

120 Hz oscillations in the flash visual evoked potential are strictly phase-locked and limited to the first 100 ms

SVEN P. HEINRICH AND MICHAEL BACH

Elektrophysiologisches Labor, Univ.-Augenklinik Freiburg, Germany

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Abstract

Flash stimulation elicits a visual evoked potential (VEP) as part of the electroencephalogram (EEG). This VEP is known to contain strong oscillatory activity around 120 Hz, which ceases 100 ms after the flash. It was unclear so far whether this time limit represents an averaging artifact due to loss of intertrial phase coherence or indicates a veridical cessation. Here we present results obtained from single-trial analysis of the EEG. These show that the oscillations exhibit virtually perfect phase locking and do in fact cease around 100 ms after the stimulus. Thus, the cessation of oscillatory activity in the VEP is not due to increasing intertrial phase jitter. Comparison with simultaneous retinal recordings exclude the possibility of direct crosstalk from the retina, but suggest that the oscillations are propagated from the retina to the cortex with a time lag of 48 ms.

Keywords: Visual evoked potentials, Oscillations, High frequency, 120 Hz, Cortex

Introduction

Oscillatory activity currently receives much attention in the investigation of the neural basis of visual perception (e.g. Munk & Neuenschwander, 2000; Sannita, 2000). In addition to well-established oscillations in the electroretinogram (ERG) (Brown, 1968), a number of authors reported oscillations above 100 Hz in the early visual evoked potential (VEP). These are assumed to be of cortical or subcortical origin. This includes oscillations before 60 ms following flash stimulation (Cracco & Cracco, 1978; Rubinstein & Harding, 1981; Harding & Rubinstein, 1983) as well as a second epoch of oscillatory activity at 50–100 ms, which was found in the magnetoencephalogram (MEG) (Lopez & Sannita, 1997), in direct recordings from the optic tract (Yokoyama et al., 1999) and in the VEP (Allison et al., 1977).

It is not clear why these VEP oscillations are confined to the first 100 ms after stimulus presentation. There are several possible explanations for their cessation:

1. The oscillations cancel out in the VEP due to increasing phase differences between trials. A temporal jitter equally distributed in the range of ± 4.2 ms is sufficient for a complete suppression at 120 Hz.
2. Oscillatory activity actually ceases, possibly due to a transition between different processing stages.

3. The oscillations persist on the level of single neural assemblies. However, the sum potential which constitutes the VEP fails to show these oscillations due to phase asynchrony between different sources.

The present study was aimed to narrow down the possibilities. As opposed to previous studies a single-trial analysis approach is used. This allows one to assess the amount of intertrial phase jitter. In contrast, the “classic” averaged VEP only represents the phase-locked components of the EEG, that is, it is composed of those oscillations which have, in each trial, the same phase relative to the stimulus. Other components are eliminated by the averaging process.

Methods

Subjects viewed a Ganzfeld bowl (Roland Consult Ganzfeld Q400), where flashes of $4.6 \text{ cd/m}^2 \cdot \text{s}$ were presented at randomized intervals of 0.5–0.7 s, corresponding to an average of 1.67 Hz. Flash duration was 4 ms. EEGs were recorded at four occipital positions [Oz according to standard nomenclature (American Encephalographic Society, 1994), OTL (between O1 and PO7), OTR (between O2 and PO8), and Pz] with a linked-ears reference. Signals were amplified, bandpass-filtered (0.33–1000 Hz), and digitized at a sampling rate of 4 kHz. The vertical electrooculogram (EOG) was also recorded to detect eye blinks. For one subject, the ERG was recorded instead of the EOG from one eye using DTL electrodes (Dawson et al., 1979; Bach, 1998) to assess a possible contamination of the VEP by retinal potentials. A total of 2000–2200 trials were recorded in four blocks for each subject resulting in 1600–2100 trials after artifact rejection. Eight subjects partici-

Address correspondence and reprint requests to: Michael Bach, Univ.-Augenklinik, Killianstr. 5, 79106 Freiburg, Germany. E-mail: bach@uni-freiburg.de

pated and gave their informed consent prior to the experiment. All experiments were conducted in accordance with the Declaration of Helsinki (World Medical Association, 2000).

