Beyond Post Dural Puncture Headaches

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MICHIGAN MEDICINE

Nothing to Disclose

Special Thanks to Dr. Wade Cooper for input on this lecture

Case

- ER contacts you to evaluate a patient for a blood patch
- 22 YO F ASA 2 who 2 days earlier presented to the ER with 4 day history of worsening headache
- Long standing history of headaches, first occurred in adolescence
- Several ER visits for headache
- Two days earlier was in the ER for “the worst headache of my life”

Initial Encounter: LP results

- Negative for heme
- Negative for elevated WBC

Initial Encounter

- Head CT negative
- Afebrile, negative meningeal signs
- No concern on CN exam
- Was discharged home after IV ketorolac and steroid burst and review of negative LP

Subsequent Encounter

- Now presents again to the ER and has worse headache
- “definitely worse with standing and walking”, but does not go away completely when she lays down
- Hydration and IV caffeine have failed to help
- Describes it as throbbing and rating her pain 10/10
- Would you do a blood patch?

Objectives

- Be able to diagnose a migraine headache and understand what characteristics set it apart form a post dural puncture headache
- Understand the epidemiology of the most common headaches
- Review the pathophysiology of migraine headaches
- To be familiar with common and emerging treatment options

How do you define a headache?

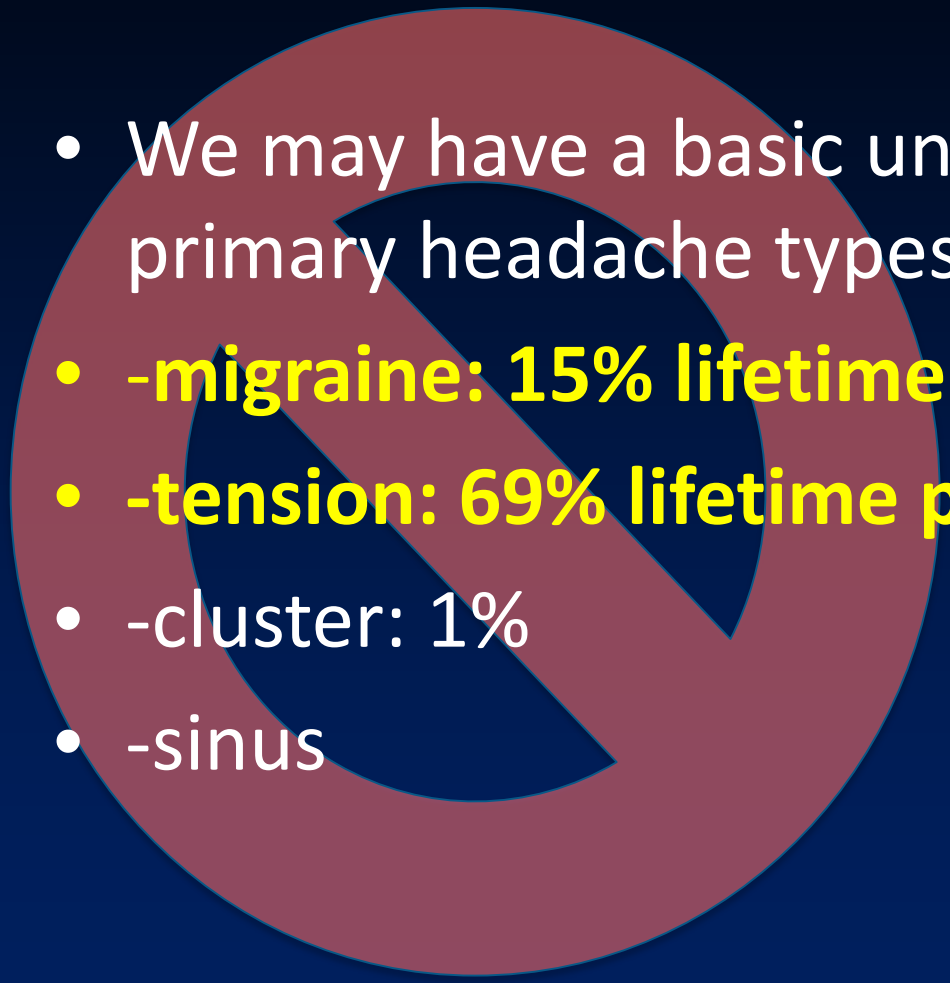
- We may have a basic understanding of the most common headache types:
- -migraine
- -tension
- -cluster
- -sinus

How do you define a headache?

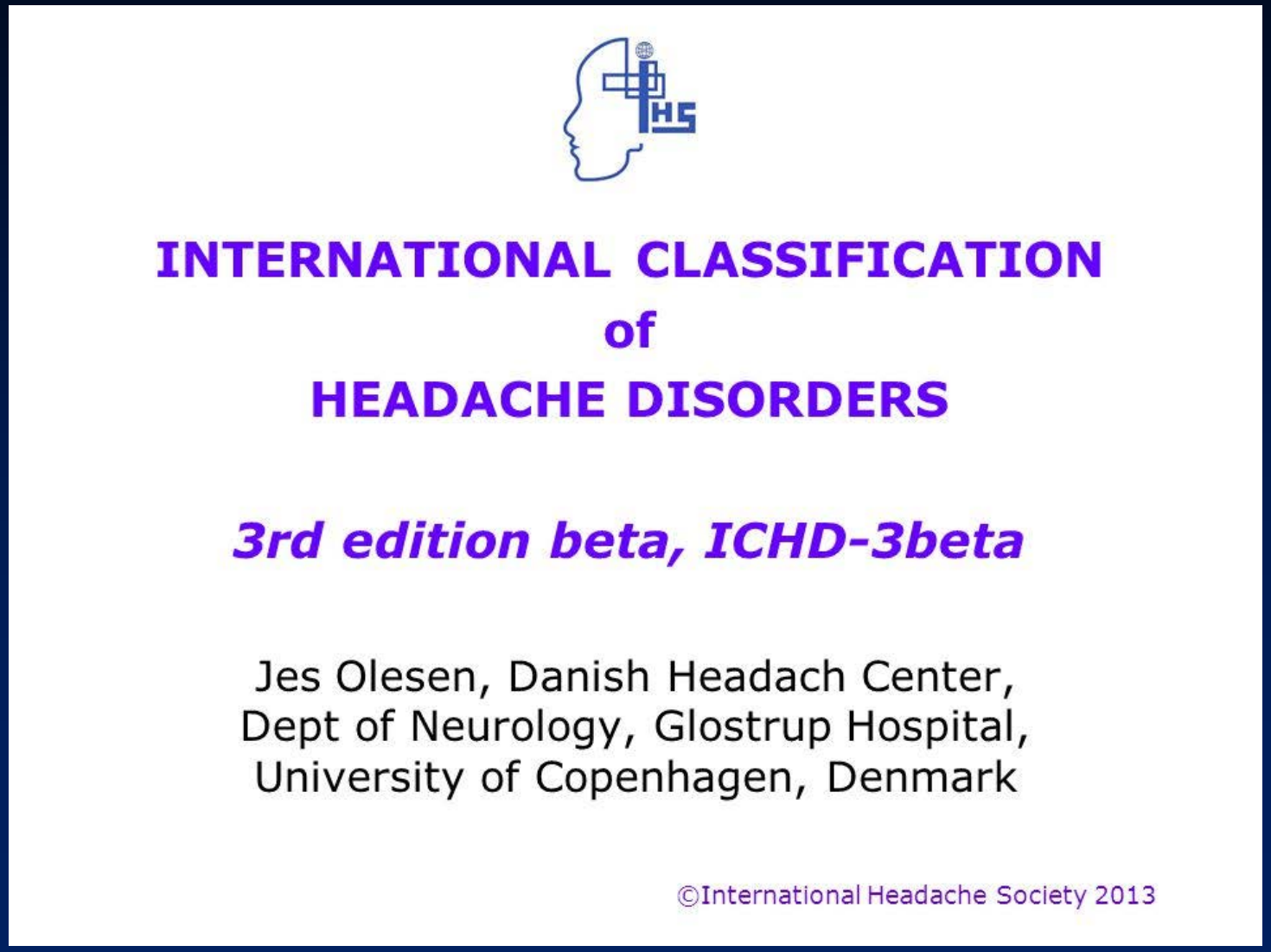
- We may have a basic understanding of the most common primary headache types:
- **-migraine: 15% lifetime prevalence**
- **-tension: 69% lifetime prevalence**
- -cluster: 1%
- -sinus: estimates vary

How do you define a headache?

- We may have a basic understanding of the most common primary headache types:
- **-migraine: 15% lifetime prevalence**
- **-tension: 69% lifetime prevalence**
- -cluster: 1%
- -sinus



International Classification of Headache Disorders (ICHD-3 beta)



International Classification of Headache Disorders (ICHD-3 beta)

- Classification Outline
- Part one: the primary headaches
  - 1. Migraine
  - 2. Tension-type headache
  - 3. Trigeminal autonomic cephalgias
  - 4. Other primary headache disorders
- Part two: the secondary headaches
  - 5. Headache attributed to trauma or injury to the head and/or neck
  - 6. Headache attributed to cranial or cervical vascular disorder
  - 7. Headache attributed to non-vascular intracranial disorder
  - 8. Headache attributed to substance or its withdrawal
  - 9. Headache attributed to infection
  - 10. Headache attributed to disorders of homoeostasis
  - 11. Headache or facial pain attributed to disorder of the cranium, neck, eyes , ears, nose, sinuses, teeth, mouth or other facial or cervical structure
- Part three: painful cranial neuropathies, other facial pains and other headaches
  - 12. Painful cranial neuropathies and other facial pains
  - 13. Other headache disorders

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Classification Simplified

Primary

- Tension
- Migraine
- Cluster

Secondary

- Bad Hombres….
- Age of onset > 40
- Thunderclap
- Those with neurological findings
- Associated with systemic findings (fever)

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- Tension
- Migraine
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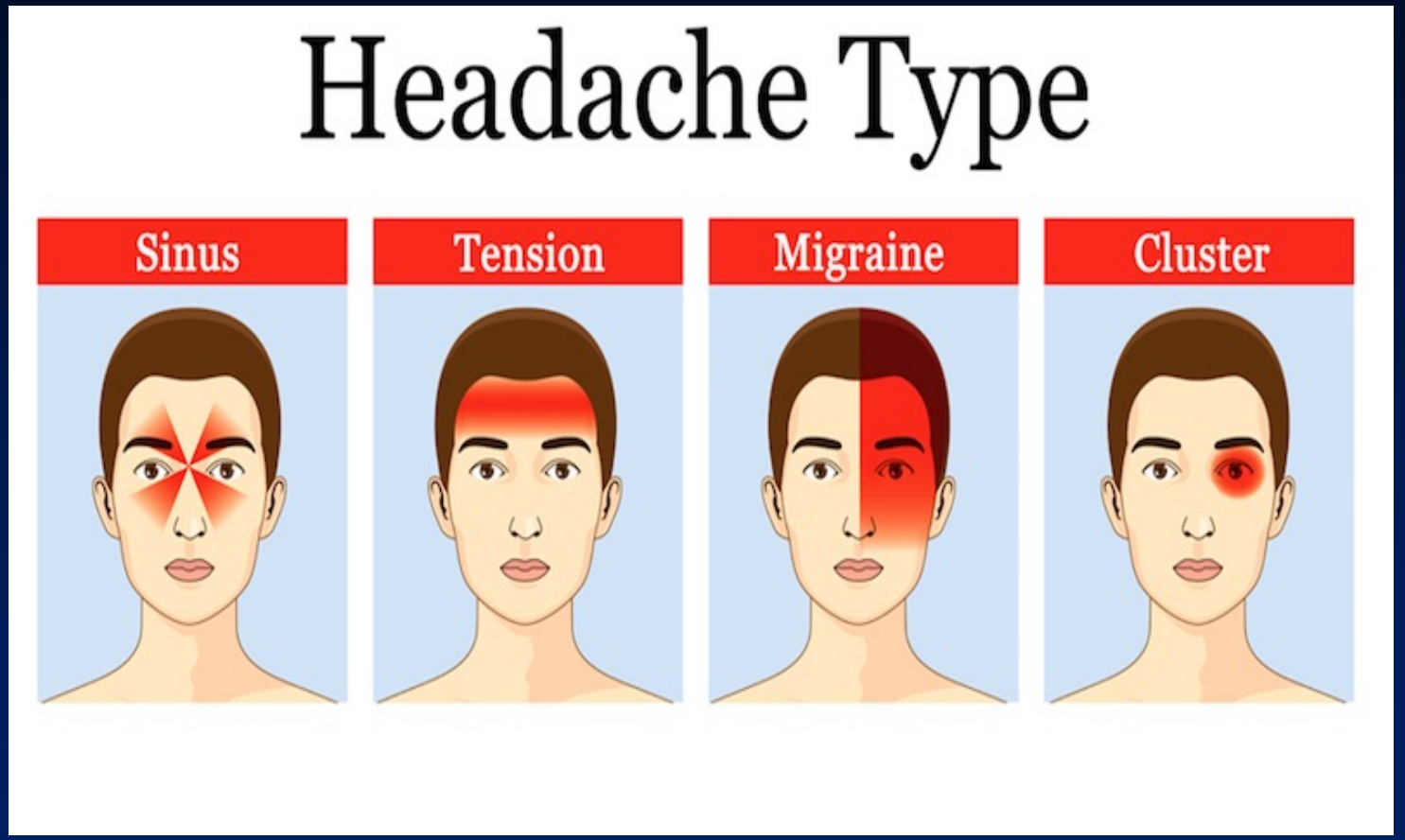
- Sinus
- Hormonal



