HEADACHE

Headache syndromes

Headache

Is is pain in any region of the head. Its the commonest disorders of the nervous system.

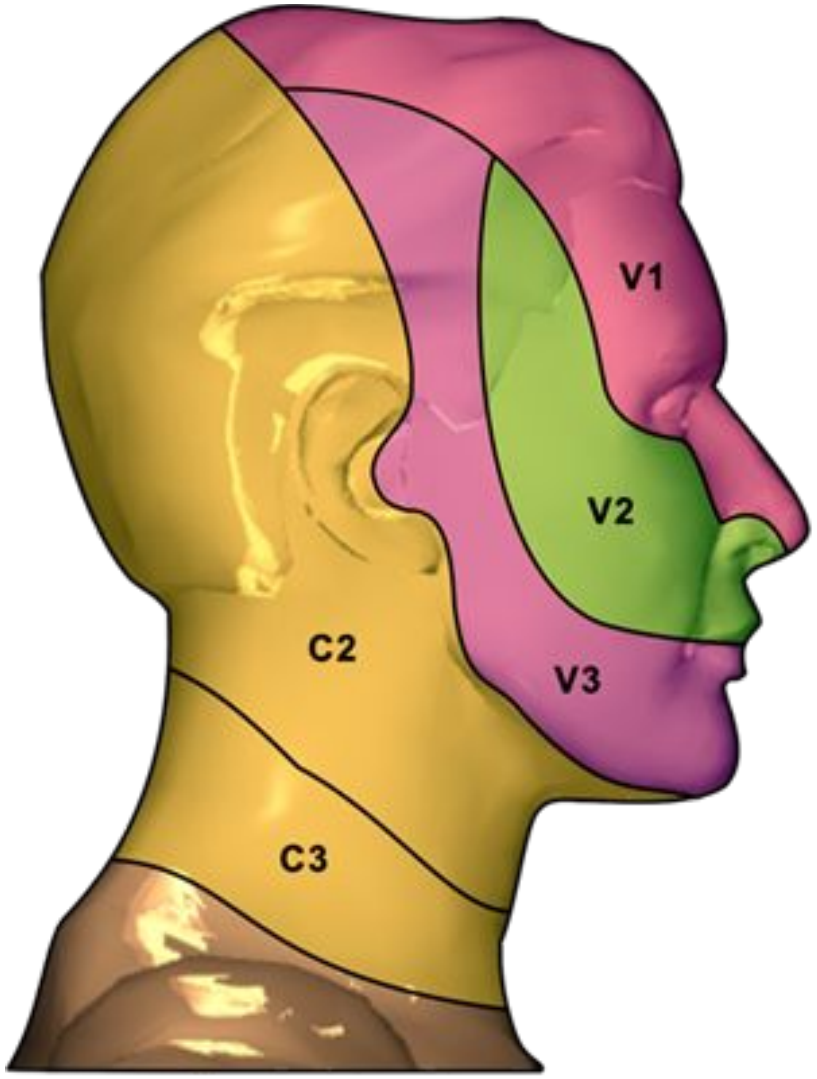
It has been estimated that almost half of the adult population have had a headache at least once within the last year.

Chronic headache (present in > 15 days / month) affects 1.7– 4% of the adult population.

Headache syndromes (disorders) are characterized by

- Recurrent or chronic
- Affect quality of life
- Affects work performance.

