

Asymmetry of motion VEP in infantile strabismus and in central vestibular nystagmus *

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Abstract. Norcia *et al.* [1] found a nasal-temporal asymmetry of visually evoked potentials (VEP) elicited by motion stimuli in patients with infantile strabismus. Patients with infantile strabismus typically present with an asymmetry of the monocular optokinetic nystagmus (OKN). We here address the question whether the asymmetry of the motion VEP indicates a sensory defect in the afferent visual pathway that could explain the OKN asymmetry. We recorded the VEP to a horizontally oscillating vertical sinusoidal grating in 20 patients with infantile strabismus (esotropia, asymmetry of the monocular optokinetic nystagmus, latent nystagmus) and in 10 normal controls. No asymmetry occurred in the 10 controls. Eight of the 20 patients with infantile strabismus showed a clear difference between the VEPs evoked by back and forth movements with a mirror-like asymmetry between the two eyes (phase shift $180 \pm 20^\circ$). However, there was no significant correlation between the degree of VEP and OKN asymmetries. Therefore, we assume that the VEP asymmetry does not reflect the primary cause of the OKN asymmetry. Rather, the OKN asymmetry may be due to a sensory-motor defect in the efferent subcortical pathway, and the VEP asymmetry could be an epiphenomenon. Some of the VEP asymmetry may be a consequence of the latent nystagmus typically released under monocular stimulation, leading to adaptation of the afferent retino-cortical pathway. This suggestion is supported by a marked VEP asymmetry that we found in two patients with an acquired central vestibular nystagmus, an abnormality most likely not combined with a primary defect of the retino-cortical pathway.

Introduction

Patients with infantile strabismus show a reduced optokinetic response to temporally-directed motion. This results in a nasal-temporal asymmetry of the optokinetic nystagmus (OKN) if only one eye is stimulated. We are addressing the question whether the OKN asymmetry is due to a sensory defect in the afferent visual pathway, or to a sensory-motor defect in the efferent cortico-oculomotor pathway.

Norcia *et al.* [1] found a nasal-temporal asymmetry of visually evoked potentials elicited by motion in patients with infantile strabismus. These

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authors suggested that the asymmetry of the motion VEP indicates a sensory defect in the afferent visual pathway or the visual cortex, and that this sensory defect could explain the asymmetry of the OKN. Although their paradigm did not allow to determine whether it was the nasalward or the temporalward movement that evoked the smaller response, their hypothesis was supported by the fact that the asymmetry was out of phase by about 180° between the two eyes. To further test their hypothesis, we searched for a quantitative correlation between the asymmetries of the VEP and the OKN. Moreover, we considered the possibility that the VEP asymmetry could be a consequence of a latent nystagmus (LN) which can be released in patients with infantile strabismus when they are tested monocularly for VEP asymmetry.

Materials and methods

Subjects

Twenty patients with infantile convergent strabismus (aged 10 to 33 yr.) were examined, usually on the day before squint surgery. Their strabismus had commenced during the first 6 months of life. For inclusion in the study, we required asymmetry of the monocular OKN, detectable by observation using a manually moved tape. In addition, a patient with upbeat nystagmus (a 24-year-old nurse, oscillopsia since 6 months, slow phase velocity $5^\circ/\text{s}$) and another patient with downbeat nystagmus (81 yr, oscillopsia since 2 years, slow phase velocity $3^\circ/\text{s}$) were examined. Both of them did not exhibit strabismus. Upbeat and downbeat nystagmus are similar to latent nystagmus as they are not suppressed by fixation and are accompanied by a (vertical) OKN asymmetry. Although the specific cause of the nystagmus in the two cases could not be detected by MRI and CT, it is generally accepted that upbeat and downbeat nystagmus represent a central vestibular imbalance caused by a lesion in the posterior cranial fossa [2]. 10 normal subjects were also examined.

Motion VEP

The stimulus consisted of a monocularly presented sine wave grating (spatial frequency $2.8 \text{ cyc}/^\circ$) which was square-wave alternated with an amplitude of $\frac{1}{4}$ period at 7.15 Hz. The VEP was recorded from an Oz-Fz derivation, amplified with a bandpass of 3–70 Hz (first order filter, Toennies physiologic amplifier) and digitized with a sampling interval of 2.4 ms over a sweep length of 1.12 s. The sweep length contained exactly 16 alternations of the stimulus so that frequency overspill could not occur in the subsequent Fourier transformation. Further analysis was done in the frequency domain: Normally, nasally and temporally directed shifts of the grating evoke identical responses.

