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The influence of age on the electroretinogram and visual evoked potential

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Abstract, Changes in the ERG and VEP across the life span were investigated. The dark adapted and scotopic ERGs both showed a progressive increase in the implicit times of the A and B waves and a reduction in the amplitude of the AB configuration. There was also an increase in the implicit times of the oscillatory potentials of the photopic ERG.

The flash and pattern onset-offset VEP both showed changes in waveform with age whilst the waveform of the pattern reversal VEP was constant. The amplitudes of the components of the flash and pattern reversal VEP were very high in the teenage group, but once reduced, were constant from the twenties onwards, showing no further consistent age changes.

The latencies of the components of the pattern VEPs showed an increase with age which could be accounted for by the reduction in retinal illuminance due to the decrease in pupil diameter with age. However, the increase in the latency of the flash major positive (P2) component was greater than that expected from the decrease in retinal illuminance alone, suggesting that this is due to neural factors.

Introduction

The electroretinogram (ERG) and visual evoked potential (VEP) are important clinical techniques for the diagnosis of pathology in the eye and visual pathway. Age-related changes in the electrical responses of the retina and cortex are an important consideration when analysing clinical data. Various workers have separately investigated the effect of age on the normal ERG to flash stimulation (Karpe et al., 1950; Zetterstrom, 1956; Zeidler, 1959; Straub, 1961 ; Peterson, 1968; Weleber, 1981 ; Martin and Heckenlively, 1982) and on the flash VEP (Kooi and Bagchi, 1964; Copenhaver and Perry, 1964; Dustman and Beck, 1966; 1969, Buchsbaum et al., 1974; Dustman et al., 1977; Cosi et al., 1982) and the pattern reversal VEP (Asselman et al., 1975; Celesia and Daly, 1977; Allison et al., 1979, 1983; Stockard et al., 1979; Shaw and Cant, 1981; Snyder et al., 1981; Sokol et al., 1981; Halliday et al., 1982). There are few studies on age-related changes in VEPs evoked by pattern onset-offset stimulation, which is a subject of considerable interest (de Vries-Khoe and Spekreijse, 1982; Spekreijse et al., 1973; Jeffreys, 1977).

This paper reports a study on the influence of age on the components of the dark-adapted low intensity ERG and photopic ERG, and the VEP to flash, pattern reversal and pattern onset-offset stimulation on progressive age groups of normal subjects. Psychophysical measures on the same subjects are reported in the following paper (Wright and Drasdo, 1985). These results were required as control values for a number of clinical studies (eg. Wright et al., 1984a, 1984b; Harding et al., 1984) and will be of interest to others working in the field as not all these tests have been covered by previous studies of ageing. Comparison of these tests in the same large group of normals is of particular interest as no equivalent study is known to the authors.

Selection of subjects

Subjects were paid volunteers with no history of ophthalmic or neurological pathology. The purpose of the study and the techniques involved were explained fully to all subjects. Full refractive correction was worn where necessary and all subjects had a visual acuity of 6/6 or better (thus excluding any significant ophthalmic pathology). The proportion of males and females in each group was balanced as evenly as possible. The lower age limit was 20 years for the ERG study and 10 years for the VEP study.

Methods

ERG

A drop of 0.4% Benoxinate was instilled into the lower fornix of each eye and the subject was asked to fixate a red spot in the centre of the circular photostimulator screen. A gold leaf electrode (Arden et al., 1979) was then placed centrally with respect to the pupil in the lower fornix to make contact with the corneo-scleral junction. The reference electrode (a standard silver, silver-chloride electrode) was positioned posterolaterally to the outer canthus. The electrode linkages were $F_8 - F_{p2}$ and F_7 to F_{p1} , where F_{p2} and F_{p1} were the right and left gold leaf electrodes respectively. A pair of wide angle goggles fitted with diffusing opal lenses and side flaps were subsequently placed on the subject's face in order to produce Ganzfeld stimulation.

Diffuse light flashes were provided by a Grass photostimulator (PS22) viewed at a distance of 30 cm. The photopic flash ERG to red stimulation was recorded first, followed by the dark adapted low intensity flash ERG to white stimulation. The potentials were amplified and filtered by an Elema-Schonander EEG machine and averaged by the PDP8E computer. The parameters are shown in Table 1.

