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CLINICAL INVESTIGATION

Development and surgical removal of an epiretinal membrane in infantile nystagmus syndrome: a new type of oscillopsia

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Abstract

Purpose To report and discuss a focal oscillopsia in a small area of the visual field produced by, and after the removal of, an epiretinal membrane (ERM) in an individual with infantile nystagmus syndrome (INS) since birth with no associated afferent visual deficits.

Study Design A retrospective case report.

Methods A chart review, including clinical and electrophysiological data. A 74 y/o man with INS and an epiretinal membrane was studied. Detailed studies of the retina post-removal of an epiretinal membrane, with consequent changes in best-corrected visual acuity (BCVA), and subjective oscillopsia compared to INS waveforms. OCT measurements and eye-movement data from digital video and scleral search-coil systems were used.

Results The monocular ERM produced an unexpected focal area of torsional/vertical oscillopsia (noted 1 year prior to the ERM surgery) in the portion of the visual field that corresponded with distortions from the ERM. The remainder of the visual field, corresponding with normal healthy retina was unaffected and stable in all planes. Post-removal, BCVA improved with redevelopment of the foveal pit and focal oscillopsia became less noticeable but remained due to the retinal distortion.

Conclusions In patients with INS, complete oscillopsia suppression across the visual field requires undistorted vision. If a retinal area of visual distortion develops or results from retinal surgery, a symptomatic island of oscillopsia in one or more planes may result.

Keywords Epiretinal membrane · Nystagmus · Oscillopsia · Surgery

Introduction

Infantile nystagmus syndrome (INS, formally called, "congenital nystagmus") [1] is a bilateral conjugate nystagmus that can be pendular, jerk, elliptical, or circular and exhibits distinct waveforms [2]. Visual function can be near normal and oscillopsia, the perception of an unstable oscillating visual world, is rare [3]. Abadi and Bjerre suggest a significantly higher percentage of oscillopsia at some point (40% of 224 subjects) [4]. There is a large body of literature reporting research on oscillopsia [5–18]; this is the first report examining the association between an epiretinal membrane (ERM), its removal, and oscillopsia. When oscillopsia occurs in patients with INS, it is full field (global), typically transient, and can be brought on by exhaustion, illness, or sensory deficits that reduce contrast.

We report a patient with INS (unassociated with visual sensory deficits) who developed an ERM resulting in uniocular oscillopsia only in the small area of visual field corresponding to the ERM.

Patients and Methods

Clinical information was obtained from the patient's medical record/chart, and from electrophysiological data.

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Eye-Movement Recording

Written consent was obtained from the subject before testing. All test procedures were carefully explained to the subject before the recording began, and were reinforced with verbal commands during it. The work adhered to the tenets of the Declaration of Helsinki and was IRB approved. The subject was seated in a chair with a headrest and either a bite board or a chin stabilizer, far enough from an arc of red LEDs to prevent convergence effects (> 5 feet). At this distance the LED subtended less than 0.1□ of visual angle. The room light could be adjusted from dim down to blackout to minimize extraneous visual stimuli. Both a high-speed digital video system and search-coil system were used for the eye-movement recordings [19].

Results

Case Report

The patient was a 74-year-old white man with no relevant past medical history, no prior eye surgery, and a past ophthalmic history of INS and intermittent esotropia. Best-corrected visual acuity (BCVA) with manifest refraction was 20/40 OU (OD: +1.25 S, +2.75 C, ax 60 and OS: +1.00 S, +2.75 C, ax 120); BCVA was also tested OU with the patient's normal glasses (7 PD BO prisms added to his refraction). The induced convergence and improved foveation of this binocular (optically aligned) patient maximized his BCVA; he has always had, and still has, normal stereo acuity. However, the resulting acuity remained 20/40; on a previous visit, prior to the development of the ERM and cataracts, his visual acuity was 20/25.

He presented with a chief complaint of, "When I read, some of the letters appear fuzzy (despite correction) and are moving." When he occluded his left eye (RE fixation), the letters were clear and stable. However, when he occluded his right eye (LE fixation), the letters were both blurred and oscillated mainly in the torsional plane possibly containing a small, transient vertical component; a more detailed description can be found in a preliminary report [20]. Although the RE provided a clear and stable picture of the visual scene during binocular viewing, its occlusion resulted in a significant deficit in reading both printed material and an even greater deficit in attempting to read street signs while driving. It was also noted by the patient that during LE fixation, all horizontal lines or edges within and to the left of the fixation point appeared to bow downwards, producing a small area of curved distortion (top portion of Fig. 1).