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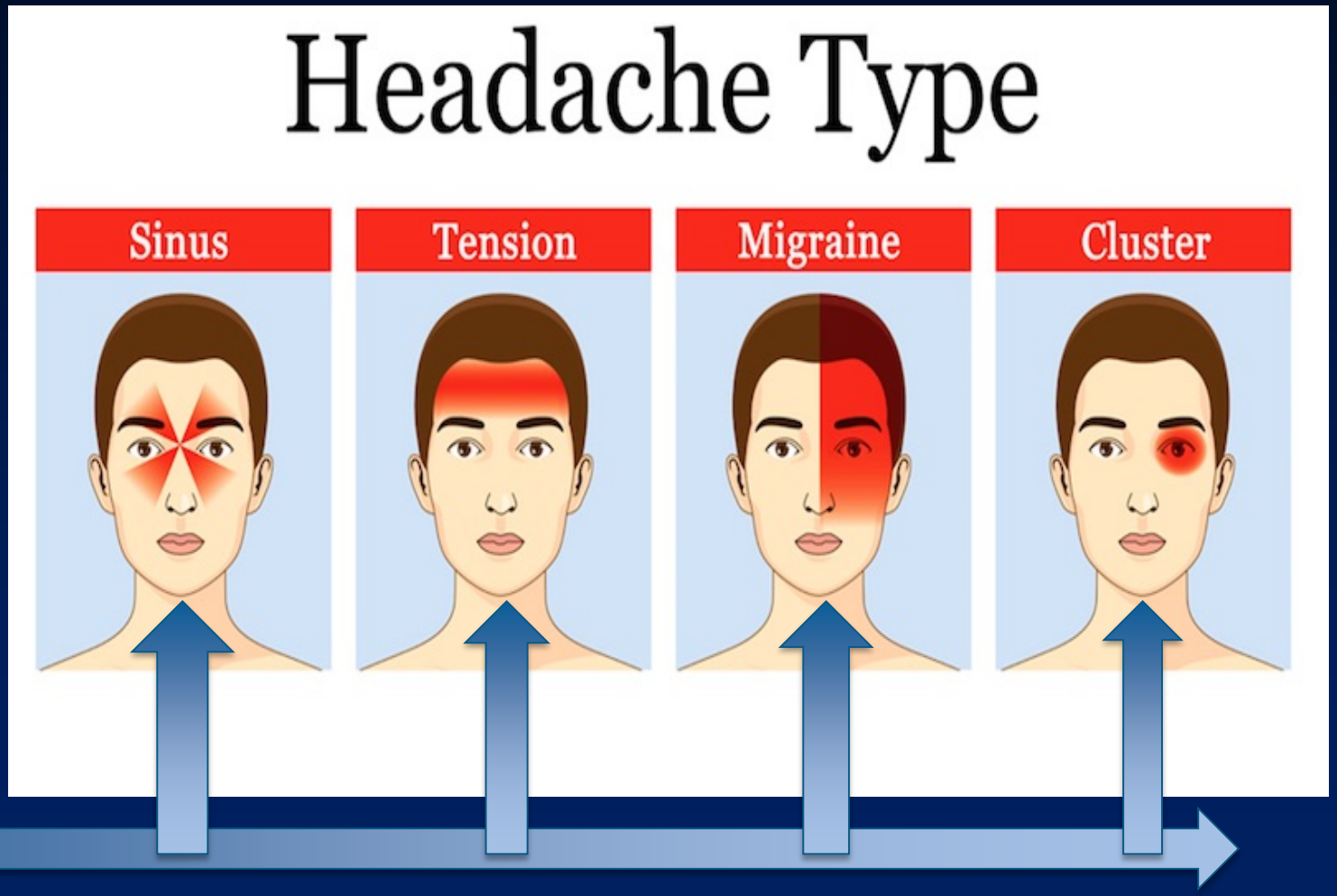
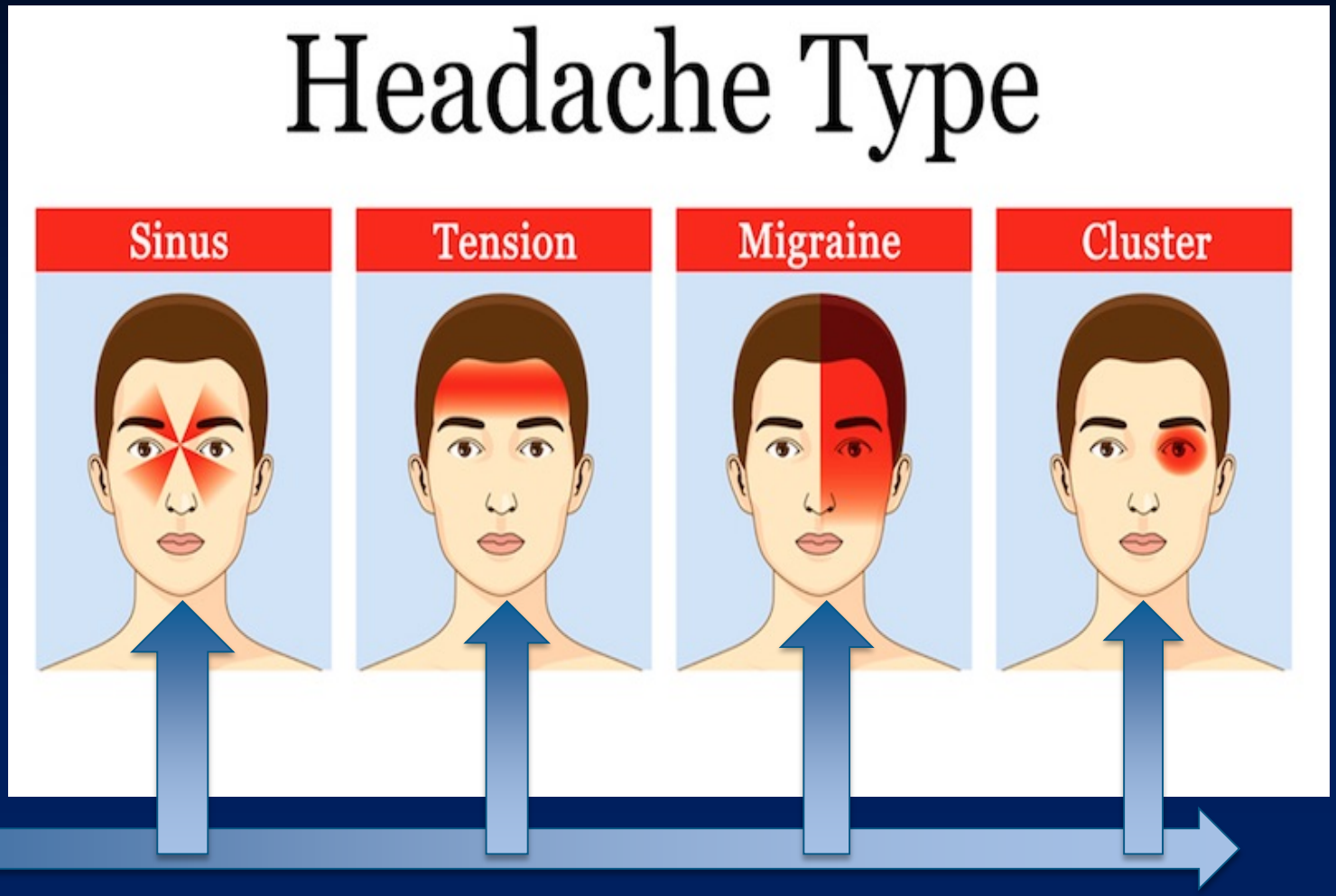


Classification Simplified

Primary

- **Tension**
- **Migraine**
- Cluster
- Sinus
- Hormonal



Tension Headache

- Most common type of primary headache
- Also referred to as: stress headache, daily persistent headache, chronic non-progressive headache
- Affect 1.4 billion people (20.8% of the population)
- Affect woman > men
- Lifetime prevalence 69%

Tension Headache

- Mild to moderate pain around head or behind eyes
- May be described as a “band around the head”
- No visual changes and no N/V
- Not exacerbated by activity
- Generally less severe than migraine

Tension May Overlap with Migraine

- While they can have overlap, they have distinct clinical presentations

Treatment of Tension Headaches

- Ibuprofen/NSAIDS
- Acetaminophen
- Caffeine
- Muscle relaxers
- Magnesium
- Gabapentanoids
- Topical compounds and TENS

Migraine

Epidemiology

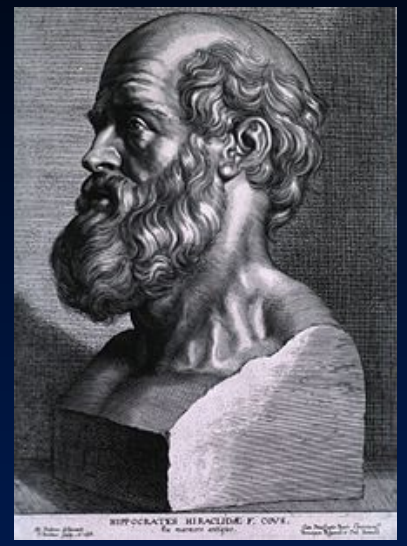
- Females 18%
- Males 5%
- 15% lifetime prevalence

Economical Impact

- Of that, 54% severe, 46% moderate
- Results in cost of $11,000,000,000 per year

History

- First mentioned about 6000 years ago
- First detailed description – Hippocrates
- First classification –
- Arataeus of Cappadocia (1st Century, AD)



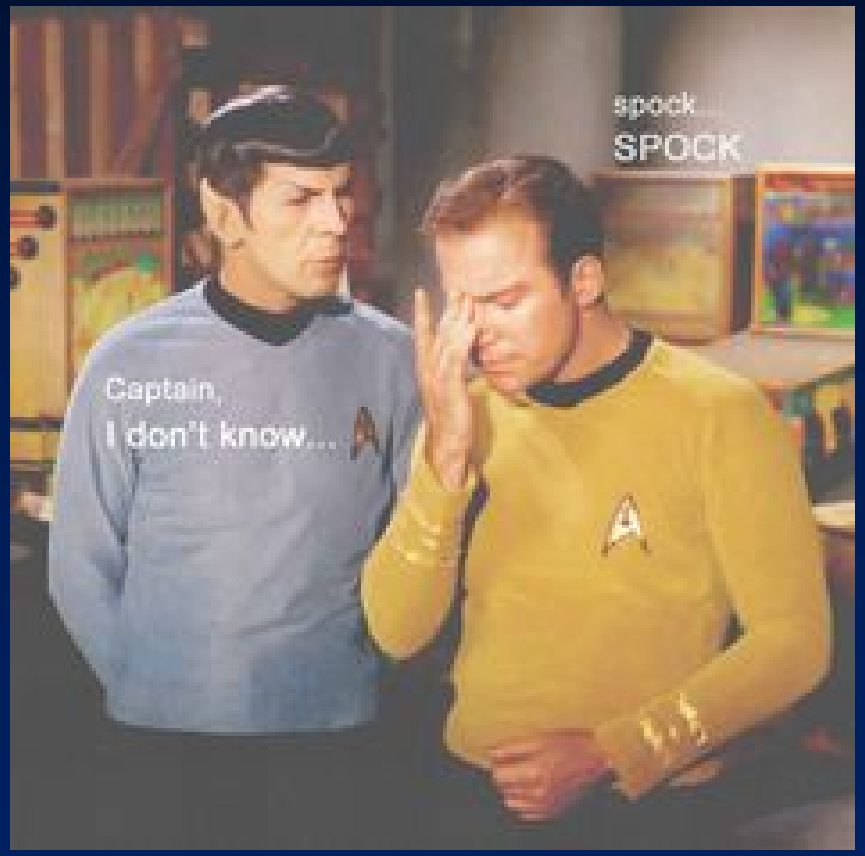
History

- First Pathophysiological details – Galen (2nd Century, AD)
  - Brain-abdomen connection
  - Blood vessel involvement

- Vascular Theory – Thomas Willis (17th Century)
  - First to use coffee in migraine treatment

Migraine: Clinical Diagnosis

- Pulsatile headache of moderate to sever pain
- Typically in one side of the head
- Sensitive to light and sound
- Worse with physical activity
- Associated with N/V



