GAZE-EVOKED NYSTAGMUS AND ITS DIFFERENTIAL DIAGNOSIS

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DEFINITIONS

Gaze-evoked

Gaze-evoked nystagmus (GEN) is a jerk nystagmus, not present in primary position, elicited by attempted maintenance of eccentric eye position. GEN may have a linear or a decreasing-velocity exponential slow phase; the latter has sometimes been referred to as gaze-paretic nystagmus but, unless it is due to a muscle or nerve paresis, the GEN terminology is preferred. Distinction should be made between nystagmus that is truly gaze evoked and that which is gaze modulated. Many types of nystagmus vary with gaze angle but are present in primary position and are not, therefore, GEN.

Gaze-modulated

Gaze-modulated nystagmus is a jerk nystagmus, present in primary position, that is increased by lateral gaze. The slow phases may be linear, decreasing-velocity or increasing-velocity exponentials. Examples of gaze-modulated nystagmus are vestibular nystagmus (VN), latent/manifest latent nystagmus (LMLN) and congenital nystagmus (CN). Both VN and LMLN vary in intensity with gaze angle according to Alexander’s law; the nystagmus increases as gaze is directed in the direction of the last phases. CN increases as gaze is directed away from the null and if the null is near primary position, CN may be mistaken for GEN (especially in the absence of a patient history or in a case of head trauma seen in the emergency room). These types of nystagmus increase with lateral gaze but, since their genesis is not due to gaze off primary position, they are not types of GEN.

Overlap

Nystagmus that is modulated according to Alexander’s law may be classified type I, II or III depending on the field of gaze in which the nystagmus first appears. Thus, a type I nystagmus (appearing only in lateral gaze) may easily be mistaken for GEN. The interrelationship between the various types of gaze-evoked and gaze-modulated nystagmus is summarized in Figure 1.

Figure 1. The relationship between gaze and nystagmus.

GAZE-MODULATED

Normal Types

The type of gaze-modulated nystagmus seen in normals is VN, induced by caloric irrigation of the auditory canal, rotation, electrical stimulation or head shaking. The nystagmus has linear slow phases whose direction is dependent on the stimulus to the canals. The amplitude of VN varies with gaze direction according to Alexander’s law.

Pathological Types

The pathological types of gaze-modulated nystagmus are: VN, including alcohol-induced positional nystagmus (APN); periodic alternating nystagmus (PAN); LMLN; and CN. VN is a linear jerk nystagmus whose direction is determined by the particular type and side of the lesion producing it. PAN is a slowly varying jerk nystagmus that increases then decreases in one direction, stops or is replaced by a pendular nystagmus for a short period, increases then decreases in the other direction and again stops for a short period; this cycle repeats but may be altered by gaze angle changes. LMLN is a jerk nystagmus in the direction of the fixating eye when the other is either covered or centrally suppressed. It is always accompanied by strabismus. CN is a nystagmus exhibiting specific waveforms that are learned in infancy to extend foveation and increase acuity. There is usually a null angle in gaze or convergence that can be exploited therapeutically to maximize acuity.

Mechanisms

Several mechanisms may produce gaze-modulated nystagmus. They include: a tonic imbalance that varies according to Alexander’s law (VN) (1,2), a time-varying tonic imbalance (PAN) (3,4), egocentric direction confusion (LMLN) (5) and high-gain instability (CN) (6,7). In the case of alcohol ingestion, the decrease in specific gravity of the cupula in the canals causes APN which is later compensated for by the decrease in specific gravity of the endolymph (8,9). When the blood alcohol decreases, the return to normal specific gravity of the cupula again causes APN; this is also compensated for as the endolymph increases in specific gravity.

