# NEUROPSYCHIATRY

RC Education Rounds

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# LATERALITY

- Sensorimotor = usually contralateral
- Language and verbal memory = usually left
- Non-verbal memory, praxis, gnosis = usually right

# ANTERIORITY

- Anterior
  - Personality – disinhibition, loss of empathy, stimulus-bound
  - Cognitive – dysexecutive, working memory, **nonfluent aphasia (L), expressive aprosody – trouble expressing emotions in speech (R)**
  - Motivation – apathetic, loss of initiative
- Posterior
  - Personality, executive cognition, motivation spared
  - Contralateral hemisensory loss
  - **Fluent aphasia (L), receptive aprosody – inability to understand emotions expressed by others speech (R)**
  - VS deficits, spatial disorientation, hemi-neglect

# VERTICALITY

- Cortical
  - Frontal (anterior) behaviors and cognitive deficits
  - Aphasia
  - Apraxia agnosia
  - Recall
  - Retrieval deficit
  - Hemi-motor or hemi-sensory symptoms
- Subcortical
  - **Executive deficits**
  - **Retrieval memory deficit****
  - **Slowing**
  - **EPS**

# FRONTAL LOBES

- **Dorsolateral prefrontal cortex (DL-PFC)**
  - Monitors info in **working memory**
  - Needed for planning and manipulating info
  - Attentional processes
  - Executive function – planning goals
  - **Motor planning**, **set shifting**, strategy, activation
  - May see difficulty following instructions
  - **Tests of executive dysfunction = clock draw, trails B, Luria sequence**
- Orbitofrontal circuit (OFC)
  - Lesions cause personality changes, emotional lability, irritability, disinhibition, outspokenness, reduced concern or worry, imitation or utilization behaviors
  - Ie. Phineas Gage
- **Anterior Cingulate Circuit (ACC)**
  - Mediates **motivated behavior**, reversal learning, reward processes and evaluation
  - Lesions result in reduced spontaneous activity, evident in **akinetic mutism, abulia, consider catatonia**
  - May see extreme amotivation

# PHINEAS GAGE

- Penetrating brain injury in orbitofrontal cortex bilaterally
- Dramatic change in behavior – capricious, childish, obstinate
- Poor social judgment – profane, sexually inappropriate, impulsive, loss of empathy for others
- Relatively preserved intellect, motivation, basic cognition
- Now = personality change due to traumatic brain injury, disinhibited type

# TEMPORAL LOBE

- Essential for memory and understanding of the world
- Superior temporal sulcus = receives inputs from visual, auditory and somatic regions
- Middle and inferior temporal gyri = visual object recognition
- **Medial temporal lobes, hippocampus, entorhinal, perirhinal, parahippocampal cortex = long term memory**
- Temporal pole = conceptual knowledge, social conceptual information processing
- Lesions = dense global amnesia, Wernicke's aphasia

# PARIETAL LOBE

- Anterior parietal = somatosensory processing
- Posterior parietal lobe = cognitive function
- Perception and attention, localizing objects in different spatial locations
  - Lesions may cause visual disorientation, mislocalization, constructional apraxia (cube draw), discriminative sensory loss – tactile agnosia, graphesthesia
- Visuomotor and motor control
  - Lesions may cause optic ataxia, ocular apraxia, limb apraxia (ideomotor)
  - Ie. Apraxia in Alzheimer's disease
- Language and number processing
  - **Conduction aphasia – fluent speech but phonemic errors, intact comprehension but poor repetition**
  - Dyscalculia
- Role in short term or working memory

