

Spatiotemporal dynamics and functional correlates of evoked neural oscillations with different spectral powers in human visual cortex



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HIGHLIGHTS

- Spectral power analysis of VEPs in response to flash visual stimuli showed distinct spatiotemporal characteristics recorded from visual cortices in epilepsy surgery patients with intracranial recordings.
- High γ (60–150 Hz) evoked oscillations (EOs) predominantly belonged to the electrodes with simple form visual responses, whereas low γ (30–60 Hz) and lower frequency (LF) <30 Hz EOs were observed from those with intermediate form and LF EOs with complex form responses.
- Phase-locked EOs in these frequency bands may have special neuroanatomical and functional organization during early visual processing in human.

ABSTRACT

Objective: To investigate spatiotemporal characteristics and functional correlates of evoked oscillations (EOs) at different frequency bands in human visual cortex.

Methods: Flash visual evoked potentials (FVEPs) were recorded from 11 epilepsy patients with intracranial electrodes placed over the occipital and adjacent cortices. Spatiotemporal characteristics of spectral powers and correlation with various visual responses elicited by electrical cortical stimulations were analyzed in the same electrodes.

Results: High γ (60–150 Hz) EOs were first recorded in the cuneus and lingual gyri around the calcarine sulcus. Low γ (30–60 Hz) EOs appeared also in the mesial occipital cortex slightly later and lasted longer than high γ EOs. In contrast, lower frequency (LF) <30 Hz EOs were recorded more diffusely from occipital surfaces with delayed onset and longer duration. High γ EOs were predominantly associated with simple form visual responses, whereas low γ and LF EOs were with intermediate form and LF EOs with complex form responses.

Conclusions: FVEP spectral power analysis directly recorded from human visual cortex showed distinct spatiotemporal distributions in high and low γ , or LF bands that have different functional correlates.

Significance: Phase-locked EOs in these frequency bands may have special neuroanatomical and functional organization during early visual processing.

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1. Introduction

Visual evoked potential (VEP) is a standard diagnostic method widely used to evaluate the visual system integrity (Celesia, 1984). VEP also provides an opportunity to look into the cortical dynamics related to early visual processing (Asano et al., 2009).

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In clinical settings, negative or positive peaks of VEP waveforms after visual stimulation are obtained, and their latencies and amplitudes are analyzed. It has been shown that the potential peaks are superimposed with neural oscillations with different frequency bands. The evoked response is a phase-locked component to the stimulus onset obtained from time-domain averaging across trials, whereas the induced activity is a random component with varying latency after stimulation (Pantev, 1995; Tallon-Baudry et al., 1996). While most previous studies have been focused on visually induced neural oscillations (Tallon-Baudry et al., 1996; Tallon-Baudry, 2009; Schwarzkopf et al., 2012), VEPs have been studied mainly from scalp recordings (Cracco and Cracco, 1978; Mushin et al., 1984; Chin et al., 1985; Kraemer et al., 1999; Shepherd et al., 1999; Di Russo et al., 2002), occasionally from intracranial recordings (Arroyo et al., 1997; Asano et al., 2009). Considering that high frequency activities are significantly attenuated when recorded from the scalp (Pfurtscheller and Cooper, 1975), detailed spectral analysis of neural oscillations in VEP need to be elucidated from intracranial recordings.

Intracranial electrodes in epilepsy surgery patients to localize a seizure focus offer unique opportunities to record neuronal activities directly without significant attenuation (Crone et al., 2011). The current study aimed to analyze spatiotemporal dynamics of visually evoked neural oscillations with different spectral powers using intracranial electrode recordings in epilepsy patients. The electrode coverage of the mesial and inferior visual cortices in our patients also provided an excellent spatial resolution that could hardly be achieved by surface recordings. We previously mapped various visual experiences in response to electrical cortical stimulation (ECS) on different areas of the visual cortex in epilepsy patients (Lee et al., 2000). In order to infer functional relevance of neural oscillations with different spectral powers during early visual processing, the current study compared different frequency components of the VEPs in response to flash visual stimuli directly from cortical areas and observed different visual responses elicited by ECS. Our results showed that flash visual stimuli evoked neural oscillations at different frequency bands with distinct spatiotemporal dynamics and suggested that the evoked oscillations (EOs) at different frequency bands might be involved in different functions during early visual processing.

2. Methods

2.1. Patient selection

Eleven epilepsy surgery candidates participated in the current study. All patients underwent intracranial electrode monitoring over the occipital and adjacent cortical areas. All procedures were performed for clinical purposes, and informed consent was obtained from all patients. The study protocol was approved by the local Institutional Review Board.

2.2. Flash VEP data acquisition from intracranial electrodes

For flash VEP (FVEP), visual stimuli were 1.1 Hz light flashes delivered by light-emitting diodes using goggles with an output power of 3 J/flash, consistent with the international recommendations by the International Federation of Clinical Neurophysiology (IFCN) (Deuschl and Eisen, 1999). The peak light intensity was 1000 lux from 50 cm distance, decreasing to 50% of peak value within 50 μ s, with luminance at 3000 cd/m². Cortical responses were recorded by Viking IV intraoperative monitoring unit (Nicolet Ltd, Minster, OH, USA). All input signals were filtered at 0.016–300 Hz with a 60 Hz notch filter, digitized at sampling rate of

2 kHz, and averaged over 500 trials (Pantev, 1995). Data was converted into ASCII code and resampled at 1 kHz for further off-line analyses (Molotchnikoff and Shumikhina, 2000). Electrode impedance was <10,000 Ω for subdural electrodes. All electrodes were referenced against a single relatively inactive subdural electrode at the periphery (Crone et al., 2001).

