Intern. J. Neuroscience, 1989, Vol. 44: pp. 185–195
Reprints available directly from the publisher
Photocopying permitted by license only

CORTICAL AND RETINAL REFRACTORY PERIODS IN THE HUMAN VISUAL SYSTEM

WOLFGANG SKRANDIES and ASTRID RAILE

Max-Planck-Institute for Physiological and Clinical Research 6350, Bad Nauheim, F.R.G.

(Received January 8, 1988)

Refractory periods of the visual system were investigated in 12 healthy subjects by simultaneously recording retinal (ERG) and cortical (VEP) evoked electrical activity. Double-flash stimuli were presented at different interstimulus intervals, and response components evoked by the second flash were analyzed in detail, and related to psychophysical detection thresholds. With short interstimulus intervals ERG b-wave peak latencies were increased and b-wave amplitudes were significantly reduced, while P100 component latencies of the VEP were significantly influenced only at long interstimulus intervals. Regression analysis of the individual data as well as analysis of the retinocortical transmission times showed that the cortical latency changes were not simply caused by changes on the level of the retina. Additional influences of the interstimulus interval on nonretinal structures of the human visual system must be assumed.

The subjective psychophysical detection thresholds were significantly higher than the threshold values at which reliable electrical or cortical response components could be elicited.

Keywords: human electrophysiology, visual evoked potential, electroretinogram, double flash discrimination, retinocortical transmission time

Refractory periods of given parts of the nervous system define times of reduced neural excitability. In human studies, electrical potentials evoked by sensory stimuli presented at short interstimulus intervals can be recorded in order to analyze refractory periods of sensory systems. The temporal characteristics of the human visual system have been investigated electrophysiologically both at the level of: (1) the retina, and (2) the visual cortex. Experiments have been performed with recordings of visual evoked potentials (VEPs) in order to study refractory periods of the visual cortex in both normal subjects and clinical patients (Schwartz & Shagass, 1964; Bergamasco, 1966; Mitchell *et al.*, 1983; Riemslag *et al.*, 1985). Electroretinographical (ERG) recordings have shown that retinal refractory periods can be determined in a similar way. The electrical responses of the human retina to light flashes presented successively are influenced by stimulus parameters like temporal frequency and intensity of the test light as well as by the subjects' state of adaptation (Dodt, 1951; Mahneke, 1957; Burian & Spivey, 1959; Sverak & Peregrin, 1960). The ERGs elicited by the second flash of a stimulus pair depend on the interstimulus interval, and changes of ERG amplitude and latency are commonly interpreted as indicating refractory periods of the retina.

Since the VEP activity is influenced not only by cortical mechanisms but depends also on information processing already occurring at the retinal level (Skrandies, 1987a), we were interested in the refractory behavior of both retinal and cortical electrical response components when paired visual stimuli were presented at different intertimulus intervals. In the present investigation, simultaneous recordings of ERG and VEP activity were obtained which may help to answer the question of whether

We thank Professor E. Dodt for support of our work and helpful discussions, and Professor D. Lehmann for reading the manuscript.

peripheral (retinal) and central (cortical) stages of the visual system are affected in a similar way by variation of the interstimulus interval. Such data may help to understand whether time dependent changes of VEP components are caused by changes in retinal information processing alone, or whether different, additional processes account for the findings on refractory periods of the visual cortex. In addition, we will show how subjective, psychophysical thresholds in a double-flash discrimination task relate to electrophysiological thresholds determined by recordings of ERG or VEP activity.

METHODS

A pilot study was carried out with five subjects; twelve healthy adults between 20 and 34 years of age were used in the final experiments. All subjects had normal or corrected-to-normal visual acuity and had participated earlier in electrophysiological experiments.

Three occipital recording electrodes were placed along the midline at the inion, and at 10% and 20% of the nasion-inion distance above the inion referred to a frontal electrode at Fz. The electroretinogram (ERG) was recorded with a Henkes contact lens electrode placed in the left eye. In order to minimize influences of the occipital VEP activity on the ERG, for ERG recordings a reference electrode was used at the ipsilateral outer canthus (Skrandies, 1987a).

The signals were bandpassed between 1 and 250 Hz, amplified, and averaged (n = 64) by a Medelec ER94a Sensor system. The recording epoch was 300 ms. Stimuli were delivered by a GRASS PS22 photic stimulator at a rate of 1 pair of flashes per second. Intensity 16 was used which corresponded to a luminance of about 1500 cd/m^2 as measured with flashes fused at 300 Hz. A black and white translucent checkerboard pattern of 80% contrast with a checksize of 23′ arc was presented as a circular test field with a diameter of 4.95° arc at a distance of 150 cm. In order to control for adaptation effects, a steady background illumination of 50 cd/m^2 was used. Double-flash intervals ranged between 10 and 135 ms, the exact intervals were determined by measuring stimulus artifact latencies occurring at the eye electrode. We note that the photoelectric artifact latencies picked up by the electrode were identical to those measured with a photodiode in control experiments.

