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Objective measurement of contrast sensitivity and visual acuity with the steady-state visual evoked potential

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Abstract Since the appearance of Campbell and Maffei's and Harter and White's reports it has been well established that the visual evoked potential (VEP) can be used to predict psychophysical contrast sensitivity and visual acuity and is thus suited as an objective technique to assess these fundamental aspects of vision. Nevertheless, the technique has not become a standard diagnostic tool, being too time-consuming to apply and suffering from variable reliability under pathological visual conditions. In addition, there are problems of reliability in normal subjects. By using an unconventional stimulus – temporally sinusoidal 16-Hz on-off modulation of sine-wave gratings – we demonstrated that these problems can be alleviated in normal subjects. This stimulus avoids the low signals in the visible range that frequently occur with conventional pattern-reversal stimuli, it leads to high correspondence between normal observers, and it is much faster to apply than are transient VEPs. Initial applications of this stimulus to amblyopes yielded promising results. The steady-state VEP could consequently turn into a viable diagnostic procedure in disturbances of visual contrast perception.

Key words VEP · On-off modulation · Transient sustained theory · Contrast sensitivity · Visual acuity

Zusammenfassung Seit den Berichten von Campbell und Maffei (1970) und Harter u. White (1968) ist es gut gesichert, daß das visuell evozierte Potential (VEP) zur Bestimmung der visuellen Kontrastempfindlichkeit und Sehschärfe eingesetzt werden kann und damit die Basis eines objektiven Verfahrens zur Erfassung dieser grundlegenden diagnostischen Maße darstellt. Das Verfahren wurde aber bis heute kein klinisches Routineverfahren; Hinderungsgründe sind mangelnde Zuverlässigkeit unter pathologischen Bedingungen und zu hoher Zeitaufwand. Darüber hinaus bestehen gewichtige Zuverlässigkeitsprobleme bereits bei Normalsichtigen. Wir haben eine unkonventionelle Reizmodulationsform benutzt – sinusförmige Ein/Aus-Modulation mit 16 Hz bei Sinusgittern – und zeigen, daß mit ihr diese Probleme beim Normalsichtigen verringert werden können: Niedrige Signalamplituden im Bereich bester Sichtbarkeit, wie sie bei der konventionellen Musterumkehr auftreten, werden vermieden; die interindividuelle Variabilität ist verringert, und im Vergleich zum transienten VEP ist die Meßdauer gering. Erste Anwendungen der Reizform bei amblyopen Patienten erbrachten ermutigende Ergebnisse. Das stationäre VEP könnte damit zu einem nützlichen Diagnostikum bei Störungen der Kontrastverarbeitung werden.

Schlüsselwörter VEP · Ein/Aus-Modulation · Tonisch/phasisch · Kontrastempfindlichkeit · Sehschärfe

Introduction

Contrast sensitivity and visual acuity are among the basic diagnostics for visual function. Like all psychophysical measures, their assessment depends on the subject's conscious perception; and although such "subjective" tests are fast, valid, reliable, and objective (objective since their result is independent of the test conductor), there are situations where one would want to circumvent the subject's consciousness. One example is the testing of preverbal infants; another is the diagnosis of malingerers; and a third is the use in pediatric ophthalmology, where, for a variety of reasons, responses of any kind are difficult to obtain. For these purposes the so-called "objective" tests have been developed, and the visual evoked potential (VEP) has found application in that it can provide such estimates of both contrast sensitivity ([3]; reviews in [26, 42]) and visual acuity [7, 8, 12, 24–27, 30, 35, 40, 46].

Campbell and Maffei [3] have introduced the "regression technique" for determining contrast thresholds: when VEPs are recorded for a series of stimulus contrasts and VEP amplitude is extrapolated to zero, the corresponding threshold contrast closely matches the subjective threshold. Such a procedure is usually performed with grating patterns of various spatial frequencies such that a full contrast-sensitivity function is obtained. A similar extrapolation along the spatial frequency axis had earlier been used to obtain an estimate of grating acuity [8]; yet earlier, a similar result had been reported for the acoustic system by Keidel and Spreng [14].

More than 20 years later, not all problems that prevent a widespread practical application have been solved. Techniques have improved, noticeably through the introduction of automated sweep techniques [25, 28, 33, 34, 42, 48], the refinement of data-analysis techniques [23, 26, 29, 31, 33, 37, 41, 49, 50], especially those concerning phase reliability, and the careful examination of the influence of stimulus characteristics. VEP equipment is readily available and the measurements in question can be performed on any standard system. However, although the VEP prediction accuracy of psychophysical thresholds is generally satisfactory in normal subjects, there are alarming reports about results obtained under pathological conditions that severely limit the practical applicability. A recent extensive study by Ohn et al. [27], for example, that comprised patients suffering from optic nerve disease, macular disease, functional amblyopia, and cataracts, found mispredictions in acuity exceeding ±2 octaves in every third eye. Both over- and underestimation occurred. Especially sobering were the results in the optic-nerve-disease group, where 30% of the cases had mispredictions exceeding ±3 octaves.

Such reports are in sharp contrast to frequent reports of high prediction accuracy in normal subjects. However, in previous reports we have warned [44] that also in normal subjects there are dramatic deviations from the prototypical inverted-U shape of the VEP amplitude/spatial-frequency function that underlies the common regression procedures [10, 43–45, 47]. In the large majority of subjects there is a certain range of spatial frequencies where, despite good stimulus visibility, a poor evoked response is obtained. These peculiarities are prominent for the ubiquitous 8-Hz pattern-reversal sine-wave grating stimuli, but neither transient modulation nor use of checkerboard patterns will cure the situation [44]. Worse, for transient and slow-repetition steady-state modulation the difficulties are obscured since, due to the lower recording speed, fewer spatial frequencies or check sizes are tested and critical regions are overlooked. These signal peculiarities do not in principle invalidate the regression technique [44, 45]. They do, however, significantly affect the reliability of predictions and, thus, limit their usefulness.