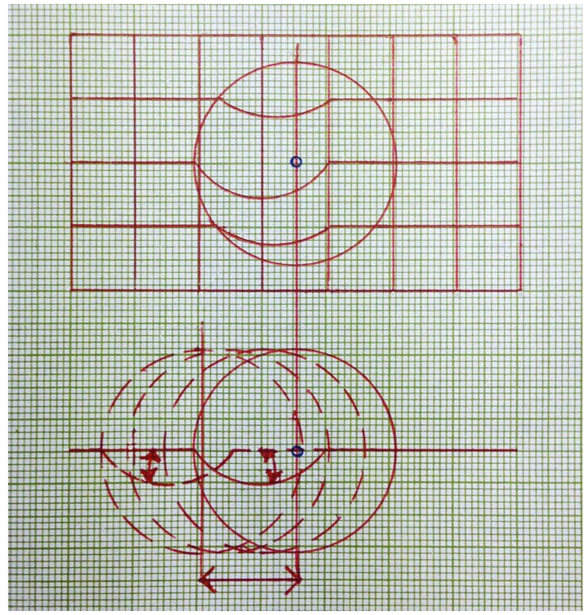

Fig. 1 Illustration of the perceived downward bowing of horizontal contours of images on and to the left of the fovea and para-foveal area (top) of the affected eye and the perceived torsional oscillation of the bowed distortion caused by the horizontal component of the nystagmus oscillation (bottom). Perceived motion of the horizontal line passing through the fixation point was chosen to illustrate the torsional oscillation of all horizontal contours within the distorted retinal area (see text). The target grid, with 2° by 2° spacing between all grid lines, is drawn approximately to the same scale as the thickness diagrams in Fig. 3, the fixation point is the small circle in the center of the foveal area, and the horizontal component of the infantile nystagmus (indicated by the horizontally shifted distortion area) is drawn to correspond to the ~3° peak-to-peak horizontal components shown in the top part of Figure 4; the mechanism would not differ if we used some of the lower amplitude cycles

Surgery

After retrobulbar anesthesia, the left eye was prepped and draped and a lid speculum was placed between the lids. A 25-guage trocar and cannula system were placed in the usual fashion for phakic 3-port vitrectomy. A complete vitrectomy was performed and the posterior hyaloid was separated from the retinal surface. The ERM was peeled in a single large sheet from the macula using barbed MVR blade. The pre-retinal peeling was extended mid periphery using the vitreous cutter. The cannula was removed and left at low normal intraocular pressure. Subconjuctival injection of 10 mg Decadron and 20 mg of Vancomycin were conducted in the inferonasal fornix. The eye was dressed with TobraDex ointment, homatropine drops, a light patch, and a Fox shield. The eye was free of iatrogenic damage and stable; there were no operative complications.

The patient's symptoms were still present immediately after surgery. However, as the foveal architecture gradually returned to normal, his pre-op symptoms of image blur slowly improved and oscillopsia became less noticeable but did not actually change; i.e., the amplitude remained the same. The vertical bowing of horizontal features remained the same. The rate of improvement in his visual symptoms mirrored the rate of improvement in his retinal anatomy. OS acuity improved as the foveal pit redeveloped and as a result of ERM removal, BCVA with BO prisms improved from 20/40 with the ERM to 20/25 post-ERM removal.

OCT and Eye Movements

The anterior segment exam was unremarkable with the exception of 1+ NSC and 1-2+ cortical changes OU. The optic nerve was pink and sharp with a C:D ratio of 0.5 OU. The vitreous was clear OU. The macula had an ERM with loss of the foveal pit. The ERM was dense, long standing, homogeneous and entered throughout the macula. No optic nerve, vascular, or peripheral retinal disease was present. The vessels had normal caliber. The peripheral retina had no holes, tears, or detachment. OCT was obtained and demonstrated an ERM with loss of foveal depression. The RE fundus was normal. Figs 2 and 3 show the macular photographs and OCT profiles of the LE from pre-op to two years post-op. Fig. 2 (pre-op), contains fundus photographs and OCT scans OU for comparison. Unlike the normal RE, the LE foveal pit is completely closed under the ERM.