2.3. Localizations of intracranial electrodes on 3-dimensional brain surface rendering

All patients underwent preoperative brain MRI and postoperative computerized tomography (CT) scans with intracranial electrodes. MRI was performed using a GE Signa 1.5-T unit (GE Medical Systems, Milwaukee, WI, USA). For high-resolution 3-dimensional (3D) volumetric MRI, the spoiled gradient recalled (SPGR) MR images were acquired as 124 contiguous no gap coronal slices of thin section in 1.5 mm with a repetition time of 33.3 ms, an echo time of 7.0 ms, 22 cm field of view (FOV), and 256 \times 256 matrix size. A GE Hispeed Advantage (GE Medical Systems, Milwaukee, WI, USA) was used for CT scanning. The scanning parameters were 120 kp, 220 ma, 1 s helical, 3 mm slice thickness no gap, the standard algorithm, display FOV 21 cm, scan FOV of head, and 512 \times 512 sampling matrix.

The electrodes were 4 mm diameter platinum–iridium disks with 1 cm center-to-center inter-electrode distances (AdTech Medical Instruments Corp., Racine, WI, USA). The anatomical locations of electrodes were determined by 3D MRI/CT co-registration using Analyze 9.0 (AnalyzeDirect Inc., Overland Park, KS, USA) (Lee et al., 2000). To display the electrodes on the individual patient's own brain surface, we created a triangular mesh surface model of each patient using FreeSurfer (<http://surfer.nmr.mgh.harvard.edu>) (Makris et al., 2006). Finally, electrode positions across patients normalized to the Montreal Neurological Institute (MNI) coordinates were mounted on 3D MRI co-registered in standard space (Fig. 1A) using SPM5 implanted MATLAB v7.7 (MathWorks, Natick, MA, USA).

2.4. Flash VEP spectral powers color display on the 3D cortical surface

Spectral powers of cortical signals were analyzed using a fast-Fourier Transform (FFT) (Fig. 1B and C). Baseline correction was applied for 250 ms epoch after stimulus onset. Spectral power (expressed in μ V) was computed with time resolution of 1/1000 s and frequency resolution of 250 Hz. Grand averaged power spectrum was averaged for different frequency components over all electrodes from all 11 patients. Absolute powers were obtained by square means of powers (expressed in μ V²) at different frequency bands from all electrodes and from those electrodes with significant VEP waveforms, respectively. The range of frequency bands was determined from the spectral power distribution patterns of our dataset. Since we identified distinct power distribution patterns at different frequency ranges, we separated FVEPs into three frequency bands: 60–150 Hz (high γ), 30–60 Hz (low γ), and lower frequency (LF) less than 30 Hz bands. To produce 3D color display of spectral powers in these frequency bands, calculation of spectral power was repeated using a moving window of 1 ms increment without overlap. Instantaneous amplitudes were estimated from analytic signals using Hilbert transform of filtered VEPs (Tass et al., 1999). For all FVEP waveforms, we determined the onset and offset latencies, durations, and peak latency of instantaneous amplitude, using MATLAB. In Fig. 2A, we illustrated how to determine these values in an example of raw VEP that showed the largest amplitude with mixed frequency components (G19 electrode in patient #1).