Although the basic regression approach of predicting thresholds from suprathreshold responses is sound, difficulties may arise from choices that are made in the attempt to obtain reliable VEP responses. One example is the use of checkerboard stimuli, which generate large signals but have variable predictive value. Another example is the extrapolation far from the threshold. Such strategies improve intrasubject VEP signal reliability but reduce its *prediction validity*. As Ohn et al. [27] note, a majority of their mispredictions occur with low signal-to-noise ratios and the absence of spatial tuning in the amplitude/check-size plot. Whereas the inappropriateness of checkerboards for assessing the contrast-sensitivity function (CSF) is obvious, their usefulness for acuity measurement is also doubtful (see Steele et al. [40]).

Reliance on an acuity estimate without taking into account the spatial tuning of VEP amplitudes – often motivated by the fissured appearance of the latter function in normals when checkerboards and pattern reversal are used – is a problem in itself. Frisén and Frisén [6] have shown that in macular edema "so called normal visual acuity requires no more than 44% of the normal quantity of foveolar neuro-retinal channels." This speaks for having available an interpretable tuning function.

Signal reliability needs to be improved without compromising prediction validity. The techniques for doing so are available and are mentioned above: sweep techniques, phase criteria, reliability estimates, and exploitation of close-to-threshold data, among others. In the present report we advocate avoiding pattern-reversal stimulation and replacing it with on-off (appearance/disappearance) modulated patterns. Such stimuli improve the basic intersubject reliability and lend themselves to application of the above-mentioned techniques. This report is based on data that have largely been presented previously [45] and that are discussed herein with the applicability to clinical conditions in mind.

Previously [45] we have shown that a likely cause of reduced amplitude in pattern-reversal stimulation is a superposition of the electrical activity of visual mechanisms that differ in their spatiotemporal characteristics.

Such characteristics have been described as being transient and sustained [16] and we have found the sources of VEP activity, as isolated by principal component analysis, to have characteristics that are well described by this dichotomy. A neurophysiological basis for mechanisms functionally described as transient/sustained might lie in pathways originating from different kinds of retinal ganglion cells, namely, those belonging to the parvocellular and magnocellular system, respectively (see Kaplan et al. [11] for a review of the neurophysiology and Kulikowski et al. [17] for a conference proceedings devoted to this question), but this remains under debate. Of practical importance was our finding that VEPs evoked by fast-rate on-off modulated gratings show characteristics that resemble sustained activity, i.e., are sensitive to high spatial frequencies, and have reduced intersubject amplitude variability, minimized interactions between detecting mechanisms, and high phase constancy. They thus lend themselves to application of the regression technique.

Materials and methods

We used our computer-based, automated sampled-sweep technique [42] to obtain steady-state VEPs to different kinds of temporal modulation and compared them with psychophysical thresholds obtained on the same setup. The computer (an LSI-11/73) generates temporally modulated sine-wave gratings on a CRT monitor, acquires one channel of electroencephalogram (EEG) data, and processes the data off-line. Details of the setup [42] and the methods of analysis [41] have been described in separate reports.

Stimuli

Vertical sine-wave gratings of various contrasts and spatial frequencies, sinusoidally modulated in time, were presented on an analog x-y-z CRT display having a mean luminance of 17 cd/m^2 (512 horizontal resolution, continuous y-deflection, continuous gray scale). The frame rate was 64 Hz and was locked to signal sampling.

Each sweep set consisted of 18 gratings of equal contrast but graded spatial frequency ranging from 0.5 to 25 cpd. In each sweep the set members were presented, one after the other, for 3 s each with a 1-s pause in between, repeatedly in ascending and descending order such that each stimulus was shown six or eight times. Of the 3-s period over which each stimulus was presented, only for the trailing 2 s was an EEG recorded to let the VEP reach a new steady state each time (cf. Seiple and Holopigian [37] for a comparison with continuous sweeps). The net recording time for each spatial frequency was thus 12–16 s, and a complete sweep took about 7–9 min. Most recordings were run at 40% Michelson contrast. Subjects viewed the screen binocularly at a distance of 128 cm. A white cardboard screen limited the test field to 5° of visual angle.

The results obtained using two kinds of temporal modulation are presented herein: sinusoidal pattern reversal at 8 Hz, i.e., 16 reversals per second (rev/s); and sinusoidal on-off (appearance/disappearance) modulation at 16 Hz. In the latter (less conventional) case the modulating function is given by

$$C(t) = 1/2\ C_m \times (1+\sin \omega_t t),$$

where contrast $C=(L_{max}-L_{min})/(L_{max}+L_{min})$ according to the Michelson definition and C_m represents the maximal contrast. Note that space average luminance is constant in time for both kinds of stimulation; the temporal contrast mean is zero for pattern reversal and is equal to $C_m/2$ in the on-off case, i.e., the on-off stimulus contains a static component of half the maximal contrast.

Data recording and analysis

One channel of raw EEG was recorded with the active electrode located 2 cm above the inion and the reference electrode on the forehead at two-thirds of the distance from the inion to the nasion. Electrode impedance was kept below 2 kOhm. The EEG was bandpassfiltered between 1 and 25 Hz with a 12-dB/oct filter slope and was sampled at 64 Hz and stored. Raw traces recorded at a low sampling rate are not informative and are not shown herein. The off-line analysis happens in three steps: averaging with a period length of $1/\omega_t$, Fourier analysis, and vector averaging over stimuli having equal parameters. This is equivalent to a Fourier analysis of the raw data [41]. As a result, 96–128 periods contribute to 1 amplitude/phase data pair. Frequency components of up to 16 Hz were considered. The component most closely related to stimulus properties is that at the reversal rate for pattern-reversal stimulation and at the modulation rate for on-off stimulation, i.e., 16 Hz in both cases; only these components are shown herein. The reliability of amplitude and phase were assessed by methods developed from those detailed by Strasburger [41]. Noise was estimated by recording while the subject fixated on the wall. Amplitudes for this condition were around 0.4 µV and phases were random. Note that true noise, i.e., signal energy that is uncorrelated to the stimulus, is lower than this estimate ([42], Appendix). This value is therefore unsuitable for calculating a signal-to-noise ratio.

