Binocular Interaction Reflected in Visually Evoked Cortical Potentials as Studied with Pseudorandom Stimuli

Eiju Sato, Mariko Taniai, Atsushi Mizota, and Emiko Adachi-Usami

**PURPOSE.** To study the interaction of visual signals from both eyes with visual evoked cortical potentials (VECPs) elicited by pseudorandom binary sequence (PRBS) stimuli.

**METHODS.** A PRBS was used to drive two independent LED arrays to elicit VECPs. The right and left eyes were simultaneously stimulated by two different series of PRBS stimuli. The impulse response function of each eye was calculated from the raw data by cross-correlating the PRBS and the response. The effect of changing the luminosity of the LEDs parametrically on the responses obtained from the two eyes was evaluated.

**RESULTS.** The impulse response, obtained from 10 volunteers with normal vision, had characteristics similar to responses to the conventional VECP, with a major positive peak at 110 ms (P110). When two eyes were bilaterally exposed to two PRBS stimuli of the same luminosity, the P110 amplitudes of both eyes were decreased by the same amount from that obtained by stimulating only one eye. When the luminosity in the two eyes was different, the VECP amplitude in the eye with the dimmer stimuli decreased, and the amplitude in the contralateral eye increased.

**CONCLUSIONS.** The results clearly demonstrate that interocular luminance interaction can be detected electrophysiologically in normal subjects by using PRBS-driven stimuli in which the feasibility of recording response from the two eyes independently.

Signals from the two eyes interact in the visual cortex and thereby contribute to a variety of visual perceptions. In normal humans, various types of binocular interactions have been reported (e.g., summation, suppression, and facilitation). These phenomena have been identified and evaluated by psychophysical methods and by noninvasive physiological methods, such as visually evoked cortical potentials (VECPs), in normal subjects and in patients.

Several investigators have reported that the amplitude of the monocular VECP decreases when the contralateral eye is steadily illuminated or when the image moves on the retina. This decrease has been termed interocular suppression, and the degree of suppression increases as complexity of the contralateral stimulus increases. When assessing the degree of suppression induced by the stimulation of the contralateral eye, VECPs can be used as an objective test to evaluate ocular interaction by comparing the responses recorded from one eye with those in the contralateral, nonstimulated eye with the response elicited when the contralateral eye is stimulated. However, there is a problem in assessing binocular interaction, because there is substantial variation of the VECP amplitudes when recorded separately in the two eyes. In a routine VECP examination, the two eyes are separately recorded because there is no other way to identify the responses from both eyes separately. It may be advantageous to stimulate both eyes simultaneously under the same stimulus condition, not only to shorten the recording time but also to study interocular interaction.

One of the favorable methods is those of using multi-input stimuli with pseudorandom binary sequence (PRBS). Fricker and Sanders and Srebro and Wright were the first to use pseudorandom methods to record VECPs in the late 1970s. The PRBS stimulus methods have been applied to investigate the nonlinearity of VECPs and to study the temporal frequency characteristics of the visual system. We have applied the PRBS method to temporally modulate dichoptic flash stimuli to investigate binocular luminance interactions in normal subjects by developing a stimulating system for simultaneous recording in both eyes, which could shorten recording time and avoid the disadvantages of separate differing recordings. We studied in the hope that our PRBS method could be applied for clinical use of VECPs to determine binocular interaction.

**MATERIALS AND METHODS**

**Subjects**

Ten volunteers between the ages of 26 and 32 years were tested (five men and five women). None had neurologic or ophthalmic diseases, and monocular and binocular visual acuity was 20/20 or better with or without correction. All had stereopsis, as assessed by random dot stereograms. Informed consent was obtained from all volunteers, in accordance with the provisions of the Declaration of Helsinki.

**Experiment 1**

To investigate the feasibility of recording VECPs simultaneously from the two eyes independently, we developed a stimulus system. The PRBS was derived from a 10-stage shift register with a clock rate of 33.3 Hz, which gives a clock interval of 30 ms. This produced a maximal-length sequence (m-sequence) with 1023 states.

The output of the PRBS was used to trigger pulses for the 5-ms flash stimuli and 25-ms dark intervals (Fig. 1). To produce a different PRBS for the contralateral eye, the order of the sequence was reversed, because the PRBS and the reversed order of the PRBS are nearly uncorrelated if the sequence is long enough. The stimuli were delivered to the two eyes with a relative temporal shift of 15 ms, so that flashes were never presented to both eyes at the same time, thus eliminating unexpected summation and fusion phenomena that would have interfered with the readings (Fig. 1).

