JCN Open Access REVIEW

pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2021;17(3):337-343 / https://doi.org/10.3988/jcn.2021.17.3.337

Update on Nystagmus and Other Ocular Oscillations

Seong-Hae Jeong[a]
Ji-Soo Kim[b,c]

[a]Department of Neurology, Chungnam National University Hospital, Chungnam National University School of Medicine, Daejeon, Korea
[b]Department of Neurology, Seoul National University College of Medicine, Seoul, Korea
[c]Dizziness Center, Clinical Neuroscience Center, Seoul National University Bundang Hospital, Seongnam, Korea

This review reports on recent advances in understanding nystagmus and other involuntary eye movements. Advances in quantitative evaluations of eye movements using oculography, computational model simulations, genetics, and imaging technologies have markedly improved our understanding of the pathophysiology of involuntary eye movements, as well as their diagnosis and management. Patient-initiated capture of eye movements, especially when paroxysmal, and the online transfer of these data to clinicians would further enhance the ability to diagnose involuntary eye movements.

Key Words eye movement, nystagmus, saccadic oscillation.

INTRODUCTION

Ocular oscillations mainly comprise nystagmus and saccadic intrusions/oscillations.[1-10] Nystagmus refers to repetitive and involuntary to-and-fro eye movements that are initiated by a slow drift of the eyes away from the object of interest.[8] Nystagmus should be distinguished from other oscillatory eye movements, especially saccadic intrusions and oscillations.[5,8] Unlike in nystagmus, the initial abnormal eye movement is a saccade in saccadic intrusions/oscillations.[5,6,8]

Eye movements are generated by signals transmitted from the eyes and inner ears to structures located in the brainstem and cerebellum, where they are closely monitored and modulated.[8] Human eye movements include saccades, smooth pursuit, the vestibulo-ocular reflex (VOR), optokinetic eye movements, vergence, and fixation, and each such subclass of eye movements is generated and modulated by its own neural network.[8] The eye-velocity signals generated for each eye movement are integrated in the neural structures (neural integrators) in order to hold the gaze steady in the required position.[11] Dysfunction of these structures and the resultant imbalance or instability in each subclass of eye movements may generate involuntary eye movements. Nystagmus may occur when the subsystems involved in slow eye movements (smooth pursuit, the VOR, optokinetic eye movements, and vergence) or the gaze-holding mechanisms are impaired. In contrast, saccadic intrusions/oscillations may be ascribed to instability of the networks involved in generating saccades.[12]

Identifying and characterizing nystagmus and saccadic intrusions/oscillations provide valuable information about lesion sites and pathophysiology.[5,6,8,10] The present review provides an update of the major findings in nystagmus and other oscillatory eye movements since 2017.

Received September 17, 2020
Revised October 7, 2020
Accepted October 8, 2020

Correspondence
Ji-Soo Kim, MD, PhD
Department of Neurology, Seoul National University College of Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro 173beon-gil, Bundang-gu, Seongnam 13620, Korea
Tel +82-31-787-7463
Fax +82-31-719-6828
E-mail jisookim@snu.ac.kr

GENERAL FINDINGS

Peripheral disorders

The presentation of significant spontaneous nystagmus is associated with hospitalization for ≥5 days and nystagmus persisting at 1 month after discharge (with a cutoff of 12.1°/s) in patients with vestibular neuritis (VN).[13] Two of three patients with delayed endolymphatic hydrops showed a typical horizontal-torsional nystagmus beating to the healthy side, whereas the third showed initial upbeat nystagmus with a slight torsional component that evolved into horizontal-torsional nystagmus beating to the healthy side. Initial upbeat nystagmus might reflect inhibition of the superior semicircular canal in the involved ear.[14]

Central disorders

In Wernicke's encephalopathy, spontaneous upbeat nystagmus often changes into downbeat nystagmus (DBN) during eccentric gazes and convergence, or after vestibular stimulation.[15] Furthermore, initial upbeat nystagmus may evolve into permanent DBN.[15] Hypothetical explanations for these transitions and their evolution include directional vulnerability to thiamine deficiency of the vertical gaze-holding networks in the dorsomedial medulla, and impaired processing of otolith information.[15,16] Differentiating neuromyelitis optica spectrum disorder (NMOSD) from multiple sclerosis (MS) is important for both ensuring appropriate treatments and minimizing irreversible neural damage.[17] When the brainstem is involved, the presence of horizontal gaze-holding nystagmus with bilateral lesions involving the medial vestibular nucleus and nucleus prepositus hypoglossi favor a diagnosis of NMOSD over MS.[18] Recording eye movements revealed gaze-holding nystagmus and superimposed pendular nystagmus in five of seven patients with MS and ocular oscillations.[19] The gaze-holding nystagmus showed all the features of a leaky integrator, while the pendular nystagmus presented with all the features of an unstable integrator.[19,20] Simulations using a computational model aided in conceptualizing the underlying pathophysiology of these abnormal eye movements in a common disorder.[19] Quantitative evaluation of eye movements using video-oculography revealed pendular nystagmus and ocular bobbing in a comatose patient with a pontine hemorrhage,[21] with the authors proposing three hypothetical models to explain these eye movements that involved the inferior olive, neural integrator, and omnipause neurons.

