Differential Diagnosis and Management of Brainstem and Cerebellar Infarctions

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Objectives

1. Apply the process of differential diagnosis in the examination and management of brainstem and cerebellar infarctions versus acute vestibular pathology.

2. Identify the constellation of functional impairments associated with specific brainstem, cerebellar and vestibular syndromes.

3. Utilize the oculomotor examination to identify lesion locations associated with brainstem, cerebellar and vestibular structures.

4. Determine the long-term outcomes of the brainstem and cerebellar lesions.
Incidence of Vertigo and Dizziness – Emergency Department

- Vertigo and Dizziness account for 4 million Emergency Department visits annually in the US. (Newman-Toker et al 2013)

- Of all cases of dizziness, 32.9% due to oto-vestibular causes. (Newman-Toker, Hsieh et al, 2008)

Acute Vestibular Syndrome (AVS) – Peripheral or Central in Origin

Symptoms – Rapid Onset
- Severe, continuous vertigo or dizziness
- Nausea with retching or vomiting
- Gait instability
- Head motion intolerance
- Nystagmus

Evolves over seconds to hours
Duration of Symptoms – Days to weeks.
Acute Vestibular Syndrome (AVS) – Peripheral or Central in Origin

Causes of AVS:
- Peripheral – vestibular neuritis or nonbacterial labyrinthitis.
  - 75% of all cases.
- Central – brainstem or cerebellar stroke
  - 25% of all cases.
  - Half of cases have no focal neurological signs.

35% of stroke cases presenting to ED with dizziness are misdiagnosed (Kerber KA et al, 2006)

Acute Vestibular Syndrome of Central Origin

- 4 – 6% of ED visits associated with dizziness and vertigo have cerebrovascular causes
  - 160,000 – 240,000 visits (Newman-Toker 2013)

- Missed cerebellar stroke at the initial ED visit may confer up to an eightfold increased risk of death (Tarnutzer AA, CMAJ 2011)

- Symptoms often isolated and don’t meet criteria for a TIA (Paul Nicola M, 2013 Lancet Neurology)
Posterior Circulation Stroke in Population Based Study in UK

Oxford Vascular Study 2002 - 2010

- Of 1034 consecutive patients with definite stroke:
  - 73% (N=759) - carotid territory
  - 27% (N=275) - vertebrobasilar territory

- 22% with posterior circulation had at least one event in 90 days prior to stroke

- Isolated transient neurological attacks were 15x’s more likely before a vertebrobasilar stroke than carotid stroke.
  - Symptoms include isolated vertigo, vertigo plus other symptoms, isolated double vision, transient generalized weakness, binocular visual disturbances.

Clinical Examination Important in Identifying Acute Central Vestibular Pathologies

Imaging not sensitive acutely. In the first day:

- CT scans identified 16% of posterior fossa infarctions.

- MRI with diffusion-weighted imaging identified 80% of posterior fossa infarctions.

Left Lateral Medullary Syndrome. (A) T2 Weighted axial MRI. (B) MRI with diffusion-weighted imaging

http://www.bmj.com/content/348/bmj.g3175
Clinical Implications

- Accurate diagnosis of stroke is necessary to:
  - Initiate appropriate treatment
  - Prevent adverse outcomes resulting from missed opportunities for thrombolysis or surgical intervention

Differential Diagnosis - Brainstem CVA
The Rule of 4 of the Brainstem

Gates, 2005
Brainstem Anatomy

Step 1: Determine if Medial v. Lateral Brainstem Lesion
The Rule of 4 of the Brainstem

1. 4 structures in the “midline' beginning with M – medial brainstem lesions.
2. 4 structures to the side beginning with S – lateral brainstem lesions.

Medial Brainstem – #1 Structure CST

Medial Structure – Motor Pathway or Corticospinal Tract.
Lesion - contralateral weakness of arm and leg.
**Medial Brainstem - #2 Medial Lemniscus**

Medial Structure – Medial Lemniscus.
Lesion - contralateral loss of vibration and proprioception in arm and leg.

**Medial Brainstem - #3 MLF**

Medial Structure – Medial Longitudinal Fasciculus (MLF). Connections between abducens, oculomotor, trochlear, and vestibular nucleus.
Lesion – Ipsilateral Internuclear Ophthalmoplegia (INO).
Inability to adduct eye. Ability to converge.
Differential Diagnosis and Management of Brainstem and Cerebellar Infarctions

Medial Brainstem - #4 Motor CN Nuclei

Motor CN Nuclei – Lower motor neuron.
• Oculomotor (CN III)
• Trochlear (CN IV)
• Abducens (CN VI)
• Hypoglossal (CN XII)

Lesion: Ipsilateral involvement.