Subjective, psychophysical fusion thresholds were obtained by the method of limits, and the mean values of three ascending and three descending temporal threshold values were computed for each subject. Electrophysiological measurements were obtained with single flashes, and at long double-flash intervals which were successively reduced. Control runs with the single-flash condition were interspersed throughout the recording session in order to control for sequence effects. The peak latencies and amplitudes of the ERG b-wave, and the peak latencies of the P100 component of the VEP were measured and further analysed. For the VEP we decided to measure only the occipitally dominant positive component that turned out to be reliable over subjects and that had an approximate latency of 100 ms; consequently this component will be referred to as P100 component. Since we found that for small interstimulus intervals response components to the second flash could not be measured reliably, a subtraction procedure was employed (see Figure 1): The response evoked by single flashes was subtracted from the double-flash response, and the resulting waveshapes displayed the activity evoked by the second flash alone. This method has been used before by a number of authors (e.g., Schwartz and Shagass, 1964; Mitchell *et al.*, 1983). In addition, we analysed the retino-cortical transmission times which were

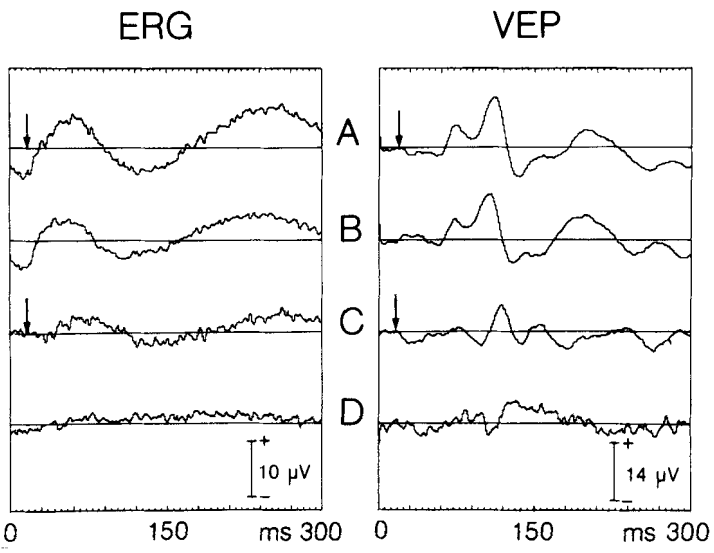

FIGURE 1 A. ERG and VEP averaged responses obtained with double flashes at an interstimulus interval (ISI) of 18 ms. Occurrence of the second flash is indicated by arrow. B. ERG and VEP averaged responses obtained with single flashes. C. Subtraction procedure: result of subtracting the single-flash responses from the double-flash responses. Occurrence of the second flash is indicated by arrow. D. Control condition: result of subtracting two single-flash responses from each other. Bandpass from 1 to 250 Hz. Note the different amplitude scales for ERGs and VEPs.

defined as latency differences between the ERG b-wave and the P100 component of the VEP.

In order to identify reliably the P100 component and to prevent confusion with other components, the following criteria were employed:

(1) Changes of component latency had to be continuous when interstimulus interval changed continuously. With very long interstimulus intervals the response to the second flash had the same latency as that evoked by a single flash, and a gradual reduction in interstimulus interval was accompanied by a gradual change in latency (see also Diamond, 1977).

(2) A latency time window with a lower limit of 75 ms was employed. We also note that due to these strict criteria, at short interstimulus intervals the VEP data of only four subjects were used for further analysis (see Results section).

Amplitude and latency data were statistically compared using paired *t*-tests with an alpha level of 5%; linear regressions between ERG and VEP component latencies were computed on the individual data of each of the twelve subjects, and these results were further analysed.

