Investigative Ophthalmology & Visual Science, Vol. 30, No. 9, September 1989

Retinocortical Time Exhibits Spatial Selectivity

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We recorded simultaneous electroretinograms and visual evoked potentials to pattern-reversal stimulus in ten normal subjects employing check sizes subtending 7.5, 15, 30, 60, 120, 240 and 480 min of visual arc. The mean peak latency of the pattern electroretinogram (PERG) b wave decreased logarithmically with increasing check size. The mean peak latency of the pattern visual evoked potential (PVEP) P100 component was shortest for 30 min check size and was longer at both smaller and larger check sizes, a phenomenon termed spatial selectivity. Retinocortical time (RCT) was calculated as the latency difference between the PVEP P100 peak and the PERG b wave. The RCT also exhibited spatial selectivity similar to that of the PVEP P100 component; mean RCT was shortest for 30 min check size and was longer at both smaller and larger check sizes. Implications are discussed in light of our current knowledge of the origins of the PERG and PVEP and visual processing of pattern-reversal stimuli. Simultaneous recording of PERGs and PVEPs in patients with disease of the afferent visual pathways employing a large range of check sizes may increase the diagnostic sensitivity of visual electrophysiologic testing. Invest Ophthalmol Vis Sci 30:2045–2049, 1989

Studies on the distribution of the major positive wave (P100) of the pattern-reversal visual evoked potential (PVEP) suggest it is generated by neurons in area 17, the primary visual cortex.[1–6] Several variables may affect P100 latency, including age,[7,8] sex,[3] pattern type,[9,10] reversal time,[3,11,12] luminance[3,13] and check size.[1] Lueders and his colleagues[1] noted that when check size was less than 15 min or greater than 2° of visual arc, P100 latency significantly increased. These authors suggested that at small check sizes, the prolonged latency was due to blurring of the retinal image. There is evidence, however, that the anterior visual pathways do exhibit spatial frequency dependence.[14]

The electrical activity of the retina in response to pattern-reversal stimulus identical to that which elicits the PVEP can be recorded from electrodes on or around the eye (the pattern electroretinogram). The pattern electroretinogram (PERG) is thought to arise from ganglion cells or be dependant upon the ganglion cell layer for its genesis.[15–17] In 1964, Vaughan and Katzman[18] demonstrated the use of simultaneous electroretinograms and visual evoked potentials to flash stimulus in patients with diseases of the afferent visual pathways; this methodology has been recently employed with pattern-reversal stimulus.[19–26] When simultaneous PERG and PVEPs are recorded, retinocortical time can be calculated as the latency difference between the PERG major positive wave (b wave) and the PVEP major positive wave (P100).[19,24,26] We recorded simultaneous PERGs and PVEPs in normal subjects to determine the effect of check size on b wave latency, P100 latency and retinocortical time.

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Presented in part at the American Electroencephalographic Society Annual Scientific Meeting, October 2–5, 1988, San Diego, California.

Submitted for publication: June 7, 1988; accepted March 13, 1989.

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Materials and Methods

We tested ten subjects whose age ranged from 24 to 46 years (mean 28.8, SD 6.43; seven men, three women). All had best-corrected visual acuity of 20/20 or better. None had ophthalmologic or neurologic dysfunction. Informed consent was obtained after the nature of the procedure had been explained fully.

PERGs and PVEPs were recorded simultaneously to stimulation of the left eye; the right eye was patched. The PERG was recorded from a gold foil electrode inserted into the lower fornix of the eye, foil touching the lower limbus, with a gold cup electrode placed 2.5 cm posterior to the left lateral canthus serving as reference. The PVEP was recorded from a gold cup electrode placed 3 cm above the inion, with a gold cup electrode placed 3 cm above the nasion serving as reference. A gold cup electrode placed at the vertex served as ground. Impedance of each of the electrodes was below 5000 Ohms.

