New techniques in diagnosis of eye muscle palsies: a review[1]

A Huber MD[2]
University Eye Clinic, Zurich, Switzerland

The symptomatology of eye muscle palsies can be summarized by the term 'paralytic strabismus', which is characterized by the well-known phenomena: abnormal position of the visual axes with variable angle of squint, limitation of movement of the eyes in the direction of the paralysed muscle, compensatory head position and, above all, double vision with maximum separation of the images in the main direction of action of the affected muscle. For neuro-ophthalmological diagnosis the identification of a paralysed muscle or muscles is of utmost significance. In simple cases, the analysis of ocular movements in the diagnostically important eight cardinal directions and the assessment of motor limitation by comparison with any of the well-known motility schemes are sufficient. In complicated situations, especially in cases of multiple eye muscle palsies, the Hess-Lancaster coordinometer represents the method of choice for detecting the single paretic muscles and at the same time the frequent secondaries, such as contraction of the ipsilateral antagonist and hyperfunction of the contralateral synergist. These tests furnish information only in a qualitative way about the distribution of the paralysed muscles in the whole oculomotor system.

However, quantitative data about the important parameters of eye movement, such as excursion, velocity, acceleration etc. under the pathological conditions of palsy, can only be gained by the modern methods of oculography. For recording eye position and movements in an objective way, electro-oculography is one of the methods used in our ocular motility laboratory. By placement of electrodes on the skin around the eye, potential differences can be measured between electrodes in the plane of any movement. The source of the energy is the potential difference between the electropositive cornea and the electronegative retina, setting up an electrostatic field that rotates with the eye. By placing the electrodes on the skin of the face close to the inner and outer canthi or above or below the eye, vertical and horizontal eye movements can be recorded without any interference from head movements. The method is useful and convenient for recording movements in the approximate range 0.5–40°.

Apart from the electro-oculographic method, we use a photoelectric device (eye-trac-instrument) which operates on the principle of optically detecting the position of the limbus and converting the optical information into a voltage signal that may easily be recorded on an oscilloscope or pen-recorder. The system yields a linear measurement of horizontal eye position over the range of about 15°. As the photoelectric methods do not differentiate head from eye movements, the head requires special fixation.

A still newer system we have recently introduced is the selspot system (Figure 1). Small light-emitting diodes of a diameter of only a few millimetres are attached to the central surface of a close-fitting scleral contact lens. With the aid of fine wires the light-emitting diode is connected to the light-emitting diode control unit. The heart of the whole system is a specially developed photodetector with four electrodes. When the infrared light from the light-emitting diode on the surface of the contact lens is focused on the detector, a photo-current, divided among the four electrodes, will occur. Thus the photoelectronic camera (Figure 2) detects the position of the diode for registration and analysis of static as well as dynamic processes in real time. In other words, the current produced by the photodetector can be used to obtain two signals, linearly related to the X and Y coordinates of the light-emitting diode. These signals can be displayed directly to the surface of an oscilloscope, where the axial movement of the light-emitting diode, identical to the movement of the contact lens and to that of the moving

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[2] Correspondence to: Stadelhoferstrasse 42, Zürich 8001, Switzerland

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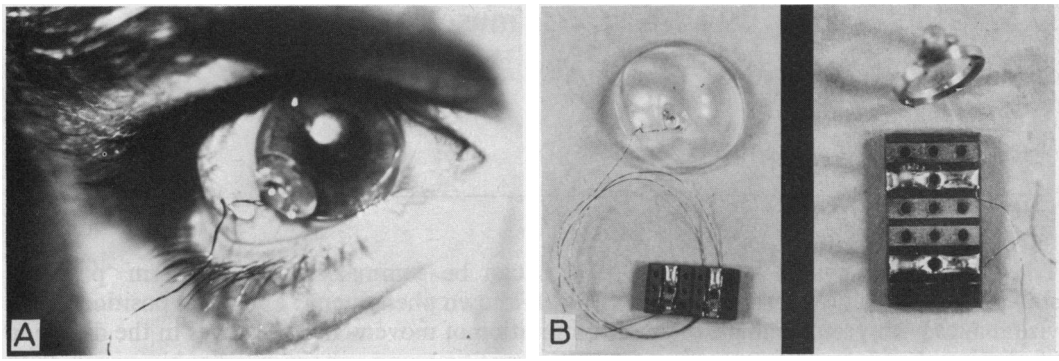