RESULTS

Figure 1A shows the ERG and VEP responses obtained with a double-flash stimulus with an interstimulus interval of 18 ms. Obviously, the components evoked by the second flash cannot be identified unambiguously in these traces. However, when the single-flash response (Figure 1B) was subtracted, a difference waveform resulted which reflected the response components to the second flash only (Figure 1C). The resulting latency of the P100 component was 136 ms, that of the ERG b-wave was

50 ms. In order to establish that such a difference waveform has physiological meaning and is not produced by chance, we applied the subtraction procedure also to all pairs of single-flash responses. This yielded no consistent waveshape indicating that the waveshapes in Figure 1D were not different from the noise level. The data in Figure 1 demonstrate that the subtraction procedure identified retinal and cortical electrical activity elicited by the second flash alone in the double-flash condition. When we first analyzed only the original double-flash response waveshapes in a pilot study on five subjects, it was hard reliably to identify the components evoked by the second flash when interstimulus intervals shorter than about 85 ms were used. Thus, all results presented below were obtained using the subtraction procedure. We also compared the original latency and amplitude values elicited at long interstimulus intervals with those obtained by the subtraction procedure, and we could verify that no distortions were introduced by subtracting the signals.

A complete series of difference waveshapes obtained with single flashes and at 11 different interstimulus intervals is illustrated in Figure 2. On the left, the ERGs are

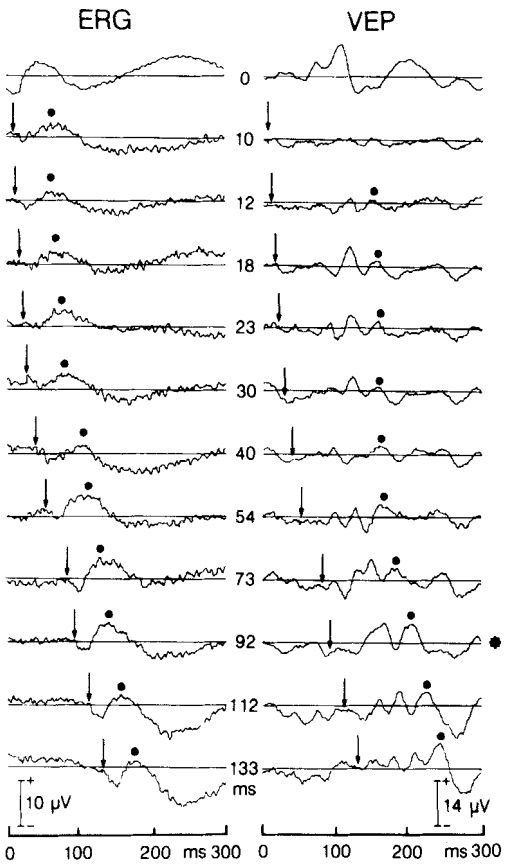

FIGURE 2 Series of difference waveshapes obtained with single flashes and with double flashes at 11 different interstimulus intervals (ISIs). Left column: ERGs; right column: VEPs recorded at Oz. Occurrence of the second flash is indicated by arrow. Subjective threshold for double-flash perception was at 95 ms, indicated by '*'. There is a continuous change in component latency when the interstimulus interval is successively shortened. Bandpass from 1 to 250 Hz. Note the different amplitude scales for ERGs and VEPs.

shown, and it is clear that also with short interstimulus intervals response components elicited by the second flash can be identified unambiguously. The corresponding VEP waveshapes recorded from Oz are given in the right column of Figure 2. Since there were no systematic and significant differences between the three occipital recording channels only the VEP data obtained at Oz will be discussed in detail.

The systematic shortening of the interstimulus interval was accompanied by a continuous change of the component latencies of both the ERG b-wave and the P100 component. It is obvious from Figure 2 that at short interstimulus intervals VEP components could not be identified unambiguously, and we found that only 4 of 12 subjects showed reliable VEP components at interstimulus intervals below 40 ms. We also note that the subjective threshold for the detection of a double flash (at 95 ms, asterisk in Figure 2 appeared to be independent of the occurrence of electrophysiological response components: ERG components could be identified down to an interstimulus interval of 10 ms, and also VEPs below 92 ms interstimulus interval were reliably recordable (see below).

The component latencies of both the ERGs and VEPs in Figure 2 varied systematically with different interstimulus intervals: short interstimulus intervals yielded longer latencies than single flashes or double flashes with long interstimulus intervals. The average latency data of the ERG b-wave and the P100 component of 12 subjects are illustrated in Figure 3A and C.

The mean ERG b-wave latencies elicited by the second flash at different interstimulus intervals were not constant (Figure 3A). Short and long interstimulus intervals had different effects, and we compared: (1) single-flash latencies and mean latencies elicited by short interstimulus interval stimuli (mean values computed from responses obtained with interstimulus intervals between 10 and 35 ms) and (2) single flash latencies and mean latencies elicited by long interstimulus interval stimuli (mean values computed from responses obtained with interstimulus intervals between 100 and 135 ms).

