second most commonly activated site. Gamma-augmentation in the subcentral gyrus began earlier than in any other sites, and reached significance at least 200 ms prior to the onset of sound generation (Supplementary Video S2).

3.3. Different phonemes elicited distinct spatial patterns of gamma-modulations in oral sensorimotor areas

In both patients, significant gamma-augmentation involved various oral sensorimotor areas differentially across different phonemes, immediately prior to the generation of sounds (Figure 3). The spatial pattern of gamma-modulations in the Rolandic region within 4 cm from the Sylvian fissure effectively distinguished phonemes. In Patient 1, articulation-related gamma activity distinguished consonants significantly better than vowels; there were a total of 23 spatial patterns of gamma-modulations within such inferior Rolandic sites (Supplementary Table S1); 14 of the 24 consonants (58.3% [95%CI: 38.8 to 75.5%]) and 3 of the 20 vowels (15.0% [95%CI: 5.2 to 36.0%]) were associated with their own unique spatial pattern of gamma-modulations. Likewise, Patient 2 had a total of 20 spatial patterns of gamma-modulations within such inferior Rolandic sites; 42.9% of consonants (95%CI: 24.5 to 63.5%) and 20.0% of vowels (95%CI: 8.1 to 41.6%) were associated with their own unique spatial pattern of gamma-modulations.

3.4. Different phonemes elicited gamma-augmentation and -attenuation differentially in the same Rolandic site

In both patients, a post-central site located about 3 cm above the Sylvian fissure showed gamma-augmentation and -attenuation differentially elicited by different phonemes (Figure 5). In Patient 1, the post-central site C5 (Figure 2) showed gamma-augmentation associated with phonemes /m/ and /θ/, but gamma-attenuation associated with /l/, /ʒ/, /ʌ/, /əɪ/, /au/, and /ju:/. In Patient 2, the post-central site D5 (Figure 2) showed gamma-augmentation associated with phonemes /p/ and /f/, but gamma-attenuation associated with /d/, /n/, /r/, /g/, and /h/.

3.5. Difference between consonant- and vowel-related gamma activities

Group-level comparison suggested that the peak amplitudes of gamma activity elicited by consonants were greater, compared to those by vowels, in three post-central sites in Patient 1 (corrected $p < 0.05$; Figure 6); in these three sites, consonants increased gamma-amplitude by 40% on average (range: 31 to 53%), while vowels 15% (range: 11 to 20%). Also, in a pre-central site, the peak amplitudes of gamma activity elicited by consonants were somewhat greater than those elicited by vowels (53% vs 34%; uncorrected $p = 0.008$), but this difference did not survive the Bonferroni correction (Figure 6). In this patient, the peak latency was earlier during articulation of consonants compared to that of vowels in a subcentral and two post-central sites (corrected $p < 0.05$; Figure 6), where the peak latency of consonant-related gamma-augmentation was, on average, 170 ms earlier than those that were vowel-related.

In Patient 2, the difference in the peak amplitude between consonant- and vowel-related gamma-augmentation was much smaller in effect size (Supplementary Figure S1). The peak amplitudes of gamma activity elicited by vowels were slightly greater, compared to those by consonants, in two pre-central sites in this patient (corrected $p < 0.05$). In these two sites, vowels elicited gamma-augmentation by 24% on average (range: 9 to 39%), while consonants 16% (range: 2 to 29%). In this patient, the peak latency was 100 ms earlier during articulation of consonants compared to that of vowels in a post-central site (uncorrected $p = 0.019$), but this difference did not survive the Bonferroni correction.

3.6. Difference between tongue- and lip-related gamma activities

Group-level comparison in Patient 1 suggested that the peak amplitudes of gamma activity elicited by tongue-related consonants were greater, compared to those by lip-related ones, in one pre-central site about 3 cm above the Sylvian fissure (69% vs 38%; corrected $p < 0.05$; Figure 6). Conversely, the peak amplitudes of gamma activity elicited by lip-related consonants were greater, compared to those by tongue-related ones, in a post-central site about 4 cm above the Sylvian fissure (32% vs 23%; uncorrected $p = 0.04$; Figure 6) as well as in a subcentral site (96% vs 87%; uncorrected $p = 0.02$), but neither difference survived the Bonferroni correction.

