

# THE NERVOUS SYSTEM

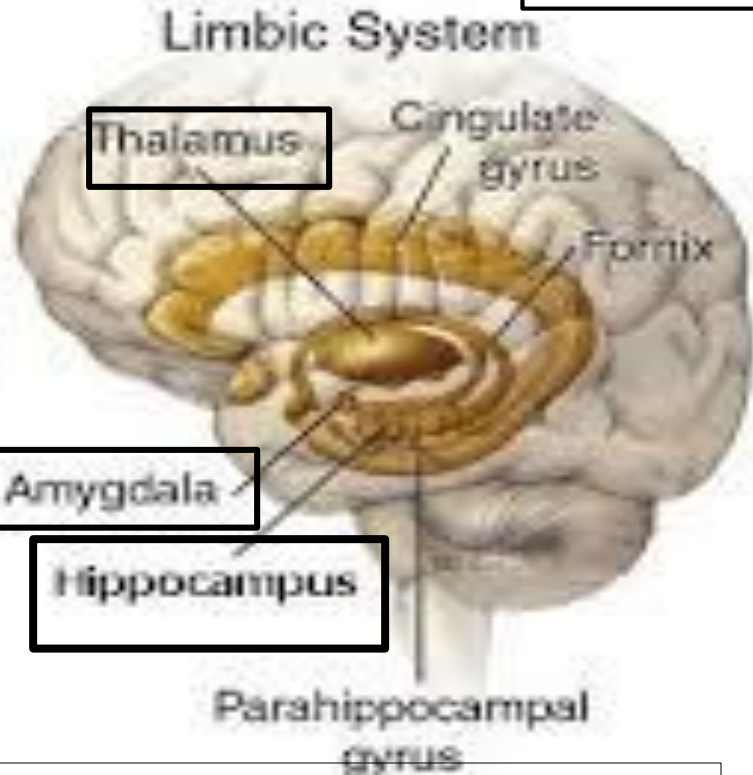
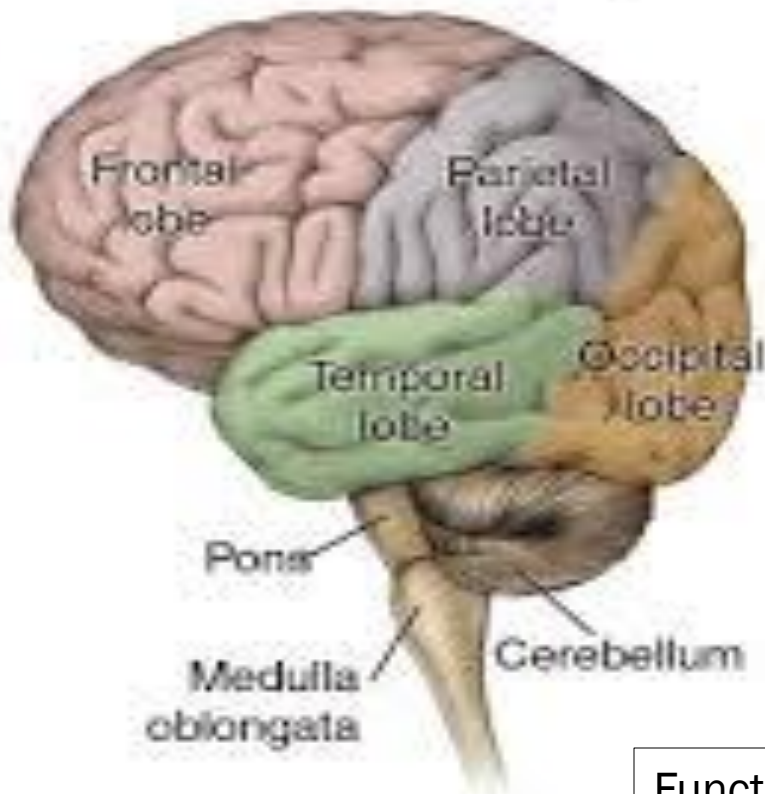
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MODERATOR