At 2 months post-op the foveal pit of the LE had begun to reopen with a small depression at the foveola. Six months post-op, the LE showed a more well-developed depression at the foveola; although it was not as well-developed as the depression in the RE. The average-thickness plot for the LE showed an area of thickness below the foveola and thickened area extending nasally. That area corresponds to the superior-temporal position of the perceived, small-area of para-foveal distortion in the LE described above. Fig. 3, pre-op to 2 years post-op, shows the OCT scans of the LE with a further increase in the depression at the foveola, approaching that of the normal RE.

Fig. 4 illustrates the amplitude and phase relationships between the horizontal, torsional, and vertical components of this patient's INS. They are included to demonstrate the

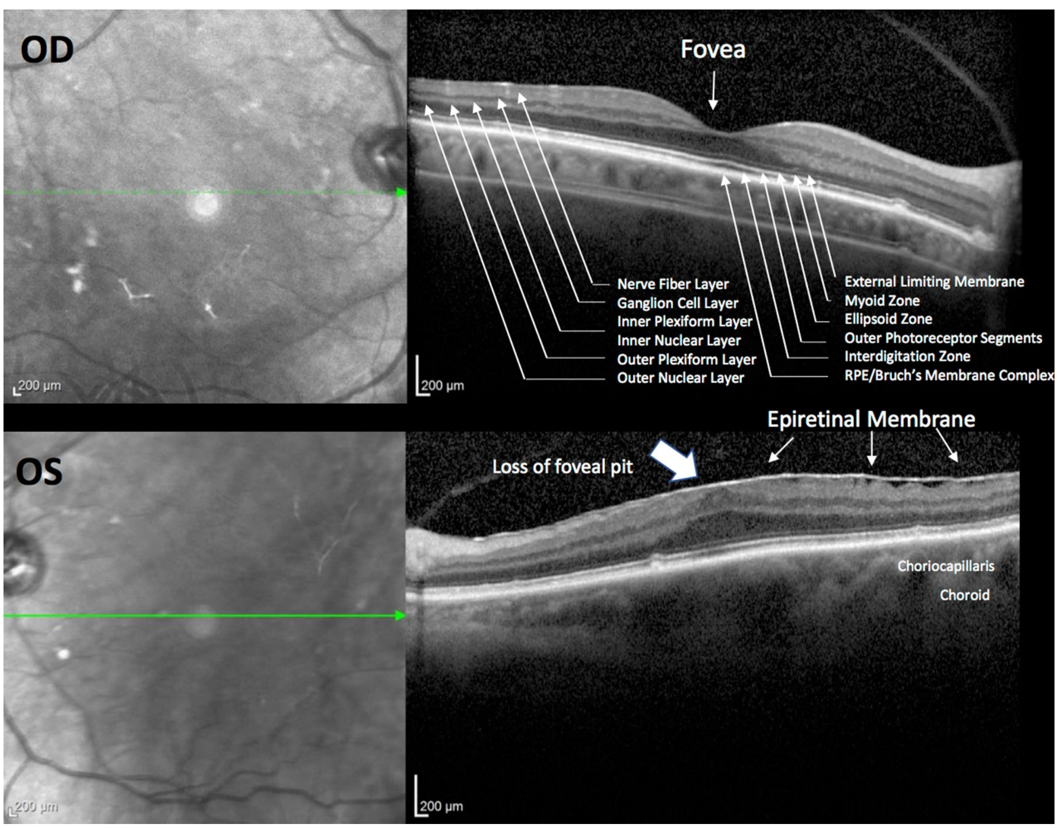

Fig. 2 Fundus photographs, and OCT scans of the normal right (OD) and affected left (OS) foveal areas taken before ERM surgery. For comparison to the left eye in this and Fig. 3, the layers of the right eye are labeled as is he ERM in the left eye