The Rule of 4 of the Brainstem

Gates, 2005

1. 4 structures in the “midline’ beginning with M – medial brainstem lesions.
2. 4 structures to the side beginning with S – lateral brainstem lesions.
**Lateral Brainstem - #1 Spinothalamic Tract & #2 Sensory Nucleus of V**

Lateral Structures – Spinothalamic Tract (5) and Sensory Nucleus of V (6)

Lesion - altered sensation of pain and temperature affecting contralateral arm and leg -and- ipsilateral face.

**Lateral Brainstem - #3 Spinocerebellar Pathway**

Lateral Structure – Spinocerebellar pathway (7).

Lesion – Ipsilateral ataxia of the arm and leg.
**Lateral Brainstem - #4 Sympathetic Pathway**

Lateral Structure – Sympathetic pathway (8).
Lesion – Ipsilateral Horner's Syndrome. Partial ptosis, miosis and anhidrosis.

![Sympathetic Pathway](image)

**Transverse Rostral Medulla**

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**Step 2: Determine Level of Brainstem Lesion**

![Brainstem Model](image)
The Rule of 4 of the Brainstem

Gates, 2005

- 4 cranial nerves in the medulla, 4 in the pons and 4 above the pons (2 in the midbrain).

- 4 midline motor nuclei divide equally into 12 – III, IV, VI, and XII.

- 4 side nuclei (lateral) are located in the pons/medulla - V, VII, IX, and XI.

- 2 nuclei exceptions – I, II.

Determine CN Involved
Lesion Level Based on Location CN Nucleus

Medial CN Nuclei – Lower motor neuron:
- Oculomotor (CN III)
- Trochlear (CN IV)
- Abducens (CN VI)
- Hypoglossal (CN XII)

Lesion: Ipsilateral involvement.
**Differential Diagnosis and Management of Brainstem and Cerebellar Infarctions**

**Determine CN Involved Lesion Level Based on Location CN Nucleus**

**Lateral CN Nuclei** – Sensory &/or Lower motor neuron:
- Trigeminal (CN V)
- Facial (CN VII)
- Glossopharyngeal (CN IX), Vagus (X)
- Spinal Accessory (XI)

Lesion: Ipsilateral involvement.

**Vertebrobasilar Artery Supplies Brainstem**

**Branches**
- Posterior Inferior Cerebellar A. (PICA)
- Anterior Inferior Cerebellar A. (AICA)
- Superior Cerebellar A.
Vertebrobasilar A. Branches that Supply Brainstem and Cerebellum

Branches

- Posterior Inferior Cerebellar A. (PICA) supplies medulla and inferior cerebellum
- Anterior Inferior Cerebellar A. (AICA) supplies pons and mid cerebellum
- Superior Cerebellar A. supplies midbrain and superior cerebellum

Blood Supply to Medial v Lateral Brainstem

Branches that supply interior of brainstem.
- **Paramedian Branches** – supply medial brainstem.
- **Circumferential Branches** – supply lateral brainstem (side)
  - Short circumferential
  - Long circumferential (dorsolateral).
### Posterior Inferior Cerebellar Artery Infarct

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Structures Possibly Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertigo, Ny, nausea, and vomiting</td>
<td>vestibular nuclei, flocculus</td>
</tr>
<tr>
<td><strong>Dysphagia and hoarseness due to ipsilat paralysis palate, pharynx, and larynx. Intractable hiccups.</strong></td>
<td>Nucleus Ambiguous and exiting fibers of CN IX and X</td>
</tr>
<tr>
<td>Limb ataxia ipsilat, gait ataxia</td>
<td>Inferior cerebellar peduncle</td>
</tr>
<tr>
<td>Pain and temperature loss contralat limbs</td>
<td>Spinothalamic tract</td>
</tr>
<tr>
<td><strong>Facial hemianesthesia ipsilateral</strong></td>
<td>Spinal trigeminal tract, nucleus</td>
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<td>Facial Paralysis ipsilat</td>
<td>Facial nerve fascicle</td>
</tr>
<tr>
<td>Lateral Rectus Weakness ipsilat</td>
<td>Abducens nerve</td>
</tr>
<tr>
<td>Dysmetria of saccades, lateropulsion of eyes</td>
<td>vestibular nuclei</td>
</tr>
<tr>
<td>Horner’s Syndrome ipsilat</td>
<td>Sympathetic fibers</td>
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### Anterior Inferior Cerebellar Artery Infarct

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<td>Labyrinth, vestibular nerve, vestibular nuclei, flocculus</td>
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<td><strong>Tinnitus, hearing loss ipsilateral</strong></td>
<td>Cochlea, auditory nerve, cochlear nuclei</td>
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<td>Gait and limb ataxia ipsilat</td>
<td>MCP, anterior inferior cerebellum</td>
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Oculomotor System Divided by Anatomical Location

- **Nuclear** – Cranial Nerve nuclei (III, IV, VI, VIII)
- **Infranuclear** – CN III, IV and VI and extraocular muscles.
- **Internuclear** – Medial longitudinal fasciculus (MLF). Connections between oculomotor, trochlear, abducens, and vestibular nuclei.
- **Supranuclear** – cortical structures and pathways that descend into the brainstem and are rostral to the ocular motor nuclei.