# BRAIN AND CENTRAL NERVOUS SYSTEM

## Gross Anatomy

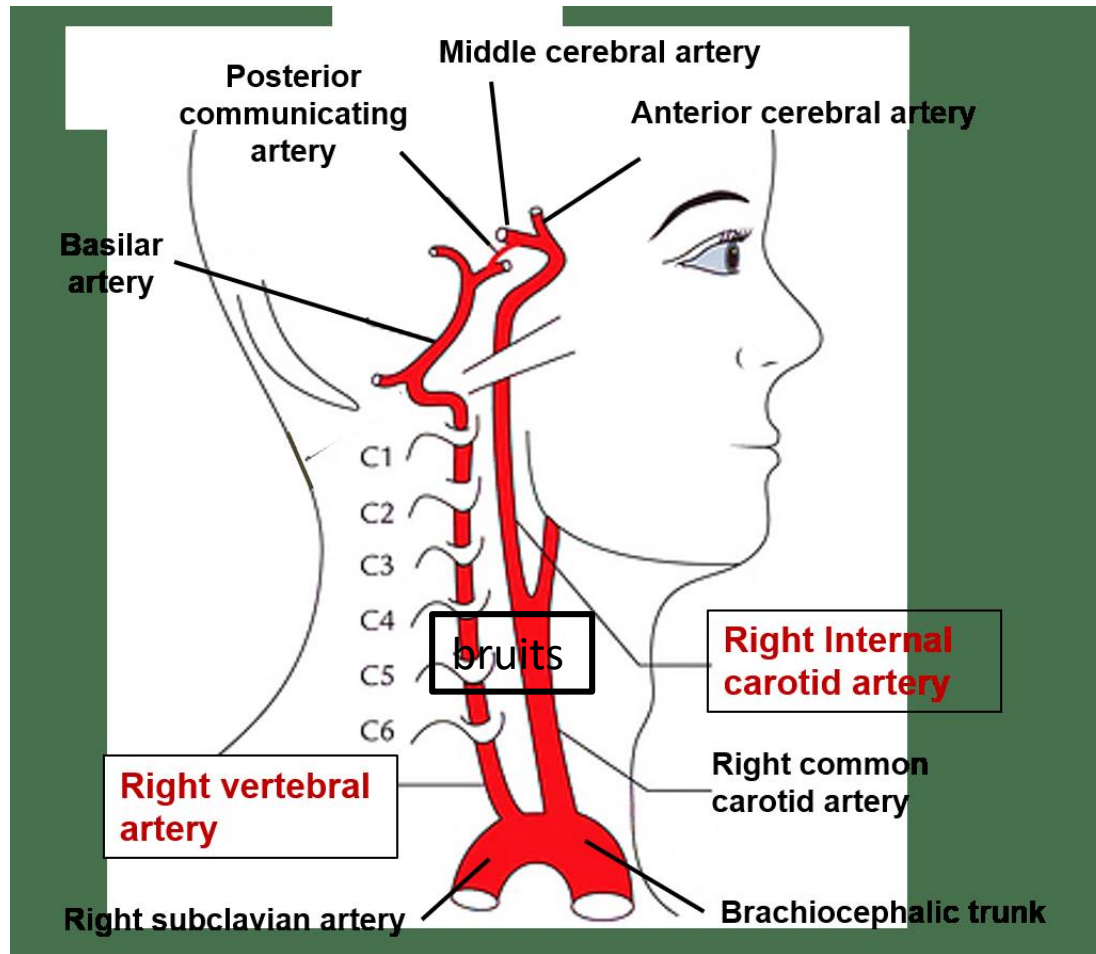
## Anatomy of the Brain

Controls behavior



Functional MRI and PET scanning as Research Tool

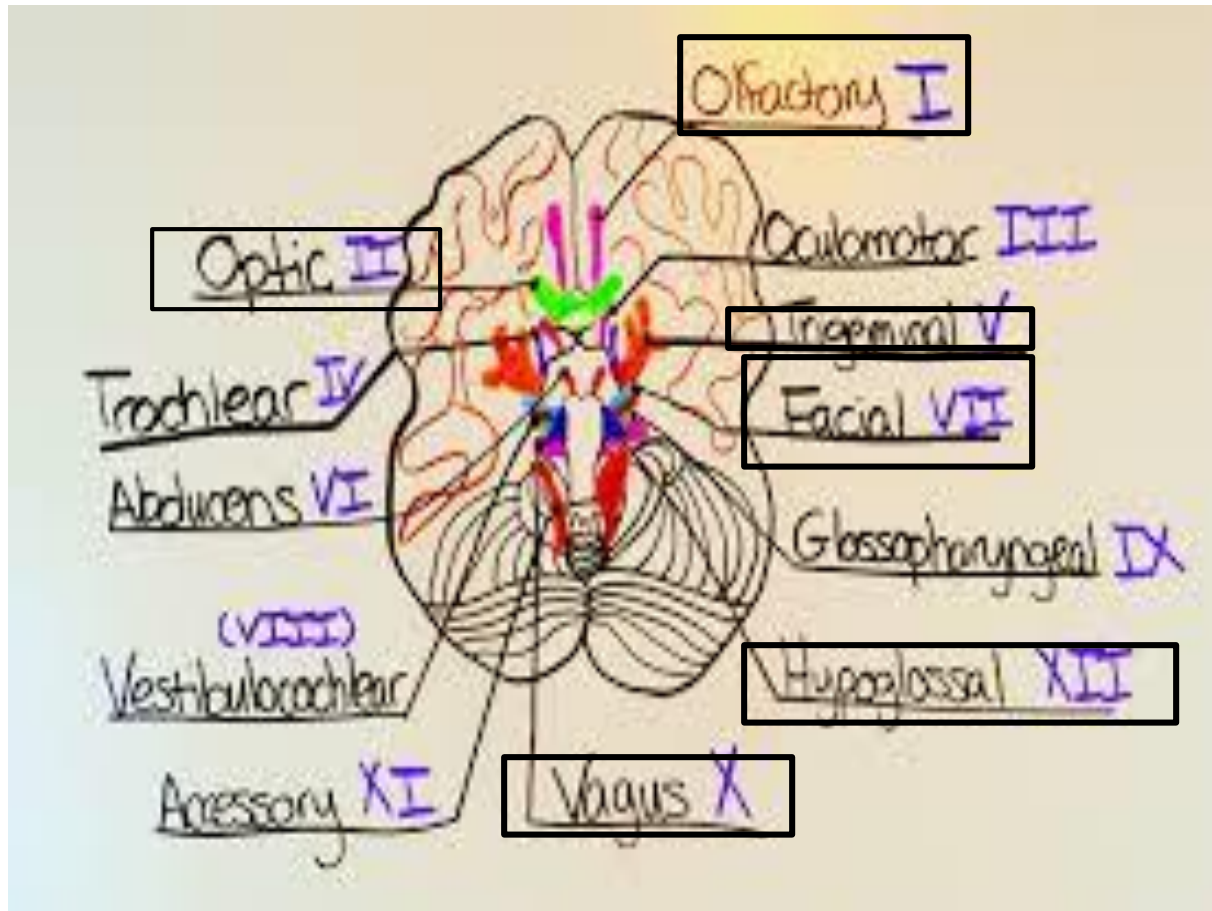
# Arterial Blood Supply to the Brain



# Neurotransmitters; carry impulses across synapses

- ❖ Dopamine (reward-motivation) L dopa is the precursor to dopamine and treats **Parkinson's**
- ❖ Serotonin (SSRIs) Depression
- ❖ Acetylcholine (alpha adrenergic-parasympathetic)
- ❖ Norepinephrine (blood pressure and stress) (Beta adrenergic)
- ❖ Epinephrine/adrenalin(Beta adrenergic)
- ❖ GABA-(gamma-aminobutyric acid) (pain-Neurontin)
- ❖ Glutamine