VEP

Standard silver-silver chloride electrodes were placed at O_2 and O_1 on the scalp and referred to a mid-frontal electrode (F_z) . The resistance of the skinelectrode interface was reduced to below 5 Kohms. The signals were amplified

| Stimulus parameters | Photopic | ERG type Dark-adapted 12 dark-adapted for 10 min prior to stimulation | | |
|---------------------|---------------------|--|--|--|
| Stimulus intensity | I16 | | | |
| Stimulus colour | Red (Kodak | | | |
| | Wratten No. 29) | White | | |
| Stimulus duration | 10 us | 10 _{us} | | |
| Stimulus frequency | 3 _{Hz} | 1 flash every 10s. | | |
| Gain setting | 200 uV/cm | $200 \,\mathrm{uV/cm}$ | | |
| Time constant | 0.15 s | 0.3s | | |
| Low pass filter | 700 Hz | 70 Hz | | |
| Sweep time | 100 ms | 100 ms | | |
| No. of sweeps | 25 | 4 | | |

Table 1. Stimulus parameters for ERG recording

by an Elema-Schonander EEG machine, time constant 0.3 sec, high frequency filter 15 Hz (3 dB attenuation). The two channel EEG was monitored throughout the VEP recording. Fifty sweeps were averaged by a PDP8E computer.

The flash VEP was evoked by an unstructured white light flashing twice per second. The flash was produced by a Grass PS22 photostimulator at Intensity 2 (stimulus intensity of each flash 68 cd/m^2 per second). The patterned stimuli were back projected checkerboards of 56, 19 and 13 min check size. A circular field with an angular diameter of 28° was used for the 56' and 19' checkerbords, and a foveal 3 ~ field for the 13' checkerboard. The contrast of the checks was 0.76 and the mean luminance 1050 cd/m^2 . The ambient luminance was 42 cd/m^2 . Pattern reversal twice per second was produced by the oscillation of a surface silvered mirror mounted on a pen motor. Pattern onset-offset stimulation was produced by the rotation of a lenticular perspex disc with a clear sector in the beam of the projector (Drasdo, 1976) twice per second. Within each cycle the pattern was presented for 150 msec and replaced by a homogenous field of equal mean luminance for 350 msec.

The results were analysed by 2-way analysis of variance for unrelated samples (Keppel, 1973). There was no statistically significant difference between the VEP results from the two eyes so, for clarity, only the VEP results from the right eye are shown.

Results

ERG study

Waveforms typical of the photopic and dark adapted ERGs recorded in this study are shown in Figures 1 and 2. The graphs below the waveforms give the mean values of the amplitudes and peak latencies for each age group. All of

Figure 1. (a) Typical waveform of the photopic ERG to red stimulation; (b) and (c) Graphs showing the mean amplitudes of the AB configuration and the mean latencies of the A and B waves and oscillatory potentials for each age group of normal subjects. Positive potentials are represented by an upward deflection, in accordance with ERG convention. (Results are shown for right eye only).

the subjects demonstrated the components of the ERGs shown in Figures 1 and 2.

The results of the dark adapted and photopic ERGs are given for six separate 10 year age groups (range 20-77 years) in Table 2. Statistically significant progressive age changes were found for the peak latencies of the A and B waves which demonstrate a gradual increase (p < 0.05 and p < 0.01 respectively) and the amplitude of the AB configuration which shows a gradual decrease (p < 0.05). For the photopic ERG, the peak latencies of the A and B waves and oscillatory potentials, and the amplitude of the AB configuration all showed progressive age related changes that were significant at the 1% level.