Infranuclear and Nuclear Control of Eye Movements: Extraocular Muscles and Innervation
Extraocular Muscles - Actions in 9 Planes

<table>
<thead>
<tr>
<th>Extraocular M</th>
<th>Primary Action</th>
<th>Secondary Action</th>
<th>Tertiary Action</th>
<th>CN Innervation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral Rectus</td>
<td>Abduction</td>
<td>None</td>
<td>None</td>
<td>VI</td>
</tr>
<tr>
<td>Medial Rectus</td>
<td>Adduction</td>
<td>None</td>
<td>None</td>
<td>III</td>
</tr>
<tr>
<td>Superior Rectus</td>
<td>Elevation</td>
<td>Incyclotorsion</td>
<td>Adduction</td>
<td>III</td>
</tr>
<tr>
<td>Inferior Rectus</td>
<td>Depression</td>
<td>Excyclotorsion</td>
<td>Adduction</td>
<td>III</td>
</tr>
<tr>
<td>Superior Oblique</td>
<td>Incyclotorsion</td>
<td>Depression</td>
<td>Abduction</td>
<td>IV</td>
</tr>
<tr>
<td>Inferior Oblique</td>
<td>Excyclotorsion</td>
<td>Elevation</td>
<td>Abduction</td>
<td>III</td>
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Extraocular Muscle Actions Illustrated for Right Eye
http://www.improveeyesighthq.com/eye-muscles.html

Extraocular Muscles tested in 9 Planes
http://clinicalexamskills.blogspot.com/

Eye Muscle Innervation

Nuclear - final common pathway –
- Oculomotor Nucleus (CN III)
- Trochlear Nucleus (CN IV)
- Abducesens Nucleus (CN VI)

http://www.gopixpic.com/
Oculomotor Nuclear Complex – Innervation
Midbrain at Level of Superior Colliculus

- Oculomotor Nuclear Complex compartmentalized and organized by muscle action – SR, IR, IO, MR.
- Oculomotor Fascicle maintains functional organization.

Organization of Eye Movements

Key Point
- Midbrain center for control of vertical eye movements and vergence
- Pons center for control of horizontal eye movements

Lesion: Deficits ipsilateral to side of lesion.
Insertions of Extraocular Muscles Aligned with Canal Planes

Canal/Otolith Generate Eye Movement within Canal Plane

<table>
<thead>
<tr>
<th>Canal/Otolith</th>
<th>Eye Movement Direction</th>
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<tbody>
<tr>
<td>Horizontal</td>
<td>Horizontal</td>
</tr>
<tr>
<td>Anterior</td>
<td>Upward</td>
</tr>
<tr>
<td>Posterior</td>
<td>Downward</td>
</tr>
<tr>
<td>Otolith</td>
<td>Torsional</td>
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</tbody>
</table>

Vestibular System:
Three Major Planes of Action

Planes of Motion

Pitch

Roll

Yaw

Pitch Axis

Roll Axis

Yaw Axis
**Vestibular Ocular Reflex**  
Each canal generates rotational VOR within the plane of the canal. Excitatory connections illustrated.

1°  2°  3°

**AC - Upward Eye Movement**  
**PC - Downward Eye Movement**  
**LC - Contralateral Horizontal Eye Movement**

**Vestibular Nerve - CN VIII**  
*Illustrated for Right Inner Ear*

- **Superior Branch Innervates:**
  - Crista Ampullaris of Anterior and Lateral Canal
  - Macula of Utricle

- **Inferior Branch Innervates:**
  - Crista Ampullaris of Posterior Canal
  - Macula of Saccule
Vestibular Nuclear Complex
Organized by Plane of Motion

Canal Planes of Motion

Superior Branch:
- Fibers from AC project to Superior vestibular nucleus – vertical (upward) VOR
- Fibers from LC project to Medial vestibular nucleus – horizontal VOR

Inferior Branch:
- Fibers from PC project to Superior and Medial vestibular nucleus - vertical (downward) VOR

Vestibular Ocular Reflex

Otolith organs generate translational VOR.

- Surge – Forward/backward
- Sway - Side/side
- Heave - Up/down
Vestibular Nuclear Complex Organized by Plane of Motion

Otolith Organs Planes of Motion

**Superior Branch:**
- Fibers from utricle project to Medial, Lateral and Descending vestibular nucleus - forward/backward and side/side.

