

2/12/08 - DNT - Functional neuroanatomy

**OBJ1 What is meant by a functional anatomic system?**

"A population of neurons that serves a specific functional role."

**OBJ2 Discern the relationship between damage to a system and clinical symptoms**

Generally, if a functional system is damaged, the function it serves is lost or disrupted. However, you can see *positive* symptoms (e.g., flashes of light in retinal detachment; motor seizures; hallucinations).

**OBJ3 Describe the layout of paradigmatic simple (linear) systems (sensory, motor, autonomic) and draw the neuronal connections for an example of each**

Simple: the functional anatomic system is connected to an end organ via the PNS.

3 paradigms:

1. Basic sensory (3-neurons: primary, secondary, tertiary)
  1. Pathway: 1°->relay nucleus; 2°->*thalamus*; 3°->cortex
  2. Systems: There are 6
    - i. Special senses (vision, taste, hearing, balance)
    - ii. General senses (epicritic [light touch & proprioception], protopathic [pain & temp])
  3. **Example:** Visual system ( -> = axon )
    - i. 1° Bipolar cell -> 2° ganglion cell -> 3° geniculate cell -> primary visual cortex (striate)
2. Basic motor (2-neurons: UMN, LMN)
  1. CN LMNs are (mostly) in brainstem; peripheral LMNs are in ventral horn
  2. **Example 1:** Corticobulbar tract
    - i. There is partial redundancy in this system; thus unilateral strokes (UMN damage) leave the upper contralateral face with some mobility.
  3. **Example 2:** Corticospinal tract
    - i. There is also partial redundancy in this system.
3. Basic autonomic (3-neurons: First, Second, Third-order neurons)
  1. Pathway: 1° Hypothalamus -> 2° Brainstem or spinal cord -> 3° Autonomic ganglion or NMJ -> end organ
  2. Each system has sympathetic and parasympathetic subsystems
  3. **Example 1:** Pupillomotor (most important clinically)
    - i. Parasympathetic – 1° Hypothalamus -> 2° Edinger-Westphal -> 3° Ciliary ganglion -> iris sphincter
    - ii. Sympathetic – 1° Hypothalamus -> 2° intermediolateral cell column cervical cord -> 3° stellate ganglion -> iris dilator muscle
  4. **Example 2:** Exocrine motor
  5. **Example 3:** Vasomotor

**OBJ4 List 3 types of complex (nonlinear) systems (diffusely projecting, reciprocal circuits, distributed networks) and list an example of each**

Complex: no specific associated end-organ, and the entire circuitry is confined to the CNS.

1. Diffusely projecting (shotgun)
  1. Clinical correlation: Small lesions can have major clinical consequences

2. **Example 1:** Brainstem reticular activating system
3. **Example 2:** Dopaminergic reward pathway
2. Reciprocal circuits (on & off switches)
  1. Clinical correlation: Hyper or hypo activity from partial circuit damage
  2. **Example 1:** Basal ganglia circuitry
  3. **Example 2:** Memory circuitry
3. Distributed networks
  1. Clinical correlation: Small lesions to hubs (like Wernicke's area) will cause loss of function, even if the actual computation areas (cortex) are intact.
  2. **Example 1:** Language
  3. **Example 2:** Prefrontal motor cortex
  4. **Example 3:** Parietal association cortex

3 paradigms:

1. Diffusely projecting (one-to-many)
2. Reciprocal circuits (feed-forward & feedback loops)
3. Distributed networks (many-to-many, often with a hub)




## MISC

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2/12/08 - DNT - Regional-functional neuroanatomy - Brainstem & cranial nerves

### OBJ1

Describe basic brainstem structure (midbrain, pons, medulla) and recognize key landmarks in horizontal histologic sections that identify the brainstem level

1.  Midbrain
  1. Connections: basal ganglia
2.  Pons
  1. Connections: cerebellum
3.  Medulla
  1. Connections: body

**OBJ2** List the tripartite role of the brainstem (conduit, cranial, and visceral control functions) and give an *example* of each role