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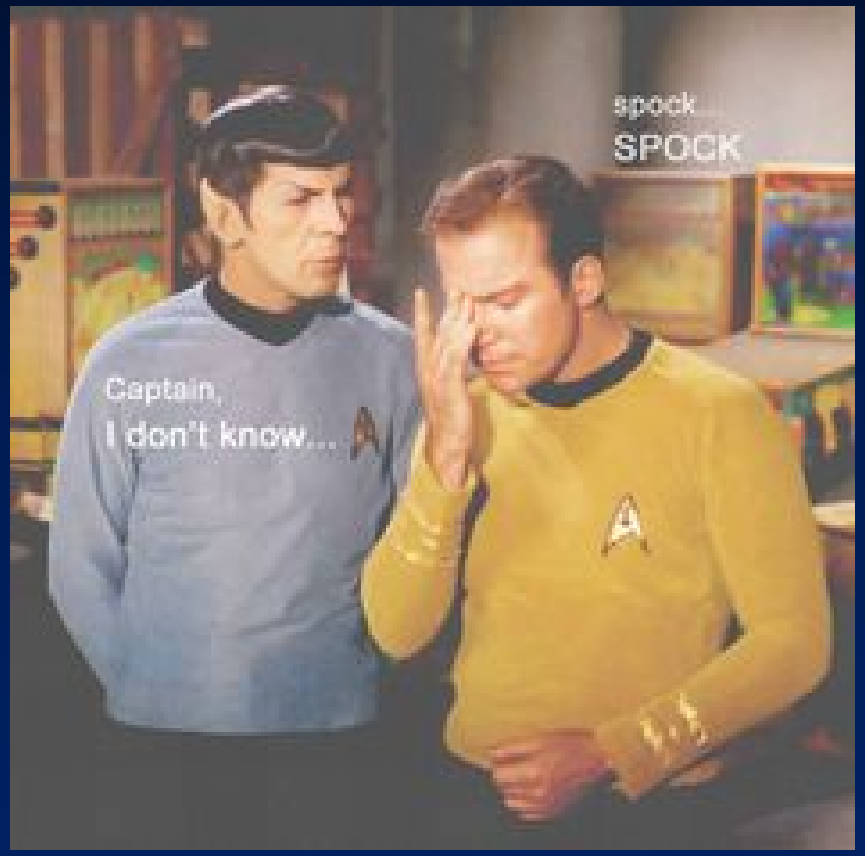


Diagnostic Criteria: Migraine

A. At least five attacks fulfilling criteria B-D

B. Headache attacks lasting 4-72 hours

C. Headache has at least two of the following characteristics:

1. unilateral location
2. pulsating quality
3. moderate or severe pain intensity
4. aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)

D. During headache at least one of the following:

1. nausea and/or vomiting
2. photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis

Diagnostic criteria: Aura

A. At least two attacks fulfilling criteria B and C

B. B. One or more of the following fully reversible aura symptoms:
   1. visual
   2. sensory
   3. speech and /or language
   4. motor
   5. brainstem
   6. retinal

C. C. At least two of the following four characteristics:
   1. At least one aura symptom spreads gradually over >5 minutes, and/or two or more symptoms occurring in succession
   2. Each individual aura symptom lasts 5-60 minutes
   3. At leas one aura symptom is unilateral
   4. The aura is accompanied, or followed within 60 minutes, by headache

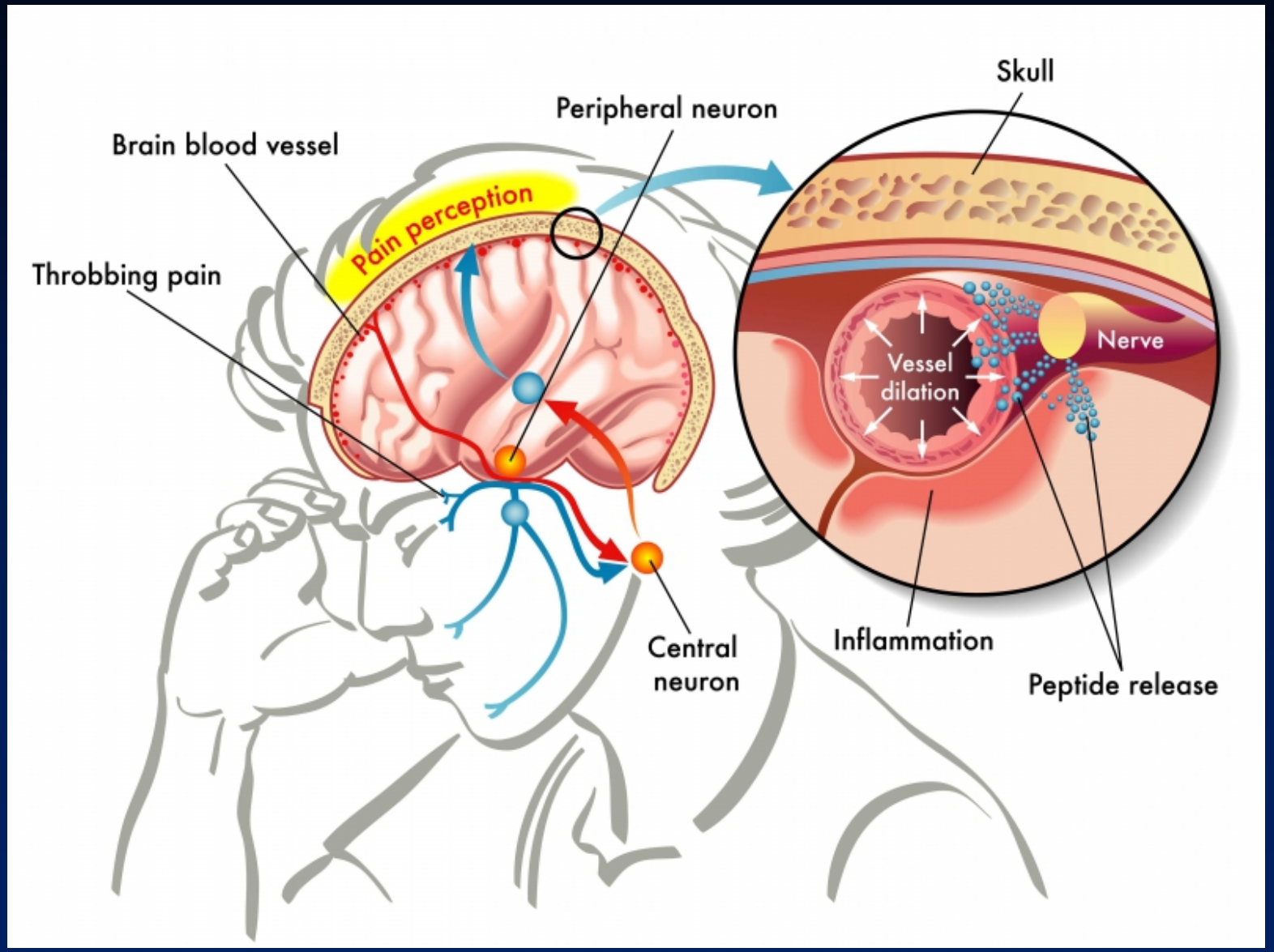
D. D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded

Top 5 triggers for Migraine

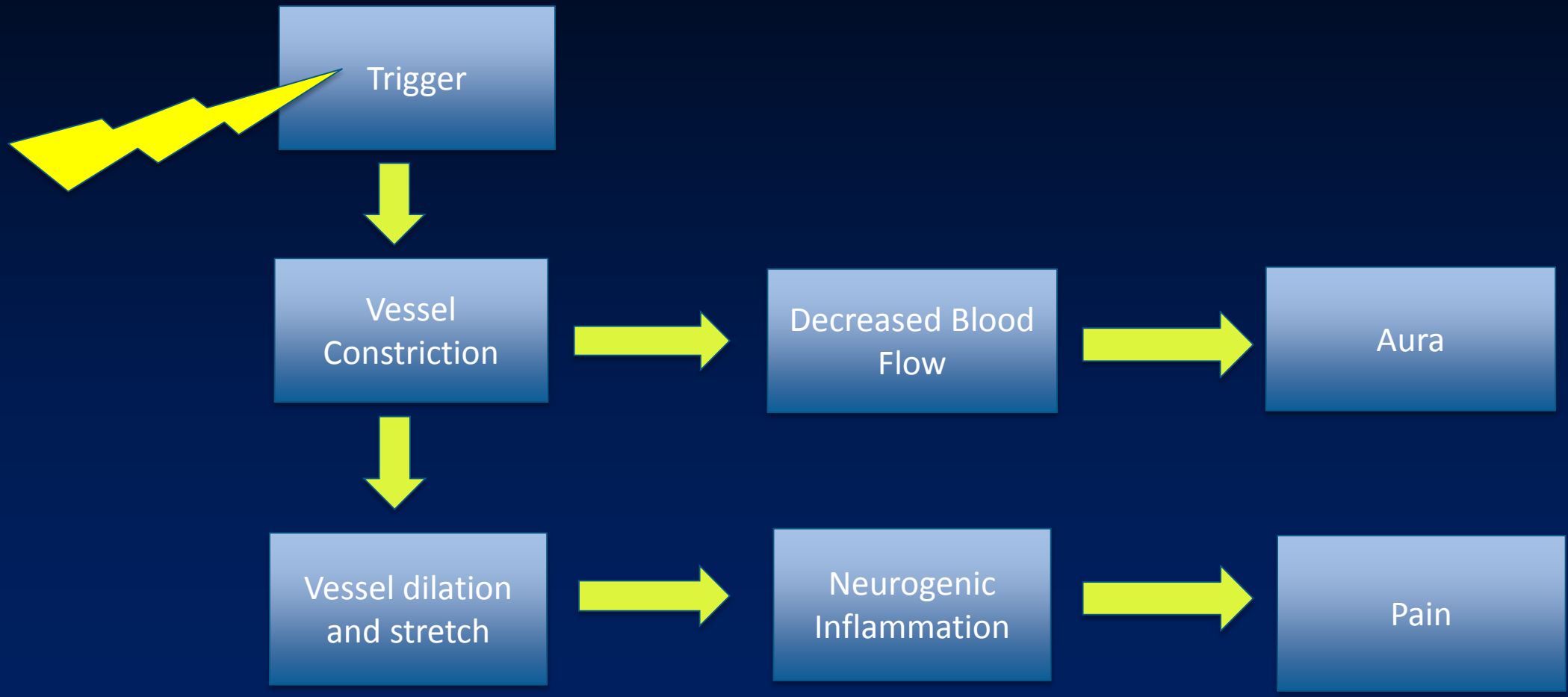
Pathophysiology

- Vascular Theory (1940) vasoconstriction that causes aura leads to compensatory vasodilation that in turn stimulates perivascular nociceptors (by stretching) causing pain
- Cerebral blood vessels, venous sinuses and dura mater are innervated by V CN (opthalimic division) and (posterior fossa area) by upper cervical dorsal roots (C1, C2)
- Stimulation of V CN ganglion leads to SP and CRGP release and plasma protein extravasation (sterile inflammation)