Figure 1. A, contact lens with light-emitting diode (LED) fitted on patient's eye. Fine wires connect LED with LED control unit. B, infrared LED attached to central surface of contact lens (left) and infrared LED attached to metallic corneal ring (Goldmann) with corresponding wire elements (right)

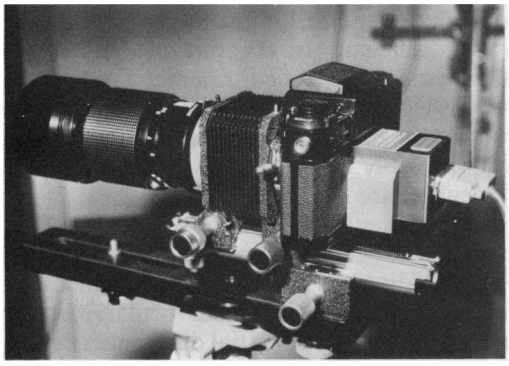

Figure 2. Photoelectronic camera with photodetector (right), and objective (left)

eye, in horizontal, vertical or oblique planes, can be observed directly. One of the main features of this method is the very high linearity (Figure 3).

For the evaluation of pathological eye movements, such as in palsies, the following types of eye movements are recorded: saccadic eye movements; pursuit movements; reading movements; optokinetic nystagmus.

The oculogram obtained by the above-mentioned different oculographic methods is interpreted in the following way: (*a*) the course of the movement of the eye to be examined is studied directly from the oculographic curve; (*b*) horizontal or vertical excursions are measured from the oculographic curve; (*c*) the velocity curve (differential movement curve) tells us about the course of the speed of the eye movement; (*d*) by placing the tangent to the steepest part of a section of an eye movement curve, the peak angular velocity can be measured; (*e*) by placing the tangent to a corresponding steep section of the velocity curve one

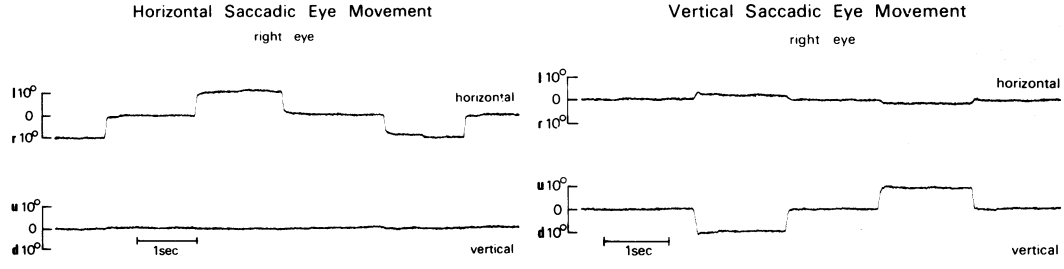

Figure 3. Selspot oculogram of normal horizontal and vertical saccadic eye movement

gets an angle in comparison to the baseline which is an indication for the size of peak acceleration.

Thus by simple evaluation of the eye movement and velocity curves we can obtain quickly three most important quantitative parameters of eye movements: the excursion, the peak velocity and the peak acceleration. The average peak velocity of normal subjects varies for abduction between 300 to 600°/sec and for adduction between 250 and 500°/sec. The average peak acceleration in normal individuals shows values of 17'000 to 40'000/sec^2 for abduction and values of 12'000 to 18'000/sec^2 for adduction. Sometimes it is not difficult to see by direct observation the difference in the speed of saccadic eye movements when a normal muscle is functioning, compared with a slower, relaxed-type movement noted with stimulation of a paretic extraocular muscle. However, in many cases especially in slight pareses, quantitative measurements of saccadic movements are indispensable. Such a measurement performed by oculography gives an indication of the severity of the pareses and, when repeated at intervals, an indication of the degree of a possible recovery. This information is of value also to the surgeon in deciding when to operate and in choosing the appropriate procedure for maximum functional recovery. In a case of left VI nerve paresis, the horizontal saccades are demonstrated