Results

Psychophysics

Figure 1 shows psychophysical contrast-sensitivity functions for three conditions: static gratings and the two dynamic conditions used for VEP recording, all obtained on the same setup used for the VEP. Five of the subjects who

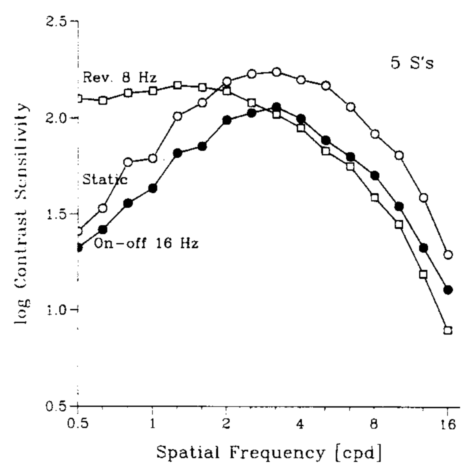
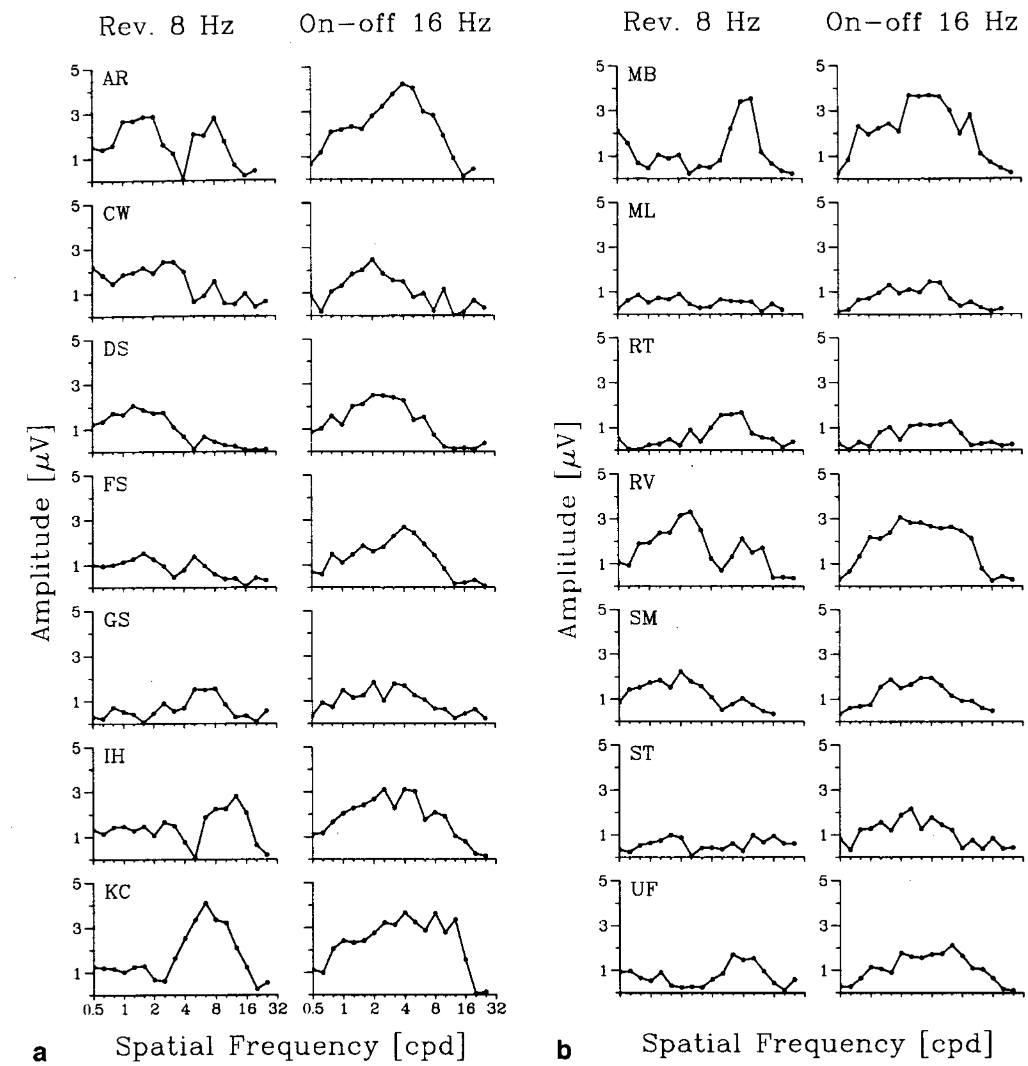


Fig. 1 Mean contrast sensitivity of 5 subjects for 3 conditions of temporal modulation: pattern reversal at 8 Hz, i.e., 16 rev/s (*open squares*), sinusoidal on-off modulation at 16 Hz (*filled circles*), and static gratings (*open circles*). Data from Strasburger et al. [45]

Fig. 2 VEP amplitude as a function of grating spatial frequency, for 14 subjects. *Left column:* Pattern reversal at 8 Hz (16 rev/s); *right column*: on-off modulation at 16 Hz. The maximal pattern contrast, C_m, was 40%. Data from Strasburger et al. [45]



participated in the VEP studies took part here; the method of adjustment with a simple criterion of "something visible" was used.

As other authors have reported, there is a relative improvement in sensitivity at low spatial frequencies for pattern-reversal modulation as compared with static presentation [13, 16]. This is usually interpreted as reflecting transient activity at low spatial frequencies [16, 18]. On-off stimulation at the given high rate of modulation, however, does not show such transient components; rather, the function resembles that of static gratings. Note that the vertical offset between the latter two functions largely stems from the different contrast scales used: the mean contrast ($C_m/2$) of on-off modulated gratings is half that of static gratings; the different scales are retained to distinguish better the functions in the graph. Note that grating acuity, by regression, is around 30 cpd for both static and on-off modulated gratings, whereas pattern reversal leads to somewhat lower acuity.