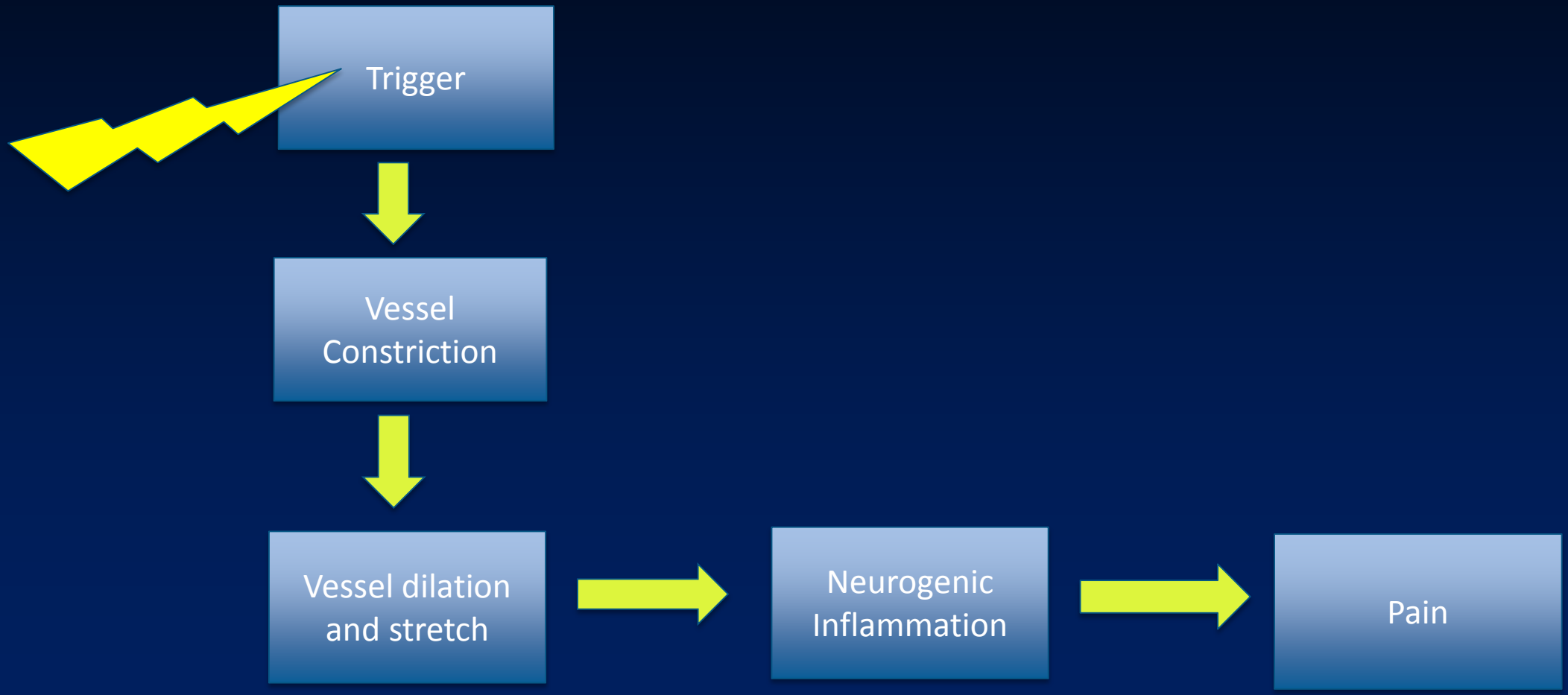
Vascular Theory



Pathophysiology – vascular trigger



Vascular theory has largely been discounted



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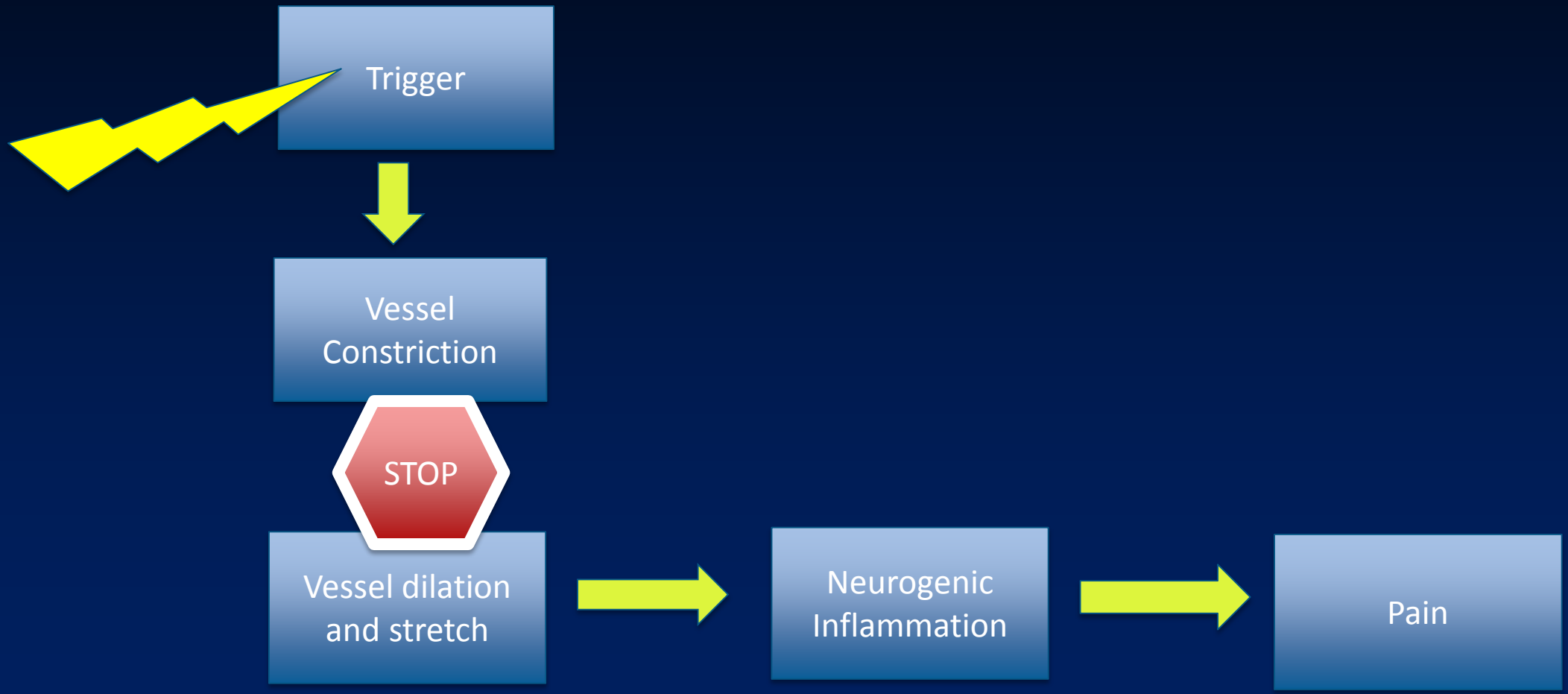

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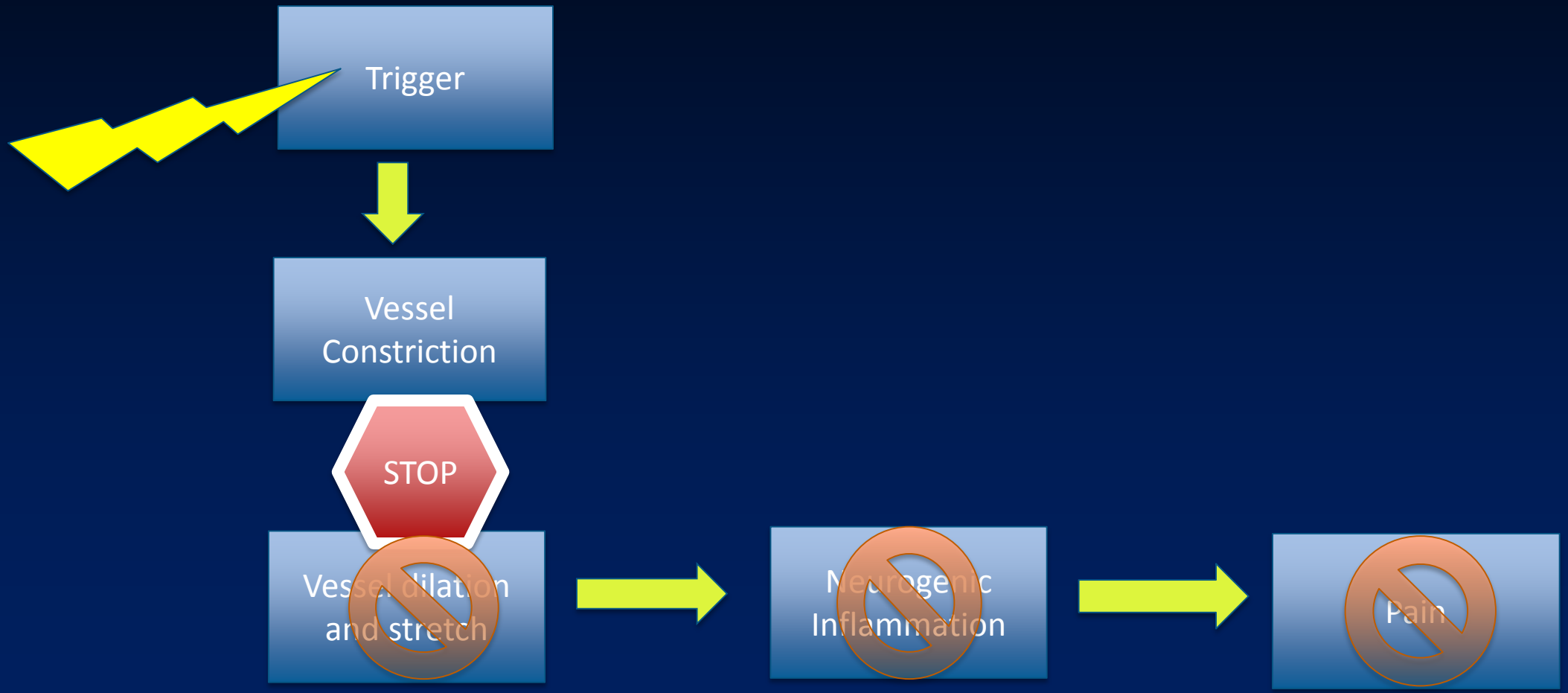

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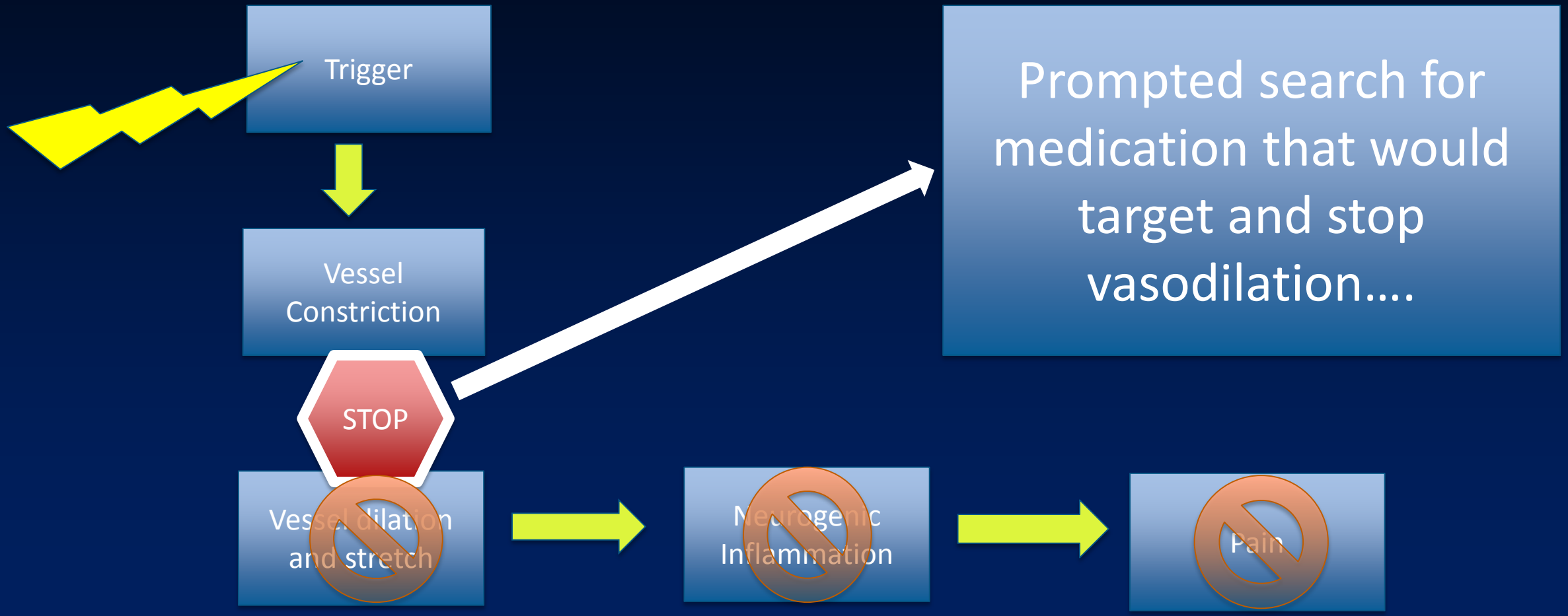


Triptans were born

- Goal was to find a medication that selectively vasoconstrictor cerebral blood vessels
- Succeeded in 1984 with sumatriptan (Imitrex)
- Triptans do work to abort migraine

Triptans work to abort migraines….

- But probably has little to do with the fact that they cause vasoconstriction
- Has more to do with secondary effect on serotonin
- In the 1960's researchers noted an association between low blood serotonin and migraine headaches
- Seratonin causes vasoconstriction…

This may explain why medications used to treat depression often work to *prevent* migraines

Recognizing the impact serotonin has led to new thinking about pathophysiology of migraines

- Thought that changes in the brain itself cause the pain syndrome

New Theory

- Cortical Spreading Depression
- CSD – “seizure like phenomenon – a spreading wave of electrical silence in which cortical neurons go quiet”

Cortical Spreading Depression

- 1944 – Leao
- Initial wave of excitation followed by wave of depression
- The wave is spreading from occipital lobe towards frontal
- Spreads 3-6 mm/min