Figure 2. (a) **Typical waveform of the dark-adapted low intensity** ERG; (b) **and** (c) **Graphs showing the mean amplitudes of the AB configuration and the mean latencies of the A and B waves for each age group of normal subjects. Positive potentials displayed upwards. (Results are shown for right eye only).**

VEP study

Waveform. **Examples of typical VEPs recorded in this study, and their nomenclature, are shown in Figure3. A notable feature of our results was the difference in waveform between the youngest age group (10-19 years) and the middle to older groups for the flash and pattern onset VEP.**

Inspection of the flash VEP waveforms showed that the predominant P2 component was very consistent and could be identified in the VEPs of 69 of the 70 subjects in the study. The later N3, P3 and N4 components were more **variable, but showed no changes in incidence with age. However, the incidence of the early P1 component seemed to be closely related to age. No P1** component was identified in the flash VEP of any of the 10–19 year **group, while 5 were identified in each of the 20--29 and 30-39 year groups, 6 in each of the 40-49 and 50-59 year groups and 9 in each of the 60-69**

Table 2. Giving means ± 18D for the components of the dark-adapted and photopic ERG for each age group of normal subjects Table 2. Giving means \pm 1SD for the components of the dark-adapted and photopic ERG for each age group of normal subjects

Pattern reversa! VEP (56 minute check)

Pactern onset-offset VEP (56 minute check)

Figure 3. Examples of the flash, pattern reversal and pattern onset-offset VEP waveforms recorded in this study. Positive potentials represented by a downward deflection, in accordance with EEG convention. (Results are shown for right eye only).

and 70-79 year groups. In place of P1 the younger groups showed a negative component with a latency intermediate to N1 and N2 (Figure 4).

The pattern reversal response was very consistent. Of the 70 subjects and 3 check sizes, the major positive (P100) component was reliably identified in 209 of the 210 VEPs. However, the pattern onset-offset VEP was much more variable. In many cases the waveforms were ambiguous and the usual CI, CII and CIII components could not be identified. This was particularly difficult in the 10-19 year group, where 8 of the 10 subjects showed a very large positive wave in place of the onset VEP, followed by a later positive offset response (Figure 5). This positive onset component appeared to be a combination of CI and CIII, as it was of an intermediate latency. The number of subjects showing a standard onset waveform increased to 5 when the foveal stimulus was used. From the 20-29 year group upwards there were no further changes in incidence related to age. The CII and CIII components were very variable throughout the life span, being identified in as few as 5

Figure 4. (a) Comparison of flash VEP waveforms from a teenage and elderly subject. The VEP is larger in amplitude in the teenager, but the early components are more prominent in the 70 year old. Responses from the right eye are shown, positive potentials displayed downwards; (b) and (c) Graphs showing mean flash P2 latency and mean N2- P2 amplitude (\pm 1 standard error) for each age group of normal subjects.

subjects in a group on a number of occasions. The CI component was fairly consistent in all groups (with the exception of the 10-19 year olds as already described) while an offset response was identified in all the groups, including the 10-19 year group. The 40-49 year age group was notable in that it was the only group in which all 10 subjects had a pattern onset VEP showing CI, CII and CIII components.

The statistical significance of latency and amplitude measures was determined using analysis of variance tests. As an equal number of subjects is

Figure 5. Ambiguous pattern onset-offset waveforms in one subject showing the difficulties encountered in the measurement of such VEPs. (a) shows a standard waveform with CII at 101 msec; (b) can be interpreted either as two negative components or a single negative split in two by a positive wave at 115 msec; (c) CII is completely obscured by a large positive wave which could be either CI and CIII or a combination of the two.

required for the analysis, the results from the $10-19$ year group were excluded from the tests for pattern onset and the early flash components.

Latency. The only flash VEP component showing a significant change with age was the major positive component P2 which showed a progressive increase from a mean latency of 114.5 ms in the $10-19$ year group to 134.25 in the 70-79 year group ($p < 0.001$). The N2 component was earlier in the 20-29 year group, due to the apparent merging of N1 and N2 in subjects without a P1 component, as already described. However, apart from this, no consistent trend with age was found (Table 3, Figure 4).

Pattern reversal latency was found to be more consistent throughout life, but showed a significant increase in the older age groups ($p < 0.01$). The overall latency increase was more marked for the smaller checks, being 6ms, 2.5 ms and 11 ms for the 56, 19 and 13 minute checks respectively (Table 4).

