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REVIEW ARTICLE

Nystagmus

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ABSTRACT

Nystagmus is an important clinical sign. Often it may be the harbinger of an intracranial pathology, and at other times may just be a silent manifestation of a short lived vestibular imbalance; yet at other times it may be an intermittently visible sign that may have to be induced, and again, at others it may be the only evidence to support an ongoing pathology. Given its numerous causes and presentations, it becomes important for the clinician dealing with balance disorder patients to understand the basic physiology and mechanisms that surround it.

Presented below is a brief outline of the physiology, the causes and their respective interpretations of nystagmus.

Keywords: Nystagmus, Vestibular, Vestibulo-ocular reflex.

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INTRODUCTION

The term nystagmus comes from the Greek word 'nystázein,' which means 'to drop off to sleep.' This usually means involuntary eye movements, mostly consisting of slow eye drift (of pathological cause) and a rapid reversal.[1-4]

Nystagmus is often thought of as a perplexing disorder by the physician! However, research over the last four decades has helped in understanding the pathophysiology of nystagmus and devising ways to attribute this important clinical sign to a particular balance disorder.

Basic Mechanism

In a normal individual, the labyrinths of the two sides attempt to 'push' their respective eyes to the opposite side; thus causing a conjugate slow movement of the eyes to the opposite side. Hence, they 'balance' the actions of the other in a sort of dynamic synergy. During times of an imbalance, such as in unilateral vestibular loss, the eyes are 'pushed' to the affected side by the opposite 'uninhibited labyrinth'. However, the brainstem keeps this normal/unaffected labyrinth in check and rapidly 'turns' the eyes back to the unaffected/normal side. This constant repetitive cyclic struggle between the labyrinth and brainstem results in a movement of the eyes termed as nystagmus (Fig. 1). Normally, this nystagmus persists until the underlying vestibular loss is ether cured, or taken care of by compensation (vide infra). The nystagmus, would thus gradually reduce in intensity and eventually cease.

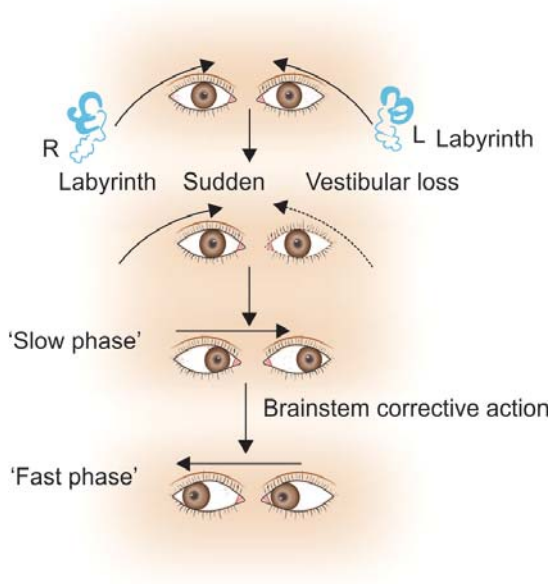

Fig. 1: A diagrammatic representation of the mechanism of nystagmus

The two phases of nystagmus are; the 'slow phase', due to the abnormality in the vestibular system; and the 'fast phase', due to the corrective central mechanism. However, while only the slow phase plays a part in image stabilization, it is the fast phase which is actually detected, and hence by convention, the direction of the nystagmus is attributed to that of its fast phase.

The terms vertigo and dizziness cover a number of multisensory and sensori-motor syndromes of various etiologies and pathogeneses, which can be elucidated only with an interdisciplinary approach. After headache, it is one of the most frequent presenting symptoms. The lifetime prevalence is almost 30%.[5] A survey of over 30,000 persons showed that the prevalence of vertigo as a function of age lies around 17% and rises up to 39% in those over 80 years of age.[6]

Types of Nystagmus

In health, there are three main control mechanisms for holding a steady gaze; fixation, the vestibulo-ocular reflex, and the neural integrator, which is a gaze-holding system which operates whenever, the eyes are required to hold gaze in the extreme lateral position.[7-9] A failure of any of these, will cause a disruption of steady fixation. There are two

types of abnormalities of fixation that can result; nystagmus and saccadic intrusions/oscillations. The difference between the two lies in the initial movement that takes the line of sight off the target-object. In the case of 'nystagmus, it is the 'slow-phase' that moves the eyes away from the target-object; whereas, in the case of 'saccadic intrusions/oscillations' it is an 'inappropriate fast movement' that moves the eyes off the target-object.