**Inferior Branch:**
- Fibers from saccule project to Medial, Lateral, and Descending vestibular nucleus - forward/backward and up/down
Supranuclear Control of Eye Movements:
Hold Image on the Fovea and Shift Gaze

Hold Image on Fovea

Visual Fixation
– Holds image of a stationary object on the fovea when the head is still.

Vestibular Ocular Reflex
– Holds image of a stationary object on the retina during brief head movements.

Optokinetic Reflex
– Holds image stable on the retina during sustained low frequency head rotation.
### Shift Gaze

**Pursuit**
- Holds images of a moving target on the retina. Head still.  
  *Needs visual stimulus.*

**Saccades**
- Rapid conjugate movement of the eyes to place the object of interest onto the fovea. Head still.

**Vergence**
- Eye movements adjust for target distance by changing the angle between the eyes.

![Cat chasing a mouse](image)

### Role of Vestibular Nuclear Complex in Generation of Eye Movements

- Vestibular Nuclear Complex involved in generation of:
  - Vestibular Ocular Reflex
  - Pursuit
  - Optokinetic Reflex

- Gain of vestibular system modified by amount of vergence.

- Pursuit deficits associated with downbeating nystagmus.
Clinical Examination

Examination - Neurological Screening

- **Motor Screen**
  - ROM
  - Muscle performance
    - Facial Nerve (CN VII)
  - Coordination
  - Gait/Balance

- **Sensory Screen**
  - Pain & Temperature
    - Anterolateral System
    - Trigeminal (CN V)
  - Proprioception
  - Vision
  - Auditory

- **Autonomic Screen**
  - Horner's Syndrome (ipsilateral)
    - Miosis
    - Ptosis
    - Anhidrosis
Oculomotor Examination

- **Observation**
  - Head/body posture
  - Position of eyelids

- **Visual Examination**
  - Acuity
  - Confrontation

- **Alignment of Visual Axes**
  - Cover/uncover test

- **Pupillary light reflexes**

- **ROM**

- **Hold Image on Retina:**
  - Fixation – primary position.
  - Gaze holding
    - eccentric gaze
    - primary position (rebound)
  - VOR
    - Impulse Test
    - Head-shaking Test
  - VOR cancellation
  - Optokinetic

- **Shift Gaze**
  - Saccades
  - Pursuit
  - Vergence

Interpretation of Clinical Findings
Bilateral Vestibular Input Makes Up Central Vestibular Tone

Lesion to vestibular pathway leads to vestibular tone imbalance. May occur in one of three planes of action:

- Pitch (sagittal, vertical canals)
- Yaw (transverse, lateral canals)
- Roll (frontal, utricles)

Plane-specific vestibular syndromes determined by:

- Ocular motor signs
- Postural signs
- Perceptual signs
Central Vestibular Syndrome in Pitch Plane

Vestibular Tone Imbalance: Pitch and Roll Plane

**Hypothesis:**

1. Signal processing of the VOR in roll and pitch is conveyed by same ascending pathway in MLF.
   - Unilateral lesion – affects function in the roll plane
   - Bilateral lesion – affects function in the pitch plane.

2. Common integrator system for eye movements in roll and pitch plane.

(Brandt and Dieterich, 1995)
Central Vestibular Tone Imbalance: Pitch Plane

Pitch Plane Signs are:
- Upbeat/downbeat nystagmus
- Forward/backward tilts
- Forward/backward falls
- Deviations of perceived horizontal.

(Brandt and Dieterich, 1995)

Vertical Slow Phase Compensatory Eye Movement Generated by Vertical Canals

RA/LP Stimulation: right anterior and left posterior – canal pairing.

Pitch Plane – Static Central Vestibular Tone
Static vertical eye position - need balance of vestibular input between sides and between vertical canals.

Anterior Canal

Posterior Canal

Up - VOR
Anterior Canal – 2 excitatory tracts – CVTT and MFL

Down - VOR
Posterior Canal – 1 excitatory tract - MLF
Why is there Overactivation of the Final Common Upgaze Pathway?

Gravity Influences Vertical Eye Position: Effects Central Vestibular Tone Balance between Bilateral Anterior and Posterior Canals
Gravity

- Gravity has an effect on the eyeball in the upright position because the center of mass is anterior to the center of rotation.

- The location of the center of mass favors downward eye movement and restrains upward eye movement.

(Harris, LR et al., 1993)

Gravity and Nystagmus

- **When the head is in the upright position:**
  - hypergravity results in sustained upbeat nystagmus due to relative over activity in the downward system
  - hypogravity results in sustained downbeat nystagmus due to relative over activity in the upward system

- **When the head is in the prone position:**
  - No nystagmus is observed in either hyper or hypo gravity

Findings confirm the influence of gravity on vertical eye position

(Clement G et al., 1989; Cheung BS et al, 1994)
CVTT “Antigravitational Pathway”
Supplements Tonic Activity of the MLF Pathway to Counter Gravity

Vestibular Tone Imbalance in Pitch Plane due to Lesions of Vertical VOR

• Nystagmus in primary position of gaze:
  – Downbeating Nystagmus
    • Greater looking laterally or down
    • Most common form of acquired involuntary nystagmus
  – Upbeating Nystagmus
    • Greater looking up

Pierrot-Deseilligny, C 2005
Wagner JN et al, 2008
Vestibular Tone Imbalance in Pitch Plane

Downbeating Nystagmus involves:
- bilateral lesion of flocculus
- unilateral lesion of vermis and lateral cerebellum.
- midline lesion crossing ventral tegmental tract (CVTT).

