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Timing of early activity in the visual cortex as revealed by simultaneous MEG and ERG recordings

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To clarify the latency of the earliest cortical activity in visual processing, electroretinograms (ERGs) and visual evoked magnetic fields (VEFs) following flash stimulation were recorded simultaneously in six human subjects. Flash stimuli were applied to the right eye and ERGs were recorded from a skin electrode placed on the lower lid. ERGs showed two major deflections in all subjects: an eyelid-negativity around 20 ms and a positivity around 60 ms corresponding to an a- and b-waves, respectively. The mean onset and peak latency of the earliest component of VEFs (37M) was 30.2 and 36.9 ms, respectively. There was a linear correlation between the peak latency of the a-wave and the onset latency of the 37M ($r = 0.90$, $P = 0.011$). When a single equivalent current dipole analysis was applied to the 37M, four out of six subjects showed highly reliable results. The generator of the 37M was estimated to be located in the striate cortex in all four subjects. Since postreceptoral activities in the retina are expected to start around the peak of the a-wave (20 ms), the early cortical activity, which appears 10 ms later than the a-wave peak, is considered to be the earliest cortical activity following flash stimulation.

Keywords: a-wave; b-wave; VEF; V1

Introduction

As compared with the timing of cortical activation following somatosensory or auditory stimulation, that of early cortical activation following visual stimulation is not well understood in humans. Previous studies using visual evoked potentials (VEPs) have reported early cortical peaks in response to flash stimuli with a latency ranging from 35 to 80 ms (Cobb and Dawson, 1960; Cigánek, 1961; Allison et al., 1977; Pratt et al., 1982; Whittaker and Siegfried, 1983; Yoneda et al., 1995). Likewise, the latency of the early striate activity evoked by pattern stimuli varied, ranging from 42 to around 100 ms in VEP and magnetoencephalographic studies (Jeffreys and Axford, 1972; Aine et al., 1995; Nakamura et al., 1997; Brecelj et al., 1998; Portin et al., 1999; Supek et al., 1999; Di Russo et al., 2001; Moradi et al., 2003; Vanni et al., 2004). Therefore, it appears that the timing of the earliest cortical activation by visual stimuli remains to be elucidated.

Changes of potential in the retina following photic stimulation can be recorded from a corneal electrode or skin electrodes placed around the eye as electroretinograms (ERGs). The ERG is a mixture of potentials generated by various retinal cell types. Human and animal studies have shown that, in general, the a-wave reflects the activity of photoreceptors (Hood and Birch, 1990) and the b-wave originates from bipolar cells (Robson and Frishman, 1999) or glias (Tomita and Yanagida, 1981). Since the photoreceptor currents create monophasic negative potentials in ERGs (Hood and Birch, 1990), the appearance of positive-going potentials indicates that photoreceptor activities are spread to the inner layers of the retina. Therefore, the peak of the a-wave approximately reflects the timing of signal transfer from the photoreceptor to the next step.

In the present study, we recorded magnetoencephalograms (MEGs) following flash stimulation to elucidate the timing of early cortical activity. MEGs can provide high temporal and spatial resolutions and are suitable for the detection of early cortical activities. In addition, we investigated the reliability of the latency of the early visual cortex using simultaneous recordings of ERGs. If the recorded magnetic activity in the early visual cortex actually reflects the earliest cortical activity, it should appear in relation to a certain ERG component with an appropriate time delay for the signal conduction from the retina to the cortex.

Methods

Subjects

Six healthy male subjects aged 27–40 years participated in this study. All were free from ophthalmic or neurological disorders and

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had a corrected visual acuity within the normal range. The study was approved in advance by the Ethical Committee of the National Institute for Physiological Sciences and written consent was obtained from all the subjects.

Stimulation and recordings

Experiments were conducted in a fully darkened shielded room. Subjects lay supine on a bed with their head fixed to the biomagnetometer with adhesive tape to prevent movement. Since electric devices, such as the Ganzfeld stimulator, could not be used in the shielded room because of magnetic noise, we used flash stimuli in the present study. Flash stimuli of 20 J (1460 cd as a point source) were delivered with a xenon light stimulator (SLS-3100, Nihonkoden, Tokyo) at an interval of 1.4 to 2.0 s. The duration of the flash was about 7 ms (Fig. 1). The light was placed outside the room and applied to the subjects through a small square window (3 × 13 cm) at a distance of 2 m from the eye, which yielded an illuminance of about 370 lx at the eye. The fixation point was a black circle 3 cm in diameter at a distance of 1.5 m from the eye, which was visible when the flash was applied. The direction of the light was about 48° below the line of fixation. To simplify the cortical response, the left eye was patched. Before the experiment, subjects were dark-adapted for 15 min. We used the scotopic background in this study since a photopic background light could not evoke a clear early cortical response even at an intensity higher than that used in the present study in our preliminary study probably due to its low illuminance at the eye. To mask the auditory noise caused by the stimulator, rubber earplugs were provided, and white noise of 50 dB was delivered from a speaker during the experiment as described previously (Okusa and Kakigi, 2002). To confirm that the auditory noise did not contribute to the recorded magnetic responses under these conditions, cortical responses to flash stimuli were recorded with both eyes covered in all the subjects.