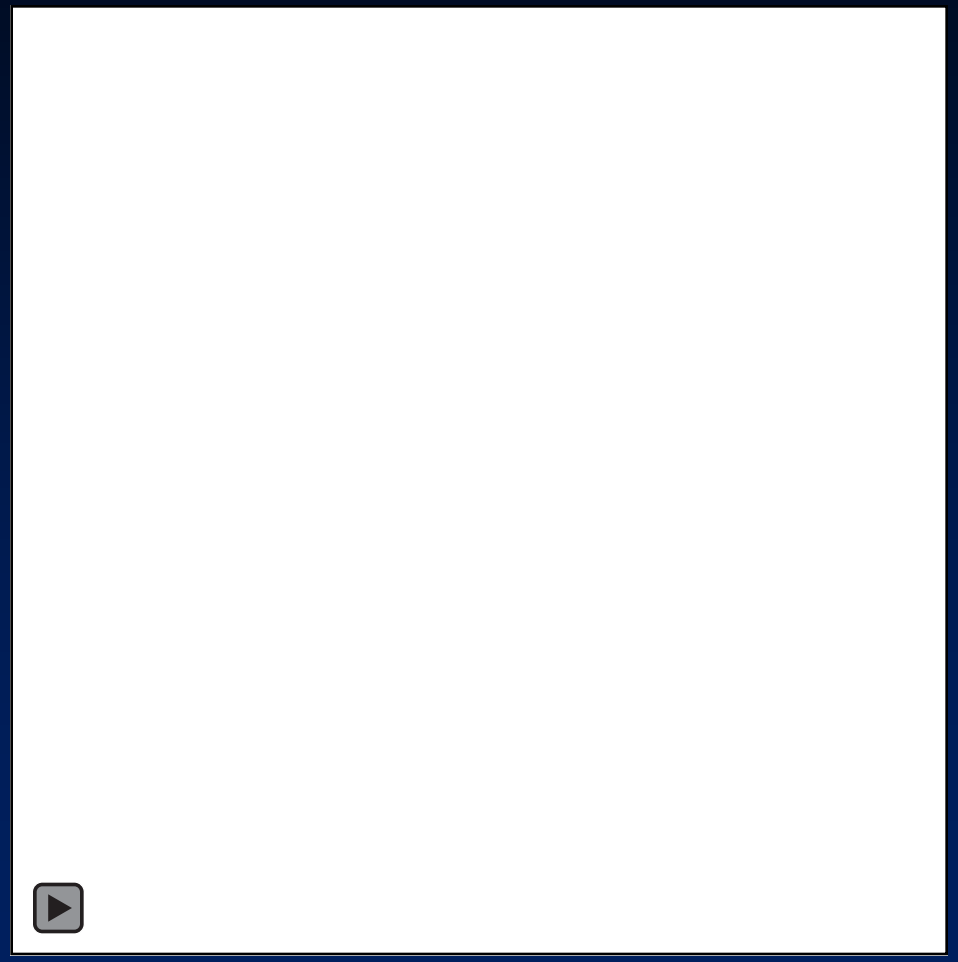
CSD

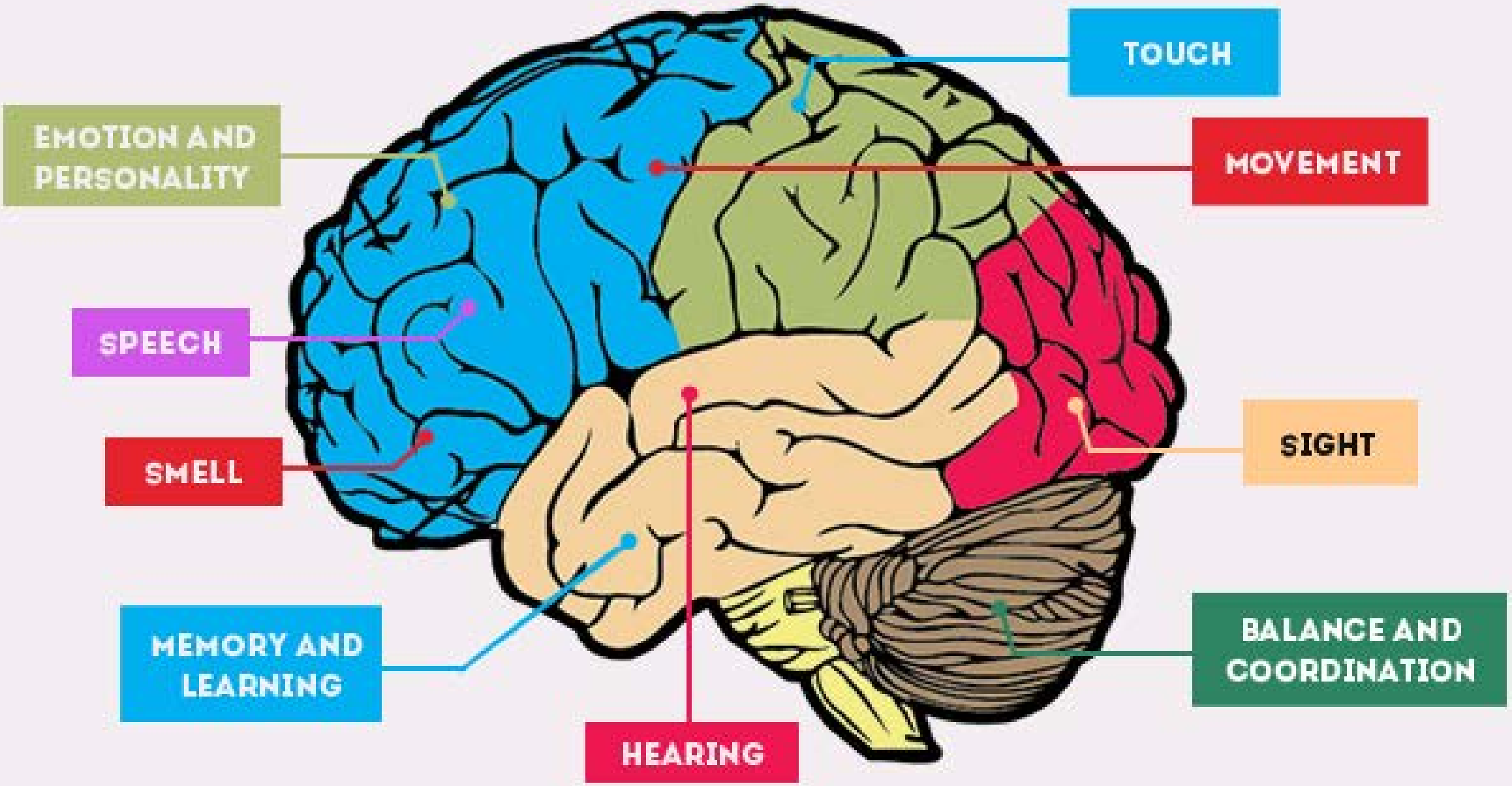
- This is a slow moving wave of depolarization
- Starts in basilar areas
- Spreads slowly (over 15-20 minutes) across cortex

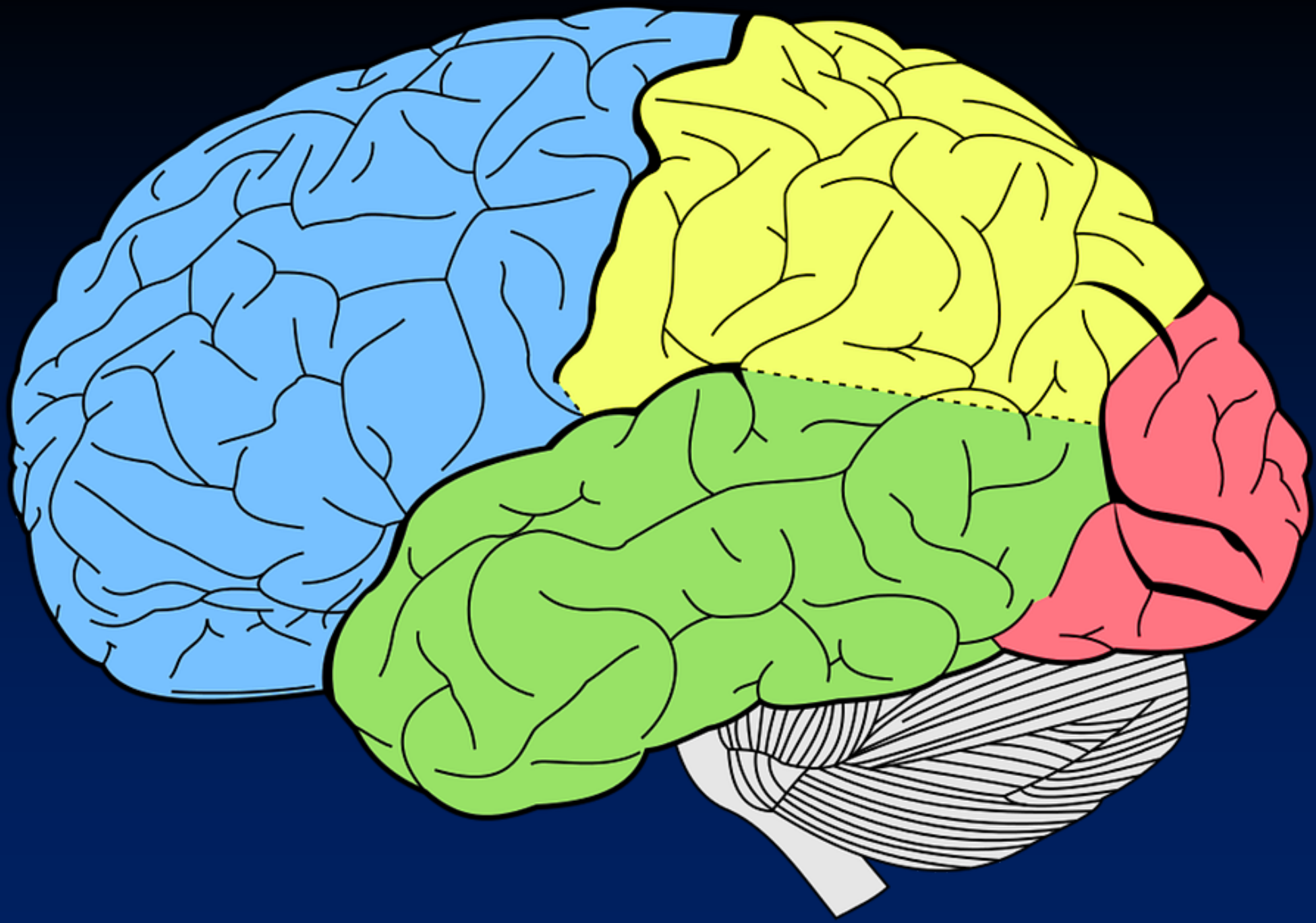
CSD

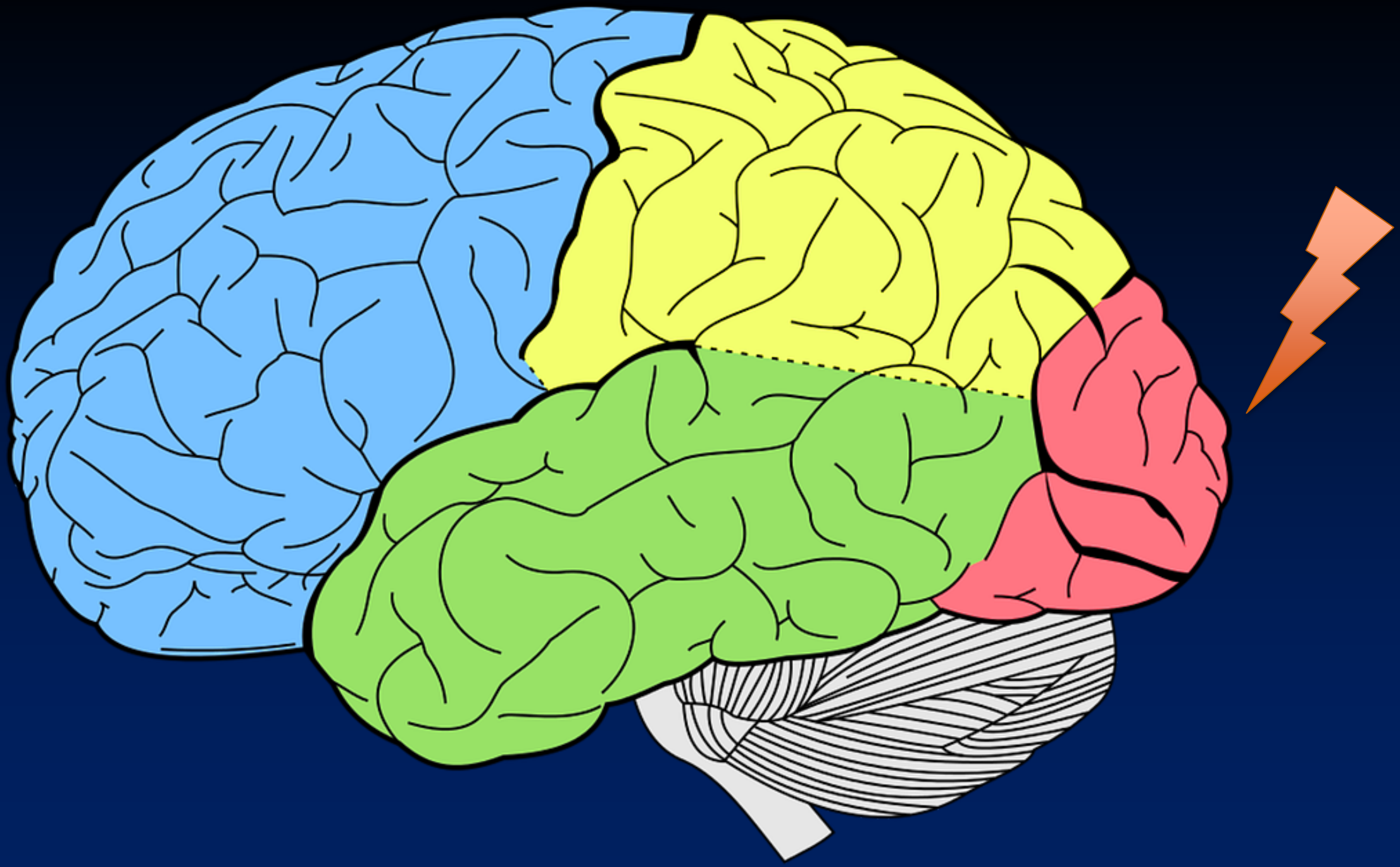
- Excitation wave:
  - Release of K+ and Glutamate depolarization
  - K+ accumulation in ECS
- Spreading depression:
  - Tissue refractory to excitation decreased blood flow causes neurological signs (aura)

