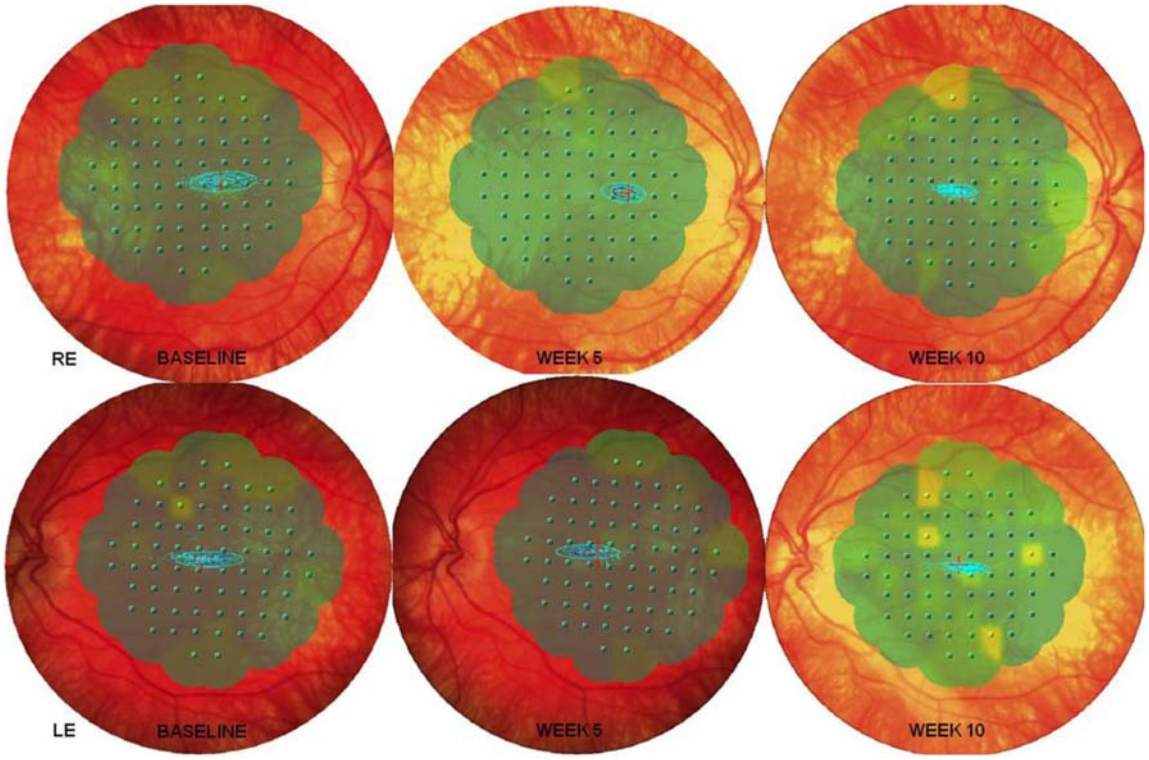

Fig. 2—Microperimetry (MP-1) images showing retinal sensitivity map and bivariate contour ellipse area at each follow-up. LE, left eye; RE, right eye.

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Rehabilitation with MP1 biofeedback training of a posterior microphthalmos case

Posterior microphthalmos is a rare disorder that affects the posterior ocular segment in cases with a normal anterior segment. They exhibit recessive form of inheritance and no associated systemic abnormalities.[1–3] Its main characteristics are high hyperopia and bilateral papillomacular retinal folds. Posterior microphthalmos with bilateral papillomacular retinal folds has been found to be associated with amblyopia probably related to the site of macular fold at the fovea.[2] Nystagmus also has been a clinical finding of this rare congenital disease.[3]