Upbeating Nystagmus involves midline lesion:
- MLF
- Nucleus of Roller
- Intercalatus Nucleus
- Midline lesion crossing ventral tegmental tract (CVTT).

(Brandt and Dieterich, 1994)

Cases:
Central Vestibular Tone Imbalance - Pitch Plane
Bilateral floccular lesions result in disinhibition of SVN

Overactivation of SR creates upward slow phase eye movements resulting in downbeating nystagmus
3,4-diaminopyridine and 4-aminopyridine suppress downbeat nystagmus in some individuals by increasing Purkinje cell activity and increasing inhibition of AC projections by the flocculus.

Medical Treatment: Medication to Suppress Downbeating Nystagmus

66 y.o. Male with Multiple Sclerosis

- Experienced oscillopsia and diplopia on left gaze when driving his car.
- Exam:
  - decreased right adduction and left monocular nystagmus on abduction = R MLF syndrome (INO)
  - But, with fixation removed, there was downbeating nystagmus
    - Increased with rightward or downward gaze
Paramedian Tract neurons excite flocculus. A lesion results in decreased inhibition of SVN and overactivation of SR creating upward slow phase eye movements and downbeating nystagmus.

**FLOCCULUS**

**CVTT**

**MLF**

**Paramedian Tract Neurons**

**SR**

**III**

**IV**

**VI**

**PONS**

**MEDULLA**

**Downbeating Nystagmus**

Nakamagoe K et al, 2013

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**47 y.o. man with Sudden Onset Marked Oscillopsia and Gait Disturbance**

- Examination revealed primary position upbeating nystagmus

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**Fig. 2.** T2-weighted MRL note the lesion (arrow) in the left paramedian part of the pons, 7 mm above the midpons level, affecting the posterior part of the basis pontis. L = Left.

http://serendip.brynmawr.edu/bb/kinser/definitions/def-pons.html

Pierrot-Deseilligny C et al, 2005
Unilateral Pontine Lesion Causing Upbeating Nystagmus

- Redundancy in innervation of Superior Recti

- Unilateral lesion at decussation of Crossing Ventral Tegmental Tract (CVTT) eliminates bilateral inputs to Superior Recti causing slow phase downward eye movement and resultant Upbeating Nystagmus (UBN)

Pierrot-Deseilligny, C et al, 2005
32 y.o. Female with Chief Complaint Dizziness - 2 weeks Duration

- Examination revealed:
  - Primary position upbeat nystagmus
  - No other neurological abnormalities

Lesion left side of dorsal caudal medulla

Lesions in the caudal medulla result in decreased inhibition to the flocculus, an increase in inhibition to the SVN and decreased activation of SR

Decreased activation of SR results in a downward slow phase and resultant upbeat nystagmus

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Upbeating Nystagmus due to Intercalatus Nucleus Lesion

Primary position upbeat nystagmus is present.

Central Vestibular Syndrome in Yaw Plane
Central Vestibular Tone Imbalance: Yaw Plane

Yaw Plane Signs are:
- Horizontal nystagmus
- Past pointing
- Rotational and lateral body falls
- Deviation of perceived straight ahead.

(Brandt and Dieterich, 1995)

Horizontal Slow Phase Compensatory Eye Movement Generated by Horizontal Canals

Horizontal Canal Stimulation: right and left horizontal – canal pairing.

Right
Left

Vestibular Tone Imbalance in Yaw Plane

Horizontal Nystagmus –
Unilateral pontomedullary lesions involving the vestibular nuclei.

Fast phase away from side of lesion.

(Brandt and Dieterich, 1994)
Vestibular Tone Imbalance in Yaw Plane - Horizontal Nystagmus

Peripheral Vestibular Lesion - Unidirectional Nystagmus
**Alexander’s Law**

Unidirectional spontaneous nystagmus increases in intensity during gaze in the direction of the quick phase.