Table 3. Effect of age on the latency and amplitude of the flash VEP

D = Standard Deviation $SD = Standard Deviation$

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| Significance level | p < 0.01 | $\dot{N} = 10$ | | p < 0.05 | $N = 10$ | Not Sig . $N = 9$ |
|--|--|-------------------------|-------------------------|-----------------------|-----------------------|-------------------------|
| $70 - 79$ | $\frac{18}{18}$ $\frac{1}{2}$ | 108.61 9.39 | 18.44 9.52 | 6.20 4.18 | $\frac{5.5}{2.71}$ | 4.36 |
| | SD | SD | $\overline{\mathbf{S}}$ | $\overline{\text{S}}$ | SD | ခ္တ |
| $60 - 69$ | 109.22 10.45 | 106.11 4.54 | 108.61 7.23 | 6.13 7.18 | 8.53 | 4.11 2.42 |
| | SD | $\overline{\text{SD}}$ | $\overline{\text{3}}$ | $\overline{\text{S}}$ | $\overline{\text{S}}$ | SD |
| $50 - 59$ | $\frac{102.89}{6.75}$ | $\frac{105.61}{7.37}$ | $\frac{106.61}{10.32}$ | 6.07 4.13 | 7.65 7.18 | 3.75 2.79 |
| | SD | $\overline{\mathbf{S}}$ | SD | GS | GS | $\frac{1}{2}$ |
| $40 - 49$ | 104.6 5.15 | 105.61 3.30 | 108.14 | 6.73 | 7.01 4.69 | 3.22 1.54 |
| | $\overline{\text{c}}$ | $\overline{\text{SD}}$ | SD | SD | $\overline{\text{S}}$ | $\frac{1}{2}$ |
| $30 - 39$ | 106.78 4.91 | 110.28 | $\frac{105}{8.52}$ | 5.1 1.82 | 5.06 | 3.47 2.03 |
| | SD | $\overline{\mathbf{S}}$ | $_{\rm SD}$ | $\overline{\text{S}}$ | $\overline{\text{3}}$ | $\overline{\text{S}}$ |
| $20 - 29$ | 101.78 7.64 | 101.83 4.24 | 106.44 | $\frac{4.54}{1.98}$ | 4.58 2.14 | 2.78 |
| | SD | Ω | $\overline{\mathbf{S}}$ | $\overline{\text{S}}$ | SD | SD |
| $Year$ 10-19 | 108.56 | 106.72 4.17 | $\frac{106.5}{8.19}$ | 11.85 3.44 | 1.49 6.44 | 4.58 2.79 |
| | $_{\rm SD}$ | $\overline{\mathbf{S}}$ | $\overline{\mathbf{S}}$ | $_{\rm SD}$ | SD | $\overline{\mathbf{S}}$ |
| $\begin{array}{c} {\rm Check}\\ {\rm (min)} \end{array}$ | 56' | 19' | 13' | 56' | ğÌ | $\frac{3}{2}$ |
| | $\begin{array}{c} Latency\\(m.s)\end{array}$ | | | $Amplitude$ (uV) | | |

 $SD = Standard Deviation$ $D =$ Standard Deviation

Table 5. Effect of age on the C1 component of the pattern onset VEP Table 5. Effect of age on the C1 component of the pattern onset VEP

D = Standard Deviation

 $SD = Standard Deviation$ $D =$ Standard Deviation

D = Standard Deviation $SD = Standard Deviation$

 $SD = Standard Deviation$ D = Standard Deviation

The pattern onset-offset response showed similar trends although, due to the variability and the small numbers in each group, significance was only reached for the CI component evoked by the smallest checks and the CII and CIII components evoked by the largest checks (Tables 5, 6, 7, 8).

Amplitude. The flash, pattern reversal and pattern offset VEPs were all found to be $2-3$ times higher in amplitude in the $10-19$ year age groups than in any of the other groups. No further trends in amplitude with age were observed. However, the pattern reversal response to a small check was an exception, showing no significant amplitude differences across the age span, including the 10-19 year age group. The anomalous pattern onset responses in the 10-19 year group were very large, but could not be included in the statistical analysis due to the difficulties of component identification as previously observed (Tables 3-8).

