

A first comparison of the human multifocal visual evoked magnetic field and visual evoked potential

Lihong Wang^{a,*}, Colin Barber^b, Ryusuke Kakigi^a, Yoshiki Kaneoke^a,
Tomohiro Okusa^a, Yaqin Wen^b

^aDepartment of Integrative Physiology, National Institute for Physiological Sciences, Myodaiji, Okazaki, 444-8585, Japan

^bMedical Physics Department, Queen's Medical Centre, Nottingham, UK

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Abstract

Our objectives were to determine the feasibility of recording reliable multifocal visual evoked magnetic fields (mfVEFs), to investigate the maximum stimulus eccentricity for which the mfVEF responses can be obtained, and to study how this changes with checksize (spatial frequency tuning). Using a checksize of 30', we recorded 8-channel pattern-onset mfVEFs three times to obtain responses from 19 channels located around theinion. Multifocal visual evoked potentials (mfVEPs) were recorded under the same conditions. Eccentricity changes with spatial frequency were studied using checksizes from 7.5' to 60'. We obtained, for the first time, reliable mfVEFs, and found they could be elicited from more peripheral stimulus elements than could mfVEPs. The larger the checksize, the greater the eccentricity reached. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

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It is generally accepted that large-area checkerboard pattern stimuli activate multiple visual areas and thus multiple visual evoked potential (VEP) sources, resulting in a complex waveform. Small-area stimuli are essential to determine the precise locations of VEP sources. Some studies [1,2] have used circumscribed stimuli such as quadrants or octants to investigate retinotopic cortical representation, but the areas are still quite large, and only a limited number of locations is feasible using conventional VEP, since such recordings must be done serially and it would take too long to record from many locations. The multifocal technique [3,11] has the advantage that it can provide multiple small-area VEPs simultaneously and independently in approximately the same time as a single conventional recording. Theoretically, it should be possible to identify the VEP contribution of each small visual field element. However, the mfVEP only gives large responses to central foveal stimulation [8,13], which limits its usefulness in detailed visual field mapping. A number of factors account for the strong foveal and weak peripheral mfVEP (and VEP in general) [12]: the higher concentration of receptive fields

in central foveal retina; the larger striate cortical generator area for the fovea and parafoveal projection; the posterior location and radial orientation of dipoles for central foveal stimulation. The latter factor maximizes the foveal VEP, since the VEP preferentially records radial currents; the anterior and more tangential dipoles which represent peripheral stimulation produce smaller VEPs. It is common to try to overcome the first two factors by use of a 'cortically-scaled' stimulus, although the wide inter-individual variation in angle and location of the calcarine fissure [7] means that this can only be an approximation. In this study, we have used magnetoencephalography (MEG) to study the third factor. MEG preferentially records tangential currents, and would thus appear more sensitive than the VEP to peripheral stimulation. In an earlier conventional visual evoked magnetic field (VEF) study, large responses to non-foveal stimulation were recorded [4]. Therefore, we propose that the mfVEF might permit recording of more precise peripheral information. To our knowledge, there are no previous mfVEF recording reports.

Our initial objective was to determine the feasibility of recording reliable mfVEFs, (i.e. MEG responses to multifocal stimulation), in particular whether the signal to noise ratio is high enough from such small areas of the visual field. The main objective was to measure to what extent the

* Corresponding author. Tel.: +81-564-55-7768/7779; fax: +81-564-52-7913.

E-mail address: lihong@nips.ac.jp (L. Wang).

mfVEF will allow us to ‘see’ visual activity from the more peripheral parts of the visual field, using the well-known variation in spatial frequency tuning with eccentricity. We recorded mfVEFs and mfVEPs under identical conditions for direct comparison of the two techniques.

Pattern-onset mfVEFs and mfVEPs were recorded to right-eye stimulation of four healthy adults (males, ages 33–57 years) with normal or corrected to normal vision. The study was approved by the Ethical Committee of the National Institute for Physiological Sciences, Okazaki, Japan; informed consent being obtained from all participants.

