Principles and Practice of Clinical Electrophysiology of Vision

Editors

John R. Heckenlively, M.D.
Professor of Ophthalmology
Jules Stein Eye Institute
Los Angeles, California

Geoffrey B. Arden, M.D., Ph.D.
Professor of Ophthalmology and Neurophysiology
Institute of Ophthalmology
Moorfields Eye Hospital
London, England

Associate Editors

Emiko Adachi-Usami, M.D.
Professor of Ophthalmology
Chiba University School of Medicine
Chiba, Japan

G.F.A. Harding, Ph.D.
Professor of Neurosciences
Department of Vision Sciences
Aston University
Birmingham, England

Sven Erik Nilsson, M.D., Ph.D.
Professor of Ophthalmology
University of Linköping
Linköping, Sweden

Richard G. Weleber, M.D.
Professor of Ophthalmology
University of Oregon Health Science Center
Portland, Oregon

Mosby Year Book

St. Louis Baltimore Boston Chicago London Philadelphia Sydney Toronto

Mosby
Year Book
Dedicated to Publishing Excellence

Sponsoring Editor: David K. Marshall
Assistant Director, Manuscript Services: Frances M. Perveiler
Production Project Coordinator: Karen E. Halm
Proofroom Manager: Barbara Kelly

Mosby-Year Book, Inc.
11830 Westline Industrial Drive
St. Louis, MO 63146

1 2 3 4 5 6 7 8 9 0 CL CL MV 95 94 93 92 91

Library of Congress Cataloging-in-Publication Data
Principles and practice of visual electrophysiology / [edited by]
John R. Heckenlively, Geoffrey B. Arden.
p. cm.
Includes bibliographical references.
Includes index.
ISBN 0-8151-4290-0
1. Electroretinography. 2. Electrooculography. 3. Visual evoked response. I. Heckenlively, John R. II. Arden, Geoffrey B. (Geoffrey Bernard)
[DNLM: 1. Electrooculography. 2. Electrophysiology. 3. Electroretinography. 4. Evoked Potentials, Visual. 5. Vision Disorders—physiopathology. WW 270 P957]
RE79.E4P75 1991 91-13378
617.7 1547—dc20 CIP
DNLM/DLC
for Library of Congress

41

Oscillatory Potential Recording

Lillemor Wachtmeister

Oscillatory potentials (OPs), which are rapid, rhythmic subwaves of low amplitude superimposed on the b-wave of the electroretinogram (ERG), may be difficult to discern in an unfiltered response. To enhance the amplitudes of the OPs and reduce the contribution of the a- and b-waves it is advisable to use a filtering technique as well as special stimulus and adaptational conditions for OP recording.

FILTERING TECHNIQUE

From Fourier analysis of the OPs it is known that the OPs in humans have a dominant frequency of about 100 to 160 Hz (Fig 41–1,A and B).[1, 2] In a clinical situation the simplest way is to use an analog band-pass filter (e.g., 80 to 500 Hz, 3-dB points) in the recording system and record the OPs with a short time constant (e.g., T= 15 ms). It is best to use a passive filter (i.e., 4 dB per octave) because too steep a filter may give ringing artifacts. Thus, a higher amplification can be used for OP recording, and the amplitudes of the individual OPs can easily be measured in a conventional way. Moreover, it is wise to increase the sweep speed of the recorder, which will facilitate measurement of the peak times of the oscillations (Fig 41–2).

For more sophisticated purposes, i.e., intraretinal recordings for current density profile studies in the primate eye, a digital filtering technique is necessary to avoid minor shifts of phase that may occur when using an analog filter.[6, 9] To measure the dominating frequency and energy content of the oscillations more refined methods have to be used, including computer techniques for analysis of power spectrum distribution or performing combined impulse response and Fourier analysis of the ERG curves (see Fig 41–1,A).[1, 2, 6]

Averaging techniques are generally not necessary in clinical practice for corneal electrode recording. For microelectrode studies in the primate retina or in the clinical laboratory when, e.g., gold foil electrodes are used, averaging of the responses may be needed.[6, 16]

In summary, for OP recording a passive analogue filter is generally adequate to selectively enhance the oscillatory response in relation to the a- and b-waves, and usually the signal-to-noise ratio allows single-response analysis.