Discussion

The results obtained in the ERG study are in general agreement with those of Martin and Heckenlively (1982) who found a significant decrease in the amplitudes and an increase in the implicit times of the A and B waves with age in both sexes for their dark adapted bright flash ERG. Similar changes have been noted for the dark adapted low intensity ERG recorded in this study. For their photopic ERG, marked reductions were reported for the A and B wave amplitudes, and a marked increase in the B wave implicit time. Our results also show a significant increase for the A wave implicit time. The marked age changes in implicit times found in this study were not observed by Weleber (1981) although it was mentioned that with more data a small correlation might have occurred. Martin and Heckenlively attributed the discrepancy in the results to the difference in methods of analysis, as they used 3 way analysis of variance and Weleber used linear regression. However, another contributing factor could be the diversity in the recording conditions of each type of ERG between laboratories, leading to varying results and thus differences in age trends.

The higher level of significance generally obtained for the parameters of the photopic ERG in comparison to those of the dark adapted ERG could be because the photopic ERG was recorded with red stimulation, which has been found to reveal greater deterioration with age than white stimulation (Williams, 1983).

Small but statistically significant differences in the parameters of the ERG and VEP between males and females have been reported (Zeidler, 1959; Peterson, 1968; Martin and Heckenlively, 1982; Vainio-Mattilo, 1951; Buchsbaum et al., 1974; Dustman et al., 1977; Allison et al., 1983; Stockard, 1979; Halliday et al., 1982). However, separate analysis of the males and females in our study showed that the ageing effects were common to both groups, so these differences did not affect our results.

The differences in VEP waveform that were found in this study have not previously been described. An understanding of these differences is clearly very important for clinical interpretation of results, particularly where younger patients are involved. In the $10-19$ year age group both the flash and pattern onset-offset VEPs show an obscuring of the early components (before llOmsec) by a single high amplitude component. The apparent replacement of the onset VEP by a large positive wave of latency between that of CI and CIII is similar to the waveform described by de Vries-Khoe and Spekreijse (1982) for the developing onset-offset VEP in children up to about 8 years of age. The authors suggest that this reflects an absence or underdevelopment of foveal contrast mechanisms. However, this seems an unlikely explanation in this case, as psychophysical results indicate that spatial and temporal mechanisms have developed to adult levels in the 10-19 year age group (Wright and Drasdo, 1985). In addition, the VEPs evoked by the foveal stimulus shows a greater similarity to those recorded in other adult age groups with respect to both pattern onset waveform (Figure 5) and pattern reversal amplitude (Table 4). It is suggested that, rather than being absent, the early components of the flash VEP and the foveal pattern onset VEP are obscured by high amplitude signals from extrafoveal areas.

In interpretation of the latency and amplitude results, the reduction in pupil size with age must be taken into account. In this study, the mean pupil diameter decreased from 4.9 mm in the 10--19 year age group to 3.15 mm in the 70-79 year age group, representing a reduction in pupil area and hence retinal illuminance, of 0.38 log units.

Halliday, McDonald and Mushin (1973) found that, for a 50 min checkerboard, a l-log unit decrease in mean illuminance resulted in a 15 ms increase in the latency of the pattern reversal VEP. An 0.38 log illuminance decrease would therefore produce an increase of about 5.7 ms, which is consistent with our results for a 56min checkerboard. Our results show a larger latency increase for small checks, consistent with other age studies (Celesia and Daly, 1977; Sokol et al., 1981). For the pattern onset VEP, Van der Tweel, Estevez and Cavonius (1979) showed that a log unit luminance reduction for 40-60 min checks produced a latency increase of 30ms. This would predict a latency increase of the order of 11.4 ms for the pattern onset CII component in our study. This is consistent with our results, although the small numbers and the variability of the pattern onset results do not permit a more detailed analysis. Halliday's amplitude measurements (1980) showed a decrease of the order of 15% per log unit luminance reduction. For the 0.38 log luminance reduction in our study, this would be equivalent to an amplitude reduction of the order of 5%, which would be negligible compared with normal amplitude variability.

For the flash VEP, previous studies have shown a $8-12$ ms increase in P2 latency per log unit (Kinney, 1977; Creutzfeldt and Kuhnt, 1967). This would predict a 3-4ms increase for the 0.38 log luminance reduction across

the life span in our study. In fact, the results showed an overall latency increase of 20 ms, which is consistent with other studies of ageing (Dustman et al., 1977; Buchsbaum et al., 1974; Cosi et al., 1982). This implies that the increase in P2 latency with age is mainly due to neural factors.