Group-level comparison in Patient 2 suggested that the peak amplitudes of gamma activity elicited by tongue-related consonants were greater, compared to those by lip-related ones, in a pre-central site about 2 cm above the Sylvian fissure (31% vs 23%; uncorrected $p = 0.006$; Supplementary Figure S1). Conversely, lip-related gamma-augmentation was larger than

tongue-related one in a post-central site about 3 cm above the sylvian fissure (42% vs 9%; uncorrected $p=0.014$). Yet, neither difference survived the Bonferroni correction.

3.7. Difference between gamma activities related to voiced and voiceless consonants

Figure 6 shows the temporal changes of gamma-amplitudes at each inferior Rolandic sites within 4 cm from the sylvian fissure; thereby, 10 out of the 12 sites showed significant gamma-augmentation elicited by at least one phoneme. Gamma-augmentation in the most-inferior pre-central site (electrode G3 in Figure 6A) commonly took place at the onset of sound generation, and the time courses of gamma-augmentation in this site were least variable across phonemes among these 10 sites (Figure 6A). Based on its functional anatomy and the temporal dynamics of gamma-augmentation, we explored whether gamma-augmentation in this site differed between eight voiced consonants (/b/, /d/, /g/, /v/, /ð/, /z/, /ʒ/, and /dʒ/, requiring vibration of vocal-folds) and the corresponding voiceless (/p/, /t/, /k/, /f/, /θ/, /s/, /ʃ/, and /tʃ/). At 160–180 ms after the onset of sound generation, greater gamma-augmentation was elicited by articulation of voiced consonants compared to that of voiceless ones ($p<0.04$; Wilcoxon-Signed rank test; Figure 7). Furthermore, the slope of gamma activity for the 50 ms after the onset of sound generation was also larger during articulation of voiced consonants compared to voiceless ones ($p=0.03$; Figure 7).

DISCUSSION

4.1. Significance of gamma and low-frequency band amplitude modulations during articulation of phonemes

This is the first study that delineated the spatial-temporal dynamics of intracranially-recorded cortical activity during articulation of all 44 American English phonemes. Cortical activation represented by gamma-augmentation_{70–110 Hz} took place exclusively in the inferior Rolandic regions before and during articulation, while that represented by low-frequency band attenuation_{10–30 Hz} was lingering and involved widespread frontal, temporal, and parietal regions (Supplementary Video S2). Our observations are consistent with the previous observations that sensorimotor tasks involving the hand or mouth elicited gamma-augmentation in smaller regions compared to alpha-beta attenuation and that the onset of movement or somatosensory stimuli was more temporally locked with task-related gamma-augmentation than alpha-beta attenuation (Crone et al., 1998a; 1998b; Leuthardt et al., 2007; Miller et al., 2007; Fukuda et al., 2008; 2010a). Our observations also support the hypothesis that measurement of event-related modulations of gamma-band activity, compared to that of low-frequency-band, may be more useful for decoding of the underlying articulatory functions.

4.2. Significance of subcentral gamma activity augmented commonly across phonemes

The subcentral site showed gamma-augmentation elicited commonly across different phonemes in both patients, and such gamma-augmentation took place at least 200 ms prior to the onset of sound generation (Figure 6; Supplementary Video S2). Direct stimulation of the subcentral site elicited sensorimotor symptoms involving the throat, larynx, or back portion of the tongue. These observations are in line with the findings in a previous fMRI study reporting that the strong hemodynamic activation for speech included the somatotopic

larynx area of the motor cortex (Brown et al., 2009). The phoneme articulation task assigned in the present study does not require semantic or syntactic function. Thus, gamma-augmentation in the subcentral gyrus may reflect cortical activity processing preparation or initiation of the movement of vocal folds for passing air through the vocal tract (MacNeilage, 1980; Scott and Johnsrude, 2003). A previous fMRI study suggested that both prolonged exhalation and phoneme articulation elicit hemodynamic activation in the inferior Rolandic regions, while the supplementary motor area was activated by phoneme articulation but not by prolonged exhalation (Loucks et al., 2007).