STIMULUS LIGHT

A white light stimulus is preferred to chromatic stimuli for OP recording because the oscillatory response contains both scotopic as well as photopic maxima in its luminosity function.[8, 10] In response to light of slow rise time, very low if any OPs can be recorded.[4, 7] Stimuli with abrupt onset must therefore be used to induce an oscillatory response (Fig 41–3).

It is well known that the threshold of the OPs is about 2 to 3 log units higher than that of the b-wave and about the same as that of the a-wave.[11, 15] Sec-

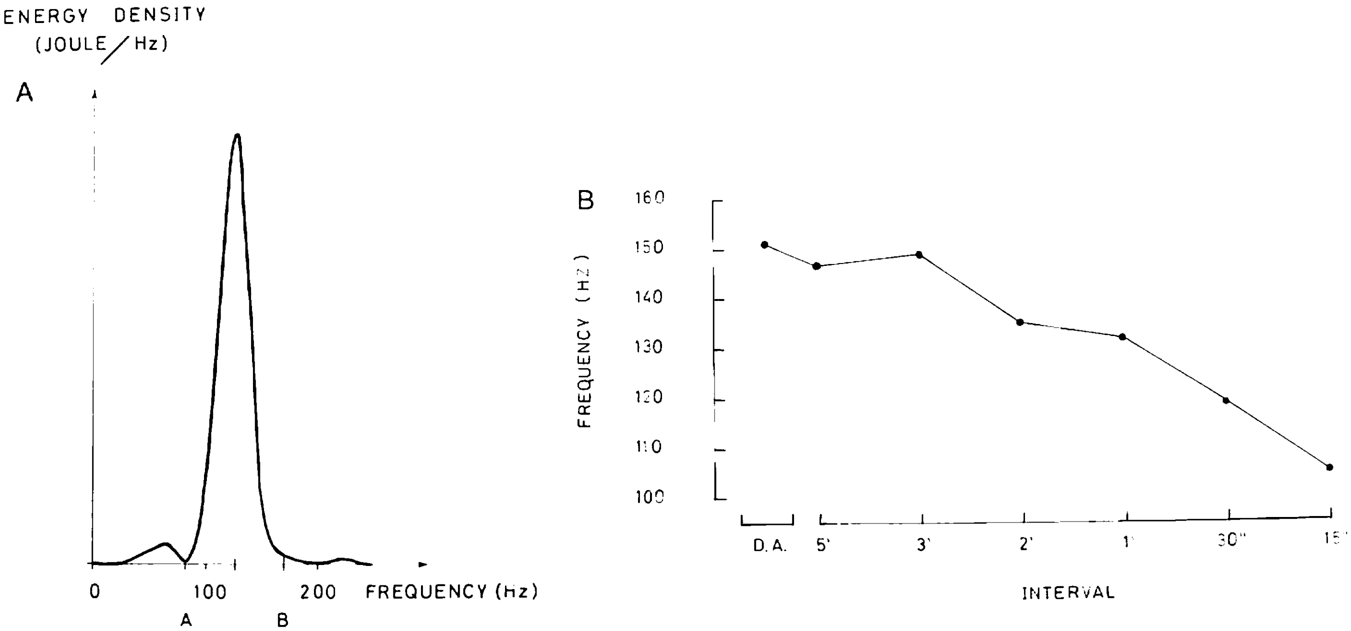

FIG 41–1.
A, energy density spectrum of OPs according to Fourier analysis. The dominant frequency in this recording was 125 Hz. The energy attributable to the OPs is the energy underlying the maximum energy peak in a certain frequency range indicated by *A* and *B*. The scale on the y-axis is linear. (From Algvere P, Wachtmeister L, Westbeck S: *Acta Ophthalmol (Copenh)* 1972; 50:737–759. Used by permission.) **B**, dominant frequency of the OPs in relation to different interstimulus intervals in response to a stimulus flash of high intensity. The frequency of the OPs declined from about 146 Hz to 105 Hz as the interval between the flashes decreased. (From Wachtmeister L: *Acta Ophthalmol (Copenh)* 1973; 51:250–270. Used by permission.)

