Pearls & Oy-sters: Divergence Nystagmus

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Pearls

- Imbalance in the vergence system may give rise to disjunctive (disconjugate) horizontal nystagmus.
- Relative overaction of slow convergence may result in divergence nystagmus.
- Divergence nystagmus has rarely been reported in patients with lesions involving the pons and cerebellum.

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Oy-sters

- While convergence or convergence-retraction nystagmus mostly indicates a dorsal mesodiencephalic lesion, divergence nystagmus occurs in lesions involving the midline cerebellum and dorsal pons.
- Divergence nystagmus supports an active neural innervation for divergence, rather than passive relaxation after convergence.

Disjunctive (disconjugate) nystagmus refers to nystagmus that beats in the opposite directions in both eyes.¹ Disjunctive horizontal nystagmus almost always occurs as the form of either convergence or convergence-retraction nystagmus in lesions involving the dorsal mesodiencephalic junction, and has been ascribed to opposing saccades or impaired vergence.^{2,3} In contrast, divergence nystagmus is extremely rare. To the our knowledge, pure or predominant form of divergence nystagmus has been described in only a few patients with lesions involving the cerebellum or pons (table e-1, [links.lww.com/WNL/B284](https://www.links.lww.com/WNL/B284)),^{2,4} even though some patients with downbeat nystagmus may show a small divergent component.⁵

This report describes 2 additional patients with divergence nystagmus in association with lesions involving the dorsal pons and midline cerebellum with a literature review. These findings support distinct neural structures for divergence in the pons and cerebellum, and indicate an active neural innervation for divergence, rather than passive relaxation after convergence.

Case Reports

Patient 1

A 27-year-old woman was consulted for neuro-otologic evaluation 3 days after resection of cerebellar pilocytic astrocytoma mostly occupying the middle portion of the midline cerebellum around the fourth ventricle (figure, A). Before the surgery, the patient had had headache and intermittent fever for a few weeks. The findings of preoperative neurologic examination were unremarkable except swaying tandem gait. The operation was uneventful, but an extra-cranial ventricular drainage was placed the next day due to cerebellar and pontine edema and resultant hydrocephalus.

At the time of consultation, 5 days after the operation, neurologic examination showed spontaneous divergence nystagmus during visual fixation, gaze-evoked nystagmus during lateral gazes, more to the left, and limitation of abduction in the left eye. Convergence was intact.

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(A) One day after the operation, MRI of patient 1 shows a near complete resection of the tumor, but edema along the resection margin, mostly in the paramedian tegmentum of the pons and midline cerebellum. (B) Oculography of patient 1 shows divergence nystagmus during visual fixation with a mean slow phase velocity of $2.0^{\circ}/s$ in the right eye and $3.0^{\circ}/s$ in the left eye. (C) Without visual fixation in darkness, the nystagmus is mostly right-beating in patient 1. (D) MRI of patient 2 shows a mixed solid and cystic mass involving the right cerebellum and pons with a compression of the fourth ventricle. (E) Oculography of patient 2 shows divergence nystagmus during visual fixation with a mean slow phase velocity of $4.5^{\circ}/s$ in the right eye and $4.8^{\circ}/s$ in the left eye. The divergence nystagmus is associated with conjugate upbeat and extorsional nystagmus in both eyes. (F) Without visual fixation in darkness, the nystagmus is mostly left-beating with a small upbeat component in patient 2. The upward deflection indicates rightward or upward eye motion in each recording. Torsional recording is not displayed due to severe noises. (G) Illustration of the neural structures and their connections involved in the control of vergence. FEF = frontal eye field; FN = fastigial nucleus; IN = interposed nucleus; IPL = inferior parietal lobule; LH = horizontal position of the left eye; LV = vertical position of the left eye; MSA = midbrain supraoculomotor area; MST = medial superior temporal area; MT = middle temporal area; NRTP = nucleus reticularis tegmenti pontis; OV = oculomotor vermis; RH = horizontal position of the right eye; RV = vertical position of the right eye.

Saccades were hypermetric rightward and hypometric leftward. Smooth pursuit was impaired bilaterally. Bedside head impulse tests showed perverted responses (downward corrective saccades after horizontal head rotation) in both horizontal directions. Ataxia was noted in the left upper and lower extremities. The patient was unable to sit unaided. Other findings of neurologic examination were unremarkable.

Video-oculography (VOG) 7 days after the surgery documented divergence nystagmus during visual fixation (figure, B), which changed into mostly right-beating nystagmus without visual fixation in darkness (figure, C; video 1). One month later, the patient reported resolution of dizziness and imbalance, and follow-up VOG documented disappearance of the divergence nystagmus.

Patient 2

An 18-year-old woman visited the emergency department with acute dizziness for 2 days probably due to a large cavernoma involving the right cerebellum and pons (3.0×5.3 cm; figure, D). She developed diplopia right after the visit. Examination showed right esotropia with limited abduction of the right eye along with rightward gaze palsy. She also showed spontaneous nystagmus beating outward in each eye and conjugate upbeat nystagmus with a clockwise component in the right eye and counterclockwise component in the left eye (figure, E; video 2). This nystagmus changed into mostly left-beating without visual fixation in darkness and during leftward gaze (figure, F; video 2). During rightward gaze, divergence nystagmus was suppressed and changed into upbeat. Convergence appeared normal. Horizontal smooth pursuit was impaired bilaterally. The patient also had hearing loss in the right ear and ataxia in the right extremities.

