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REVIEW ARTICLE

Central Vertigo

Michael Strupp, Thomas Brandt

ABSTRACT

Central vertigo can clinically manifest in three ways: Acute onset of vertigo and dizziness, recurrent attacks and chronic central vertigo. In patients with acute onset of symptoms it is essential to differentiate between central and peripheral vertigo because this has major diagnostic and therapeutic implications. A differentiation can most often be achieved by a careful neuro-ophthalmological and neuro-otological bedside examination. One should look in particular for the following five signs of central lesions: skew deviation/vertical divergence (as a component of the ocular tilt reaction), gaze-evoked nystagmus contralateral to a spontaneous nystagmus, saccadic smooth pursuit, acute nystagmus in combination with a nonpathological head-impulse test and central fixation nystagmus. The most frequent forms of central vertigo with recurrent attacks are vestibular migraine and episodic ataxia type 2. Clinically relevant types of chronic or chronic progressive central vertigo are neurodegenerative disorders affecting the cerebellum which are often associated with cerebellar ocular motor dysfunction, in particular downbeat nystagmus. Treatments of choice for a prophylactic therapy of vestibular migraine are betablocker, topiramate or valproic acid. A new treatment option for episodic ataxia type 2 and downbeat nystagmus are aminopyridines (potassium channel blockers).

Keywords: Stroke, Multiple sclerosis, Ocular tilt reaction, Skew deviation, Downbeat nystagmus, Unbeat nystagmus.

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INTRODUCTION

From an anatomical point of view central vestibular forms of vertigo can be caused by lesions along the central vestibular pathways, which extend from the vestibular nuclei in the medulla oblongata to the integration centers in the rostral midbrain and to the ocular motor nuclei (via the vestibulo-ocular reflex, VOR), and to the vestibulo-cerebellum (flocculus, paraflocculus, vermis and nodulus), the thalamus, and multisensory vestibular cortex areas in the temporoparietal cortex.[6] From a clinical point of view the most relevant anatomical structures for central vertigo and dizziness are infratentorial areas, i.e. the brain stem, the cerebellum and connecting pathways (Fig. 1). These forms of vertigo are often clearly defined clinical syndromes, such as Wallenberg's syndrome with typical ocular motor, perceptual and postural manifestations that permit a precise topographic diagnosis of brain stem lesions or cerebellar lesions. The clinical examination of eye movements and of nystagmus can also be helpful for localizing the lesion site.[7] The most relevant etiologies are ischemic lesions, multiple sclerosis (MS) plaque or hemorrhage, for instance, due to cavernomas.

Differential Diagnosis: Peripheral *vs* Central Vestibular Vertigo

In the acute phase after the sudden occurrence of rotatory vertigo the first question concerns the differential diagnosis: Is it a peripheral or a central vestibular vertigo caused by an acute stroke? In the latter case, specific diagnostics and therapy must be performed without delay. A five-step procedure to look for central vestibular or ocular motor dysfunction is recommended:[8,20]