- Example - lesion right peripheral vestibular system. Unidirectional, left beating horizontal-torsional nystagmus with increased intensity with left eccentric gaze.
Central Lesion – Gaze Evoked Nystagmus Direction Changing

Neural Integrator

- Translates velocity (pulse) signals into position (step) signals
- Involves a network of interconnected neurons
  - Horizontal, conjugate eye movement(s)
    - medial vestibular nucleus, nucleus prepositus hypoglossi, and vestibulo-cerebellum
  - Vertical and torsional eye movements
    - interstitial nucleus of Cajal and vestibulo-cerebellum
### Differential Diagnosis

**Peripheral Lesion**
- Horizontal-Torsional nystagmus beating toward the intact side. Constant velocity.
- Unidirectional nystagmus in all directions of gaze. Suppressed by vision and smooth pursuit.
- Positive head thrust
- +/- Skew deviation
- No other neurological signs

**Central Lesion**
- Horizontal-Torsional nystagmus beating towards the intact side. Variable velocity.
- Gaze–evoked nystagmus – nystagmus changes direction with gaze. May be unidirectional.
- Negative Head thrust 2/3 of patients
- +/- Skew deviation
- Other brainstem or cerebellar signs present.

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**Cases:**
**Central Vestibular Tone Imbalance - Yaw Plane**
**Isolated Vestibular Nuclear Infarction**

- 34 y.o. male with HTN developed acute spontaneous vertigo, vomiting and imbalance
  - Spontaneous left beating horizontal-torsional nystagmus
  - Gaze evoked nystagmus - Direction changing nystagmus greater on left eccentric gaze and with removal of fixation
  - No head tilt or skew deviation
- Positive head impulse test to the right
  - Caloric testing suggested ipsilesional canal paresis of 57%
- Ipsilesional cVEMPS and oVEMPS decreased/absent

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**Isolated Vestibular Nuclear Infarction**

- 67 y.o. male with Diabetes Mellitus developed acute spontaneous vertigo, vomiting and imbalance
  - Spontaneous left beating horizontal-torsional to the intact side that increased with removal of fixation
  - Gaze evoked nystagmus - Direction changing nystagmus greater on left eccentric gaze and with removal of fixation
  - No head tilt or skew deviation
  - Positive head impulse test bilaterally for HC’s and PC’s
    - Caloric testing suggested ipsilesional canal paresis of 81%
- Ipsilesional cVEMPS and oVEMPS decreased/absent
Summary

• Damage to medial vestibular nucleus results in impaired horizontal gaze holding due to role of MVN as part of neural integrator for horizontal gaze holding
• With central vestibular lesion, may have positive head impulse test and no Skew deviation but you will see direction changing gaze evoked nystagmus (GEN).

Central Vestibular Syndrome in Roll Plane
Vestibular Tone Imbalance: Pitch and Roll Plane

**Hypothesis:**

1. Signal processing of the VOR in roll and pitch is conveyed by the same ascending pathway in MLF.
   - Unilateral lesion – affects function in the roll plane
   - Bilateral lesion – affects function in the pitch plane.

2. Common integrator system for eye movements in roll and pitch plane.

Central Vestibular Tone Imbalance: Roll Plane

- Pitch Plane Signs are:
  - Torsional nystagmus
  - Skew deviation
  - Ocular torsion
  - Lateral tilt of head
  - Lateral tilt of body
  - Lateral tilt of perceived vertical.
**Pitch Plane – Static Central Vestibular Tone**

Graviceptive pathways from otoliths and vertical semicircular canals to cortex.

Pathway crosses at mid-pons.

Pitch plane signs due to unilateral lesion graviceptive pathway.

Ipsiversive at pontomedullary level and contraversive at pontomesencephalic level.

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**Vestibular Tone Imbalance - Roll Plane**

Torsional Nystagmus – Unilateral lesions involving:
- Vestibular nuclei (medial or superior)
- Lateral medulla
- MLF (associated with internuclear ophthalmoplegia
- INC
- riMLF

Fast phases of torsional nystagmus:
- contraversive in pontomedullary lesions
- ipsiversive in paramedian pontine and pontomesencephalic lesions

(Brandt and Dieterich, 1994)
Graviceptive Vestibular Pathways – Roll Plane
Real v. Perceived

Ocular Tilt Reaction
– **skew deviation** – vertical misalignment of eyes that does not map to cyclovertical eye muscles
– **ocular torsion** – lack of ocular counter roll
– **head tilt** – otolithic tone imbalance resulting medial vestibular spinal tract.
– **tilt of perceived vertical** (Wong, 2014)

Ocular Torsion

- **Physiologic Head Tilt**
- **Pathologic Head Tilt**
Ocular Tilt Reaction – Roll Plane

Real

Graviceptive pathway crosses at the pontine level.

Tonic ocular torsion and head tilt along the graviceptive pathway:
- Lesion utricle or vertical canal ipsilateral tonic deviation.
- Lesion vestibular nuclei (superior and medial) ipsiversive tonic deviation.
- Lesion MLF in pontine and pontomesencephalic brainstem and INC induces a tonic contraversive deviation.

