Introduction: A Guide to Neurolocalization
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Introduction
In clinical neurology disease of segments of the nervous system have distinct clinical signs. A neuroanatomic diagnosis occurs when a constellation of clinical signs indicate there is a lesion within a segment of the nervous system. These segments include the brain, spinal cord, and peripheral nerve/muscle. The brain can be further usefully divided into the Forebrain (cerebral hemispheres and thalamus), Brainstem (midbrain to medulla), Cerebellum and Vestibular System

Forebrain (Cerebral & Thalamic dysfunction)
A patient with a right forebrain or thalamic lesion may act confused, compulsively circle to the right and have diminished to absent postural reactions on left with a normal gait, and an absent menace on left with normal pupil light response. This is outlined below with a brief explanation.

1. **Seizure** - synchronized discharges are generated by the grey matter of the cerebral cortex. Disease in the cerebral cortex or thalamus or the connection between these structures can cause seizure. Seizures only originate from the cerebral hemispheres and thalamus.
2. **Altered mental status** - these phenomena probably revolve around an altered perception.
    a. Aggression
    b. Inappropriate urination and defecation
    c. Dementia, disorientation, lethargy, and if bilateral and severe disease- stupor, coma
    d. Head pressing, aggression, pacing, hyperexcitability
    e. Restless at night and sleeping during the day
3. **Normal gait**- the generators of gait are below the thalamus
4. **Compulsive pacing** - patient may continuously propel itself forward despite having obstacles in their path.
5. **Circling towards the side of the lesion** - with right side lesion the ability to perceive stimulus from left side maybe lost. The patient with a right side lesion only perceives information on the right side of the body and therefore may circle right or have a head turn to the right.
6. **Contralateral postural, sensory, and menace deficits** - revealed by examination:
    a. Poor/Absent postural reactions - the proprioceptive information is relayed to the ipsilateral thalamus and then crosses to the opposite somatosensory cortex.
    b. Hypalgesia - information about pain and sensation also cross to the opposite thalamus and ascend to the opposite cortex.
    c. Poor/Absent menace – visual information crosses at the optic chiasm and is ultimately projected via the thalamus to the opposite occipital cortex. The response to light does not involve the thalamus or cerebrum thus pupil size and light response are normal.

Brainstem (midbrain to medulla)
A patient with a brainstem lesion is often dull, stuporous or even comatose depending on the severity of the lesion. Gait exam often shows weakness along with ipsilateral postural reaction deficits may also be noted depending on the level of the lesion.

1. **Depression, stupor, coma** – the reticular activating system located in brainstem
2. **Abnormal gait** and posture (dysfunction is ipsilateral to lesion)
    a. Paresis and ataxia
    b. Poor postural reactions
    c. Increased to normal tone and reflex

These deficits occur because of a lesion within the white matter tracts affecting both descending motor and ascending proprioceptive tracts (see discussion below)

3. **Cranial nerve deficits at level of lesion**
    a. CN 12, 10, 9 : poor gag, dysphagia, laryngeal paralysis, megesophagus
    b. CN 8 : head tilt, nystagmus, positional strabismus, rolling or tight circles
    c. CN 7 : absent blink, droopy ear and lip, no response to noxious stimulus other than pulling head away or withdrawing globe
    d. CN 5: abnormal sensation over face, poor jaw tone, atrophy in muscles of mastication
    e. CN 6: no retraction of the globe, medial strabismus

f. CN 4: lateral rotation of bulb
g. CN 3: ptosis, ventrolateral strabismus, dilated and not responsive pupil (3,4,6) connected to vestibular nuclei and responsible for oculocephalic reflex

Cerebellum

A patient with only cerebellar lesion is bright and responsive with preserved strength and minimal postural reaction deficits. However, they have a characteristic high stepping gait, intention tremor, and occasionally a delay in the menace response. Vestibular signs are often noted with cerebellar disease and maybe manifested as head tilt, nystagmus, and/or positional strabismus.