This symmetry leads to frequency-doubling, resulting in a prominent peak at 14.3 Hz. If, in infantile strabismus, an asymmetry of the afferent visual pathway exists as suggested by Norcia *et al.* [1], nasally and temporally-directed shifts would evoke unequal responses. This asymmetry would lead to a peak at $14.3/2 = 7.15$ Hz, and the responses obtained from stimulating the right and left eyes would be out of phase by 180° . (In the following, frequencies will be rounded to 7 and 14 Hz, respectively.)

We defined an *asymmetry index* by dividing the amplitude at 7 Hz by the sum of the amplitudes at 7 Hz and 14 Hz. This ratio was used for the correlation with the oculomotor measures (Figs. 5 and 6), and averaged across the two eyes for the phase analysis (Fig. 4). We also defined a *signal-to-noise criterion* that had to be met for these analyses: In the VEP of each eye, either the peak at 7 Hz or at 14 Hz had to be twice as large as the average of the 4 neighboring frequency bins (2 on either side).

In the patients with upbeat and downbeat nystagmus and in two normal controls the experiment was repeated with the stimulus oscillating vertically rather than horizontally.

Optokinetic nystagmus

A hand-held tape with black and white stripes (visual angle 4°) was moved several times in opposite directions with a velocity of about $30^\circ/\text{s}$ before the right and the left eye (fellow eye occluded). The resulting OKN was observed and estimated according to the velocity of the slow phases. The asymmetry was graded as (1) 'slight' if the response to temporally-directed motion appeared slightly smaller than that to nasally-directed motion, (2) 'moderate' if the response to temporally-directed motion was clearly smaller, and (3) 'absolute' if the response to temporally-directed motion was completely lacking, but a decent response to nasally-directed motion could be elicited.

Latent nystagmus

Subjects were asked to fixate a 'star' projected onto the macula by an ophthalmoscope. The other eye was occluded. LN was graded by experienced observers as being (1) 'slight' if the slow phase velocity appeared to be $<2^\circ/\text{s}$, (2) 'moderate' if the slow phase velocity appeared to be $2 - 5^\circ/\text{s}$, and (3) 'marked' if the slow phase velocity appeared to be $>5^\circ/\text{s}$.

Results

Motion VEP responses

Examples of original recordings are depicted in Figs. 1–3. In the normal subject represented in Fig. 1, the symmetrical 14 Hz response clearly domi-

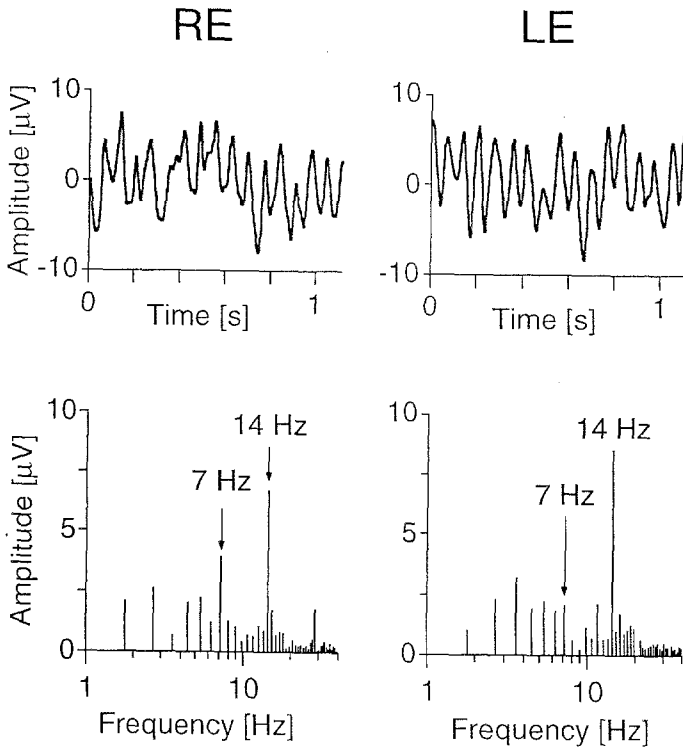


Fig. 1. Normal subject. Horizontal motion VEP from right and left eyes with respective magnitude spectra (bottom) showing a prominent peak at 14 Hz. Averaged VEP asymmetry index 0.3.

nates the asymmetrical 7 Hz response. In the patient with infantile strabismus represented in Fig. 2 and in the patient with upbeat nystagmus represented in Fig. 3, the asymmetrical 7 Hz responses dominate the symmetrical 14 Hz responses.