Patients showing positivity for serum anti-GQ1b antibody may present with an acute or fluctuating vestibular syndrome (vertigo, nystagmus, and ataxia) without ophthalmoplegia.[22] They may show various patterns of nystagmus, including spontaneous, gaze-holding, and central positional nystagmus (CPN).[22,23] Patients with lateral medullary infarction may show persistent nystagmus with dizziness/imbalance.[24] Transcranial magnetic stimulation of the cerebellum may improve dizziness that remained during the chronic phase of lateral medullary infarction along with the disappearance of ipsilesional nystagmus and a decrease in the horizontal VOR gain bilaterally.[25]

In Charles Bonnet syndrome (CBS), visual hallucinations occur after visual impairments, and they might be caused by spontaneous activities in the extrastriate visual cortex. Two patients with CBS and periodic alternating nystagmus reportedly experienced visual motion hallucinations synchronous with the nystagmus.[26] This may be explained by ocular proprioceptive inputs from the extraocular muscles projecting to either the extrastriate areas processing visual scenes, or the higher-order visual cortical areas involved in analyzing motion signals across the entire visual fields.[26]

Evaluation

Genetic testing for infantile nystagmus[27] and DBN[28,29] may improve diagnoses. Implementing home-based vestibular event monitoring by patient-initiated capture of ictal nystagmus could help in detecting nystagmus during vertiginous attacks and in the differential diagnosis of three of the most commonly encountered causes of episodic vertigo: vestibular migraine (VM), Meniere's disease, and benign paroxysmal positional vertigo (BPPV).[30,31]

SPONTANEOUS NYSTAGMUS

Infantile nystagmus

Oscillopsia refers to the illusory motion of the visual environment, and is rare in infantile nystagmus syndrome (INS).[32,33] However, new-onset oscillopsia in a patient with early-onset eye oscillations is not uncommon in routine clinical practice. It is often associated with other changes in the central nervous system, the eye, or the ocular motor system, such as decompensated strabismus, medication alterations, stroke, age-related cerebrovascular disease, and dementia.[34] In a 74-year-old male with INS, the presence of an epiretinal membrane (ERM) produced an unexpected focal area of torsional/vertical oscillopsia in the portion of the visual field that corresponded to distortions from the ERM.[34] The oscillopsia improved after removing the ERM, which suggests that suppression of the oscillopsia in INS requires undistorted vision across the visual fields.

Predicting future visual function is important in children with infantile nystagmus. A recent longitudinal cohort study found that handheld optical coherence tomography was useful for predicting future visual acuity in infantile nystagmus.[35] Future visual acuity was predicted better by structural grad-

ing than by quantitative segmentation and preferential looking. Individuals with infantile nystagmus can read at normal or near-normal speeds. It is recommended that patients with infantile nystagmus should read horizontally oriented text in order to obtain the best reading performance.[36]

Downbeat nystagmus

DBN is a common form of acquired central fixation nystagmus that is often associated with other cerebellar signs. Despite its distinctive clinical features, the mechanisms of DBN remain to be elucidated.[28] A recent genome-wide association study found a significant association between DBN and variation in the fibroblast growth factor 14 (FGF14) gene located on chromosome 13. FGF14 is expressed in Purkinje cells (PCs), and its reduction leads to decreases in the spontaneous firing rate and excitability of PCs, which are compatible with the pathophysiology of DBN.[29] In addition, mutations in the FGF14 gene cause episodic ataxia type 9[37] and spinocerebellar ataxia type 27 (SCA27).[28] FGF14-associated phenotypes also highlight the overlap between progressive and episodic ataxias, similar to those observed in mutations involving CACNA1A.[37] SCA27 is a typical childhood-onset disorder that presents with tremor, gait ataxia, parkinsonism, depression, and anger outbursts. Given the genetic relationship between SCA27 and DBN, idiopathic DBN could be a late-onset and milder manifestation of SCA27.[28] While DBN is typically observed in dysfunction of the lower cerebellum, the association of DBN with motor neuron diseases indicates the need to look for neuromuscular disorders in patients with this type of nystagmus.[38-40] SCA38 is characterized by DBN, intermittent strabismus, and hearing loss in addition to gait ataxia, and is associated with lower total scores on the Scale for the Assessment and Rating of Ataxia (SARA) and higher levels of docosahexaenoic acid, which should also be validated for DBN.[41] There are rare cases of DBN being observed during attacks of Meniere's disease, which are probably due to asymmetry in the vertical VOR or saccular dysfunction.[42] Thus, Meniere's disease should be considered in recurrent audiovestibulopathy and ictal DBN.