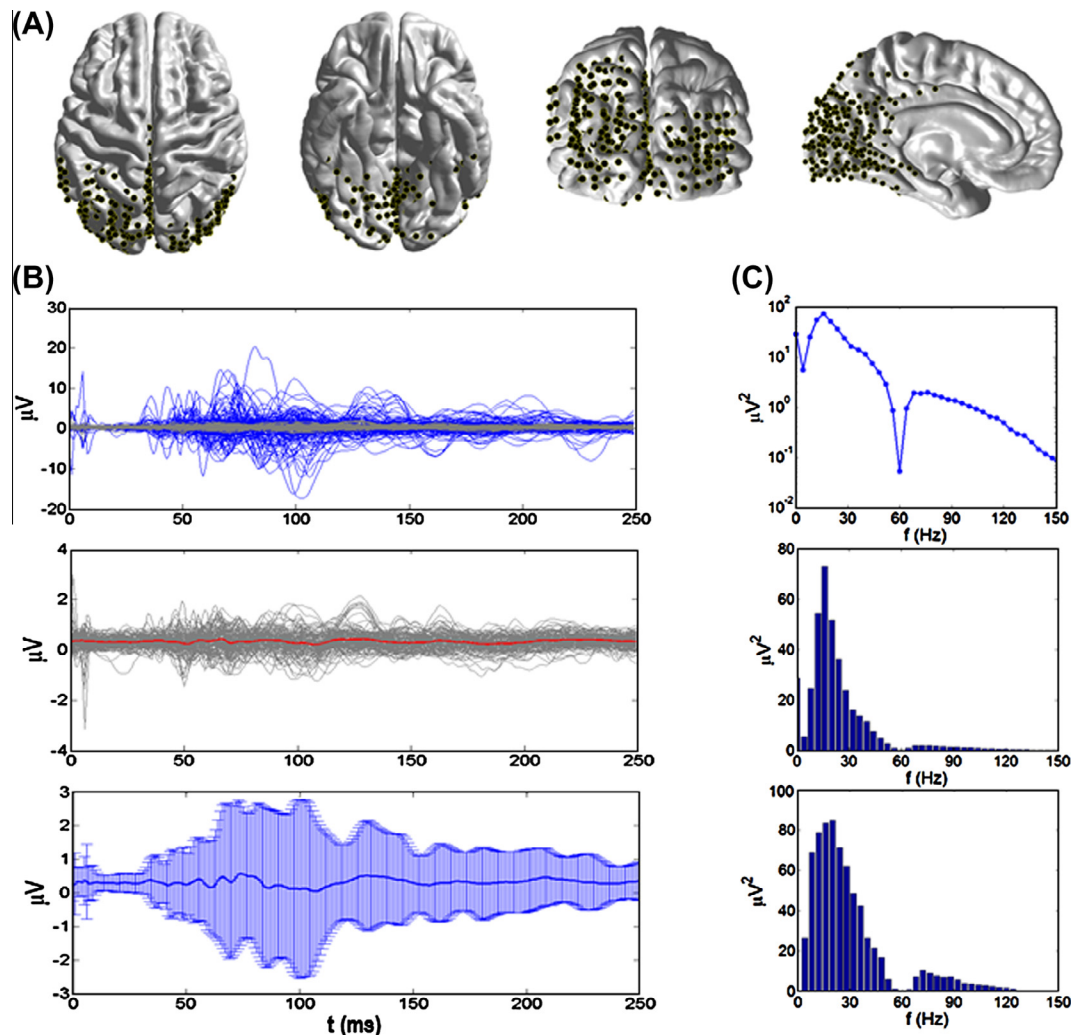


Fig. 1. Cortical location of 3D electrode maps and FVEP recordings drawn from electrodes over all 11 patients. (A) Three-dimensional maps on the brain surface renderings for the intracranial electrodes with statistically significant FVEP waveforms. (B) Individual waveforms of FVEPs from all electrodes with amplitudes larger (blue) and smaller (gray) than 2 μV (upper and middle panels), and the average amplitudes and standard deviations of all FVEPs across the time axis (lower panel). (C) Grand averaged power spectrum using FFT (upper panel), square means of powers at different frequency bands from all electrodes (middle panel) for all electrodes, and spectral powers from statistically significant VEPs (lower panel). Powers under 60 Hz clearly revealed that the power was peaked at 16 Hz and then dropped in higher than 30 Hz, which was the rationale for us to divide the waves further into lower frequency (LF) less than 30 Hz, low γ (30–60 Hz), and high γ (60–150 Hz) frequency bands.

2.5. Electrical cortical stimulation

Electrical cortical stimulation (ECS) was performed using a standard presurgical functional mapping method (Lee et al., 2000). Electrical currents were directly applied to brain cortex using a Grass S12 Isolated Biphasic Stimulator (Quincy, MA, USA) that generates 300 μV square waves at 50 Hz for 5 s. Electrical stimuli were initially delivered to each pair of neighboring electrodes. For the electrode pairs that elicited any positive visual responses, each electrode was tested again as an active electrode with a silent reference electrode in the electrode array to confirm which electrode was responsible for that specific response. If a visual response occurred, patients reported this verbally and were asked to draw the shape. Reported shapes were categorized into simple, intermediate, and complex forms according to their outline and shape as described in the previous study (Lee et al., 2000). Briefly, the simple form was defined as a white or black spot or a blob of flashing light, the intermediate form as a geometric shape, triangle, diamond, or star, and the complex form as a more complicated formed visual hallucination or illusion. Averaged

time–frequency spectral power map was plotted for each visual response type separately to investigate their functional relevance based on ECS cortical mapping.

2.6. Statistical analysis

To examine whether the oscillatory activity was random baseline fluctuation or not, we used a bootstrap test, where null hypothesis H_0 = random signal and $P < 0.02$ was set for a statistically significant oscillation in a given frequency band. For Bootstrap test, a more conservative P -value ($P < 0.02$) was set to provide statistical significance, using a method based on surrogate averages from our dataset as proposed in recent studies on evoked potentials (Lv et al., 2007; McCubbin et al., 2008).

One-way analysis of variance (ANOVA) was used to compare the onset, offset, peak latency, duration, and power of each frequency band of FVEP. A general linear model (GLM) was computed to test the main effects for cortical locations (medial, inferior, lateral) \times frequency bands (high and low γ , LF). For the functional correlates of different frequency bands, a GLM was tested for the

