PATIENTS occasionally present with complaints of visual loss and yet initial examinations can reveal no structural abnormalities. The diagnosis of such patients requires a careful step-by-step approach, to determine whether the visual loss is a product of the body or of the mind, according to speakers at a symposium held at the Congress of the European Association for Vision and Eye Research (EVER). "When the patient says that he cannot see and the doctor cannot immediately see why, a non-organic visual loss has to be excluded," said Werner Spileers MD, PhD, Katholieke Universiteit Leuven, Leuven, Belgium. Non-organic loss can take many forms, ranging from hysterical visual loss to malingering for financial gain. But some diseases which affect vision have signs and symptoms that are not readily apparent, Prof Spileers noted.

Methods that can be of value in deciding whether visual loss is organic or non-organic include testing of visual acuity, visual fields and pupillary reflexes, as well as electroophysiological testing and imaging techniques. It is often the simplest tests that reveal the most, he pointed out. The first thing to consider when diagnosing such patients is whether the visual loss is optical or neuroretinal in origin. Optical causes include refractive errors and all abnormalities of ocular media. Neuroretinal disturbances are those which occur anywhere from the retina to the visual cortex. To find if there is an optical performance issue it is necessary to first perform or repeat a skilled refraction on the patient to accurately determine the best potential vision. When visual disturbance persists with best correction, a pinhole test will show improved acuity if the deficit is a result of optical abnormalities of the tear film, cornea or lens.

Relative afferent pupillary defects

Should the cause of visual loss remain elusive, another simple and inexpensive examination is the swinging flashlight test. It allows detection of relative afferent pupil defects and can often reveal whether or not an eye has neural pathology. The test involves first shining the light in one eye and then in the other to examine pupillary reflexes. If the pupil of one eye dilates in response to shining light in that eye after withdrawal of the light from the other eye, and there is no gross retinal pathology present, it is a pretty sure indication that the relative afferent pupillary defect is generally in the contralateral eye. "It's important to notice that a relatively small lesion on the optic nerve head already results in a clear-cut relative afferent pupillary defect and that such a defect is possible in the presence of near normal visual acuity." Relative afferent pupillary defects never result from lesions in the lateral geniculate or cortex, neither do they result from media opacities and cataracts and amblyopia. Moreover, if the visual loss is purely non-organic in origin it will never cause a relative afferent pupillary defect.

At the same time, the absence of a relative afferent pupillary defect does not rule out the possibility of bilateral symmetrical optic nerve, chiasmal or optic tract pathology, since pupillary response is measured in relation to the other eye, Dr Spileers cautioned. Relative afferent pupillary defect is present the next step of the examination is to perform visual field testing in both eyes. Where there is a nonhemianopic lesion it is most likely the result of a pre-chiasmal lesion. However, a hemianopic defect strongly suggests the presence of a compressive lesion at the level of the optic chiasm if it is bitemporal or beyond the chiasm in case of a homonymous hemianopic defect. Neuromaging is required to locate the lesion, and may help in determining the nature thereof. If there is no afferent pupillary defect they should look behind the geniculate body. If there is neither an optical problem nor an afferent pupillary defect, additional tests to detect subtle changes in the macula include fluorescein angiography and OCT may be indicated. The presence of metamorphopsia on Amsler grid testing can also reveal subtle macular changes that might have been missed on ophthalmoscopy.

Perimetry can also be useful in detecting positive signs of non-organic visual loss. For example, confrontational visual fields tested at two different distances should show different patterns, otherwise it is a sign that the patient is consciously influencing the results.

Electrophysiology testing can be very helpful

The objective data provided by electrophysiological testing are indispensable to the diagnosis and management of patients with visual loss, said Graham Holder, BSc, PhD, Moorfields Eye Hospital, London, UK. "In those patients where abnormal function is not accompanied by visible changes in the fundus, electrophysiology enables the characterisation of the disease and may suggest potential targets for multifocal screening. In non-organic visual loss the role of electrophysiology is to demonstrate normal function in the presence of symptoms that suggest otherwise."

Electrophysiological tests involve measurement of visually evoked potentials (VEP) and the electroretinal response to visual stimulation. In both types of testing the delay, reduction or absence of a signal is indicative of organic visual loss. Moreover, interpretation of the VEP is partly in which the signal is altered can help pinpoint where in the visual system the dysfunction originates from, he noted. Patients undergoing VEP testing have electrodes mounted over their visual cortex at the back of their head. The electrodes receive signals from the cortex in response to visual stimuli, which can include a simple changing pattern of alternating black and white bars or checkerboard patterns on a video screen, or diffuse flashes of light. As VEPs are a measure of cortical response to visual stimuli, the VEP recordings can be affected by any disturbance of the visual cortex from the tear film to the cortex. They are useful in detecting conditions which cause a delay in the VEP signal, such as optic neuritis and multiple sclerosis.

