Central and Peripheral Vestibular Disease: A Matter of Life and Death

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Introduction

The vestibular system provides information to the brainstem and somatosensory cortex regarding head position, acceleration, and deceleration and provides us with our sense of balance. Clinical signs of dysfunction include side-stepping as though drunk, abnormal head or eye position and spontaneous eye movement. Examination of the patient will allow an assessment of whether the dysfunction is from the nerve and therefore peripheral to the brain or from the brainstem or central. This distinction is critical because central diseases are often life-threatening unless identified and treated, whereas peripheral disease often improves on its own or with minor intervention. There are many causes of peripheral and central vestibular disease but special attention should be given to meningoencephalitis of unknown etiology (MUE) because it is common and often lethal if not treated promptly. This talk will discuss common and distinguishing features of central and peripheral vestibular disease, common causes for diseases in each location and available treatments and prognosis for MUE.

Vestibular Anatomy and Function

Movement of endolymph over the hair cells of the receptors of the inner ear (semicircular canal, saccule, and utriculus) provides input to the vestibular nerve. The cell bodies for the vestibular nerve are located in 4 paired nuclei located within the brainstem nestled around the fourth ventricle and choroid plexus. The receptor apparatus the detects acceleration, deceleration as well as the static position of the head. There are many outputs from the vestibular nuclei:

1) Vestibular system controls eye position and coordinated movement by synapsing on **cranial nerve 3, 4, and 6** via the medial longitudinal fasiculus (MLF). The generation of physiological nystagmus by moving the head left and right is called the vestibulo-ocular reflex. This reflex relies on structures deep within the brainstem and when abnormal and not related to drug therapy, there is an indication of severe brainstem dysfunction.
2) The **vestibulospinal tract** connects the vestibular nuclei with the nerve and muscle and will increase extensor tone to support the body against gravity during movement
3) Vestibular system has projections via the caudal cerebellar peduncle to the **cerebellum** which functions to coordinate movement of the eyes, neck, trunk, and limbs in relation to movement of the head as well as static head position.
4) Vestibular influences on the **vomiting center** in the reticular formation of the brainstem account for the motion sickness often noted in people and possibly in dogs with vestibular dysfunction.
5) There is a conscious awareness or perception of balance and equilibrium and although the pathway is not currently well defined, there is a thalamic relay of information to the **somatosensory cortex.**

Besides the receptors of the inner ear there are visual and proprioceptive inputs into the vestibular system. Blindfolding a vestibular patient and then lifting them off the floor often increase the sense of poor balance. Also, congenitally blind patients often have spontaneous nystagmus.

Central vs. Peripheral Vestibular Disease

Peripheral vestibular disease has a fairly consistent clinical presentation. A useful tool to think about central disease is that dogs whose clinical signs do not look like they peripheral likely have central disease. Please see Table 1.

Peripheral Vestibular Disease

Peripheral vestibular disease typically has a sudden onset and can be associated with vomiting at its onset. Patients have rotary or horizontal nystagmus at a rate of 60 beats per minute or greater and a head tilt of about 20 degrees from midline. The nystagmus can change from rotary to horizontal but its fast phase should remain opposite the direction of the head tilt. Persistent weakness and postural deficit are not noted and after a few hours of acclimating these dogs are bright and responsive and able to ambulate. These patients may lean, side-step or rarely roll in the same direction as the head tilt.
The three most common causes of peripheral vestibular disease are infection of the middle ear extending into the inner ear's bony labyrinth that contains the vestibular receptors (OTMI), the old dog peripheral

vestibular or idiopathic vestibular syndrome (dogs typically older than 5, cats of any age), and the low thyroid state, especially when the cholesterol is elevated.

Central Vestibular Disease

One specific example of central disease is called paradoxical vestibular disease because the signs are different or opposite of what would be expected for peripheral disease. In this syndrome, the lesion is within the brain in the caudal cerebellar peduncle or floculonodular lobe of the cerebellum and the head tilt is opposite the side of the lesion. Some clinical signs of non-peripheral or central vestibular disease include dull mentation, side- stepping/leaning towards head tilt, sway back and forth, hypermetria, tremors, weakness, non-ambulation, postural deficit, nystagmus at a rate under 60 beats per minute, extreme head tilt, cranial nerve deficits besides those associated with Facial nerve and Horner's tract (commonly seen with OTMI). Common causes of central vestibular disease include neoplasia like meningioma (larger breeds), meningoencephaltiis of unknown etiology (MUE), and infarcts of the cerebellum (larger breeds). Please see Table 2.

Non-Vestibular Eye Movement

There have been 2 recent reports describing non-vestibular system spontaneous eye movements called saccadic oscillations and convergent-retraction nystagmus. Common to these spontaneous and fast eye movements is that there is no slow phase or drift of the eye. Convergence-retraction nystagmus is a pulse movement of the eye, and not a nystagmus since there is no drift of the eyes and the lesion is in the midbrain and does not involve the vestibular system. In addition to having a head tilt, the 3 dogs reported would rhythmically converge the eyes and retract them into the orbit, especially when they tried to direct the gaze upwards. These dogs tend to hold there head up with their neck extended because they are unable to elevate their gaze. All 3 dogs with this symptom suffered cerebrovascular accidents with their symptom's improving within 48 hours and eventually resolving.

