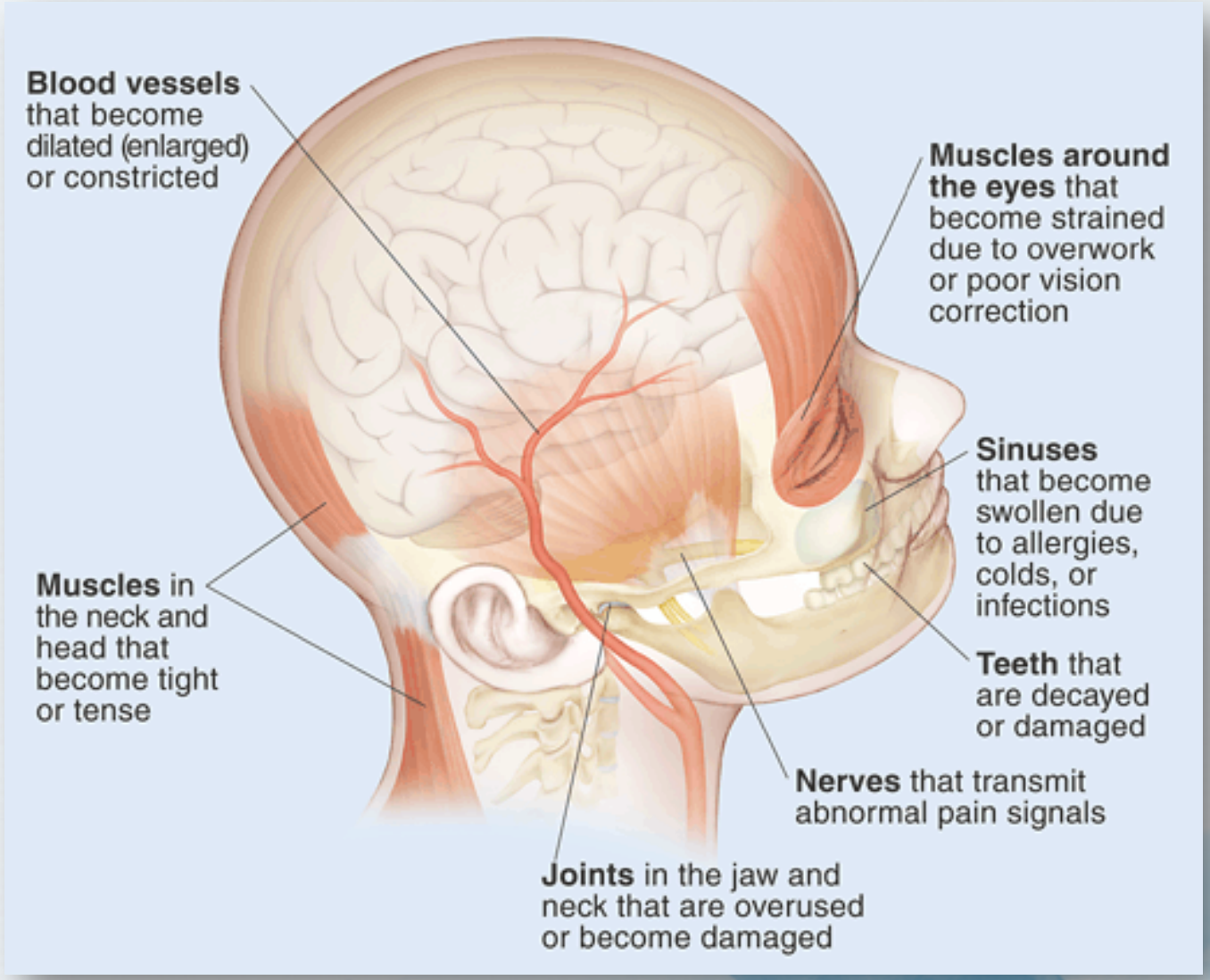
# PATHOPHYSIOLOGY

# Structures Related with Headache



# Primary vs. Secondary Headache

**Primary Headache**

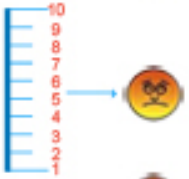
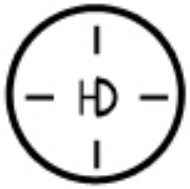
Not a symptom of or caused by another disease or condition

**Secondary Headache**

A symptom of or caused by an underlying disease or condition, such as tumor or infection

Mayo Clinic. Headache causes – symptoms. Available at: http://www.mayoclinic.org/symptoms/headache/basics/causes/sym-20050800. Accessed 15 January 2015.