# BASAL GANGLIA

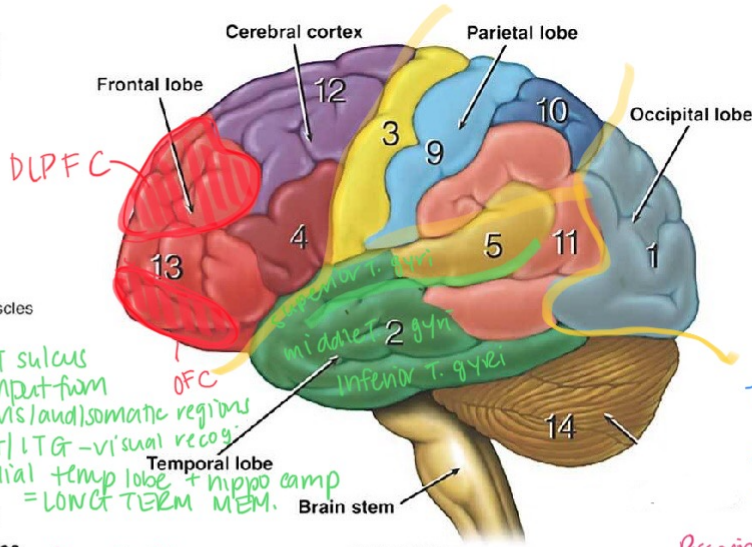
- Vital forebrain nuclei, rich connections to cortex, thalamus, brainstem
- Lesions result in severe consequences for behavior and cognition
- Patients with basal ganglia disease show signs of frontal lobe dysfunction (**frontal subcortical paradox**) → cortico-basal ganglia-thalamo-cortical loops
- Implicated in Parkinson's disease, Huntington's, Progressive Supranuclear Palsy, FTD

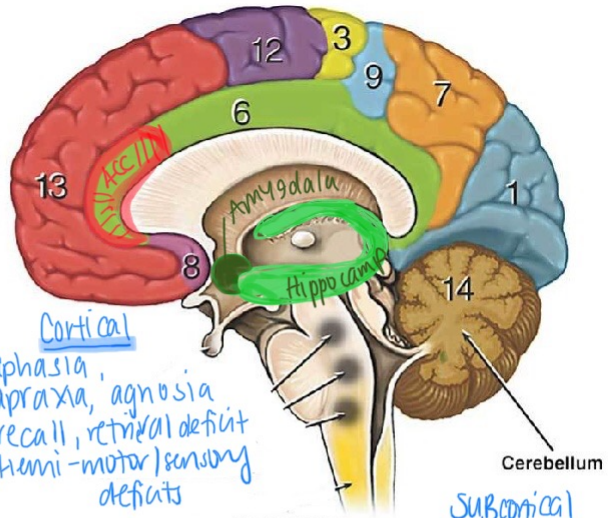
## Functional Areas of the Cerebral Cortex

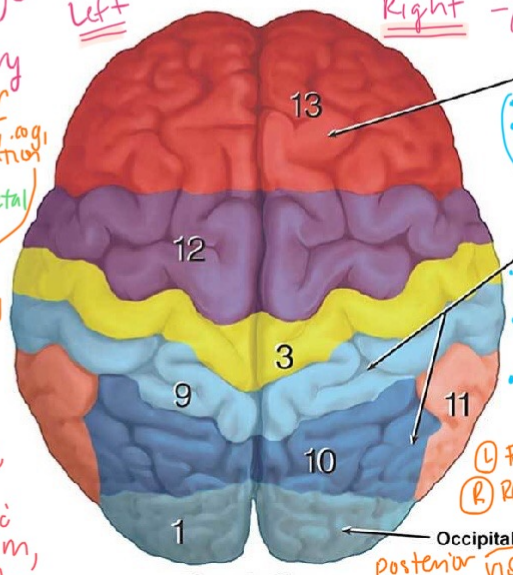
1. **Visual Area:** Sight, Image recognition, Image perception
2. **Association Area** Short-term memory, Equilibrium, Emotion
3. **Motor Function Area** Initiation of voluntary muscles
4. **Broca's Area** Muscles of speech
5. **Auditory Area** Hearing
6. **Emotional Area** Pain, Hunger, "Fight or flight" response
7. **Sensory Association Area**
8. **Olfactory Area** Smelling
9. **Sensory Area** Sensation from muscles and skin
10. **Somatosensory Association Area** Evaluation of weight, texture, temperature, etc. for object recognition
11. **Wernicke's Area** Written and spoken language comprehension
12. **Motor Function Area** Eye movement and orientation
13. **Higher Mental Functions** Concentration, Planning, Judgment, Emotional expression, Creativity, Inhibition