Graviceptive Vestibular Pathways – Roll Plane

Skew Deviation

Graviceptive pathway:
- Lesion utricle ipsiversive hypotropia.
- Lesion vestibular nuclei (superior and medial) ipsiversive hypotropia.
- Lesion MLF in pontine and pontomesencephalic brainstem and INC induces contraversive hypotropia.
- Lesion thalamus and cortex variable. Dependent on lesion above or below decussation.
**Graviceptive Vestibular Pathways – Roll Plane Perception of Vertical**

Tilt of perceived vertical ie subjective visual vertical (SVV)

Graviceptive pathway:
- Lesion utricle and vertical canal ipsiversive SVV.
- Lesion vestibular nuclei (superior and medial) ipsiversive SVV.
- Lesion MLF in pontine and pontomesencephalic brainstem and INC induces contraversive SVV.
- Lesion thalamus and cortex variable. Dependent on lesion above or below decussation.

(Brandt and Dieterich, 1995)

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**Test of Subjective Visual Vertical - Bucket Test**

(A) Patients sit upright looking into a translucent plastic bucket so that the bucket rims prevent any gravitational orientation clues. (B) On the bottom inside the bucket, there is a dark, straight line. The examiner rotates the bucket clockwise or counterclockwise to an end position and then slowly rotates it back towards the zero degree position. Patients indicate ‘stop’ at the position where they estimate the inside bottom line to be truly vertical. The examiner reads off the degrees on the outside scale. Ten repetitions have to be performed.

Zwergal 2009
TESTING- Bucket Test

- Healthy subjects align the bar within 1 – 2.5° of vertical
- Subjects with central (and peripheral) pathology align the bar greater than 2.5° from true vertical

<table>
<thead>
<tr>
<th>SVV Application</th>
<th>Pathologic SVV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute peripheral vestibular neuritis</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>Wallenberg syndrome</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>INO</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>Midbrain</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>Vestibular pseudoneuritis</td>
<td>&gt; 90%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bucket Test</th>
<th>SVV Monocular Left</th>
<th>SVV Monocular Right</th>
<th>SVV Binocular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal n=30</td>
<td>1.2 ± .7</td>
<td>1 ± .8</td>
<td>.9 ± .7</td>
</tr>
<tr>
<td>Acute peripheral or central vestibular dysfunction n=30</td>
<td>8.9 ± 5.2</td>
<td>8.4± 4.8</td>
<td>8.3 ± 5</td>
</tr>
</tbody>
</table>

Zwergal 2009

Association between Ocular Torsion and SVV

- Compared optic disc angles (torsions) with SVV deviations in 55 subjects with acute, focal brainstem and cerebellar lesions
- R2 = 0.73

Frisen L, 2012
Skew Deviation vs. Trochlear Nerve Palsy

• Differentiating skew deviation from trochlear nerve palsy requires looking at Ocular Torsion
  – Skew – higher eye is incyclotorted
  – Trochlear nerve Palsy – higher eye is excyclotorted

Skew Deviation vs Cranial Nerve IV Palsy

Left Peripheral Vestibular Lesion or Left posterior circulation lesion (medullary level)

Head tilt ipsilesional

Left Trochlear Nerve Palsy

Elevation of involved side Hypertropia

Head tilt contralesional in order to level eyes
Ocular Tilt Reaction v. Trochlear N Palsy

<table>
<thead>
<tr>
<th>Ocular Tilt Reaction</th>
<th>Superior Oblique Palsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intorsion of higher eye/extorsion of the lower eye</td>
<td>Extorsion of higher eye</td>
</tr>
<tr>
<td>Binocular tilt of subjective visual vertical</td>
<td>Monocular tilt of subjective visual vertical</td>
</tr>
<tr>
<td>Head tilt compensatory for altered subjective visual vertical</td>
<td>Head tilt compensatory for vertical diplopia</td>
</tr>
</tbody>
</table>

Skew Deviation v. Trochlear Nerve Palsy

**Upright-Supine Test**

- **Skew deviation**
  - Imbalance of graviceptive vestibular pathway
  - Modify position of head relative to gravity reduces tone imbalance
    - Ocular torsion decreases by 83%
    - Vertical misalignment decreases by 74%

- **Trochlear Nerve Palsy**
  - Weakness superior oblique muscle
  - Modifying position of head relative to gravity has no effect
    - Ocular torsion decreases by 2%
    - Vertical misalignment increases by 5%

(Wong et al., 2011)
HINTS to Diagnose Stroke in Acute Vestibular Syndrome

**Head Impulse Nystagmus Test of Skew**

3 step bedside examination superior to MRI

Stroke suspected if **any** of the following exist:
- Normal head impulse test
- Gaze evoked nystagmus - Direction changing nystagmus in eccentric gaze
- Skew deviation (vertical ocular misalignment)

*In cases where there was a false positive on the head impulse, the coexisting presence of skew deviation or direction changing nystagmus correctly identified all those w/ stroke*  

(Kattah 2009)

Interpretation of HINTS Findings

- Head Impulse Test may be positive.
  - Positive in 39% of patients with central vestibular lesions *[(Cnyrim et al, 2008)]*.
  - Positive if lesion to medial vestibular nucleus.