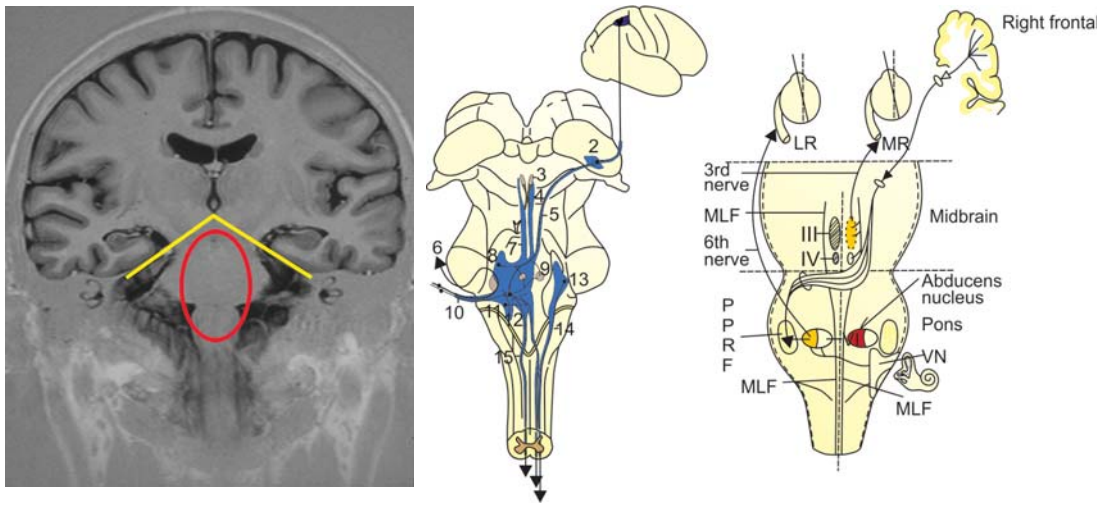


Fig. 1: From a clinical point of view, central vertigo is most often caused by infratentorial lesions affecting the brainstem, the cerebellum or connecting pathways (left). Most often central vestibular lesions are associated with central ocular motor dysfunction because the vestibular and the ocular motor system use similar or adjacent nuclei and pathways

- Skew deviation/vertical divergence (as part of the ocular tilt reaction)
- Gaze-evoked nystagmus contralateral to a spontaneous nystagmus
- Saccadic smooth pursuit
- Nonpathological head-impulse test in patients with an acute nystagmus,
- Central fixation nystagmus (which contrary to peripheral vestibular spontaneous nystagmus is not suppressed by visual fixation).

The presence of a skew deviation/vertical divergence, a gaze-evoked nystagmus in the opposite direction to that of a spontaneous nystagmus, saccadic smooth pursuit, a normal head-impulse test in a patient with acute vertigo and nystagmus,[24] and a fixation nystagmus indicate a lesion of the brain stem (in particular a vestibular pseudoneuritis, Fig. 2), or more seldom a lesion of the cerebellum. However, one has to point out that a central lesion is possible if the head-impulse test is pathological. This 5-step procedure yields a sensitivity of more than 95% for evidence of a central lesion; this sensitivity is higher than that possible with an early magnetic resonance imaging (MRI) with diffusion-weighted sequences (88%).[20]

Central Vestibular Anatomical Structures

The most important structures in central vestibular forms of vertigo are the neuronal pathways mediating the VOR. They travel from the peripheral labyrinth over the vestibular nuclei in the medullary brain stem to the ocular motor nuclei (III, IV, VI) and the supranuclear integration centers in the pons and midbrain (interstitial nucleus of Cajal, INC; and rostral interstitial nucleus of the medial longitudinal fascicle, riMLF).[4,7] Ascending pathways travel contralaterally and ipsilaterally[32] over the posterolateral thalamus up to a network of vestibular areas in the parietotemporal cortex and the insula, e.g. the parietoinsular vestibular cortex (PIVC), areas in the superior temporal gyrus, and inferior parietal lobes, which are, e.g. responsible for perception.[4] Descending pathways lead from the vestibular nuclei along the medial and lateral vestibulospinal tract into the spinal cord to mediate postural control. In addition, there are numerous pathways to the vestibulocerebellum.

Etiology

Central vestibular syndromes are most often the result of lesions of these pathways or of core areas caused by infarction, hemorrhage (in particular due to canvernomas) multiple sclerosis (MS) plaques, for instance in the root entry zone of the 8th cranial nerve (Fig. 2) or rarely tumors. More seldom are pathological stimuli as occur in paroxysmal brain stem attacks (with ataxia and dysarthria) in MS or lacunar infarctions. Vestibular epilepsy is even rarer.

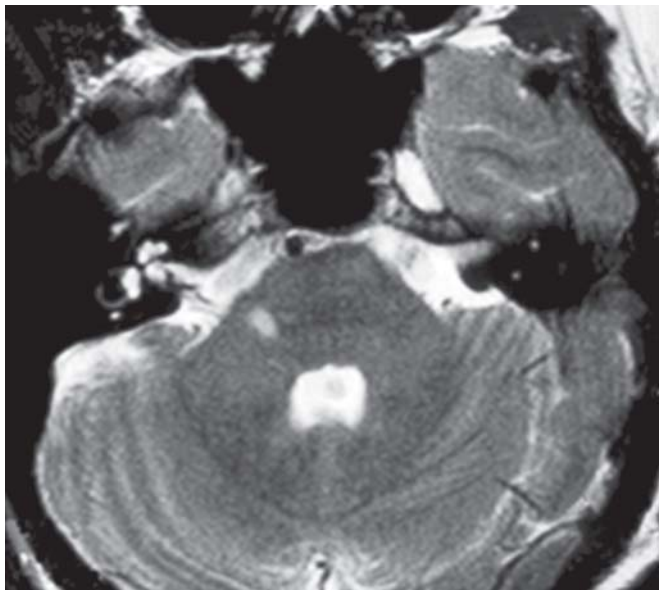


Fig. 2: Magnetic resonance image of a patient with vestibular pseudoneuritis, a disorder of the vestibulo-ocular reflex in the yaw plane. The T2-weighted shows an MS plaque in the root entry zone of the eighth cranial nerve on the right side

