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Four-dimensional map of the human early visual system

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HIGHLIGHTS

- We generated a 4D map of neuronal modulations elicited by full-field photic stimulation.
- The visual cortex showed an eccentricity-dependent gradient in the post-activation suppression.
- Our unique ECoG dataset effectively clarified the neuronal events underlying VEP components.

ABSTRACT

Objective: We generated a large-scale, four-dimensional map of neuronal modulations elicited by full-field flash stimulation.
Methods: We analyzed electrocorticography (ECoG) recordings from 63 patients with focal epilepsy, and delineated the spatial-temporal dynamics of visually-elicited high-gamma$_{70\text{-}110\ Hz}$ amplitudes on a standard brain template. We then clarified the neuronal events underlying visual evoked potential (VEP) components, by correlating with high-gamma amplitude measures.
Results: The medial-occipital cortex initially revealed rapid neural activation followed by prolonged suppression, reflected by augmentation of high-gamma activity lasting up to 100 ms followed by attenuation lasting up to 1000 ms, respectively. With a number of covariate factors incorporated into a prediction model, the eccentricity representation independently predicted the magnitude of post-activation suppression, which was more intense in regions representing more parafoveal visual fields compared to those of more peripheral fields. The initial negative component on VEP was sharply contoured and co-occurred with early high-gamma augmentation, whose offset then co-occurred with a large positive VEP peak. A delayed negative VEP peak was blunt and co-occurred with prolonged high-gamma attenuation.
Conclusions: Eccentricity-dependent gradient in neural suppression in the medial-occipital region may explain the functional difference between peripheral and parafoveal/central vision. Early negative and positive VEP components may reflect neural activation, whereas a delayed negative VEP peak reflecting neural suppression.
Significance: Our observation provides the mechanistic rationale for transient scotoma or mild flash-blindness, characterized by physiological afterimage preferentially formed in central vision following intense but non-injurious light exposure.

1. Introduction

Humans manage to live under the sun, and are repeatedly exposed to gross and extensive changes in low-level visual information in daily life. For example, you might remember that the sunlight dazzled your eyes when you stepped out from a movie theater. Experimental studies using visual-evoked potentials (VEP) and electrical stimulation suggest that such visual perception is associated primarily with neural processing in the medial-occipital region (Barett et al., 1976; Ducati et al., 1988; Winawer and Parvizi, 2016; Bosking et al., 2017). Electrophysiological studies of animals suggest that flash stimuli elicit neural activation in

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the striate cortex (also known as primary visual cortex or, simply, V1) within 100 ms after stimulus onset, as reflected by increased firing rate and augmentation of high-gamma activity above 70 Hz; in turn, the offset of visual stimuli elicits neural suppression as reflected by attenuation of high-gamma activity below the baseline level (Leopold and Logothetis, 1998; Ray and Maunsell, 2011). Studies of patients with focal epilepsy, using electrocorticography (ECoG), also replicated flash-related high-gamma augmentation followed by attenuation in the early visual cortex (Asano et al., 2009b; Matsuzaki et al., 2012). Yet, it still remains undetermined if there is a large-scale spatial difference across the human medial-occipital region in the dynamics of neural processing for full-field visual stimulation. We expect that functional difference, if present in an eccentricity-dependent manner, would improve our understanding of the early visual cortex for parafoveal and far peripheral fields. *How can we test this?* Quantitative measurement of neural responses from deep portions of the medial-occipital cortex may be difficult using noninvasive methods such as scalp EEG or magnetoencephalography. ECoG provides a unique opportunity of direct recording from the human cortical surface, but spatial sampling is generally limited in individual patients undergoing presurgical evaluation of focal epilepsy because extensive ECoG sampling from the nonepileptic striate cortex is frequently not feasible nor clinically warranted. Here, we overcame such limited spatial sampling, by combining ECoG signals derived from a large number of patients, each of whom had a small number of strip electrodes placed on the medial-occipital cortex which turned out to be non-epileptic following chronic ECoG monitoring. This approach allowed us to delineate visually-elicited neural modulations on a standard brain template in a four-dimensional manner. The main goal of this study is to determine if the early visual cortex in the medial-occipital region would have eccentricity-dependent difference in visually-elicited high-gamma dynamics.

The second goal of this study is to determine the neural events underlying the components of VEP (American Clinical Neurophysiology Society, 2006; Odom et al., 2016). Both on scalp EEG and intracranial ECoG recording, normal VEP at the occipital lobe consists of a negative peak at a latency of <100 ms (referred to as N1 here), a positive peak around 100 ms (referred to as P2), and subsequently followed by a second, delayed negative peak (referred to as N3). VEP peak latencies are often utilized for clinical diagnosis, and it would be valuable to provide the empirical data addressing whether each VEP peak indeed reflects neural activation or suppression in human early visual cortex. As suggested in studies with monkeys (Wilke et al., 2006; Whittingstall and Logothetis, 2009), we hypothesized that the initial negative VEP component would co-occur with high-gamma augmentation, reflecting neural activation (Ray et al., 2008; Crone et al., 2011; Magri et al., 2012). Conversely, we hypothesize that the delayed VEP components would rather co-occur with high-gamma attenuation; thus, reflecting neural suppression.