We used an 8-channel VERIS system (EDI, San Francisco, CA) to generate the stimuli and perform the multifocal analysis. The 64-element checkerboard stimulus, which was presented by a projector located outside the magnetically shielded room, subtended a total visual angle of 16° (Fig. 1a). Each of its $2 \times 2^\circ$ elements, containing a checkerboard of 4–256 checks, depending on the checksize, appeared from a uniform gray background of the same mean luminance, according to a pseudo-random m-sequence. The total recording time was approximately 8 min, divided into 16 segments for comfort. Because of the special nature of the m-sequence, responses to each of the elements can be extracted independently, i.e. we obtained 64 responses, corresponding to these 64 small stimulus areas, from each electrode or magnetometer. The maximum luminance was 106 cd/m^2 , and the minimum 9 cd/m^2 , producing a contrast of 84.4%.

We recorded the pattern-onset mfVEF by means of a 37-channel biomagnetometer (Magnes, BT Inc. San Diego, CA). The device was 144 mm in diameter and its radius of curva-

ture was 122 mm. The outer coils were 72.5° apart. Each coil was 22 mm. The analogue mfVEF data were amplified (100 000 \times) and filtered (3–100 Hz) before being transferred back to VERIS system for the multifocal analysis. We monitored eye movement during recording. Segments with high noise levels or eye movement contamination were discarded and re-recorded. The subjects used a central red cross to maintain fixation for the whole of each segment. They were allowed to relax briefly between segments.

First we recorded the pattern-onset mfVEF with a checksize of $30'$. To locate the dipole sources corresponding to each local VEF, we recorded three sets of mfVEFs to obtain responses from 19 of the 37 BTi channels (Fig. 1b). To confirm reproducibility, we repeated the recordings. Second, we recorded pattern-onset mfVEPs (for the best 8 of the 19 channels in the mfVEF) under identical stimulus conditions and recording positions as the mfVEF, using a template of the detector positions to position the electrodes. Third, we recorded a conventional pattern-onset VEF using a left lower foveal stimulus to match local area F4 (Figs. 1a and 2c) in the mfVEF. The checksize for this recording was also $30'$. Fourth, we recorded pattern-onset mfVEFs for checksizes of 7.5, 15, 20, 30, 40 and $60'$ to investigate spatial frequency tuning variation with eccentricity. The best eight of 19 channels were selected as before. All the above were recorded in Okazaki. To confirm data reliability, we recorded mfVEPs also in Nottingham, using 19 channels as in Okazaki.

We obtained 64 local responses from each channel, analyzing only the first-order kernels in this study. The