Central Vestibular Syndromes

To differentiate central vestibular forms of vertigo from other forms, it is helpful to refer to how long the symptoms last:

- Short rotatory or postural vertigo attacks lasting seconds to minutes or for a few hours are caused by transient ischemic attacks within the vertebrobasilar territory, vestibular migraine, paroxysmal brain stem attacks with ataxia/dysarthria in MS, and the rare vestibular epilepsy.
- Attacks of rotatory or postural vertigo lasting hours to several days, generally with additional brain stem deficits, can be caused by an infarction, hemorrhage or MS plaques in the brain stem and/or vestibule-cerebellum, seldom by a long-lasting attack of vestibular migraine.
- Persisting postural imbalance and dizziness, combined with a tendency to fall, is usually caused by permanent damage to the brain stem or the cerebellum bilaterally, e.g. downbeat nystagmus syndrome due to impaired function of the flocculus/paraflocculus or most often transient in upbeat nystagmus syndrome due to paramedian pontomedullary or pontomesencephalic damage (infarction, hemorrhage, tumor, intoxication).

Central Vestibular Syndromes in the three Planes of Action of the VOR

Based on the functional anatomy central vestibular syndromes can be classified into three different forms depending on the plane: Sagittal (pitch) plane, vertical (roll) plane and horizontal (yaw) plane. The clinical findings correlate with this classification. For instance, impaired

function in the pitch plane is characterized by a vertical down- or upbeat nystagmus, in the roll plane by an ocular tilt reaction and yaw plane by pure horizontal nystagmus.

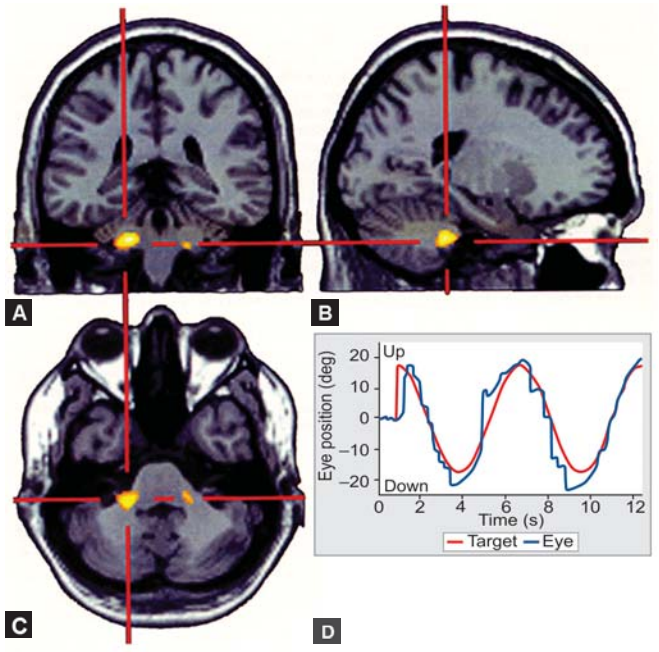
Vestibular Syndromes in the Sagittal (Pitch) Plane

Vestibular syndromes in the sagittal (pitch) plane are characterized by a vertical nystagmus, i.e. a downbeat or an upbeat nystagmus. They have so far been attributed to lesions in the following places: paramedian bilaterally in the medullary and pontomedullary brain stem, the ponto-mesencephalic brain stem with the adjacent cerebellar peduncle, in the paramedian pons, or the cerebellar flocculus/parafloccullus bilaterally.[23] Despite the numerous clinical studies performed on upbeat and downbeat nystagmus as well as the many hypotheses proposed to explain their pathomechanism, so far the pathophysiology of the disorders has not been clarified.[25]

Downbeat Nystagmus

The downbeat nystagmus (DBN) syndrome is a fixation nystagmus that beats downward in primary gaze position, is exacerbated on lateral gaze and in head-hanging position, and can have a rotatory component. It is the most frequently acquired fixation nystagmus and is accompanied by a combination of visual and vestibulocerebellar ataxia with a tendency to fall backward, past-pointing upward and a disturbance of vertical gaze pursuit.[23] DBN is often associated with other oculomotor, cerebellar, and vestibular disorders, e.g. gaze pursuit, OKN or the visual suppression of the VOR. The intensity of idiopathic DBN is dependent on head position—it is less in upright than in supine or prone positions—and on the time of day—it is stronger in the morning than at noon or in the afternoon.[26] The syndrome is frequently persistent.