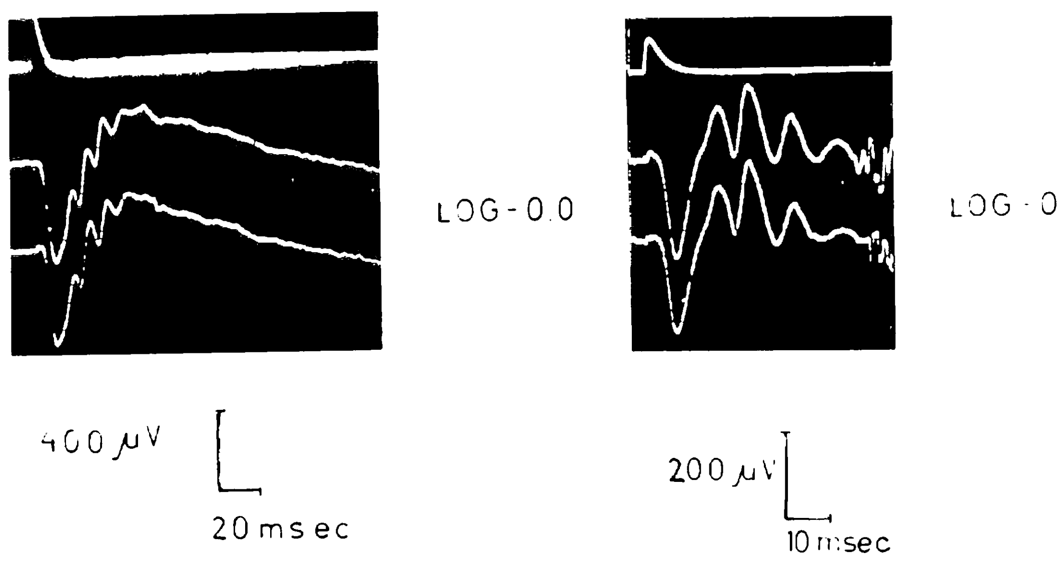

FIG 41–2.
ERG recordings performed with a long time constant (unfiltered) in response to stimulus light of high intensity at an interval of 30 seconds *(left)*. The response to the second and third flashes is shown. On the *right* are OPs of the ERG recorded with a short time constant (T = 15 ms) selectively attenuating the a- and b-waves, during the same stimulus conditions. (From Wachtmeister L: *Acta Ophthalmol (Copenh)* 1973; 51:250–270. Used by permission.)

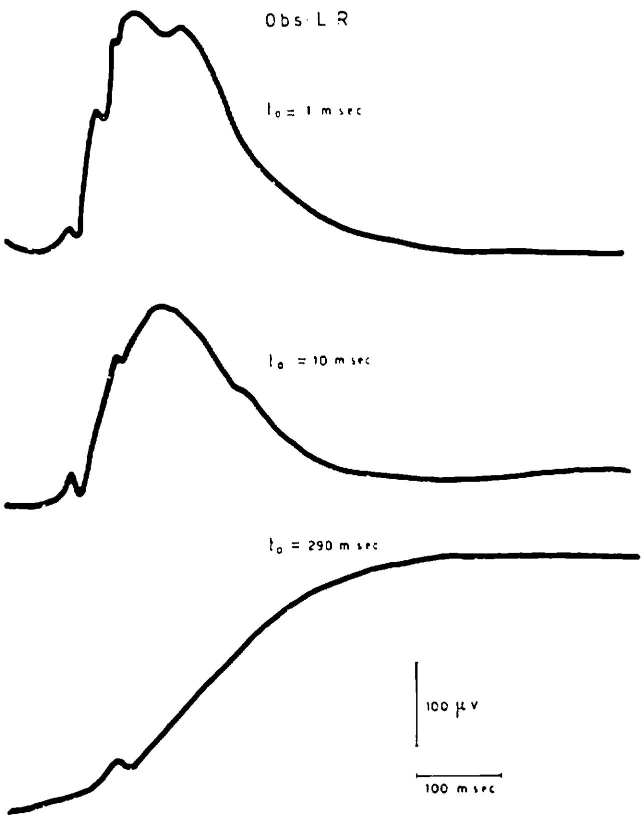

FIG 41–3.
ERG responses recorded with a long time constant and stimulus of the same intensity but with different rate of rise. In response to a slowly rising stimulus *(bottom)* a very low amplitude OP can be recorded. In response to stimulus with rapid rate of rise the OPs clearly appear *(top)*. (From Rhonchi L, Grazi S: *Optica Acta* 1956; 3:188–195. Used by permission.)

ond, the amplitude of the OPs as well as their energy increase linearly over a range of at least 3 log units (Fig 41–4).[11, 15] The stimulating light should therefore be relatively intense to elicit the OPs, e.g., in the range of about 5×10^4 photopic cd/m^2.