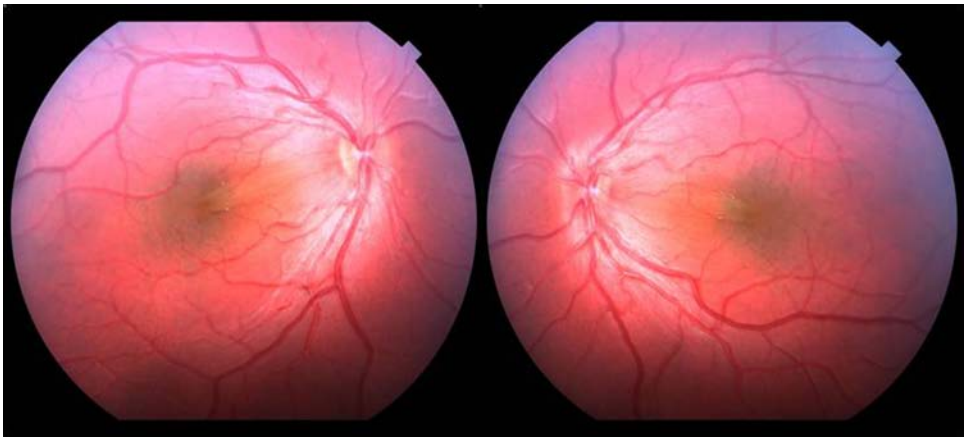

Fig. 1—Fundus colour photograph showing bilateral papillomacular fold with hard exudates at the edge and in the context of the retinal fold close to the fovea.

We report a case of a 7-year-old female with posterior microphthalmos with bilateral papillomacular folds, presenting with nystagmus and bilateral amblyopia. Best corrected visual acuity was 0.4 logMAR, and cycloplegic spherical equivalent refraction was +14.00 D in both eyes. She had horizontal saccadic nystagmus. The anterior segment and ocular alignment at distance and near were normal. Optical coherence tomography (OCT) measurements showed an anterior chamber depth of 2.61 mm in the right eye (RE) and 2.68 mm in the left eye (LE), and a cornea white-to-white diameter of 11.01 mm in the RE and 10.61 mm in the LE. The axial length measured using A-scan echography was of 17.15 mm in the RE and 17.21 mm in the LE.

Fundus examination after pupil dilation showed bilateral papillomacular retinal folds extending from the fovea nasally (Fig. 1). Spectralis OCT (Heidelberg Retina Angiograph (HRA) + OCT; Heidelberg Engineering, Heidelberg, Germany) scans showed neurosensory folding involving the inner layers, the outer plexiform layer, and part of the inner nuclear layer. The external limiting membrane and photoreceptor inner segment–outer segment junction showed a normal profile. The retinal pigment epithelium choriocapillaris complex and the underlying choroid showed normal profile and morphology (Fig. 2).

Microperimetry examinations using the MP1 instrument (Nidek Technologies Srl, Padova, Italy) were performed under dark conditions after pupil dilation: a red circle of

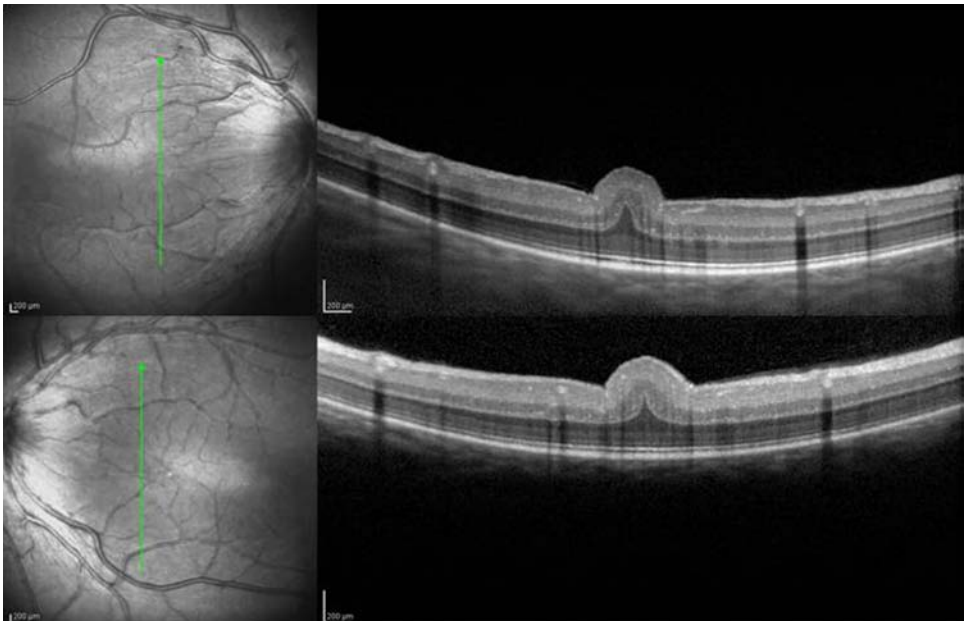

Fig. 2—Spectral-domain optical coherence tomography (vertical scan) scans showing the presence of neurosensory folding involving the inner layers, the outer plexiform layer, and part of the inner nuclear layer. The external limiting membrane, photoreceptor inner segment–outer segment junction, and the retinal pigment epithelium–choriocapillaris complex showed normal profile and morphology.