## PRIMARY HEADACHE

| Type of Headache | Pain Location | Quality of Pain | Pain Severity | Duration | Unique Features |
|---|---|---|---|---|---|
| Tension type Headache |  |  |  |  | No other Symptoms except for band-like tightness or presure pain caused by muscle contractions of head & neck. |
| Sinus Headache |  |  |  |  | Bad-braeathe, Nasal discharge almost always preceded by cold, respiratory infections and allergies. |
| Migraine |  |  |  |  | neurological dysfunction nausea, photophoba, phonophobia, parasthesions, disorientation, mental cloudiness and "TRIGGERS". |
| Cluster Headache |  |  |  |  | Eyeredress/tearing congested & Runny nose. |

# Causes of Primary Headaches

- No underlying disease is responsible for the symptoms
- Caused by problems with or over-activity of pain structures in the brain
- Some primary headaches can be triggered by lifestyle factors:
- Alcohol – especially red wine
- Certain foods (*e.g.*, processed meats containing nitrates)
- Changes in sleep or lack of sleep
- Poor posture
- Skipped meals
- Stress

Mayo Clinic. Headache causes – symptoms. Available at: http://www.mayoclinic.org/symptoms/headache/basics/causes/sym-20050800. Accessed 15 January 2015.

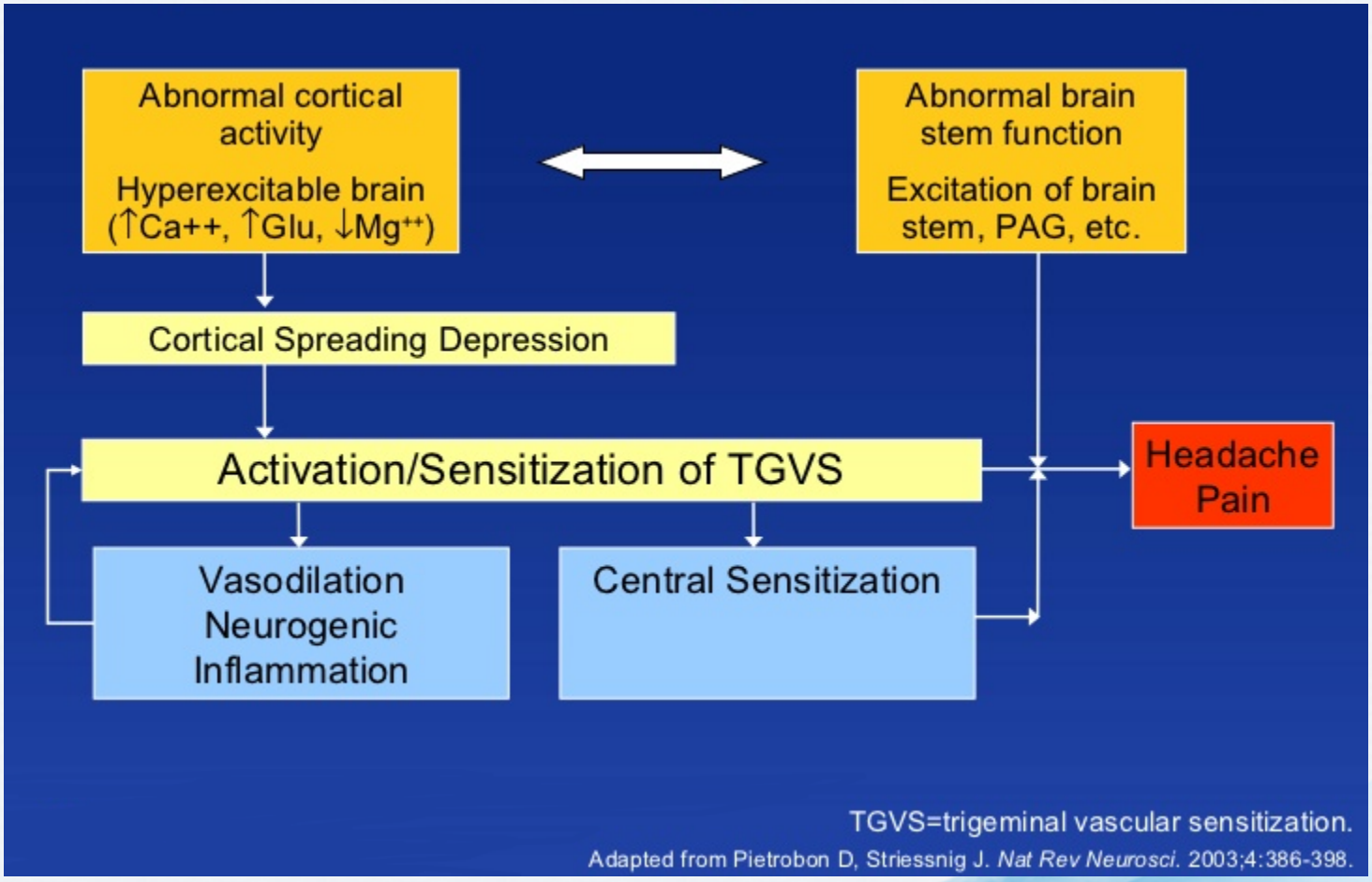
# Causes of Secondary Headaches

- Acute sinusitis
- Arterial tears
- Blood clot in the brain (non-stroke)
- Brain aneurysm
- Brain arteriovenous malformation
- Carbon monoxide poisoning
- Chiari malformation
- Concussion
- Dehydration
- Dental problems
- Ear infection (middle ear)
- Encephalitis
- Giant cell arteritis