A saccade is a willful or directed rapid eye movement between fixations points. The saccadic system of eye movement allows us to shift and direct a voluntary gaze and in your instance read this sentence. Saccadic oscillations of the eye result from lesions of the non-vestibular pathways that control saccadic movements and are characterized by a fast, saccadic eye movement without a slow phase. One example is opsoclonus which is a burst of rapid, multidirectional (horizontal, vertical, rotary) eye movement without an initial slow phase. Another example is macrosaccadic oscillation where a shift in the gaze generates a rapid eye movement that oscillates around a fixation point with a build up and then decrease in amplitude – these movements are separated by an intersaccadic interval of about 200 milliseconds. In a recent report of 4 dogs and 1 cat with saccadic oscillations, 1 resolved on its own, 2 required prednisone and 2 had a progressive storage disease called neuronal ceroid lipofuscinosis confirmed with genetic testing and eventually necropsy. Beware that there are non-vestibular eye movements with a specific appearance, central lesion location, and to date a limited set of differential diagnoses.

Meningoencephalitis of Unknown Etiology (MUE)

MUE is a group of diseases all thought to be immune mediated. Necrotizing disease of the grey matter (NME) and white matter (NLE) and Granulomatous meningoencephalitis (GME) are all examples of MUE. GME has a predisposition for the brainstem and often presents with central vestibular signs and is thought to account for up to 25% of all cases of canine CNS disease. Female, small breed dogs 4-8 years of age are predisposed and the diagnosis is made by a combination of clinical suspicion, MRI, CSF and infectious test results. A recent prospective prospective study of 39 MUE dogs treated with prednisone and then 4 weeks later Cytosine arabinoside provides insight into the prognosis with MUE. 13/39 (33%) died in the first 72 hours and 22/39 (56%) died within the first 52 days and the study had an overall mean survival time of 26 days (range 0-2250 days). In progressive MUE, prompt recognition and treatment with Prednisone 0.5 -1 mg/kg, BID, plus a chemotherapy (Cytosine arabinoside, Lomustine, Procarbazine) and/or immune modulation with (Cyclosporine and less commonly Leflunomide, Azathioprine, or Mycophenolate) is thought to provide best chance of a return to normal. In that same study, 12/39 (31%) of dogs returned to normal.

Conclusion

Vestibular disease is a common presenting complaint and assessing the disease to be central or peripheral provides the owner with the best sense of the appropriate diagnostic plan, treatment and prognosis. Having the image of a typical peripheral case in your mind and comparing all cases against this image can allow for best determination of the likelihood of central disease. Prompt treatment of the diseases that cause central vestibular signs is essential for a good outcome.

Table 1. Clinical Signs of Disease in the Central or Peripheral Vestibular System

Observation	**Central Disease**	**Peripheral Disease**
Mentation	Dull	Normal
Gait	Side step opposite head tilt Hypermetria Weakness	Side-steps towards side of lesion
Postural Reactions	Delayed or absent	Normal
Head Tilt	Absent or extreme	20 Degrees
Cranial Nerve Deficits	Any	+/- Facial, +/- Horner's tract
Nystagmus	Vertical or positional (chronic) Fast phase towards lesion Fewer than 10 beats/second	Rotary or horizontal Fast phase away from lesion Greater than 60 beats/minute No slow phase (saccadic)
Positional Strabismus	Ventral on side of head tilt Dorsal opposite head tilt	Ventral on side of head tilt
Neck Pain	Yes	No

Table 2. Categories of Disease that Cause Central or Peripheral Vestibular Disease

Category	**Central Diseases**	**Peripheral Diseases**
Malformation	Rostrocerebellar fluid accumulation Caudal occipital malformation syndrome (COMS) Hydrocephalus	Congenital vestibular disease
Metabolic	Hypothyroidism (± infarction)	Hypothyroidism
Neoplastic	Primary intracranial neoplasms Metastatic neoplasms	Primary aural neoplasia Vestibular neurofibroma
Infectious & Inflammatory	Viral: Canine distemper virus, Feline infectious peritonitis Bacterial: Abscess, Rocky mountain spotted fever, Ehrlichiosis, Bartonellosis, Anaplasmosis	Otitis media interna (OMI) Nasal- and otopharyngeal polyps

	Protozoal: Toxoplasmosis, Neosporosis Mycotic: Cryptococcosis, Blastomycosis, others Non-infectious (MUE)	Idiopathic vestibular disease (vestibular neuronitis)
Trauma	Brainstem trauma	Inner ear trauma
Toxic	Metronidazole	Ototoxic drugs (systemic and topical)
Vascular	Cerebrovascular disease	

Selected References

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