Emergent operation was arranged due to worsening nausea and declining mental status due to perilesional edema and increased intracranial hypertension. The pathologic finding was consistent with cavernous hemangioma. Three days after the surgery, follow-up examination with VOG showed a resolution of the divergence nystagmus along with improved headache, dizziness, and nausea. Only small upbeat nystagmus remained without visual fixation in darkness. The patient also showed improvement of the right abduction limitation, rightward gaze palsy, hearing loss, and ataxia on the right side.

Discussion

Our patients showed divergence nystagmus mostly during visual fixation in association with lesions involving the midline cerebellum and dorsal pons.

Disjunctive horizontal nystagmus may be ascribed to an imbalance of vergence eye movements.¹ The predominance of convergent form of horizontal disjunctive nystagmus may be explained by the physiology of vergence eye movements. The

vergence neurons found in the mesencephalic reticular formation fire in a direct proportion to vergence angle and velocity, mainly during convergence.³ Those neurons can be subdivided into tonic cells (related to vergence angle), burst cells (related to vergence velocity), and tonic-burst cells (related to both vergence angle and velocity).³ These premotor neurons are mainly involved in convergence, and only a few are engaged in divergence.⁶

Divergence has been considered a passive eye movement resulting from relaxation of convergence, and divergence palsy has been ascribed to impaired relaxation after convergence.⁷ Indeed, there has been limited evidence of pure vergence signals being released from the abducens nucleus.³ Furthermore, convergence and following divergence are engaged together, and the peak velocity of divergence is related to the preceding convergence tone and starting angle.³ A previous study also failed to find any localized pathology that may account for divergence paralysis, and instead reported a variety of more diffuse etiologies including Wernicke encephalopathy and Parkinson disease.⁸ In these disorders, the divergence paralysis has been explained by bilateral abducens paresis, impaired inhibition of convergence due to diffuse neural dysfunction, or orbital dysfunction (elasticity theory).⁸

Recent studies, however, have proposed a divergence center within the pons, the nucleus reticularis tegmenti pontis (NRTP), which probably has a connection with the deep cerebellar nuclei (figure, G).⁷ The NRTP affects vergence angles and increases firing rates for both near and far responses.⁶ Vergence eye movements are either slow (smooth) or fast (saccadic).³ The NRTP is mostly involved in smooth pursuit and slow vergence.³ Lesions involving the NRTP impair the slow vergence, especially the divergence,⁹ while fast vergence movements are related to other pontine nuclei.³

The NRTP has neural connections with the cerebellum.⁷ Two specific nuclei in the cerebellum, the interposed and fastigial nuclei, have connections with the supra-oculomotor area and mesencephalic reticular formation in the midbrain.⁶ These 2 cerebellar nuclei located either within or close to the vermis appear to have a differential effect on each type of vergence eye movements. The fastigial nucleus specifically synapses close to the Edinger-Westphal nucleus, suggesting its involvement in the near responses.³ While the fastigial nuclei are involved more in convergence, the interposed nuclei show more activities during divergence and distance fixation.⁶ In lesions involving the cerebellar vermis, only slow divergence was reduced, while fast vergence was unaffected.⁶

Divergence paralysis was reported in patients with lesions involving the paramedian and left inferior portion of the pontine tegmentum, thalamus, and midbrain.⁹ Patients with thalamic lesions may show esotropia (thalamic esotropia), likewise in our patients.¹⁰ Thalamic esotropia has

been explained by damage to the prefrontal cortico-oculomotor fibers and resultant disinhibition of the oculomotor neurons innervating the medial rectus, disruption of the supranuclear fibers inhibiting convergence, or damage to the divergence neurons.^{8,10} However, thalamic esotropia is frequently associated with vertical gaze palsy and convergence-retraction nystagmus, rather than divergence nystagmus.¹⁰ Instead, lesions involving the NRTP and cerebellum and causing divergence abnormalities support the theory of a separate divergence neural pathway or “divergence center.”^{7,8}

We report 2 patients with divergence nystagmus in association with lesions involving the midline cerebellum and dorsal pons. Imbalance in the vergence system may give rise to disjunctive horizontal nystagmus. While convergence or convergence-retraction nystagmus mostly indicates a dorsal mesodiencephalic lesion, divergence nystagmus may suggest a lesion involving the midline cerebellum and dorsal pons. Divergence nystagmus supports an active neural innervation for divergence, rather than passive relaxation after convergence.

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Disclosure

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Eunjin Kwon, MD	Seoul National University Bundang Hospital, Seongnam, South Korea	Analyzed and interpreted the data and wrote the manuscript
Ju-Young Lee, MD	Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, South Korea	Analyzed and interpreted the data and revised the manuscript
Hyo-Jung Kim, PhD	Seoul National University Bundang Hospital, Seongnam, South Korea	Analyzed and interpreted the data
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Ji-Soo Kim, MD, PhD	Seoul National University Bundang Hospital, Seongnam, South Korea	Designed and interpreted the data and revised the manuscript

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