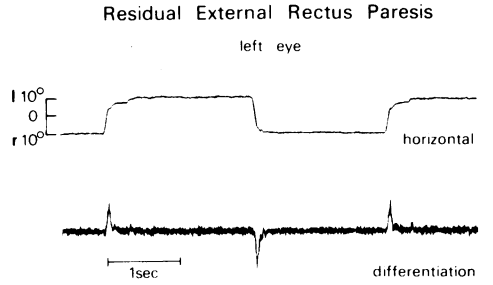

Figure 4. Selspot oculogram of neurogenic external rectus paresis, left eye. Upper curve demonstrates distinct slowing of abduction to the left (curve sections going up) in contrast to intact abduction to the right (curve section going down). Lower curve representing velocity curve shows reduced velocity of abduction to the left (peaks up) in contrast to normal velocity of abduction to the right (peak going down)

at the beginning of the affection (Figure 4) and six months later. The electro-oculogram manifests the normalization of the originally distinctly decreased excursion and reduced angular velocity of the left eye on attempting to look to the left. In the acute phase of the paresis, the saccades to the left are slow with greatly reduced excursion and with definite lower velocity spikes (which contrasts distinctly with the oculographic picture six months later). By studying the saccadic eye movements and their parameters it is therefore possible to follow the reinnervation of a paretic eye muscle. In some cases of mild paresis, a decrease in saccadic velocity is an even more sensitive indicator of abnormality in the oculomotor apparatus than the electromyogram, which in the early stages of paralysis is often normal. Apart from saccadic velocity measurements, the evaluation of acceleration values in different time intervals also furnishes an instructive image of the course of a paresis. Similar results can be obtained by the study of alterations of pursuit movements, optokinetic nystagmus and reading movements.

Limitations of eye motion, detectable by oculography, are present not only in peripheral neurogenic pareses, but also in myopathies and myasthenias. In myasthenia gravis the characteristic fatigue phenomena can be oculographically demonstrated by the corresponding alterations of the saccadic movements. Saccadic eye movements have a constant amplitude-velocity relationship that cannot be altered voluntarily. In ocular myasthenia there are two basic types of saccade fatigue to be observed: either progressive decrease in amplitude, or progressive decrease in velocity, or both (hypometric saccades). Three minute after 10 mg i.v. edrophonium chloride (Tensilon) there occurs a significant increase in average saccade amplitude and maximum velocity which contrasts with the negative effect (or even decrease)

in healthy control subjects. Sometimes the saccades after edrophonium chloride may become even more intensive than normal, so-called hypermetric. Optokinetic nystagmus is an equally reliable and sensitive oculographic test and a specific indicator of myasthenia. There is also fatigability of nystagmus amplitude and unequivocal responsiveness to intravenous edrophonium chloride. Saccade and optokinetic fatigue and its reversal by edrophonium chloride are reliable tests not only for ocular involvement in myasthenia, but are sufficiently sensitive to uncover subclinical eye muscle pareses in cases with no clinical appearance of ophthalmoplegia.

Anomalies of eye movements occur in many disorders involving the central nervous system. It is obvious that the more refined methods of oculography are not only likely to provide additional details of movement disorders, but may also demonstrate anomalies that completely escape clinical observation.

In patients with internuclear ophthalmoplegia, oculography demonstrates adduction movements to be significantly slower than in normal subjects and significantly slower than abduction velocities. Therefore, measurements of saccadic velocity may be useful in detecting internuclear ophthalmoplegia or confirming the presence of suspected internuclear ophthalmoplegia.

In multiple sclerosis, apart from oscillating and jerky nystagmus, ocular dysmetria and flutter-like oscillations represent characteristic motor anomalies easily demonstrated by oculography. Ocular dysmetria is an overshoot or undershoot of the eyes on changes of fixation from one object to another; the error in eye position is corrected by several oscillations of progressively diminishing amplitude until accurate fixation is attained. Flutter-like oscillations are intermittent to-and-fro oscillations of the eye, not lasting more than a few seconds, occurring either spontaneously or associated with changes of fixation. Apart from dysmetria, there is other clinical evidence of cerebellar involvement in patients with multiple sclerosis: the stepwise pursuit movements, the replacement of smooth pursuit movements by a stepwise pattern. These stepwise pursuit movements are present not only in the majority of multiple sclerosis patients, but also in cases of spinocerebellar degeneration and cerebellopontine angle tumours, thus suggesting the cerebellum as common denominator in all three disease groups.