- Glaucoma
- Hangovers
- Influenza
- Intracranial hematoma
- Medications to treat other disorders
- Meningitis
- Monosodium glutamate
- Overuse of pain medication
- Panic attacks
- Post-concussion syndrome
- Pressure from tight-fitting headgear
- Pseudotumor cerebri
- Toxoplasmosis
- Trigeminal neuralgia

**A wide range of possible causes with varying severity**

Mayo Clinic. Headache causes – symptoms. Available at: http://www.mayoclinic.org/symptoms/headache/basics/causes/sym-20050800. Accessed 15 January 2015.

# Proposed Mechanisms of Migraine



# Migraine Mechanisms

- Trigeminal vascular system serves as a common pathway for migraine with and without aura
- How migraine pain is triggered and the cascade of events following original activation are not completely understood
- Connection between cortical spreading depression (CSD) and activation of trigeminal nerve afferents
  - Activation of trigeminal nerve → a series of meningeal and brainstem events consistent with what is observed during a migraine attack
  - Triggering CSD →long-lasting blood flow increase in middle meningeal artery
  - Increased blood flow depends on trigeminal and parasympathetic activation

1. American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

# Migraine Mechanisms

- Bidirectional conduction along trigeminal nerve sensitizes surround nerve fibers
  - Conveys painful stimuli to trigeminal nucleus caudalis in brainstem for transmission to higher centers
  - Leads to the throbbing pain, nausea, photophobia, and phonophobia that characterize migraine