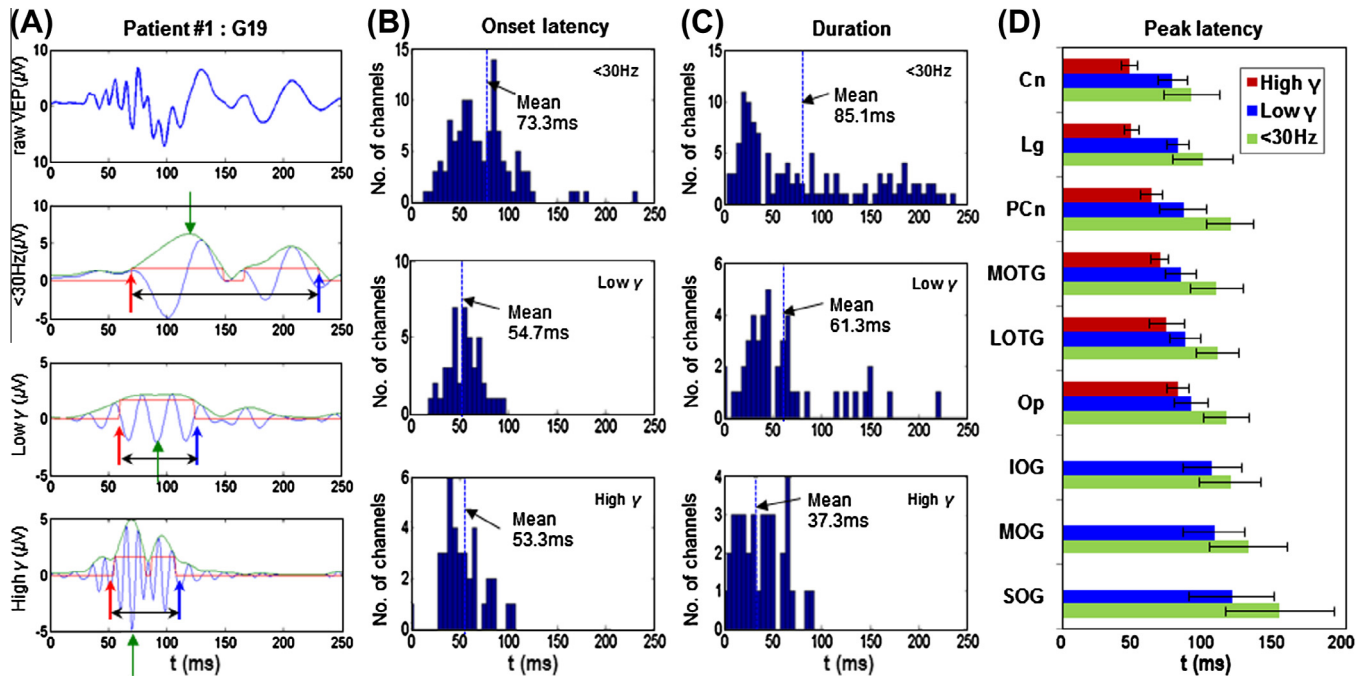


Fig. 2. Analysis of individual FVEP waveforms. (A) An example of FVEP waveform that shows the largest amplitude with mixed frequency components (G19 electrode in patient #1). Waveforms of raw FVEP (upper), <30 Hz lower frequency, low γ and high γ from 2nd to 4th rows, respectively. Red, blue and green arrows denote the start, end and peak latencies of significant FVEP at each frequency band. Duration between start and end time points of each signal was depicted by black arrows. Initial time points (B) and durations (C) of all FVEP waveforms, and peak time points in each anatomical location (D) from all 11 patients were indicated in the graphs. Note that the high γ EOs appeared the earliest (53.3 ms mean onset latency) and lasted the shortest period of time (37.3 ms on average) after the flash stimulation, whereas low γ and LF EOs occurred later (54.7 and 73.0 ms) and lasted longer (61.3 and 85.1 ms). Abbreviations: Cn, cuneus; Lg, lingual gyrus; PCn, precuneus; MOTG, medial occipitotemporal gyrus; LOTG, lateral occipitotemporal gyrus; Op, occipital pole; IOG, inferior occipital gyrus; MOG, middle occipital gyrus; SOG, superior occipital gyrus.

main effects of visual response (simple, intermediate, complex forms) and frequency factors (high and low γ , LF). Bonferroni correction was used for post hoc analysis. All statistical analyses were performed using a MATLAB and SPSS® v19.0 with $P < 0.05$ as a statistical significance except for bootstrap test.

3. Results

3.1. Spatio-temporal dynamics of flash VEP waveforms

Eleven patients (5 females and 6 males) aged from 11 to 35 (25.4 ± 7.1) years participated in the current study (Table 1). The 243 out of 1050 electrodes that showed statistically significant FVEPs from all 11 patients were depicted on a standard brain template (Fig. 1A). The electrodes that showed EOs were located in the cuneus, precuneus, and lingual gyri of the medial surface, medial and lateral occipitotemporal gyri of the inferior surface, occipital pole, inferior, middle, and superior occipital gyri of the lateral cortical areas. Individual waveforms from all electrodes over all 11 patients were plotted as separate lines with amplitudes of larger and smaller than $2 \mu\text{V}$, with mean and standard deviations demonstrated across the time axis (Fig. 1B). Grand averaged power spectrum using FFT (upper panel), square means of powers at different frequency bands from all electrodes (middle panel) from all electrodes over all patients, and spectral powers from statistically significant VEPs (lower panel) were demonstrated, respectively (Fig. 1C). Spectral power distributions of VEPs showed a maximum power at frequency around 16 Hz and distinct power distributions in lower and higher than 60 Hz (notch filter effect) and almost negligible in higher than 130 Hz, which was the rationale for us to divide the waves further into high γ (60–150 Hz), low γ (30–60 Hz), and lower frequency (LF) <30 Hz.

In an example of FVEP waveform from the patient #1 in Table 1, EOs in high or low γ bands were superposed on the LF at different time points; 50 to 110 ms for high γ , 60 to 125 ms for low γ , and 75 to 230 ms for LF (Fig. 2A). From all significant FVEP waveforms, the onset latencies seemed shorter for high or low γ than LF EOs (53.3 ± 9.8 , 54.7 ± 12.9 , and 73.3 ± 18.2 ms, respectively; $F_{2,258} = 2.471$, $P = 0.086$; Fig. 2B). High γ lasted shorter than low γ or LF EOs (37.3 ± 13.6 , 61.3 ± 21.5 , 85.1 ± 32.7 ms; $F_{2,258} = 5.707$, $P = 0.004$; Fig. 2C). Peak time points were illustrated in each anatomical location (Fig. 2D). High γ EOs showed peak amplitudes first in the cuneus and lingual gyri around 50 ms, later in the precuneus, and then peaked in the medial and lateral occipital temporal gyri mostly before 100 ms, but did not spread to other cortical gyri in the lateral cortical surface. Low γ EOs were peaked in the most cortical gyri of the medial and inferior occipital areas slightly later than high γ EOs. In contrast to the high γ , low γ EOs also appeared in the lateral occipital cortex with a delayed time course peaked around or after 100 ms. LF EOs clearly showed peak amplitudes later than other frequency bands in all cortical areas, around 100 ms in the cuneus and lingual gyri, and then peaked later in the precuneus or other cortical gyri of the inferior and lateral occipital areas. Onset and end latencies were shorter in the medial or inferior occipital surfaces compared with the lateral cortex ($P = 0.001$ and 0.021 , respectively).