Seesaw nystagmus

While the pathogenesis of pendular seesaw nystagmus remains elusive, dysfunction of the visuovestibular mechanisms that control eye movements may play a pivotal role.[43] Pendular seesaw nystagmus has been described most frequently in large parasellar tumors, and has been attributed to either the effects of commonly associated visual field defects or secondary midbrain compression.[44] Based on a patient with paraneoplastic seesaw nystagmus and opsoclonus due to breast cancer and antineuronal nuclear autoantibody type 2, increased excitability of the excitatory burst neurons in the interstitial nucleus of Cajal and resultant reverberations of the reciprocally excitatory circuit was proposed as the mechanism underlying pendular seesaw nystagmus.[44]

Windmill nystagmus

Windmill nystagmus is characterized by a clocklike rotation in the direction of nystagmus.[8] Like in other abnormal eye movements observed in the blind, windmill nystagmus is explained by a lack of visual feedback from the image motion on the retina that stabilizes the velocity-storage mechanism or gaze-holding network. Given that windmill nystagmus was observed in association with subacute progressive vision loss for 3 months, the time span required for the development of impaired gaze-holding or velocity-storage mechanism may be shorter than thought previously.[45] Furthermore, windmill nystagmus has been observed in a patient with paraneoplastic cerebellar dysfunction but normal vision, which suggests that this form of nystagmus can occur in the absence of any vision loss.[46]

Divergence nystagmus

There are rare cases of divergence nystagmus being observed in patients with lesions involving the dorsal pons and midline cerebellum, while convergence or convergence-retraction mostly indicates an upper midbrain lesion.[47] Divergence nystagmus supports that divergence is generated by active neural innervation rather than by passive relaxation after convergence.

TRIGGERED NYSTAGMUS

Rebound nystagmus

Rebound nystagmus is a common cerebellar sign that is observed when the eyes return to the primary position following a period of prolonged eccentric gaze-holding. Even in healthy subjects, rebound nystagmus may be evoked after extreme (±40°) eccentric gaze, which is modulated by the presence of vision.[48] The slow phase of rebound nystagmus is directed toward the former eccentric gaze position and the rapid phases away from it.[49] Since the initial velocity of rebound nystagmus is correlated with the velocity decay of gaze-holding nystagmus, rebound nystagmus may be explained as gaze-holding nystagmus relative to a new set point with the lowest eye drift.[50] Thus, it might be easier to detect rebound nystagmus when the patient is instructed to look at a target at an eccentric position (e.g., 10°) opposite to the prior eccentric gaze.[50]

Positional nystagmus

Even though CPN is much less common than BPPV, it is important to distinguish these two conditions.[51] The Bow and

Lean Test (BLT) was first introduced to examine the affected ear in patients with horizontal semicircular canal BPPV (HC-BPPV) by observing the direction of horizontal nystagmus induced during the test.[52] A recent study of 225 patients with vertical nystagmus observed during the BLT found that DBN in the bowing position and no nystagmus in the leaning position was the most common type (190/225, 84.4%), and that 163 (72.4%) of the patients had posterior semicircular canal BPPV.[53] The nystagmus induced during positional maneuvers may be atypical for the involved canal in about 8% of patients with BPPV.[54]

Successful canalith repositioning for each type of BPPV requires accurate identification of the involved canal, which is mostly based on comparison of the intensity of nystagmus induced during the supine head-roll test in HC-BPPV.[55] The accuracy of bedside lateralization of the affected side is acceptable in HC-BPPV when the nystagmus asymmetry exceeds 30%;[56] otherwise the latency for nystagmus inversion is shorter when the head is turned to the affected side in geotropic HC-BPPV and longer in apogeotropic HC-BPPV.[57]

The occurrence of orthotropic nystagmus—with the nystagmus beats upward with the torsional component toward the involved ear—in the second position of the Epley maneuver may indicate successful repositioning.[58] A recent study found that orthotropic nystagmus in the third position of the Epley maneuver was more sensitive than orthotropic nystagmus in the second position in predicting treatment efficacy (88.9% vs. 50.9%),[59] whereas there was no significant difference in their specificity.[59] Observing orthostatic nystagmus during the Epley maneuver is thus helpful in predicting the result of canalith repositioning maneuvers.