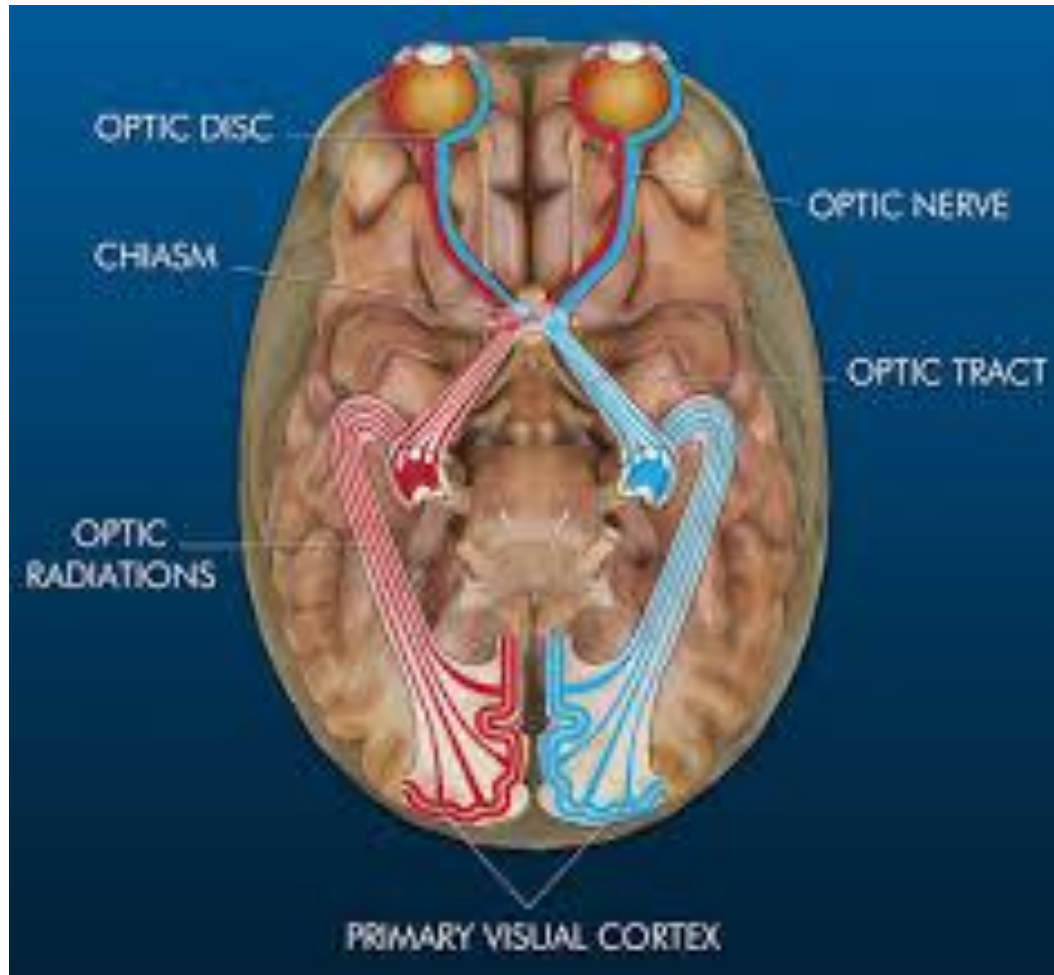
# Cranial Nerve Diagram: 12 altogether



# Neurologic Exam when you go to see you Primary Care Physician

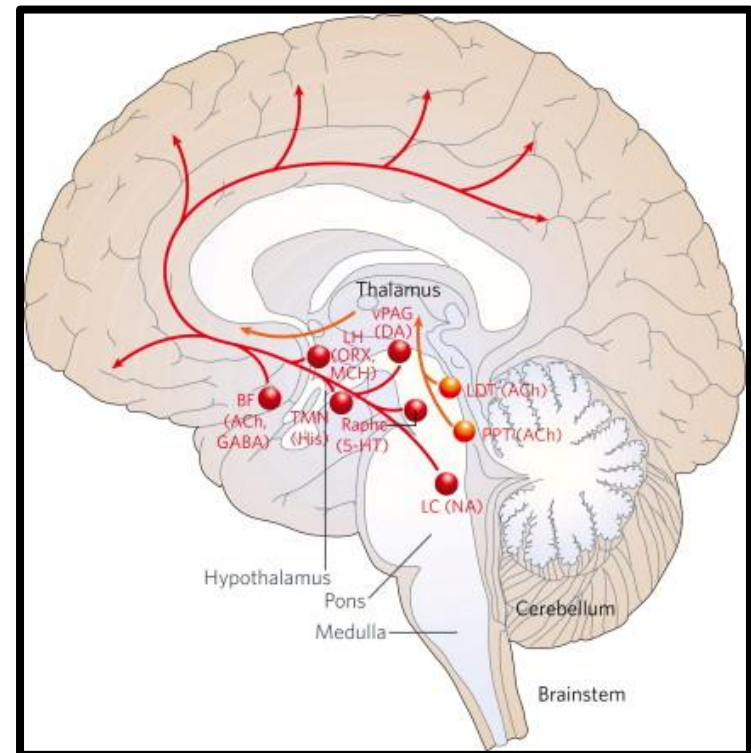
- Sensorium and memory
- Pupils (R&R&RLA)
- Funduscopic exam to examine the retina
- Eyes movements
- Check Reflexes with reflex hammer
- Strength evaluation and proprioception
- Balance