FVEPs in different frequency bands were color plotted from the medial (patient #1), lateral, and inferior (patient #10) cortical areas, who had extensive electrode coverage in these surfaces, on the patients' own 3D brain rendering (Fig. 3). Similar to the trends described above, the early FVEP responses in high and low γ EOs were elicited in the cuneus and lingual gyri near the calcarine sulcus. Interestingly, high and low γ EOs were temporally overlapped in the medial occipital cortex, but the high γ appeared and disappeared earlier than low γ EOs. Low γ EOs

Table 1

Clinical characteristics including intracranial electrode locations in all 11 patients.

No.	Age (y)	Gender	Age at onset (y)	Seizure semiology	Final localization ^a	Pathology	Total No. of electrodes implanted	No. of electrodes with significant FVEP	Intracranial electrodes coverage	Surfaces covered by electrodes
1	26	F	12	CPS, sGTC	Lt POLE	CD	96	34	Lt TPO	Med, Lat
2	23	M	7	CPS, sGTC	Lt TLE	Astrocytoma	40	8	Lt TO	Lat, Inf
3	11	M	0.5	CPS, sGTC	Rt PLE	Gliosis	60	28	Rt TPO	Med, Lat
4	26	M	7	CPS, sGTC	Lt TLE	CD	96	34	Lt TO	Med, Inf
5	28	M	3	CPS, sGTC	Lt TOLE	CD	92	21	Lt TPO	Med, Lat
6	25	F	19	CPS, sGTC	Rt TLE	Gliosis	48	8	Rt TO	Lat, Inf
7	15	F	2	CPS, sGTC	Lt TLE	CD	160	28	Lt TO	Lat, Inf
8	31	F	27	CPS, sGTC	Lt TLE	Oligoastrocytoma	94	17	Lt TO	Lat, Inf
9	32	M	9	CPS, sGTC	Lt TOLE	CD	164	7	Lt TO	Med, Inf
10	27	F	15	CPS, sGTC	Rt TLE	HS, gliosis	88	31	Rt TO	Lat, Inf
11	35	M	11	CPS, sGTC	Rt TOLE	CD	112	27	Rt TPO	Lat, Inf

No., number; yrs, years; M, male; F, female; CPS, complex partial seizure; sGTC, secondary generalized tonic–clonic seizure; Lt, left; Rt, right; TLE, temporal lobe epilepsy; PLE, parietal lobe epilepsy; TOLE, temporo-occipital lobe epilepsy; POLE, parieto-occipital lobe epilepsy; CD, cortical dysplasia; HS, hippocampal sclerosis; TPO, temporo-parieto-occipital; TO, temporo-occipital; Med, medial; Lat, lateral; Inf, inferior.

^a Final epilepsy localization based on surgical resection.