ERGs were recorded using a pair of disc electrodes placed at the center of the right lower lid as close as possible to the lid margin, and 2 cm lateral to the lateral canthus. We used an infraorbital electrode to record ERGs in this study, since (1) a standard contact lens electrode appears not suited to our study with a long experimental time (approximately 20 min) because of possible corneal abrasions, (2) among various areas of facial skin, the largest ERG response can be obtained from infraoribital areas (Noonan et al., 1973; Rubinstein and Harding, 1981) and (3) reliable ERGs can be obtained using skin electrodes when a signal averaging technique is used (Noonan et al., 1973; Rubinstein and Harding, 1981). Visual evoked magnetic fields (VEFs) were recorded with a 37-channel axial-type first-order biomagnetometer (Magnes, Biomagnetic Technologies, San Diego, CA) as described previously (Kakigi et al., 2000). The probe was centered about 3 cm above the inion of the subject. The ERGs and VEFs were recorded with a filter of 0.1–200 Hz (zero-phase lag, −6 dB/oct) at

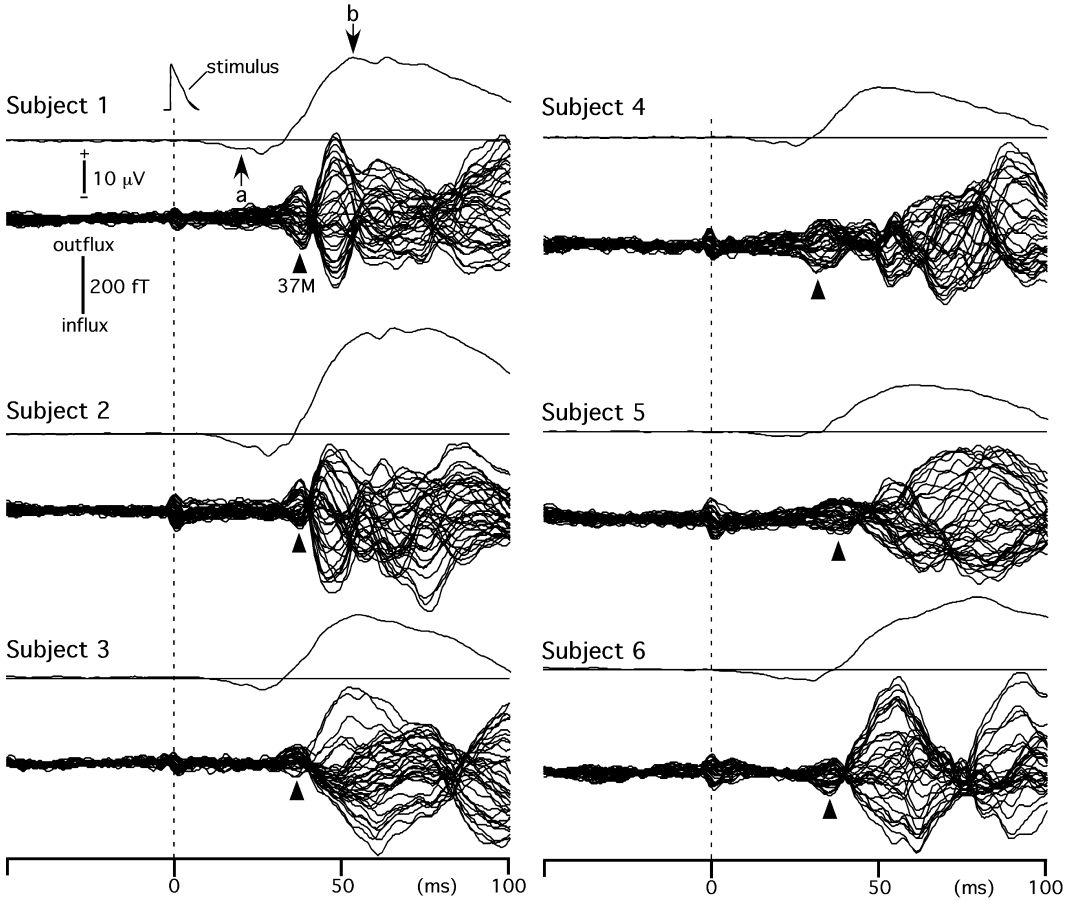

Fig. 1. ERG and MEG waveforms of all subjects. Time course of a stimulating light recorded by a photodiode is shown in the tracings of subject 1. ERG, electroretinogram; MEG, magnetoencephalogram.