4.3. Significance of gamma activity distinguishing phoneme classes

The most inferior portion of the precentral gyrus demonstrated articulation-related gamma-augmentation more intense during articulation of voiced consonants compared to during that of voiceless ones (Figure 7). Behavioral studies have shown that voiced consonants are generated with the vocal folds vibrating, while voiceless ones without (Tabain et al., 2002; Slis, 2009). There is only minimal difference in locations of oral structures such as lip and tongue between the corresponding voiced and voiceless consonants. We also found that gamma activity in this precentral site began to increase at the onset of sound generation and began to decrease around the offset of sound (Figure 6A). Taken together, such gamma-augmentation may directly reflect the cortical processing controlling movement of vocal-folds. Although less likely, one cannot completely rule out the effect of auditory perception of self-vocalization on ECoG gamma measures at the most inferior precentral site, because of the proximity with the planum temporale. Further studies combining electrical stimulation may better clarify the causal significance of gamma-augmentation differentially elicited by articulation of different phonemes.

In addition, the present study replicated the previous fMRI and ECoG observations that lip- and tongue-related phonemes were differentially associated with activation in distinct primary sensorimotor cortices (Pulvermüller et al., 2006; Brown et al., 2008b; Bouchard et al., 2013).

4.4. Significance of articulation-related gamma-augmentation and -attenuation

The present study demonstrated that articulation of consonants, compared to that of vowels, was associated with more variable patterns of gamma-modulations in Patient 1 (Supplementary Table S1); furthermore, the peak latency of gamma-augmentation in some Rolandic sites was earlier in consonants than in vowels. These ECoG findings are consistent with the observations in previous behavioral studies that articulation of consonants is generally associated with more complex configuration of articulatory structures required prior to exhalation of the air, as well as larger contact and airflow pressure at the place of articulation (Black, 1950; Arkebauer et al., 1967). Other behavioral studies reported that accurate articulation of consonants as compared to vowels requires more accurate positioning of oral structures such as lip and tongue (Flege et al., 1988; McFarland et al., 1996). The present study also suggested that some Rolandic sites can elicit gamma-augmentation during articulation of phonemes while gamma-attenuation during that of different phonemes (Figure 5). This ECoG finding indicates that articulation requires some

degree of coordination of agonist and antagonist muscles in oral structures (Sanguineti et al., 1997; Dang and Honda, 2004).

We failed to observe gamma-augmentation in the left inferior-frontal gyrus. Rather, we demonstrated significant gamma-attenuation involving both inferior-frontal and superior-temporal gyri in both patients (Supplementary Video S2). A plausible explanation for this ECoG finding is that such gamma-attenuation may reflect transient functional suppression in these cortical regions during automatic, self-paced vocalization of phonemes containing no semantic or syntactic information. The task assigned in the present study does not require judgment of phonological similarity or relation to others. It is also possible that our patients may have covertly engaged semantic or phonological processing during the resting period.

4.5. Methodological issues

ECoG analysis and electrical stimulation in the present study indicated that the sampled Rolandic region was associated with somatotopic organization of lips, tongue and larynx in a superior-to-inferior direction. Thereby, we failed to replicate the presence of larynx function above the level of sensorimotor lip areas, as demonstrated by previous ECoG and fMRI studies (Brown et al., 2008b; Bouchard et al., 2013). This discrepancy can be partly attributed to sampling limitations in our study. We utilized standard subdural grid electrode arrays with inter-electrode distances of 1 cm, while the previous ECoG study implanted dense arrays with inter-electrode distances of 4 mm (Bouchard et al., 2013). In the present study, each macro-electrode supposedly records electrical activities from on the order of 100,000 neurons (Modolo et al., 2010); thus, we cannot rule out the possibility that augmentation and attenuation of gamma-band activities were cancelled out within a single electrode site.

The number of trials may have influenced the results of time-frequency analysis of ECoG signals during articulation of each phoneme. For example, absence of significant gamma-augmentation during articulation of /u:/ in Patient 1 (Supplementary Table S1) does not infer that there was no augmentation but rather that statistical analysis of individual phoneme's effects did not have a sufficient power to detect a difference.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Movies delineate articulation-related cortical processing in distinct perisylvian regions.
- Gamma activity at 70–110 Hz in oral sensorimotor sites distinguished phonemes.
- Gamma activity in a larynx motor site distinguished voiced and voiceless phonemes.

Figure 1. Location of subdural electrodes

The regions of interest in the present study include the inferior Rolandic area within 4 cm from the sylvian fissure (white squared area). Previous studies using electrical stimulation have suggested that this region contains the primary sensorimotor cortex for the lip, tongue, and throat (Boling et al., 2002). The Rolandic site immediately below the bottom of central sulcus is referred to as the subcentral region (Electrode F4 in Patient 1 and F3 in Patient 2).