1. Conduit (long tracks)
  1. I.e., an incidental role. Long tracts from cortex to body *pass through* here - Sensory input, motor output
  2. Examples:
    - i. Corticospinal; dorsal column medial lemniscus; spinothalamic (anterolateral) & more
2. Cranial
  1. I.e., an intended role. This contains the actual entry & exit points for CNs.
  2. Damage: Motor *downstairs d's* – diplopia, dysphagia, dysarthria, dysphonia; gaze palsy, facial weakness, chewing difficulty. Sensory – anosmia, visual loss, facial numbness, headache, hearing loss, dizziness.
3. Visceral control
  1. I.e., this contains the control sites for semi-autonomous control functions.
  2. Examples:
    - i. Midbrain
      1. Eye movements – vertical gaze & vergence
      2. Visceral – PAG (pain/pleasure)
      3. Motor – substantia nigra (extrapyramidal/motor)
    - ii. Pons
      1. Eye movements – horizontal gaze center
      2. Visceral – RAS, locus ceruleus, raphe nuclei (arousal/mood)
    - iii. Medulla
      1. Eye movements – gaze-holding
      2. Visceral – respiratory & cardiovascular

**OBJ3** Describe brainstem organization in 3 dimensions: front-back; top-bottom; medial-lateral

1. Front-back
  1. Front (basis): long motor tracts
    1. These descend from cerebral peduncles
    2. 2/3 of this goes to the *cerebellum*, **not** the spinal cord. Unilateral damage to this 2/3 leads to few clinical defects.
    3. **Cerebellar peduncles:** inferior & middle are input to cerebellum; superior is output
  2. Middle (tegmentum): long sensory tracts, CN nuclei, & visceral centers
    1. **This is the meat.**  
This is largely the part of the brainstem that isn't just stuff passing through, but is actually brainstem-generated activity.
  3. Back (tectum): CSF space (aqueduct/4<sup>th</sup> ventricle/subarachnoid), colliculi
    1. 4 colliculi; superiors generate saccades, inferiors process auditory info for eye movement
2. Top-bottom
  1. Top (midbrain)
    1. Cranial: 3-4
    2. Control: vertical gaze & vergence; Subs. N.
  2. Middle (pons)

1. Cranial: 5-8
2. Control: horizontal gaze, locus ceruleus, raphe nuclei
3. Bottom (medulla)
  1. Cranial: 9-12
  2. Control: gaze-holding, respiratory & cardiovascular
3. Medial-lateral
  1. Medial (motor)
    1. Corticospinal, MLF, medial lemniscus (epicritic), somatic motor CN 3/4/6/12
    2. NB: Moving your face & jaw is generally special, not somatic, motor, and is more intermediate than medial. Eye movement is medial.
  2. Intermediate (visceral)
    1. Special motor CN 5/7/9/10/11, parasympathetic EW, sympathetic tracts, special
    - 2.
  3. Lateral (sensory)
    1. Spinocerebellar (inferior peduncle), anterolateral (protopathic), somatic sensory CN 8
    2. Does NOT share blood supply with medial brainstem.
    3. **Lateral brainstem strokes** cause no weakness or paralysis. They can mimic inner ear problems, though.

## MISC

Pineal gland (epithalamus): involved in circadian rhythms, can compress dorsal midbrain if it develops masses. This can impair upgaze & light reflexes but not accommodation, and can cause obstructive hydrocephalus.

Diencephalon: thalamus, mamillary bodies. The mm bodies are impacted in Wernicke (confusional) – Korsakoff (amnesic) syndromes in *thiamine* deficiency.

Hypothalamus: command center for autonomic functions.

2/13/08 - DNT - Functional pathoanatomy & pathophysiology

## OBJ1

Recognize key principles of nervous system organization and cite concrete examples of how they inform lesion localization.

## 9 PILLARS

1. Between neurons
  1. Functional segregation
    - i. Loss of function in subsystems that segregate in only one place suggestion a lesion in that one place.
    - ii. Example: Vision. Night vs day vision; loss of just one can best be explained by a lesion at the photoreceptors, since those modalities do not segregate at any other location.
  2. Redundancy
    - i. Unilateral cortical lesions do not produce loss of brainstem or CN functions that have redundant cerebral innervation. Partial redundancy leads to partial deficits.
    - ii. Example: In L UMN loss to face (CN7), only the lower part has no redundant innervation, so only the lower part has obvious motor deficits.