There seem to be various forms of DBN with different degrees of disturbance. Various mechanisms are currently under discussion, in particular, an impairment of the vertical gaze-pursuit system with spontaneous upward drift. Here the flocculus/parafloccullus seems to play a special role, since its damage leads to a disinhibition of the vestibular pathways of the superior vestibular nucleus to the oculomotor nucleus. This fits with findings from functional imaging studies that have proven that patients with idiopathic downbeat nystagmus have a hypometabolism or a reduced activity in the flocculus/parafloccullus as well as in the pontomedullary brain stem (Figs 3A to D).[15,16] In contrast, structural MRI found atrophies of the gray matter not in the flocculus/parafloccullus but in the lateral portions of the cerebellar hemispheres (lobule VI) and in the oculomotor vermis.[15]



Figs 3A to D: Functional MRI in patients with downbeat nystagmus. A reduction of the activations in the flocculus on both sides was also observed in patients with downbeat nystagmus during vertical gaze pursuit movements (Kalla et al, 2006)

As mentioned above DBN is often caused by a bilaterally impaired function of the flocculus/parafloccullus[16] often associated with an atrophy of the cerebellum, rarely due to drugs, in particular anticonvulsant. It is even more rarely induced by a lesion on the floor of the fourth ventricle. Accordingly idiopathic cases occur most often (38%), degenerative disorders of the cerebellum in 20% of cases, vascular lesions in 9%, malformations in 7%; the more seldom causes like toxic drug damage, lesions in MS and paraneoplastic syndromes, vestibular migraine, vitamin B_{12} deficiency or traumatic and hypoxic injuries occur in decreasing frequency.[31] It can, however, also be caused, but more seldom, by a paramedian lesion of the medulla oblongata, for example, in MS, hemorrhage, infarction or tumor.

There are two subgroups of the idiopathic form of DBN: one with clear cerebellar signs without cerebellar pathology in MRI and the other a combination with bilateral vestibulopathy, peripheral polyneuropathy, or a cerebellar syndrome, suggesting a multisystem degeneration. In 89% of patients with CANVAS syndrome (cerebellar ataxia with neuropathy and bilateral vestibular areflexia syndrome) a circumscribed atrophy of the cerebellum of the anterior and dorsal vermis and crus I was seen in MRI.[22,29]