Headache



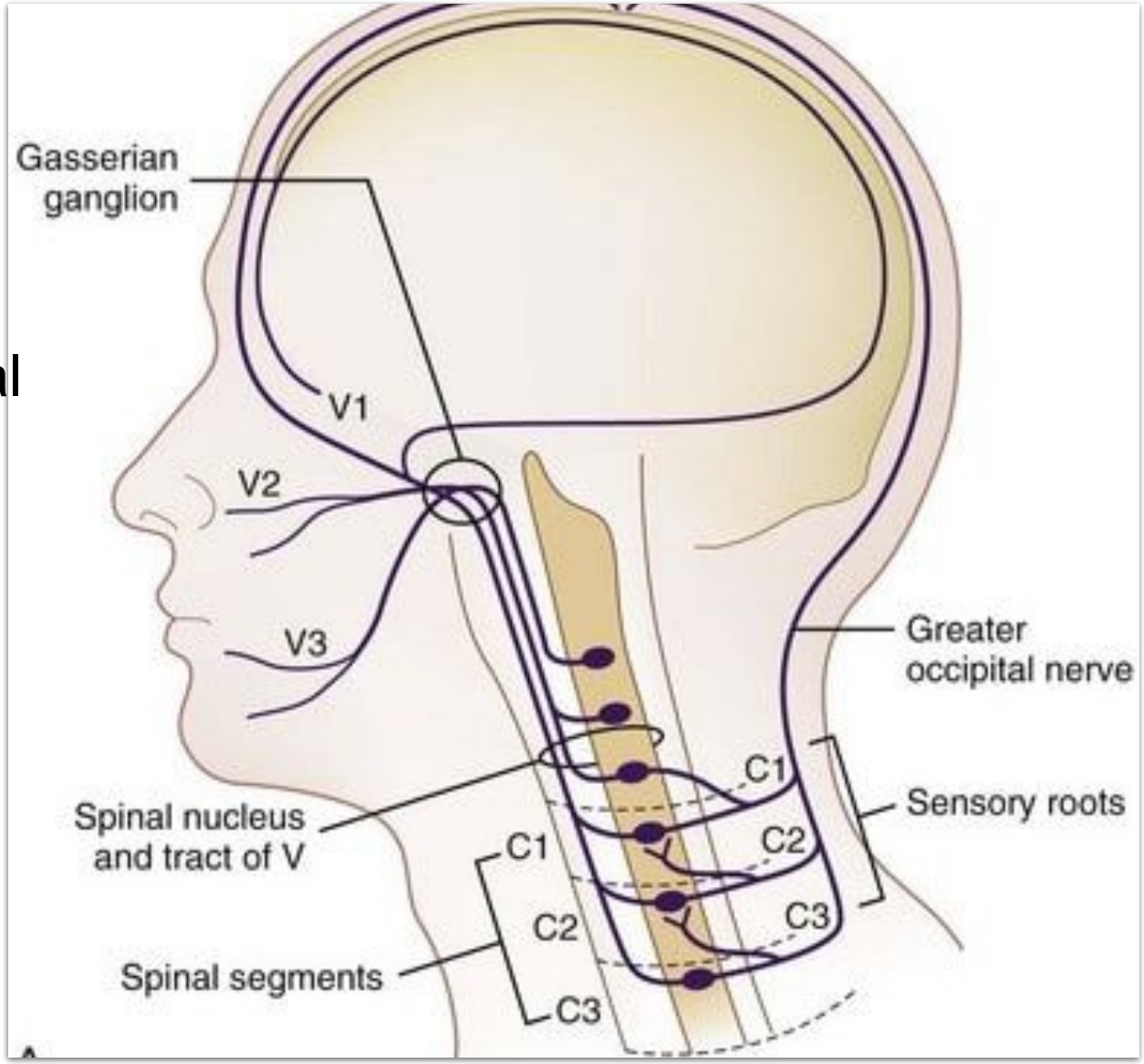
V1 - Ophthalmic Division of Trigeminal Nerve (Upper Face)
V2 - Maxillary Division of Trigeminal Nerve (Mid Face)
V3 - Mandibular Division of Trigeminal Nerve (Lower Face)