The oscillatory response integrates temporally up to about 10 ms during relatively photopic conditions,[14] and the stimulus light can thus be quite short for OP recording.

In summary, a stimulator generating white light of a rapid rate of rise, high intensity, and short duration (e.g., a Grass photostimulator) is very suitable for testing the oscillatory response in a clinical situation. A full-field stimulator should be used as when the main components of the ERG are recorded.

ADAPTATIONAL CONDITIONS

In dark adaptation in response to one single flash no prominent OPs can be recorded.[3, 11] Special adaptational conditions are a prerequisite to maximize the oscillations. The adaptational conditions have been studied systematically, and it has been found that OPs of maximal energy are recorded when the sensitivity of the eye was changed from scotopic to photopic vision or vice versa, i.e., during mesopic conditions.[1–3, 12, 13] The optimal conditions of adaptation can be induced in different ways: giving a series of flashes in the dark-adapted state and recording the OPs in response to the last flash, light-adapting to a steady background illumination, or recording the OPs during recovery in the dark after

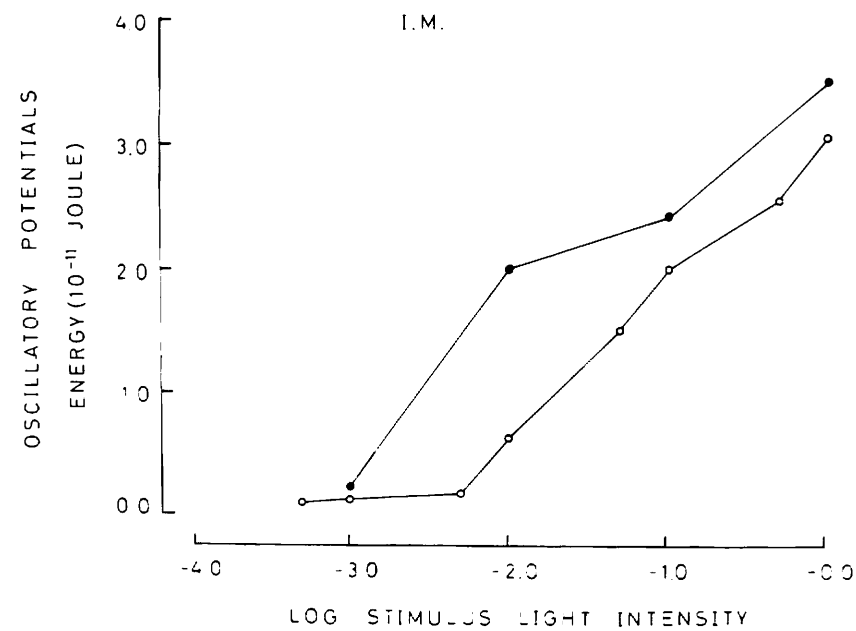

FIG 41–4.
Calculated energy of the OPs in relation to stimulus intensity. The *black and white circles* indicate different protocols for conditioning flashes. *Black circles* represent a protocol with conditioning flashes of maximal intensity, and *white circles* designate a protocol with the same intensity of conditioning flashes as the stimulus flash. (From Algvere P, Wachtmeister L, Westbeck S: *Acta Ophthalmol (Copenh)* 1972; 50:737–759. Used by permission.)