In Parkinson's disease there is a distinct prolonged execution of saccadic eye movements: whereas in a normal subject a saccade of 20° is executed in 70 msec, in parkinsonism the prolongation can go as far as 400–800 msec. Also in parkinsonian patients the smooth pursuit movements are replaced by a stepwise saccadic pattern (also called 'ocular cogwheel'). In addition to the above disorders of saccadic and pursuit movement, the reading pattern in parkinsonism turns out to be severely changed: the characteristic stepwise pattern interrupted by regressions for the next line is replaced by irregular, often undulating curves where the regular change of the saccade and fixation phases is missing.

In conclusion, one may say that oculography represents an ideal method for the analysis of pathologic eye motility and furnishes some important measurable parameters for the prognostic and therapeutic evaluation of oculomotor disorders of different types.

After the identification of the paralysed muscle or muscles, the next step consists of localizing the process leading to the eye muscle palsy. By localization of a certain lesion one can often also gain important information about its aetiology and thereby valuable indication for successful treatment. In practice, however, the differentiation between myopathies, affection of the neuromuscular transmission (myasthenias), peripheral neurogenic palsies and supranuclear palsies may be extremely difficult, because disturbances on these different levels may produce very similar pictures of oculomotor disorders. However, electromyography (Figure 5) of the eye muscles gives us the ability to localize an eye motility disorder along the motor unit from its beginning in the muscle over the neuromuscular transmission through the peripheral neurone up to supranuclear centres. Essentially these disorders manifest themselves in the electromyogram by alterations of the wave-form of the action potentials, by more or less pronounced fall out of motor units, by alteration of the frequency of discharge, or by alterations of the pattern of discharge (eventually traced from antagonistic muscles).

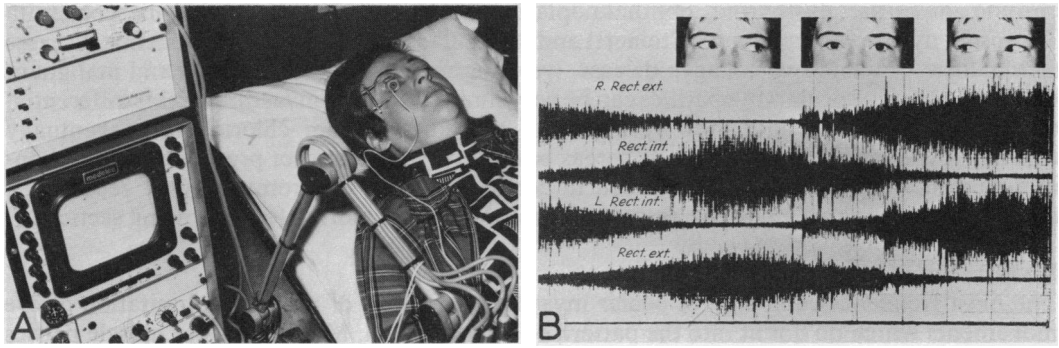

Figure 5. A, electromyography of extraocular muscles: oscillograph (left), and coaxial electrode inserted into right inferior rectus with attached cable connection (right). B, electromyograms of four horizontal recti in different gaze positions, demonstrating distinctly Hering's law of reciprocal innervation

Ocular myopathies

Since the introduction of electromyography as a tool in analysis of extraocular muscle disorders, the diagnosis of ocular myopathy seems to have become more frequent. There is no doubt that until recently many affections of the eye muscles have been interpreted erroneously as being of neurogenic origin. Ocular myopathy is an affection of the eye muscle which is not caused or accompanied by a lesion of the corresponding oculomotor nerve. An ocular myopathy must be suspected if the oculomotor palsies cannot be classified into a peripheral neurogenic or central scheme of disorder. The progressive affection of eye muscles belonging to different oculomotor nerves suggests myopathy. However, in many cases it will be impossible to differentiate clinically between the motility disturbance due to a lesion of the oculomotor nerve and that due to an affection of the muscle itself. Here only electromyography is able to establish a differential diagnosis. The crucial criterion of a myogenic eye muscle palsy in the electromyogram is the striking disproportion between the high degree of electrical activity and the very poor effect on the motility of the affected eye muscle, even upon maximum effort. In the skeletal muscles, a further characteristic and constant sign of myopathy is the shortening of the potentials and a diminution of their amplitudes. The potentials of the ocular muscles already being of short duration, it is very difficult if not impossible to register their shortening. On the other hand, in ocular myopathy the reduction of amplitude can be observed usually very distinctly (Figure 6).