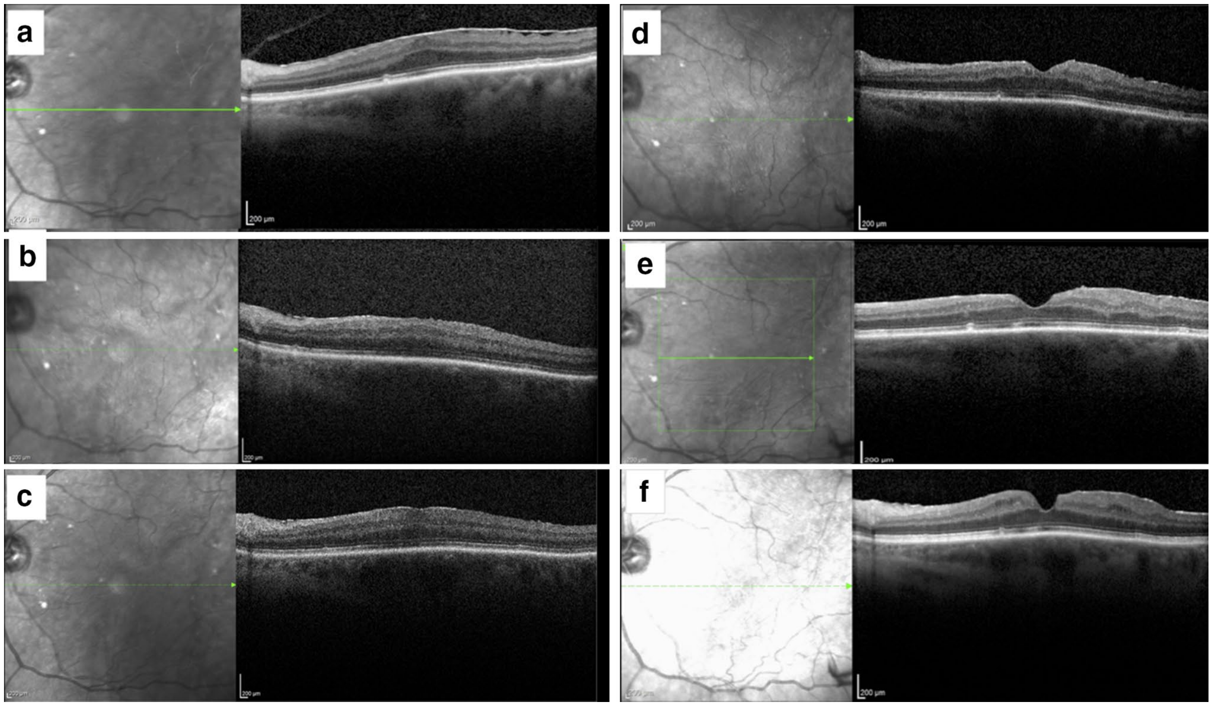

Fig. 3 Fundus photographs, OCT scans of the affected left foveal area showing return of normal foveal anatomy. (A) pre-op; (B-D) 1-3 months post-op; (E) 1 year post-op; (F) 2 years post-op. Note the absence of an ERM in (B-F) (compare to (A) and Fig. 2)

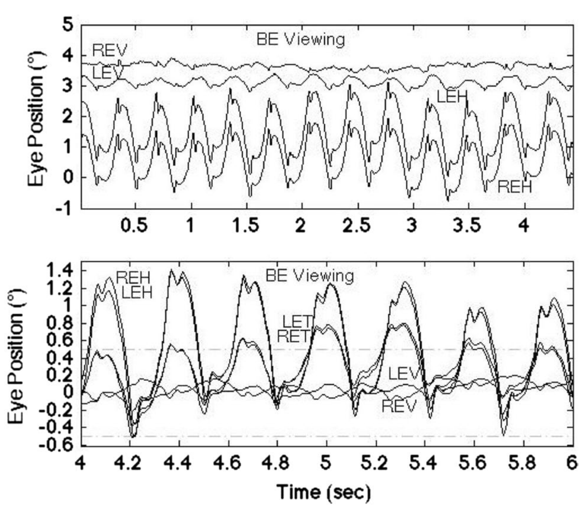

Fig. 4 Horizontal, vertical, and torsional components of the patient's infantile nystagmus. The horizontal and torsional components of each eye are variable and conjugate whereas the vertical components reveal a sub-clinical see-saw nystagmus. Top panel data from a digital video system and bottom panel from a search coil system. Positive movements are rightward, upward, and clockwise (all, from the patient's point of view). The LEH, LEV, and REV data in the top panel are shifted vertically for clarity and the dash-dot lines in the bottom panel indicate the foveal extent. BE, both eyes; RE, right eye; LE, left eye; H, horizontal; V, vertical; T, torsional