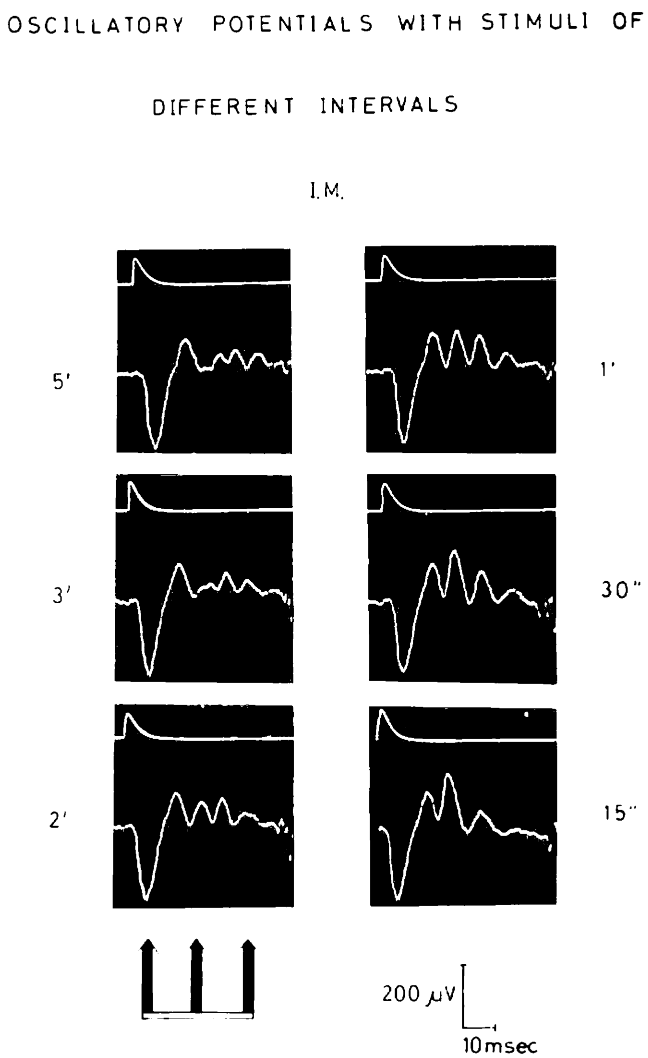

FIG 41–5.
OPs of the ERG recorded with a short time constant (T = 15 ms) during dark adaptation in response to flashes of high intensity delivered at different intervals, which are indicated. Most prominent OPs are recorded at an interval of 30 seconds. (From Wachtmeister L: *Acta Ophthalmol (Copenh)* 1973; 51:250–270. Used by permission.)

a bright preillumination. Generally, the most practical way is to use a series of flashes, i.e., use conditioning flashes of high intensity and record the ERG in response to the last flash, in a dark-adapted situation.

The rationale for such a protocol is illustrated in Figures 41–5 to 41–7. Conditioning flashes were used and the ERG recorded in response to a third stimulus flash. By changing the interstimulus interval the optimal state of adaptation to elicit the OPs was investigated. The amplitudes of the OPs were found to be highest when an interval of 30 seconds was used (Fig 41–5). The energy of the oscillations was low when the interval between the flashes was long (Fig 41–6). When the interstimulus interval decreased, the energy of the OPs augmented tenfold and reached a maximum at a 30-second interstimulus interval. Figure 41–7 shows the sensory threshold of retinal sensitivity measured in a Goldmann-Weekers adaptometer during the same recording conditions. When longer interstimulus intervals than 30 seconds was used, the retinal sensitivity was below the level that corresponds to the rod-cone break (about 6×10^{-3} lux), and with shorter interstimulus intervals than 30 seconds the sensory threshold was above the Kohlrausch knee and determined by the cones. Thus, optimal OPs were recorded when the retinal sensitivity was at the border between scotopic (rod) and photopic (cone) vision, e.g., in the mesopic range.

For special recording conditions like microelectrode studies in the intact primate eye, when it is important to collect as much data as fast as possible to shorten the time of an experiment, a shorter interstimulus interval may be used. A flicker-like (0.5 to 1 Hz) stimulus can be applied to elicit the OPs, which will be of somewhat lower amplitudes, a compromise that has to be accepted. In such an experimental situation an averaging technique is usually necessary. If so, it is important to discharge the first ERG response in the dark adapted eye because it is completely different from the following ones.

In summary, the most practical way of inducing optimal (i.e., mesopic) recording conditions to maximize the oscillatory response is to give conditioning flashes and record the OPs in response to the last (e.g., third) flash in a dark-adapted (30-minute) state. The interstimulus interval to be chosen depends on the flash intensity. If a bright flash (about 5×10^4 photopic cd/m^2) is used, an interstimulus interval of 30 or 15 seconds is a good choice.