Visual evoked potentials

VEP amplitude responses as a function of spatial frequency for the two conditions of modulation are shown side by side in Fig. 2 for different subjects. The left column shows pattern reversal and the right column, on-off modulation. The peak pattern contrast, C_m, was constant at 40%. Only 14 subjects are represented for clarity (of 23 paid volunteers of both sexes aged between 19 and 39 years with normal or corrected-to-normal vision).

Pattern-reversal functions show large variability between subjects, as has repeatedly been reported before. Often, amplitudes are surprisingly low at intermediate spatial frequencies and in these functions this might look like a "notch" in an otherwise inverse U-shaped function. No such notch is found in the right column for on-off modulation and, apart from differences in the overall amplitude, the curves for different subjects look remarkably similar. For about 10% of all subjects we obtained very low ampli-

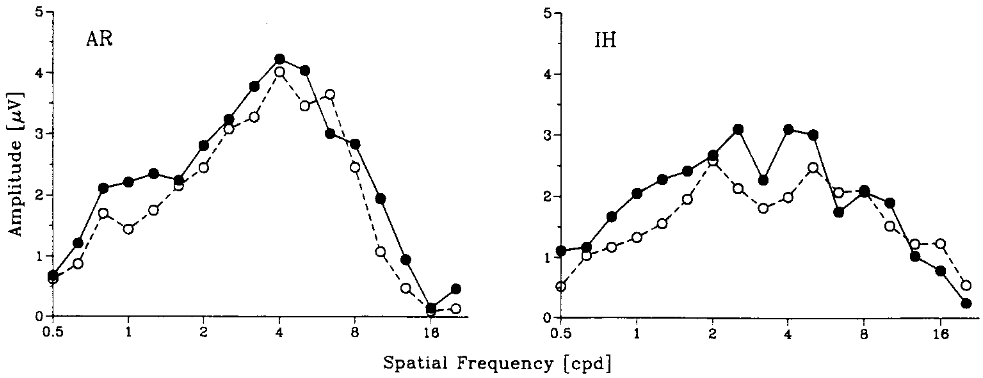


Fig. 3 Retesting of the amplitude/spatial-frequency curve (*closed symbols*) after 3 weeks (*open symbols*) for 2 subjects

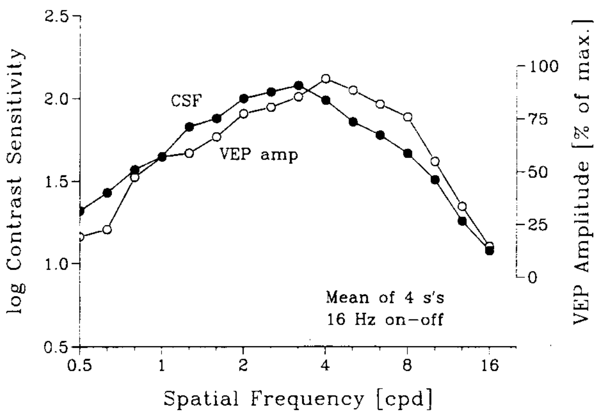


Fig. 4 Comparison of the shape of the VEP amplitude curve at 40% contrast (*VEP amp*) with that of the psychophysical contrast-sensitivity function (*CSF*). On-off modulation at 16 Hz; mean of 4 subjects. The *ordinate scales* were chosen for a least-squares fit. Data from Strasburger et al. [45]

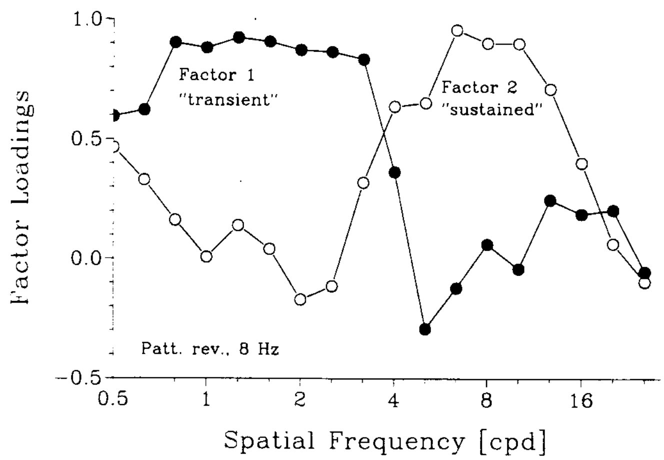


Fig. 5 Factor loadings of the two main factors in a principal component analysis of pattern-reversal (*Patt. rev.*) amplitude data. These two factors account for 62% of the variance between subjects. They can be thought of as representing underlying generators of electric brain activity. Data from Strasburger et al. [45]

tudes (data not shown). In all these cases, however, when we increased the contrast to 80% we again got results similar to those shown. Within subjects the results are highly reliable, as is shown by retesting after several weeks (Fig. 3).

The overall shape of the on-off amplitude versus spatial-frequency response is similar to that of a contrast-sensitivity function. This is illustrated in Fig. 4, which shows the mean amplitude for all subjects together with a contrast-sensitivity function that has been rescaled for an optimal fit. Note the corresponding scales on the left and right sides. The transformation that led to this fit is given by

$$S = 0.0128A + 0.92,$$

where S is the predicted sensitivity in log percent and A is the normalized VEP amplitude in percent.

As an answer to the question as to where the variability in the pattern-reversal data stems from, we run a principal component analysis on the data [45]. Without going into detail, it can be said that the VEP can be construed as stemming from two sources, or factors, which are shown in Fig. 5. These factors can be thought of as representing underlying generators of activity, one peaking at low spatial frequencies (transient) and the other peaking at higher ones (sustained; for terminology cf. Kulikowski [15]; for a spatiotemporal model cf. Anderson and Burr [2]). Each subject has its own mix of contributions from these sources, leading to the observed VEP variability.