As outlined in Fig. 1, four separate analysis procedures were applied using Igor Pro (WaveMetrics, Inc., Lake Oswego, OR):

1. $V(t)$: The standard flash-VEP was obtained by averaging the single trials. In addition, a 40-Hz lowpass filter was applied.
2. $B(t)$: After regular averaging, the VEP was submitted to a 75–175 Hz Hanning-weighted (i.e. 50-Hz effective width) bandpass filter, yielding the “high-frequency VEP”. This procedure represents those applied in the previous studies.
3. $E(t)$: Each trial was first bandpass filtered (75–175 Hz Hanning-weighted). The single-trial signal envelope was then averaged over all trials. We will refer to this as “total oscillatory activity”. It represents both phase-locked and non-phase-locked activity and therefore allows one to assess Alternative (1) laid down in the Introduction.
4. The VEP was subtracted from each trial before the same procedure as in (3) was applied. This resulted in the “non-phase-locked activity” since the VEP represents the phase-locked activity, which is present in each trial.

Signal envelopes were computed as

$$e_i(t) = \sqrt{b_i^2(t) + h_i^2(t)},$$

where $b_i(t)$ denotes the bandpass-filtered signal of the i th trial [obtained from raw data for analysis type (3) and with the VEP subtracted for type (4)] and $h_i(t)$ its Hilbert transform (Oppenheim & Schaffer, 1975). Averaging the signal envelopes rather than the bandpass-filtered signal itself is essential for eliminating the influence of phase jitter. Envelope values are positive by definition, resulting in a nonzero average even without a stimulus. To account

for this, a prestimulus baseline value was subtracted from the envelope averages. Grand means were computed with data from each subject weighted according to the corresponding number of valid trials per subject.

Results

Fig. 2 shows standard (40-Hz low-passed) VEPs, high-frequency VEPs, and total oscillatory activity for the Oz electrode position. Subjects are sorted by the amplitude of the high-frequency VEP. All subjects produced clear standard flash-VEPs. The high-frequency VEPs, $B(t)$, which were obtained from the regularly averaged trials, exhibit oscillatory activity around 120 Hz in the first 100 ms for all subjects, though to widely varying degrees. For some subjects, two oscillatory epochs can be distinguished, one before and one after 50 ms. The total oscillatory activity, $E(t)$, which is based on the single-trial analysis, also varies between subjects, but never extends beyond 100 ms after the stimulus. No sizable total oscillatory activity could be extracted for three subjects arranged at the bottom of the figure.

Fig. 3 displays the grand means of the total oscillatory activity and of the non-phase-locked activity. The grand mean of the total oscillatory activity is clearly enhanced between 0 and 100 ms, but less pronounced at the more temporal electrode positions. It consists of two maxima at around 40 and 70 ms at Oz and Pz. The second peak appears delayed by 10 ms at OTR and is not distinct at OTL.

The total oscillatory activity at time intervals later than 100 ms does not exceed the prestimulus activity. The trough around 150 ms after the stimulus indicates a decrease below baseline. The non-phase-locked activity is less modulated than the total oscillatory activity. It does not rise sizably above baseline level, but shows a dip at around 70 ms. After 100 ms, it closely follows the total oscillatory activity not exceeding the baseline.

The time course of the ERG activity differs markedly from the cortical activity (Fig. 4): Most ERG activity is found at 0–60 ms