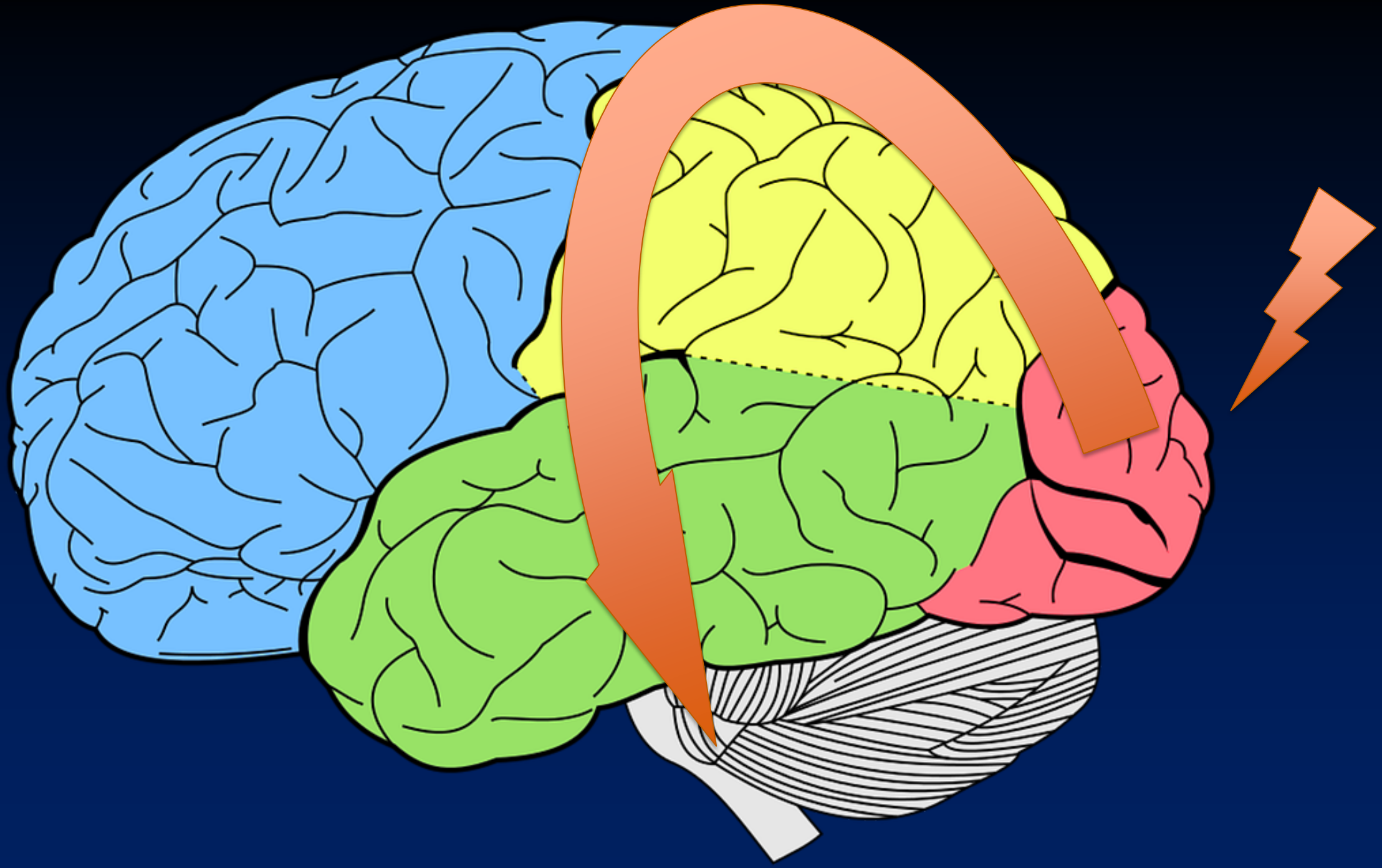
CSD

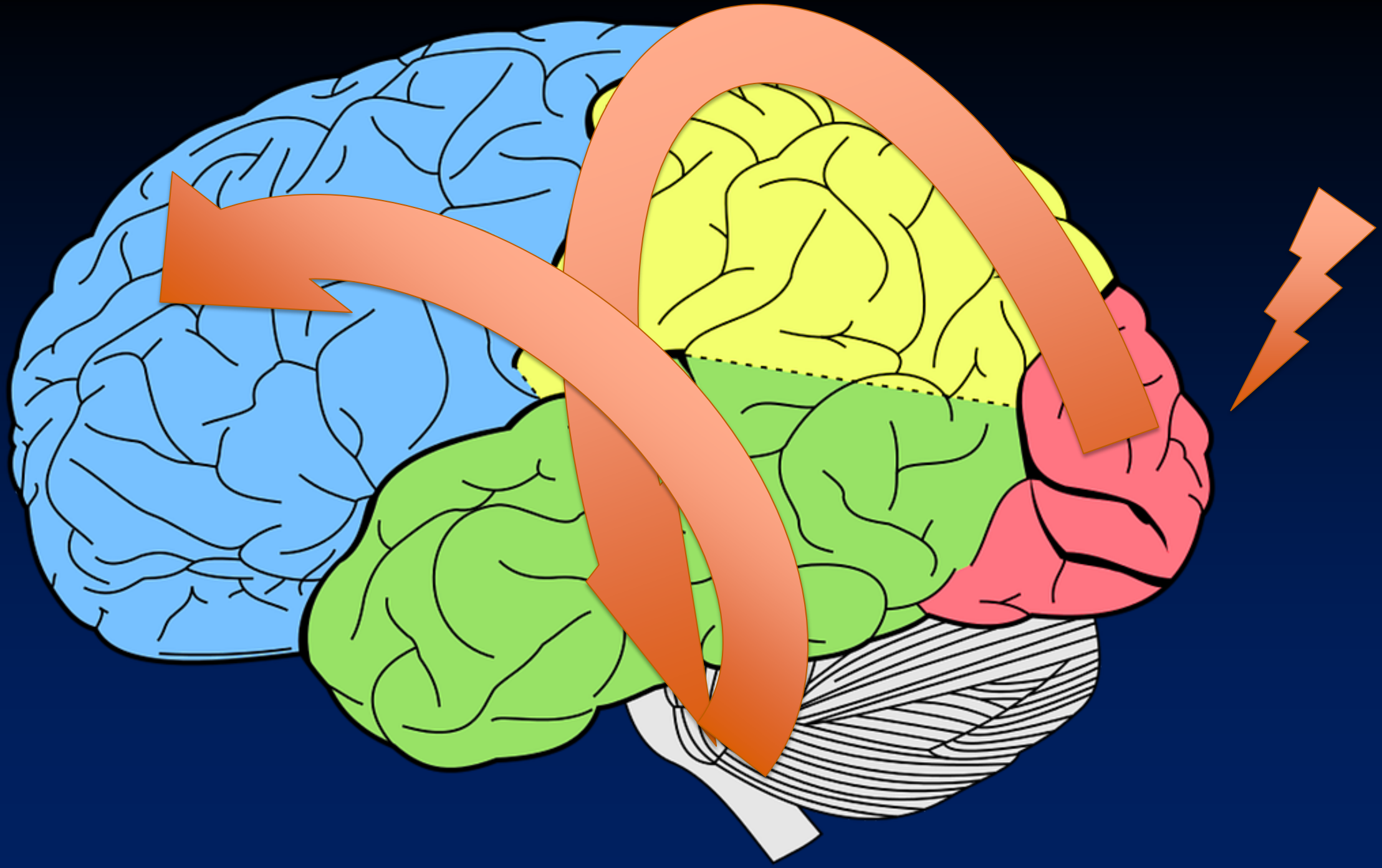


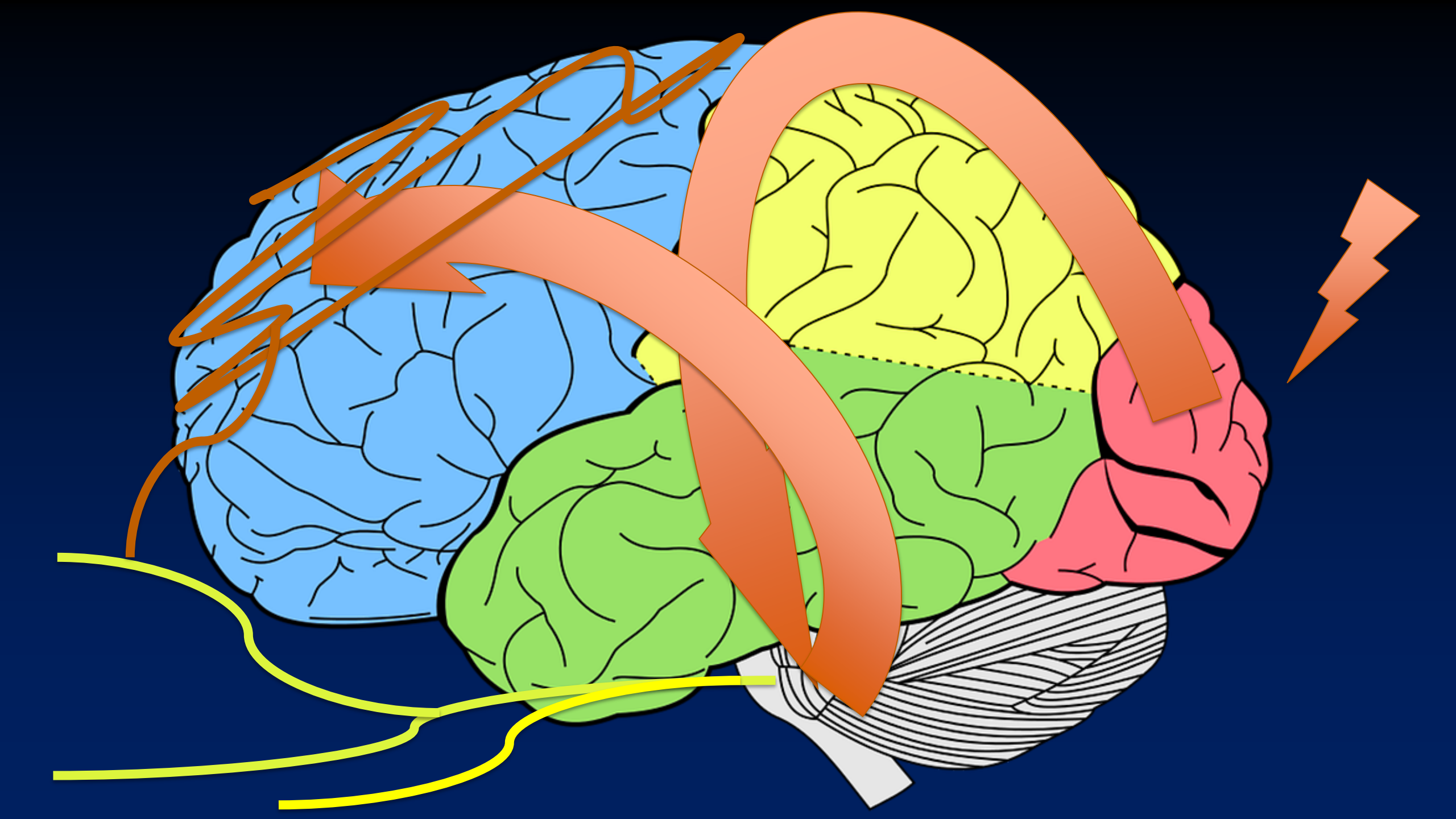

TOUCH
EMOTION AND PERSONALITY
MOVEMENT
SPEECH
SIGHT
SMELL
MEMORY AND LEARNING
BALANCE AND COORDINATION
HEARING











Pathophysiology - CSD

V CN activation → Vasodilation → Neurogenic Inflammation → Pain

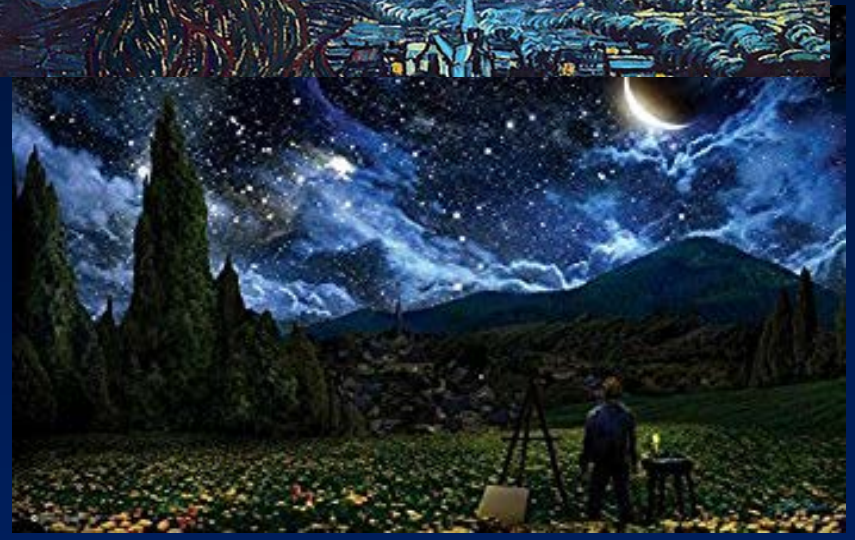
Pathophysiology - CSD

Surface Cortex

Aura

Interior Cortex

No Aura



V CN activation

Vasodilation

Neurogenic Inflammation

Pain

What is the big deal about Aura anyway?