Discussion

Implications for clinical application

Reliability and speed

The most important aspect from the standpoint of clinical applicability is probably the increased amplitude reliability. As VEP amplitudes have generally quite good *retest* reliability [44], the present results in this respect (Fig. 3) are not too surprising. However, litte use can normally be made of this in the diagnosis of visual abnormalities due to the high *intersubject* variability. The on-off VEP recorded at high rates seems to us a major step toward the goal of reliability. We have interpreted the "cleaner" appearance of on-off VEPs as being a result of decreased contributions of transient mechanisms when the modulation rate is beyond the maximal response of these [45], but regardless of how the data are interpreted there is little doubt that on-off modulation reflects stimulus visibility more accurately than does pattern reversal.

Another point of importance for clinical application is the speed of acquisition. Herein lies an advantage of steady-state over transient VEPs: the same reliability can be obtained in much less time [41]. With optimized equipment, only a few minutes are required for meaningful results.

Note that the favorable results for on-off modulation do not obtain for on-off modulation in general but seem to be linked to the high rate. In the present study we systematically tested at only one other temporal frequency for on-off modulation, 8 Hz, and found the results to be inferior for practical purposes in all cases. At this frequency the alpha rhythm might add to the variability (cf. Spekreijse et al. [39]). At a yet lower modulation rate and sinusoidal modulation it was difficult to evoke reliable potentials at all. Studies currently under way (Parry and Hadjizenonos, personal communications) seem to imply that the useful range might be 14–25 Hz or more, but it is too early to be specific in this respect. Another open question is whether the sinusoidal shape of modulation at high rates is crucial or whether the more readily available square-wave modulation might be sufficient.

When the on-off stimulus is used, speed can be significantly further improved by using phase-sensitive recording, since phase, for this stimulus, shows little variation with both contrast and spatial frequency [45]. Phase-locking techniques have been well developed by Nelson et al. [23]; their applicability is usually hindered by the observation that phase is much more variable than Nelson et al. assume (e.g., Strasburger et al. [44]). This limitation does not apply to the 16-Hz on-off stimulus, and phase locking can thus be favorably applied (cf. Seiple and Holopigian [37]).

Contrast sensitivity

To measure a full-contrast sensitivity function by the regression method, one would in any practical application proceed differently, using, for example, contrast sweeps and not spatial-frequency sweeps and adopting further automation. The point we wish to make is the advantage of using on-off modulation as compared with contrast reversal in any such technique. Basically, the regression technique works well, as others have reported, provided the signal-to-noise ratio is sufficient. However, in pattern reversal at a temporal frequency that is routinely used there are small or large regions of spatial frequency in which amplitudes and signal-to-noise ratios are rather poor – and unexpectedly so (Fig. 2). These cases of low response amplitude at conditions of good target visibility occur at all spatial frequencies and thus cannot easily be avoided. With coarse sampling, these cases are often either overlooked or misinterpreted. Increasing the contrast can worsen the signal, and the signal-to-noise ratio can be optimal close to the contrast threshold [44]. With checkerboard patterns instead of sine waves the notches seem to occur equally often [44], yet with 16-Hz on-off modulation these paradoxical signals rarely occur, if ever. Thus, a contrast regression can be performed at all spatial frequencies, including those that lie in a notch for pattern reversal. Furthermore, the better intersubject amplitude reliability reduces the sources of ambiguity, leading to more confidence in the results.

The data shown in Fig. 6 were not obtained with optimal precision of contrast sensitivity prediction in mind, and more sophisticated methods for this purpose are available (see below). Nonetheless, they show the improvement relative to pattern reversal. Basically, the regression technique works well with pattern reversal, as others have reported. At low spatial frequencies there are, however, deviations between the VEP estimate and the psychophysical measure (left panel): psychophysically there is a relative sensitivity enhancement that is not followed by the VEP estimate. In the on-off case, psychophysical and VEP regression functions are of more similar shape (right panel). Since the psychophysical 16-Hz on-off sensitivity function (see Fig. 1) is rather similar to that for static gratings – which is usually of interest – the corresponding VEP regression is the better predictor. For both kinds of modulation there is, with the present extrapolation, a considerable offset between the psychophysical findings and the VEP results. For on-off modulation the offset is constant at 0.66 log units (factor of 4.5) and will not affect the prediction accuracy, provided it remains unchanged under changed conditions. It is, however, desirable to eliminate this difference. Partly it can be attributed to the definition of on-off contrast (factor of 2), as mentioned above, by assuming that not maximal but rather mean contrast, or the deviation from mean contrast, is the appropriate basis of comparison. The remaining offset (0.35 log units) might be removed by more sophisticated extrapolation (see below).

There is the chance that the regression technique could be circumvented and amplitude data could directly be used as a sensitivity predictor. For this to be feasible, one would need to show that the coefficients contained in the above-mentioned amplitude transformation equation hold for a larger sample and also for abnormal vision. This does not seem very likely. Furthermore, one would reduce the reliability, and in an automated procedure the additional gain in speed would not seem worthwhile.

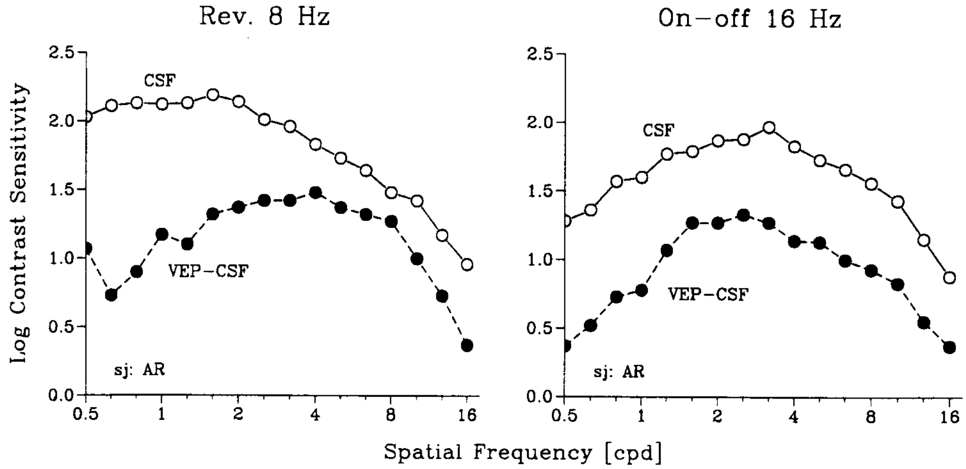


Fig. 6 Contrast-sensitivity function (*CSF*) as obtained through the VEP regression technique (*filled symbols*) and psychophysically (*open symbols*). *Left:* Pattern reversal (*Rev.*); *right*: on-off modulation. For the offset between the curves see Discussion. Data from Strasburger et al. [45]