# Optic Chiasm (the cross; right to left, left to right)



# Consciousness

- The reticular activating system (RAS) is composed of an ascending tract and a descending tract. The ascending RAS is **responsible for human consciousness level and integrates the functions of the brain stem with cortical, cerebellar, thalamic, hypothalamic, and sensory receptor functions.**





# Right Brain versus Left Brain: Importance?

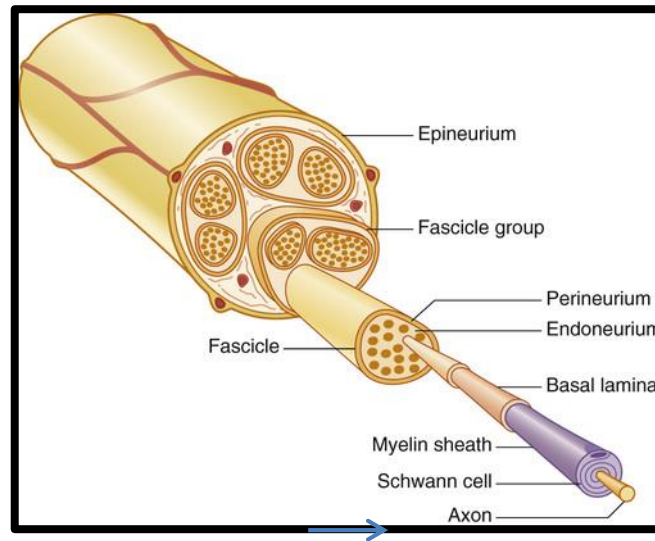
- Right brain more adept at spatial and nonverbal concepts and being more creative and emotional (a scientist or musician) imagination, holistic and abstract thinking
- Left Brain are more analytical and methodical. They are better at things like reading, writing, and computations. (an accountant or author) logic

No proof that one is dominant but the differences do appear to be real between the two sides.

# Autonomic Nervous System or **Involuntary** nervous system

- ❖ Sympathetic nervous system: the ‘fight or flight’ response to stress mediated by adrenaline/epinephrine or nor-epinephrine. The response to stress includes pupil dilation, increased sweating, increased heart rate, increased strength and increased blood pressure. The adrenal gland and solar plexus secretes adrenalin.
- ❖ Parasympathetic nervous system; involuntary functions of the body such as peristalsis, slowing of the heart, constriction of the pupil. Mediated by acetylcholine. The Vagus nerve, the tenth cranial nerve, is a parasympathetic nerve trunk.

# A peripheral nerve



# Brain Health

- Memory supplements?
- Being alone and the need for social interaction
- Sweat once a day and do something that scares you every day.
- Sleep habits and circadian rhythms
- Exercise and keep active.
- How to avoid falls and balance

# Brain Cancer

- a. Most brain cancers arise as metastasis from other primary tumor sites (5x)
- b. 15,000 deaths per year from primary brain cancer with the majority being glioblastomas (49%) and lower grade gliomas (30%) which affect younger patients (astrocytomas, oligodendrogliomas)
- c. Treatment:
  - Surgery (mainstay)
  - Radiation
  - Chemotherapy with temozolamide
- d. The five-year survival rate for glioblastoma patients is only 6.8 percent,

# Amyotrophic Lateral Sclerosis/Lou Gehrig's Disease

- Slowly progressive (5-8 years) but uniformly fatal demyelinating disorder (neural sheaths) of both upper and lower motor neurons with about 13,000 deaths per year. **Retain cognitive function**
- Onset between age 50 and 70: mean 55 and more common in men and 10 percent familial
- Progressive Respiratory symptoms most devastating
- No known treatment; Riluzole a glutamate inhibitor can be given with 3-6 month survival benefit.

