Electrophysiology and colour perimetry in dominant infantile optic atrophy

T A Berninger, W Jaeger, H Krastel

Abstract
A typical finding in dominant infantile optic atrophy (DIOA) is the variation of the phenotypic expression of the DIOA gene even within one family. It is of special interest for genetic consultation to evaluate an examination method for detecting subclinically involved patients. Seven patients of two families were examined. Three of them had the typical symptoms of DIOA: reduced visual acuity, tritan defect, temporal pallor of both optic discs, and a relative central scotoma for white test spots. In visual evoked cortical potentials (VECP) the amplitudes were reduced, and in one patient the latencies were slightly delayed and two patients considerably so. The amplitude of the negative component of the PERG was markedly reduced, while the positive component was normal. In the remaining four family members normal retinal and cortical responses were recorded under standard conditions and visual fields and colour vision (FM 100 hue) were also normal. However, static perimetry with blue test spots showed in two family members enlarged central scotomas, thus proving that they had subclinical DIOA.

A tritan defect forms the decisive diagnostic clue to most cases of dominant infantile optic atrophy (DIOA). François and Verriest found that the colour arrangement tests are particularly suitable for diagnosing such acquired tritan defects. In particular the desaturated Panel D15 has proved to be successful in the early detection of tritan defects in dominant optic atrophy. These findings are inconsistent with Koellner's rule that lesions of the receptor and bipolar retinal layers cause loss of blue-yellow sensitivity and that lesions of the ganglion cells and pre-geniculate pathways affect red-green.14 Histological findings, however, identified the retinal ganglion cells as the site of primary damage in DIOA. Further, it is striking that the phenotypic expression of the DIOA gene varies even within a family, ranging from severely affected patients who have both red-green and blue-yellow defects to those scarcely affected in whom not even a tritan defect can be observed. Visual fields tested in the usual clinical manner frequently show only mild abnormalities or at times appear normal.15 Even the optic nerve may show only questionable pallor or appear normal in some individuals. Krill et al therefore recommended that an experienced ophthalmologist should examine the optic nerve head so that subtle changes might also be detected.

The aim of this study was the evaluation of methods for detecting subclinical involved patients with DIOA.

Patients and methods
Two families (family A: five members; family B: two members) were examined. We recorded the best corrected visual acuity and the results of slit-lamp biomicroscopy, Tübingen automatic perimetry (TAP) (family A), the Goldmann visual field test (family B), the Farnsworth-Munsell 100-hue test (A2, A3, A4, A5), the Panel D-15 desaturated test (A1, B1, B2), funduscopy, pattern reversal evoked cortical potentials (VECP), and pattern reversal electroretinogram (PERG) tests.

VISUAL EVOKED CORTICAL POTENTIALS (VECP)
The standard conditions for the VECP were as follows: Checkerboard pattern stimuli were generated on a black-and-white TV monitor. The field size of the screen subtended 14.5° by 18.5° and the checks were 38 min of arc. The mean luminance was 30 cd/m² and the modulation depth was 0.97. The checks were temporally alternated at a modulation rate of four reversals/s (2 Hz). The active electrode was attached 2–3 cm above the inion. The right ear was earthed and the reference electrode fixed to the left ear. All VECP recordings were monocular. In some cases the mean luminance was reduced to 10 cd/m² and the modulation depth to 0.2 (reduced contrast test).

PATTERN ELECTRORETINOGRAM (PERG)
Arden gold foil electrodes were used. The reference electrode was placed on the ipsilateral temple, thus minimising retinal and cortical contamination. The stimulus was provided by a checkerboard pattern reversal on a TV screen of 14.5° by 18.5°. The visual angle of each square was 50 min of arc, modulation depth 0.97, reversing rate 4 rev/s (2 Hz).

Retinal and cortical potentials were amplified by a Medelec AA6 with bandpass setting 0-16 and 32 Hz and averaged by a Nicolet 1170. Four samples of 64 sweeps were used to obtain the final result.

COLOUR VISUAL FIELD
With the Tübingen automatic perimeter (TAP) white and blue test spots of 0.16° diameter were presented for 200 ms. Yellow adaptation (Schott OG 530 nm cutoff filter) was applied to isolate the activity of the blue system. Luminance distribution was adjusted to compensate for the loss of sensitivity towards the periphery (for details see Krastel et al). A small foveal scotoma was obtained for normal subjects using blue test spots, which is due to the foveal tritanopia.
COLOUR VISION

Colour vision was tested by Farnsworth-Munsell 100-hue, Panel D-15 desaturated test, tritanomaly, and spectral increment thresholds.

Results

VISUAL EVOCA TED CORTICAL POTENTIALS

The visual evoked potentials were only abnormal in the severely affected patient (A3, B1, B2) (Fig 1). In B1 and B2 a positive-negative-positive (PNP) complex was observed. In contrast, patient A3 had a broad positive deflection with only a slight delay of the P-100 latency.

PATTERN ELECTRORETINOGRAM

PERGs were obtained in all patients. Normal positive components were measured in all seven patients. The negative components of the patients A1, A2, A4, and A5 were also in the normal range. However, a significantly reduced negative component was found in other patients (A3, B1, B2) with definite DIOA.

COLOUR VISUAL FIELD

The visual fields of both members of family B were tested with a Goldmann perimeter. A central scotoma was found in both patients. All members of family A were tested with the TAP. With the white test spot a central scotoma was observed only in patient A3. His father (A1) and his eldest sister (A4) also had a normal visual field for blue test spots, but the mother (A2) and the younger sister (A5) both had an enlarged central scotoma (Figs 3 and 4).

COLOUR VISION

Four patients (A2, A3, A4, A5) were tested with the Farnsworth Munsell 100-hue test and three (A1, B1, B2) with the Panel D-15. Colour arrangement tests detected an obvious defect only in those patients (A3, B1, B2) who showed significant signs of the disease. However, we observed one obligate and one possible carrier of the gene, who according to the conventional tests (visual acuity, colour arrangement, white perimetry) seemed to be not involved. For reasons of colour perimetry (see Discussion) we regarded these patients (A2, A5) as subclinically affected. The results of the tritanomalscopy and spectral sensitivity are published elsewhere.²²
positive component which is not specific to changes in retinal distribution of contrast, followed by a negative wave showing spatial tuning across temporal frequency. Recently Holder observed that the positive component of the PERG is reduced in macula diseases while in optic nerve disease the negative component of the PERG is selectively decreased, and this has been confirmed. DIOA is a clear-cut case of damage confined to the optic nerve, and our findings in the patients A3, B1, and B2 thus strengthen the claim that the negative PERG component is affected in optic nerve defects. Papst et al. observed a normal positive component of the PERG in their patients, as we did in cases (A3, B1, B2). However, again normal results were obtained for our subclinically involved family members (Fig. 2).

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