The single-flash b-wave latency was significantly shorter than that of the double-flash response at interstimulus intervals between 10 and 35 ms (mean difference: 8.58 ms; $t = 5.29$; $p < 0.0005$), whereas there was no significant b-wave latency difference between the single-flash and double-flash response latencies with interstimulus intervals ranging from 100 to 135 ms ($t = 0.34$; n.s.).

The amplitudes of the ERG b-wave also covaried with interstimulus intervals (Figure 3B): at interstimulus intervals between 10 and 35 ms the response amplitudes to the second flash were significantly smaller than single-flash evoked amplitudes (mean difference: 3.1 μV; $t = 10.72$; $p < 0.00005$). At long interstimulus intervals (between 100 and 135 ms) the ERG b-wave amplitudes elicited by the second flash were not significantly different from the single-flash evoked amplitudes ($t = 0.77$, n.s.).

The VEP latency data showed a similar behavior as the ERG b-wave latencies. Figure 3C presents the mean P100 latencies as a function of interstimulus interval. Statistically significant differences between the single-flash component latencies and the double-flash latencies were, however, restricted to long interstimulus intervals: the mean values obtained with interstimulus intervals between 100 and 135 ms were significantly longer than the single-flash latencies (mean difference: 2.92 ms; $t = 1.86$; $p < 0.05$). We note that with short interstimulus intervals latencies only in 4 of 12 subjects could reliable P100 components be obtained. With short interstimulus intervals, the mean P100 latencies of 4 subjects were longer by 13.25 ms than the single-flash latencies. This latency difference was, however, not statistically significant ($t = 1.70$, n.s.), probably due to the large intersubject variation.