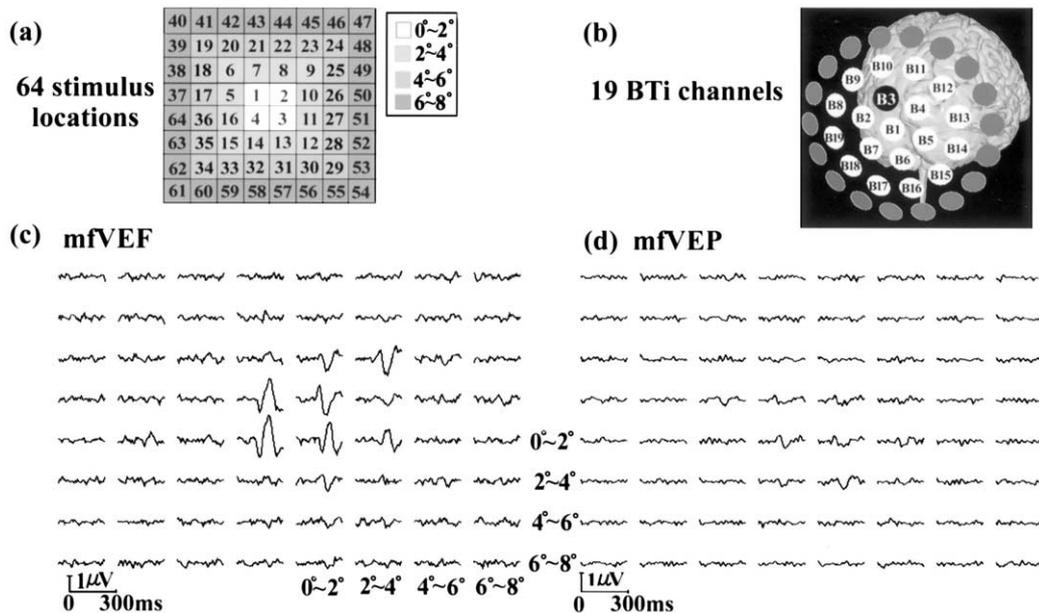


Fig. 1. (a) 64-element checkerboard subtending total stimulus angle of 16° . Each element contains a checkerboard of 4–256 checks depending on checksize and appeared in a pseudo-random m-sequence, permitting extraction of the responses corresponding to each element, i.e. each stimulus location. The locations are numbered serially (F1–F64) from center to periphery. (b) Sensor positions of 19 of the 37 channels. Examples of mfVEF (c) and mfVEP (d) recordings from channel B3 in subject CB show that mfVEF responses are clearly larger and more eccentric than mfVEP responses.

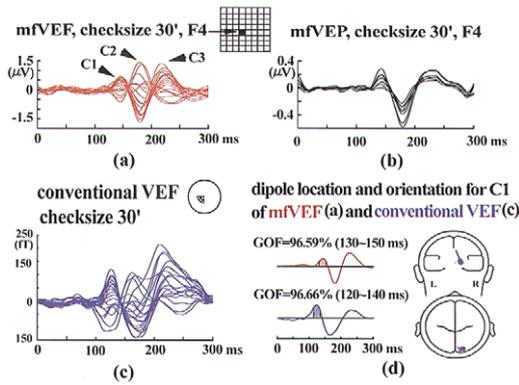


Fig. 2. (a) Superposition of 19-channel mfVEF responses to F4; (b) superposition of 8-channel mfVEP responses to F4; (c) superposition of 19-channel conventional VEF responses; (d) similar dipole location and orientation of the component C1 were found in mfVEF responses to F4 and the conventional VEF.

peak latency and amplitude of each component in the response to each stimulus element (i.e. each small visual field) from the 19 channel recordings was measured, and the eccentricity effect on peak latency and amplitude examined using one-way repeated measures ANOVA, with eccentricity as the covariates. For computation of theoretical source generators for each local mfVEF response, we used brain electric source analysis (BESA) in a three-layer spherical head model. Goodness-of-fit (GOF) values larger than 90% are considered to indicate a good dipole model.

Repeatable mfVEF responses were obtained from all four subjects. The signal to noise ratio was good enough to see clear responses to stimulation of central and paracentral visual fields (Fig. 1c). When we superimposed local mfVEF responses from the 19 channels, three peaks were clearly visible. These are labeled: C1, (130~150 ms); C2, (150~180 ms); C3, (190~210 ms) (Fig. 2a). The latency varied with checksize. With the same stimulus conditions, similar responses were obtained from the mfVEP (Fig. 2b). The waveforms and the latencies of the three components were almost the same. The conventional VEF (Fig. 2c) showed considerable similarity, but with some differences in wave shape and latency. These are believed to be due to timing differences between multifocal and conventional stimuli; specifically the temporal pattern-to-gray ratios, leading to a different degree of pattern adaptation, which is known to produce waveform changes [6]. However, the dipole location and orientation of C1 was almost the same as that of the mfVEF (Fig. 2d). The mfVEP recording in Nottingham showed three components too, with the latencies similar to the conventional VEF recording.

The three components of the mfVEF could be seen from stimulus elements located as far as 8° from fixation, in three of the four subjects; mfVEFs were apparent at greater eccentricities than the corresponding mfVEPs (Fig. 1c,d). The larger the checksize, the greater the eccentricity at which a response could be seen (Fig. 3). A decrease in