Apogeotropic CPN may occur in lesions mostly involving the vestibulocerebellum (nodulus, uvula, and tonsil), and is explained by dysfunction of the tilt-estimator circuit incorporated in the velocity-storage mechanism.[60] Persistent geotropic positional nystagmus may be observed in patients with unilateral cerebellar lesions involving the tonsil along with other central oculomotor signs such as impaired horizontal smooth pursuit and positional DBN.[61] In contrast, persistent geotropic direction-changing positional nystagmus may be an isolated finding of a variant form of HC-BPPV, and is explained by a change in the specific gravity of the cupula relative to the surrounding endolymph (also called a light cupula).[62] However, the pathogenesis underlying light cupula is not known, and no effective treatments are currently available.[63,64]

Episodic positional vertigo, which is typical of BPPV, may also be a manifestation of VM.[65] One such patient with migraine developed left-bearing nystagmus while upright without visual fixation, as well as persistent geotropic horizontal nystagmus without latency or fatigability during the supine head-roll test.[65] The associated symptoms were successfully controlled with topiramate and eletriptan. However, between the attacks the patient exhibited apogeotropic horizontal nystagmus without responding to repetitive repositioning maneuvers.[65] Patient-initiated monitoring of eye movements revealed spontaneous vertical nystagmus and persistent positional nystagmus, which are highly specific for VM during the attacks.[30]

Positional alcohol nystagmus (PAN) has also been explained by a buoyancy mechanism.[66,67] A recent study proposed a rapid change in the serum osmolarity and resultant dyshomeostasis of the inner ear fluid as the mechanism underlying PAN.[68] There are rare reports of vertical nystagmus resulting from metabolic disturbances due to electrolyte imbalances, especially hypomagnesemia,[69] hydroxyzine,[70] and ranitidine.[71]

Optokinetic nystagmus

The right frontal eye field (rFEF) is involved in visual perception and eye movements.[72,73] Along with many subcortical regions, the rFEF is activated during optokinetic stimulation. The function of these cortical activations remains unclear, in particular regarding whether these regions are responsible for perceptual and/or oculomotor roles during optokinetic stimulation and for the resultant optokinetic nystagmus (OKN). Combined transcranial magnetic stimulation and electroencephalography and an optokinetic-stimulation motion-discrimination task revealed multiple related yet dissociable roles within the FEF, which included perceptual processing during optokinetic simulation, generation of OKN, and maintenance of alpha oscillations.[74]

A prospective observational study of 73 patients with SCA1, SCA2, and SCA3 found that a higher motor disability subscore on the International Cooperative Ataxia Rating Scale (ICARS) was associated with greater oculomotor dysfunction as measured with OKN-saccadic impairment grading but not with the ocular disorder subscore on the ICARS.[75] This suggests that OKN saccades could be a better and more sensitive bedside clinical tool for quantifying oculomotor dysfunction in degenerative ataxias.[76]

Head-shaking nystagmus

Head shaking in the horizontal plane at 2 to 3 Hz for 10 to 20 s may induce nystagmus in central as well as peripheral vestibular lesions. Head-shaking nystagmus (HSN) is also frequently found in patients with HC-BPPV, with the nystagmus mostly beating to the lesion side in geotropic HC-BPPV and to the healthy side in apogeotropic HC-BPPV.[77] HSN in BPPV may be explained by altered endolymph or cupular dynamics due to otolithic debris in the semicircular canal.[77]

Interictal HSN may be observed in patients with recurrent spells of spontaneous vertigo without any other evidence of

peripheral or central vestibulopathy, and it may be vigorous. Given that the time constant of HSN in these patients (=12 s) is larger than in those with VN, VM, and Meniere's disease, this disorder appears to represent a distinct entity. This may be due to a hyperactive and asymmetric velocity-storage mechanism that gives rise to intermittent attacks of spontaneous vertigo, especially when the marginal compensation of the underlying pathology is disrupted by endogenous or exogenous factors.[78]

Vibration-induced nystagmus

Skull vibration stimulates both the otolith and canal structures, and instantaneously triggers nystagmus by inducing or augmenting a preexistent vestibular asymmetry.[79] Vibration-induced nystagmus may be observed in up to 20% of healthy controls,[80] and may be useful for screening children with hearing loss for vestibular asymmetry when combined with other tests of vestibular function.[81]

Other types of triggered nystagmus

Hyperventilation instantaneously increases the randomness of the waveforms, but with only a small change in the intensity of nystagmus. The increase in waveform randomness can have detrimental effects on function.[82] Sound- or pressure-induced horizontal nystagmus is a rare finding in bilateral vestibular paresis, but associated elevations of the summation and action potentials on electrocochleography suggest the presence of hydrodynamic changes involving the inner ear.[83] Dizziness and nystagmus were observed in a patient who was living in a house that had been tilted by an earthquake.[84] Such nystagmus may be explained a velocity-storage mechanism that had been subject to chronic gravitational stimulation of the otoliths.

OTHER OCULAR OSCILLATIONS

The Heimann-Bielschowsky phenomenon (HBP) describes a monocular slow pendular oscillation, mostly vertical, that mostly develops years after severe vision loss. The pathogenesis remains unknown, but vertical fusion disruption due to monocular vision loss has been hypothesized to be the underlying mechanism.[85] Recognition of HBP is important since this would prevent unnecessary investigations or treatments.[86,87] There are rare cases of monocular nystagmus being observed in spasmus nutans (INS characterized by nystagmus, head nodding or titubation, and anomalous head posture), MS, and alternating hemiplegia of childhood. Monocular nystagmus, which decreases with the administration of flunarizine, was recently described in an infant with an ATP1A3 gene mutation causing alternating hemiplegia of childhood.[88]

In conclusion, careful evaluation of nystagmus and saccadic intrusions/oscillations would provide valuable information on the lesion location and the involved pathomechanism. Recent advances in quantitative evaluations of eye movements using oculography, computational model simulations, genetics, and imaging technologies have markedly improved our understanding of the pathophysiology of involuntary eye movements, as well as their diagnosis and management. Patient-initiated capture of eye movements, especially when paroxysmal, and the online transfer of these data to clinicians would further enhance the ability to diagnose involuntary eye movements.

