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Robust sensory gating in the cortical visual evoked potential using two spatially separated stimuli

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ABSTRACT

Objective: Sensory gating has been reported to be either absent or weak in the cortical visual evoked potential (VEP) response to diffuse or spatially overlapping stimuli. In this study, the authors evaluated sensory gating to two spatially separated visual stimuli.
Methods: Spatially separated stimuli were presented either singly or in combination at the same or different onset times and the VEP recorded at either Oz, or O1 and O2, referenced to Cz.
Results: When one visual stimulus is flashed on, the VEP response to another non-overlapping stimulus is almost completely suppressed.
Conclusions: The VEP does not reflect the bulk activation of retinotopically organized visual cortex, but rather it primarily reflects a distributed mode of visual cortical activity that only indicates that at least one visual stimulus was presented, and not how many or in what order.
Significance: Other studies performing intracortical recordings of the local field potential (LFP) in visual cortex have identified a slow-distributed component that exhibits the same nonlinearity found here in the VEP, suggesting that these two phenomena are related.

1. Introduction

Sensory gating is the phenomenon whereby the electroencephalographic response to one stimulus is reduced in magnitude by the presentation of a preceding ('conditioning') stimulus. It is sometimes referred to as a "recovery function" or "recovery cycle". Sensory gating has been commonly seen in the cortical evoked potential response to auditory stimuli (Adler et al., 1982; Hong et al., 2008). However, a previous study using flashes of light viewed diffusely through closed eyelids found no evidence for sensory gating (Adler et al., 1985), and another, using large overlapping white circles, found gating effects that were statistically significant but small in magnitude (Gjini et al., 2008). A study using diffuse flashes of light found sensory gating in the human VEP which was strong for flashes separated by 20 ms or less but that became much less robust for longer inter-stimulus intervals (Schwartz and Shagass, 1964). Another study using large-field contrast-reversing checkerboard gratings found no consistent effect of one stimulus on the magnitude of the response to a following stimulus, although there were significant latency effects for inter-stimulus intervals of 30 ms or less (Mitchell et al., 1983). The goal of this study was to explore the degree of sensory gating in the VEP to two spatially separated stimuli, which instead of activating the same cortical regions in sequence, should sequentially activate different retinotopically organized areas of visual cortex regions. Using spatially separated stimuli could elicit different behaviors than using spatially congruent stimuli.

Despite many years of research, it is still not clear precisely what aspects of neuronal activity are reflected in the scalp-surface recorded cortical visual evoked potential (VEP) (Fahle and Bach, 2006). Intracortical recordings of the local field potential (LFP) have identified a fast local component, which in visual cortex has been referred to as "retinotopic", and a slow-distributed component, which has also been referred to as "non-retinotopic" (Bringuier et al., 1999; Doty, 1958; Ebersole and Kaplan, 1981; Gawne, 2010; Kitano et al., 1994, 1995; Kasamtsu et al., 2005; Mitzdorf, 1985). Because the slow-distributed component of the LFP is widely distributed across cortex, it might be expected to contribute strongly via volume conduction to the surface-recorded VEP. What is most relevant to the current study is that the slow-distributed component is highly nonlinear: the response to a stimulus at one location suppresses the response to a stimulus at another location (Kitano et al., 1994; Nauhaus et al., 2009). The purpose of this

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study was to determine if the nonlinearity present in the slow-distributed component of the LFP is also present in the scalp-surface-recorded VEP.

2. Materials and methods

Subjects were 18 adults between the ages of 23 and 52, of normal health, and with acuity corrected to normal. They were seated in a Faraday cage that had a viewing port made of electrically conductive glass. Three gold cup electroencephalogram (EEG) electrodes were placed on the skin in standard EEG locations Oz, Pz, and Cz. The skin was scrubbed with Lemon Prep (Mavidon, Lake Worth, FL) until good contacts were made at each location, impedance <5 KΩ. We also verified that when each subject was instructed to close their eyes and relax, that prominent alpha-band rhythms were observed. Electrode gel (Grass, EC2 West Warwick RI) was used to ensure good electrode contact. Two additional pairs of electrodes were used to monitor the horizontal and vertical electro-oculogram (EOG). A custom-built EEG amplifier was used with Oz referred to Cz, and Pz ground. In some experiments, however, we only used a single vertical channel of EOG but two channels of EEG, O1 and O2, both referenced to Cz. The amplifier had a gain of 200 and a flat passband between the frequencies of 0.1 and 1000 Hz. The output of the EEG amplifier was further amplified and filtered by a four-pole low-pass linear-phase Bessel filter (Warner Instrument Corp., Model LPF202, Hamden, CT) set at a cutoff frequency of 200 Hz. No notch filters were used. A post-recording software filter was used that had a Gaussian kernel with a standard deviation of 6 ms, which acts as a linear-phase low-pass filter with a cutoff frequency of 20 Hz. The entire filtering chain did not create any phase distortion or 'ring' in any way.

For visual activation of the occipital lobe, there is generally one dominant response vector which is readily picked up by the electrode configurations used here. For this reason the multifocal VEP typically only uses a single active recording site (Fortune and Hood, 2003). Additionally, as will be covered in Section 4, testing the linearity of summation that might occur via volume conduction is independent of either the number or configuration of recording electrode pairs. Thus, high-density recording would not have altered our results.