1. American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

# Migraine and Sensitization

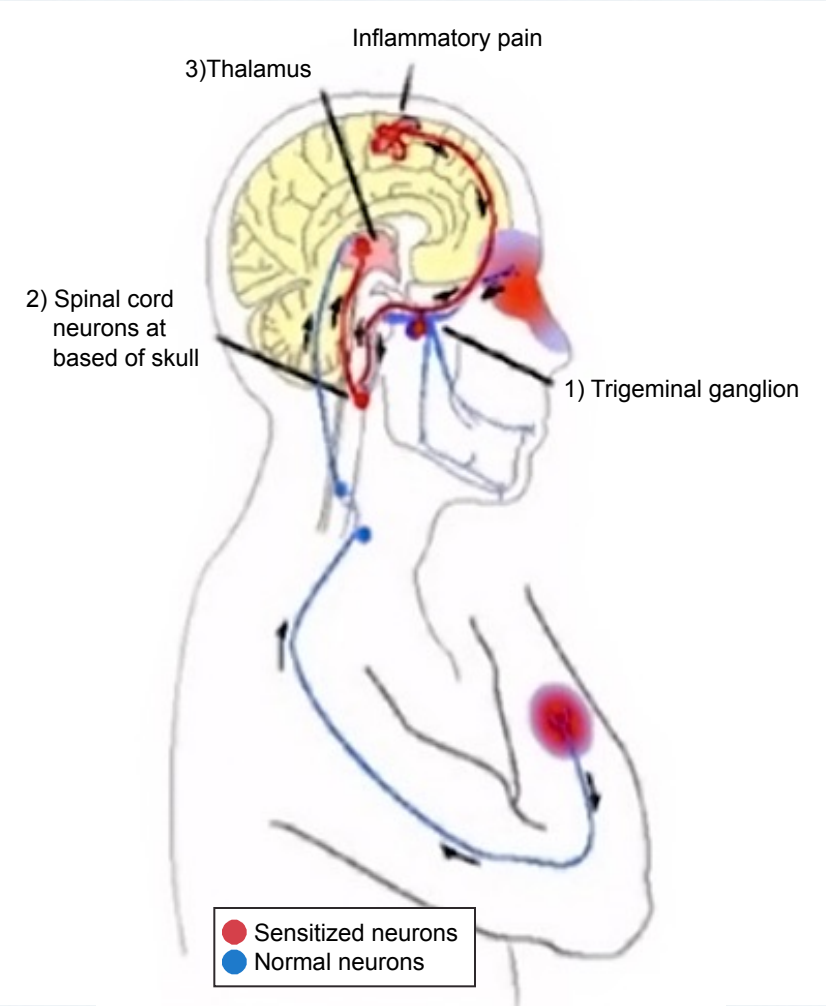
- Patients often report increased sensory sensitivity during a migraine attack

- Symptoms may be regulated by central or peripheral mechanisms
  - Peripheral sensitization → throbbing, exacerbation of pain with movement
  - Central sensitization → cutaneous allodynia (increased sensitivity to touch)