NORMAL OSCILLATORY POTENTIALS

There are few studies on the OPs in a normal population. The appearance of the OPs in normal eyes depends on the protocol used for OP recording (see the previous section). Bresnick et al.[5] studied a group of nondiabetics and diabetics by using a strobe light in a Ganzfeld bowl as a stimulus light for uniform retinal illumination, conditioning flashes after 30 minutes of dark adaptation, and a 30-second interflash interval, and the last two responses were recorded separately. The response of higher quality of the last two was used for analysis. Measurement of the OPs was accomplished with a caliper-square

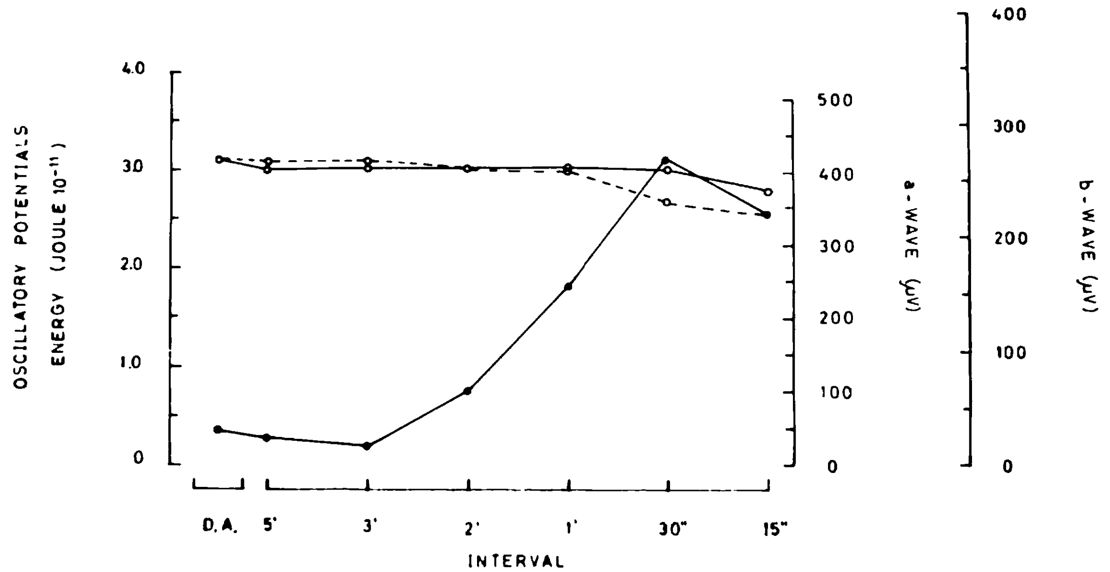

FIG 41–6.
Calculated energy of the OPs shown in Figure 41–5 and amplitudes of the a- and b-waves in relation to the interval between stimulus flashes of high intensity. *Black circles* indicate energy of the OPs, *open circles* and *continuous line* designate amplitude of the a-wave, and *open circles* and *dashed line* indicate the amplitude of the b-wave. (From Wachtmeister L: *Acta Ophthalmol (Copenh)* 1973; 51:250–270. Used by permission.)

method combined with a computer program (Fig 41–8). They found that 95% of a nondiabetic population has a summed amplitude of the OPs higher than 75 µV.

It has been claimed that the peak latencies of the OPs show less variation in a normal group than do the amplitudes and are a better indicator of retinal pathology.[17] Yonemura and Kawasaki[17] studied 35 human subjects (10 to 64 years old) by using a xenon discharge tube (20 J) as a light source that delivers a conditioning flash as well as the stimulus light after 5 minutes of dark adaptation. They found the summed amplitude of the OPs to be 276.9 ± 63.7 µV (normal range, 149.5 to 404.3 µV). The peak latencies of the OPs (O_1 to O_4) were as follows: O_1, 14.2 ± 0.36 ms (13.5 to 14.9); O_2, 20.6 ± 0.7 ms (19.2 to 22.0); O_3, 27.0 ± 1.19 ms (24.6 to 29.4); and O_4, 34.0 ± 1.44 ms (31.1 to 36.8).

