Pattern visual evoked potentials in hyperthyroidism

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SUMMARY Pattern reversal visual evoked potentials (VEPs) have been elicited in 16 female hyperthyroid patients before and after treatment and compared with those from a similar group of age and sex matched control subjects. No effect on latency was seen, and although larger amplitude values were noted in the thyrotoxic group these too were not significant. We would conclude that hyperthyroidism per se has little effect on the pattern reversal VEP, and any observed effect on these potentials is probably due to other factors.

Thyroid disease is a known cause of nervous system dysfunction. Hypothyroidism has been reported to affect both the electroencephalogram (EEG)¹ and the visual evoked potential (VEP) to flash stimulation, the feature of note in the latter being a delay in conduction.² In more recent studies utilising the VEP to pattern stimulation this observed delay was shown to show reversibility after appropriate treatment.^{3,4} While hyperthyroidism has been shown to produce a so-called 'fast' rhythm EEG⁵ (a feature which was observed to disappear when the patients became clinically euthyroid), to our knowledge only one study has investigated VEPs in hyperthyroidism⁶ and this adopted flash stimulation. No effect on latency was observed, though larger amplitudes were noted.

It is obviously important to be aware of any abnormalities in the VEP that are due to hyperthyroidism if electrodiagnostic techniques are to be used in the treatment of any optic nerve disease which may result from such thyroid dysfunction. The intention of this study therefore was to investigate the pattern VEP in hyperthyroid patients before and after treatment and to compare the results with an appropriately matched group of control subjects.

Patients and methods

Sixteen hyperthyroid patients (mean age and SD=38.3 and 7.2 yr), all female, and with biochemically proved (untreated) thyrotoxicosis, were recruited

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from the endocrine clinic. Patients with eye disease unrelated to thyroid disease or receiving drug therapy which could influence the VEP were excluded. All patients had a full ophthalmic assessment which consisted of measurement of corrected visual acuity, biomicroscopy, tonometry, funduscopy, exophthalmometry, and assessment of ocular motility and visual fields. Apart from the results of exophthalmometry and ocular motility assessment the patients were found to be normal. Most of the group had mild thyroid eye disease consisting of slight proptosis and lid retraction. Two patients developed extraocular muscle involvement during the study; however, there were no cases of corneal ulceration or optic nerve compression. VEP investigations were performed on patients in the thyrotoxic state and then repeated at least six months after they had been rendered euthyroid. Control of the disease was medical (nine cases), surgical (three cases), and by radioactive iodine (four cases).

The control group comprised 16 female subjects who were age matched to the patient group not only with respect to mean and standard deviation (37.6 ± 10.5 yr) but also in the distribution of ages. They were selected on the criterion that they were ophthalmologically normal in all respects.

ELECTROPHYSIOLOGY

The checkerboard stimulus was produced by a video pattern generator on a high quality TV monitor. Luminance modulation of the pattern was selected to give the pattern reversal mode of stimulation at a rate of 2 per second. The checksize of the stimulus was 50'

and the visual field subtended, $17^\circ \times 14^\circ$. The overall luminance of the TV screen—with and without pattern—was maintained constant at 10.4 Cd M^{-2} . Pattern contrast (defined as $(L_{\max} - L_{\min}) / (L_{\max} + L_{\min})$ where $L_{\max}$ and $L_{\min}$ are the luminance of the bright and dark checks respectively) was adjusted to be 95%.

Silver/silver chloride disc electrodes were attached to the scalp with collodion in the following positions as defined by Jasper⁷: active—Oz, reference—Cz, earth—Pz. A Medelec electrophysiological recording unit was used to amplify, average, and store the evoked potentials. The amplifier band width was 0.8–80 Hz, and either 64 or 128 epochs of 300 ms duration were averaged depending on the size of the response. Two averages were obtained under each stimulus condition to check for consistency, and quantitative analysis was performed on the average of these two. The patients were given short periods of rest between each separate measurement so as to minimise fatigue and any concomitant increase in response variability. With respect to latency, the P100 component was analysed, and for amplitude a peak-peak measure between components P100–N150 was adopted. A permanent record of the responses was made on an X-Y plotter.

Monocular stimulation was adopted in all investigations, the subject being instructed to maintain fixation and focus on a small LED marker attached to the centre of the screen. This was monitored during the investigation by closed circuit TV.

Prior to the commencement of the test the subject was preadapted to the luminance of the blank screen for 5 minutes. This was the only source of illumination in an otherwise darkened room. The test was concluded with the measurement of the subject's pupil size under experimental conditions.