**Not all patients have central sensitization but most patients have peripheral sensitization**

1. American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

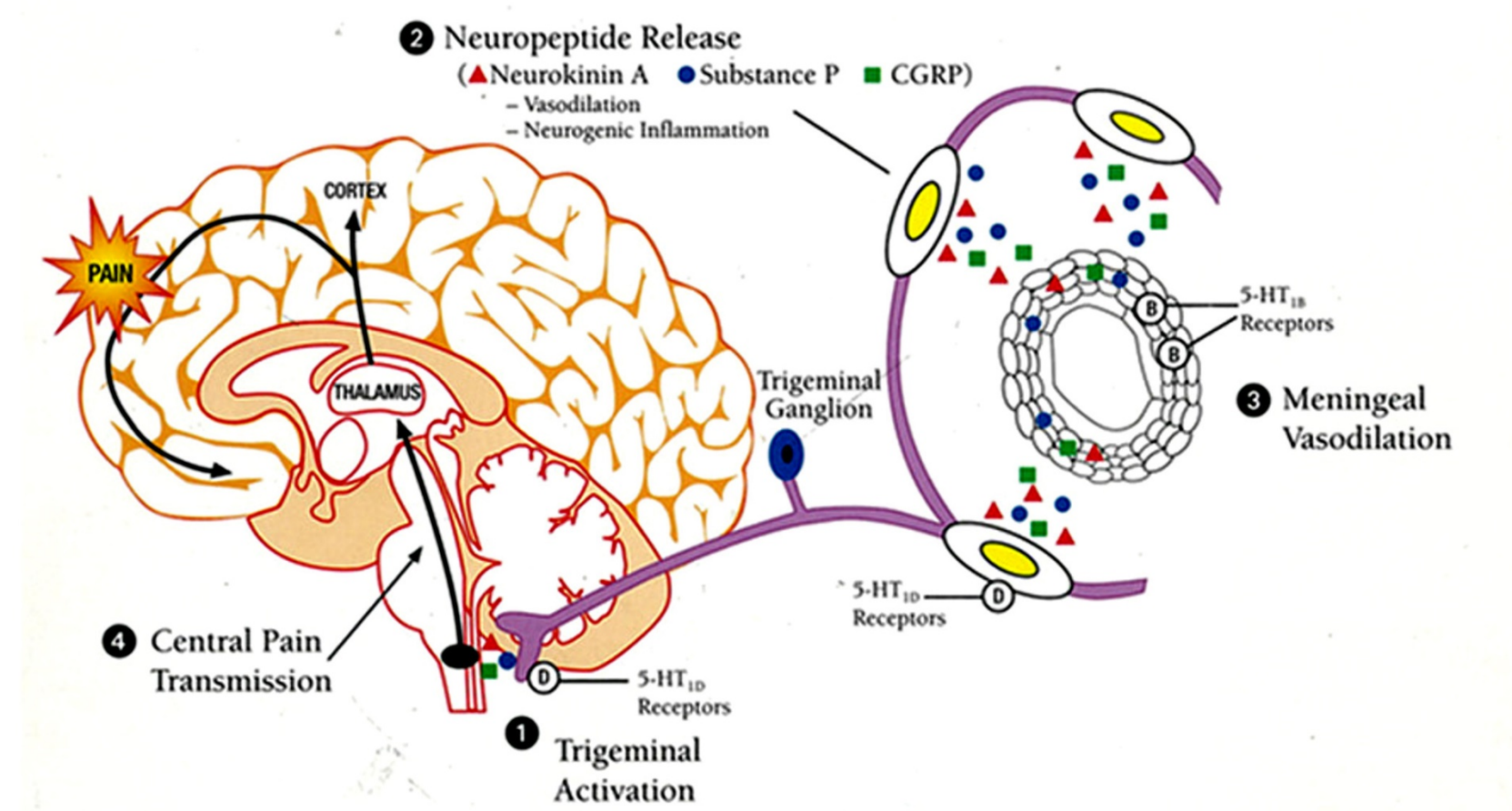
# Central Sensitization in Migraine




- Migrateurs develop increased to stimuli due to increased excitability
- About 2/3 of migraine patients suffered from *cutaneous allodynia* during attacks due to central sensitization

Burstein R et al. *Ann Neurol.* 2000;47:614-624; Burstein R et al. *Headache.* 2002; 42:390-391

# The Process of Migraine Pain



# Migraine Aura

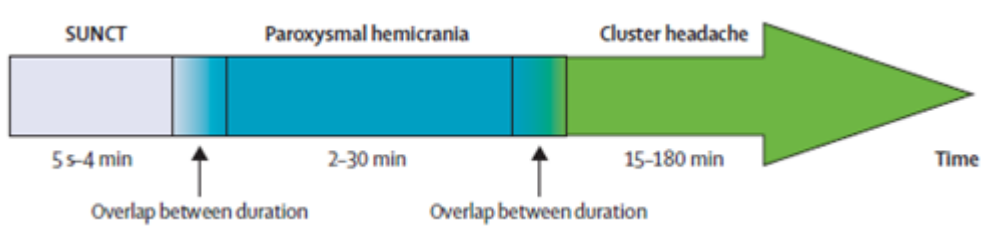
**Only 15% of patients with migraine experience aura**

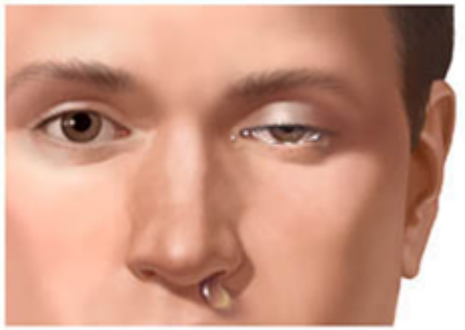
- Rate of expansion calculated at ~3-6 mm/min
- Initial hyperemia is followed by oligemia, which spreads from the occipital cortex at a rate of 2 to 6 mm/min
- Headache usually starts while cerebral blood flow is diminished

Lashley KS. *ArchNeurol Psych.* 1941;46:331-9; Lauritzen M. *Brain.* 1994;117(Pt 1):199-210; Olesen J *et al. Ann Neurol.* 1990;28(6):791-8; Woods RP *et al. N Engl J Med.* 1994;331(25):1689-92.