2. Materials and methods

The inclusion criteria consisted of patients with focal epilepsy who underwent functional brain mapping using flash stimuli during extraoperative ECoG recording at Children's Hospital of Michigan or Harper University Hospital in Detroit. The exclusion criteria consisted of: (i) age younger than 4 years (Nakai et al., 2017), (ii) presence of massive cortical malformations affecting the calcarine, central or lateral sulcus, (iii) seizure onset zone, interictal spikes, or epileptogenic lesions involving the medial-occipital cortex (i.e.: lingual and cuneus gyri below and above the calcarine sulcus, respectively; Fig. 1), and (iv) history of previous epilepsy surgery. Sixty-three patients satisfying the inclusion and exclusion criteria were studied (age range: 4–44 years; 32 females; Table 1). The study was approved by the Institutional Review Board at Wayne State University, and informed consent was obtained from the patients or guardians of patients.

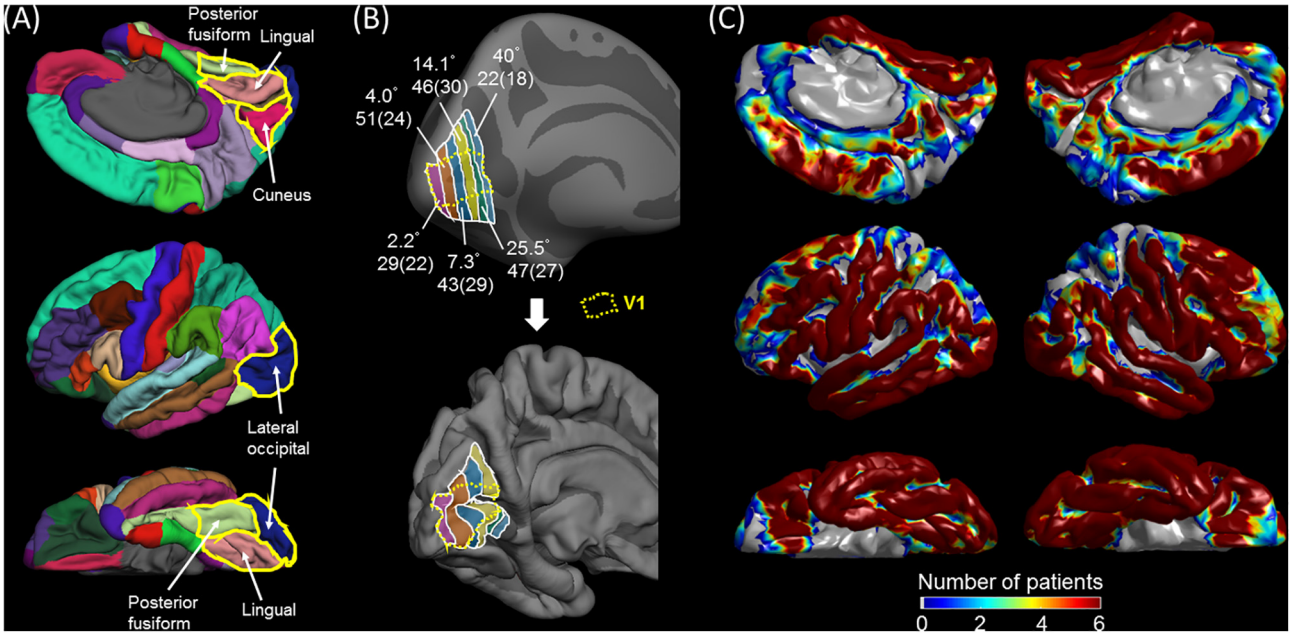

Fig. 1. Regions of interest (ROIs), eccentricity estimates, and distribution of subdural electrodes. (A) The medial-occipital cortex was defined to consist of the lingual (pink; below the calcarine sulcus) and cuneus regions (wine red; above the calcarine sulcus). The lateral occipital (blue) and posterior fusiform regions (light green) were defined as previously reported (Desikan et al., 2006; Nakai et al., 2017). (B) The inflated (upper) and pial (lower) images of the left hemisphere of the FreeSurfer averaged brain denote the medial-occipital regions with mean receptive-field eccentricity of 2.2, 4.1, 7.3, 14.1, 25.5, and 40.0° (Benson et al., 2012; Griffis et al., 2015). The boundary of striate cortex (V1; Hinds et al., 2008) in the medial-occipital surface is delineated with a broken line. The number of analyzed electrodes within a given eccentricity region for either hemisphere is indicated (along with number of contributing patients in parentheses). (C) The distribution of subdural electrodes, included in further analyses, is indicated at the whole-brain level. It should be noted that subdural disk electrodes inherently fail to sample ECoG activities generated by the deep cortex along the calcarine sulcus. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)