- Researchers presented findings in 2016 that patients who have migraine with aura are 2.4 times more likely to have CVA
- Compared to migraine without aura
- Study lasted 25 years and included nearly 13,000 adults age 45-64

- Androulakis XM, *et al*. Ischemic stroke subtypes and migraine with visual aura in the ARIC study. Neurology. 2016 Dec 13;87(24):2527-2532. Epub 2016 Nov 9.

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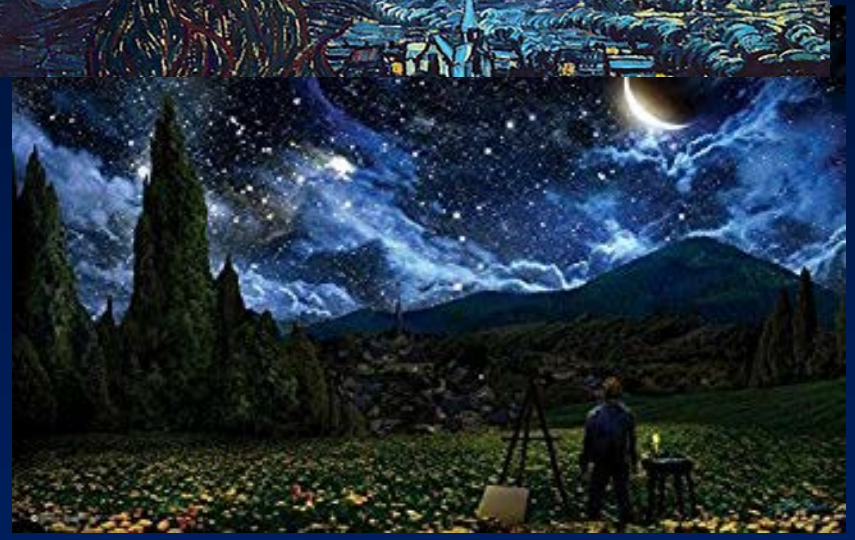

V CN activation

Vasodilation

Neurogenic Inflammation

Pain

V CN activation

- C-fibers
- Activated by K+ and H+ released in the process of CSD
- CGRP and SP release
- Vasodilation
- This understanding sets the stage for new therapies

A few more words about classification

Episodic vs. Chronic

- Over 90 % of patients who suffer from migraine have episodic migraines (fewer than 15 per month)
- Greater than or equal to 15 = chronic

Diagnostic Criteria: Status Migrainousus

- Status Migrainosus

A. A headache attack fulfilling criteria for migraine
B. Unremitting for >72 hours
C. Pain and/or associated symptoms are debilitating

Back to our case…

Case

- ER contacts you to evaluate a patient for a blood patch.
- 22 YO F ASA 2 presents to the ER with 4 day history of worsening headache 2 days prior
- Long standing history of headaches, first occurred in adolescence
- Several ER visits for headache
- 48 hrs. earlier was in the ER for “the worst headache of my life”

Case

- Head CT negative
- Was discharged home with after IV ketoralac and steroid burst
- Now presents again to the ER and has worse headache. “a little worse with standing and walking”
- Hydration and IV caffeine have failed to help
- Describes it as throbbing and rating her pain 10/10
- Would you do a blood patch?

Case

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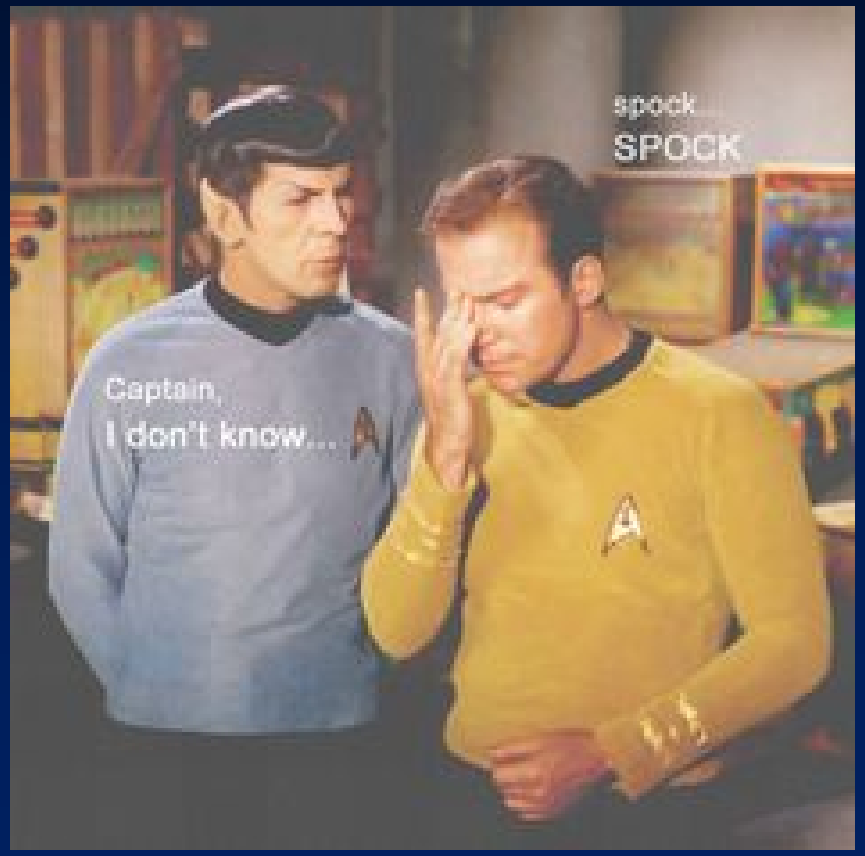
- Now presents again to the ER and has worse headache. “a little worse with standing and walking”
- Hydration and IV caffeine have failed to help
- Describes it as throbbing and rating her pain 10/10
- Would you do a blood patch?
- She fulfills criteria for status migranosus

Migraine: Clinical Diagnosis

- Pulsatile headache of moderate to sever pain
- Typically in one side of the head
- Sensitive to light and sound
- Worse with physical activity
- Associated with N/V
- Status if >72 hrs



Fun Facts…

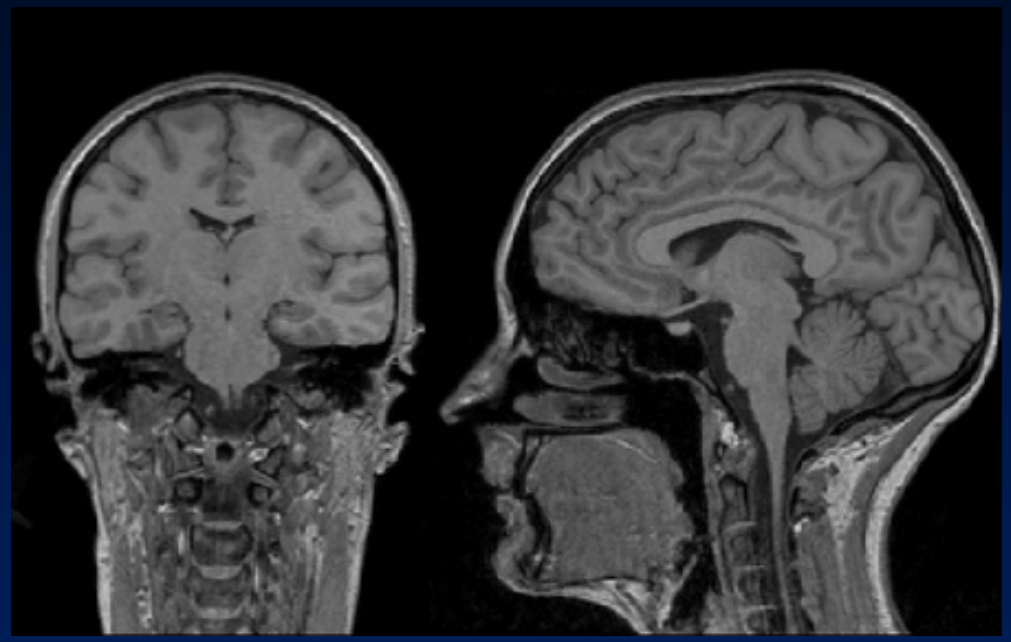
- The most common diagnosis for a patient presenting to the ED with the worst headache ever is…..
- Migraine
- The most common diagnosis for a patient present to the ED with a change in Headache pattern is….
- Migraine
- The most common type of headache is….
- Hangover

Red Flags

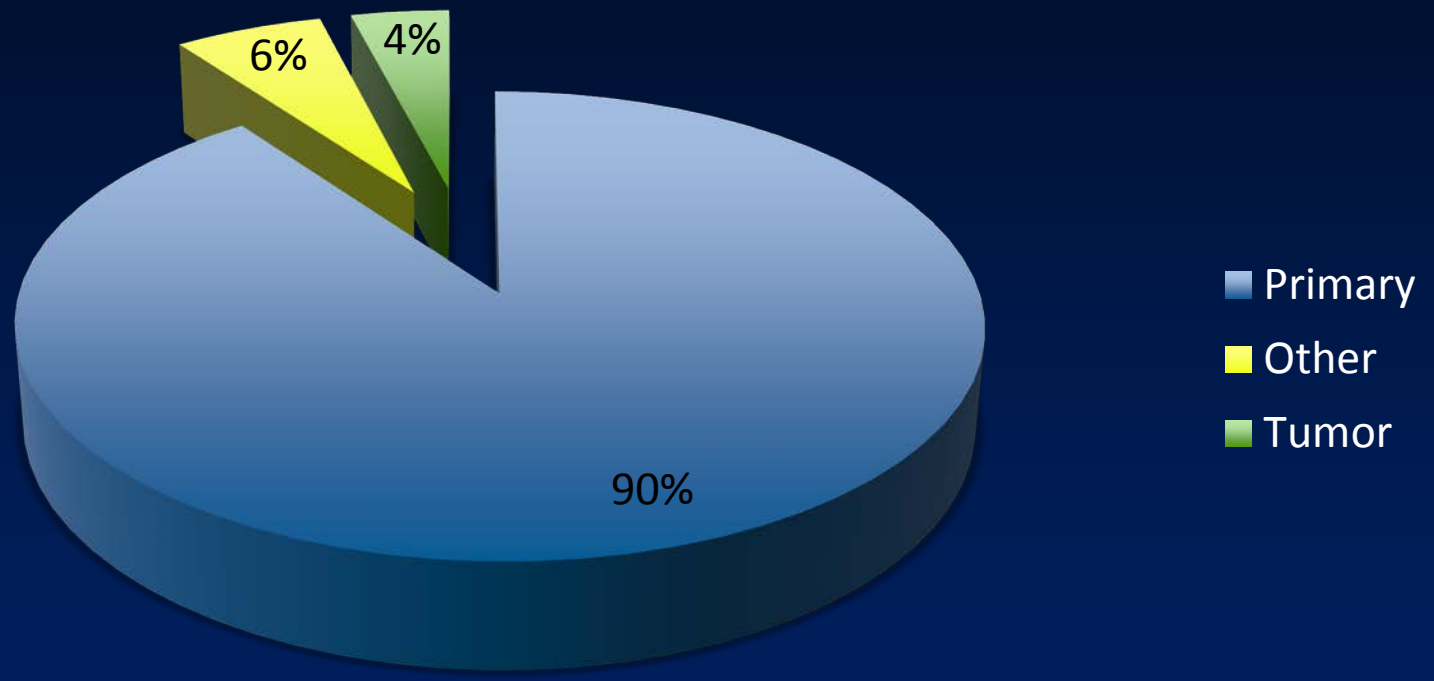
- Systemic: fever, weight loss
- Abnormal Neuro Signs: confusion, rigidity
- New onset at older age
- Headache pattern change
- Abrupt onset, “worst headache”
- Exertional headache pattern

When to Scan

- Abnormal neuro examination
- Headache pattern change
- Refractory headache
- Atypical features (age of onset, etc)
- Prolonged/complicated aura



New onset headache is likely a primary headache



Treatment

Two Strategies

- Abortive
- Prophylactic

Abortive Treatment

- Ergotamine – 1928
  - Nasal spray
  - DHE-45 IV infusions, mainstay of status migraine treatment
- Triptans – early 1990's
  - Sumatriptan (Imitrex) PO, SQ, NS, TD
  - Sumatriptan/Naproxen (Treximet)
  - Zolmitriptan (Zomig) PO, NS
  - Rizatriptan (Maxalt) PO, ODT
  - Naratriptan (Amerge)
  - Amotriptan (Axert)
  - Frovatriptan (Frova)
  - Eletriptan (Relpax)

Contraindications

- Poorly controlled HTN
- Severe hepatic or renal impairment
- Hx basilar migraine
- Hx. Of hemiplegic migraine
- CAD, untreated
- MAO inhibitor use
- Avoid during pregnancy

Considerations

- Should not be used within 24 hrs. post ergotamine-containing medication use
- Treatment should be limited to 2 does per day (at least 2 hrs. apart) and no more then 2 days per week.