multiplanar complexity of the INS; as will be explained in the Discussion, the nystagmus itself could not be responsible for partial oscillopsia of the visual field. The horizontal and torsional waveforms are conjugate and the foveation periods overlap. Vertically, there is a sub-clinical see-saw nystagmus [19]. It is only during foveation periods that clear, high-resolution vision is possible in INS. These eye-movement recordings were made prior to the development of the ERM and are part of a large database of recordings of this individual made over a span of 50 years during which the waveforms and other INS characteristics never changed either before or after the ERM developed. The eye-movement data from this individual (S001) are available at omlab.org.

Discussion

New onset oscillopsia in early onset eye oscillations is most often associated with other changes in the CNS, the eye (as in this case) or ocular motor system, e.g., decompensated strabismus, medications, stroke, age related cerebro-vascular disease, dementia, etc. In a patient with INS, who normally fully suppresses oscillopsia, its sudden occurrence could indicate an overlaying acquired nystagmus. In this case, the peculiar characteristics of the small area of torsional oscillopsia and its uniocular nature initially suggests that the patient's ERM, or possibly cataracts, were interfering with the normal oscillopsia suppression mechanism common to INS. There are common central processes for central (foveal) and peripheral (parafoveal and eccentric retinal) suppression employed as compensatory mechanisms utilized in most forms of childhood strabismus, these may be utilized in the non-preferred eye of patients with asymmetric, or disconjugate eye oscillations in childhood. Although those mechanisms may play a part, they could not fully suppress the focal oscillopsia in this case.

In order to deduce a plausible explanation for this small-area, uniocular oscillopsia in a patient with INS and global suppression of oscillopsia, we needed to first consider all known, related mechanisms. INS cycles contain two distinct portions. The first is the foveation period, a brief moment when the image falls on or near the fovea and the velocity of nystagmus is relatively slow. At and slightly lateral to the null angle, foveation periods have increased duration as compared to more lateral gaze angles. During the remainder of the nystagmus cycle (prior to and after the foveation period), the image falls outside the fovea and is in a state of rapid motion (including saccades), precluding high acuity. Perceptual stability requires complex compensatory mechanisms to suppress the sensation of global image movement. Based on our studies of oscillopsia and modeling of the OMS, the most probable mechanism is efference copy (EC), which utilizes a copy of the motor signal to each ocular muscle that combines with signals from the visual cortex to preclude perceived oscillopsia due to that eye movement [3, 21–26]. EC allows cancellation of the perception of world movement while the image is moving at high velocity and is outside the fovea. This allows construction of a clear and stable image during the foveation period of an INS cycle. The clarity of this image is retained and reinforced by the foveation period from the next cycle. The net result is the perception of a clear and stable target/world.

Because the two eyes often do not oscillate with exactly the same waveform (amplitudes may be different between the two eyes), EC suppression of global image motion must occur independently for each eye. In binocular INS individuals, both clear and stable images are fused into a single binocular perception of the target; in those with strabismus and nystagmus, only the stable image from the fixating eye is used and the other suppressed. The ERM in this patient produced distortion of only a small portion of the para-foveal image in the affected left eye. Therefore, when the attempt was made to superimpose global image motion from that distorted area (LE) onto the presumed undistorted motion (as from the RE), the processes of global oscillopsia suppression and fusion were interfered with or, as suggested by the observations in this paper, precluded. The result in this case was monocular torsional oscillopsia of only the small distorted area during monocular viewing and reduced monocular torsional oscillopsia of that distorted area superimposed on a stable global image during binocular viewing conditions. This latter perception of small-area oscillopsia (due to less than total suppression of the left eye) was less prevalent and less disturbing.

In INS, the whole visual field remains stable despite ongoing changing waveforms, amplitudes, and frequencies of the nystagmus in each eye. Oscillopsia and its suppression are full-field, global effects related to the nystagmus motor signal. E.g., vibrating one eye with a finger results in full-field oscillopsia in both normal persons and those with INS. Thus, even a putative change in the INS with the onset of the ERM (in one, two, or all planes), could not produce a small-area, torsional, uniocular oscillopsia.