Author Contributions

Supervision: Ji-Soo Kim. Writing—original draft: Seong-Hae Jeong. Writing—review & editing: Ji-Soo Kim.

ORCID iDs

Seong-Hae Jeong https://orcid.org/0000-0001-5055-9986
Ji-Soo Kim https://orcid.org/0000-0002-1508-2024

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Acknowledgements

This study was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (no. NRF-2016R1D1A1B04935568).

REFERENCES

1. Stahl JS, Leigh RJ. Nystagmus. *Curr Neurol Neurosci Rep* 2001;1:471-477.
2. Straube A. Nystagmus: an update on treatment in adults. *Expert Opin Pharmacother* 2005;6:583-590.
3. Rucker JC. Current treatment of nystagmus. *Curr Treat Options Neurol* 2005;7:69-77.
4. Rucker JC. An update on acquired nystagmus. *Semin Ophthalmol* 2008;23:91-97.
5. Rucker JC. Pearls: nystagmus. *Semin Neurol* 2010;30:51-53.
6. Thurtell MJ, Leigh RJ. Nystagmus and saccadic intrusions. *Handb Clin Neurol* 2011;102:333-378.
7. Strupp M, Kremmyda O, Adamczyk C, Böttcher N, Muth C, Yip CW, et al. Central ocular motor disorders, including gaze palsy and nystagmus. *J Neurol* 2014;261 Suppl 2:S542-S558.
8. Leigh RJ, Zee DS. *The Neurology of Eye Movements*. 5th ed. New York: Oxford University Press, 2015.
9. Choi JY, Kim JS. Nystagmus and central vestibular disorders. *Curr Opin Neurol* 2017;30:98-106.
10. Rucker JC. Nystagmus and saccadic intrusions. *Continuum (Minneap Minn)* 2019;25:1376-1400.
11. Fukushima K, Kaneko CR, Fuchs AF. The neuronal substrate of integration in the oculomotor system. *Prog Neurobiol* 1992;39:609-639.
12. Sharpe JA, Fletcher WA. Saccadic intrusions and oscillations. *Can J Neurol Sci* 1984;11:426-433.
13. Kim SJ, Lee HY, Lee MY, Choi JY. Initial degree of spontaneous nystagmus affects the length of hospitalization of patients with vestibular neuritis. *Otol Neurotol* 2020;41:836-842.
14. Reynard P, Karkas A, Gavid M, Lelonge Y, Bertholon P. Delayed endolymphatic hydrops. Special emphasis on nystagmus associated with episodes and contribution of chemical labyrinthectomy. *Eur Ann Otorhinolaryngol Head Neck Dis* 2018;135:321-326.