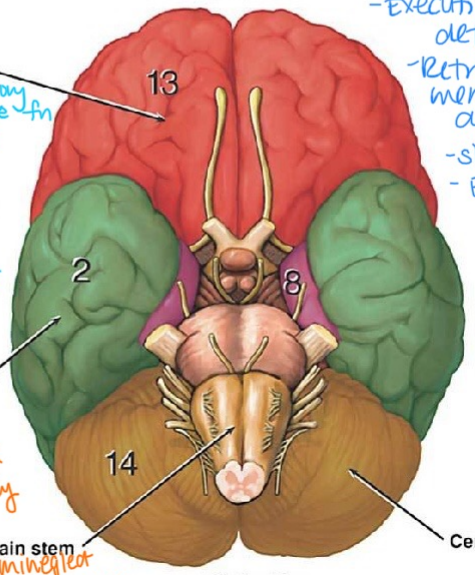
## Functional Areas of the Cerebellum

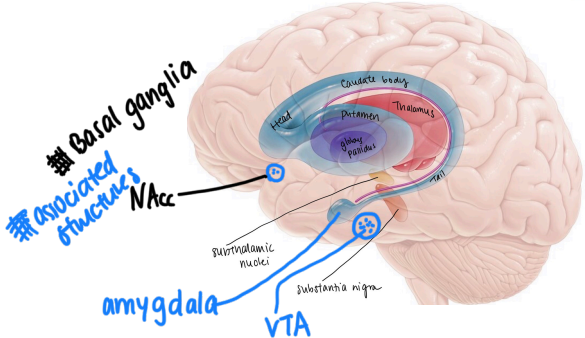
14. **Motor Functions** Coordination of movement, Balance and equilibrium, Posture



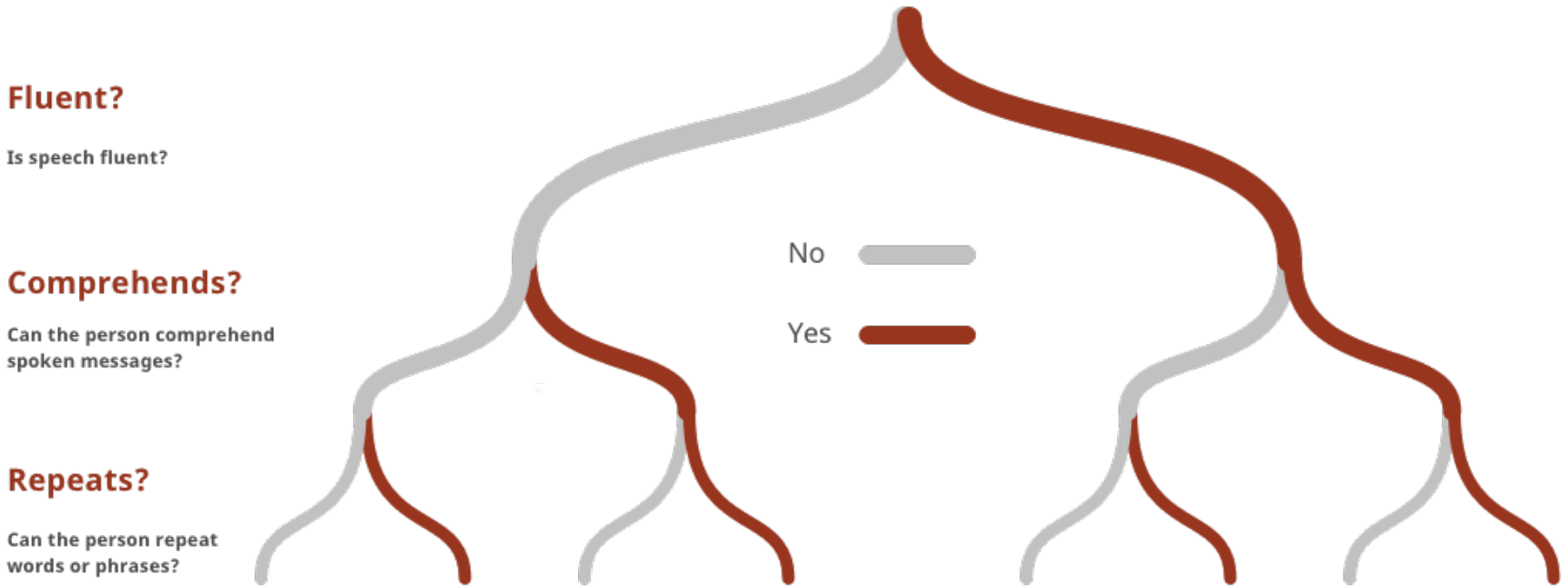




Limbic system = amygdala, hippocampus, hypothalamus [?] these are KEY areas
Cortical areas = limbic lobe, OFC, hippocampus, fornix
Subcortical areas = amygdala, NAcc, septal nuclei