Full-field and pattern electroretinography

In the full-field flash ERG, the stimulus is a flashing light, and the retina’s electrical response provides an indication of its overall performance. The ERG waveform to a bright white flash in a dark adapted eye has two main components, an initial negative going a-wave, resulting from the photoreceptors converting light into electricity, and a positive b-wave, largely arising from ON-bipolar cells. When the flash used is a dim light and the eye is fully dark-adapted, the electrical response generates a b-wave which comes from the rod ON-bipolar cells, which serves as a measure of rod system sensitivity. A bright flash will generate the a-wave which is produced by all the photoreceptors together to generate the combined rod-cone response. To specifically measure cone sensitivity, the patient’s eyes must first be light-adapted to suppress rod activity. Under these conditions, stimulation with a single flash or a flickering light provides a sensitive measure of the inner retinal function.

For the pattern electroretinogram (PERG) the stimulus is usually a reversing black and white checkerboard. Patients undergoing the test have electrodes placed on the cornea and the skin near the eye. They then view the stimulus, which is similar to that used in VEP testing. Since the technique requires the patient to fixate on the centre of a checkerboard pattern, it measures the macular response with no contribution from the peripheral retina.

In PERG recordings, much of the positive P50 component (the main positive component, latency 50 msec) arises from the retinal ganglion cells, but is “driven” by the macular photoreceptors, and thus acts as an objective measure of macular function. The negative N95 component arises exclusively in the ganglion cells.

“The main role of the pattern ERG is to assess the function of the macula and retinal ganglion cells objectively, which allows improved interpretation of the VEP. Once you know how the central retina is responding to the same stimulus that produces the VEP you can interpret the VEP far more meaningfully.”

Dr Holder went on to demonstrate the above points with a number of clinical cases, including children with Batten disease and Leber Hereditary Optic Neuropathy where an initial diagnosis of non-organic visual loss was changed by electrophysiological testing, and claimed visual loss following a road traffic accident which could be confirmed as having a non-organic basis.

Multiple causes for unexplained visual loss

A diverse range of conditions can masquerade as non-organic visual loss. They include early manifestations of hereditary retinal disease, retinal manifestations of non-ophthalmic conditions and vitamin A deficiency, said Bart Leroy MD, PhD, Department of Ophthalmology and Centre for Medical Genetics, Ghent University Hospital, Ghent, Belgium. Dr Leroy described the case of a 24-year-old man who had undergone LASIK in both eyes for correction of high myopia. He afterwards complained of night vision problems but said his daytime vision was satisfactory. He subsequently underwent six LASIK re-treatments until finally he required corneal grafts in both eyes. Some months after the keratoplasty procedures, a cousin of the patient was diagnosed with retinitis pigmentosa. On ophthalmoscopy examination the appearance of the fundus was typical of what is usually found in myopic eyes. However, fluorescein angiography showed that bull's eye maculopathy was present in both eyes. Moreover, visual field testing revealed a gross scotoma in the mid periphery of both eyes and the patient’s full-field ERG was virtually flat, confirming a diagnosis of retinitis pigmentosa. Dr Leroy also described a 67-year-old woman who reported seeing shimmering light for four months. Her visual acuity was 7/10 in her right eye and 9/10 in her left eye. She was regarded as a psychosomatic case and had been seen by three ophthalmologists previously. Visual field testing showed that she had a central scotoma and small defects on the periphery in both visual fields. Her fundi had a completely normal appearance and fluorescein angiography revealed no abnormalities either. Non-organic visual loss full-field ERG testing showed that she had a virtually extinguished rod function. On the basis of these findings, and because she had been previously cured for a malignant bowel tumour, Dr Leroy diagnosed the patient as having a carcinoma- or melanoma-associated...
retinopathy until proven otherwise. A thorough examination revealed that the patient had an adenocarcinoma of right lung. “Cancer-associated retinopathy is due to cross-reacting antibodies against either enolase or recoverin, and loss of photoreceptors ensues. The ERGs are very often bad from early on. Some cases can be helped with corticosteroid treatment, although it is uncertain whether this may not also suppress the patient’s immune reaction against the tumour cells.” Another case of unexplained visual loss Dr Leroy described involved a 29-year-old man who had dry eyes for seven years, and had vague complaints about his vision which remained unresolved despite visiting eight ophthalmologists. Slit-lamp examination showed flecks on the patient’s conjunctiva, which itself had a dry appearance. These were highly suggestive of Bitot spots. Electrophysiological testing showed abnormal dark adaptation responses, and abnormal overall rod/cone function. Another symptom the patient had was profuse acne, which he said had been getting worse over recent years. When queried on his medical history, the patient said he had undergone multiple operations on his small intestine. With this in mind, a diagnosis of vitamin A deficiency was made. “Vitamin A is absorbed through the small intestine so small intestine operations, like those now being performed for obesity, can cause malabsorption. The vitamin is essential in the cornea and the conjunctiva as well as all other epithelia and in the retinal photoreceptors,” Dr Leroy added. The patient has since recovered well, following repeated administration of high doses of vitamin A, he noted. “One has to be smart in that electrophysiological findings have to be put into a clinical context. You have to listen to your patients and ask extra questions. A patient is very much more than a pair of eyes and one has to watch out, things are not always what they seem to be,” he added.