Signals were digitized for 500 ms intervals at a rate of 1000 Hz using a 16-bit A/D converter and custom software written in MS-DOS. The entire data acquisition system had a sensitivity of 0.032 μV/bit. A photocell was taped to the video display and positioned such that a positive signal was generated with each stimulus, and all timings verified accurate to less than 1 ms by recording and analyzing the resultant data using the same amplifiers, filters and software as was used in the recording from the human subjects. Analysis was done in MATLAB (The Mathworks, Natick, MA) using custom-written routines.

Subjects were instructed to fixate on a small (0.08° square) white dot presented in the middle of a video monitor (Korea Data Systems, Garden Grove, CA). The monitor was displayed at a refresh rate of 85 Hz, measured 54.3 cm diagonally, and was positioned 57 cm from the subject's eye. Two stimuli, each 1.6 degrees square, were presented centered 2.26 degrees from the fixation point. Stimulus 1 was located in the lower left, and stimulus 2 in the upper left, visual field. Stimuli were flashed on either separately or together with different inter-stimulus delays. There were eight distinct conditions presented in shuffled random order with an inter-trial interval that varied randomly from 500 to 750 ms. The stimulus timings were constrained by the 85 Hz video refresh rate. Stimulus 1 was always flashed on at time = 43 ms, and stimulus 2 at time = 90 ms, for an inter-stimulus delay of 47 ms. There were three stimulus pairings: a checkerboard followed by a checkerboard (Fig. 1A), and checkerboard followed by a red[1] circle (Fig. 1B), and a red circle followed by a checkerboard (Fig. 1C). This allowed us to investigate whether the interactions between stimuli were affected by the stimuli having the same or different forms. The gray background had a luminance of 6.96 cd/m^2, the black and white of the checkerboard stimuli had luminances of 0.74 and 87.58 cd/m^2, and the red circle had luminance of 27.38 cd/m^2. Additionally, the single stimuli making up each combination were presented separately, as well as a blank control stimulus (Fig. 1D–H). The responses to the blank control stimuli as a function of time were subtracted off from all other responses to cancel out a small but consistent effect that was due to the initiation of the recording epoch.

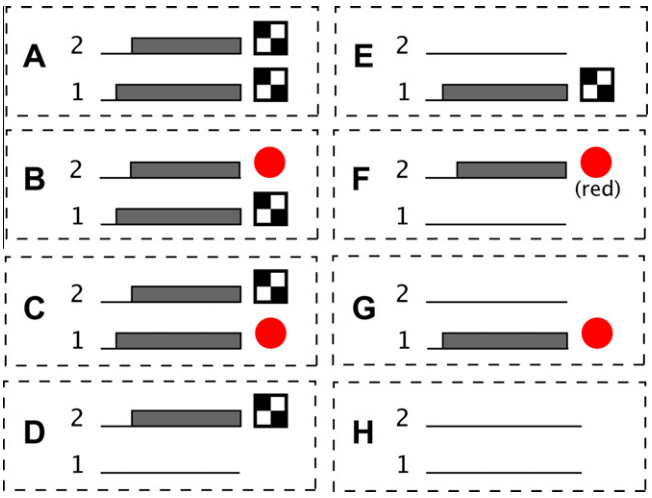

Fig. 1. Schematic of each of the eight conditions in this paradigm. The solid gray bars indicate the time the stimuli are on within each 500 ms recording epoch. These eight conditions were repeated 200 times in shuffled random order for each of 18 subjects. Stimulus 1, presented in the lower left visual field, was always flashed on 47 ms before stimulus 2, which was presented in the upper left visual field. The stimuli were actually black and white checks on a uniform gray background: the black border around the stimuli was not present in the actual display. Stimulus combinations included: (A) checkerboard followed by a checkerboard, (B) checkerboard followed by a solid filled red circle (may be a gray disk in a B&W reproduction), (C) red circle followed by a checkerboard, (D–G) all single stimuli from A to C presented separately, and (H) blank field.

For 13 subjects we performed a similar experiment, except that we only used the checkerboard stimuli, and we presented the stimuli at three different delays: simultaneously, 47 ms, and 90 ms. Additionally, the stimuli were larger, subtending 2.4° each. Using longer inter-stimulus delays is problematic, because the number of trials where the eyes do not move decreases rapidly with longer recording epochs, and with longer inter-stimulus delays it is hard to rule out small-magnitude stimulus-dependent eye movements. For this experiment, we used only the vertical channel of the EOG, and recorded two channels of VEP data, with both O1 and O2 referred to Cz.

Responses were discarded when the EOG signal indicated a blink or eye movement, and when the peak-to-peak VEP amplitude was greater than 80–120 μV (VEP thresholds set separately for each subject). We presented the stimuli 200 trials per unique stimulus condition for each subject, but rejecting bad trials meant that the median value for the smallest number of trials for any single condition for each subject was 167, with a range from 75 to 193.

For the purposes of this study we were only concerned with the first strong positive peak, which is by far the strongest and most consistent part of the VEP, at least under these conditions. The la-

[1] For interpretation of color in Figs. 1, 3 and 4, the reader is referred to the web version of this article.