# Types of Aphasia




- nonfluent
- short phrases w/ ++ frustrat$^{n}$

Transcortical
✓ repeat b/c ∅ impact arcuate fasiculus *

- Fluent
- Long sentences w/ ∅ meaning
- Difficulty understanding SPEECH, unaware of own mistakes

- arcuate fasiculus damage
∴ only repitition is POOR

- only naming impaired

**Phonemic Error** – closely related to word (ie. Chair, hair)
**Semantic Error** – closely related object
**Neologism** – whole new word

# APHASIAS

- Wernicke's Aphasia
  - Fluent
  - Impaired repetition
  - Impaired comprehension
  - Impaired naming
  - Long sentences with no meaning, neologisms
  - **Difficulty understanding speech of themselves and others, unaware of mistakes**
  - Left hemisphere
  - Posterior, cortical
- Broca's Aphasia
  - Non-fluent, short, meaningful phrases with great effort
  - Able to understand the speech of others
  - **Get frustrated**
  - Recurrent utterances, automatisms
  - Anterior left hemisphere
- Conduction Aphasia
  - Arcuate fasciculus damage, damage to insula or auditory cortex
  - Comprehension is normal, expression is fluent, repetition poor
- Transcortical Aphasia
  - **Able to repeat**, does not include arcuate fasciculus that connects Broca's and Wernicke's
- Global Aphasia
  - Everything is impaired
- Anomic Aphasia
  - Only naming is impaired
  - Grammatic but empty speech
  - Auditory comprehension preserved
  - Alzheimer's
- **Naming can be impaired in all aphasias**, most can name pen and watch

# STROKE

- **Leading cause of adult neurological disability**
- **2.8% prevalence**, silent stroke 6-28%
- Post-stroke disorders:
  - **Depression 35%**
    - Higher risk if severe functional dependence, previous depression, social isolation, major events pre-stroke, **female gender**, previous stroke
    - Both biologic (lesion location, inflammation) and psychologic (reaction to major life event)
    - Poor rehabilitation outcome, poor cognitive recovery, increased mortality, social withdrawal, worsened QOL, increased caregiver burden, risks of suicide
    - Increased mortality (10% higher at three years, even 29 years later)
    - All patients with stroke should be considered at risk for depression, **assess prior history and risk factors, do screening initially and at 3 mo intervals and after rehab**
    - Challenges: time, communication difficulty, cognitive impairment, anosognosia (lack of awareness), overlap of depression and medical illness, stigma
    - Psychotherapy – supportive, problem solving, build coping skills
    - Anti-depressants are effective – escitalopram, citalopram, sertraline, mirtazapine, venlafaxine, duloxetine; tailor tx to patient
    - Takes weeks to work, psychoeducation
    - **Watch with warfarin – highest risk with Prozac, Paxil, Luvox**
    - Stimulants – limited research, can be effective, generally safe but risks exist
    - ECT – effective treatment for serious cases, prev stroke not contraindication
    - Some evidence for tDCS, NNT 3-5
    - One study for prevention with Cipralex, NNT5; Sertraline NNT5 – may decrease mortality
    - Not yet in guidelines
    - **Problem solving therapy increased time to mortality**
  - Anxiety 25%
  - Pathologic affect 20%
  - Catastrophic reaction 20%
  - Apathy 20%
  - **Mania or psychosis rare**
  - Delirium in over 30%
  - **Dementia in over 25%**
  - Perceived neglect in childhood – 23% increase stroke on autopsy

# TBI

- **85% mild**
- **3 age peaks – 0-4, 15-24, >75**
- **Male>female, 2:1**
- 1-2% of population living with persistent disability due to TBI
- With post-concussive symptoms, **natural history is spontaneous recovery with time**
  - At three mo – 24-84% symptomatic
  - 6 mo – 30%
  - **12 mo <15%**
- Treat in step-wise, hierarchical manner
  - **First address depression, anxiety, irritability, sleep disorder, headache**
  - Then address balance, dizziness, fatigue, cognitive impairment, tinnitus, noise intolerance
- **Key predictor for severity of longer term impairment is extent of diffuse axonal injury**