Nystagmus can be defined as periodic, most often involuntary eye movements that normally consist of a slow (causative or pathological) phase and a quick eye phase, which brings the eyes back to the initial position. Nystagmus is quite common: Its prevalence lies around 0.1%.[10,11] Nystagmus may be either congenital or acquired.

Nystagmus is basically an involuntary oscillation of one or both eyes, about one or more axes. It can be broadly divided into three categories:

- *Induced nystagmus*: Which can be induced physiologically (optokinetic nystagmus, end-point nystagmus and vestibular nystagmus)
- *Congenital or infantile nystagmus*: Which is present at birth or soon after
- *Acquired nystagmus*: Which occurs secondary to some inducing factor (neurological disease or drug toxicity).[8-10,12-14]

Spontaneous Nystagmus

Spontaneous nystagmus has been defined as that nystagmus which appears in the upright position of the head, in darkness and at least 3 feet away from any form of stimulus. It has not been included in the above classification, as it over laps between the congenital, vestibular and some other types. In fact, the term 'spontaneous' is a misnomer, as except in cases of congenital nystagmus, it shall always result following a stimulus, whether ongoing, or in the past.

There is always the possibility of spontaneous nystagmus being confused with certain cases of anterior and lateral semicircular canalolithiasis, as in such cases, there could be the possibility of a nystagmus occurring in the head-upright position even at rest. It is thus very important to understand that spontaneous nystagmus depends on nothing but itself, and this independence should be checked.

It is a known fact that rotatory vertigo appears only when the velocity of the slow phase of the nystagmus exceeds 10 degrees/second, especially when the head is at rest, i.e. spontaneous nystagmus. This association is relatively constant, and in conditions when the rotatory vertigo does not appear, one must check to rule out a 'central' cause of the vertigo.

Etiopathogenesis

Clinically, nystagmus can be characterized by the plane/s of oscillation, the direction/s of gaze at which it occurs, the degree of conjugacy, the waveform, it's amplitude and it's frequency. A reasonable indicator of the nystagmus can be obtained by merely viewing the eyes. This can be further supplemented by the use of Frenzel's glasses, electro-nystagmography, videonystagmography, etc. When the nystagmus consists of a slow drift of the eyes in one direction followed by a fast corrective movement in the neutral position, it is termed as jerk nystagmus. When the eyes oscillate like a sine wave, the nystagmus is termed as pendular nystagmus.

Physiologically Induced Nystagmus

In a normal individual, nystagmus can be induced by self-rotation. This is physiological nystagmus and occurs so as to keep the images seen by the eyes, steady on the retina during rotation.

There are three forms of physiologically induced nystagmus; vestibular, optokinetic and end-point nystagmus.

Vestibular nystagmus occurs during self-rotation even in darkness. It occurs due to the signals sent by the vestibular labyrinth to the vestibular nuclei and the cerebellum.[7-9] This nystagmus can also be induced by irrigating the ears with warm and cold water/air. A unilateral irrigation will result in horizontal, torsional or oblique conjugate nystagmus depending on the position of the head. Both a convection mechanism and a direct temperature effect on the canal's sensory apparatus have been proposed to account for the involuntary oscillations[8] (Figs 2 to 5).

Nystagmus and the Vestibulo-ocular Reflex (VOR)

The vestibulo-ocular reflex is the reflexive eye movement in response to head movement. It is an important reflex that keeps the image on the retina during head movements. It is often confused with nystagmus, but the two are distinctly varied. While the VOR is a normal reflex, a defect in the VOR can cause nystagmus; Yet, all nystagmuses are not due to defective VOR, as there can be 'central' causes, ocular causes. Nystagmus can be physiological under certain conditions, and when these physiological limits are crossed, they can become pathological. What is important to remember is that the purpose of any neural connection between the vestibular nuclei and end organs, and the ocular muscles is to keep the image on the retina at rest and during motion.