Acuity

Grating acuity corresponds – by definition – to the rightmost point on the contrast-sensitivity function. Thus, testing time can be reduced when only the right portion of the amplitude/spatial-frequency function is recorded. This is not possible with the pattern-reversal VEP, however, since it is never clear whether a given response is dervied from factor 1 or factor 2 (Figs. 1, 5), i.e., whether an acuity estimate by spatial-frequency regression erroneously reflects a midpoint instead of the high-spatial-frequency end of visibility. Moreover, even when the full range of spatial frequencies is tested, the response in the higher-spatial-frequency lobe (corresponding to factor 2, open symbols in Fig. 5) can be weak or missing altogether, as in the case of subject DS in Fig. 2 a, such that the cutoff point of the *low*-spatial-frequency lobe is erroneously taken as the acuity estimate. These problems do not arise with 16-Hz on-off modulation leading to more consistent results.

Figure 7 shows a demonstration for a typical myopic subject. The subject's acuity has been manipulated by using plus and minus lenses of various powers. Each time, an amplitude response is obtained. One can see how the cutoff point shifts with varying corrections, the optimum being at –1.25 D. The second part of this figure correlates the cutoff point to the (psychophysically obtained) Landolt acuity (according to DIN norms [4]). The plotted regression line, forced through the origin, is given by

$$a = 0.0578 \times \omega,$$

where a is the acuity in degrees^{-1} and ω is the spatial frequency in cpd. It explains 98% of the variance. With suitable equipment, acuity can be assessed within 30 s once electrodes have been applied.

Note that these results were obtained with a circular stimulus field on only 5° diameter. Clinical studies often use larger fields; e.g., Ohn et al. use $10° \times 10°$ [27], Steele et al. use $8° \times 11°$ [40], and Petersen et al. use $7° \times 10°$ [30]. The contribution of peripheral vision to the VEP [9], which particularly distorts results in macular disease [27, 30], is thus reduced.

Under- or overestimation of thresholds?

Correlative relationships such as that shown in Fig. 7 are sufficient for accurate predictions as long as the statistically obtained parameters are stable under varying conditions. Experience has shown, however, that parameters change, particularly under pathological viewing conditions, and it is worthwhile to ask further. Since both acuity measures are on the same physical scale, 1/(gap width), in degrees^{-1}, they can be directly compared with each other, and the expected relationship is a straight line, through the origin, of slope "1". When the abscissa is expressed as spatial frequency, as in the graph, this expected relationship is

$$a = 1/30 \times \omega,$$

(a is the acuity in degrees^{-1} and ω is the spatial frequency in cpd), since a square-wave grating of 30 cpd has a gap of 1′ and at the spatial threshold only the fundamental of such a grating is perceived. Note that our psychophysical results (Fig. 1) are in agreement with this.

The actual relationship has the steeper slope of 0.0578, i.e., VEP extrapolations of spatial frequency are systematically lower (thresholds are higher) by a factor of 1.7 (0.24 log units). In the preceding section we obtained a similar underestimation of contrast sensitivity. The occurrence of underestimation was not specific to the kind of temporal modulation. It is hard to see why VEP sensitivity should be lower than subjective sensitivity since conscious perception requires electrical activity, not vice versa. To use not zero volt as the regression intercept but some nonzero level, as sometimes proposed, seems a poor

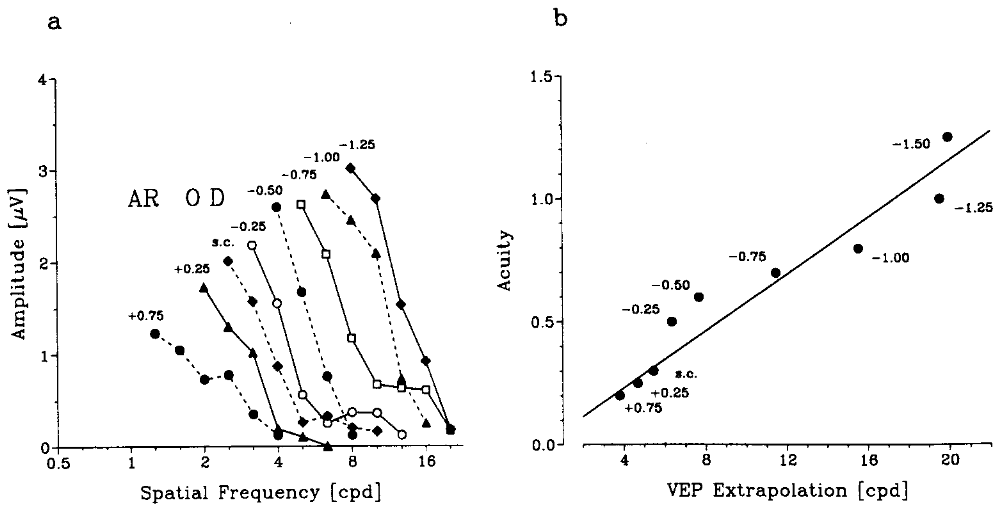


Fig. 7 a, b Relationship between grating acuity and VEP. **a** The high-spatial-frequency part of VEP amplitude response functions as recorded with the subject wearing lenses of various powers (numbers in diopters; right eye; myopic subject). **b** The extrapolated thresholds are then compared with the psychophysical grating acuity. A regression line, forced through the origin, is given by $a = 0.0578 \times \omega$ and explains 98% of the variance (a: acuity in degrees^{-1}; $a = 1.0$ corresponding to a 1′ gap; ω: spatial frequency in cpd). Note that equal gap widths for psychophysics and VEPs correspond to a shallower slope of $1/30 = 0.033$. In other words, the VEP acuity in this graph is systematically lower, with an acuity of 1.0 corresponding to less than 30 cpd in VEP gratings