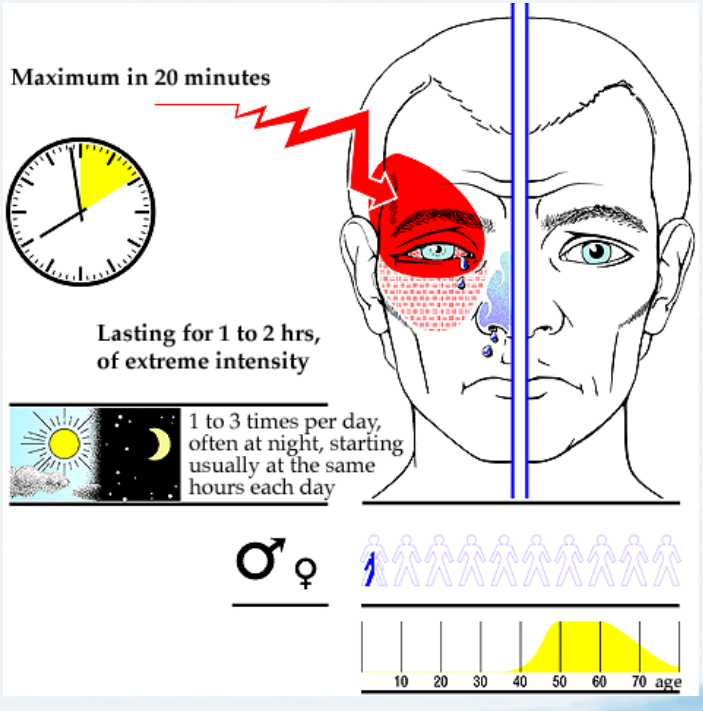
# Trigeminal Autonomic Cephalgias (TACs)

## Overlap between attack duration in TACs



Watery eye, drooping eyelid, runny nose



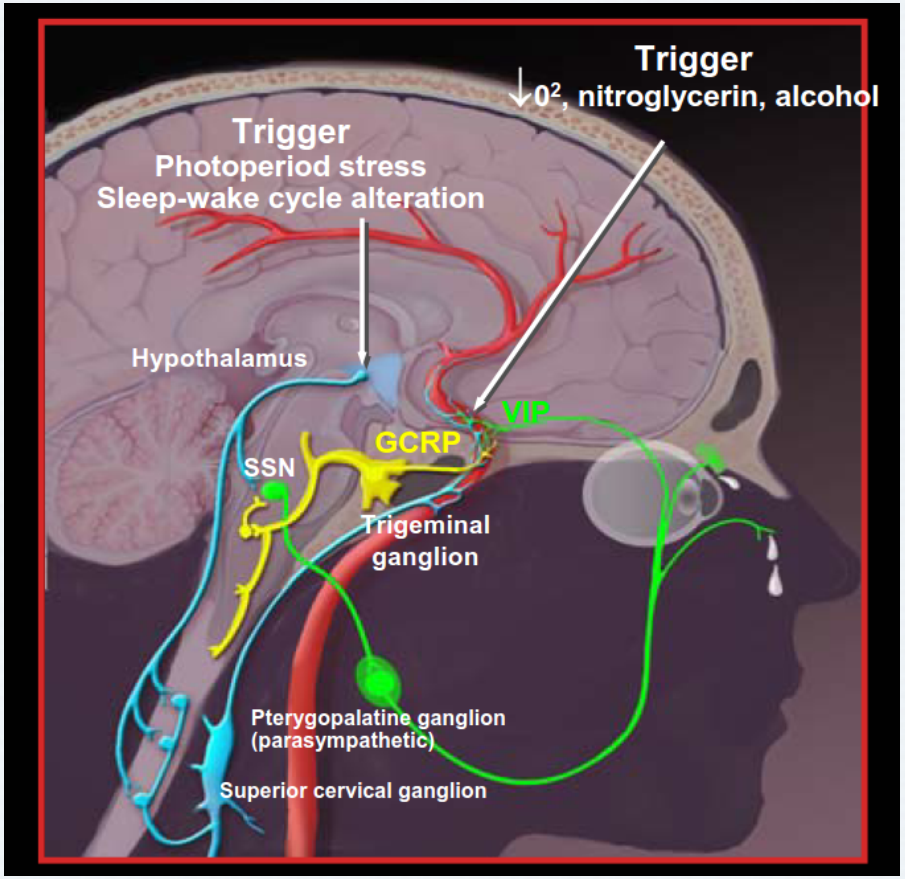

SUNCT = short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing

# Cluster Headaches (Trigeminal Autonomic Cephalalgias)

- Attacks of severe, strictly unilateral pain that is orbital, supraorbital, temporal, or any combination of these
- Duration: 15 minutes to 3 hours
- Frequency: one every other day to eight times/day
- Associated symptoms:
  - Ipsilateral conjunctival injection
  - Lacrimation
  - Nasal congestion
  - Rhinorrhea
  - Forehead and facial sweating
  - Miosis
  - Ptosis and/or eyelid edema
  - Restlessness/agitation

Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia.* 2013;33(9):629-808.