**Multiple Sclerosis; an autoimmune inflammatory demyelinating disease three to four time more common in females than males**

- Nonspecific symptoms beginning between the ages of 20 and 40: slurred speech, fatigue, dizziness, tingling, altered sexual, bowel and bladder function, cognitive; runs a variable course.
- Common disorder about 720,000 cases in US with variable course and no diagnostic lab test (**MRI**)
- Link to Epstein-Barr virus (may be main cause)
- FDA has approved 15 plus drugs for treatment (average cost per year \$80,000)-these drugs alter the immune response of lymphocytes.

# Guillain-Barre Syndrome

- A rare autoimmune disease that affects the peripheral nerves and usually occurs 4-6 weeks after a viral infection.
- The weakness often spreads from legs to the arms and in 50 percent of cases cranial nerves are involved.
- Most recover completely over a 6-12 months period.

- Treatment:

IV immune globulin

Infusion of antibodies

Plasma exchange



Mental Illness: poorly understood and difficult to diagnose and treat with a severe shortage of mental health professionals and a social stigma that acts as a barrier to treatment and delay in treatment.

- Three major **psychosis**: Schizophrenia, Bipolar and Psychotic Depression.
- An estimated one in 300 have schizophrenia, 2.8% have bipolar disorders and about 25% of adults experience severe depression at some time during their lives. **Depression is the most common cause for absenteeism**
- Bipolar-(Manic-Depressive) Type one--severe diagnosed when it lasts 7 or more days with 80% psychosis (talkative, decreased need for sleep, grandiosity, increase pleasurable activities with increase in substance abuse and suicide.
- The DSM-5 coding system is used to categorize mental disorders (imprecise and controversial)
- Screening in PCP offices for depression with PHQ-9 and BDI tests

# Treatment for Mental Illness

- One large study showed that 13.2% of Americans aged 18 and over reported taking antidepressant medication in the past 30 days.
- Significant Depression usually SSRI (Zoloft and Prozac). Sometimes SNRI (Cymbalta and Sertraline)
- Bupropion (Wellbutrin) a tranquilizer to quit smoking (helps 50% of the time)
- Large number of psychotropic drugs to treat mood disorders; **most takes weeks to kick in; most have significant side effects; and treatment often is 'trial and error'**.
- New drugs like Ketamine and others that are faster acting

## Autism Spectrum Disorder: cause unknown and varies in severity: now often called neurodiversity

- Related to brain development that impacts how a person perceives and socializes with others, causing problems in social interaction and communication. The disorder also includes limited and repetitive patterns of behavior.
- ASD begins before the age of 3 years
- About 1 in 44 with a 4 to 1 ratio boys vs girls
- Doctors look at the child's developmental history and behavior to make the diagnosis

### *A few characteristics: (different and 'nerdy' and obsessed)*

- Avoids eye contact,
- Has little interest in other children or caretakers,
- Limited display of language (for example, having fewer words than peers or difficulty with use of words for communication)
- Getting upset by minor changes in routine

# Neuroplasticity

- It is defined as the ability of the nervous system to adapt to changing circumstances such as traumatic brain injury or stroke by reorganizing its structure, functions, or connections.
- There are at least four major forms of functional neuroplasticity that can be studied in humans: homologous area adaptation, cross-modal reassignment, map expansion, and compensatory masquerade.
- Stem cells reside in the brain throughout life creating new neurons.

# Meningitis, Encephalitis, and Brain Abscess

- Viral meningitis is fairly common due to enteroviruses (85-95% and seasonal)

**Presents with stiff neck or nuchal rigidity**

- Encephalitis can be caused by the Herpes simplex virus and is treated with acyclovir and dexamethasone.
- Lumbar puncture with examination of cerebrospinal fluid is diagnostic; (meningoencephalitis PCR panel (polymerase chain reaction) for screening)
- MRI is better than CT scan for diagnostic purposes.

# Parkinson's and Parkinsonism that has a broad range of presentations

- Cause: Due to loss of Dopamine producing cells in the basal ganglia (substantia nigra) at the base of the brain (10 types of cells identified and intense research is underway as to the cause)
- Symptoms: tremors, **rigidity**, gait, mask face, mood change, hallucinations, dementia (dementia occurs later in the disease than with Alzheimer's)
- Early symptoms of anosmia, sleep disorders, constipation, depression, restlessness, anxiety, orthostatic hypotension (may occur many years before)
- Treatment: directed at increasing dopamine. Levodopa the mainstay but a whole array of meds prescribed by neurologists. Newer agents include monoamine oxidase B inhibitors, catechol-O-methyltransferase inhibitors, and adenosine A2A receptor antagonists.
- Deep brains stimulation of basal ganglia can be used and is often effective- do not know why this works.