### iii. Specifics

#### 1. Unilateral brainstem or *unilateral* cerebral (no redundancy)

1. Unilateral horizontal gaze palsy 3/6
2. Hemi-facial numbness
3. Hemi-oropharyngeal numbness
4. Unilateral shoulder shrug weakness
5. Unilateral tongue deviation

#### 2. Unilateral brainstem or *bilateral* cerebral (redundancy)

1. Unilateral 3/4/6 palsy
2. Unilateral CN5 paralysis
3. Unilateral *complete* CN7 paralysis
4. Unilateral taste loss
5. Unilateral hearing loss
6. Unilateral paralysis of soft palate or vocal cords
7. Unilateral weakness of SCM

#### 3. Trophic influences

- i. LMN: areflexia, fasciculation (acute), atrophy (chronic)
- ii. UMN: Babinski, spasticity (chronic), hyperreflexia (chronic)

### 2. Between chains

#### 1. Density

- i. Small lesions in tightly-packed bundles cause big deficits. Thus, white matter lesions often do better than gray matter lesions.

#### 2. Magnification

- i. Cortical representation is magnified based on importance, so lesions of important areas will produce *smaller* regions of impairment.

#### 3. Proximity

- i. In convergence or divergence, patterns of loss indicate localization. Discontiguous deficits can be caused by chain convergence from different body regions.
- ii. Example: MCA stroke causing face and hand deficits while leaving the torso intact

### 3. Between systems

#### 1. Orientation

- i. Segmental symptoms (ventrodorsal/axial): narrow level of nervous system that is dysfunctional.
  1. Ex: Cognitive circuitry, CN nuclei, Spinal horns, roots, nerves
- ii. Long tract symptoms (rostrocaudal/longitudinal): only localize if they fit a pattern.
  1. Ex: Sensory, motor, coordination, autonomic

#### 2. Adjacency

- i. Lesions produce dissociated loss of function in nonadjacent pathways. Different pathways may decussate at different levels.
- ii. Ex: *Crossed syndrome*
  - CN palsy ipsilaterally with lower muscle deficit contralaterally due to brainstem damage.

#### 3. Reflexes

- i. Reflexes bypass processing steps. Reflex integrity implies a central lesion. Damaged reflexes imply a segmental lesion.

**OBJ2** Define 'law of parsimony' and explain its relevance to approaching lesion localization  
Occam's razor: do not posit plurality without necessity.

**OBJ3**

List the 3 key questions that must be answered to localize lesions and describe how to answer them (What's the level? Intra- or extra-axial? Can you explain it with 1 lesion?)

1. What's the level?
  1. Supratentorial (CN1-2)
    1. Mnemonic: Attic A's (aphasia, amnesia, agnosia, apraxia, abulia, anosmia, anopsia)
  2. Infratentorial (CN3-12)
    1. Mnemonic: Downstairs D's (diplopia, dysarthria, dysphagia, dysphonia)
      - i. These can result from supratentorial lesions, so watch out.
  3. Spinal
    1. Mnemonic: Basement B's (breathing, bowel, bladder, and 'broken reflexes)
2. Intra- or extra-axial?
  1. Intra (brain or spinal cord)
  2. Extra (nerves, NMJ, end organs, meninges)
3. Can you explain it with 1 lesion?
  1. That is, one lesion in *space*.
  2. Territory/tissue specific deficits (arteritis) may not count as one lesion *in space*, despite being one *type* of lesion.

2/19/08 - DNT – Headache syndromes & migraine I

**OBJ1** List what hurts in the head (i.e., **never the brain**)

The brain parenchyma never hurts. In the head, you have primary (benign) and secondary (not benign) sources of pain.

**OBJ2** Recognize the red flag symptoms and signs of dangerous headaches

1. Dangerous headaches
  1. SNOOP (systemic, neurologic, onset sudden, older than 50y, pattern change)
    - i. Rules of thumb (from bad to worst):
      1. Persistent (>72h) = maybe bad
      2. Abrupt = often bad
      3. HA + fever = usually bad
      4. HA + diplopia = almost always bad
        1. This is NOT migraine
      5. HA +  $\Delta$ MMS = almost always bad
    - ii. Specifics:
      1. Brain tumor HAs
        1. Dangerous if  $\uparrow$ ICP threatens hydrocephalus or herniation.
        2. The classic is morning  $\uparrow$ ICP from fluid redistribution after orthostasis, but this is rare.
2. Benign headaches
  1. Symptoms:
    - i. Analgesic rebound cycle – worst in AM, rises over time. Due to tolerance to pain meds. Need to detox over weeks.