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From the Department of Ophthalmology and Visual Science, Graduate School of Medicine, Chiba University, Chiba, Japan. Submitted for publication November 6, 2001; revised April 9, 2002; accepted April 20, 2002. Commercial relationships policy: N. The publication costs of this article were defrayed in part by page charge payment. This article must therefore be marked ‘advertisement’ in accordance with 18 U.S.C. §1734 solely to indicate this fact. Corresponding author: Eiju Sato, Department of Ophthalmology and Visual Science, Graduate School of Medicine, Chiba University, Inohana 1-8-1, Chuo-ku, Chiba, 260-8670, Japan; esato@ophthalm.m.chiba-u.ac.jp.
PRBS stimuli were delivered to the two eyes separately by two sets of 12 high-intensity, white-light–emitting diodes (LEDs; NSPW-500BS; Nichia Co., Tokushima, Japan), that were mounted in the right and left frames of light-proof goggles. The LEDs were covered with a diffuser to obtain uniform light stimuli. The array size for one eye was \(2.5 \times 3.5\) cm and consisted of three rows of four LEDs. The vertical and horizontal visual angles were 90° and 100°, respectively.

VECPs were recorded between an active electrode placed at Oz and a reference electrode placed on the left earlobe. The ground electrode was connected to the right earlobe. The elicited potentials were amplified (AVB-11; Nihon Kohden, Tokyo, Japan) by 10^5 with a band-pass filter setting of 1.5 to 100 Hz. The amplified responses were fed to a personal computer to process the responses.

Impulse response functions were calculated from the raw data by cross-correlating the PRBS stimuli and the response, according to the Sutter m-transform method.12 The responses are expressed in microvolts.

One recording session consisted of four cycles of the PRBS stimuli (30,720/4 ms). Each recording period was started 10 seconds before the initiation of the PRBS cycle. The total recording time was approximately 2.5 minutes. The subjects were instructed to keep both eyes open, look forward, and try not to blink or move their eyes. First, VECP waveforms elicited by simultaneous dichoptic PRBS stimuli were studied under constant luminance of 320 candelas (cd)/m².

**Experiment 2**

We studied VECP changes in one eye as the luminance of the stimulus was increased to the other eye. The effect of varied luminance on VECPs from the one eye (left eye) under either constant luminance of 320 cd/m² or without stimulation to the contralateral eye was tested. The mean luminance of the stimulus of the right eye was varied in three steps: 20, 80, and 320 cd/m². The amplitude of the first positive component from the scalp electrode, which appeared approximately at 110 ms (P110), was evaluated.

**RESULTS**

**Experiment 1**

The VECPs elicited from the right and left eyes of one subject and extracted by cross-correlating the PRBS stimulus with the raw data are shown in Figure 2. These VECPs were elicited by simultaneous dichoptic PRBS stimuli of 320 cd/m² to each eye. The extracted waveforms were similar to those of the conventional VECP, with a small initial negative wave followed by a larger positive peak from the scalp electrode at approximately 110 ms. We termed this component P110 for convenience.

The mean ± SD of the implicit times of P110 in the right and left eyes were 110.8 ± 5.8 ms and 111.4 ± 5.7 ms, respectively, and the mean P110 amplitudes were 4.39 ± 1.42 and 3.94 ± 1.66 μV, respectively, in the 10 subjects. The differences in the P110 amplitudes and implicit times for the two eyes were not statistically significant. These findings demonstrated that there was good reproducibility in the implicit times and amplitudes of the VECPs.

When the right eye was stimulated with a PRBS stimulus luminance of 320 cd/m² and the left eye was kept in the dark without stimulation, the VECPs extracted from the right eye showed a well-defined response, and as expected, those obtained from the nonstimulated left eye showed no distinct response (Fig. 3). In the 10 subjects, the mean ± SD of the P110 amplitude was 5.93 ± 2.26 μV in the stimulated eye; no
distinct response was measurable in the nonstimulated eye. The mean amplitude was significantly larger than that recorded when both eyes were stimulated with a luminance of 320 cd/m². These results confirm that the VECPs derived from the right and left eyes were separately extracted by our PRBS method.

**Experiment 2**

By changing the stimulus luminance for the right eye to 20, 80, and 320 cd/m² while the left eye was exposed to a PRBS stimulus luminance of 320 cd/m² or was kept in the dark without stimulation, the amplitude of the P110 wave in the right eye increased as the stimulus luminance increased, regardless of whether the left eye was in the dark or was presented with a stimulus of 320 cd/m² (Fig. 4).