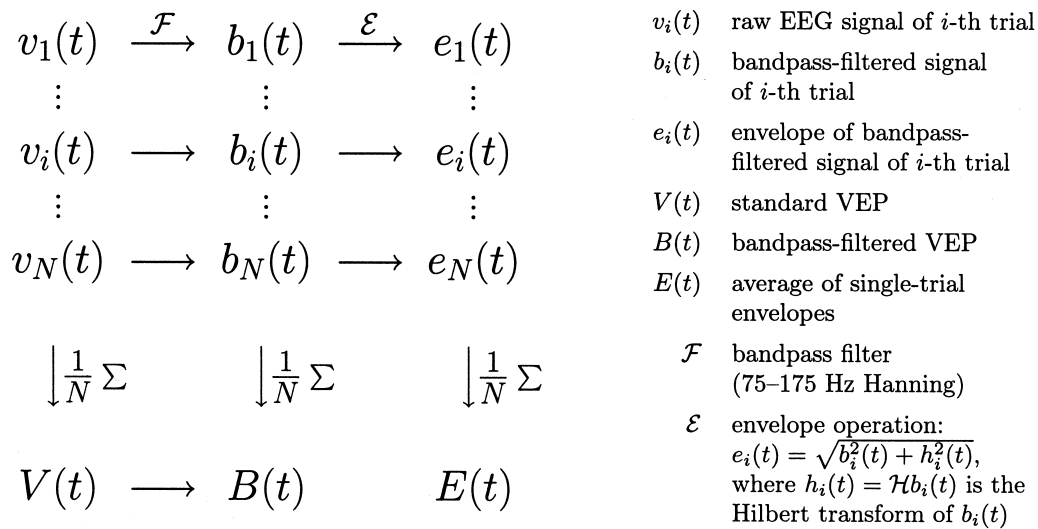


Fig. 1. Data analysis scheme: The left column represents the standard VEP averaging procedure. Applying a high-frequency bandpass-filter yields the high-frequency VEP $B(t)$ (center column). The total oscillatory activity $E(t)$ is computed by averaging the envelopes of the bandpass-filtered single trials (right column). Due to the envelope operation only the signal amplitude is averaged irrespective of the actual phase. This assures that phase jitter does not cause the oscillatory activity to cancel out during averaging. The non-phase-locked activity is obtained by applying the same analysis procedure to $n_i(t) = v_i(t) - V(t)$ rather than $v_i(t)$.

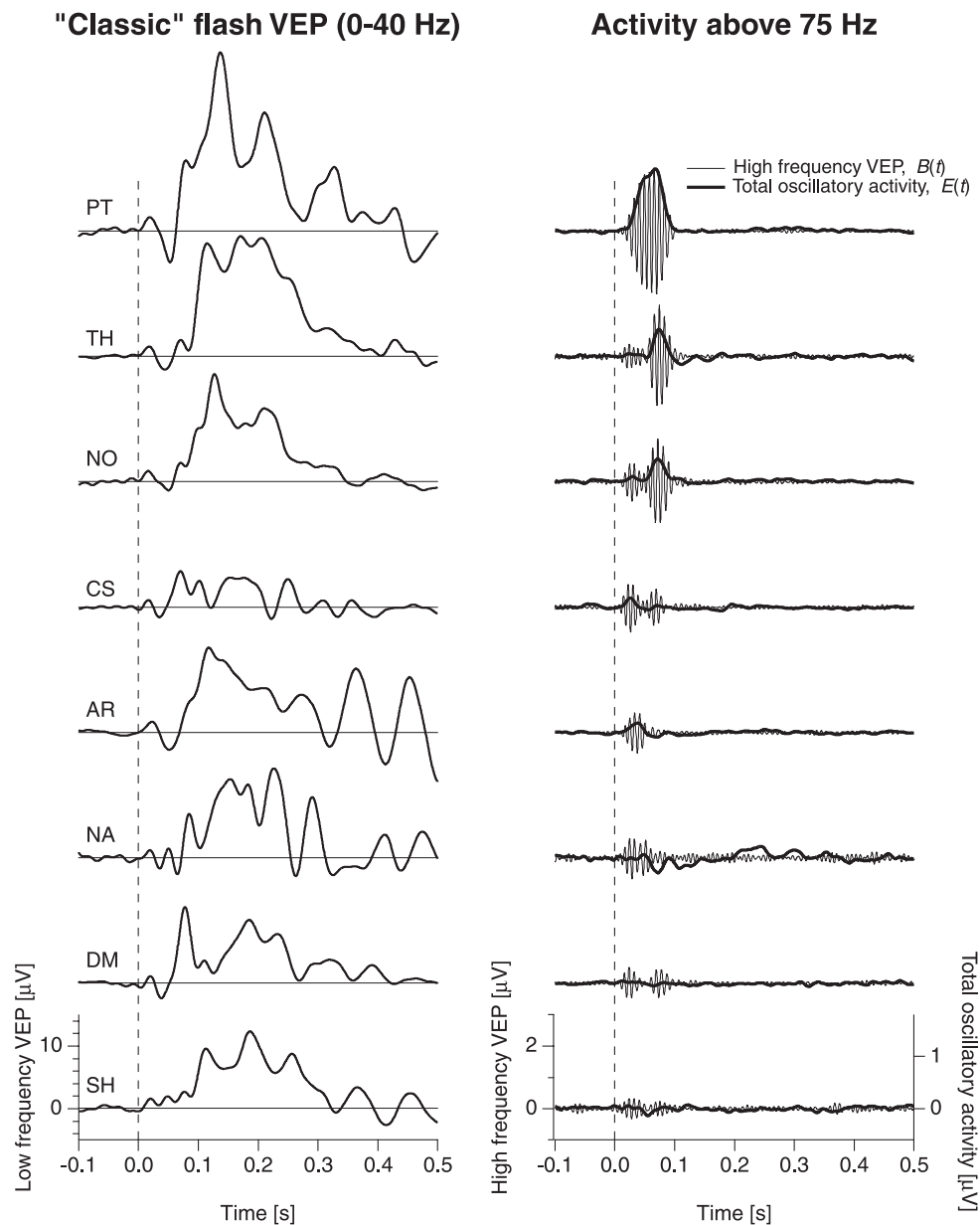


Fig. 2. Left: Standard VEPs (40 Hz low-passed) for each subject. Right: Corresponding high-frequency VEPs and total oscillatory activity (both with 75–175 Hz Hanning filter). Dashed vertical lines indicate the time of the flash. Subjects are identified by their initials and sorted by the magnitude of the high-frequency VEP. Two epochs of high-frequency activity can be distinguished in most subjects around 0–50 ms and 50–100 ms. In subjects with high amplitudes, these epochs coincide with enhanced total oscillatory activity.