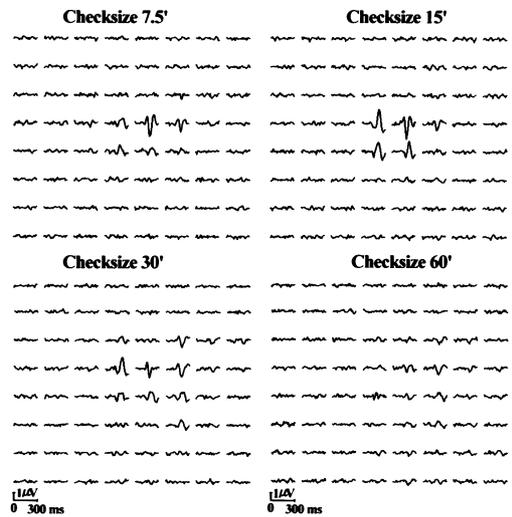


Fig. 3. mfVEF changes with the checksize in subject R.K., recorded from channel B2. The larger the checksize, the more eccentric the mfVEF could be seen.

amplitude with checksize (spatial frequency tuning) was clear in the central responses.

The repeated measures one-way ANOVA showed the influence of different eccentricities (2°-F4, 4°-F14, 6°-F32). The latency of the three components did not change significantly with eccentricity, whereas the amplitude of C1 declined significantly with increasing eccentricity ($F = 26.702$, $P < 0.001$).

Using BESA, we also studied the dipole location and orientation changes with eccentricity. As shown in Fig. 4, the dipole location for C1 followed the anatomical structure, the dipole orientation becoming more tangential to the skull at 6°.

Our results showed that the signal to noise ratio was good enough to recognize local mfVEF responses from both central and paracentral visual fields. They were repeatable. With the same stimulus conditions, mfVEFs and mfVEPs exhibited three very similar components with exactly the same latencies, confirming the reliability of the mfVEF recordings.

Comparing the mfVEF with the mfVEP, we found that

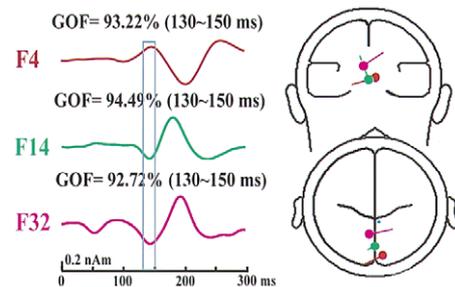


Fig. 4. The dipole location and orientation changes with eccentricity. The dipole to the stimuli at 6°-F32 was more tangential and anterior. Please note that the head model shown is only a sketch, and does not reflect the real anatomical location.

the mfVEF responses were more robust at all stimulus locations, and extended more peripherally. Larger mfVEF responses might be expected because of the greater transparency of the skull to magnetic than electric currents [5], but the effect is surprisingly large, even for cortical sources for which the orientation is not optimal. Our BESA analysis revealed that the dipole orientation became more tangential for the paracentral and peripheral visual fields, giving bigger mfVEFs than mfVEPs for more peripheral stimuli as expected. Dipole orientation was thus confirmed as an important factor for weak peripheral mfVEPs and VEPs in general.

The results of the checksize experiment show that the larger the checksize, the greater eccentricity reached by the response. Previous conventional VEP studies have compared VEPs to foveal and extra-foveal stimulation in a number of ways [9]. However, none of them could be as spatially precise as the mfVEP. The rapid fall-off in amplitude with checksize for the central elements is in line with the steep change in receptor density there. For more peripheral elements the optimum checksize is clearly larger, showing the predicted change in spatial frequency tuning with eccentricity.

The reason that our peripheral VEF was not as robust as in Brecelj et al.'s report [4] is probably due to too small a stimulus size for peripheral stimulation. Larger peripheral stimuli are needed to activate the same amount of the cortex as central stimuli [10]. However, summation of the multifocal responses to simulate a larger stimulus did not give a larger response in this study. Another possible explanation is that they used a pattern reversal, as opposed to onset, stimulus. The relation between the two kinds of response is the subject of current work. We found, in line with a previous report [13], that the latency of the three components did not change with eccentricity, but the amplitude did. The decline in amplitude with eccentricity could be due to the dipole location; the BESA results showed that the dipoles for more peripheral stimulus were located more anteriorly.

We have successfully recorded the mfVEF for the first time and shown it to be a robust response. Our results support the contention that dipole orientation is one reason for the limitation of mfVEPs (and all VEPs) to central stimulation. The mfVEF can to some extent overcome this limitation and record both foveal and more peripheral responses.

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