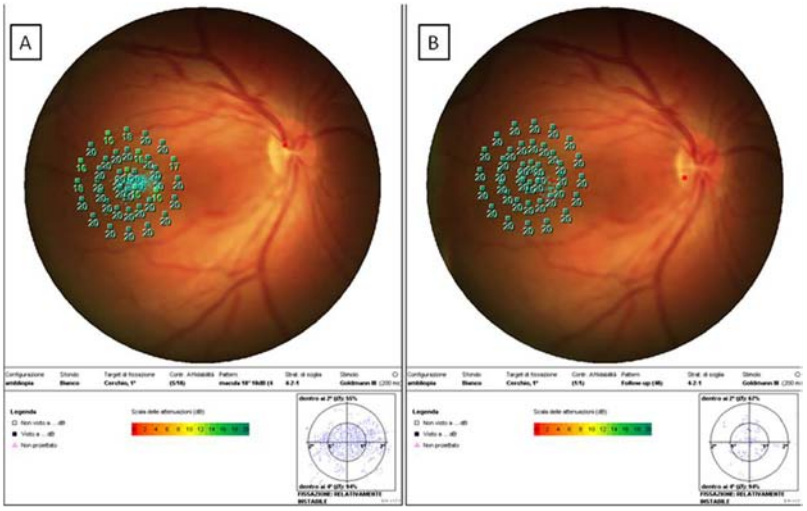

Fig. 3—A, Image shows fundus-related perimetry of right eye at baseline presenting relatively unstable fixation behaviour in the foveal area, with 55% of the fixation points within the 2-degree diameter circle and 94% of the fixation points within the 4-degree diameter of the central retina. B, Image shows improvement of fixation after visual rehabilitation with relatively unstable fixation, with 67% of the fixation points within the 2-degree diameter circle and 94% of the fixation points within the 4-degree diameter of the central retina.

1 degree was used as fixation target, white background luminance of 4 apostilbs, stimulus size Goldmann III with projection time of 200 milliseconds, and a customized grid of 40 stimuli covering the central 10-degree diameter circle of the central retina. A 4-2-1 staircase strategy was used. At baseline, mean retinal sensitivity was 19.2 dB in the RE and 19.9 dB in the LE. Fixation behaviour was relatively unstable with 55% of the fixation points within the 2-degree diameter circle and 94% of the fixation points within the 4-degree diameter of the central retina in the RE, and 74% of the fixation points within the 2-degree diameter circle and 98% of the fixation points within the 4-degree diameter in the LE.

The low-vision rehabilitation program administered consisted of 10 training sessions of 10 minutes for each eye, performed once a week using the MP-1 biofeedback training module. The fixation target used was a flickering black and white checkerboard pattern.

Following the training sessions, best corrected visual acuity was 0.18 logMAR in both eyes. Mean retinal sensitivity was 20 dB in both eyes. Fixation behaviour was relatively unstable in the RE, with 67% of the fixation points within the 2-degree diameter circle and 94% of the fixation points within the 4-degree diameter of the central retina, and was stable in the LE, with 89% of the fixation points within the 2-degree diameter circle and 98% of

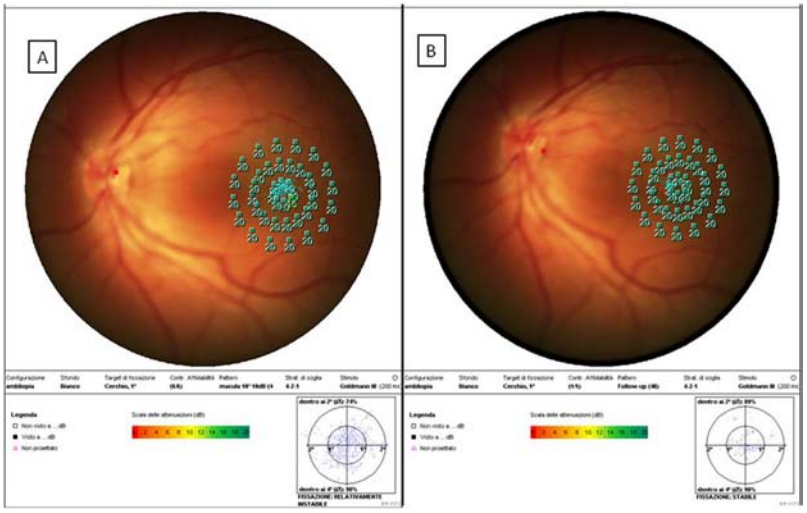

Fig. 4—A, Image shows fundus-related perimetry of left eye at baseline presenting relatively unstable fixation behaviour in the foveal area, with 74% of the fixation points within the 2-degree diameter circle and 98% of the fixation points within the 4-degree diameter. B, Image shows improvement of fixation after visual rehabilitation with stable fixation, with 89% of the fixation points within the 2-degree diameter circle and 98% of the fixation points within the 4-degree diameter.