All signals were recorded, amplified and averaged using a commercially available system (Nicolet Compact-Four, Nicolet, Madison, WI). For the PERG, the

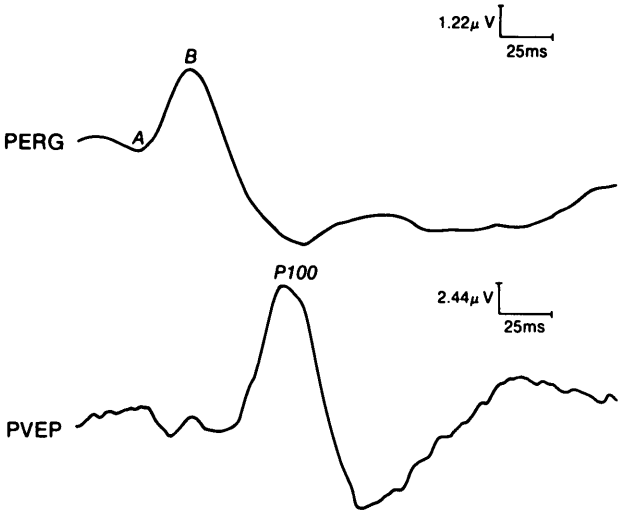

Fig. 1. Simultaneously recorded pattern electroretinogram and visual evoked potential with waveform components labelled. Relative positivity at the first input results in an upward deflection.

preamplifier was set for a sensitivity of 100 μV/full scale with band-pass filters (−3 dB) at 1 and 30 Hz. An artifact rejection system was employed which rejected potentials greater than ±47.5 μV due to eye blinks and extraocular movement. For the PVEP, the preamplifier was set for a sensitivity of 100 μV/full scale with band-pass filters (−3 dB) at 1 and 100 Hz. Sweep time was 250 msec and sample rate was 4098 points/sec. One hundred sweeps were averaged for each check size and plotted on an X-Y plotter.

For stimulus presentation, we employed a black and white checkerboard generated by a Nicolet Biomedical Visual Stimulator (NIC 1015), projected upon a cathode ray tube. Checks reversed 2.1 times per sec. Subjects were seated 70 cm from the screen and instructed to fixate upon a target in the center of the cathode ray tube. All subjects could accommodate to 70 cm. Responses were measured employing checks subtending 7.5, 15, 30, 60, 120, 240 and 480 min of visual arc. The order of stimulus presentation was randomized with respect to check size. The cathode ray tube measured 16° by 20° of visual arc. Contrast between black and white checks was 76% and mean luminance 115.6 candela/m^2. Average background luminance was 8.3 candela/m^2.

For the PERG, latency of the b wave was measured from onset of stimuli to the peak of the major positive component. For the PVEP, P100 latency was measured from onset of stimuli to the peak of the major positive component. Retinocortical time was calculated as the latency difference between the PERG b wave and the PVEP P100 component (see Fig. 1).

Statistical modeling was performed based on preliminary analysis of the data. The validity of the use of repeated measures analysis of variance on the variation of each variable within patients (by check size) was tested using the Huynh-Feldt procedure.[27-29] The repeated measures analysis of variance approach was found to be inappropriate ($P < 0.0001$); hence, the multivariate regression approach was used.[28,29] Tests of significance for polynomial fits of various degrees were performed using orthogonal polynomials.

Calculations were performed using the SPSS[30] and BMDP[31] statistical packages.

Results

Mean PERG b wave latency decreased logarithmically with increasing check size (see Table 1 and Fig. 2). Mean PVEP P100 latency was shortest with 30° checks and increased progressively with both smaller and larger checks (see Table 1 and Fig. 2). Mean RCT was also shortest with 30 degree checks and increased progressively with both smaller and larger checks (see Table 1 and Fig. 2).

Table 2 shows the results of statistical modeling of b wave latency, P100 latency, and RCT versus check size. Multivariate regression analysis confirmed the apparent linearity of b wave latency versus log check size. For both P100 latency and RCT, the quadratic and cubic coefficients were highly significant ($P < 0.001$, Table 2).

Discussion

An inverse relationship between check size and PERG b wave latency has previously been reported.[32]

Table 1. PERG b wave latency, PVEP P100 latency, and RCT, by check size

Check size	*PERG b wave latency (msec)**	*PVEP P100 latency (msec)**	*Retinocortical time (msec)**
7.5 min	57.55 ± 2.60 (52.5–62.5)	111.90 ± 3.37 (107.5–119.5)	54.40 ± 4.93 (48.0–63.5)
15 min	56.00 ± 1.99 (53.0–58.0)	100.30 ± 4.95 (91.5–107.5)	44.30 ± 5.36 (34.5–54.5)
30 min	54.30 ± 2.50 (51.5–59.0)	95.95 ± 4.98 (85.0–103.0)	41.65 ± 6.16 (27.5–50.0)
1°	52.20 ± 2.03 (49.0–55.5)	99.60 ± 3.73 (95.0–106.5)	47.4 ± 3.99 (42.0–54.0)
2°	50.75 ± 1.88 (48.0–53.0)	105.00 ± 5.01 (96.0–110.5)	54.25 ± 4.70 (46.5–59.5)
4°	49.60 ± 1.27 (47.0–51.0)	109.75 ± 6.93 (99.0–118.0)	60.10 ± 7.42 (48.5–69.0)
8°	48.90 ± 1.24 (47.5–51.5)	110.65 ± 6.50 (98.5–117.0)	61.70 ± 6.17 (51.0–68.5)

* Mean ± 1 SD (minimum–maximum).