**OBJ3** Describe the 9 headache-causing diseases in frontline settings that are *catastrophic* (ACT CANADA or DATA C2A2N)

1. ACT CANADA - with gratitude to Andrew Hughes - (DATA C<sup>2</sup>A<sup>2</sup>N)
  1. **Arteritis**
    - i. Sx: Headache + age>50y
    - ii. Dx: Sed rate (ESR/CRP) or biopsy
    - iii. Rx: Corticosteroids
  2. **Carbon monoxide**
    - i. Sx: any age, common in winter, better on vacation, poor ventilation + dizziness + confusion
    - ii. Dx: CO detectors, COHb
    - iii. Rx: Fix appliances, ventilation
  3. **Thrombosis of dural venous sinuses**
    - i. Sx: worse in AM or flat, loss of venous pulsations +/- papilledema
    - ii. Dx: LP, venography
    - iii. Rx: Anticoagulation
  4. **Colloid cyst of 3<sup>rd</sup> ventricle**
    - i. This is the only one that is excluded by a normal CT/MRI
    - ii. Sx: age 40 + intermittent, severe, brief HAs + bifrontal + better when supine + syncope (intermittent obstructive hydrocephalus / **ball valve** effect)
    - iii. DX: CT or MRI
    - iv. Rx: Surgical resection
  5. **Aneurysm**
    - i. Sx: age>40y + abrupt onset +/- meningismus + diplopia
    - ii. Dx: CT then LP then angiography
    - iii. Rx: Surgical clip or endovascular embolization
  6. **Norepinephrine (phea)**
    - i. Sx: Any age + episodic HA + palpitation + sweating + anxiety
    - ii. Dx: Plasma free metanephrines
    - iii. Rx: Surgery
  7. **Angina**
    - i. Sx: age>40 + bifrontal
    - ii. Dx: EKG or stress test
    - iii. Rx: CABG
  8. **Dissection**
    - i. Sx: Headache +/- minor trauma +/- Horner's
    - ii. Dx: MRA-DSA angiography
    - iii. Rx: Anticoagulation
  9. **Angle closure glaucoma**
    - i. Sx: age>40 + Chinese/Eskimo + worse in darkness (2° dilation) + one eye blurred (HA + eye pain)
    - ii. Dx: Gonioscopy
    - iii. Rx: Iridotomy
  10. **Infections**
  11. **ICP**
  12. **Infected pituitary (apoplexy)**

## MISC

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### Headaches II

**OBJ1** List clinical manifestations of migraine

## 1. Definition

1. DNT's definition: Migraine is a syndrome characterized by pain, autonomic changes (GI>cranial), polysensory hypersensitivity, and neurological dysfunction (mixed + & -).
2. Migraine with aura is a polygenic channelopathic disorder of excitability.
3. Classic = visual aura; common = without aura; acephalgic migraine = aura without headache.

## 2. Timeline

1. Vulnerability, trigger, prodrome (hrs-days), visual aura (min-hr), hemicranial headache (hrs-days), anorexia NV (hrs-days), photophobia phonophobia (hrs-days)
2. Triggers can be high potency (easily discovered, enough in themselves to cause migraines) or low potency (require multiple triggers to coincide, hard to discover).
  - i. Catamenial migraine
    1. Menstrually related
  - ii. Migraine with clear food trigger
    1. Alcohol

## 3. Manifestations

## 1. Visual aura

- i. Positive leading edge
  1. Organized, geometric, spreading
  2. Hemifield start
- ii. Negative wake
  1. Scotoma/blur
  2. Within borders of positive arc
- iii. Slow tempo, lasts 5-30 minutes
  1. Watch out - **TIA**s also last 5-30 minutes

2. Hemicranial. **Pain behind eye, on opposite side from hemifield with visual manifestations.** Pulsatile pain. Photophobia.

**OBJ2**

Outline the trigeminovascular and neurogenic inflammation hypotheses in genesis of migraine pain and relationship to current migraine therapy

## 1. Trigemino-vascular

1. Initiation (seconds to minutes)
  - i. Trigeminal nucleus in pons is a major site of brain activation in migraine
  - ii. Migraine begins in CNV nucleus, spreads to cortex.
  - iii. Rx: avoid trigger
2. Escalation (hours)
  - i. This is a neurochemical feed-forward loop.
  - ii. Rx: abortive (5HT agonists)
3. Persistence (days)
  - i. Vascular problems cause nerve-generated inflammation of vessels
  - ii. Nerve generated inflammation feeds back, causing more vascular problems
  - iii. Rx: NSAIDs, steroids

**OBJ3**

Recognize similarities and differences in clinical manifestations and pathophysiology of cluster headache (and other trigeminal autonomic cephalalgias).