and 90–160 ms after the stimulus while the activity in the cortical potentials occurs between 60 and 100 ms. The lag between the first maxima is 48 ms.

Discussion

In all subjects, we found oscillations at 120 Hz in the averaged VEP resembling those described by Lopez and Sannita (1997) for the MEG. They probably correspond to the VEP “wavelets” depicted by Allison et al. (1977). No increases in total oscillatory activity were found beyond 100 ms after the flash in any of the subjects. For subjects with small high-frequency VEP amplitudes,

the modulations in the total oscillatory activity were smaller than in the VEP or even absent. This is probably due to a low signal-to-noise ratio and the fact that the EEG background noise does not cancel out in the signal envelopes as efficiently as in the conventional averaging procedure.

Let us consider some possible sources of artifacts:

1. *Auditory intrusion:* Since the stimulator used LEDs instead of the usual high-voltage discharge lamps, auditory evoked potentials can be excluded as a possible source.
2. *Crosstalk from ERG oscillations:* Rubinstein and Harding (1981) suggest that the scalp distribution indicates a non-

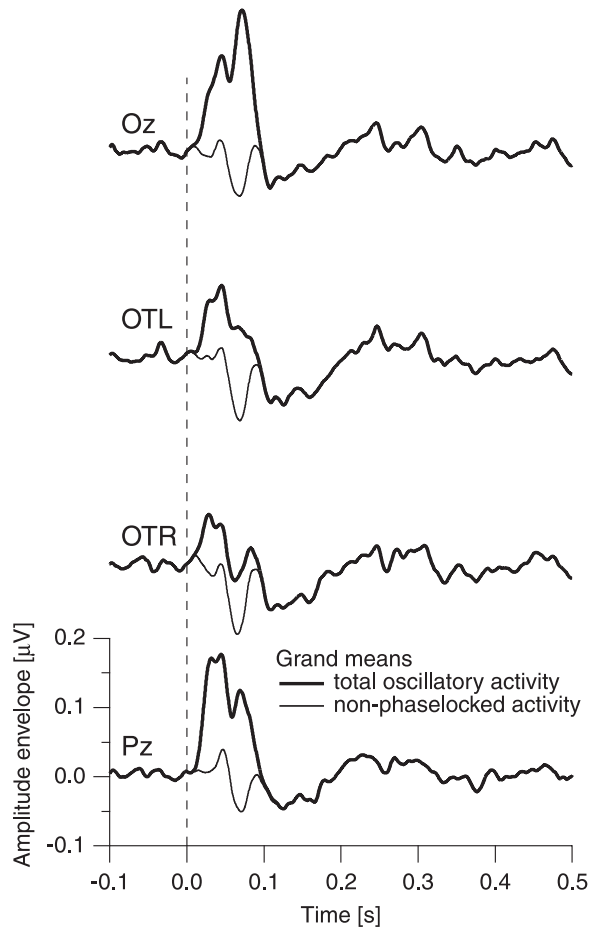


Fig. 3. Grand means of high-frequency total oscillatory activity (thick traces) and non-phase-locked activity (thin traces) for all four channels. The vertical dashed line at 0 s represents the time of the flash. The total oscillatory activity is clearly enhanced between 0 and 100 ms, while the non-phase-locked activity is not increased. This implies a high degree of phase locking.

retinal origin also for the early (<50 ms) oscillations. Using intracerebral recordings, however, Ducati et al. (1988) conclude that the early oscillations might be coming from both retinal and cortical generators. In our recordings, the retinal activity had a time course clearly different from that of the cortical activity (Fig. 4). Therefore electrical crosstalk between retinal potentials and cortical recordings can be excluded as a source of the cortical oscillations for the epoch between 50 and 100 ms.