1. **Intention tremor** – cerebellum is responsible for smoothing out movement
2. **Wide-based stance**
3. **Abnormal gait -** high stepping, hypermetric or over-reaching gait, hypometria possible but more difficult to see
4. **No paresis -** dogs with pure cerebellar lesions are not weak as the cerebellum coordinates but does not initiate gait
5. **Delayed or exaggerated postural reaction** - cerebellum is the integrator of proprioceptive information
6. **Menace deficit** - ipsilateral menace deficit as this response coordinated through cerebellum

Vestibular Disease

The vestibular system is responsible for the sense of balance. This system includes receptors (semicircular canals) in the inner ear, the connecting nerve and nerve root, and the 4 nuclei nestled in the brainstem around the 4th ventricle. Peripheral vestibular disease is from involvement of the receptor system, nerve, or nerve roots. Central vestibular disease is generated from lesions that involve the vestibular nuclei, portions of the cerebellum, or less commonly the high cervical region. It is very useful to be able to distinguish central from peripheral disease because the diagnostic work-up and prognosis are so different. As you might imagine there is some overlap in the clinical signs of peripheral and central disease, however, there are some distinguishing features of central vestibular disease.

Signs with peripheral vestibular disease:

- Head tilt (usually about 20 degrees)
- Leaning, rolling, tight circles opposite side of the head tilt
- Nystagmus fast phase opposite side of head tilt and rate > 60 beats per minute
- Positional strabismus on the same side as head tilt

Signs with central vestibular disease:

- Dull or depressed
- Absent or extreme head tilt often on same side as other deficits
- Nystagmus - vertical, change in direction of the fast phase, fast phase towards head tilt
- Cranial nerve deficits other than Facial nerve or Horner's syndrome
- Abnormal gait (high stepping, side stepping left and right, side step toward head tilt, spinal cord ataxia)
- Postural reaction deficits
- Neck pain can be seen with many diseases of the brainstem

*If overall clinical presentation is different, opposite or paradoxical to what you would expect from a typical peripheral case then highly suspect central disease. Some examples would be an extreme head tilt without nystagmus, side stepping towards the side of the head tilt, or a waxing and waxing progressive course of disease.

** Note that acutely both peripheral and central vestibular patients may have postural reaction deficits. Dogs with central disease tend to stay the same or get worse versus dogs with idiopathic or reversible peripheral disease will often start to get better in the following 24 hours.

Clinical Signs Distinguishing Central from Peripheral Vestibular Disease

Observation	Brainstem / Central	Nerve / Peripheral
Mentation	Dull	Normal
Gait	Weak, spinal cord ataxia, side step to side of head tilt, side step left and right	Side step, lean or tight circles towards head tilt
Postural Reaction	Delayed or absent	Normal
Head tilt	Absent or extreme (> 30 degree)	Present and about 20% off midline
Cranial Nerve Deficits	Yes	Facial, Horner's tract permissible
Nystagmus	Vertical Fast phase towards head tilt Changing direction of fast phase Fewer than 60 beats per minute	Horizontal or/and rotary Fast phase opposite head tilt More than 60 beats per minute
Positional Strabismus	Present without head tilt	Ventral on side of head tilt
Neck pain	Maybe present	Absent
Typical progression of clinical signs	Progressive, wax and wane	Sudden onset improving

Spinal Cord
The divisions of the spinal cord with distinct clinical signs include cervical disease (C1-C5), cervical intumescence (C6-T2), thoracolumbar (T3-L3) and lumbar intumescence / cauda equine (L3-cauda equine)

UMN vs LMN
Gait generation is primarily a brainstem phenomenon. The upper motor neuron (UMN) system starts in the brainstem and relays information to and from the lower motor neuron system (LMN) consisting of the muscle and nerve. The axonal portions of the UMN neurons descend within the white matter of the spinal cord until synapsing on the LMN cell body located in the grey matter of the spinal cord. As previously stated, the LMN starts in the grey matter of the spinal cord and synapses on the muscle triggering muscle depolarization and contraction.