Upper Body Quarter

C2 - Occipital Protuberance
C3 - Supraclavicular Fossa

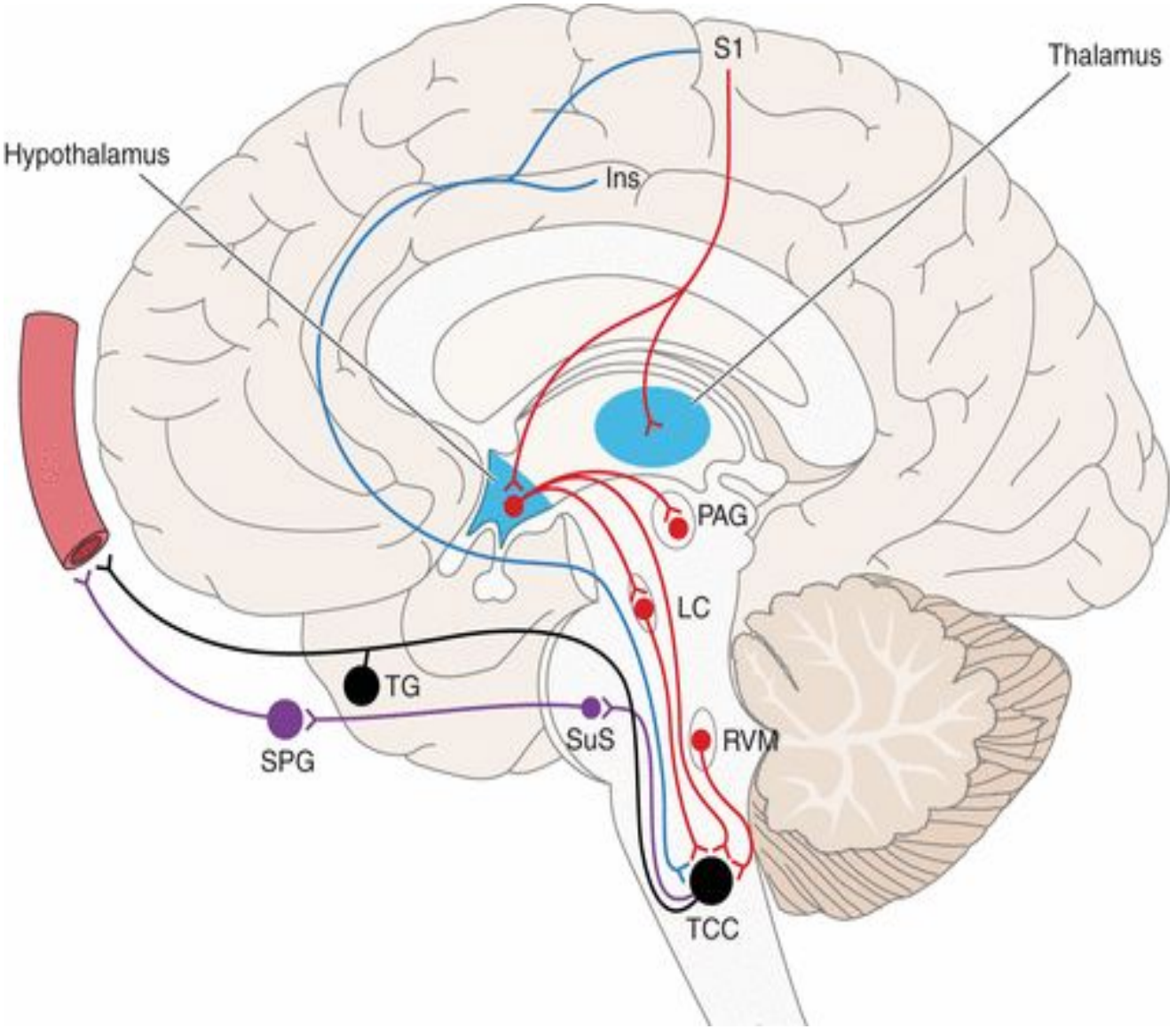
Headache

Trigeminocervical complex



Headache

Trigeminocervical complex modulation



Common causes of headache

Primary headache

Not resulting from medical condition

- Tension-type 69%
- Migraine 16%
- Idiopathic stabbing 2%
- Exertional 1%
- Cluster 0.1%

Secondary headache

Due to an underlying medical condition

- Systemic infection 63%
- Head injury 4%
- Vascular disorders 1%
- SAH <1%
- Brain tumor & ↑ICP 0.1%
- Referred pain

Red Flags for Secondary Headache Disorders

1. Systemic symptoms including fever
2. New headache with cancer, immunosuppression, or pregnancy
3. Neurologic deficit & Papilledema
4. Sudden or abrupt onset
5. First or worst headache
6. Onset after 65 years
7. Positional headache
8. Precipitated by sneezing, coughing, or exercise, Valsalva maneuver, or sex
9. Progressive headache and atypical presentations
10. Painful eye and autonomic features
11. Posttraumatic onset of headache

Migraine

Is a common episodic neurological disorder characterized by recurrent attacks of throbbing headache, most often unilateral and associated by nausea, phonophobia, and photophobia. In 1/5 is preceded by visual or sensory symptoms (aura).

Migraine is most common in women usually appears before middle age and has a strong genetic component.