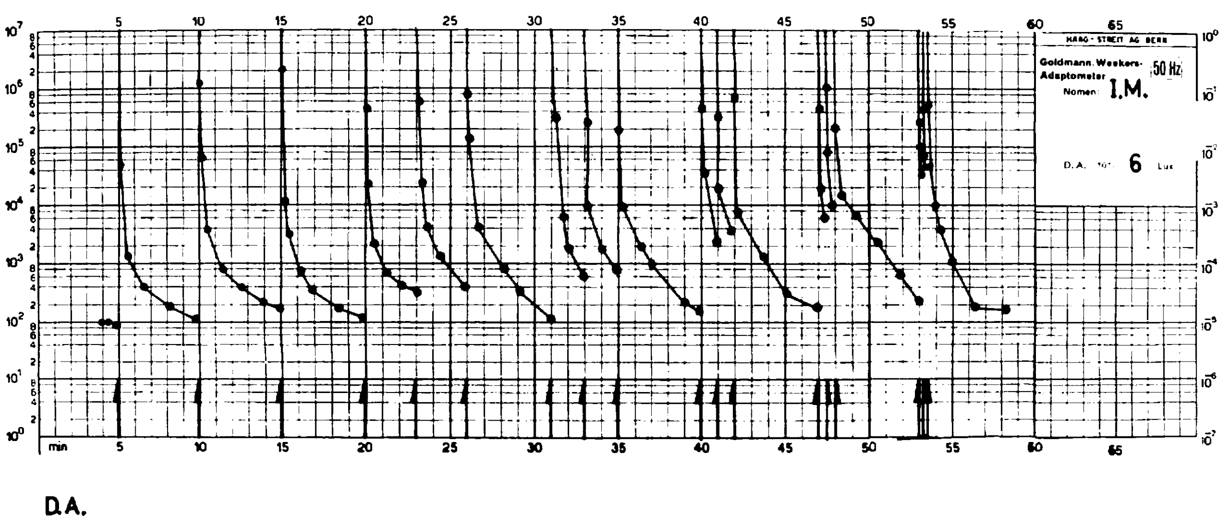

FIG 41–7.
Visual sensory threshold in the dark after light adaptation by stimulus flashes of high intensity elicited at different intervals as in Figure 41–5. (From Wachtmeister L: *Acta Ophthalmol (Copenh)* 1973; 51:250–270. Used by permission.)

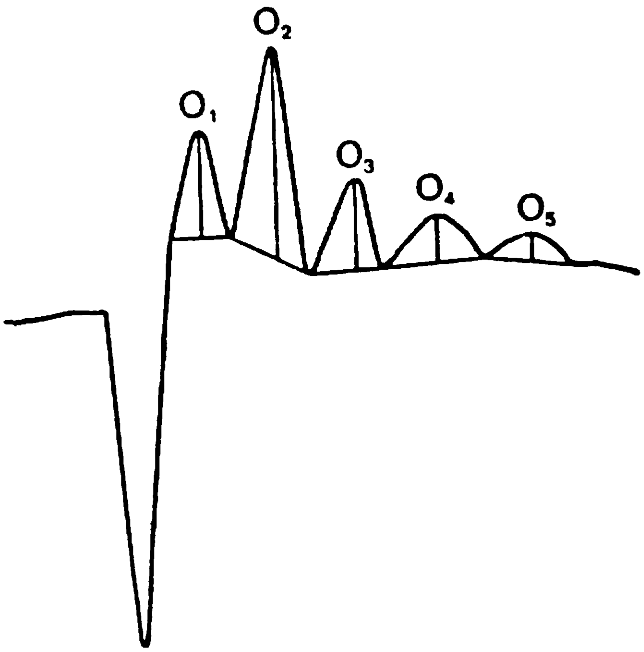

FIG 41–8.
Measurements of the amplitudes of the OPs. The amplitude of the individual peaks is determined by connecting adjacent troughs and measuring the height from the OP peak to a line so drawn. The summed OP amplitude is calculated by adding individual OP amplitudes. (From Bresnick G, Korth K, Groo A, et al: *Arch Ophthalmol* 1984; 102:1307–1311. Used by permission.)