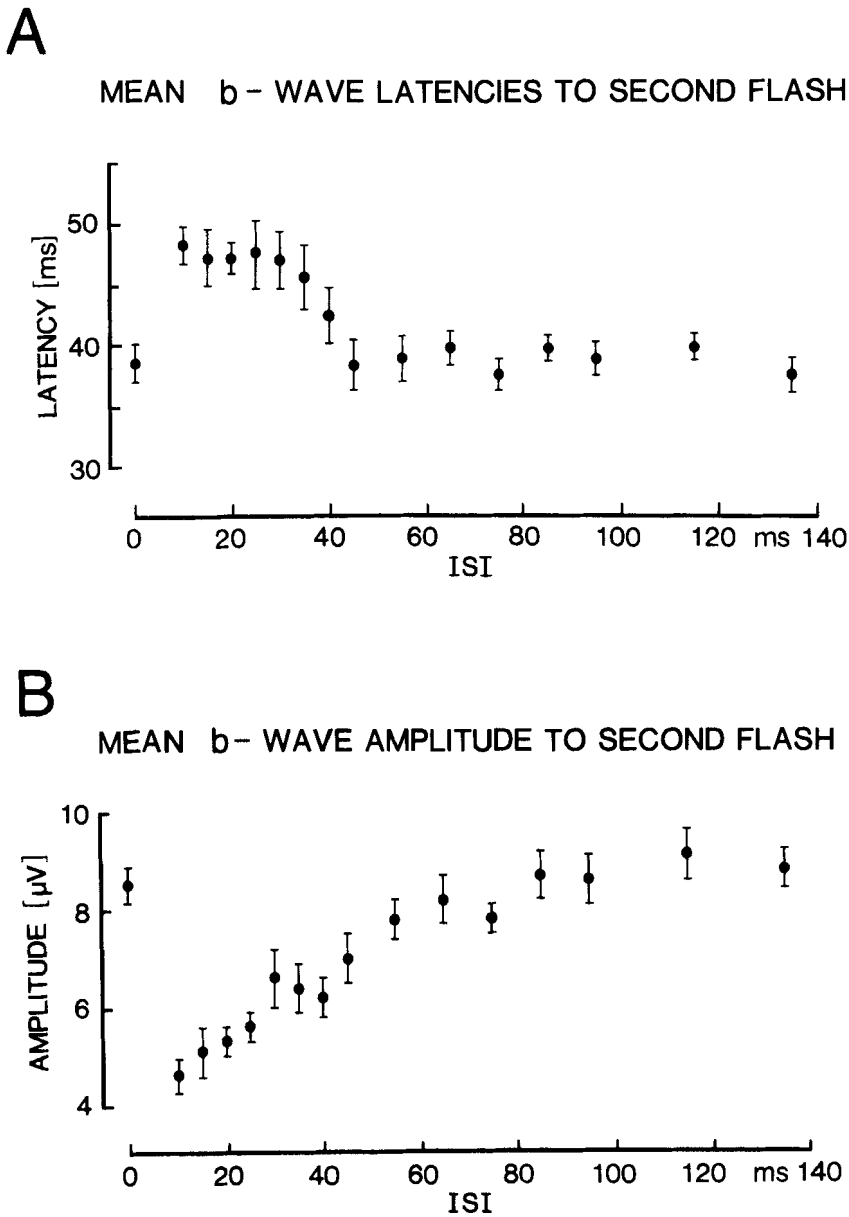

FIGURE 3 Grandmean component latencies and amplitudes of 12 subjects elicited by the second flash as a function of interstimulus interval (ISI); means and standard errors are given. A. ERG b-wave latencies; the single-flash latency (ISI = 0 ms) is significantly shorter than that of the second flash at ISIs between 10 and 35 ms ($t = 5.29$, $p < 0.0005$). B. ERG b-wave amplitudes; the single-flash amplitude (ISI = 0 ms) is significantly larger than that of the second flash at ISIs between 10 and 35 ms ($t = 10.72$, $p < 0.0005$). C. VEP latencies; the single-flash latency (ISI = 0 ms) is significantly shorter than that of the second flash at ISIs between 100 and 135 ms ($t = 1.85$, $p < 0.05$). At short interstimulus intervals only four subjects showed reliable components, and no significant difference is observed. D. Retinocortical transmission times defined as latency differences between P100 component of the VEP and the ERG b-wave; there are no statistically significant differences between single-flash and double-flash transmission (Refer to text for further details).

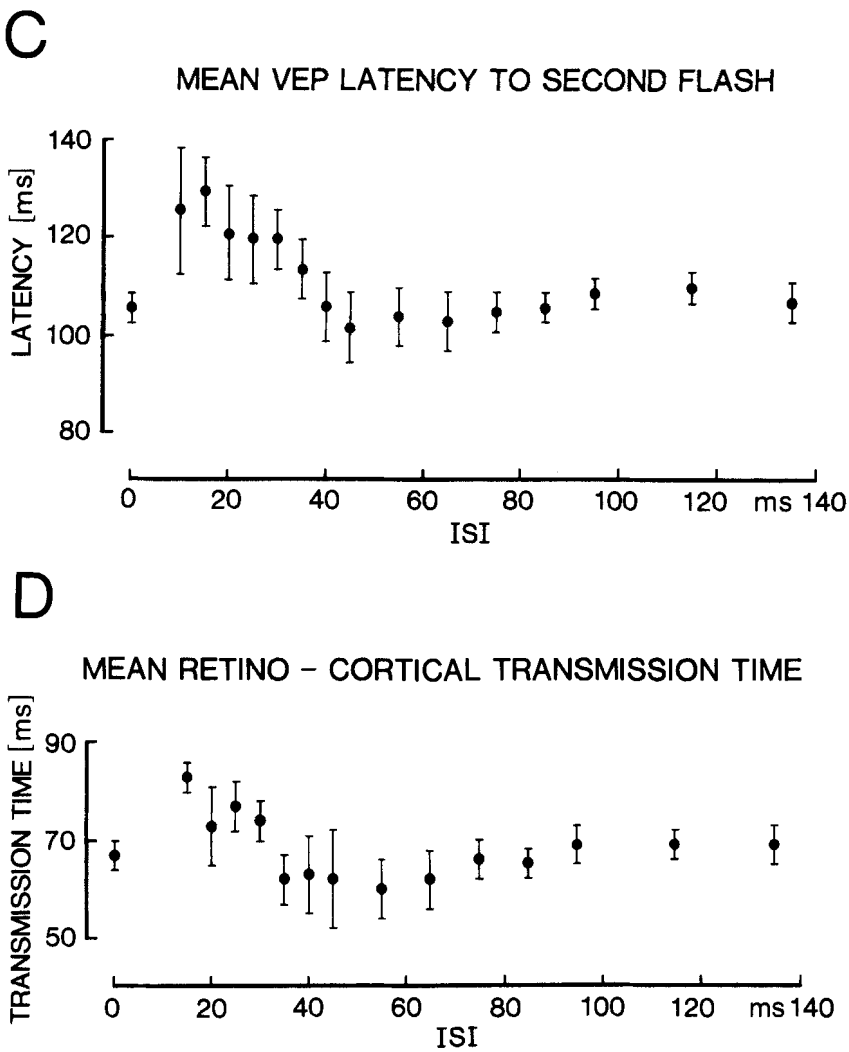

FIGURE 3 (continued).