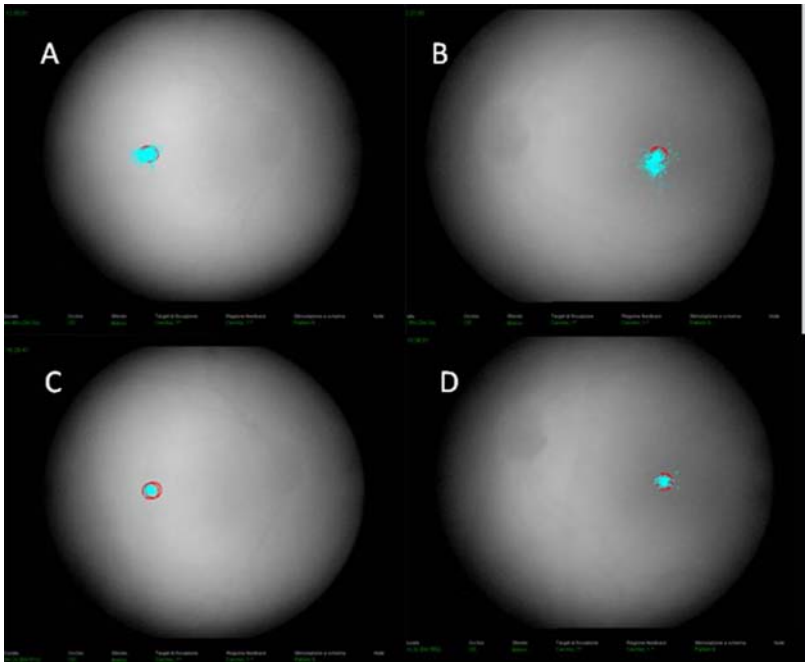

Fig. 5—A and B, Images show fixation stability at baseline of right and left eye, respectively. C and D, Images show evidence of an increase of fixation stability with concentration of fixation points in a smaller area.

the fixation points within the 4-degree diameter (Figs. 3, 4, and 5).

At baseline in the RE, total shift of fixation on x-axis (Xmax – Xmin) was 6.92 degrees (2.31 – [–4.61]) and total shift of fixation on y-axis (Ymax – Ymin) was 3.73 degrees (1.99 – [–1.74]) with a mean velocity of 2.51 deg/s; after rehabilitation, total shift of fixation on x-axis (Xmax – Xmin) was 5.42 degrees (3.68 – [–1.74]) and total shift of fixation on y-axis (Ymax – Ymin) was 3.12 degrees (1.56 – [–1.56]) with a mean velocity of 2.43 deg/s. In the LE, total shift of fixation on x-axis (Xmax – X min) was 8.23 degrees (4.55 – [–3.68]) and total shift of fixation on y-axis (Ymax – Ymin) was 8.17 degrees (5.86 – [–2.31]) with a mean velocity of 3.69 deg/s; after rehabilitation, total shift of fixation on x-axis (Xmax – Xmin) was 4.05 degrees (2.80 – [–1.25]) and total shift of fixation on y-axis (Ymax – Ymin) was 3.37 degrees (1.25 – [–1.12]) with a mean velocity of 2.30 deg/s.

Microperimetric rehabilitation with audio feedback has been described in patients with macular diseases and loss of foveal function. It was used to train patients to use preferred retinal loci (PRL) or to create another PRL in the proximity of the fovea.[4–6]

In our patient, microperimetric rehabilitation training with pattern stimulation improved fixation behaviour, retinal sensitivity, and visual acuity. In the presence of a central scotoma, it has been postulated that biofeedback training can help the brain to use an input from a new PRL to access the foveal occipital cortex. Auditory feedback stimulate the attention of the patient with increasing the time spent on the PRL. Furthermore, a pattern fixation target enhances inner retina integration processes and optimizes stimulus processing, recognition, and in-brain transmission.[7] In our case, stimulation of fixation with a pattern stimulus coupled to auditory biofeedback probably increasing foveation time improved stability of fixation. Moreover, increased foveation time probably reduced nystagmus and, consequently, improves visual function.