Upbeat Nystagmus

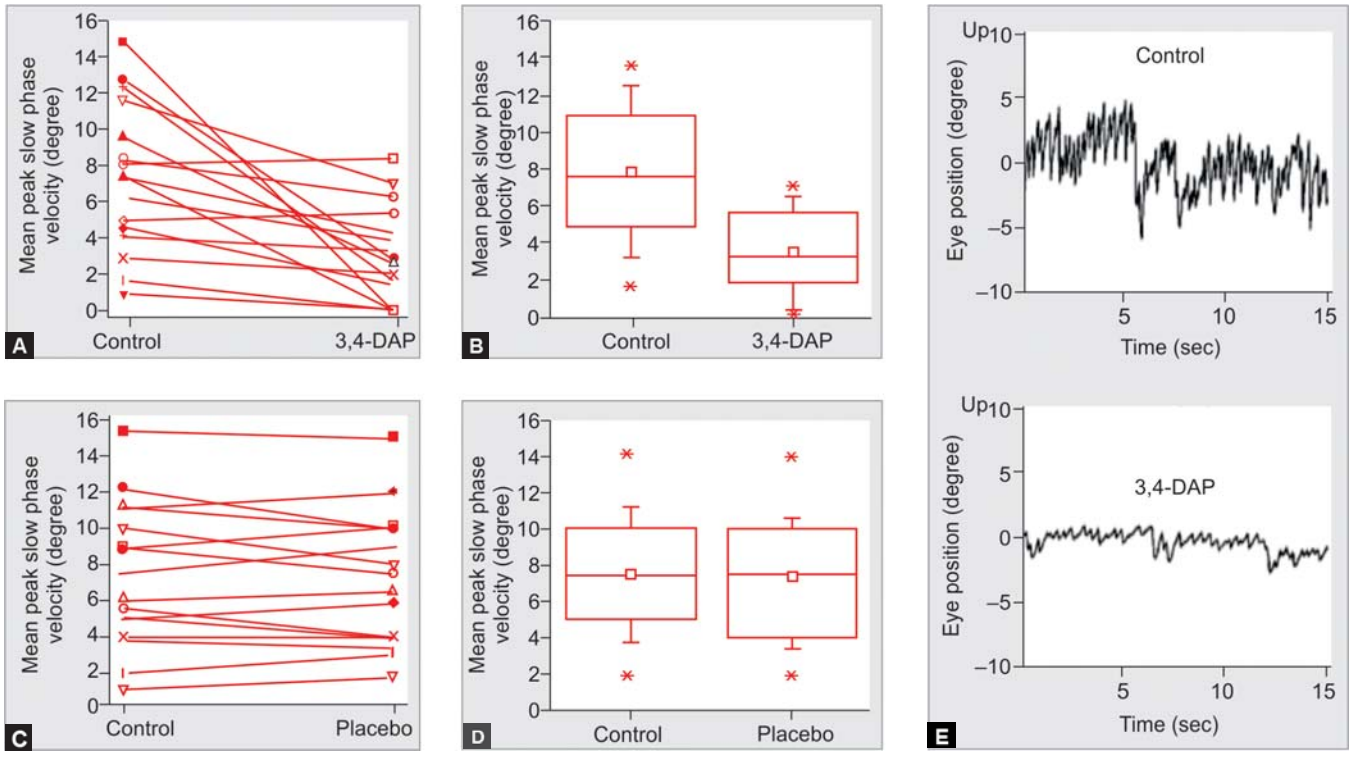
Upbeat nystagmus (UBN) is rarer than DBN. It is also a fixation-induced jerk nystagmus that beats upward in

primary gaze position, is partially dependent on position, and is combined with a disorder of the vertical smooth-pursuit eye movements, a visual and vestibulospinal ataxia with a tendency to fall backward, and past-pointing downward. On the one hand, the pathoanatomical location of most acute lesions is paramedian in the medulla oblongata, in neurons of the paramedian tract, close to the caudal part of the perihypoglossal nucleus, which is responsible for vertical gaze-holding.[25] On the other, lesions have been reported to be paramedian in the tegmentum of the pontomesencephalic junction, the brachium conjunctivum and probably in the anterior vermis. The symptoms persist as a rule for several weeks but are not permanent. Because the eye movements generally have larger amplitudes, oscillopsia in upbeat nystagmus is very distressing and impairs vision. UBN due to damage of the pontomesencephalic brain stem is frequently combined—especially in MS patients—with a unilateral or bilateral internuclear ophthalmoplegia (INO), indicating that the MLF is affected. The main etiologies are bilateral lesions in MS, brain stem ischemia or tumor, Wernicke's encephalopathy, cerebellar degeneration and dysfunction of the cerebellum due to intoxication.

Therapy for DBN and UBN

It is therapeutically expedient to try to treat the symptoms of persisting downbeat nystagmus with various drugs.[28] In the last years the potassium channel blockers 3,4-diaminopyridine and 4-aminopyridine have been proven to have a positive effect, above all in DBN (Figs 4A to E) and also in single cases of UBN.[14,17,18,27,30] Since 4-aminopyridine is more effection than 3, 4-diaminopyridine, 4-aminopyridine is nowadays preferred.[19] 4-aminopyridine can intensify the Purkinje cell activity[13] and thus improve the reduced inhibiting influence of the cerebellum on vertical eye movements. Since epileptic attacks or heart rhythm disorders—especially at higher dosages-can occur, an electrocardiogram (EKG) should be performed before and ca. 30 minutes after the first ingestion of 5 mg 4-aminopyridine in order to detect early any lengthening of the QT interval.[27] The standard dosage is 5 mg tid. The sustained-release form of 4-aminopyridine (Fampyra TM) is also effective.