	Episodic Tension-Type	Migraine without Aura
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Lasts hours	Y	Y
Bilateral	Y	40%
Severe pain	Sometimes	Y
Pressure/tightness	Y	50%
Respond to serotonin	Y	Y

### CLUSTER HEADACHES ('suicide headaches')

1. NOTE: distinguish from carotid dissection.
2. Unilateral orbital or temporal severe pain
3. Rapid onset, short duration (<90min)
4. Agitation, restlessness
5. Autonomic features
  1. Lacrimation, conjunctival injection, nasal stuffiness (rhinorrhea), **ptosis**, eyelid edema
6. Migrainous symptoms: nausea, photophobia, phonophobia, aura
7. Age of onset: 2<sup>nd</sup>-4<sup>th</sup> decade (mean 32 years). 1y – 80y.
8. Periodicity & pathophysiology
  1. *Circannual periodicity* – cluster periods.
  2. *Circadian periodicity* – cluster attacks.
  3. Explanation: **hypothalamic dysfunction**. Altered secretory rhythms of pituitary hormones. Decreased NAA/Cr ratio in hypothalamus.

### MISC

#### HEADACHES

1. Primary (episodic, tension, migraine, cluster or trigeminal cephalalgias in order of prevalence)
  1. BENIGN
  2. Source: Central pain centers (PAG, CN5, hypothalamus, thalamus)
2. Secondary (meningitis, tumor, aneurysm)
  1. NOT BENIGN
  2. Sources:
    - i. ACT CANADA
    - ii. Arterial dissection – leading cause of stroke in adults <45y
    - iii. Giant cell arteritis – blindness
    - iv. Dural thrombosis – intracerebral hemorrhage in young women or postpartum
    - v. Subarachnoid hemorrhage from aneurysm – 50% mortality

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2/20/08 - DNT – Vertigo and the Pathophysiology of bedside vestibular eye signs

### OBJ1

Describe role and function of a normal vestibular system, particularly its influence on normal eye movements. (The 6<sup>th</sup> sense.)

#### VESTIBULO-OCULAR SYSTEM

1. Goals

1. Keep us unaware of which way is up
2. Prevent us from crumpling to the ground
3. Keep vision steady when moving our heads
2. VOR
  1. Connection between balance organs and eye-movement structures that keeps vision steady when we move.
  2. Vision takes 100ms to process, which would be too slow to correct for bouncy movement, so the VOR does this before the signal ever gets to the cortex.
  3. Mechanism: rolls eyes in direction opposite of head movement.
  4. Try it yourself:
    - i. If our head is moving quickly relative to the world, the VOR corrects for it.
    - ii. In contrast, if the world is moving quickly, we can't correct for it.
3. Anatomy
  1. Vestibular nuclei (CN8) are connected directly to CN3/4/6.
4. Functional anatomy
  1. Angular VOR (aVOR)
    - i. Baseline tonic firing at rest.
    - ii. Head turning toward canals = ON.
    - iii. 3 sets of canals:
      1. Horizontal/axial/yaw (R&L of same side)
        1. Turn head right, right canal turns on, pushes eyes left.
      2. Vertical/Sagittal/pitch (anterior canal & posterior canal of both sides)
        1. Tilt head down, activate both ACs, pushes eyes up.
      3. Torsional/Coronal/roll (anterior canal & posterior canal of same side)
        1. Roll head to right, activates AC & PC of right side, intorts eyes.
    - iv. Test aVOR with **head thrust test**
      1. Eyes should stay focused on you if VOR is intact.
  2. Otolith-ocular reflexes
    - i. Vestigial system for lateral-eyed animals since "turning" their head is actually head tilt, and they tort their eyes to compensate for this.
    - ii. This is suppressed by the modern cerebellum & lateral medulla+midbrain.
    - iii. You desuppress this if the cerebellum is injured.
  3. Cerebellar gaze-holding
    - i. Constant force is required to gaze in an eccentric position. The force is generated by the medulla, and calibrated by the vestibulocerebellum.