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Visual function and risk genotypes in maternally inherited diabetes and deafness

Maternally inherited diabetes and deafness (MIDD) is an autosomal dominant inherited syndrome caused by the mitochondrial DNA (mtDNA) nucleotide mutation A3243G. It affects various organs including the eye with external ophthalmoparesis, ptosis, and bilateral macular pattern dystrophy.[1,2] The prevalence of retinal involvement in MIDD is high, with 50% to 85% of patients exhibiting some macular changes.[1] Those changes, however, can vary between patients and within families dramatically based on the percentage of retinal mtDNA mutations, making it difficult to give predictions on an individual's visual prognosis.

MIDD progresses slowly over several years and has a good visual prognosis when confined to the perifoveal region.[3,4] However, atrophic areas can progress toward the fovea with central vision loss mimicking geographic age-related macular degeneration (AMD). Associations between mtDNA mutations and AMD have been proposed, with patient's mtDNA showing high levels of single nucleotide polymorphisms (SNPs).[5] A common SNP in the complement factor H region has been repeatedly associated with AMD, and the similarity of atrophic changes in MIDD with geographic AMD raises the question of a common pathway.[3] Bilateral macular pattern dystrophy in MIDD has been well documented in localized areas of reduced neuroretinal function using multifocal electroretinography (mfERG)[6] and fundus autofluorescence.[3] No study, however, has longitudinally investigated vision function loss using microperimetry in MIDD and the relationship with AMD high-risk genotypes.

A 50-year-old female patient diagnosed with MIDD and confirmed with mtDNA A3243G mutation in 2000 presented to our research laboratory first in 2007. She was glucose intolerant and had no neurosensory hearing loss. The patient's history revealed a mother and sister with no MIDD-related symptoms and a brother with deafness and vision problems caused by myopia. The study was approved by the Queensland University of Technology (QUT) Ethics Committee, and informed consent was obtained from the participant.

The patient was followed up over 4 years (3 visits: 2007, 2009, and 2011). We performed mfERG (VERIS III, Redwood City, USA) according to the International Society for Clinical Electrophysiology of Vision (ISCEV) standard[7] (visits 2007 and 2009), optical coherence tomography (OCT; Stratus OCT; Zeiss, Oberkochen, Germany; visits 2007, 2009, and 2011) and microperimetry (MP1-microperimeter; Nidek Technologies, Padua, Italy) (visits 2009 and 2011). The mfERG responses were recorded with DTL-electrodes, and established recording and analysis techniques were used.[8,9] We determined trough-to-peak response densities (N1P1-RD) and peak implicit times (P1-IT), and responses were averaged into 4 rings.[8] For microperimetry, we used a 2-1 threshold strategy, a Goldman IV stimulus, and the macula (Humphrey 10-2) program (68 stimuli, 20 degrees), and mean sensitivity (MS) was determined. We applied the MP-1 "follow-up" testing method in 2011, which allows repeating the previous test on exactly the same retinal area using the same test parameters applied in 2009.

At her first visit in 2007, the participant's visual acuity was 6/30 and 6/7.5 in her right and left eye, respectively (Table 1). On fundus examination, chorioretinal atrophic areas were present in both eyes, sparing the fovea in her left eye (Fig. 1). No signs of diabetic retinopathy were evident. MfERG (in 2007 and 2009) demonstrated corresponding reduced N1P1-RD and centrally impaired P1-IT (Fig. 2) compared with normative data[6,10] (Table 2). The OCT revealed central retinal thinning in her right eye and normal central retinal thickness in her left eye compared with normative values[11] (Table 1). On follow-up in 2009, retinal atrophic changes, as well as visual acuity and mfERG responses, remained stable, but there was a reduction in central retinal thickness in her right eye (Tables 1 and 2). In 2009, microperimetry was performed and demonstrated reduced MS corresponding to the atrophic areas (Fig. 1, top). In 2011, visual acuity had deteriorated by one line in her left eye but was stable in her right eye with no change in central retinal thickness (Table 1). MfERGs were not performed during this visit. With microperimetry, a stable fixation could be achieved (between 93% and 100% stable within 2 and 4 degrees) at both assessments and a progression of the disease toward the fovea in her left eye was found in addition to further

Table 1—Visual acuity and central retinal thickness (optical coherence tomography) in a patient with maternally inherited diabetes and deafness at 3 time points over 4 years

Year	VA-RE	VA-LE	OCT-RE	OCT-LE
2007	6/30	6/7.5	185	214
2009	6/30	6/7.5	158	203
2011	6/30	6/9.5	154	210

VA, visual acuity; RE, right eye; LE, left eye; OCT, optical coherence tomography.