strategy for both theoretical and empirical reasons. A plausible explanation, however, is that such deviations simply reflect deviations from the assumed log/linear relationship of signal amplitude and contrast (or spatial frequency), especially at low contrast. There is little evidence that such a relationship holds at all signal levels. Any deviation from that relationship will lead to prediction errors that become larger, the further from threshold the data are that are used as a basis for prediction. Far-from-threshold data are generally used since they are less contaminated by noise, with noise both artificially increasing the amplitude and reducing the reliability [41]. However, both problems can be overcome [1, 26]. Low-amplitude reliability can be improved by using phase-stability criteria: noise has a random phase. When the phase is nonrandom, the signal is different from noise [26, 29, 31, 37, 41, 49, 50]. The artificial increase in amplitude by noise contamination can be taken into account by fitting an appropriate function, the Rice function, which is curved at low signals [26].

An example of how phase can be used, by inspection, to differentiate low signal amplitudes from noise is given in Fig. 8, which shows the VEP phase as a function of lens power. A similar graph could be plotted with spatial frequency on the abscissa. For clarity, only coherent phases, i.e., of above-noise signals, are shown, the exception being two values at 8.0 cpd (at −0.25 and −0.5 D). For example, at 6.3 cpd and −0.25 D lens power the phase remains coherent, although the amplitude is quite low at 0.26 μV (cf. Fig. 7a). In contrast, at 8.0 cpd and −0.25 D the phase is not coherent, although the amplitude is a little higher at 0.39 μV. Note that phase-locked recording would automatically reduce amplitudes at noncoherent phases.

How fast is fast?

Will fast-rate modulation predominantly stimulate fast neural mechanisms? The role of temporal frequency in VEPs is clouded by mysticism. The large majority of VEP results are uninformative as to which neural channels, fast or slow, are activated. This is because VEPs are routinely acquired by square-wave modulation, and it is not clear which harmonic is the most effective. A conventional 5-Hz stimulus, for example, contains a strong 15-Hz component and can be considered slow or fast, depending on which component acts physiologically. Even the "slow"-repetition *transient* VEP will trigger "fast" (transient) neurons. The observation that below-4-Hz sine-wave modulation evokes little response at all shows that a certain "transientness" is required for any VEP, i.e., that only a certain temporal frequency band – somewhere above 5 Hz – is effective.

Surprisingly, 16-Hz on-off stimulation seems to trigger predominantly "slow", or so-called sustained, mechanisms: First, psychophysically the contrast sensitivity is very similar to that of static gratings, but this might simply reflect that only the static component is well perceived. Second, however, the VEP response for this stimulus goes up to quite high spatial frequencies that seem untypical of fast neurons. Perhaps the static stimulus component preactivates sustained neurons and the modulation makes such activation visible in the VEP. Quantitative psychophysical models of sustained and transient channels show that both go up to about equally high temporal frequencies and that 16 Hz is within both response bands [2]. How this modulation acts under pathological conditions, in which fast neurons are preferentially affected, is a question that needs to be addressed empirically.

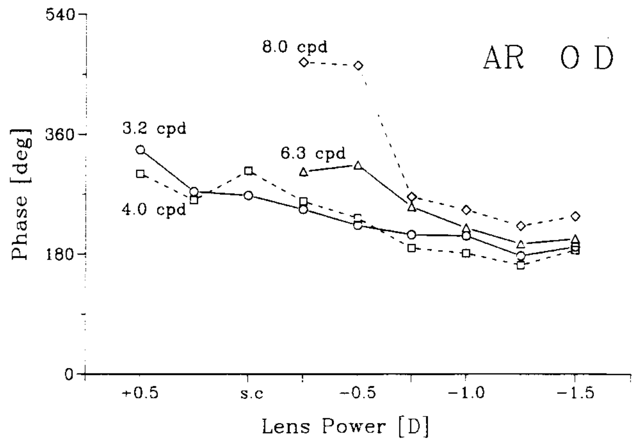


Fig. 8 VEP phase as a function of lens power. For clarity, only coherent phases, i.e., of above-noise signals, are shown, except two values at 8.0 cpd (at −0.25 and −0.5 D). For example, at 6.3 cpd and −0.25 D lens power the phase remains coherent, although the amplitude is quite low at 0.26 μV (cf. Fig. 7a). In contrast, at 8.0 cpd and −0.25 D the phase is not coherent, although the amplitude is a little higher at 0.39 μV. As an approximate criterion of coherence we excluded values that differed by more than ±45° from the expected value