The amplitudes of the VEP components showed large intersubject variation, and, thus, were not used for further analysis in the present study. Amplitude variation increased with short interstimulus intervals; this may account for the fact that with interstimulus intervals below 40 ms VEP component latencies elicited by the second flash could not be determined unambiguously.

The latency changes of the P100 component, however, were not simply caused by changes on the retinal level. We investigated the relationship between ERG and VEP components by: (1) analyzing the retinocortical transmission times, and (2) computing linear regressions between ERG and VEP latencies for the individual data of each subject.

Retinocortical transmission times were defined as latency differences between the b-wave of the ERG the P100 component of the VEP. Figure 3D shows the mean

retioncortical transmission times of 12 subjects as a function of interstimulus interval. In contrast to the influence of interstimulus interval on the ERG or VEP component latencies (Figures 3A and C) there were no statistically significant differences in retinocortical transmission times between single-flash evoked activity and double-flash evoked activity at any interstimulus interval. This means that the variations apparent in Figure 3D could not be substantiated statistically.

Further support for the independence of ERG and VEP component latency changes was obtained with regression analyses. Such computations were performed on the individual data of each of the twelve subjects, and the results yielded no consistent relationship between ERG and VEP component latencies: Only three subjects showed significant positive correlations, one subject showed a negative correlation, while eight subjects displayed no significant correlations between ERG and VEP component latencies. Examples are given in Figure 4 which illustrate the relationship between the latency of the ERG b-waves and the VEP components obtained in three different subjects. As noted above, for most of the subjects (67%) only nonsignificant correlation coefficients were obtained. This indicates that the cortical latency changes were not directly caused by changes at the retinal level since longer latencies of the ERG b-wave were not accompanied by a similar prolongation of the VEP component latencies.

In general, the subjective, psychophysically determined double-flash discrimination thresholds were different from the threshold values at which reliable electrical response components were evoked. This was true for both retinal and cortical activity. In the subject population the perceptual thresholds were significantly higher (mean interstimulus interval: 82.5 ms) than the VEP thresholds (mean interstimulus interval: 49.7 ms). This difference was statistically significant ($t = 3.08$; $p < 0.01$). Even lower time thresholds were obtained with the ERG (mean interstimulus interval: 13.7 ms) which were significantly different from the subjective thresholds ($t = 16.80$; $p < 0.00001$).

In order to examine the possibility of backward masking in our data (i.e., an inhibitory effect of the second flash on the activity generated by the first flash), the response latencies and amplitudes elicited by the first flash were investigated over the complete range of all interstimulus intervals. There was neither consistent, statistically significant influences of the second flash on the activity elicited by the first flash for the ERG nor the VEP components. Response component latencies and amplitudes remained constant, independent of the interstimulus intervals of the double-flash stimuli.

DISCUSSION

In the present experiments we observed influences of short interstimulus intervals on the amplitudes and latencies of the ERG b-wave. At interstimulus intervals shorter than 40 ms the ERG responses elicited by the second flash of a stimulus pair were significantly smaller in amplitude, and showed longer latencies than the corresponding responses evoked by single flashes. A similar decrease of b-wave amplitudes at short interstimulus intervals was described by Mahneke (1957), Burian and Spivey (1959), and Sverak and Peregrin (1960) who also reported much lower time thresholds for photopic ERGs in a double-flash condition. In a similar line, Elenius (1969) showed in a completely color-blind patient that the double-flash ERG was dominated by cone activity, and Dodt and Wadensten (1954) and Elenius and Zewi (1958) demonstrated that the photopic flicker ERG was absent in colorblind patients.