In interpreting the Frequency spectra, the following should be noted: If a VEP record displays a strong upward or downward trend as in Fig. 2 (probably remnants of eye-movement or blink artifacts rejected from averaging), this trend is seen as a repetitive sawtooth shape by the Fourier analysis. Consequently, in addition to the response at 7 and/or 14 Hz and to broadband-noise, the spectrum contains sawtooth-components following a $\frac{1}{f}$ -law. Thus the amplitude at 7 Hz is superimposed by $\frac{1}{4}$ of the amplitude at 1.8 Hz (lowest spectral line at 0.89 Hz not shown in the figures). Nevertheless, responses stand out clearly against the trend artifact estimate of $\frac{1}{4}$ of the amplitude at 1.8 Hz, even in Fig. 2.

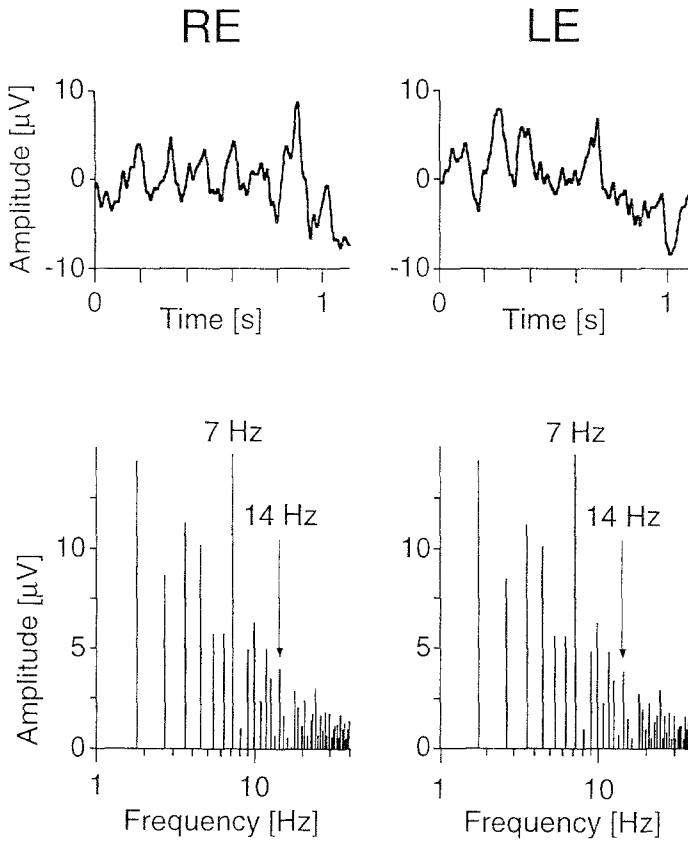


Fig. 2. Patient with infantile strabismus. Horizontal motion VEP from right and left eyes. Magnitude spectra show a prominent peak at 7 Hz. Averaged VEP asymmetry index 0.7.

Asymmetry of the motion VEP

The signal-to-noise criterion required for further analysis was met by all 10 normal subjects, by 16 of the 20 patients with infantile strabismus and by the 2 patients with acquired central vestibular nystagmus.

In the 10 normal subjects, the median of the asymmetry index across eyes and subjects was 0.25 in the horizontal plane and (2 subjects) 0.3 in the vertical plane. In the 16 patients with infantile strabismus a VEP asymmetry index (averaged across the two eyes) of <0.5 was found in 4, and of >0.5 in the remaining 12 cases (Fig. 4). Only 8 of 16 cases showed responses of the two eyes that were out of phase by $180 \pm 20^\circ$, i.e., a mirror-like asymmetry comparable to that of the OKN (Fig. 4).