Laboratory-induced retinal image stabilization (RIS) of a small, central portion of visual space resulted in that portion being perceived as oscillating horizontally (the main direction of his INS) while the larger, physically stable but retinally unstabilized visual surround was perceived as stable [3]. However, the subject found that he could reverse those percepts so that the RIS portion was perceived as stable but the stable world around it was perceived as oscillating horizontally. Thus, the brain could perceive either retinally stabilized or unstabilized images as stable but not both at the same time. The inability to accomplish the same perceptual reversal of a retinal distortion-induced torsional oscillopsia of the LE might suggest an interference with the basic mechanism by which torsional oscillopsia is suppressed in INS. However, there is no evidence for that or that global torsional oscillopsia differs from horizontal or vertical oscillopsia. Finally, there was no global torsional oscillopsia.

The bilateral cataracts in this case were in the early stages of development and did not significantly impair vision. It was unlikely that these bilateral early cataracts could be the cause of the focal monocular blurring and oscillopsia. It is well known that monocular or binocular blurring (either by the addition of high-plus lenses or simply removing one's refractive correction) does not cause oscillopsia in INS. Patients with INS do not develop oscillopsia if wearing correction for only one eye or if holding a plus lens in front of one eye. Such evidence contradicts the prior speculation [20] that blurring might be the cause of the focal oscillopsia in a patient. Removal of the cataracts did not affect the focal oscillopsia in this case.

It is also unlikely that the development of a translucent stationary, monocular ERM produced oscillopsia by the same mechanism as oscillopsia produced by after-images from flash bulbs and migraine auras [27], which are also stationary on the visual cortex. The focal oscillopsia caused by the ERM was torsional whereas those caused by an after-image or migraine-aura are horizontal (the major component of the INS). The reason for this difference was not evident until we considered the downward bowing of horizontal contours in the foveal area. Because the overall visual scene was perceived as stable, despite its complex multiplanar motion on the retina (e.g., the horizontal and vertical grid lines outside of, and the vertical lines within, the distorted area shown in Fig. 1 were perceived as stable), we conclude that the efference-copy mechanisms that normally suppress global oscillopsia in INS were still functioning properly in all planes.

However, if one superimposes a horizontal motion on the perceived downward bowing horizontal portions of the visual scene within the small area of retinal distortion (as illustrated in the bottom portion of Fig. 1), the net result would be a perception that they were oscillating torsionally. That is, as the distorted area of the retinal image moves to the left, the right side of the distorted image (shown solid in Fig. 1) would appear to rise while the left side (also shown solid) would appear to fall until, at the leftward peak of the motion, the perception would appear as the dashed line. As the distorted area of the retinal image moves back rightward, the opposite torsional motion of the distorted, bowed area will be perceived—the net result is the perception of a torsional oscillation to the left of and within the fovea (as observed by the patient). Thus, the small-area torsional oscillopsia experienced by this patient could be explained by the major horizontal retinal motion produced by his INS and the small-area, bowed distortion of his horizontally moving retinal image. The latter produced an unexpected torsional motion in the distorted cortical image mapped from that distorted retinal area that did not match the efference-copy-expected horizontal motion and produced this torsional oscillopsia.

In summary, we have presented a case where the unique confluence of a monocular ERM and INS produced an unexpected focal area of torsional/vertical oscillopsia, limited to the distorted portion of the visual field corresponding to the ERM (i.e., an "island of oscillopsia" within the perceptually stable total visual field). The remainder of the visual field, corresponding with normal healthy retina was stable and unaffected. In this patient, efference copy, the main oscillopsia suppression mechanism of INS, remained intact but oscillopsia still developed. In addition, the plane of retinal distortion influenced the plane of oscillopsia. The reduction of the original focal oscillopsia caused by the ERM-induced retinal distortion required removal of the ERM and the subsequent reduction of that distortion as the retinal foveal pit redeveloped. Thus, developmental or surgically induced retinal distortions may produce small-area oscillopsia in INS patients. This acquired, distortion of the retina resulted in new motion perception which could not be suppressed by a visually mature central nervous system, resulting in oscillopsia, similar to many forms of acquired nystagmus in adulthood.

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Conflicts of interest L. F. Dell'Osso, None; S. S. Huang, None.

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