Since generally UBN slowly resolves after an acute occurrence, therapy for its symptoms is often not



Figs 4A to E: Effect of 3,4-diaminopyridine (3,4-DAP) on downbeat nystagmus (DBN). Influence of 3,4-DAP on the average velocity of the slow phase of DBN (measured by 2D-videography). The figures (A to D) show the average velocity of the slow phase of DBN for each patient. (A) Controls *vs* 3,4-DAP; (C) controls *vs* placebo. Both groups (B) and (D) show a so-called box plot with average, median and 50% percentile values as well as the standard deviation for the controls *vs* 3,4-DAP (B) and controls *vs* placebo (D). 3,4-DAP reduced the maximal velocity of the slow phase of DBN from 7.2°/s to 3.1°/s 30 mins after ingestion of 20 mg 3,4-DAP ($p < 0.001$). In (E) is an original recording of the vertical eye positions before and 30 mins after ingestion of the medication [from (Strupp et al, 2003)]. Since 4-aminopyridine is more effective than 3,4-diaminopyridine nowadays 4-aminopyridine is preferred

necessary. In cases of very disturbing oscillopsias due to large amplitudes of the nystagmus or longer duration one can try 4-aminopyridine (3 × 5 mg/d orally)[14] or memantine (2 × 10 mg/d orally). If both are ineffective, one can try baclofen (2 × 5 mg/d orally).[1]

Vestibular Syndromes in the Vertical (Roll) Plane

These syndromes indicate an acute unilateral deficit of the 'graviceptive' vestibular pathways, which run from the vertical canals and otoliths in the brain stem over the ipsilateral (medial and superior) vestibular nuclei and the contralateral MLF to the ocular motor nuclei and integration centers for vertical and torsional eye movements (INC and riMLF) in the rostral midbrain.[4] Unilateral lesions of the vestibulocerebellar structures (e.g. the uvula, nodulus, dentate nucleus) can also induce signs in the roll plane.[2] More rostral to the midbrain, only the vestibular projection of the VOR for perception in the roll plane (determination of the subjective visual vertical, SVV) runs over the vestibular nuclei, the posterolateral thalamus[12] to the parietoinsular vestibular cortex in the posterior insula.[5] The crossing of these pathways at pontine level is especially important for topographic diagnosis of the brain stem. All signs of lesions in the roll plane—single components or a complete ocular tilt reaction (i.e. head tilt, vertical divergence of the eyes, ocular torsion, SVV deviation)—exhibit an ipsiversive tilt (ipsilateral eye lowermost) in cases of a pontomedullary lesion (medial and superior vestibular nuclei) below the decussation in the brain stem. All signs in the roll plane— perceptual and postural—exhibit contraversive deviations (contralateral eye lowermost) in cases of unilateral pontomesencephalic lesions of the brain stem above the decussation and indicate a deficit of the MLF or of the supranuclear center of the INC. Perceptual deficits in the sense of pathological deviations of the SVV occur during unilateral deficits along the entire VOR projection and of the vestibulocerebellum. They are one of the most sensitive signs of acute brain stem lesions (in ca. 90% of cases of acute unilateral infarctions).[11] Deviation of the SVV in the acute phase is more pronounced in patients with lesions of the vestibular nuclei (Wallenberg's syndrome) than in patients with vestibular neuritis; this means an average of 9.8° as opposed to 7°.[9] The remission of the perceptual deficits over a period of ca. 2 to 4 weeks is very similar in both diseases.

The etiology of these unilateral lesions is frequently an infarction of the brain stem, or the paramedian thalamus as well as hemorrhages, which extend into the rostral midbrain.[11] The course and prognosis depend also here on the etiology of the underlying illness. In the frequent ischemias a significant and generally complete recovery from the symptoms in the roll plane can be expected within days to weeks due to central compensation over the opposite side.[9,10]