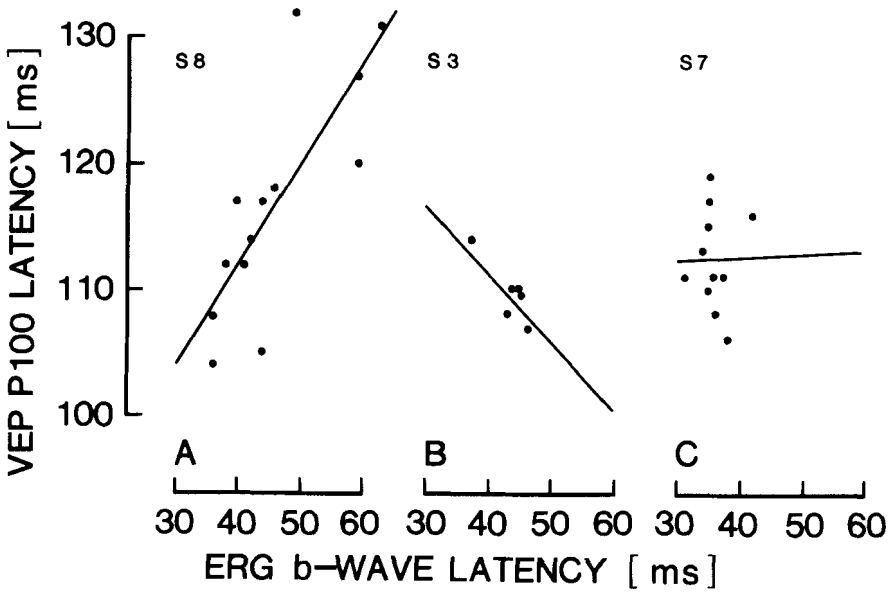

FIGURE 4 Linear regressions between the latency of the ERG b-waves and the P100 components of the VEP obtained from three different subjects illustrating intersubject variation. In the subject population, three subjects (25%) showed significant positive correlations (example in A), one subject (8%) showed a negative correlation (example in B), while eight subjects (67%) displayed no significant correlations between ERG and VEP component latencies (example in C).

The influence of short interstimulus intervals on the VEP activity displayed a similar tendency in our data: At interstimulus intervals below 40 ms only four of twelve subjects showed recordable evoked brain activity. This is in line with the results of Bergamasco (1966) and Riemslag *et al.* (1985) who found an absolute refractory period for the VEP when interstimulus intervals were shorter than 40 ms. Similarly, Musselwhite and Jeffreys (1983) reported that the stimulus onset asynchrony values of paired visual stimuli had to exceed 40 ms in order to obtain an electrical response to double stimuli. Earlier findings by Gastaut *et al.* (1951) suggested that, in both humans and cats, with visual stimuli there is an absolute refractory period of 20 ms, and relative refractory period of 40 ms. Our limit of 40 ms is in very good agreement with these earlier studies considering the fact that Riemslag *et al.* (1985) and Musselwhite and Jeffreys (1983) did not present light flashes but used a pattern onset paradigam.

In our data, component latencies evoked by the second flash at short interstimulus intervals were not significantly different from the single-flash evoked component latencies. This finding is surprising since Mitchell *et al.* (1983) demonstrated longer component latencies at short interstimulus intervals. Those results, however, were based on checkerboard reversal stimuli.

On the other hand, in the present experiments long interstimulus intervals were followed by significantly prolonged P100 latencies. This illustrates that retinal and cortical evoked activity were influenced in a different way by the interstimulus interval: ERG latencies were significantly prolonged at short interstimulus intervals while VEP latencies were affected significantly only at long interstimulus intervals. Only four of twelve subjects showed reliable VEP components with interstimulus intervals below 40 ms. At short interstimulus intervals VEP component latencies

showed a similar tendency as the ERG b-wave latencies. These VEP components, however, could not be obtained in all subjects, and due to the large intersubject variation this effect was not significant.

Support for different behavior of ERG and VEP activity also comes from the analysis of the retioncortical transmission time which displayed no significant covariation with the interstimulus interval. In addition, latencies of the VEP components could not be predicted from the ERG latencies. Most of the subjects (67%) displayed only nonsignificant correlation coefficients between ERG and VEP component latencies when linear regressions were computed. This also suggests that changes in VEP component latencies are not simply caused by changes in retinal activity at different interstimulus intervals, but additional influences of the interstimulus interval on nonretinal structures of the human visual system must be assumed.

Absolute refractory periods occurred for cortical electrical activity mainly at interstimulus intervals below 50 ms while retinal potentials could be recorded with interstimulus intervals down to about 10 ms, suggesting a much greater temporal sensitivity of retinal structures. Data from animal experiments support this finding: Levick and Zacks (1970) reported, for cat retinal ganglion cells, that double flashes elicited only single responses with interstimulus intervals below 30 ms while with interstimulus intervals between 32 and 40 ms two response components could be recorded. With light flashes of high intensity Dodt and Enroth (1954) obtained flicker fusion frequencies of cat retinal ganglion cells and ERGs in the order of 60 to 70 Hz which correspond to an interstimulus interval of about 15 ms. In addition, Eysel and Burandt (1984) showed that in subcortical structures of the cat visual system neuronal flicker responses can be recorded with frequencies above 100 Hz. Corticol neurons appear to have generally higher time thresholds as Galleti *et al.* (1979) illustrated: Simple phasic neurons in visual areas 17 and 18 of the cat were shown to have a response duration in the order of about 50 ms, independent of the duration of the light stimulus. All these single unit data directly support our finding that retinal structures have a better temporal resolution than cortical structures.