# Pathogenesis of Cluster Headaches (Trigeminal Autonomic Cephalalgias)

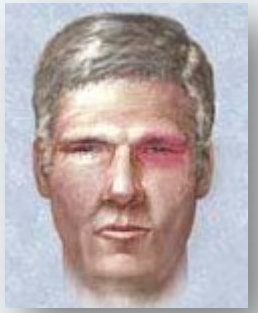



**A unifying pathophysiologic explanation of cluster headache is not yet available**

Edvinsson L, Goadsby PJ. *Eur J Neurol*. 1998;5:329-451.

# Pathophysiology of Cluster Headaches

- May involve an autosomal dominant gene
- Carotid and ophthalmic artery vasodilation and an increased sensitivity to vasodilator stimuli during an attack may be triggered by trigeminal parasympathetic reflexes
- May involve autonomic function abnormality with increased parasympathetic drive and decreased sympathetic function



- May be a disorder of circadian rhythm: attacks often begin during sleep
- Reduced oxygenation may trigger attacks
    - Increased prevalence of sleep apnea in patients with cluster headaches

Beck E *et al. Am Fam Physician.* 2005;71(4):717-24.

# Tension-Type Headache

- Depression
- Anxiety
- Stress
- Noise
- Alcohol
- Medications

- Transient stabbing pain
- Episodic
- Chronic

**Persistent, variably severe headache**

# Tension-Type Headache (TTH)

- Very common: lifetime prevalence 30 to 78%
- Four subtypes:
  - Infrequent episodic
  - Frequent episodic
  - Chronic
  - Probable
- Increased pericranial tenderness with manual palpation
  - Typically interictal, further increased during actual headache, and increases with intensity and frequency of headaches

**It can be difficult to discriminate between TTH and migraine without aura**

**Patients with frequent headaches often suffer from both disorders**

Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia.* 2013;33(9):629-808.

# Pathophysiology of Tension-Type Headache (TTH)

- Complex and multifactorial pathology with contributions from central and peripheral factors[2]
- May be due to abnormal neuronal sensitivity and pain facilitation – not abnormal muscle contraction
- Associated with exteroceptive suppression, abnormal platelet serotonin, and decreased cerebrospinal fluid beta-endorphin
- Extracranial myofascial nociception and hypersensitivity of neurons in the trigeminal nucleus caudalis may play a role
- May involve central sensitization at spinal dorsal horn/ trigeminal nucleus due to prolonged nociceptive inputs from pericranial myofascial tissues

Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia.* 2013;33(9):629-808; Singh MK. Muscle contraction tension headache. Available at: http://emedicine.medscape.com/article/1142908-overview. Accessed 15 January 2015.