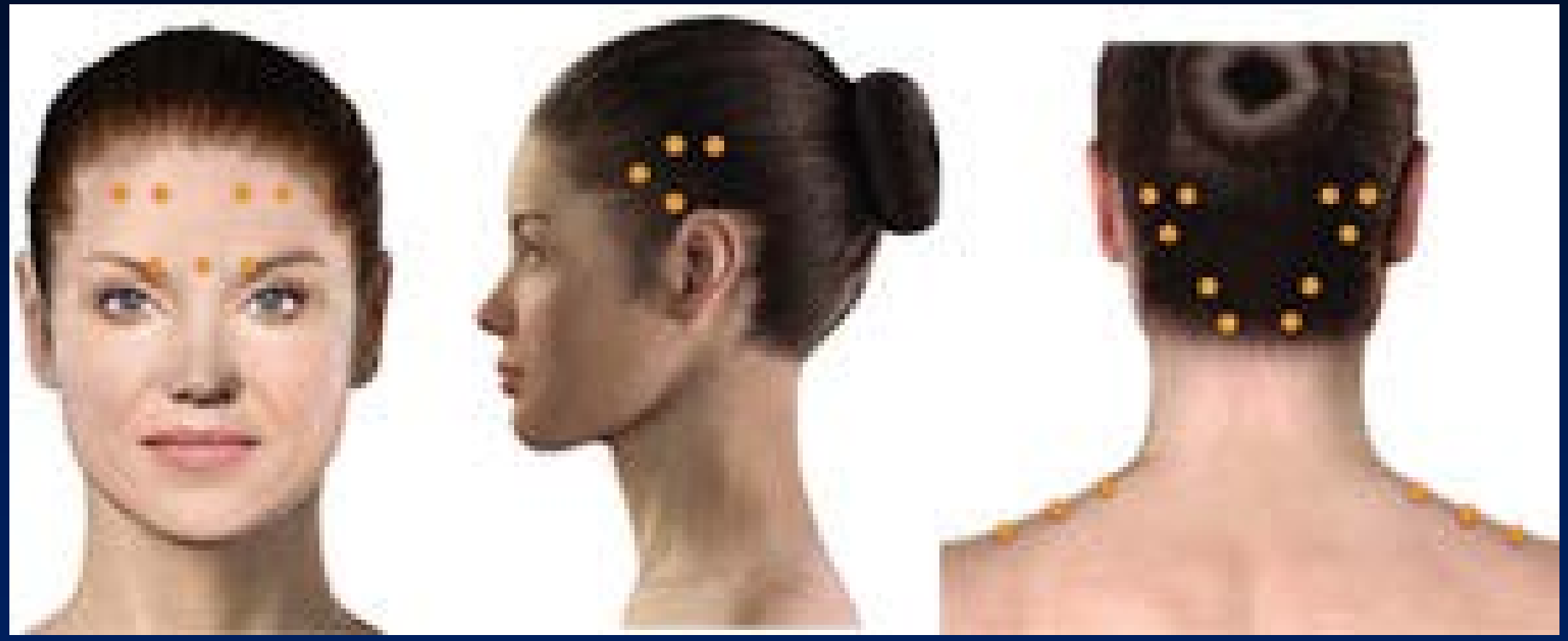
Prophylactic Treatment

- Response may take 2-4 weeks
- Beta blockers (propranolol 120-240 mg/day)
- Ca-channel blockers (verapamil 180-360 mg/day)
- Anticonvulsants (topiramate 100-200 mg, divalproex sodium 500-1000 mg)
- Antidepressants (TCA, SNRI, MAOI: amitriptyline 25-100 mg, duloxetine 30-60 mg, phenelzine 30-45 mg)

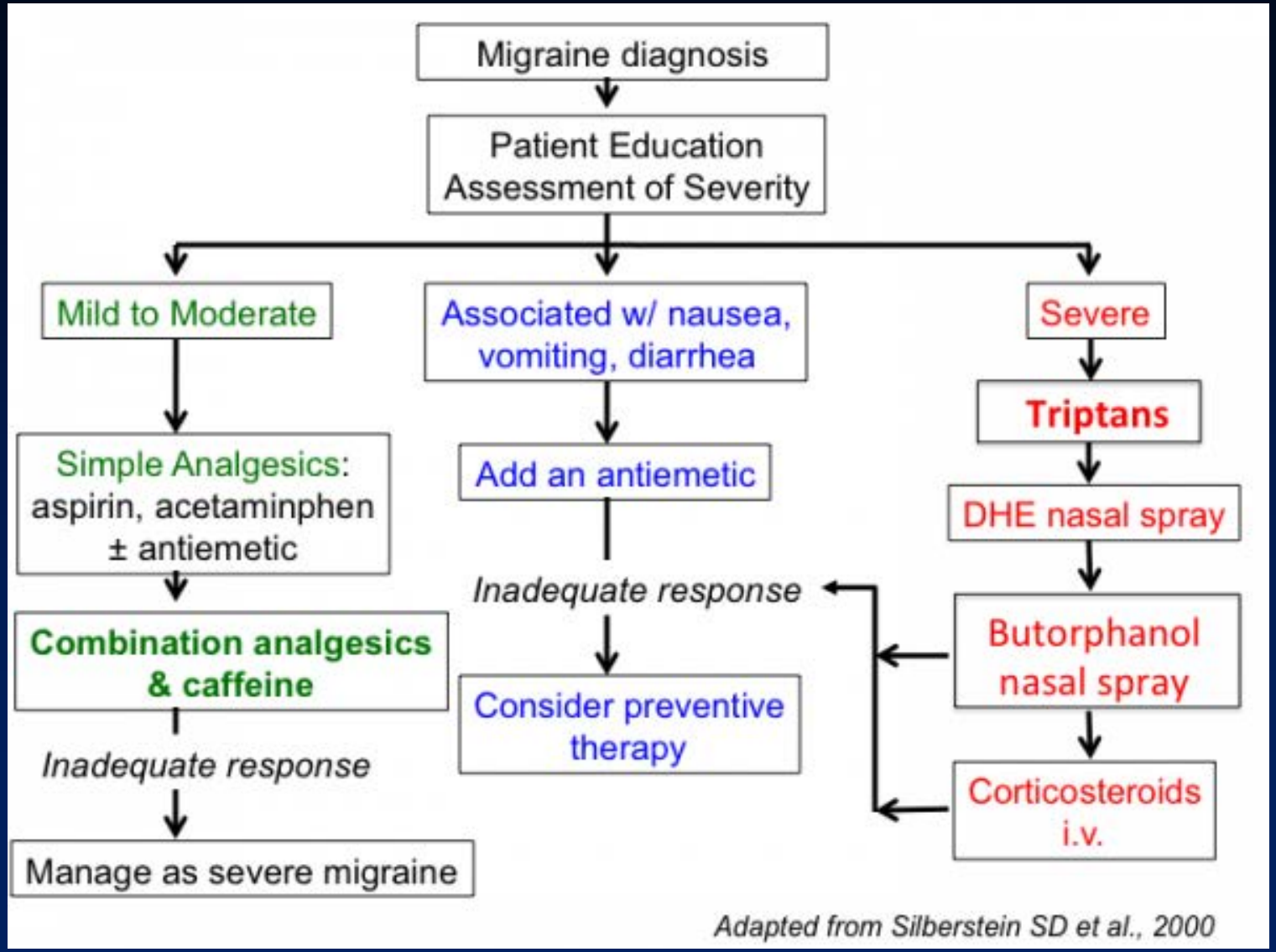
Prophylactic

- Botulism toxin-A (Botox)

31 injections



Treatment


Migraine diagnosis
Patient Education
Assessment of Severity
Mild to Moderate
Associated w/ nausea, vomiting, diarrhea
Severe
Simple Analgesics: aspirin, acetaminphen ± antiemetic
Add an antiemetic
Triptans
DHE nasal spray
Inadequate response
Combination analgesics & caffeine
Butorphanol nasal spray
Consider preventive therapy
Inadequate response
Corticosteroids i.v.
Manage as severe migraine
Adapted from Silberstein SD et al., 2000

New Developments in Treatment

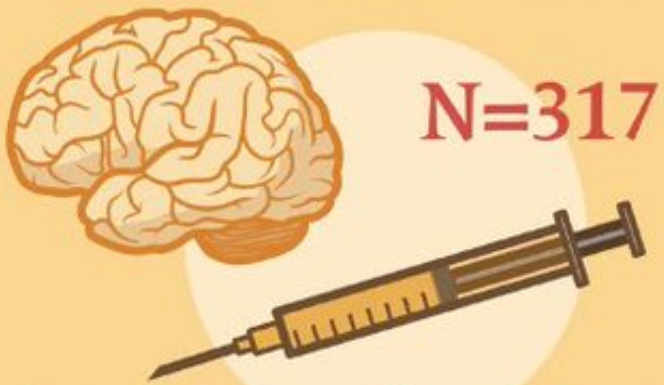
erenumab

- An anti CGRP monoclonal antibody, targets CGRP receptor
- STRIVE trial (2017) tested injections as preventive for episodic migraines in 955 patients across 121 clinical sites
- Six month trial

  – Goadsby *et al* N Engl J Med 2017; 377:2123-2132

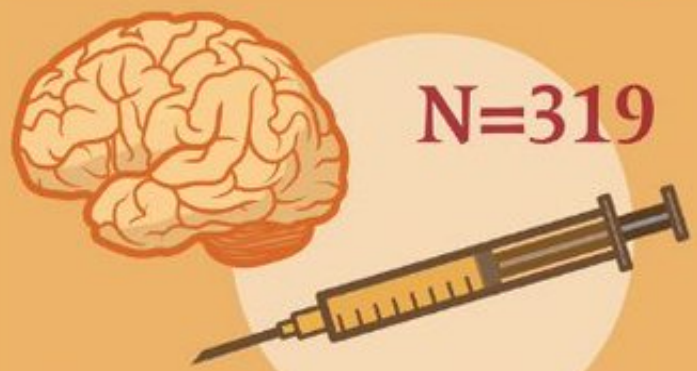
A Controlled Trial of Erenumab for Episodic Migraine

MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PHASE 3 TRIAL



N=317

Erenumab, 70 mg



N=319

Erenumab, 140 mg

N=319

Placebo

Reduction in mean migraine days/mo (baseline to months 4–6)

3.2 days

3.7 days

1.8 days

Either treatment vs. placebo, P < 0.001

≥50% Reduction in mean migraine days/mo

43.3% of patients

50.0% of patients

26.6% of patients

The NEW ENGLAND JOURNAL of MEDICINE

Goadsby et al. 2017

fremanezumab

- Targets CGRP molecule itself
- Tested in mid 2017 on 1,130 chronic migraine patients
- When injected quarterly for 12 weeks, headache reduced from 13.2 days to 8.9

– Silberstein *et al.* N Engl J Med 2017; 377:2113-2122

The devil is always in the details…

- Estimated cost
- At least $8500/year

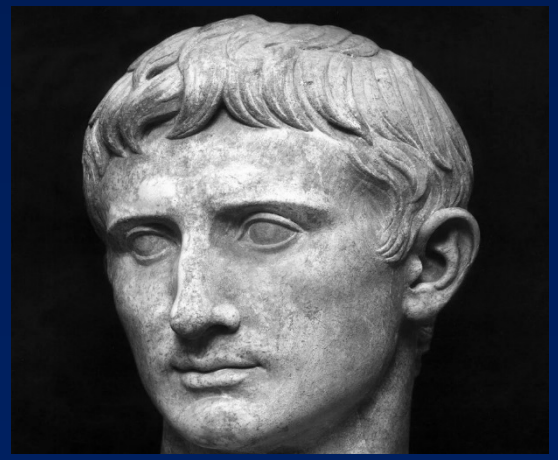
Non Pharmacological Treatment

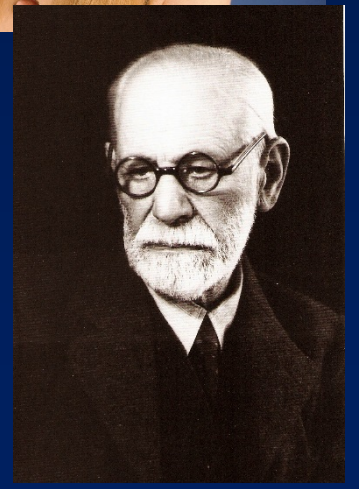
- Avoid Triggers
- Diet (low tyramine, low caffeine)
- Regular Meal Pattern
- Regular Sleep Pattern
- Biofeedback
- Stress management and psychotherapy

Interventional Options

- Occipital Nerve Blocks
- Sphenocath
- Medial Branch denervation for cervicogenic headache

If you have migraines, you are in good company…





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