Differential Diagnosis

The differential diagnosis includes: VN due to both central and peripheral deficits, positional nystagmus due to alcohol, PAN due to central vestibular dysfunction (4), LMLN associated with either a fixed or variable tropia (10), CN (11) (with or without a latent component) and the nystagmus blockage syndrome (12).
GAZE-EVOKED NYSTAGMUS

Normal types

The types of gaze-evoked nystagmus seen in normals are physiological (endpoint) nystagmus (PHYN) and rebound (RBDN) or centripetal (CNTPN) nystagmus. The GEN seen in normals is of lower amplitude (slower slow-phase drift) and is more symmetrical than that due to pathology. PHYN is induced by lateral gaze in normals. It often has a latency of several seconds before onset, is jerk in type, small in amplitude, irregular, variably sustained, may be dissociated, and occurs in darkness (13). Abel et al. (14) divided PHYN into 3 types: 1) fatigue nystagmus, 2) unsustained end-point nystagmus, and 3) sustained end-point nystagmus. They found that, regardless of the particular type of end-point nystagmus developed by their subjects, the slow phases were linear rather than exponential in form. This enabled differentiation from pathological gaze-evoked nystagmus. End-point nystagmus was found to begin with only 20 degrees lateral deviation in some subjects. The latency for the development of fatigue nystagmus was variable between subjects. In addition, there could be dynamic overshoots in the fast phases of this nystagmus. The existence of PHYN at gaze angles considerably less than maximal makes the term “end-point” nystagmus misleading. RBDN appears as nystagmus in primary position after prolonged lateral gaze. It beats in the opposite direction to the lateral gaze and GEN that preceded it. Sometimes, the GEN damps in lateral gaze and RBDN develops in the opposite direction (CNTPN) while the subject is still in lateral gaze. Recently, Shallo-Hoffmann et al. reported on both PHYN and RBDN in normals (15). They found that roughly 50% of their 20 normals developed PHYN at gaze angles of 40 to 50 degrees and that all 5 of their tested subjects who had PHYN also developed RBDN. In contrast to earlier reports, they found that RBDN could be elicited in a lighted room with fixation targets; in darkness, the RBDN was more robust.

Pathological types

The pathological types of gaze-evoked nystagmus are: non-specific GEN, including drug-induced nystagmus (DIN); gaze-paretic (GPN) or muscle-paretic (MPN) nystagmus; RBDN or CNTPN; and Brun’s nystagmus (BRUN). GEN is the most common form of nystagmus encountered in clinical practice. In the absence of drugs, horizontal GEN indicates posterior fossa (brainstem and/or cerebellar) dysfunction; more exact localization is not possible at this time without analysis of associated neurological signs and symptoms. GEN has been reported in: Arnold-Chiari malformation (22); spino-cerebellar (olivopontocerebellar) degeneration (23,24); lateral medullary syndrome (Wallenberg) (25); autosomal recessive spastic ataxia of Charlevoix-Saguenay (26); ataxia telangiectasia (Louis Bar) (27); and medulloblastoma (28). Multiple sclerosis sometimes causes nystagmus in extreme lateral gaze (deviational nystagmus). When horizontal GEN is bilateral, upward-beating vertical GEN is often present; it is rarely present without bilateral horizontal GEN. Downward-beating GEN is usually absent.

The most common causes of bilateral GEN are sedative or anticonvulsant drugs. GEN has been reported with phenytoin (29), diphenylhydantoin (29,30) and barbiturates (31,32). Another type of gaze-evoked DIN is alcohol-induced gaze nystagmus, usually called alcohol gaze nystagmus (AGN) (33,34). Esser and Brandt wrote an excellent review of various types of DIN (35).

Occipital lobectomy in primates has been found to produce GEN (36) and may indicate that, in man, cortical lesions can also cause GEN.

There is no consistency in the literature on the use of the terms “GEN”, “GPN” or “MPN” although the latter is usually reserved for nystagmus due to neuromuscular weakness. I suggest, in agreement with Leigh and Zee (37), that the term “GPN” be reserved for nystagmus that is due to a paresis of gaze and, further, that it be restricted to paresis of neuromotor origin to distinguish it from MPN. Differentiation between GPN and MPN would then be made by the condition responsible since they are both de-
ABDUCTION "NYSTAGMUS" OF INTERNUCLEAR OPHTHALMOPLEGIA (INO)

The so-called abduction "nystagmus" of INO consists of a jerk-type oscillation of the abducting eye in the direction of lateral gaze. This gaze-evoked oscillation is actually not a nystagmus but a saccadic pulse train (SPT); this consists of a series of saccadic pulses (SP) not sustained by the step of innervation that is part of normal gaze-evoked oscillation. Unusual oculomotor phenomena in a lateral medullary syndrome, J Neurol Neurosurg Psychiatry, 31, 360-367, 1968.

REFERENCES