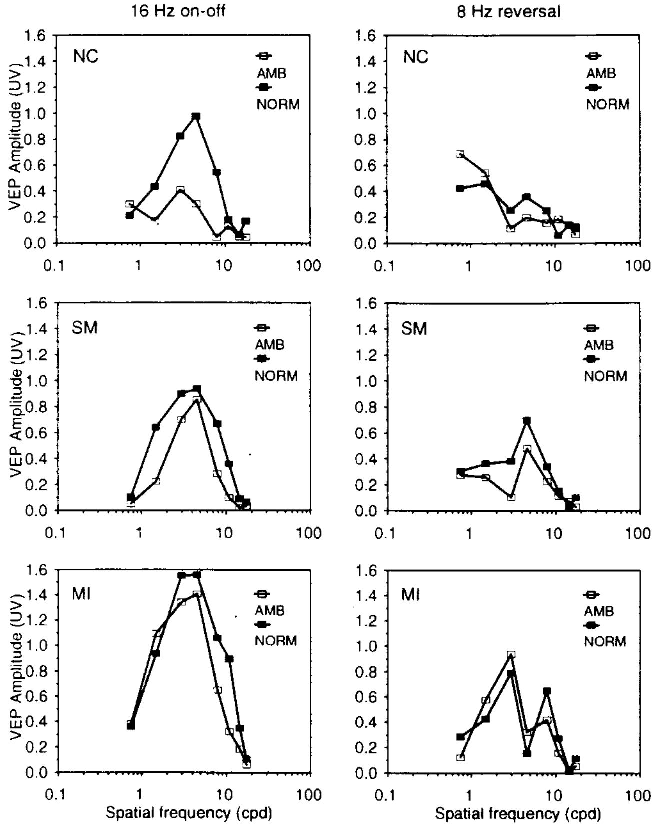


Fig. 9 Comparison of on-off modulation at 16 Hz and pattern-reversal stimulation at 8 Hz in three cases of amblyopia. *Left:* On-off modulation; *right:* pattern reversal. Amblyopic eyes are indicated by *empty squares*, and normal eyes are represented by *filled squares*. NC is an anisometropic amblyope (amblyopic eye, 6/18; fellow eye, 6/5). SM is an anisometropic amblyope (amblyopic eye, 6/9; fellow eye, 6/6). MI is a strabismic amblyope (amblyopic eye, 6/9; fellow eye, 6/5). VEPs were recorded using a CED 1401 signal analyzer (Cambridge Electronic Design, Cambridge, UK). Active electrodes were placed at Oz and referenced to linked ears, with the forehead serving as the ground. The sampling rate was 256 Hz; the recording epoch for each spatial frequency was 4 s. The data presented are the means of 3 determinations each composed of 10 samples of the recording frequency. Stimuli were vertical sinusoidal gratings either reversed in phase at 8 Hz or presented in the onset-offset mode at 16 Hz without any change in mean luminance between onset and offset. The spatial frequency was varied between 0.75 and 17.4 cpd. The mean luminance was 20 cd/m^2 and the contrast change between different phases of the stimuli was 0.4. The field size was 5° and the viewing distance was 244 cm. In all, 10 amblyopes were tested, and the results obtained in 3 typical amblyopic subjects are demonstrated. (Reproduced with permission from N. R. A. Parry: Objective assessment of infant vision, report to the North Western Regional Health Authority, UK)

Preliminary observations in abnormal cases

Pathological conditions of the visual pathway that present particular problems for the VEP regression method include neuropathies [22, 27, 36], amblyopia [5, 19–21, 32, 34, 38], macular disease [27, 30], diabetic retinopathies [30, 40], and nystagmus. Overestimation of acuity in macular disease seems mainly due to the use of test fields that allow a large contribution of nonfoveal vision to the VEP. The 5°-diameter field used in this study is expected to largely avoid these distortions. In neuropathies, the main problem lies with low amplitudes and poor signal-to-noise ratios that render the regression technique meaningless. Thus, the improved reliability of the present stimulation type promises favorable results. Whether the temporal frequency employed plays an adverse role (cf. above) needs to be examined, and this is part of a different study.

An obvious method of testing the technique is to record from patients with amblyopia. Although the clinical benefits of using VEPs in adult amblyopes is limited, this type of pilot study can provide insight into the value of the method; there are no optical complications, the degraded visual acuity is not artificial, and the patients can be relied upon to cooperate. One potential problem that must not be overlooked is the role of fixation. Depending on the type of amblyopia, the quality of fixation may vary, and this might account for the divergence of findings in the literature when VEPs have been obtained using amblyopic eyes [5, 19–21, 32, 34, 38]. The data presented in Fig. 9 are illustrative of the merits of on-off versus reversal stimulation rather than purporting to reveal anything new about amblyopia per se. Having been used on amblyopic subjects as a means of deciding on optimal stimulus conditions, the technique is being applied on a trial basis in a pediatric ophthalmology clinic.

In Fig. 9 it is evident that 16-Hz on-off modulation reflects the differences in contrast sensitivity more accurately and reliably than does pattern reversal. Levi and Harwerth [19, 20] also used 16-Hz on-off stimulation specifically to investigate amblyopia, and their findings are similar to ours except that they did not make a direct comparison with contrast reversal. In the present paper we make a different point: if VEPs are to be of any value in clinical conditions, they must reflect the underlying physiological processes as faithfully as possible. Contrast-reversing gratings are a powerful stimulus to movement perception, and we should not be surprised that they overestimate static visual acuity in infants.

Levi and Harwerth [19, 20] have also demonstrated that 16-Hz on-off modulation gives VEP amplitude versus spatial-frequency responses that resemble the contrast-sensitivity function. Their strabismic amblyopes did not show a difference in VEP amplitude between the two eyes for a 0.5-cpd grating but did show a difference above 2 cpd up to the highest frequency visible. Their anisometropic amblyopes, on the other hand, demonstrated a reduced VEP amplitude over the whole spatial-frequency range tested (0.5–16.0 cpd). Unlike these results, our data show no difference between strabismic and anisometropic amblyopes.

Conclusions

That the VEP could be used clinically to assess contrast sensitivity and visual acuity in cases where psychophysical methods are difficult to employ is a long-standing promise that has not yet quite been fulfilled. The main criticisms have concerned the large intersubject variability of VEP data, the long test times, the ambiguity of results, and the reduced correspondence between VEP and psychophysics in cases of impaired vision. The first three points are addressed by the present report; VEPs from fast-rate, on-off modulated stimuli have low intersubject variability, allow speedy acquisition, exhibit spatial tuning that reflects contrast sensitivity, and are well suited to assess contrast sensitivity and acuity. Impaired vision is being addressed in the next phase of this study. Our preliminary data show that even in mild cases of amblyopia, 16-Hz on-off modulation provides an accurate reflection of contrast sensitivity.

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