15. Kattah JC, Tehrani AS, du Lac S, Newman-Toker DE, Zee DS. Conversion of upbeat to downbeat nystagmus in Wernicke encephalopathy. *Neurology* 2018;91:790-796.
16. Kattah JC, McClelland C, Zee DS. Vertical nystagmus in Wernicke's encephalopathy: pathogenesis and role of central processing of information from the otoliths. *J Neurol* 2019;266:139-145.
17. Huh SY, Min JH, Kim W, Kim SH, Kim HJ, Kim BJ, et al. The usefulness of brain MRI at onset in the differentiation of multiple sclerosis and seropositive neuromyelitis optica spectrum disorders. *Mult Scler* 2014;20:695-704.
18. Lee SU, Kim HJ, Choi JH, Choi JY, Kim JS. Comparison of ocular motor findings between neuromyelitis optica spectrum disorder and multiple sclerosis involving the brainstem and cerebellum. *Cerebellum* 2019;18:511-518.
19. Gupta P, Shaikh AG. "Leaky" and "unstable" neural integrator can coexist-paradox observed in multiple sclerosis. *J Neuroophthalmol* 2020;40:226-233.
20. Das VE, Oruganti P, Kramer PD, Leigh RJ. Experimental tests of a neural-network model for ocular oscillations caused by disease of central myelin. *Exp Brain Res* 2000;133:189-197.
21. Chang TP, Gold DR, Otero-Millan J, Huang BR, Zee DS. Pendular oscillation and ocular bobbing after pontine hemorrhage. *Cerebellum* 2019 Dec 27 [Epub]. Available from: https://doi.org/10.1007/s12311-019-01086-6.
22. Lee SU, Kim HJ, Choi JY, Kim JK, Kim JS. Acute vestibular syndrome associated with anti-GQ1b antibody. *Neurology* 2019;93:e1085-e1092.
23. Jung I, Kim HJ, Kim JS. Fluctuating ataxia and nystagmus in association with anti-GQ1b antibody in HIV infection. *J Neurol Sci* 2017;382:123-125.
24. Lee TK, Park JY, Kim H, Choi KD, Kim JS, Sung KB. Persistent nystagmus in chronic phase of lateral medullary infarction. *J Clin Neurol* 2020;16:285-291.
25. Johkura K, Kudo Y, Sugawara E, Watanabe K, Nakamizo T, Yamamoto M, et al. Effects of cerebellar magnetic stimulation on chronic post-lateral medullary infarction dizziness: a proof-of-principle cohort study. *J Neurol Sci* 2018;392:56-62.
26. Minakaran N, Soorma T, Bronstein AM, Plant GT. Charles Bonnet syndrome and periodic alternating nystagmus: moving visual hallucinations. *Neurology* 2019;92:e1072-e1075.
27. Rim JH, Lee ST, Gee HY, Lee BJ, Choi JR, Park HW, et al. Accuracy of next-generation sequencing for molecular diagnosis in patients with infantile nystagmus syndrome. *JAMA Ophthalmol* 2017;135:1376-1385.
28. Shaikh AG, Manto M. Genome-wide association study points new direction for downbeat nystagmus research. *Cerebellum* 2020;19:345-347.
29. Strupp M, Maul S, Konte B, Hartmann AM, Giegling I, Wollenteit S, et al. A variation in FGF14 is associated with downbeat nystagmus in a genome-wide association study. *Cerebellum* 2020;19:348-357.
30. Young AS, Lechner C, Bradshaw AP, MacDougall HG, Black DA, Halmagyi GM, et al. Capturing acute vertigo: a vestibular event monitor. *Neurology* 2019;92:e2743-e2753.
31. Shaikh AG, Bronstein A, Carmona S, Cha YH, Cho C, Ghasia FF, et al. Consensus on virtual management of vestibular disorders: urgent versus expedited care. *Cerebellum* 2021;20:4-8.
32. Dell'Osso LF, Daroff RB. Congenital nystagmus waveforms and foveation strategy. *Doc Ophthalmol* 1975;39:155-182.
33. Leigh RJ, Dell'Osso LF, Yaniglos SS, Thurston SE. Oscillopsia, retinal image stabilization and congenital nystagmus. *Invest Ophthalmol Vis Sci* 1988;29:279-282.
34. Dell'Osso LF, Huang SS. Development and surgical removal of an epiretinal membrane in infantile nystagmus syndrome: a new type of oscillopsia. *Jpn J Ophthalmol* 2018;62:249-255.
35. Rufai SR, Thomas MG, Purohit R, Bunce C, Lee H, Proudlock FA, et al. Can structural grading of foveal hypoplasia predict future vision in infantile nystagmus? A longitudinal study. *Ophthalmology* 2020;127:492-500.