On the basis of the clinical and electromyographic findings, the following ocular myopathies can be differentiated: chronic progressive ocular muscle dystrophy (v Graefe), acute and

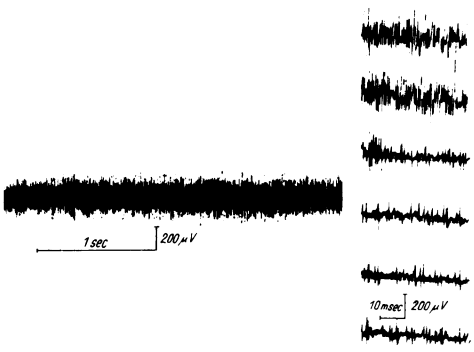

Figure 6. Electromyogram of ocular myopathy: striking disproportion of high degree of electrical activity and very poor effect on motility. Right side demonstrates shortening of potentials and diminution of amplitudes

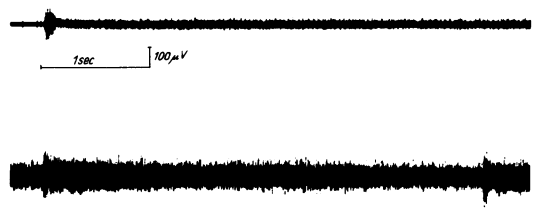

Figure 7. Electromyogram in ocular myasthenia. Above: progressive decrease in electrical activity of muscle during sustained effort with fall out of motor units up to neuromuscular block. Below: intravenous injection of edrophonium chloride (Tensilon, 10 mg i.v.) producing distinct increase of electrical activity in paretic muscle (increase of frequency of firing and amplitude of potentials). Reappearance of interference pattern

chronic myositis, dysthyroid ophthalmoplegia, ocular myotonias (myotonia congenita Thomsen, dystrophia myotonica Steinert) and the ocular myopathies due to systemic diseases (sarcoidosis, amyloidosis, collagen disease, lymphogranuloma, toxoplasmosis and malignant tumours). As some ocular myopathies can be very similar to ocular myasthenia, this differential diagnosis has to be established by means of the edrophonium chloride test, eventually combined with electromyography. Whereas ocular myasthenias react promptly to edrophonium chloride (especially when observed in connection with electromyographic recording), myopathies never give a positive response to edrophonium chloride (see following section).

Myasthenia gravis (Erb-Goldflam)

The most frequent ocular sign of ocular myasthenia consists of ptosis and limitation of eye movements which do not fit into the pattern of a nerve lesion. Myasthenic eye muscle palsies vary in their intensity with the time of the day or with the state of the patient's fatigue. For diagnosis of ocular myasthenia edrophonium chloride (Tensilon 10 mg i.v.) is the method of choice. Ptosis and external ophthalmoplegia, as well as subjective diplopia may disappear completely for a short time. In a considerable portion of cases the edrophonium chloride test turns out to be negative, although myasthenia is present. To enhance objective sensitivity to ocular muscle response in such doubtful cases, the test must be used in combination with electromyography. The electromyographic pattern of myasthenia in extraocular muscles is that of progressive decrease in electrical activity of the affected muscle during sustained effort, characterized by a progressive fall out of motor units and a drop of potential amplitude, such that the initial interference pattern disappears and only a few motor units remain in action. Conclusive for myasthenia is the combination of electromyography with injection of edrophonium chloride after the decline of response in the fatigue test: within seconds after injection there is recruitment of motor units and increase of amplitude to the level of the interference pattern, which again falls off after a few minutes (Figure 7). The importance of this electrical response to edrophonium chloride lies in the fact that the reaction is pathognomonic for myasthenia and occurs even when no visible effect on ocular motility can be registered. Recently also the method of single-fibre electromyography has been applied to myasthenic eye muscles. With the use of single-fibre electromyography, neuromuscular disturbances can be detected before impulse blocking occurs. The single-fibre electrode is inserted into the slightly voluntarily activated paretic eye muscle and a position sought where action can be obtained. There is temporal variability, the so-called 'jitter', between the two action potentials of the same muscle fibre at consecutive discharges. This is mainly due to a variation in the neuromuscular transmission time in the two motor end-plates involved. In myasthenic eye muscles the jitter is increased to abnormal values, indicating a reduced safety factor; with progressing increase in jitter impulse blocking also occurs. Most important for diagnostic purposes is the fact that in cases with purely ocular myasthenia an increased jitter can be found not only in ocular, but also in clinically unaffected skeletal muscles (for instance extensor digitorum communis). Thus single-fibre electromyography may well become the single most useful physiological test for neuromuscular function and at the same time for diagnosis of ocular or general myasthenia.