Investigators have suggested that the PERG is composed of two responses, a local luminance response and a pattern-specific response.[33-35] The local luminance response is maximal when large areas of the retina are stimulated (ie, large check size); in the extreme case of one large white check, the local luminance response is identical to the classical flash electroretinogram (FERG). While the FERG b wave is thought to be generated in Müller cells,[36] the PERG is thought to be generated in the proximal retina[37] and to be at least partially dependant upon the ganglion cell layer for its genesis. Evidence for this is derived from work in vertebrate models which suggests that the PERG parallels the functional integrity of ganglion cell axons. Following surgical section of the optic nerve in cats[15] and monkeys,[16] the amplitude of the PERG reduces to zero over the period of time thought to coincide with Wällerian degeneration of ganglion cells; the FERG, however, remains unchanged. One would expect that a potential generated in the Müller cells would have an earlier latency than a potential generated in the more proximal ganglion cells; in fact, the b wave latency of the FERG is shorter than that of the PERG. In our study, the mean b wave latency employing the smallest checks (7.5 min) was 58.4 msec. As check size increased, b wave latency decreased logarithmically, and approached the mean FERG b wave latency derived from a large number of subjects studied in our laboratory (unpublished data) of 44 msec; to the best of our knowledge, the logarithmic nature of this curve has not been discussed.

We propose, then, that the decrease in PERG b wave latency with increasing check size may be due to changes in the relative proportions of its two components: an increase in the local luminance component (which is probably generated in Müller cells and has a shorter latency) and a decrease in the pattern-specific component (which is probably generated in ganglion cells and has a longer latency). This would imply that the PERG b wave latency can never become shorter than the FERG b wave latency. Our interpretation is supported by the observations of Harrison et al,[17] who recorded PERGs in a 19-year-old man 30 months after surgical transection of the optic nerve. They noted a significantly reduced PERG amplitude in the affected eye. They also noted the b wave latency in the affected eye to be 6 msec earlier than that of the contralateral eye employing 50 min check size, and 12 msec earlier than that of the contralateral eye employing 12 min check size. This suggests that the pattern-specific response, preserved only in the normal eye, contributed to the increased latency with smaller checks on that side.