# Dementias

- 1) Alzheimer's disease: 60% of patients (Beta-amyloid and Tau Protein with tangles)—cause unknown (APOE-e4 genetic link). No effective treatment although there is a new blood test for Tau protein that is 96% accurate in diagnosing Alzheimer's: anticholinergics and NMDA (glutamate) receptor antagonists may temporarily delay the need for NH placement but no long term benefits.
- 2) Arteriosclerotic; multiple mini-strokes, Transient Ischemic Attacks (TIAs)
- 3) Temporal Frontal Lobe Dementia; usually starts with difficulty in speech and behavioral problems. More rapidly progressive.
- 4) Lewy Body Dementia; more behavioral problems and shorter course and hallucinations
- 5) TDP- 23 deposition dementia in ¼ over the age of 90

**For all dementias try to avoid too many meds; less is more and antipsychotics are not well tolerated.**

## New drugs approved by the FDA for Alzheimer's.

- Aducanumab, Donanemab, Lecanemab, and Remternetug are amyloid targeting immunotherapy drugs. These drugs are expensive (about \$25,000 or more per year) and may slow the progression of the disease?
- They are monoclonal antibody that reduces the buildup of amyloid plaques in the brain and used mainly in early cases.



# Strokes; two types--ischemic and hemorrhagic (12 percent)

- **Unlike heart attack do not give aspirin because of possible intracranial bleeding**
- Cincinnati Criteria: *Facial droop, Arm drift, Slurred Speech: All three present = 87% chance of stroke.*
- Emergency CT scan to differentiate (takes little time)
- Window of 3-4.5 hours from when symptoms first started (with new angiography techniques can estimate amount of viable brain beyond stroke (flair and penumbra) and possible large vessel disease and in some cases extract the clot to retrain maximal function up to 24 hours.)
- IV anticoagulant and fibrinolytic: plasminogen activator (tPA) and Alteplase. Cannot give after 4.5 hours.
- Carotid bruits (large vessel occlusion that can be reversed with endovascular thrombectomy.)

# More on strokes: Risk factors

- Hypertension; target 130/80 and ACE, ARBs and diuretics more effective than Beta blockers and CA channel blockers in preventing strokes.
- Lipid LDL (low density lipoproteins, if >100 treat with statins; in high risk shoot for LDL of 70 that decreases cardiovascular events: **diet, statins and Ezetimibe**)
- Anti-platelet medications: ASA (baby), Plavix, and Ticagrelor (in acute phase ASA and Plavix in combination has survival benefits x 21 days)

**Migraine headaches** are throbbing headaches that last 4 hours to 3 days with 40 million Americans afflicted. It is the second leading cause for absenteeism.

1. The headache is characterized by unilateral or bilateral throbbing pain, nausea and vomiting, photophobia, impairment (they are incapacitated)  
Most individuals can feel the headache coming on.
2. Many areas of the brain effected including the meninges, blood vessels, brain stem, trigeminal nerve and the thalamus (pain center) on MRI scans
3. Migraines represent 90% of the complaints about headache seen in the PCPs office.