Peripheral neurogenic eye muscle palsies

Peripheral neurogenic eye muscle pareses or palsies are a consequence of a lesion of the peripheral neurone of the motor unit, i.e. a lesion which may have its site from the end-plate along the axon up to the ganglion cell in the nuclear region of the eye muscle nerve. The relationship of certain muscles to the oculomotor nerve, the trochlear nerve and the abducent nerve leads to characteristic patterns of palsy. Important information about the neurogenic nature of an eye muscle palsy is furnished by disturbances of pupillary reaction and accommodation mechanism, and concomitant signs of other brain nerves or structures of the brainstem or even the brain itself. But diagnostic difficulties are very often present and not easy to overcome. Electromyography here contributes to a distinct improvement of the diagnostic possibilities: a neurogenic paresis or paralysis manifests quite a different pattern of

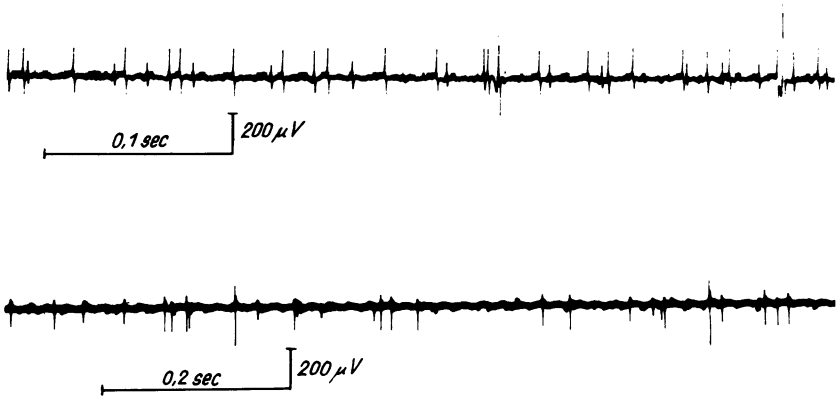

Figure 8. Electromyogram in peripheral neurogenic eye muscle palsy. Above: diminution of number of motor units going parallel to degree of the paresis. Below: appearance of fibrillation potentials (without relation to volition) after two or three weeks as sign of denervation of muscle

electrical activity of the affected muscle from a myogenic palsy or myasthenia. The most characteristic phenomenon in the EMG represents a diminution of the number of motor units parallel to the degree of the paresis. In cases of complete interruption of impulse conduction, there appear after two or three weeks fibrillation potentionals which occur spontaneously without relation to volition (Figure 8). The reinnervation of a paretic eye muscle manifests itself first of all by the disappearance of fibrillation potentials which are replaced by new-formed motor unit potentials of typically high-polyphasic character. Thus by means of electromyography it is possible to follow the different phases of reinnervation of a paralysed eye muscle. Moreover, it is important to know that electrical signs of reinnervation very often precede the clinically visible signs of reappearing action of the paretic muscle. In a case of a neurogenic extraocular muscle palsy, which after eight weeks does not manifest any signs of reinnervation, but fibrillation potentials, one has to be prepared for incomplete or even no recovery. Thus the results of electromyography gain cardinal importance in the planning of surgical treatment of paralytic strabismus. Sometimes deficient eye motility after third nerve paresis is the result of misdirection of regenerating nerve fibres. This occurs when axons growing from the central stump to the periphery contact 'foreign' muscles. The various forms of such an aberrant third nerve regeneration can only be demonstrated and analysed by means of electromyography.