36. Gantz L, Sousou M, Gavrilov V, Bedell HE. Reading speed of patients with infantile nystagmus for text in different orientations. *Vision Res* 2019;155:17-23.
37. Piarroux J, Riant F, Humbertclaude V, Remerand G, Hadjadj J, Rejou F, et al. FGF14-related episodic ataxia: delineating the phenotype of episodic ataxia type 9. *Ann Clin Transl Neurol* 2020;7:565-572.
38. Delva A, Thakore N, Pioro EP, Poesen K, Saunders-Pullman R, Meijer IA, et al. Finger extension weakness and downbeat nystagmus motor neuron disease syndrome: a novel motor neuron disorder? *Muscle Nerve* 2017;56:1164-1168.
39. Pinto WBVR, Farias IB, Badia BML, Libardi Silva LH, Yanagiura MT, Chieia MAT, et al. Finger extension weakness and downbeat nystagmus motor neurone disease (FEWDON-MND). *Pract Neurol* 2019;19:424-426.
40. Anagnostou E, Papadimas G, Rentzos M, Zambelis T. Downbeat nystagmus and lower motor neuron disease: 14 years follow-up. *J Neurol* 2018;265:714-716.
41. Gazulla J, Orduna-Hospital E, Benavente I, Rodríguez-Valle A, Osorio-Caicedo P, Alvarez-de Andrés S, et al. Contributions to the study of spinocerebellar ataxia type 38 (SCA38). *J Neurol* 2020;267:2288-2295.
42. Lee SU, Kim HJ, Choi JY, Kim JS. Ictal downbeat nystagmus in Ménière disease: a cross-sectional study. *Neurology* 2020;95:e2409-e2417.
43. Yat-Ming Woo P, Takemura S, Ming-Yan Cheong A, Chi-Ho Chu A, Chan Y, Wong HT, et al. Pendular seesaw nystagmus in a patient with a giant pituitary macroadenoma: pathophysiology and the role of the accessory optic system. *J Neuroophthalmol* 2018;38:65-69.
44. Rizvi MT, Cameron L, Kilbane C, Shaikh AG. Paraneoplastic seesaw nystagmus and opsoclonus provides evidence for hyperexcitable reciprocally innervating mesencephalic network. *J Neurol Sci* 2018;390:239-245.
45. Lee SU, Jo SY, Kim HJ, Choi JY, Kim JS. Windmill nystagmus in a patient with subacute visual loss. *J Neurol* 2018;265:2737-2739.
46. Lee SU, Kim HJ, Oh SW, Song EY, Choi JY, Kim JS. Pearls & oy-sters: windmill nystagmus in paraneoplastic cerebellar degeneration. *Neurology* 2018;91:e1831-e1833.
47. Kwon E, Lee JY, Kim HJ, Choi JY, Kim JS. Pearls & oy-sters: divergence nystagmus. *Neurology* 2021;96:290-293.
48. Otero-Millan J, Colpak AI, Kheradmand A, Zee DS. Rebound nystagmus, a window into the oculomotor integrator. *Prog Brain Res* 2019;249:197-209.
49. Bodranghien F, Bastian A, Casali C, Hallett M, Louis ED, Manto M, et al. Consensus paper: revisiting the symptoms and signs of cerebellar syndrome. *Cerebellum* 2016;15:369-391.
50. Bögli SY, Straumann D, Schuknecht B, Bertolini G, Tarnutzer AA. Cerebellar rebound nystagmus explained as gaze-evoked nystagmus relative to an eccentric set point: implications for the clinical examination. *Cerebellum* 2020 Feb 19 [Epub]. Available from: https://doi.org/10.1007/s12311-020-01118-6.
51. Büttner U, Helmchen C, Brandt T. Diagnostic criteria for central versus peripheral positioning nystagmus and vertigo: a review. *Acta Otolaryngol* 1999;119:1-5.
52. Choung YH, Shin YR, Kahng H, Park K, Choi SJ. 'Bow and lean test' to determine the affected ear of horizontal canal benign paroxysmal positional vertigo. *Laryngoscope* 2006;116:1776-1781.
53. Choo OS, Kim H, Jang JH, Park HY, Choung YH. Vertical nystagmus in the bow and lean test may indicate hidden posterior semicircular canal benign paroxysmal positional vertigo: hypothesis of the location of otoconia. *Sci Rep* 2020;10:6514.
54. Fath L, Vuong-Chaney H, Rohmer D, Lamy M, Baumgartner D, Simon F, et al. Unusual locations of benign paroxysmal positional vertigo: rare entity or regular occurrence? *Otol Neurotol* 2020;41:e735-e743.