## OBJ2

Derive pathophysiologic mechanisms of vestibulo-ocular signs that distinguish benign inner ear disease from stroke.

### ABNORMAL VESTIBULAR

1. Symptoms & signs
  1. Symptoms
    - i. Dizziness
      1. Where your ears say one thing, but the brain disagrees
      2. 4 types: vertigo (hallucination of angular motion, implying asymmetry), presyncope, disequilibrium (unsteady walking), or 'vague lightheadedness'
      3. Nonvestibular causes: orthostatic, cardiac, intoxication, concussion, panic attack
      4. Vestibular causes: BPPV, migraine & meniere, bilateral vestibulopathy (AGs), neuritis, brainstem/cerebellar stroke, MS

5. Why care?
  - In urgent care, 25% of pts >50y with new, isolated vertigo have cerebellar stroke.**
- ii. Oscillopsia, diplopia
2. Signs
  - i. Abnormal VOR
  - ii. Nystagmus
    1. Pendular (slow-slow) – rare in population.
      1. Assoc with oscillopsia.
      2. Usually from brainstem lesion.
    2. Jerk (slow-fast) – uncommon, but common among dizzy people.
      1. Assoc with dizziness/balance probs.
      2. Results from vestibular or gaze-holding lesions.
  - iii. Ataxia & lateropulsion (tendency to fall to the side)
2. Pathophysiologic mechanism
  1. Nystagmus
    - i. Slow phase is pathology; something is driving the eyes like a normal VOR.
      1. This is a *failure of gaze-holding center* (medulla) or of its calibrator (cerebellum)
    - ii. Fast phase is cerebrally driven.
  - iii. Spontaneous (vestibular) vs gaze-holding
    1. Vestibular: tonic asymmetry (in a labyrinth) that produces perpetual drift.
    2. Gaze-holding: asymmetry only when eye is in an eccentric position.

## DISTINGUISH EAR DZ FROM STROKE

1. Timing approach
  1. Common / Benign
    - i. Brief – BPPV, vasovagal
    - ii. Intermediate (hrs) – migraine-Meniere, panic
    - iii. Long (hrs-days) – Neuritis, labyrinthitis, drugs, meds, toxins
  2. Uncommon / Dangerous
    - i. Brief – Cardiac dysrhythmias, TIAs
    - ii. Intermed – TIA, hypoglycemia
    - iii. Long – stroke, TIA
2. Imaging
  1. Neuritis – May see tiny 8<sup>th</sup> nerve enhancement by 3Tesla (very powerful; world record is <15T) MRI with high-dose Gad. Have you ever felt gad? It's remarkably sticky. Please keep it out of my arteries.
  2. Stroke – Will see brainstem or cerebellar strokes on MRI.
3. **Vestibulo-ocular physiology**

(4 possible regions: cerebellum, midbrain, pons, CN8. Algebra: 4 variables require 3 tests for dx.)

  1. Integrity of VOR response [**Head thrust test**]
    - i. In vestibular neuritis, response is abnormal.
    - ii. In cerebellar stroke, the response is normal.
      1. The VOR pathway **does not** go through the cerebellum (no time for that!)
  2. Vertical ocular alignment [**Skew deviation/eye cover test**]
    - i. Vestibular otolith-ocular reflexes are suppressed by modern cerebellum & brainstem

- ii. Only unmasked in central damage.
- 3. Nature of the nystagmus
  - i. Spontaneous vestibular nystagmus
    - 1. Results: *Unidirectional*; worse when looking toward fast phase; exists even at rest.
    - 2. Cause: medial cerebellar stroke; lateral pontine stroke; vestibular neuritis.
  - ii. Gaze-holding nystagmus [**only strokes cause this**]
    - 1. Results: No nystagmus at rest; worst when looking laterally; beats *in direction of gaze*.
    - 2. Cause: lateral cerebellar stroke; medial medulla stroke.
  - iii. Mixed vestibular & gaze-holding nystagmus [**only strokes cause this**]
    - 1. Results: Beats *in direction of gaze*; exists even at rest.
    - 2. Cause: Medial/lateral cerebellar stroke; medial/lateral medullary stroke.

## MISC

35% of dizzy strokes are missed in the ED.

Alexander's Law: Amplitude of nystagmus increases when looking in the direction of the fast phase.