Figure 2. The results of electrical stimulation mapping

Electrical stimulation mapping in both patients indicated the somatotopic organization of the Rolandic region, where the primary somatosensory-motor areas for the hand, lip, tongue, and throat (larynx) were located in a superior-to-inferior direction. Absence of stimulation-induced symptoms does not mean that the stimulation cortex does not have a function, since electrical stimulation mapping does not have an optimal sensitivity for localization of the eloquent cortex (Kojima et al., 2012).

Figure 3. Common and differential Rolandic gamma-augmentation elicited by articulation of different phonemes

(A) The top row shows the sound spectrograms during articulation of phonemes /t/, /l/, and /3/ in Patient 1. (B) The second row indicates the fundamental frequency of sounds, which ranged between 310 and 330 Hz. (C) The results of time-frequency ECoG analysis are shown. Electrode F4 in the left subcentral region (Figure 1) showed early gamma augmentation commonly across phonemes. Electrode E3 in the precentral gyrus, D5 in the postcentral gyrus, and C4 in the precentral gyrus showed differential gamma-augmentation specific to phonemes /t/, /l/, and /3/, respectively.

Figure 4. Spatial-temporal characteristics of gamma-modulation 70–110 Hz during articulation of phonemes

In Patient 1, electrode F4 in the left subcentral region (red arrows) showed gamma-augmentation, commonly at least 280 ms prior to the onset of sound of phonemes /t/, /l/, and /z/. Electrode E3 in the precentral gyrus, D5 in the postcentral gyrus, and C4 in the precentral gyrus (each denoted by a black arrow) showed differential gamma-augmentation specific to phonemes /t/, /l/, and /z/, at the onset of sound generation. The superior-temporal and inferior-frontal gyri rather showed gamma-attenuation.

Figure 5. Gamma-augmentation and -attenuation in the same postcentral site in Patient 1

The top row indicates the fundamental frequency of phoneme sounds /θ/, /ʒ/, and /ʌ/, which ranged between 310 and 330 Hz. Electrode G3 in the precentral gyrus showed gamma-augmentation associated with phonemes /ʒ/ and /ʌ/. Electrode C5 in the postcentral gyrus showed gamma-augmentation associated with /θ/ but gamma-attenuation associated with /ʒ/ and /ʌ/.

Patient 1

(B)

Red : consonants

Blue: vowels

Figure 6. Phoneme-articulation-related gamma modulations₇₀₋₁₁₀ Hz in Patient 1

(A) The temporal dynamics of gamma-modulations related to each phoneme at each inferior Rolandic site are shown. X-axis represents the time relative to the onset of phoneme sound generation. Y-axis represents the magnitude of gamma-modulation relative to that during the resting period; 0 indicates no changes in gamma-amplitude₇₀₋₁₁₀ Hz, while 1.0 indicates amplitude augmentation by 100%. All sites other than electrodes F3 and E4 showed significant gamma-augmentation related to at least one of the 44 phonemes (see: *). (B) Each square delineates one standard error $\pm$ the median of the peak and peak latency of gamma-augmentation related to articulation of consonants (red) and vowels (blue). In

electrodes D5, E5, and F5, consonant-related gamma-augmentation was larger than vowel-related one (corrected $p < 0.05$; see solid lines). In electrode D4 (see broken line), the peaks of gamma-augmentation related to articulation of consonants was somewhat larger than that related to vowels (uncorrected $p < 0.05$ but corrected $p > 0.05$). In electrodes F4, F5, and C5, the peak latency of consonant-related gamma-augmentation was earlier than that of vowel-related one (corrected $p < 0.05$). (C) In electrode D4, the peak of gamma-augmentation related to articulation of tongue-related consonants was larger than that related to lip-related ones (corrected $p < 0.05$). In electrodes F4 and C5 (see broken lines), the peaks of gamma-augmentation related to articulation of lip-related consonants was somewhat larger than that related to tongue-related ones (uncorrected $p < 0.05$ but corrected $p > 0.05$).

Figure 7. Temporal dynamics of gamma-activity_{70–110} Hz during articulation of voiced and voiceless consonants in a precentral site in Patient 1

Red line shows the gamma-amplitude at a given moment averaged across all voiced consonants with standard error bars. Blue line shows that related to voiceless consonants. 0 indicates no changes in gamma-amplitude_{70–110} Hz, while 0.2 indicates amplitude augmentation by 20%. *: Voiced consonants, compared to voiceless ones, elicited larger gamma-augmentation at these moments.