These results suggest that flash P2 latency is the most sensitive VEP indicator of the neural factors associated with ageing. This is particularly interesting in view of our results which show that pre-senile dementia (which could be described as an extreme form of ageing) produces a delay of the flash P2 component, but does not affect the latency of the pattern reversal, pattern onset-offset or flash P1 components (Harding et al., 1981, Wright et al., 1984b). These results therefore, contribute to our knowledge of the electrophysiological mechanisms involved with ageing and maturation. They emphasise the importance of fully understanding the changes in latency, amplitude and waveform with age and using appropriate controls in any clinical studies using the ERG or VEP for the diagnosis of pathology.

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References

- Allison T, Goff WR and Wood CC (1979) Auditory, somatosensory and visual evoked potentials in the diagnosis of neuropathology: Recording considerations and normative data. In: Lehmann D, Callaway E, eds. Human evoked potentials $-$ applications and problems. New York, Plenum Press p $1-16$
- Allison T, Wood CC and Goff WR (1983) Brainstem auditory, pattern reversal visual, and short latency somatosensory evoked potentials: latencies in relation to age, sex and brain and body size. Electroenceph Clin Neurophysiol 55:619-636
- Arden GB, Carter RM, Hogg C, Siegel IM and Margolis S (1979) A gold foil electrode: extending the horizons for clinical electroretinography. Invest Ophthal 18:421-426
- Asselman P, Chadwick DW and Marsden CD (1975) Visual evoked responses in the diagnosis and management of patients suspected of multiple sclerosis. Brain 98: 261-282
- Buchsbaum MS, Henkin RI and Christiansen RL (1974) Age and sex differences in averaged evoked responses in a normal population with observations on patients with gonadal dysgenesis. Electroenceph Clin Neurophysiol 37:137-144
- Celesia GG and Daly RF (1979) Effects of aging on visual evoked responses. Arch Neurol 34:403-407
- Copenhaver RM and Perry NW (1964) Factors affecting visually evoked cortical potentials such as impaired vision of varying etiology. Invest Ophthal 3:665-673
- Cosi V, Vitelli E, Gozzoli L, Corona A, Ceroni M and Callieco R (1982) Visual evoked potentials in aging of the brain. In: Courjon J, Mauguiere F, Revol M, eds. Clinical applications of evoked potentials in neurology. New York, Raven Press, pp 109-115
- Creutzfetdt OD and Kuhnt U (1967) The visual evoked potential: physiological, developmental and clinical aspects. Electroenceph Clin Neurophysiol: 26 (Suppl):29-41
- Drasdo N (1976) A method of eliciting pattern specific responses and other electrophysiological signals in human subjects. Brit J Physiol Opt 31:14-22
- Dustman RE and Beck EC (1966) Visually evoked potentials: amplitude changes with age. Science 151:1013-1015
- Dustman RE and Beck EC (1969) The effects of maturation and aging on the waveform of visually evoked potentials. Electroenceph Clin Neurophysiol 26:2-11
- Dustman RE, Schenkenberg T, Lewis EG and Beck EC (1977) The cerebral evoked potential: Life span changes and twin studies in man: Desmedt JE, ed. Visual evoked potentials in man. Oxford, Clarendon Press, pp 363-377
- Halliday AM (1980) Event related potentials and their diagnostic usefulness. In: Kornhuber HH, Deecke L, eds. Motivation, motor and sensory processes of the brain. Progress in Brain Research, Vol 54. Amsterdam, Elsevier/North Holland Biomedical Press, pp 470-485
- Halliday AM, Barrett G, Carroll W and Kriss A (1982) Problems in defining the normal limits of the visual evoked potential. In: Courjon J, Mauguiere F, Revol M, eds. Clinical applications of evoked potentials in neurology. New York, Raven Press, pp **1-10**
- Halliday AM, McDonald Wl and Mushin J (1973) Delayed pattern evoked responses in optic neuritis in relation to visual acuity. Trans Ophthal Soc UK 93:315-324