2/22/08 - DNT – TNDs, TIAs, Neuro-electrical auras: pathogenesis of episodic neurologic symptoms

### OBJ1 List clinical manifestations of migraine aura

1. As above (hyperpolarized edge with depolarized wake); **nonsynaptic transmission**
2. Sensory auras are common
  1. Modality specific triggers are also common
  2. Visual, somatosensory, vestibular, auditory, gustatory, olfactory
3. Cognitive auras are uncommon
4. Motor auras (rare)
  1. Hemiplegic migraine
  2. Paraplegic migraine (formerly called basilar migraine; vascular theory now debunked)
  3. Progression typical

Migraines involve 3mm/min spread across the cortex. The size of the visual field defect grows as it spreads away from the fovea; however, this is because the fovea is magnified in the cortex. The depression there actually remains ~ the same size. The transmission could be seen as **nonsynaptic** based on timescale alone.

Cerebral blood flow decreases after the aura begins, and lasts afterwards. (↓metabolic demand and ↑vasospasm)

How about pain, though? This probably comes back to CNV/Trigeminal. Cortical events may affect the **dural vascular structures**.

### OBJ2

Describe neural (spreading depression) hypothesis of migraine aura and appreciate its likely relationship to an ion channelopathy (as a cause of episodic neurologic dysfunction).

1. Spreading depression
  1. Visual -> sensory -> motor -> cognitive

2. The spread is via *extracellular fluid* to contiguous cortex; vascular distribution is irrelevant.
3. In general, the spread only spans occipital and sensory cortices.
2. Channelopathies I
  1. Not all spread stops at occipital and sensory cortices
  2. Migraines are usually polygenic inheritance, but not always
  3. '**Familial hemiplegic migraine**' (FHM) syndrome
    - i. Spread reaches motor and cognitive regions
    - ii. 2 known mutations (account for 50% of prevalence of hemiplegic migraines)
      1. Both are hereditary *channelopathies*
      2. Voltage-gated Ca<sup>++</sup> channel (FHM1); Na<sup>+</sup>/K<sup>+</sup> exchange ATPase (FHM2)
3. Channelopathies II
  1. Channelopathies may be immune-mediated, drug-induced, or hereditary.
  2. Theme: episodic neurologic deficit on short timescale.
  3. Voltage-gated
    - i. FHM, periodic paralysis, deafness, arrhythmia, episodic ataxia
  4. Ligand-gated
    - i. Myasthenia, epilepsy
  5. Gap junction
    - i. Deafness, neuropathy, cataract
4. Susceptibility
  1. Glutamate, Na<sup>+</sup>, Ca<sup>++</sup> are excitatory/depolarizers
  2. GABA, K<sup>+</sup>, Cl<sup>-</sup> are inhibitory/repolarizers.
  3. Excess excitants, insufficient inhibitors can tilt the balance of the extracellular soup towards depolarization

**OBJ3** Distinguish migraine aura from TIA and partial seizures based on temporal features.

Migraine	TIA
Spreads over space and time (5-60+ minutes)	Starts all at once
Usually sensory >>> motor	Motor involvement
+ & - signs	- signs only
Episodic head/neck pain (<72h)	Persistent head/neck pain (>72h)

If you suspect a TIA, **image the risk factor**, since TIAs often don't leave a footprint (that is why they are transient).

## MISC

TNDs = Transient neurologic deficits: TIAs, seizures, and migraines all fall into this category.

1. Mechanical TNDs
  1. Benign paroxysmal positioning vertigo (BPPV)
    - i. Dx: Triggered TND. Dix-Hallpike maneuver.
    - ii. 95% in posterior canal because of its **dependent loop**
    - iii. Rx: Epley maneuver. Start in Dix-Hallpike position, rotate 270°.
2. Ischemic

1. Transient Ischemic Attack (TIA)
  - i. Sx: Rapid onset, duration <24h (usually <1h)
  - ii. Mechanism: cardiac embolism (variable sx); thromboembolism (similar sx); stenosis (stereotyped)
3. Neuro-electrical TNDs
  1. Migraine
    - i. Sx: as described in detail above.
    - ii. Difficulty: same timeline as TIAs (5-30min)
  2. Occipital seizures
    - i. Mimic migraines
    - ii. **Sx: *simple, bright geometry (round, not zig-zag).***