Failure of Ascending Portion of UMN Tract Cause Ataxia and Postural Deficit
A lesion of the white matter can cause sensory dysfunction (ataxia, postural deficit) when the ascending tracts are affected and motor dysfunction (weakness to paralysis) when the descending tracts are affected. The ascending tracts (to the cerebellum and contralateral cortex) provide information about limb position- this is called proprioception. When ascending proprioceptive information cannot reach the cerebellum and the somatosensory cortex then the brain cannot determine where the limb is located in space leading to ataxia and postural deficit.
When a gait is referred to as 'ataxic' it means that an observer can't consistently predict where the limb will land at the end of the protraction phase. Ataxia means without order. To say a gait is disordered or the animal is ataxic, may mean the patient is long-strided, limbs are too narrow or cross midline, limbs are too wide or circumduct, interfere or all of the above. When we perform postural reactions (hopping, paw flip test, tactile placing) we are testing the patient's ability to receive information from the proprioceptors and then make the proper adjustments.

The loss of this ascending information provides for an abnormal gait with the following characteristics.

a. **Long-strided gait** - patient does not know where limb is so can be slow to initiate protraction phase of gait.
b. **Limbs cross midline** - patient does not know where limb is during protraction phase of gait so it may take a course towards midline instead of straight forward
c. **Interference** – one limb may hit the limb on the opposite side
d. **Knuckling** – the patient does not know that the dorsum instead of the palmer or plantar surface of the paw is touching the ground
e. **Circumduction or abduction** during protraction phase.
f. **Limbs too close together or too far apart**
g. **Delayed to absent postural reactions**

The ataxia described here is referred to as a proprioceptive or spinal cord ataxia, however, vestibular and cerebellar lesions can also cause ataxia with different characteristic. High stepping where there is flexion of the joints in the protraction phase is characteristic of cerebellar ataxia, whereas side-stepping as though drunk is noted with vestibular ataxia.

Failure of Descending Portion of UMN Tract Causes Weakness, Increased Tone & Reflex

Brainstem electrical activity travels in white matter of the descending UMN tracts (vestibulospinal, reticulospinal, rubrospinal, and corticospinal) and acts at the level of the intumescence. The intumescence, located at spinal cord segments C6-T2 and L3-S3, are swellings of the spinal cord from the collection of the cell bodies that form the begging of the nerve that synapse on the muscles of the limb muscles. Failure of the UMN tracts causes weakness or paralysis because of a lack of the activation of the LMN that activates the muscle. Additionally, increased muscle tone and reflex result from a loss of the inhibition (disinhibition) of the local reflex arc serving the muscles of the limb. Muscle tone must be inhibited from the upper motor neuron tracts; when this is lost more tone and more reflex develop. Lastly over a long period of time muscle atrophy is noted from disuse. In summary, dysfunction of the motor portion of the UMN tract causes:

a. **Weakness** (paresis) or if more severe, **no limb movement** (paralysis)
b. **Increased tone** and **increased reflex**
c. **Disuse muscle atrophy**

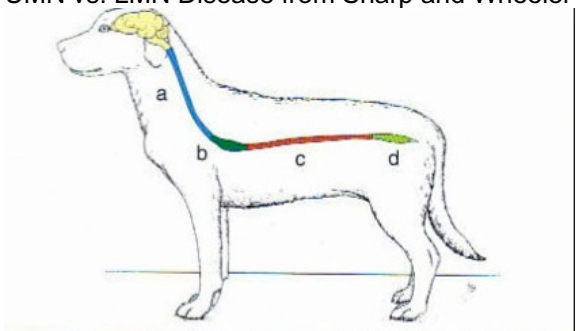
Divisions of the spinal cord

The spinal cord is shorter than the spinal canal. Therefore the number of the spinal cord segment does not always match vertebrae number. This also means that some nerve roots will run in the spinal canal before exiting at an intervertebral foramen. These roots, beyond the spinal cord running to the sciatic, pelvic, pudendal, and coccygeal nerves are called the cauda equina.

The spinal cord segments are divided into the regions above or between the intumescences.