There is no increase in non-phase-locked activity as revealed by single-trial analysis (Fig. 3). This indicates virtually perfect phase locking. The cessation of oscillations after 100 ms is not due to intertrial phase jitter, since the high-frequency VEP does not extend beyond that time and the non-phase-locked activity is not above the prestimulus values after ~100 ms. Thus, Alternative (1) presented in the Introduction can be rejected. It is not possible, however, to distinguish between the other two possible explanations: Suppression due to phase differences between different neuronal assemblies which contribute to the population response of the VEP, or, alternatively, a true cessation of neural oscillations which might be explained by different activity patterns produced by different processing stages.

A decrease below baseline is found in the total oscillatory activity between 100 and 200 ms after the stimulus. This suggests that the baseline contains activity of neurons involved in visual processing, which is either suppressed by the stimulus or shifted to other frequency bands. The latter could be part of a transition from a disordered to an ordered state as proposed by Quian Quiroga et al. (2001) as an origin of the VEP. Alternatively, this could simply be a reduction in spontaneous activity due to a recruitment of the neurons for stimulus processing without implying any specific ordering. The dip at 70 ms found in the non-phase-locked activity coincides with strong activity in the total oscillatory activity. This suggests that the phase-locked activity increases at the expense of non-phase-locked activity. Possible alternative explanations include neural refractoriness which would lead to a reduction in spontaneous activity.

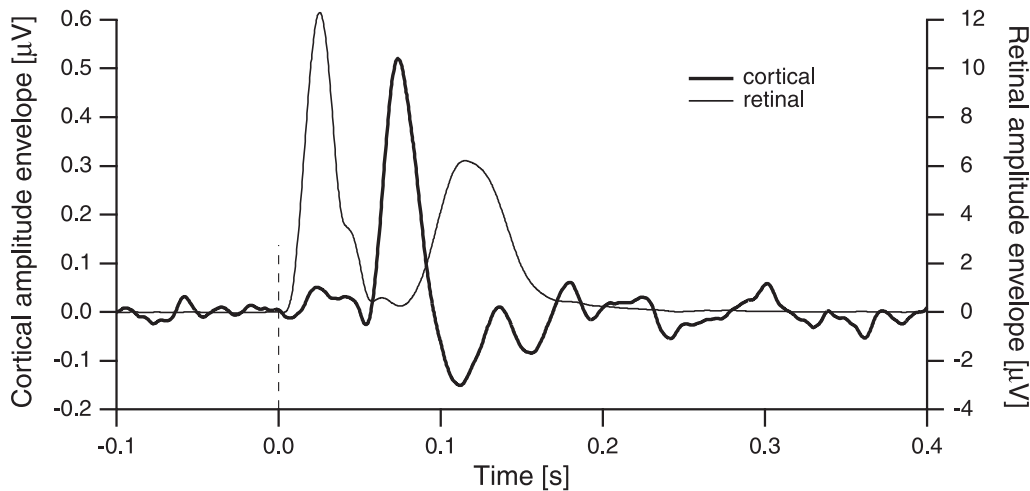


Fig. 4. Comparison of retinal and cortical total oscillatory activity for one subject (TH). The vertical dashed line at 0 s represents the time of the flash. The cortical oscillatory activity peaks around 70 ms, and the retinal activity around 25 ms. These different time courses indicate that the enhanced activity in the cortical recordings, at least in the 50–100 ms range, is not due to crosstalk from retinal potentials. The second peak around 115 ms in the retinal activity might be of electromyographic origin.

The results are in agreement with assumptions by Munk and Neuenschwander (2000) that such oscillations are propagated from previous processing stages rather than generated in the cortex itself, since only a prolonged persistence would require specific cortical mechanisms to generate or maintain the activity. Rubinstein and Harding (1981; Harding & Rubinstein, 1983) also suggested a noncortical origin and used the term “visual evoked subcortical potential” (VESP). Furthermore, Yokoyama et al. (1999) reported oscillations that resemble those presented here, but were much stronger at electrodes inserted into the optic tract than in the surface VEP. Similarly, Schroeder et al. (1992) recorded oscillations in the lateral geniculate nucleus (LGN) of macaque monkeys that were not seen in the cortical VEP. On the other hand, Lopez and Sannita (1997) argue that for methodological reasons, the oscillations found in the MEG are most likely of cortical provenance. Both views are not necessarily contradictory since an oscillation generated in subcortical regions or in the retina might be transmitted to the cortex, inducing some activity there. It has recently been shown in neural network models that signals can propagate over several stages without accumulating phase jitter, even in the presence of noise (Diesmann et al., 1999).

The present results rule out “averaging artifacts” to explain the cessation of oscillations at 100 ms. To further narrow down on the remaining possibilities, it may be fruitful to analyze the precise temporal relationship between retinal and cortical responses.

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