Vestibular Syndromes in the Horizontal (Yaw) Plane

Vestibular syndromes in the horizontal (yaw) plane with a pure horizontal nystagmus are rare. They can be caused by horizontal canal benign paroxysmal positioning vertigo.[3] Central syndromes in yaw are most often due to lesions in the area of the root entry zone of the vestibular nerve into the medulla oblongata, the medial and/or superior vestibular nuclei, and the integration centers for horizontal eye movements (nucleus praepositus hypoglossi). Other clinical signs are ipsilateral caloric hyporesponsiveness, horizontal gaze deviation, a tendency to fall to the affected side, and a past-pointing corresponding to a deviation of the 'subjective straight-ahead'. The clinical symptoms are similar to those of an acute peripheral vestibular lesion as occurs in vestibular neuritis and thus is also called 'vestibular pseudoneuritis'. In most cases, however, there is a horizontal rotatory nystagmus. A purely central yaw plane syndrome is rare, because the area of a lesion that can theoretically cause a pure tonus imbalance in the yaw plane adjoins and in part overlaps with structures in the vestibular nuclei, which are also responsible for vestibular function in the roll plane. For this reason mixed patterns are found more frequently. Thus, skew deviation is the only sensitive, but not specific sign that indicates a vestibular pseudoneuritis as opposed to vestibular neuritis.[8] Further, the horizontal head-impulse test also does not allow a clear differentiation between neuritis and pseudoneuritis: 9% of patients with a pontocerebellar infarction have a positive test as well.[24]

The most common causes include ischemic infarctions or MS plaques (Fig. 2) within the vestibular nuclei or fascicles.[21] If the lesion extends beyond the vestibular nuclei, other accompanying brain stem symptoms can be detected. Since, a unilateral medullary ischemic or inflammatory brain stem lesion is mostly present, the prognosis is favorable because central compensation takes place over the opposite side. The symptoms can be expected to resolve slowly within days to weeks. Thus, central compensation can be promoted by early balance training together with the simultaneous treatment of the underlying illness.

REFERENCES

1. Averbuch-Heller L, Tusa RJ, Fuhry L, Rottach KG, Ganser GL, Heide W, et al. A double-blind controlled study of gabapentin and baclofen as treatment for acquired nystagmus. Ann Neurol 1997;41:818-25.