When we compared the amplitude of the P110 of the right eye under the two conditions, there was a significant decrease in the amplitudes when the contralateral eye was stimulated. The means ± SDs of the P110 amplitudes at stimulus luminances of 20, 80, and 320 cd/m² were 3.22 ± 1.59, 4.79 ± 2.58, and 5.93 ± 2.62 µV, respectively. These responses were decreased by 54.3%, 41.1%, and 26.0%, respectively, when the contralateral eye was simultaneously stimulated with a PRBS stimuli of 320 cd/m². This decrease suggested that the response in the right eye was suppressed by the stimulation of the contralateral left eye.

The P110 amplitudes of the left eye, which was presented with PRBS of 320 cd/m², also decreased as the stimulus intensity of the right eye was increased (Fig. 5). The means ± SDs of P110 amplitudes of the left eye elicited by a stimulus luminance of 320 cd/m² were 4.84 ± 1.69, 4.28 ± 1.63, and 3.94 ± 1.67 µV when the contralateral eye was stimulated with luminances of 20, 80, and 320 cd/m², respectively. Thus, the degree of suppression was directly proportional to the luminance of the contralateral eye.

**DISCUSSION**

There have been several studies in which binocular interaction has been investigated with the use of VECPs as an objective measurement. In those, investigators tried to use different stimuli in the temporal and spatial domains in the two eyes: Stimulus 1 is presented to eye 1, stimulus 2 is presented to eye 2, and stimuli 1 and 2 are simultaneously presented to both eyes in the same subject. VECPs are recorded for those three conditions and compared. These earlier studies have shown that stationary and/or pattern-reversal stimuli induce an increase in the amplitude of the binocular over the monocular VECPs. However, the degree of interocular interaction varies considerably in the different reports, raising two disadvantages: that the responses from the two eyes had to be recorded simultaneously.
in different sessions, which caused the responses to vary, and that twice the recording time was needed, to compare the responses from the two eyes.

To record VECPs from the two eyes simultaneously, several investigators have taken the frequency- or phase-difference approach. Regan14 was the first to use repetitive stimuli of different frequencies for simultaneous recording of evoked potentials in vision.14 This frequency difference approach was proposed by several investigators to stimulate both eyes.15,16,17 The other method of recording simultaneously from both eyes is to vary the relative temporal phases of the two stimuli parametrically. The frequency response of the evoked potentials to these two stimuli can then provide information on the degree of binocular interaction.17,18 However, the stimuli 1 and 2 in the two eyes are temporally correlated to some extent. Therefore, the interpretation of the contribution from the two eyes to the VEP during presentation of stimuli 1 and 2 has its ambiguities. Changes in amplitudes do not necessarily represent neural events in the case of dichoptic stimuli.1 and 2 has its ambiguities. Changes in amplitudes do not necessarily represent neural events in the case of dichoptic stimuli. Therefore, the interpretation of the contribution from the two eyes to the VEP is not straightforward.13,14 The frequency domain analysis is one of the methods that can be substituted to avoid such problems.

Different from the frequency analysis, an excellent way to construct stimuli is to use a pseudorandom sequence to construct stimulus 1 and another pseudorandom sequence to construct stimulus 2 that is uncorrelated with stimulus 1. This fascinating method is PRBS, introduced by Levi and Manny,5 and Fricker and Sanders,6 and Fricker and Kuperwaser.19 The use of two independent PRBSs to control two separate stimulus presentations permits dichoptic stimulation of the two eyes. With this test arrangement, the subject views two similar but independently driven stimuli. The occipital signal from a single set of midline electrodes is amplified and cross-correlated with each of two independent reference waveforms, corresponding to the two independent PRBSs that are used to control the stimuli. In this manner, VECPs from the two eyes were obtained with dichoptic stimulation. The application of this technique has been used recently to extract local retinal responses to multifocal stimulation.2

Taking advantage of PRBS, we developed a stimulation and analysis system to compare the VECPs from both eyes simultaneously. Using our simultaneous recording and analysis method in the two eyes, we compared the VECPs of one eye with that of the contralateral eye under various stimulus luminance conditions. In our experiment, we found that the VECPs recorded with dichoptic stimuli from one eye were smaller in amplitude than the VECPs recorded when the other eye was stimulated. This decrease in amplitude suggests an inhibitory binocular interaction. When the luminance difference of the stimuli in the two eyes was increased, the VECP amplitude in the eye with the weaker stimuli decreased and the amplitude in the other eye increased.

Our PRBS-VECP method required a much shorter time to record the VECPs from the two eyes than the conventional transient flash-pattern VECP method. A simultaneous recording of the two eyes could lessen the variation in VECPs caused by recording eyes separately and could shorten recording time. Thus, our results demonstrate the usefulness of PRBS stimuli for studying binocular interactions. The shorter testing time will be especially important when this technique is applied in patients.

Acknowledgments

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References