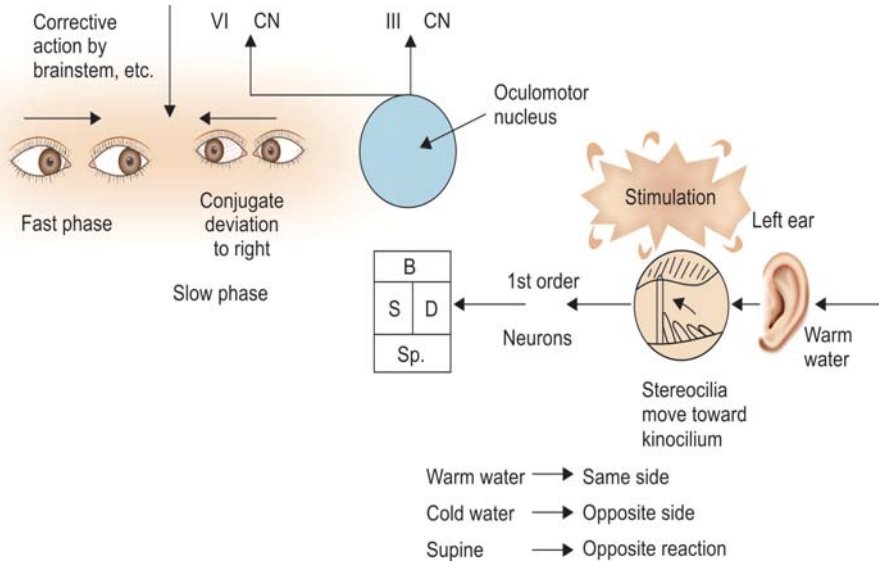

Fig. 2: Schematic diagram of the caloric irrigation procedure and the resultant nystagmus response

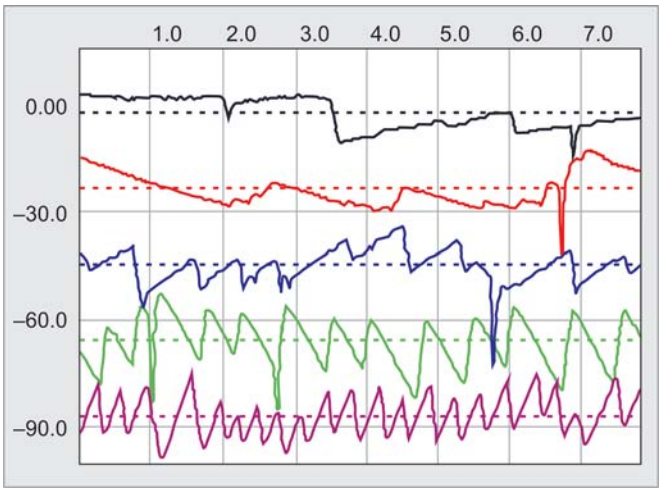

Fig. 3: The tracing for the caloric test performed—right (red and blue) and left (green and pink)

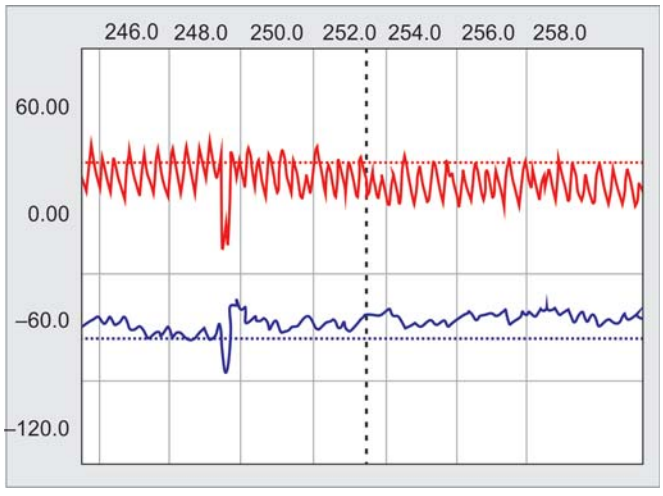

Fig. 5: The nystagmus seen due to rotational stimulation

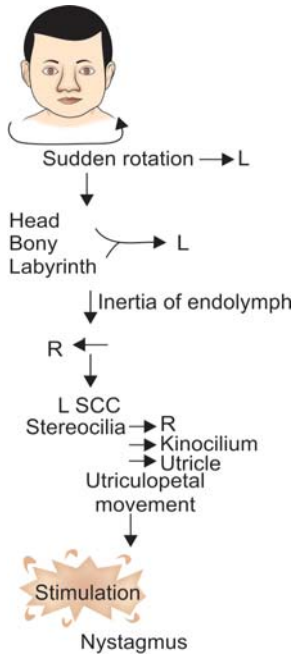

Fig. 4: A schematic diagram of the rotational test

How to Measure Nystagmus

Nystagmus can in many conditions be seen by the naked eye; occasionally when it is subtle, one may need to use Frenzel's Goggles (Figs 6 and 7), or even a videonystagmographic (VNG) (Fig. 8) evaluation may have to be performed. VNG has been explained elsewhere in this issue; however, certain modules of the VNG, such as smooth pursuit (Fig. 9), saccadic testing (Fig. 10), etc. Easily show the nystagmoid beats superimposed on the tracings (these are also visible on the electronystagmographic (ENG) evaluation). The VNG apparatus is also capable of calculating the velocity, phase and other parameters, which were initially performed manually for the ENG. Besides the graphical representation, the visual recording of eye movements can be used as a playback reference along with the graphical recording.