In the present experiments the perceptual threshold of the subject population (mean value: 82.5 ms) was of the same order as that obtained in an earlier study: Skrandies (1985) reported a mean double-flash discrimination threshold value of 92.88 ms in a population of 15 subjects. The electrophysiological time thresholds of both retinal and cortical activity were much lower than the corresponding subjective, perceptual thresholds. In a similar line, experiments using sinusoidally modulated light have shown that evoked responses could be recorded when the light was seen as fused by the subject (Van der Tweel & Verduyn Lunel, 1965). Related electrophysiological and psychophysical results were obtained with stereoscopic dynamic random-dot stimuli modulated at high temporal frequencies (Skrandies, 1987b).

REFERENCES

Bergamasco, B. (1966). Excitability cycle of the visual cortex in normal subjects during psychosensory rest and cardiazolic activation. *Brain Research*, **2**, 51–60.

Burian, H. M. & Spivey, B. E. (1959). The effect of twin flashes and of repetitive light stimuli on the human electroretinogram. *American Journal of Ophthalmology*, **48**, 274–286.

Diamond, A. L. (1977). Latency of the steady state visual evoked potential. *Electroencephalography and Clincial Neurophysiology*, **42**, 125–127.

Dodt. E. (1951). Cone electroretinography by flicker. *Nature*, **168**, 738.

Dodt. E. & Enroth, C. (1954). Retinal flicker response in cat. *Acta Physiologica Scandinavica*, **30**, 375–390.

Dodt. E. & Wadensten, L. (1954). The use of flicker electroretinography in the human eye. Observations on some normal and pathological retinae. *Acta Ophthalmologica*, **32**, 165–180.

Elenius, V. (1969). Cone and rod activity in the electroretinogram evoked by double flashes of light. *Archives of Ophthalmology*, **81,** 618–621.

Elenius, V. & Zewi, M. (1958). Flicker electroretinography in 6 cases of total colourblindness. *Acta Ophthalmologica*, **36,** 19–25.

Eysel, U. T. & Burandt, U. (1984). Flourescent tube light evokes flicker responses in visual neurones. *Vision Research*, **24,** 943–948.

Galletti, C., Squatrito, S., Maioli, M. G., & Riva Sanseverino, E. (1979). Single unit responses to visual stimui in cat cortical areas 17 and 18. *Archives Italienne of Biology*, **117,** 234–247.

Gastaut, H. Y., Roger, A., Corriot, J. & Naquet, R. (1951). Etude electrographique du cycle d'excitabilite cortical. *Electroencephalography and Clinical Neurophysiology*, **3,** 401–428.

Levick, W. R. & Zacks, J. L. (1970). Responses of cat retinal ganglion cells to brief flashes of light. *Journal of Physiology*, **206,** 677–700.

Mahneke, A. (1957). Electroretinography with double flashes. *Acta Ophthalmologica*, **35,** 131–141.

Mitchell, J. D., Hansen, S., McInnes, A., & Campbell, F. W. (1983). The recovery cycle of the pattern visual evoked potential in normal subjects and patients with multiple sclerosis. *Electroencephalography and Clinical Neurophysiology*, **56,** 309–315.

Musselwhite, M. J. & Jeffreys, D. A. (1983). Visual evoked potentials to double-pulse pattern presentation. *Vision Research*, **23,** 135–143.

Riemslag, F. C. C., Spekreijse, H. & Van Wessemn, Th. N. (1985). Responses to paired onset stimuli: implications for the delayed evoked potentials in multiple sclerosis. *Electroencephalography and Clinical Neurophysiology*, **62,** 155–166.

Schwartz, M. & Shagass, C. (1964). Recovery functions of human somatosensory and visual evoked potentials. *Annals of the New York Academy of Science*, **112,** 510–525.

Skrandies, W. (1985). Critical flicker fusion and double flash discrimination in different parts of the visual field. *International Journal of Neuroscience*, **25,** 225–231.

Skrandies, W. (1987a). The upper and lower visual field of man: electrophysiological and functional differences. *Progress in Sensory Physiology*, **8,** 1–93.

Skrandies, W. (1987b). Visual persistence of stereoscopic stimuli: electric brain activity without perceptual correlate. *Vision Research*, **27,** 2109–2118.

Sverak, J. & Peregrin, J. (1960). A contribution to the physiology of the electroretinographic double-flash test. *Ophthalmologica*, **140,** 267–280.

Van der Tweel, L. H. & Verduyn Lunel, H. F. E. (1965). Human visual responses to sinusoidally modulated light. *Electroencephalography and Clinical Neurophysiology*, **18,** 587–598.