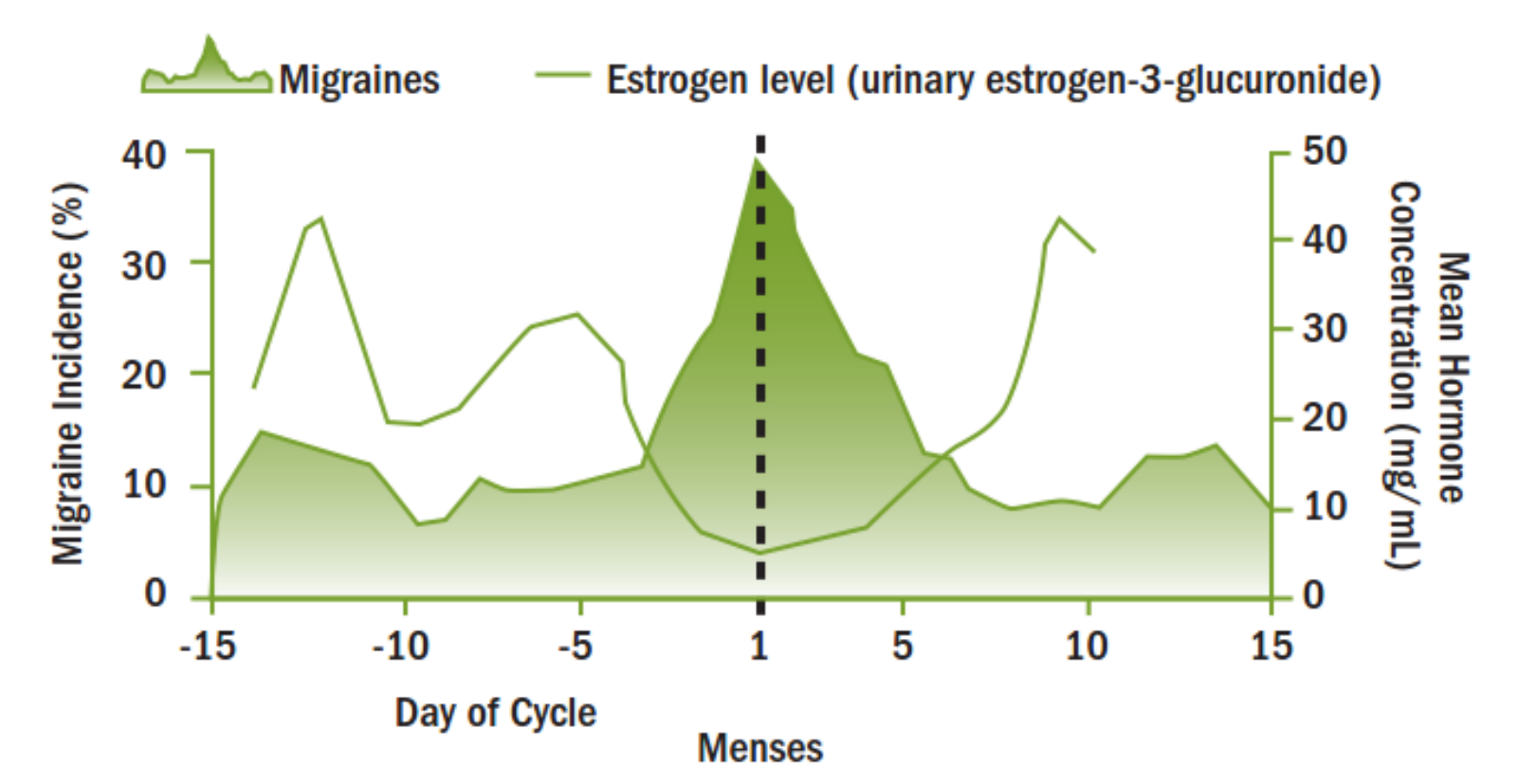
# Menstrual Migraine

- ~60% of female migraine sufferers have menstrual migraines
- Reduced estrogen at menstruation can trigger migraine in many women
- May be more persistent, painful, and resistant to treatment than migraines that occur at other times
- ICHD criteria: Migraine without aura occurring between 2 days prior and 3 days after the onset of menses and in 2 of 3 menstrual cycles
  - Some women experience migraine perimenstrually
- Headache diary should be used to record timing of menstrual migraines

ICHD = International Classification of Headache Disorders

Menstrual migraine: breaking the cycle. Available at: http://practicingclinicians.com/cms/wb/PCEv3/site/hs09_pdfs/migraine.pdf. Accessed 14 December, 2014.

# Estrogen Levels and Menstrual Migraine




Menstrual migraine: breaking the cycle. Available at: http://practicingclinicians.com/cms/wb/PCEv3/site/hs09_pdfs/migraine.pdf. Accessed 14 December, 2014.

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Headache Classification Committee of the International Headache Society (IHS). (2013). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia: An International Journal of Headache*, *33*(9), 629–808. http://doi.org/10.1177/0333102413485658

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Menstrual Migraine: Breaking the Cycle. (n.d.). Retrieved June 18, 2015, from http://practicingclinicians.com/cms/wb/PCEv3/site/hs09_pdfs/migraine.pdf

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Singh, M. (2015). Muscle Contraction Tension Headache: Background, Pathophysiology, Epidemiology. Retrieved from http://emedicine.medscape.com/article/1142908-overview

Woods, R. P., Iacoboni, M., & Mazziotta, J. C. (1994). Brief report: bilateral spreading cerebral hypoperfusion during spontaneous migraine headache. *The New England Journal of Medicine*, *331*(25), 1689–1692. http://doi.org/10.1056/NEJM199412223312505