The optokinetic nystagmus is an involuntary, conjugate, jerk nystagmus which is seen when a person gazes into a

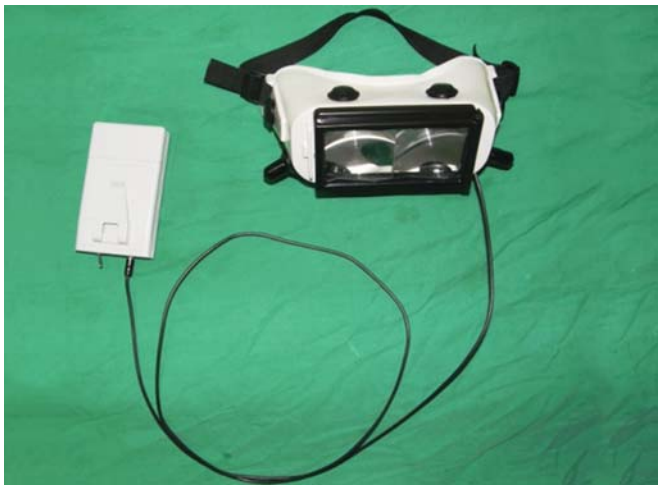

Fig. 6: The Frenzel's goggles

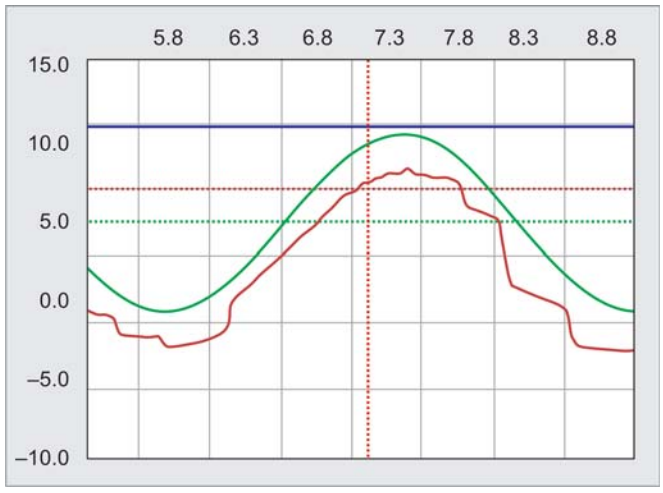

Fig. 9: The nystagmus beats superimposed upon the smooth pursuit tracing (pink) with the stimulus seen in green

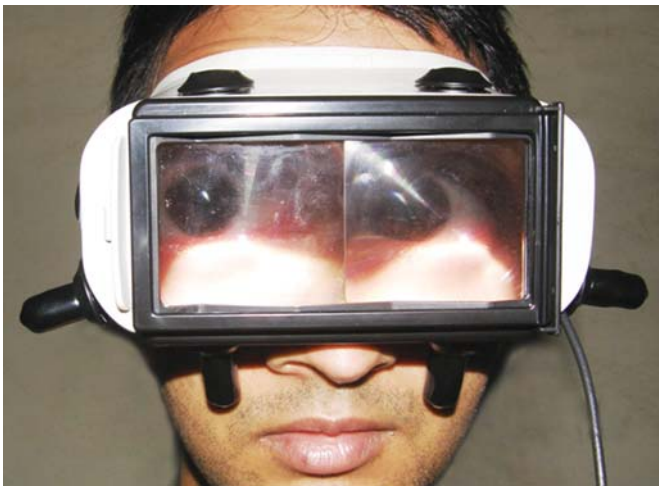

Fig. 7: A patient wearing Frenzel's goggles. The lights are turned down, as the glasses are illuminated with small bulbs, which are seen through the magnifying lens. The patient perceives blurred images and bright lights, and hence cannot make use of peripheral fixation