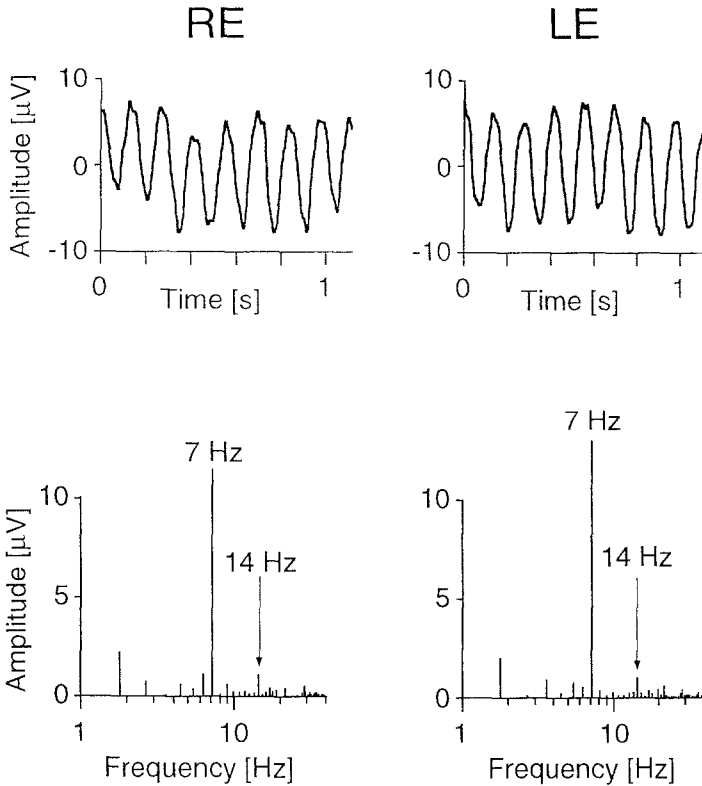


Fig. 3. Patient with upbeat nystagmus. Vertical motion VEP from right and left eyes. Magnitude spectra show a prominent peak at 7 Hz. Averaged VEP asymmetry index 0.9.

Correlation of motion VEP asymmetry and oculomotor measures

The 8 patients with infantile strabismus, whose VEP responses obtained from the right and left eyes were out of phase by $180 \pm 20^\circ$, were analyzed with respect to the strength of their OKN asymmetry (Fig. 5) and the strength of their latent nystagmus (Fig. 6). We found no significant correlation between the VEP asymmetry index and the strength of the OKN asymmetry nor between the VEP asymmetry index and the strength of the latent nystagmus ($p=.4$ and $p=.8$, respectively; Spearman Rank Correlation; average across eyes).

In the 12 patients with infantile strabismus not represented in Figs. 5 and 6, the median strength of OKN asymmetry and of LN, averaged across the two eyes and all cases, were 2.0 and 1.5, respectively. In the patients with upbeat and downbeat nystagmus, the asymmetry index of the vertical motion VEP, averaged across the two eyes and the two cases, was 0.9 and 0.7, respectively.

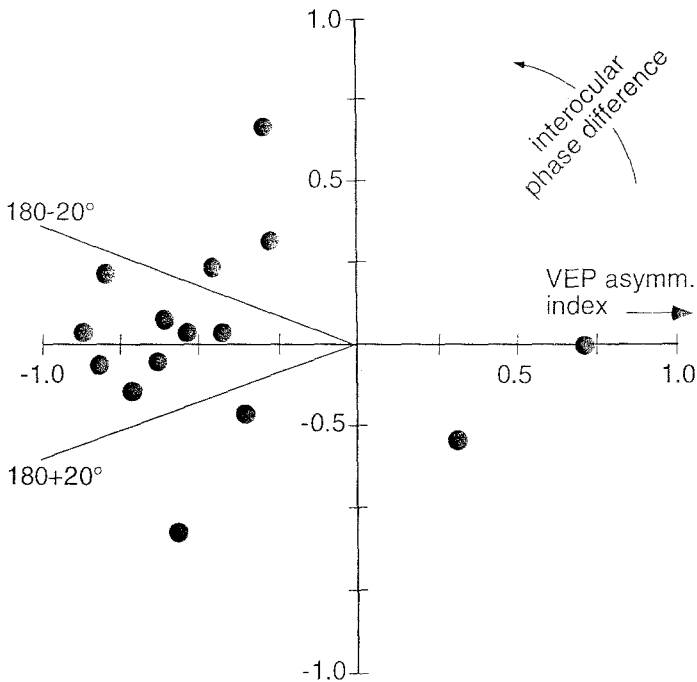


Fig. 4. VEP asymmetry and interocular phase difference of 16 patients with infantile strabismus. The distance from the origin corresponds to the asymmetry index averaged across the two eyes. The polar angle indicates the phase difference between the responses of the two eyes at 7 Hz. The interocular phase difference was within $180 \pm 20^\circ$ in only 8 of the 16 patients.