STATISTICS

In terms of absolute measurements of both latency and amplitude one value was selected for analysis at random from either the right or left eye in both control and patient groups. In addition, the magnitudes of interocular differences in latency and amplitude were also computed to facilitate comparison between distributions where interindividual differences in absolute values had been eliminated. Normal parametric distributions were assumed and therefore significance was determined by Student's *t* test. The level of significance chosen for the study was 1% ($p \leq 0.01$).

Results

Characteristic VEPs from the right and left eyes of a control subject are illustrated in Fig. 1a. The main

Fig. 1 VEPs from a control subject (a) and from a patient, before treatment (b) and after treatment (c).

components of these responses, namely the P100 and N150, are clearly evident in both RE and LE tracings. In Figs. 1b and 1c the VEPs elicited from a hyperthyroid patient before and after treatment are shown for comparison. There appeared to be little qualitative difference in the form of either set of responses, both in relation to each other or to those observed in the control subject. With respect to P100 latency, no overt differences were apparent, but amplitudes appeared to be somewhat larger in the responses from the patient than those from the control subject.

Fig. 2 Scattergrams of absolute P100 latency (a) and interocular latency difference (b) in control and patient groups. CL=confidence limit.

When the entire control and patient group data were analysed the impressions gained from the previous two subjects were essentially found to be representative of the complete study. In Fig. 2a scattergrams of P100 latency in the control group and before and after treatment in the patient group are illustrated. No apparent difference in the separate distributions was evident, a feature confirmed when mean and standard deviations were calculated (these are indicated at the top of each column). The 99% confidence level is shown drawn through the data. When interocular latency differences were considered (Fig. 2b), a similar picture was observed in

Fig. 3 Scattergrams of absolute P100 amplitude (a) and interocular latency difference (b), in control and patient groups. CL=confidence limit.

that no significant differences in the control and patient distributions or their respective means were noted.

As regards VEP amplitude, scattergrams of these data are presented in Fig. 3a. The large interindividual variability (which is characteristic of EP absolute amplitude measures in general) is seen in both control and patient groups. But even when this was allowed for there appeared to be a small shift to larger amplitudes in the distribution for (pretreatment) patients. This feature was confirmed when the means and standard deviations for the various groups were calculated. However, the increased mean in the pretreatment patient group was found to be not quite significant ($0.05 > p > 0.01$). Interestingly, what difference there was appeared to resolve in the post-treatment group. Analysis of interocular amplitude

differences, of course, eliminates one source of interindividual variability and consequently results in much narrower distributions. These are illustrated in Fig. 3b. Once again there appeared to be some difference in the pretreatment group distribution in comparison with that for the control group. However, this was not significant when the respective means were compared statistically, though four individuals in this group were outside the 99% confidence limit. It is noteworthy that, after treatment, interocular differences in three of these four became insignificant.

Discussion

It is important in the study and application of evoked potentials that due consideration be given to the influence of sex and age on both diseased and control populations. VEPs are known to be affected by such factors,⁸ and therefore to minimise their influence on the findings it is necessary to match control and pathological groups appropriately.

From the results of this study it would seem that high levels of circulating thyroid hormone have little effect on conduction in the visual pathways, as no changes in VEP latency were observed. There may, however, be some influence which serves to increase VEP amplitude (a feature which agrees with previous observations utilising the flash VEP),⁶ but the results of our trial are not statistically conclusive. In addition the broad distribution of this measure in both control and patient groups tends to militate against its use in routine clinical investigation. Thus, with the limited confidence which a trial of this size allows, we would conclude that hyperthyroidism has only a small effect on the VEP, both on presentation and throughout a course of treatment, notwithstanding the fact that no period of prolonged hypothyroidism has intervened.

The relevance of such findings in the management of thyroid eye disease must be that the observation of a delayed VEP is probably due to other factors (excluding other confounding neuro-ophthalmic disorders or artefacts due to optical or medial factors). This is certainly the case in patients who are hyperthyroid or euthyroid, and, while in hypothyroid patients some conduction delay may occur as a result of their thyroid status, it should be remembered that this does not occur in every case and, even when it does, only slowly after a prolonged alteration in thyroid hormone level.

The authors are indebted to Professor P Kendal-Taylor, Endocrine Unit, Royal Victoria Infirmary, for kindly granting access to patients investigated in this study, and to Mrs Karen Seed, senior medical physics technicians, who skilfully elicited a large proportion of the data.

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Accepted for publication 1 May 1987.