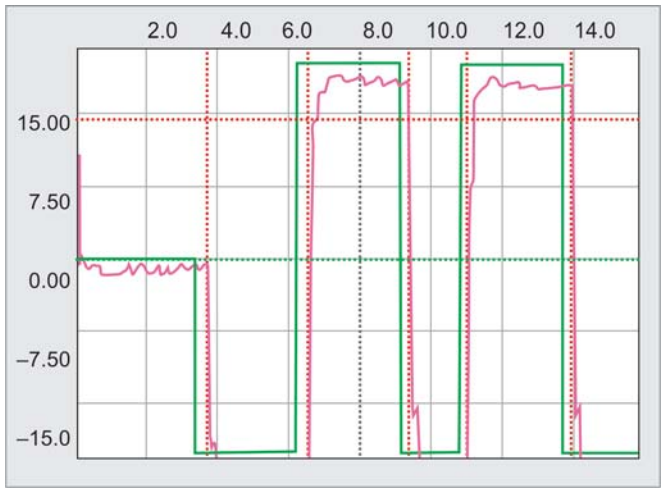

Fig. 10: The nystagmus beats superimposed upon the saccadic tracing (pink) with the stimulus seen in green

Fig. 8: The VNG test being performed; the patient sits with the eyes one meter away from the screen, the sides of which are within a 30° viewing field on either side

large moving field, e.g. looking out of the window of a moving vehicle. The oscillations are in the plane of the moving field and are generally 3 to 4° in amplitude and 2 to 3 Hz in frequency. Both the cortical and subcortical mechanisms are involved in this nystagmus which is driven by the retinal image slip velocity. Smooth pursuit inputs are of particular importance.[7,8,15-17]

On far eccentric gaze (>40°), normal individuals will show a small amplitude (<2°) conjugate, jerk nystagmus. This is termed as the end-point nystagmus and is physiological. It is thought to reflect the time constant of the gaze-holding control system and in particular, the cerebellar neural integrator.[7-9,15,18-20]

Congenital or Infantile Nystagmus

There are two common types of nystagmus which are usually seen in infancy; 'congenital nystagmus' and 'manifest latent

nystagmus'.[10,12] The oscillations in both are conjugate, horizontal and jerky, however, in 'congenital nystagmus' (CN) the slow phase velocity increases exponentially whereas in 'manifest latent nystagmus' (MLN), the slow phase velocity decreases or remains the same. Also, the fast phase of the nystagmus in MLN always beats toward the viewing eye. MLN is usually associated with the presence of strabismus and dissociated vertical divergence, is strongly visually driven and largely dependent on the attentional state of the patient.[20] CN may occur without any ocular or central nervous system anomalies, i.e. idiopathic CN. However, both MLN and CN are usually associated with various systemic disorders, such as albinism, optic nerve hypoplasia and congenital cataracts.[21-25] There are various theories proposed for the etiopathogenesis of infantile and congenital nystagmus, however none have been proven so far.

Acquired Nystagmus

The three mechanisms that normally ensure steady gaze include; visual fixation, the vestibulo-ocular reflex and the mechanism that makes it possible to hold the eyes at an eccentric eye position. Disturbances in these mechanisms give rise to acquired nystagmus.

Diseases affecting the visual system causing loss of vision will cause nystagmus due to loss of visual fixation. Diseases affecting the vestibular organ in the inner ear will result in a horizontal torsional nystagmus usually associated with vertigo. Diseases affecting the central connections of the vestibular system may result in down-beating nystagmus, torsional nystagmus, periodic alternation nystagmus or see-saw nystagmus.

The gaze-evoked nystagmus is one of the most studied and frequently-seen acquired nystagmus. It is elicited when the patient attempts to maintain an eccentric eye position. The oscillations are jerky with a decreasing velocity slow phase taking the eyes away from the desired position, followed by the corrective fast phase. It is thought to occur due to a failure of the step or tonic eye position command from the gaze holding network (the neural integrator).[8,13,19] It is very difficult to differentiate a physiological end-point nystagmus from an acquired gaze-evoked nystagmus by viewing eye movements alone.[18,19,22]

Pathologies affecting the vestibular labyrinth or nerve cause a jerk nystagmus with a linear or constant slow phase velocity. Typically, the nystagmus increases when the eyes are turned in the direction of the fast phase keeping with the principle of Alexander's law and it is suppressed by visual fixation. The direction of the nystagmus is opposite to the side of the lesion. A change in head position may exacerbate this nystagmus. In contrast, a central vestibular nystagmus which is caused by a disease of the brainstem and/or cerebellum, is not attenuated by visual fixation and may be bidirectional.