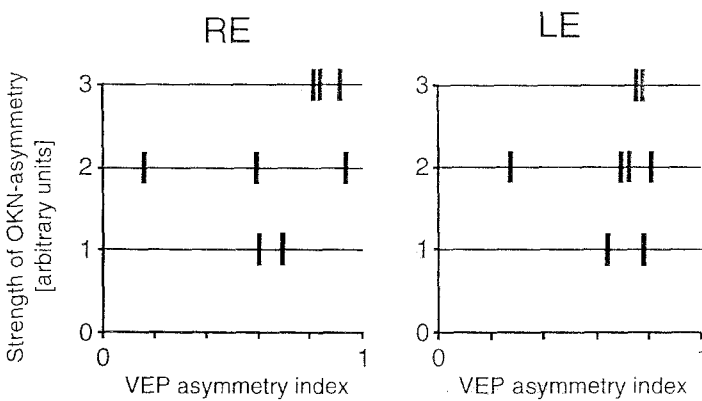


Fig. 5. No correlation between VEP asymmetry index and strength of OKN asymmetry in 8 patients with infantile strabismus ($p=.4$, Spearman Rank Correlation, average across eyes).

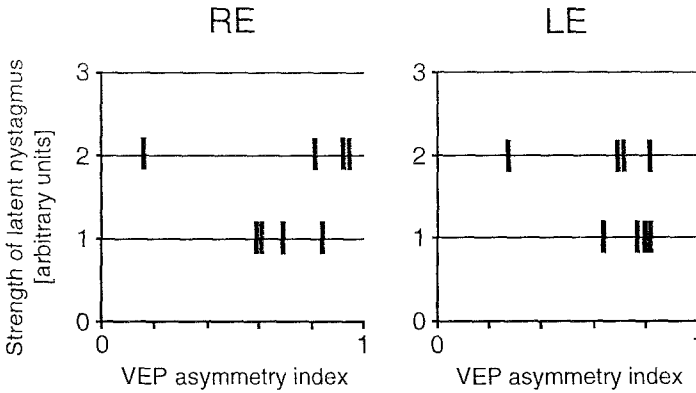


Fig. 6. No correlation between VEP asymmetry index and strength of latent nystagmus in 8 patients with infantile strabismus ($p=0.8$, Spearman Rank Correlation, average across eyes).

Discussion

In accordance with Norcia et al. [1], we found a mirror-like nasal-temporal asymmetry of the motion VEP in patients with infantile strabismus, but not in normal controls. However, we encountered such a VEP asymmetry in only 8 patients, although all 20 of them had some degree of OKN asymmetry. Moreover, we did not find a significant correlation between the asymmetry of the VEP and the OKN. This finding conflicts with the idea that the VEP asymmetry reflects the defect responsible for the OKN asymmetry [1].

As suggested by Hoffmann [2, 3, 5] and others based on neurophysiological evidence, the OKN asymmetry may not be due to a sensory defect in the afferent visual pathway or the visual cortex, but may rather be due to a sensory-motor defect in the efferent corticocolomotor pathway. There is also psychophysical evidence that supports this notion: Patients with infantile strabismus completely lacking a motor response to temporally-directed motion are able to differentiate various velocities in that direction [6]. This indicates that the pathway between the retina and the visual cortex is capable of mediating the motion signal. The sensory asymmetry in velocity perception that has been found in patients with infantile strabismus [7, 8] is subtle and can hardly be compared with the gross motor asymmetry. Moreover, the subtle asymmetry in motion perception may be the result of adaptation to the slip of the retinal image during the so-called 'manifest LN' that is present under everyday viewing conditions.

Our finding of a marked VEP asymmetry in two patients with central vestibular nystagmus suggests that some of the VEP asymmetry encountered in patients with infantile strabismus may be due to the latent nystagmus

that is released under monocular stimulation for VEP recording. The shift of the retinal image brought about by the slow nystagmus phases creates an asymmetry in the stimulus condition and might adapt the system. This interpretation is supported by the fact that, in normal subjects, adaptation of the motion VEP already sets in during the first seconds of stimulation [9]. However, LN explains only some, but not all, of the VEP asymmetry, since we did not find a quantitative correlation between LN and VEP asymmetry in patients with infantile strabismus.

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