- Harding GFA, Doggett CE, Orwin A and Smith EJ (1981) Visual evoked potentials in pre-senile dementia. In: Spekreijse H and Apkarian PA, eds Docum Ophthal Proc Ser 27:193-202
- Harding GFA, Williams DE and Innes JA (1984) The visual evoked response and visual psychophysics during Ethambutol therapy In: Proc. 2rid Evoked Potentials Symposium, London, Butterworth (In Press).
- Jeffreys DA (1977) The physiological significance of pattern visual evoked potentials. In: Desmedt JE, ed. Visual evoked potentials in man: new developments. Oxford, Clarendon Press, pp. 134-167
- Karpe G, Rickenbach K and Thomasson S (1950) The clinical electroretinogram. 1. The normal electroretinogram above fifty years of age. Acta Ophthal 28:301-305
- Keppel G (1973) Design and analysis: A researchers handbook. Englewood Clifts N.J., Prentice Hall
- Kinney JAS (1977) Transient visually evoked potential. J Opt Soc Amer 67:1465-1474
- Kooi KA and Bagchi BK (1964) Visual evoked responses in man: normative data. Ann N Y Acad Sci 112:254-269
- Martin DA and Heckenlively JR (1982) The normal electroretinogram Docum Ophthal Proc Ser 31:135-144
- Peterson H (1968) The normal B-potential in the single flash clinical electroretinogram. Acta Ophthal Suppl 99:5
- Shaw NA and Cant B (1981) Age dependent changes in the amplitude of the pattern visual evoked potential. Electroenceph Clin Neurophysiol 51:671-673
- Snyder EW, Dustman RE and Shearer PE (1981) Pattern reversal evoked potential amplitude: Life span changes. Electroenceph Clin Neurophysiol 52:429-434
- Sokol S, Moskowitz A and Towle VL (1981) Age related changes in the latency of the visual evoked potential: influence of check size. Electroenceph Clin Nenrophysiol 51:559-562
- Spekreijse H, Van der Tweel LH and Zuidema TH (1973) Contrast evoked responses in man. Vision Res 13:1577-1601
- Stockard JJ, Hughes JF and Sharborough FW (1979) Visually evoked potentials to electronic pattern reversal: latency variations with gender age and technical factors. Amer J EEC Technol 19:171-204
- Straub W (1961) Einige Erkrankungen des Sehnerven in electroretinographischer Sicht. Vision Res i :220-227
- Valnio-Mattilo B (1951) The clinical electroretinogram: The difference between the electroretinogram in men and women. Acta Ophthal 29:25-32
- Van der Tweel LH, Estevez O and Cavonius CR (1979) Invariance of the contrast evoked potential with changes in retinal illuminance. Vision Res 19:1283-1287
- Vries-Khoe LH de and Spekreijse H (1982) Maturation of luminance and pattern EPs in man. Docum Ophthal Proc Ser 31:461-475
- Weleber RG (1981) The effect of age on human cone and rod Ganzfeld electroretinograms. Invest Ophthal 20:392-399
- Williams DE (1983) The effect on visual electrophysiological investigations of substances primarily inducing a deleterious effect on the retinal ganglion cells and/or higher up in the visual pathway. Unpublished PhD thesis. The University of Aston in Birmingham, England.
- Wright CE and Drasdo N (1985) The influence of age on the spatial and temporal contrast sensitivity function. Docum Ophthal 59:385-395
- Wright CE, Drasdo, N and Harding GFA (1984a) Electrophysiological and psychophysical studies on suspected unilateral retrobulbar neuritis. Transactions of the 1st International congress of the British College of Ophthalmic Opticians, Vol 1, pp 69-93
- Wright CE, Harding GFA and Orwin A (1984b) Pre-senile dementia $-$ the use of the flash and pattern VEP in diagnosis. Electroenceph Clin Neurophysiol 57:405-415
- Zeidler I (1959) The clinical electroretinogram. The normal ERG value of the B potential in different age groups and its differences in men and women. Acta Ophthal 37:294-301
- Zetterstrom B (1956) Studies on the postnatal development of the electroretinogram in newborn infants. Stockholm, Karolinska Sjukuset