Clinical Significance and Management

Oculomotor disturbances and nystagmus are seen in many diseases of the vestibular apparatus, the nervous system, and the eyes, as well as in toxic and metabolic disorders. They often indicate a specific underlying cause. The key to diagnosis is systematic clinical examination of the patient's eye movements. A thorough knowledge of the characteristics of the nystagmus can often help to determine the site of the lesion, pathogenesis and underlying mechanisms.

In acute unilateral peripheral vestibular deficit, horizontal spontaneous nystagmus (SN) increases when patients lie on their affected ear. This phenomenon indicates an ipsilesional reduction of otolith function that normally suppresses asymmetric semicircular canal signals. In the course of vestibular compensation, the velocity of spontaneous eye drift gradually decreases. Patients with chronic unilateral vestibular deficit may yet show some SN in darkness, but not during ocular fixation in the light.[26] Nystagmus can still be detected, however, after shaking the head rapidly over 20 to 30 cycles in the horizontal plane[27] or after whole body oscillation on a turn table about an Earth-vertical axis.[28,29] This so-called head-shaking nystagmus (HSN) is considered to be a sensitive symptom for detecting asymmetries in the vestibular system.[28,30,31] The presence of HSN reflects a directional imbalance of the vestibulo-ocular reflex (VOR) in the high frequency range after unilateral vestibular lesions. During high-acceleration head rotations, the VOR is mainly generated by the excited side,[32] because the nonlinear pathway of the inhibited side is driven into inhibitory cutoff.[33]

The pseudospontaneous nystagmus (PSN) is a new clinical sign to diagnose the impaired side of lateral semicircular canal-BPPV described, for the first time, in 2005.[34] In a study by Asprella-Libonatti (2008),[35] 293 patients affected by lateral semicircular canal benign paroxysmal positional vertigo (197 geotropic and 96 apogeotropic forms) were examined. Pseudospontaneous nystagmus was observed in 222 patients (76%). After a very slow, repeated horizontal rotation of the head, in the seated position, this percentage increased to 96% (281 patients). The pseudospontaneous nystagmus and the seated supine positioning nystagmus always beat in the same direction and both were in accordance in identifying the affected side with the nystagmus evoked by the head yaw test. The differential diagnosis between spontaneous nystagmus and pseudospontaneous nystagmus is easily achieved with the

head pitch test in the sitting position: The pseudo-spontaneous nystagmus disappears with the head bent forward 30° (neutral position), it reverses its direction with the head bent 60° forward, it returns visible bringing the head in axis with the body and increases its intensity extending the head about 30° backwards. Pseudo-spontaneous nystagmus was found to be an important sign for determining the affected ear in lateral semicircular canal benign paroxysmal positional vertigo. Early identification of the affected side improves efficacy of treatment and compliance of patients.[35]

The treatment of nystagmus is based on four principles: Medical treatment, optical devices, surgery to weaken certain eye muscles, and somato-sensory or auditory stimuli. Medical treatment is the most relevant and successful means of treatment.[1,36-38] But this is probably relevant for ocular pathologies as seen in congenital nystagmus. Rest assured, nystagmus is only a clinical sign, and its treatment lies in treating its cause.

Considerable progress has been made over the last decades in the description of the clinical characteristics of different forms of nystagmus, its pathophysiology and etiology. However, because there are several forms of nystagmus and underlying central vestibulars, ocular motor and in particular cerebellar disorders, effective drugs are still awaiting prospective, randomized, placebo-controlled and—due to the low prevalence of some of these disorders—multicentre trials.[39] There are several drugs which are potentially useful, however further studies are required to validate results.

SUMMARY

Nystagmus is a clinical sign; it is not a disease by itself. The treatment thus depends upon a correct identification of the cause and subsequently treating the latter. The intensity, and sometimes even the direction of the nystagmus can divulge a lot of information to the balance specialist, especially when observed serially during the course of the disease. Nystagmus can also be a useful screening test to rule out 'central' balance disorders, which may be confirmed by other tests. With today's advancements in technology, accurate computerized measurements can be made as regards intensity, frequency, direction and nature of the nystagmus, and this has made the assessment easier. Regardless of the availability of these specialized equipments, even a basic knowledge of this sign, can lead to a reasonably accurate diagnosis, even by the naked eye.

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