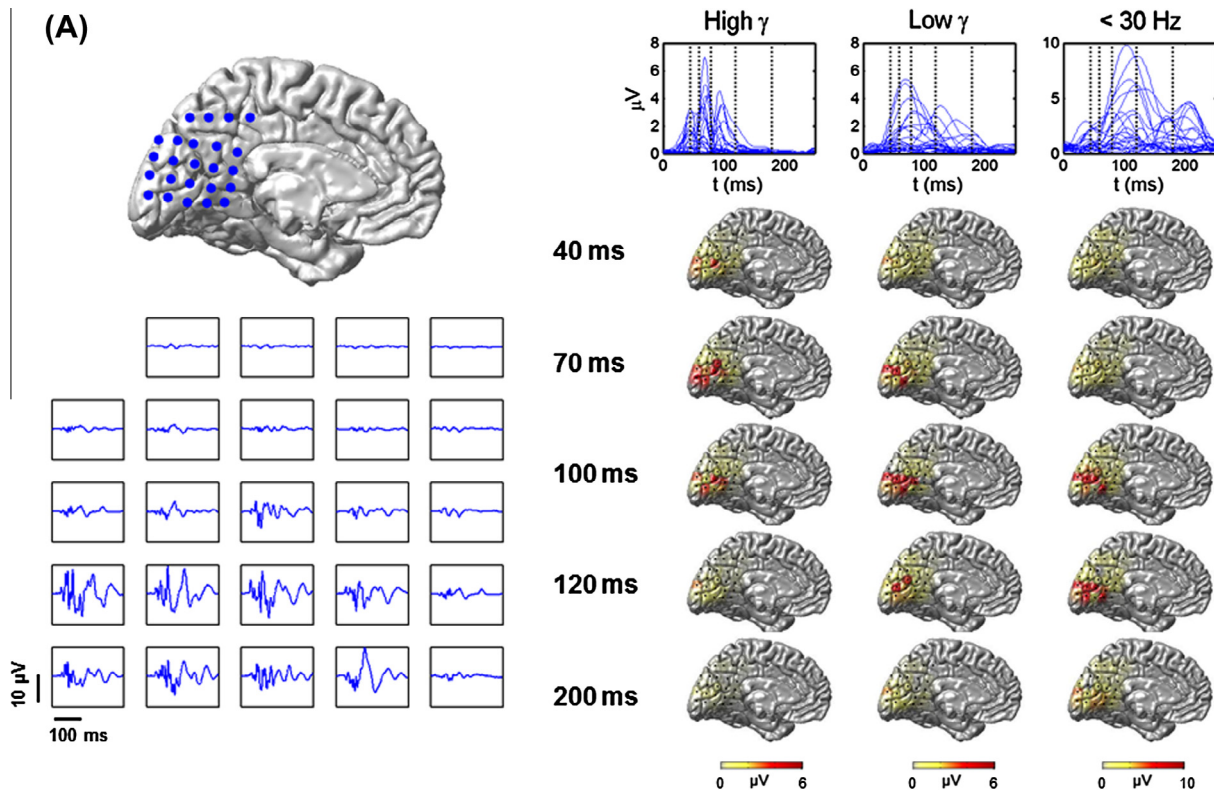


Fig. 3. Power maps of different frequency activities from the medial (A), lateral (B) and inferior (C) cortical surfaces. Powers of waveforms in high (60–150 Hz) or low γ (30–60 Hz), and lower frequency (<30 Hz) bands were color plotted at different time points. In the left column, the cortical location of the electrodes that show raw FVEP signals in the lower rows is illustrated on the patients' own 3D brain surface in the upper row by dots of the same orientation and the same color. The vertical lines in the plots at the top right corner correspond to the time points for cortical maps in the rows below them. The EOs in both high and low γ ranges were elicited at the cuneus and lingual gyrus near the calcarine sulcus at slightly different time ranges with overlap to a certain degree. Lower frequency activity appeared later at more extended areas in the occipital and occipitotemporal cortices. Data shown are from the patient #1 for the medial side, and the patient #10 for the lateral and inferior surfaces indicated in Table 1. See also the Supplementary Video S1.

occurred slightly later in the cuneus and lingual gyrus, and sequentially spread in the medial and part of lateral occipitotemporal gyri, then in the lateral cortex, especially occipital pole. In contrast, LF EOs were observed in the larger cortical areas, including medial, inferior, and lateral surfaces, and lasted longer than high or low γ EOs, even after 200 ms of stimulus onset. The 3D movies displayed powers at different frequency bands with moving windows of every millisecond for the same patients (see also the Supplementary Video S1).

3.2. Functional correlates of EOs in different frequency bands

We compared the results of FVEPs and functional mapping results using ECS. Total number of electrodes with both FVEP and positive visual responses was 43; simple form in 13, intermediate form in 25, and complex form in five electrodes, for which their cortical distributions are illustrated (Fig. 4A).

In order to investigate the functional correlates of EOs, time–frequency analysis was performed and averaged at the electrodes

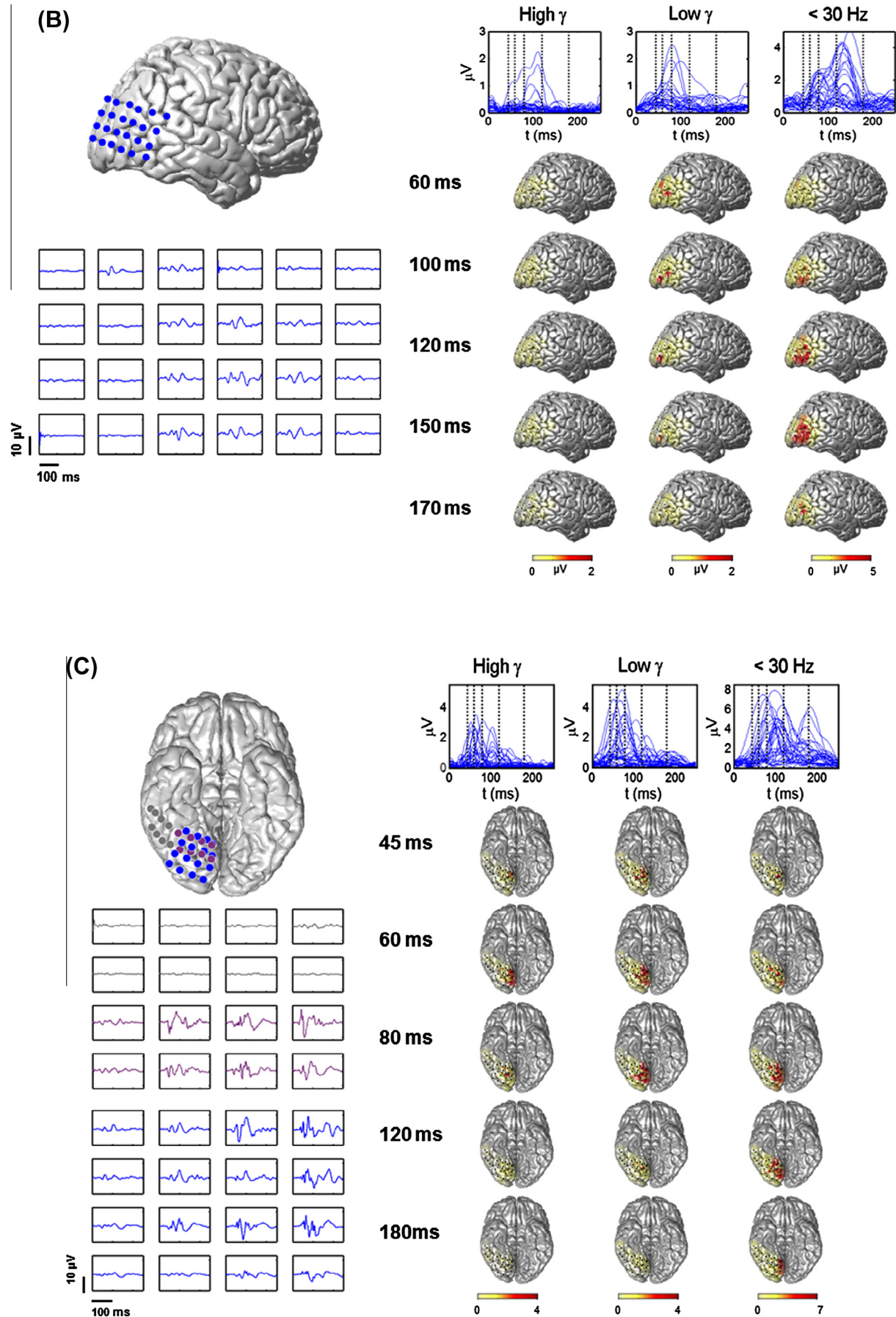


Fig. 3. (Continued)