- Gaze evoked nystagmus.
  - Due to “Leaky” integrator.
    - medial vestibular nucleus/ nucleus prepositus hypoglossi for horizontal gaze
    - Intersitial nucleus of Cajal for vertical gaze.
  - Cause.
    - Drugs eg. Alcohol, anticonvulsants, sedatives, and antidepressants.
    - Lesions to cerebellum and its projections to brainstem.

- Skew deviation rare in cases of vestibular neuritis *[(Cnyrim et al, 2008)]*. 

Property of Janet O. Helminski, PT, PhD and Janet Callahan, PT, DPT, MS, NCS. Do not reproduce or use without permission.
Head Impulse, Nystagmus, Test of Skew

<table>
<thead>
<tr>
<th>Test</th>
<th>Central</th>
<th>Peripheral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Head Impulse Test</td>
<td>39%</td>
<td>92%</td>
</tr>
<tr>
<td>Gaze-evoked nystagmus</td>
<td>56%</td>
<td>17%</td>
</tr>
<tr>
<td>Test of skew</td>
<td>40%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Rationale for Therapeutic Intervention

- Factors that Influence Recovery.
  - Extent of lesion
  - Age
  - Damage to the cerebellum
  - Diminished senses
  - Low general activity
  - Other CNS involvement
  - Identification of the problem
Summary

- Isolated brainstem lesions are misdiagnosed more than we think
- Symptoms frequently mimic AVS of peripheral causes
- Need to carefully assess oculomotor control and especially static alignment of the eyes to reveal potential UBN, DBN and torsional nystagmus that may not be readily evident when fixation is allowed.

Case:
Central Vestibular Tone Imbalance - Roll Plane

Courtesy of Tammy Ostrowski, PT
Case - History

- 75 y/o male awoke with sudden pain over right eye, pervasive imbalance, and dizziness. Unable to walk. Called 911.
- Emergency Department. MRI negative. “Not a stroke.”
- Admitted to hospital. Day two diagnosed “Posterior CVA.”
- Discharged to inpatient rehabilitation. Discharged home with home health.
- 6 weeks following onset referred to OP PT for evaluation

Case History

- Current level of function:
  - Ambulates with wheeled walker.
    - Frequent falls- 1-2x/wk.
  - Double vision (prism L eye glasses)
  - Dizziness with any movement
  - Unable to read
  - Unable to do house maintenance
  - Unable to drive
  - Loss of temperature L extremities
Differential Diagnosis and Management of Brainstem and Cerebellar Infarctions

Case History

- Past Medical History
  - HTN-controlled with medication
  - Bifocals
  - Temporal arteritis
  - Pacemaker
  - DM-controlled

- Medication: Lisinopril, Clopidogel, Amiodarone, Warfarin, Crestor, Metformin, Omeprazole, Trilipix, Flunisolide, Prednisone, Meclizine.

Case Physical Therapy Examination

- Dizziness handicapped inventory (DHI) – 56/100

- Observation
  - Right head tilt
  - Right ptosis
  - Right hypotropia

- Closes one eye when visually challenged
Oculomotor Examination

- Full ocular movements (i.e. no palsy)
- Primary Position – spontaneous, CW, torsional nystagmus with and without fixation
- Gaze evoked nystagmus
  - Right gaze – right beating
  - Left gaze – left beating
- Saccades
  - Horizontal towards left - hypometric
  - Horizontal towards right – hypermetric
  - Vertical saccades right lateropulsion
- Pursuit – catch-up saccades
- Vergence - complaints of diplopia
- Negative Head Impulse Test
**Postural Control Examination**

- Sitting - Lateropulsion with eyes closed (11° tilt towards right)

- Standing foam surface:
  - Eyes opened increased sway
  - Eyes closed loss of balance posterior and to the right within 3 seconds

**Mobility**

- Berg – 35/56
- DGI – 17/24
- Gait speed with walker – 1.27 m/sec
  - Unsteady
  - deviates towards right
- Stairs
  - Reciprocal pattern with rail
  - Moderate assist without rail

**Lateral Medullary Syndrome**

- Oculomotor Examination:
  - Spontaneous torsional nystagmus in light.
  - Skew deviation (R hypotropia)
  - Hypermetric saccades to the right
  - Gaze evoked nystagmus
  - Negative head impulse test
  - Diplopia

- Postural Examination:
  - Ambulates with walker. Falls. Severe imbalance.
  - Lateropulsion of eyes/body

- Other:
  - Loss of temperature left side.
Safe Travels