- Difficulties with **processing speed, attention, memory, executive function, and communication are common to all**
- Personality changes may include disinhibition (social, sexual, spending), labile affect (overreactive, excessive), aggressiveness, apathy, combination
- Irritability and agitation common – easily frustrated
- **1 year prevalence of depression rates as high as 50%, not associated with severity of trauma**, more in L frontal and L **basal ganglia** lesions, **dysphoria at one week**, past hx depression
- Depression increases anxiety (77%) and irritability/aggressivity (57%)
- **Antidepressants may reduce sx in depression, start low and go slow**, more susceptible to side effects, none specifically approved, SSRIs first line, stimulants an option, **SSRI** may increase risk for hemorrhagic stroke
- Non-pharmacologic – education, frequent support, multidisciplinary team, CBT
- **Psychosis in TBI – more frontal and temporal abnormalities, lower rate of negative sx than Scz**
- **PTA duration most prognostic RE long term outcome*****

post traumatic amnesia

# TBI SEVERITY

- Mild
  - GCS 13-15
  - Post traumatic amnesia **less than 1 day**
  - 0-30 minute LOC
- Moderate
  - GCS 9-12
  - **PTA >1 day to <7 days**
  - LOC > 30 min but < 24 hrs
- Severe
  - GCS 3-8
  - PTA **> 7 days**
  - LOC > 24 hrs

# MOVEMENT DISORDERS – PARKINSON'S DISEASE

- **Onset 40s-70s, mean early to mid 60s**
- **1% in people over 60**
- Major **depression 5-20%**
- Minor or subsyndromal 10-30%
- **SI common, suicide rare**
- Risk factors for depression in PD: **female, past or family psychiatric history, early onset, cognitive impairment**
- Antidepressants – pramipexole, nortriptyline, desipramine possibly useful; insufficient evidence for amitriptyline, SSRIs, MAOIs, atomoxetine, omega 3s, ECT, rTMS
- Can get **apathy with SSRIs**
- **Psychosis in <10% of untreated PDs**, **60% cumulative prevalence among tx PD**
- **Clozapine efficacious** and clinically useful, **insufficient evidence for quetiapine**, olanzapine likely not efficacious
- Some new research with pimavanserin – controversial
- **50% have MCI soon after diagnosis**, secondary to temporoparietal cortical deficits, most associated with cholinergic loss
- **First see impairments in executive function**
- **Get anxiety, emotional sx when dopamine wears off**

# IMPULSE CONTROL DISORDERS

- **Pathological gambling**
- **Hypersexuality**
- **Compulsive shopping, eating, med use**
- **Punding syndrome**: intense fascination with excessive, complex, repetitive, non-goal oriented behaviors – ie. Dismantling, sorting, re-sorting
- Can be brought on by **dopaminergic drugs (1/7 PD patients)**
- Tx:
  - **Decrease drug or decrease dopamine agonist (increase L-dopa if needed)**
  - **Switch dopamine agonist (esp. if pramipexole)**
  - **Low dose clozapine or quetiapine**
  - **Family involvement to monitor Da intake**
  - Anti-androgens or antidepressants (libido)
  - CBT
  - DBS

Note – Huntington's onset 30-40s, Parkinson's 40s-70s

# HUNTINGTON'S DISEASE

- **CAG trinucleotide repeat on chromosome 4**
- **Usual onset 30s-40s, progresses to death in about 15 yrs**
- **Loss of caudate nuclei**
- **Cognitive, psychiatric, and subtle motor signs** may appear in premorbid phase (before overt motor)
- Motor sx = **chorea, dystonia, rigidity, spasticity, myoclonus**
- End of life and reproductive issues
- Cognitive issues = executive dysfunction, perseveration, learning and memory deficits, dementia
- See **deficits on fluency, trail making B, emotion recognition**
- **Emotional = depression 50%, SI 18%, SA 10%**
- Common to have anxiety, **irritability**, OCD, apathy, hyposexuality
- **Rare to have psychosis, hypersexuality**