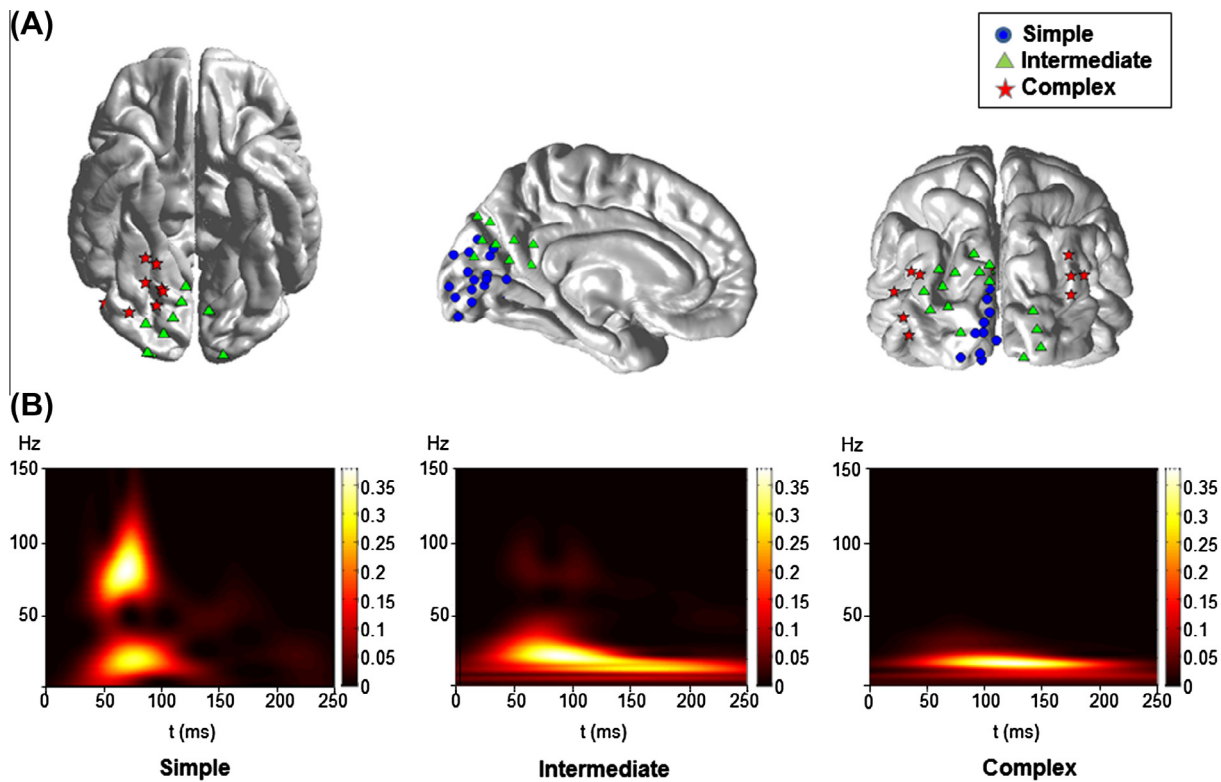


Fig. 4. Functional relationships of FVEP frequency bands and various visual responses elicited by electrical cortical stimulation. (A) 3D cortical location of electrodes showing simple (blue dots), intermediate (green triangles), and complex (red stars) forms of visual responses elicited by ECS for functional mappings. (B) Spectral power analysis of FVEPs from electrodes that showed simple (left), intermediate (middle), and complex (right) forms by electrical stimulation. Note that the FVEPs from electrodes with simple forms were largely related to the high γ EOs whereas intermediate and complex forms were more related with low γ and LF EOs.

that showed simple, intermediate, and complex form responses, respectively (Fig. 4B). High γ power was observed mainly in the electrodes with simple form response, which showed peak amplitudes between 50 and 80 ms. In contrast, the electrodes with intermediate form response showed mainly low γ and LF powers for longer duration. EOs in high or low γ bands were much less prominent in the electrodes with complex than those with simple or intermediate form responses. High γ powers were significantly higher in electrodes that showed simple form response compared with other forms ($F_{2,38} = 3.332$, $P = 0.046$), whereas differences in low γ and LF powers were not significant among different visual responses ($F_{2,38} = 0.807$, $P = 0.453$; $F_{2,38} = 1.269$, $P = 0.293$, respectively).

4. Discussion

This study demonstrated cortical generators and the functional correlates of EOs in the human visual cortex by using flash stimuli. We observed that EOs in high and low γ frequency bands were generated initially in the primary visual cortex (V1), but high γ EOs appeared earlier and lasted shorter than low γ . In contrast, LF EOs were elicited from widespread visual cortical areas encompassing the medial, inferior, and lateral surfaces with longer latencies and durations than high or low γ EOs. Cortical areas showing simple form visual responses were associated with high γ EOs at earlier time point, intermediate forms with low γ and LF EOs, whereas complex forms were related with LF EOs with longer durations, but not clearly associated with EOs in high or low γ bands.

4.1. Spatiotemporal characteristics of FVEP components

Our study demonstrated that EOs in different frequency components showed distinct temporal and spatial characteristics in human visual cortex. One of the previous scalp EEG studies demonstrated early visual oscillatory potentials after flash stimuli in midline and parasagittal scalp leads that were superimposed with fast (about 100 Hz) and slower potentials at 9–24 ms after stimulation (Cracco and Cracco, 1978). Earlier studies using scalp EEG showed that VEPs are frequency selective and they reach the maximum amplitude in high frequency band between 45 and 55 Hz (Tallon-Baudry et al., 1996; Tallon-Baudry, 2009). In another study, visual-evoked MEG activity appeared at 80–170 ms after stimulation (Supek et al., 1999).