If in a certain case the neurogenic nature of an eye muscle palsy has been more or less certainly proved, the next step consists of localizing the site of the lesion and this also with regard to aetiologic clarification and treatment. The EMG of the paretic eye muscle does not allow a topographic differentiation along the axon from the end-plate to the nuclear region. Here we have to rely upon the neuro-ophthalmological symptomatology – in other words, the neurological signs which accompany the eye muscle palsies. Some important neuro-ophthalmological syndromes with eye muscle palsies are: syndrome of the orbital apex, superior orbital fissure syndrome, cavernous sinus syndrome, Gradenigo-syndrome, cerebellopontine angle syndrome and brainstem syndromes.

Summary: New techniques of diagnosis of eye muscle palsies are discussed. Electromyography facilitates differentiation between myopathies, myasthenias, neurogenic palsies and supranuclear motility disorders; this differentiation is based on the different aspects of electromyograms according to the different levels of affection. An important aid in diagnosis of eye muscle palsies, especially for the observation of the course of eye muscle palsies is oculography: here the determination of different parameters of eye movements under normal and pathological conditions is of utmost importance. These parameters are saccadic velocity on the one hand and acceleration on the other. Oculographic measurement

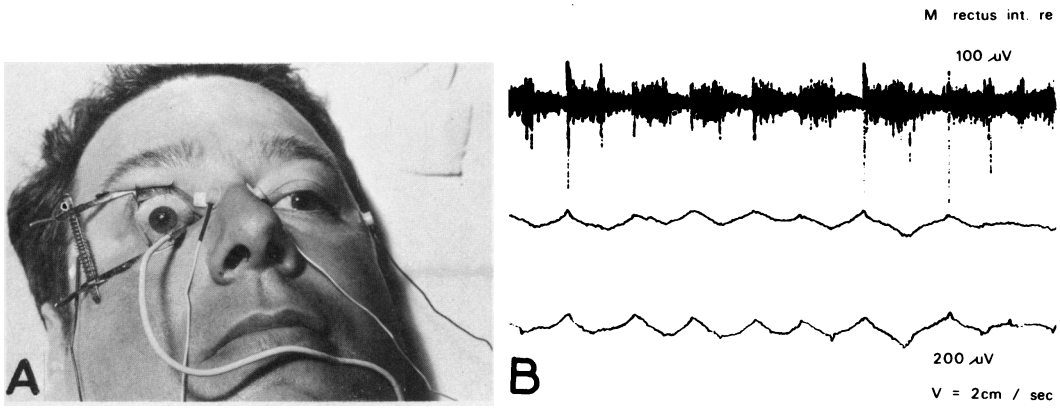

Figure 9. Combination of electromyography and electro-oculography. A, coaxial electrode inserted into right inferior rectus; four superficial electrodes attached to skin of outer and inner canthi. B, electromyogram (above) and oculogram (below) in case of congenital pendular nystagmus

of the saccadic movements gives a valuable indication of the severity of an eye muscle palsy and, when repeated, provides an important indication of the degree of recovery. A combination of electromyography and oculography permits the innervational pattern or eye muscles to be correlated with certain types of movements under normal and pathological conditions (Figure 9).

Bibliography

Esslen E & Papst W (1961) Bibliotheca ophthalmologica No. 57. Karger, Basel
Huber A (1972) *Therapeutische Rundschau* **29**, 198–203
Huber A (1977) In: Augenmuskellähmungen, Bücherei des Augenarztes. Ed. A Hamburger and F Hollwich. Enke, Stuttgart; pp 74–112
Huber A & Meyer M (1976) *Ophthalmologica* **172**, 194–204
Quéré M A (1973) *Annales d'oculistique* **206**, 450–474
van Noorden G (1966) *Archives of Ophthalmology* **76**, 162–171