P100 latency exhibited spatial selectivity, in con-

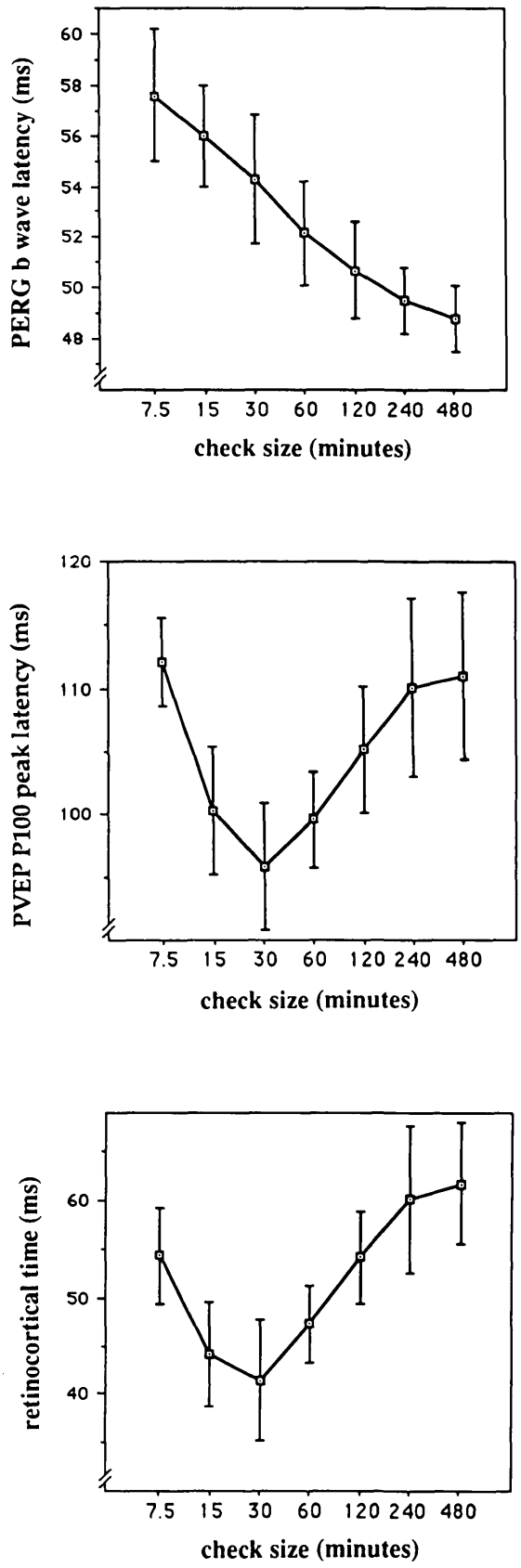

Fig. 2. The effect of check size on mean PERG b wave latency (top), mean PVEP P100 latency (middle), and mean RCT (bottom) in ten subjects. Error bars denote ± one standard deviation.

Table 2. Statistical modeling of latency versus log check size: significance levels (*P*-values) of polynomial coefficients by degree and latency

	Latency		
Degree	*b*	*P100*	*RCT*
Mean	<0.001	<0.001	<0.001
Linear	<0.001	0.11	0.0012
Quadratic	0.26	<0.001	<0.001
Cubic	0.43	<0.001	<0.001
4th–6th power	0.66–0.88	0.54–0.97	0.46–0.96

trast to the logarithmic nature of the PERG b wave latency vs. check size curve. The PERG is a relatively more homogeneous response than the PVEP, with equal contributions from foveal, perifoveal, and midperipheral regions.[38,39] The PVEP is strongly biased toward the foveal region.[7,40] It has been shown that retinal ganglion cell receptive field center size is smallest near the fovea, but increases as one moves toward the periphery.[41] The differential effect of check size on PERG and PVEP latency may be due to differences in the contributions of different cell populations.

While RCT is a comparison between the PERG b wave and PVEP P100 latency and not a true measurement, studies by Kaufman and Celesia,[19] Celesia and Kaufman[24] and Celesia et al[26] indicate that calculation of RCT may provide a model for distinguishing between macular disease and optic nerve demyelination. Patients with demyelinating disease have a normal PERG b wave latency, a prolonged PVEP P100 latency and a prolonged RCT; patients with macular disease have a delayed PERG b wave and a delayed PVEP P100, yet a normal RCT.[19,24,26] Such observations suggest that the RCT may reflect a conduction time between retina and cortex. Our observations on the relationship between check size and PERG b wave latency suggest that the validity of this model is dependent on stimulus parameters, since the contribution of ganglion cell response to the PERG may increase as check size decreases. If this model is correct, then spatial selectivity of the P100 latency might be due to some processing which occurs after the PERG b wave. From animal experiments, we know that retinal ganglion cells with different receptive field sizes have different conduction velocities.[42] Certain check sizes might evoke responses from a larger proportion of one type of ganglion cell than another; the RCT at one check size may therefore reflect the conduction velocity of a particular group of retinal ganglion cells. If this were the case, then RCT might be shortest at 30 min checks because the retinal ganglion cells that account for the majority of the response to 30 min checks may have the fastest conduction velocity. In such a model, the parallel nature of synaptic connections in the lateral geniculate[43] would preserve spatial selectivity of the RCT. The existence of bifid and trifid PVEP P100 peaks occasionally recorded may in fact be evidence of two or more parallel conduction pathways with different conduction velocities.

We conclude that, under our experimental conditions, PVEP P100 latency and calculated RCT exhibit spatial selectivity. There is disagreement as to which check size is most sensitive to afferent visual pathway dysfunction.[44] It may be that dysfunction of a specific type of retinal ganglion cell would affect RCT at one check size but not another. By recording simultaneous PERGs and PVEPs in patients with disease of the afferent visual pathways employing a large range of check sizes, we may be able to increase the diagnostic sensitivity of visual electrophysiologic testing.

Key words: electroretinogram, visual evoked potential, pattern-reversal stimulus, retinocortical time, spatial selectivity

Acknowledgments

The authors gratefully acknowledge George Wittenberg for thoughtful discussions of the data, Sylvia K. Klauber for assistance in the computer analysis, and Ray Whitney and Ellen Taylor for their technical assistance.

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