# PROGRESSIVE SUPRANUCLEAR PALSY

- **Parkinson's plus – extensive cognitive problems**
- **Many parts of basal ganglia affected**
- Behavior changes = **apathy, irritability, childishness, impulsivity**
- Executive dysfunction, memory, visuospatial, language, and social cognitive deficits
- Early signs: **loss of balance, lunging forward when mobilizing, fast walking, bumping into objects, falls**
- **Impairment of vertical gaze (supranuclear ophthalmoplegia)****
- Early **postural instability with falls**
- Frontal behavioral changes with marked cognitive slowing
- Pseudobulbar palsy

# PATHOLOGIC AFFECT

- Emotional incontinence, pseudobulbar palsy or affect
- Uncontrollable laughing or crying
- Disruption of neural networks that control generation and regulation of motor output of emotions
- Common in ALS, MS, Stroke, PD
- **Treat with SSRI or Neudexta (dextromethorphan/quinidine sulphate)**

# MS

- **Cognitive dysfunction in 40-60%**
- Reduced cognitive speed, slowed info processing
- **Retrieval of memory more affected** than encoding
- Difficulty with abstraction, attention, vigilance
- **Language largely spared**
- Little agnosia and apraxia
- **Atrophy shows more cognitive change than lesion volume**
- Use **compensatory strategies** – routine, structure, maximize strengths, remedial strategies – ie. Computer based techniques, cognitive therapy
- Pharmacology
  - Stimulants – weak benefits
  - **Cyclophosphamide or pulsed steroids – possible benefits**
  - **Donepezil – positive for verbal memory and subjective sx**
  - Disease modifying drugs – interferon beta, shows promise

# EPILEPSY

- Preictal = mood changes, irritability, hyperactivity, poor frustration tolerance; ?subconvulsive seizure activity
- **Ictal = 25% of auras**, depression, fear, anger, panic, obsessions, aggression; sudden and brief; déjà vu, depersonalization, automatisms
- Post ictal = anxiety, depression, psychosis, transient aggression and confusion
- Significant increase in prevalence of all psychiatric disorders
- Temporal lobe epilepsy = **automatisms (lip smacking, chewing),** amnestic for event, **episodic memory impairment prominent**
- Worse if frontal/temporal epilepsy, prolonged aura, frequent, severe, intractable seizures, cognitive deficits, limbic, temporal, frontal-subcortical dysfunction
- Anti-epileptic drugs
  - Positive effects = release from seizures, improved cognition; enhance GABA, antagonize glutamate
  - Negative effects = variable, **higher risk depression with phenobarb, vigabatrin, levetiracetam, topiramate**
  - Less risk depression with phenytoin, carbamazepine, gabapentin, valproate, lamotrigine, oxcarbazepine
  - Lamotrigine anti-glutamatergic – anxiety, insomnia, agitation
  - **Suicide risk higher with phenobarbital, high total daily dose of AED; lowered risk with valproate, carbamazepine and lamotrigine**

# KLUVER BUCY SYNDROME

- **Bilateral medial temporal lobe damage (including amygdala)**
- Hyperorality, hyperphagia, hypersexuality, docility, dementia, visual agnosia
- Possible consequence of **acute herpes simplex encephalitis** (targets temporal lobes)

# WERNICKE ENCEPHALOPATHY

(CN 6 palsy)

- **Triad = ophthalmoplegia, ataxia, confusion**
- Secondary to thiamine deficiency (↓MSE) vitamin B1
- **Tx with IV thiamine**
- Neuronal cell death in thalamus and **mamillary bodies**

# IMAGING

- CT = best to image skull fracture, hemorrhage, bone or blood
- MRI = permits visualization of white matter connections, small ischemic strokes, tissue contrast
- fMRI (oxygen) = better resolution than PET (glucose), index of activity
- EEG = **excessive theta, or delta during wakefulness, focal activity (slowing or bursts) all abnormal**

δ = deep

Theta = stage 2 (aka sleep spindles + K-complexes)