2. Baier B, Bense S, Dieterich M. Are signs of ocular tilt reaction in patients with cerebellar lesions mediated by the dentate nucleus? Brain 2008;131:1445-54.
3. Baloh RW, Jacobsen K, Honrubia V. Horizontal semicircular canal variant of benign positional vertigo. Neurology 1993;43:2542-49.
4. Brandt T, Dieterich M. Vestibular syndromes in the roll plane: Topographic diagnosis from brain stem to cortex. Ann Neurol 1994;36:337-47.
5. Brandt T, Dieterich M, Danek A. Vestibular cortex lesions affect the perception of verticality [see comments]. Ann Neurol 1994;35:403-12.
6. Brandt T, Dieterich M, Strupp M. Vertigo and dizziness - common complaints. London: Springer 2012.
7. Buttner-Ennever JA. Mapping the oculomotor system. Prog Brain Res 2008;171:3-11.
8. Cnyrim CD, Newman-Toker D, Karch C, Brandt T, Strupp M. Bedside differentiation of vestibular neuritis from central vestibular pseudoneuritis. J Neurol Neurosurg Psychiatry 2008;79:458-60.
9. Cnyrim CD, Rettinger N, Mansmann U, Brandt T, Strupp M. Central compensation of deviated subjective visual vertical in Wallenberg's syndrome. J Neurol Neurosurg Psychiatry 2007;78:527-28.
10. Dieterich M, Brandt T. Wallenberg's syndrome: Lateropulsion, cyclorotation and subjective visual vertical in thirty-six patients. Ann Neurol 1992;31:399-408.
11. Dieterich M, Brandt T. Ocular torsion and tilt of subjective visual vertical are sensitive brainstem signs. Ann Neurol 1993a;33: 292-99.
12. Dieterich M, Brandt T. Thalamic infarctions: Differential effects on vestibular function in the roll plane (35 patients). Neurology 1993b;43:1732-40.
13. Etzion Y, Grossman Y. Highly 4-aminopyridine sensitive delayed rectifier current modulates the excitability of guinea pig cerebellar Purkinje cells. Exp Brain Res 2001;139:419-25.
14. Glasauer S, Kalla R, Buttner U, Strupp M, Brandt T. 4-aminopyridine restores visual ocular motor function in upbeat nystagmus. J Neurol Neurosurg Psychiatry 2005;76:451-53.
15. Hufner K, Stephan T, Kalla R, Deutschlander A, Wagner J, Holtmannspotter M et al. Structural and functional MRIs disclose cerebellar pathologies in idiopathic downbeat nystagmus. Neurology 2007;69:1128-1135.
16. Kalla R, Deutschlander A, Hufner K, Stephan T, Jahn K, Glasauer S, et al. Detection of floccular hypometabolism in downbeat nystagmus by fMRI. Neurology 2006;66:281-83.
17. Kalla R, Glasauer S, Buttner U, Brandt T, Strupp M. 4-aminopyridine restores vertical and horizontal neural integrator function in downbeat nystagmus. Brain 2007;130:2441-51.
18. Kalla R, Glasauer S, Schautzer F, Lehnen N, Buttner U, Strupp M, Brandt T. 4-aminopyridine improves downbeat nystagmus, smooth pursuit and VOR gain. Neurology 2004;62:1228-29.
19. Kalla R, Spiegel R, Claassen J, Bardins S, Hahn A, Schneider E, et al. Comparison of 10-mg doses of 4-aminopyridine and 3,4-diaminopyridine for the treatment of downbeat nystagmus. J Neuroophthalmol 2011;31:320-25.
20. Kattah JC, Talkad AV, Wang DZ, Hsieh YH, Newman-Toker DE. HINTS to diagnose stroke in the acute vestibular syndrome: Three-step bedside oculomotor examination more sensitive than early MRI diffusion-weighted imaging. Stroke 2009;40: 3504-10.
21. Kim HA, Lee H. Isolated vestibular nucleus infarction mimicking acute peripheral vestibulopathy. Stroke 2010;41: 1558-60.
22. Kirchner H, Kremmyda O, Hufner K, Stephan T, Zingler V, Brandt T, et al. Clinical, electrophysiological, and MRI findings in patients with cerebellar ataxia and a bilaterally pathological head-impulse test. Ann NY Acad Sci 2011;1233:127-38.
23. Leigh RJ, Zee D. The neurology of eye movements. Oxford, New York: Oxford University Press 2006.
24. Newman-Toker DE, Kattah JC, Alvernia JE, Wang DZ. Normal head impulse test differentiates acute cerebellar strokes from vestibular neuritis. Neurology 2008;70:2378-85.
25. Pierrot-Deseilligny C, Milea D. Vertical nystagmus: clinical facts and hypotheses. Brain 2005;128:1237-46.
26. Spiegel R, Rettinger N, Kalla R, Lehnen N, Straumann D, Brandt T, et al. The intensity of downbeat nystagmus during daytime. Ann NY Acad Sci 2009;1164:293-99.
27. Strupp M, Schuler O, Krafczyk S, Jahn K, Schautzer F, Buttner U, Brandt T. Treatment of downbeat nystagmus with 3,4-diaminopyridine: A placebocontrolled study. Neurology 2003;61:165-70.
28. Strupp M, Thurtell MJ, Shaikh AG, Brandt T, Zee DS, Leigh RJ. Pharmacotherapy of vestibular and ocular motor disorders, including nystagmus. J Neurol 2011;258:1207-22.
29. Szmulewicz DJ, Waterston JA, Halmagyi GM, Mossman S, Chancellor AM, Mclean CA, Storey E. Sensory neuropathy as part of the cerebellar ataxia neuropathy vestibular areflexia syndrome. Neurology 2011;76:1903-10.
30. Tsunemi T, Ishikawa K, Tsukui K, Sumi T, Kitamura K, Mizusawa H. The effect of 3,4-diaminopyridine on the patients with hereditary pure cerebellar ataxia. J Neurol Sci 2010;292: 81-84.
31. Wagner JN, Glaser M, Brandt T, Strupp M. Downbeat nystagmus: Aetiology and comorbidity in 117 patients. J Neurol Neurosurg Psychiatry 2008;79:672-77.
32. Zwergal A, Buttner-Ennever J, Brandt T, Strupp M. An ipsilateral vestibulothalamic tract adjacent to the medial lemniscus in humans. Brain 2008;131:2928-35.

ABOUT THE AUTHORS

Michael Strupp (Corresponding Author)

Professor, Department of Neurology and Clinical Neurophysiology, German Dizziness Center, University Hospital Munich, Campus Grosshadern, Marchioninistrasse 15, 81377 Munich, Germany, e-mail: michael.strupp@med.uni-muenchen.de

Thomas Brandt

Professor, Department of Neurology, Institute of Clinical Neuroscience German Dizziness Center, University Hospital Munich, Campus Grosshadern, Marchioninistrasse 15, 81377 Munich, Germany