55. Kim JS, Zee DS. Clinical practice. Benign paroxysmal positional vertigo. *N Engl J Med* 2014;370:1138-1147.
56. Choi SY, Oh SW, Kim HJ, Kim JS. Determinants for bedside lateralization of benign paroxysmal positional vertigo involving the horizontal semicircular canal. *J Neurol* 2020;267:1709-1714.
57. Scarpa A, Cassandro C, Gioacchini FM, Viola P, Cuofano R, Kaleci S, et al. Lateralization of horizontal semicircular canal benign paroxysmal positional vertigo (HSC-BPPV) with the latency test: a pilot study. *Acta Otolaryngol* 2019;139:854-859.
58. Oh HJ, Kim JS, Han BI, Lim JG. Predicting a successful treatment in posterior canal benign paroxysmal positional vertigo. *Neurology* 2007;68:1219-1222.
59. Lou Y, Xu L, Wang Y, Zhao Z, Liu X, Li Y. Orthotropic nystagmus in predicting the efficacy of treatment in posterior canal benign paroxysmal positional vertigo. *Am J Otolaryngol* 2020;41:102472.
60. Choi JY, Glasauer S, Kim JH, Zee DS, Kim JS. Characteristics and mechanism of apogeotropic central positional nystagmus. *Brain* 2018;141:762-775.
61. Choi SY, Jang JY, Oh EH, Choi JH, Park JY, Lee SH, et al. Persistent geotropic positional nystagmus in unilateral cerebellar lesions. *Neurology* 2018;91:e1053-e1057.
62. Imai T, Matsuda K, Takeda N, Uno A, Kitahara T, Horii A, et al. Light cupula: the pathophysiological basis of persistent geotropic positional nystagmus. *BMJ Open* 2015;5:e006607.
63. Kim CH, Hong SM. Is the modified cupulolith repositioning maneuver effective for treatment of persistent geotropic direction-changing positional nystagmus? *Eur Arch Otorhinolaryngol* 2018;275:1731-1736.
64. Park JS, Kim SY, Kim MB. Effect of intratympanic steroid injection in light cupula. *Acta Otolaryngol* 2018;138:769-774.
65. Beh SC. Horizontal direction-changing positional nystagmus and vertigo: a case of vestibular migraine masquerading as horizontal canal BPPV. *Headache* 2018;58:1113-1117.
66. Money KE, Bonen L, Beatty JD, Kuehn LA, Sokoloff M, Weaver RS. Physical properties of fluids and structures of vestibular apparatus of the pigeon. *Am J Physiol* 1971;220:140-147.
67. Oman CM, Young LR. The physiological range of pressure difference and cupula deflections in the human semicircular canal. Theoretical considerations. *Acta Otolaryngol* 1972;74:324-331.
68. Han K, Lee JY, Shin JE, Kim CH. Positional alcohol nystagmus and serum osmolality: new insights into dizziness associated with acute alcohol intoxication. *Med Hypotheses* 2020;138:109606.
69. Bartolini E, Sodini R, Nardini C. Acute-onset vertical nystagmus and limb tremors in chronic renal failure. *J Emerg Med* 2019;56:e13-e15.
70. Alkan G, Emiroglu M, Kartal A. Hydroxyzine-induced vertical nystagmus. *Indian Pediatr* 2018;55:1094.
71. Robert MP, Vidal PP. Intermittent upbeat nystagmus in infancy and antihistamine medications. *Eur J Paediatr Neurol* 2018;22:571-572.
72. Moore T, Armstrong KM. Selective gating of visual signals by microstimulation of frontal cortex. *Nature* 2003;421:370-373.
73. Moore T, Fallah M. Control of eye movements and spatial attention. *Proc Natl Acad Sci U S A* 2001;98:1273-1276.
74. Mastropasqua A, Dowsett J, Dieterich M, Taylor PCJ. Right frontal eye field has perceptual and oculomotor functions during optokinetic stimulation and nystagmus. *J Neurophysiol* 2020;123:571-586.
75. Trouillas P, Takayanagi T, Hallett M, Currier RD, Subramony SH, Wessel K, et al. International Cooperative Ataxia Rating Scale for pharmacological assessment of the cerebellar syndrome. *J Neurol Sci* 1997;145:205-211.
76. Seshagiri DV, Pal PK, Jain S, Yadav R. Optokinetic nystagmus in patients with SCA: a bedside test for oculomotor dysfunction grading. *Neurology* 2018;91:e1255-e1261.
77. Lee H, Kim HA. The association of head shaking nystagmus with head-bending and lying-down nystagmus in horizontal canal benign paroxysmal positional vertigo. *J Vestib Res* 2020;30:95-100.
78. Lee SU, Choi JY, Kim HJ, Kim JS. Recurrent spontaneous vertigo with interictal headshaking nystagmus. *Neurology* 2018;90:e2135-e2145.
79. Dumas G, Curthoys IS, Lion A, Perrin P, Schmerber S. The skull vibration-induced nystagmus test of vestibular function-a review. *Front Neurol* 2017;8:41.
80. Zamora EG, Araújo PES, Guillén VP, Gamarra MFV, Ferrer VF, Rauch MC, et al. Parameters of skull vibration-induced nystagmus in normal subjects. *Eur Arch Otorhinolaryngol* 2018;275:1955-1961.
81. Sinno S, Perrin P, Smith Abouchacra K, Dumas G. The skull vibration-induced nystagmus test: a useful vestibular screening test in children with hearing loss. *Eur Ann Otorhinolaryngol Head Neck Dis* 2020;137:451-457.
82. Theeranaew W, Kim HJ, Loparo K, Kim JS, Shaikh AG. Hyperventilation increases the randomness of ocular palatal tremor waveforms. *Cerebellum* 2020 Jul 31 [Epub]. Available from: https://doi.org/10.1007/s12311-020-01171-1.
83. Heidenreich KD, Pitts CM, Angster K, Zajac T, Havard S, Melendez TL, et al. Electrocochleography results in patients with bilateral vestibular paresis and sound- or pressure-induced horizontal nystagmus. *Otol Neurotol* 2018;39:e274-e279.
84. Okamoto T, Shimizu A, Suzuki M. Dizziness after an earthquake tilted the house. *Auris Nasus Larynx* 2020;47:1070-1073.
85. Leigh RJ, Thurston SE, Tomsak RL, Grossman GE, Lanska DJ. Effect of monocular visual loss upon stability of gaze. *Invest Ophthalmol Vis Sci* 1989;30:288-292.
86. Nguyen A, Borruat FX. Teaching Video NeuroImages: Heimann-Bielschowsky phenomenon: a harmless monocular nystagmus. *Neurology* 2018;90:e731.
87. Nguyen A, Borruat FX. The Heimann-Bielschowsky phenomenon: a retrospective case series and literature review. *Klin Monbl Augenheilkd* 2019;236:438-441.
88. Tello J, Ruiz I, Herrera L, Miranda A, Alid P, Troncoso M. Monocular nystagmus in a patient with alternating hemiplegia of childhood. *Neurology* 2019;93:361.