As mentioned above, the cervical (C6,C7, C8, T1 and T2) and lumbar intumescences (L1,L,2, L3, S1, S2,S 3) are swellings of the spinal cord due to the accumulation of ventral horn cells (beginning of the nerve) that run to the limbs. Importantly lesions in the intumescence can damage the LMN and cause LMN disease (see below). Lesions above the intumescence will cause UMN to the limbs that are innervated by the intumescence.

UMN vs. LMN Disease from Sharp and Wheeler Text Book



SITE OF INJURY	THORACIC LIMB DEFICIT	PELVIC LIMB DEFICIT
C1–C5	UMN	UMN
C6–T2	LMN	UMN
T3–L3	NORMAL	UMN
L4–S3	NORMAL	LMN

Peripheral Muscle and Nerve (Lower Motor Neuron)

The nerve that innervates a muscle of the limb starts within the spinal cord. The parts of the nerve include:

a. **Cell body** - these are the large ventral horn cells.
b. **Nerve roots** - these exit the spinal cord and merge to form a numbered spinal nerve
c. **Spinal nerve** – the numbered nerves exit via intervertebral foramen and merge at a plexus
d. **Peripheral nerve** - leave the plexus as a named
e. **Endplate or synapse** – named nerve ends at nerve terminal where will release acetylcholine into the synapse with the muscle leading to muscle depolarization, calcium release, and muscle contraction.

A lesion in any part of the described system will cause what are called lower motor neuron signs. The muscle is also included in this system as muscle disease, endplate disease, nerve disease, nerve root disease, and ventral horn cell disease can all present with similar clinical signs.

a. **Short-stided, choppy gait, or lameness** - the nerve or muscle damage causes less muscle fibers to be working so overall the limb can only travel a short distance.
b. **No ataxia** - some sensory information reaches the spinal cord and this information reaches cerebellum and contralateral cortex.
c. **Less muscle tone and less reflex** - the loss of nerve or muscle means fewer muscle fibers are working.
d. **Rapid loss of muscle mass** - neurogenic atrophy can cause significant muscle loss in only 5-7 days. This stands in contrast to disuse atrophy which is an upper motor neuron phenomenon, slower, and generally less severe.

Upper Motor Neuron (Spinal Cord) and Lower Motor Neuron (Muscle / Nerve) Disease

Observation	Upper Motor Neuron	Lower Motor Neuron
Gait	Long-strided	Short-strided
Ataxia	Yes	No
Postural Deficit	Yes	No
Tone and Reflex	Increased	Decreased
Muscle Atrophy	No	Yes

Example Intracranial Diseases Presentations
(Shaded area represents processes that symmetrically affect the brain)

Disease	Onset	Progressive	Distribution	Types	Treatment
Inflammation	Sudden	Yes	Brainstem	Meningoencephaltiis Of Unknown Origin	Cyclosporine Cytosar, Lomustine,Procarbazine, Leflunomimde, Prednisone
Infection	Sudden	Yes	Brainstem	Cryptococcus Tick Borne Protozoal Distemper	Fluconazole Amphoteracin Doxycycline Clindamycin, TMZ, Ponazuril
Trauma	Sudden	Seldom	Forebrain or Brainstem		Supportive care, surgery No steroids
Neoplasia	Gradual	Yes	Forebrain or Brainstem	Meningioma Glioma Lymphoma	Surgery, Systemic or Local Chemotherapy, Radiation, Vaccine ,
Infarct	Sudden	No	Cerebellum Other	Hemorrhagic and Ischemic	Treat underlying disease Aspirin?
Malformation	Either	Yes	Forebrain	Hydrocephalus, COMS	Prednisone, Omeprazole, surgery
Metabolic	Either	Yes	Either	Low thyroid, Glucose, Electrolytes Liver shunt	Supplement Lactulose, ABs, surgery
Degenerative	Gradual	Yes	Cerebellum	Abiotrophy	None
Toxin	Sudden	Seldom	Brainstem	Metronidazole	Valium