# TORONTO REVIEW COURSE – DR. DEANNA CHAUKOS

- **DL-PFC – executive function, planning, set-shifting**
- Clock shows executive dysfunction (also shown by trails B and Luria sequence)
- OFC – personality change, Phineas Gage, disinhibition
- ACC – anterior cingulate circuite – motivation, see akinetic mutism, abulia, looks like catatonia
- **Wisconsin Card Sort Test – ability to shift learning**
- **Small stroke in brainstem (subcortical) can cause vast defects**, ie. Akinetic mutism
- Frontal lobe lesion can cause akinetic mutism too but would need large lesion, making it less likely

ø move
ø speak

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- Temporal lobes = memory in medial temporal lobes, hippocampal areas; visual object recognition
- **Dense global amnesia with bilateral removal of medial temporal lobes – anterograde memory gone, cannot form new memories**
- **Conduction aphasia = deficit in arcuate fasciculus** (connects Werenicke's to Broca's) – cant repeat, but can understand and express
- Wernicke's = cannot understand **speech or written language**, nonsensical answers, **neologisms**, cant name items
- Anterior parietal = somatosensory processing
- Posterior parietal = cognitive functions
- **Constructional apraxia – inability to repeat drawing – cube draw**
- **Balint's syndrome** = optic ataxia, optic apraxia, **simultagnosia** (bilateral inferior parietal) – parietal lobe
- **Gerstmann's syndrome** = **dyscalculia, dysgraphia**, R-L indiscrimination, finger agnosia (L angular gyrus) – parietal lobe
- **Optic ataxia – cant do finger to nose, optic apraxia – cant do saccade**
- **Alzheimer's temporoparietal hypometabolism on PET scan**

inability to perceive > 1 object at a time

ø motor movement

ø planned motor tasks

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- Basal ganglia – movement and cognition – subcortical loop
- Basal ganglia are integral parts of frontal-striatal-pallidal-thalamic circuits that mediate these capacities
- **Cortex (large stroke small impact), subcortical areas (small stroke large impact)** – ie thalamus, brainstem
- If vasculopathy with subcortical microangiopathy – likely vascular dementia
- If unilateral without finding on other side – think vascular
- **Parkinson's is global and bilateral**
- **Dementia in PD due to temporoparietal cortical deficits most associated with cholinergic loss, 50% in 10 years**
- Impaired set shifting, executive dysfunction
- Dopamine agonists cause ventral striatal dopamine OD and can induce impulse control disorders in 1/7 patients – hypersexuality, paraphilias, gambling, binge eating, impulsive shopping
- fMRI studies suggest PD reduces the cingulate cortical response to reward anticipation but increases the regional response to actual reward → unable to delay gratification

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- Huntington's – between 30-50, severe loss of caudate nuclei – see deficits early on fluency, interference control, trail making test B, emotion recognition, visuomotor integration
- **Vertical gaze issue = pathognomonic for PSP**
  - See behavior change, early loss of balance, lunging forward when mobilizing, fast walking, bumping into objects, falls, marked cognitive slowing
- **Pseudobulbar affect seen most in subcortical**, but **most described in ALS** – also stroke, MS, PDD
- If olfactory symptoms – temporal lobe epilepsy, episodic memory impairment prominent
- **Frontal lobe epilepsy - explosive behaviors**
- **Complex partial seizure – focal, impaired awareness, automatisms**, amnestic for event
- **L sided stroke historically more associated with depressive symptoms**
- Kluver Bucy syndrome = cognitive impairment, docility, puts things in mouth, hypersexuality → medial temporal lobe lesions (ie. Monkeys not scared), also see hyperphagia, dementia, visual agnosia; can be secondary to acute herpes simplex encephalitis (targets temporal lobes)

# TORONTO REVIEW COURSE – DR. DEANNA CHAUKOS

- Wernicke's encephalopathy – more likely to see atrophy of mammillary bodies
  - Triad of ophthalmoplegia, ataxia, confusion
  - Tx with 500 mg IV thiamine TID for 5 days, then 200 mg BID PO
- CT good for fracture, bone or blood – not for small infarcts; MRI better for small ischemic strokes
- **If you see excessive theta or delta during wakefulness → delirium**
- **Awake and relaxed should be 8-13 hx alpha activity**
- Focal slowing or bursts are also abnormal – brain injury, seizures
- On exam – use EEG to differentiate between delirium, depression, encephalitis etc.

# RESOURCES

- Dr. Rapoport, Dr. M Burke – Ottawa Review Course
- Dr. Deanna Chaukos – Toronto Review Course