GENERAL SUMMARY

For OP recording in clinical practice it is advisable to use a passive analog filter (e.g., 80 to 500 Hz, 3-dB points, 4 dB per octave) to selectively enhance the OPs; to use a full-field white light stimulus of short duration, rapid rate of rise, and high intensity (e.g., Grass photostimulator); and to record the OPs during a mesopic state of adaptation. Generally, the most convenient way is to use conditioning flashes of high intensity in a dark-adapted situation and to set a constant interflash interval of, for example, 15 or 30 seconds. If an averaging technique is applied, the response to the first flash in dark adaptation should be discharged because it is totally different from the later ones. Usually, conventional measurement of the amplitude and peak latencies of the individual oscillatory peaks with a caliper is adequate in a clinical situation.

REFERENCES

1. Algvere P, Wachtmeister L: On the oscillatory potentials of the human electroretinogram in light and dark adaptation. II: Effect of adaptation to background light and subsequent recovery in the dark: A Fourier analysis. *Acta Ophthalmol (Copenh)* 1972; 50:837–863.
2. Algvere P, Wachtmeister L, Westbeck S: On the oscillatory potentials of the human electroretinogram in light and dark adaptation. I: Thresholds and relation to stimulus intensity on adaptation to short flashes of light: A Fourier analysis. *Acta Ophthalmol (Copenh)* 1972; 50:737–759.
3. Algvere P, Westbeck S: Human ERG in response to double flashes of light during the course of dark adaptation: A Fourier analysis of the oscillatory potentials. *Vision Res* 1972; 12:195–214.
4. Bornschein H, Goodman G: Studies of the a-wave in the human electroretinogram. *Arch Ophthalmol* 1957; 58:431–437.
5. Bresnick G, Korth K, Groo A, et al: Electroretinographic oscillatory potentials predict progression of diabetic retinopathy: Preliminary report. *Arch Ophthalmol* 1984; 102:1307–1311.
6. Heynen H, Wachtmeister L, van Norren D: Origin of the oscillatory potentials in the primate retina. *Vision Res* 1985; 25:1365–1373.
7. Ronchi L, Grazi S: The dependence of human electroretinogram on the shape of the stimulus as a function of time. *Optica Acta* 1956; 3:188–195.
8. Stodtmeister R: The spectral sensitivity functions of human ERG wavelets. *Ophthalmic Res* 1973; 5:21–30.
9. Thijssen JM, Essink HJM, Zaicsek SPM: Time-frequency behaviour of in vitro LERG depth profiles. Presented at the Fifth International Congress of Eye Research, Veldhoven, The Netherlands, October 3–8, 1982, p 126.
10. Wachtmeister L: Luminosity functions of the oscillatory potentials of the human electroretinogram. *Acta Ophthalmol (Copenh)* 1974; 52:353–366.
11. Wachtmeister L: On the oscillatory potentials of the human electroretinogram in light and dark adaptation. *Acta Ophthalmol* 1972; 50(suppl):116.
12. Wachtmeister L: On the oscillatory potentials of the human electroretinogram in light and dark adaptation. III: Thresholds and relation to stimulus intensity on adaptation to background light. *Acta Ophthalmol (Copenh)* 1973; 51:95–121.
13. Wachtmeister L: On the oscillatory potentials of the human electroretinogram in light and dark adaptation. IV: Effect of adaptation to short flashes of light. Time interval and intensity of conditioning flashes: A Fourier analysis. *Acta Ophthalmol (Copenh)* 1973; 51:250–270.
14. Wachtmeister L: Stimulus duration and the oscillatory potentials of the human electroretinogram. *Acta Ophthalmol (Copenh)* 1974; 52:729–739.
15. Wachtmeister L, Dowling JD: The oscillatory potentials of the mudpuppy retina. *Invest Ophthalmol Vis Sci* 1978; 17:1176–1188.
16. Wanger P, Persson HE: Early diagnosis of retinal changes in diabetics. A comparison between electroretinography and retinal biomicroscopy. *Acta Ophthalmol (Copenh)* 1985; 63:716–720.
17. Yonemura D, Kawasaki K: Electrophysiological study on activities of neuronal and non-neuronal retinal elements in man with reference to its clinical application. *Jpn J Ophthalmol* 1978; 22:1–19.