# Treatments

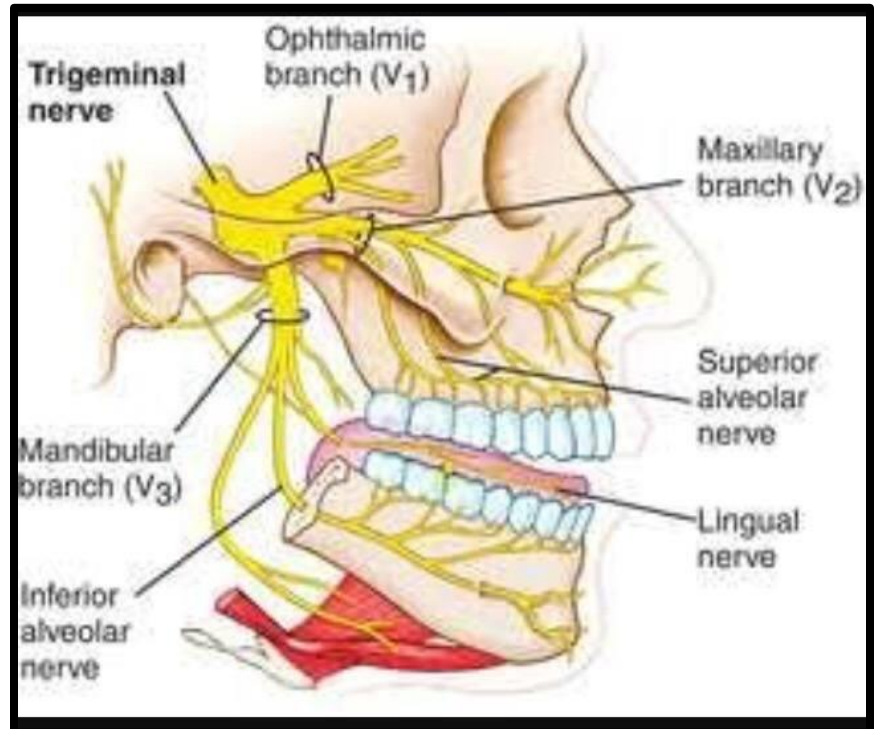
**A disorder with many treatments;** none curative but new drugs that are preventative.

- 1. Tryptans (effect on serotonin) and NSAIDS--moderately effective, mainstay of treatment
- 2. Calcitonin gene-related peptide receptor antagonists (vasodilator) (CGRP)—moderate to high effectiveness. Qulipta (atogepant) and Zavzpret (zavegepant) nasal spray
- 3. Dihydroergotamine (blocks vasospasm)—(traditional treatment) moderate to high effectiveness.
- 4. Acetaminophen-moderate effectiveness
- 5. Remote electric neuromodulation (stimulates upper arm peripheral nerves to modulate pain especially in adolescence)—moderate effectiveness
- 6. Noninvasive vagal nerve stimulation (mainly cluster headaches)-moderate
- 7. Botox (15 or more headaches per month, (It consists of 31 injections) Costly? And needs to be repeated every few months.

# Trigeminal neuralgia or tic douloureux (5<sup>th</sup> cranial nerve) and Bell's Palsy (7<sup>th</sup> cranial nerve)

- **Trigeminal neuralgia** is a rare disorder with no known cause characterized by unilateral intermittent shooting, stabbing facial pain (often debilitating)
- **Treatment:**
  1. anticonvulsants like Tegretol and gabapentin/Neurontin
  2. Sodium Channel Blockers
  3. Complex surgery to destroy portions of the nerve.

**Bell's palsy** is usually a painless condition with self limiting loss of 7<sup>th</sup> nerve function with drooping of the muscles of affected side of the face. It is felt to be related to the herpes virus and usually resolves within 3-6 months.



# Benefits of Sleep

- Critical role in immune function, metabolism, memory, learning, (retain information better right before sleep) and other vital functions
- The 5 or 6 **sleep cycles each night** lasts about 90 minutes
- **Dream sleep or rapid eye movement (REM) sleep** consumes about 90 minutes on an average night; heart rate and breathing increase and your limbs may even become paralyzed
- Need **between 7 and 9 hours** of sleep per night and people over 65 should also get 7 to 8 hours per night
- Why do we sleep? No definitive answer; but brain shrinks and may open the blood–cerebrospinal fluid barrier (BCSFB) for excretion of waste products.

# BRAIN DEATH IN ORGAN DONATION

1. Comatose and unresponsive
2. EEG for brain wave activity
3. Now have a nuclear scan that reveals total brain blackout. No longer need to rely on clinical findings and expert opinions, but still by law need multiple expert opinions.

# Obstructive Sleep Apnea (OSA) and Central Sleep Apnea(CSA)

- An epidemic due in large part due to increasing BMIs (weight in kilograms divided by height in meters squared with normal range of 18.5 – 24.9 with 30 and above equaling morbid obesity)
- As high as 37% of men and 50% of women being afflicted
- Symptoms of snoring, gaps in breathing with intercostal attempts, HPT, drowsiness and stroke.
- Treatment CPAP (Continuous positive airway pressure)
- **Opioids greatly exacerbate the complications of OSA (sudden death)**