A recent intracranial recording study demonstrated flash visual stimuli augmented γ in the anterior-medial occipital cortex with a mean latency of 31 ms (Asano et al., 2009), similar to our findings. Another intracranial study reported that high γ (80–150 Hz) oscillations were observed in more restricted regions of the medial occipital cortex at early latency of 30–90 ms, whereas slower frequency bands were observed later in more diffuse cortical areas (Matsuzaki et al., 2012). We additionally investigated FVEP in different frequency bands and documented that high γ EOs appeared earlier and lasted shorter than low γ and LF activities. Interestingly, high and low γ activities revealed similar cortical localizations especially at earlier time points, whereas LF EOs appeared not only in the medial and inferior surfaces, but also extended to the lateral cortical areas with much longer durations. In contrast, LF EOs had quite different cortical distribution, which might indicate the existence of more than one different generators involving human FVEP

oscillations. However, whether they overlap partly, whether they are functionally different generators, whether they are sequential activation in the same neuronal generators, or whether they overlap partly in either the same or different generators are still unknown.

Based on the previous report, LF and low γ activities have comparable signal shapes with scalp recording results (~ 40 Hz) (Tallon-Baudry et al., 1996). Previous studies showed scalp FVEPs recorded from patients with bilateral occipital infarction sparing the lateral occipital lobe had normal P1 potential amplitude without an early N1 component (Spehlmann et al., 1977; Celesia et al., 1991). Dipole source localization methods demonstrated multiple dipole sources generating VEP (da Silva and Spekreijse, 1991; Arroyo et al., 1997). A previous study on visual-evoked MEG activity was modeled by three sources; one in the calcarine area, two extrastriate sources in the dorsal occipito-parietal and ventral occipito-temporal areas (Supek et al., 1999). These findings may suggest the existence of different generators.

4.2. Functional correlates and possible mechanism of EOs

Our results also suggest the EOs in different frequency bands might have different functional roles especially during early visual processing in human visual cortex. In this study, high γ EOs observed in V1 at earlier time points were more closely associated with simple visual responses. The γ oscillations, particularly in high γ band, are classically known to reflect higher cortical functions rather than simple sensory response. A direct causality between spectral component of EOs and visual responses elicited by electrical cortical stimulation is not certain in this experimental setting since these two methods are quite different to compare these findings directly. However, our study showed that different types of visual responses to electrical stimulation were associated with distinct frequency bands of FVEPs in the anatomical sites where they were elicited. One possibility is that there might be major overlap between the cortical locations (in the visual pathway) where particular frequency bands of EOs were observed after flash stimulation and where different types of visual responses were elicited by electrical cortical stimulation. Another plausible explanation is that higher phase-locked frequency components might be more difficult to synchronize than lower phase-locked frequency activities, so the high frequency EOs can be seen only at early latencies in a restricted area near V1 (early in the visual pathway) while low frequency EOs can be observed at longer latencies in more widespread areas (including higher visual cortices). The spectral analysis in induced activities possibly using different visual stimuli or tasks warrants in future studies.

The mechanism why certain frequency is dominant for different aspect of visual function remains to be elucidated. Several studies proposed that the frequency bands depend on the size of cortical or neural network (Panagiotaropoulos et al., 2012; Schwarzkopf et al., 2012), conduction delays increase in large network at lower frequencies (Buzsaki and Draguhn, 2004), more refined spatial scale relates to higher frequencies, or the network configuration may influence the dominant frequency band (Cunningham et al., 2004). It was also suggested that even the same anatomical network could modulate its frequency in a task-dependent manner – for example, the same frontoparietal network can engage in coherent activity at different frequencies for different tasks (Buschman and Miller, 2007). In our results, FVEPs in different frequency bands were observed in human V1 with some time lags overlapped a certain degree, which might result from modulation in the same neuronal group, but lead to different functional roles in visual processing. Event related potentials (ERPs), phase-locked synchronized activity to stimulus onset, are deeply modulated by spatial attention (Luck et al., 2000), and the feedback of an attentional

modulation from extrastriate areas to primary visual cortex can be achieved within 200 ms of stimulus processing (Noesselt et al., 2002; Tallon-Baudry, 2009), which might have relevance to our findings.

4.3. Methodological consideration

Several methodological limitations should be noted. First, the visual responses we observed might differ from those of healthy people. We recorded FVEPs in candidates for epileptic surgery and their brain functions could be influenced by epileptic seizures. Second, subdural electrode coverage was limited in some patients, and thus, gamma band responses might be missed in the cortical areas that were not covered. However, intracranial recordings have clear merits that can record human neural activities directly from the human brain cortex, without any signal attenuation and with much more precise spatiotemporal information. Third, our study focused on intracranial VEP, more specifically on phase-locked components of neural oscillations to the flash visual stimuli. It would further reveal the functional and anatomical relevance of gamma band oscillations in the visual cortex if the spectral analyses are done for both phase-locked and nonphase-locked with various visual stimuli or tasks.

5. Conclusion

In summary, we found EOs in different frequency bands directly recorded from the human visual cortex after flash visual stimulation. FVEPs in high and low γ , or LF bands were observed with distinct spatiotemporal distributions and different functional correlates. Accordingly, phase-locked EOs in high and low γ , or LF bands may have special neuroanatomical and functional organization, especially during early stage of human visual processing.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.clinph.2013.04.341>.

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