At some point in life its affects

- 18% of females
- 6% of males

Chronic migraine (headache ≥15 days / month) affect

- 2% population

Etiology

Migraine may be due to the interplay of host susceptibility (frequently positive family history) and various triggers.

Migraine genes identified in hemiplegic migraine reveal involvement of calcium voltage gated channel.

Nitric oxide and calcitonin gene-related peptide are important mediators, and estrogen seems to ‘‘ramp up’’ the system according to the evidences :

- ✔ Female dominance
- ✔ Frequent attacks at certain time in the menstrual cycle
- ✔ Estrogen-containing oral contraception sometimes exacerbates migraine

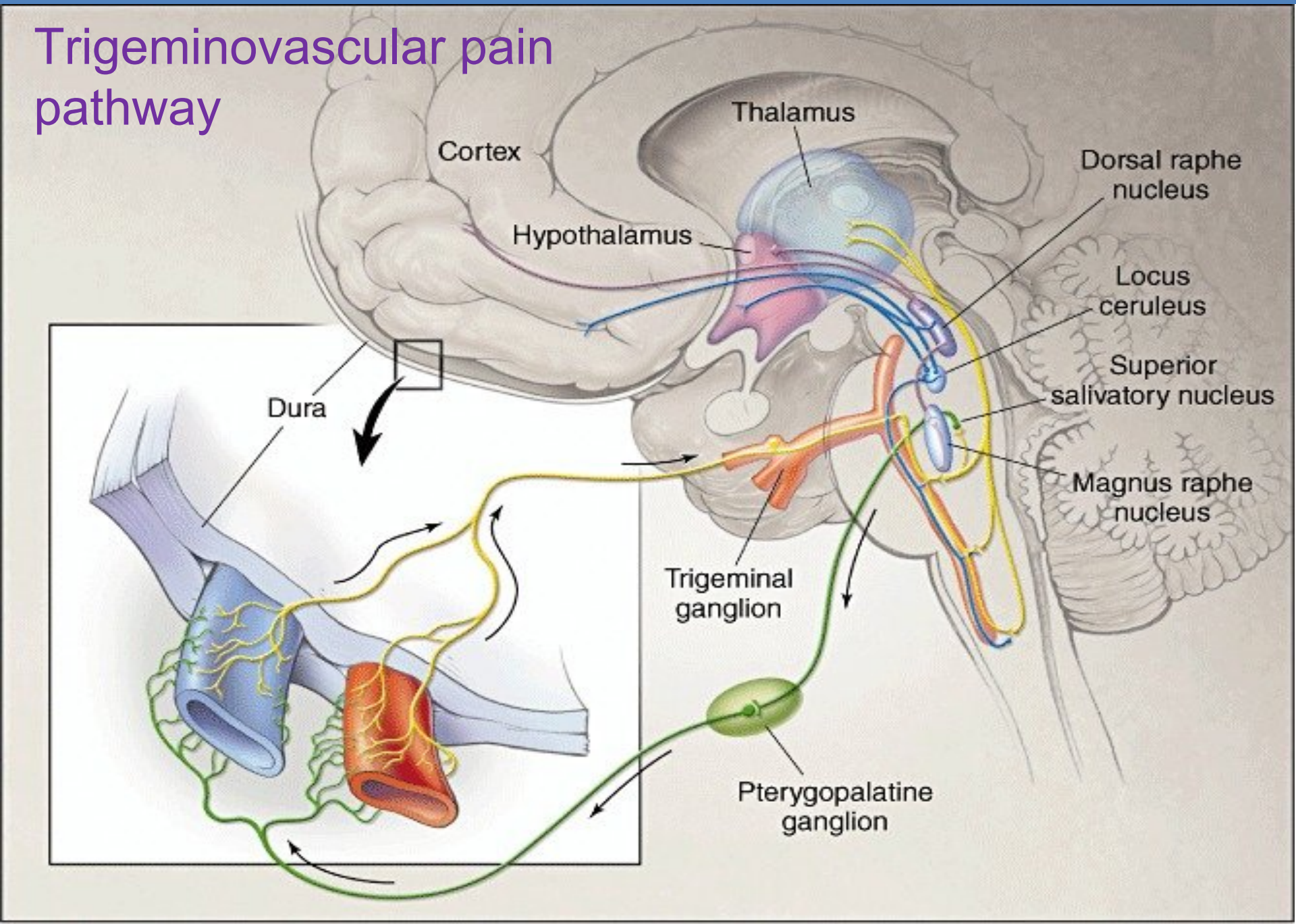
Pathophysiology

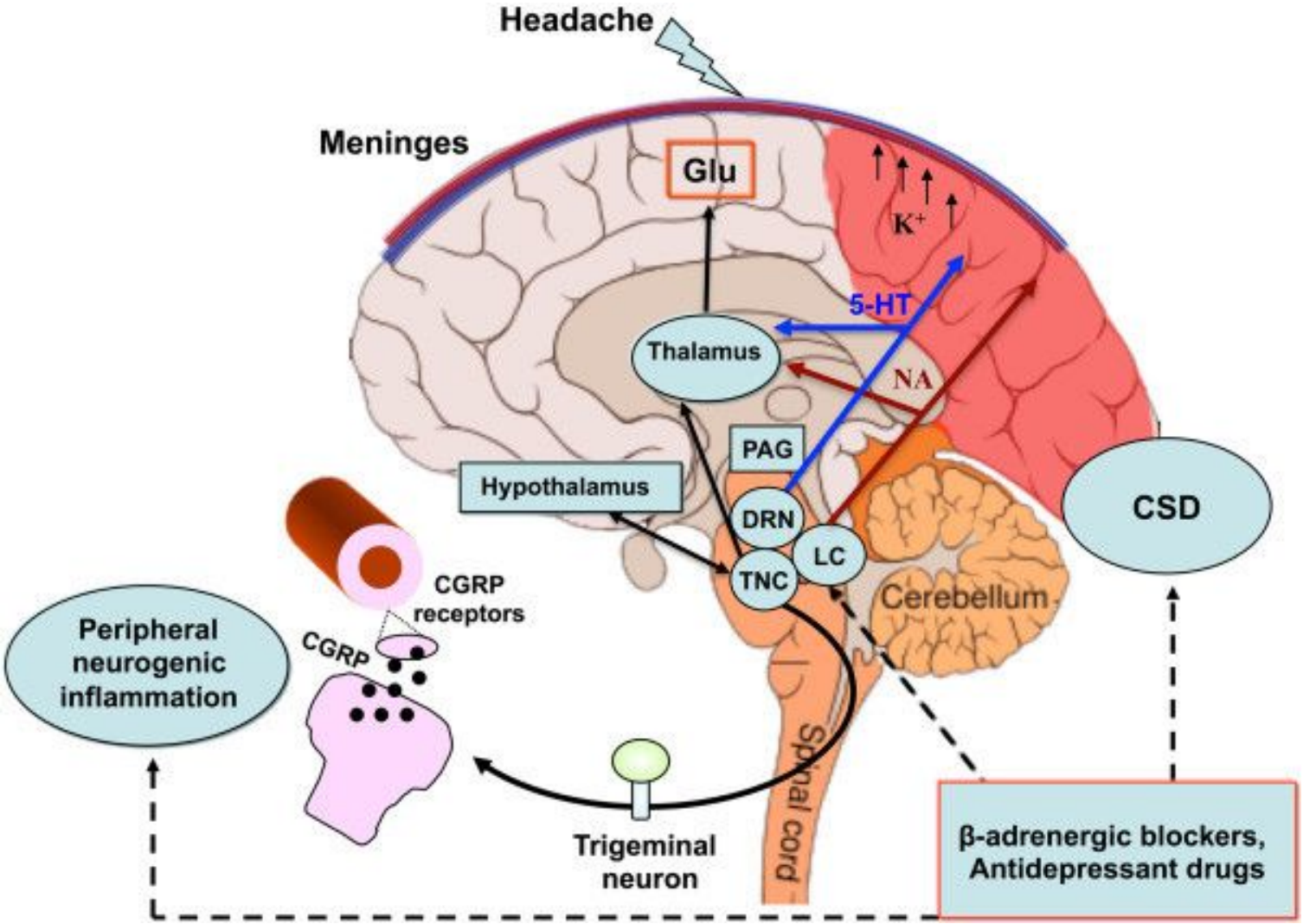
Most migraine attacks start in the brain, as suggested by

- ✔ A premonitory symptoms occur up to 12 h before the attack
- ✔ Triggered by stress, sleep deprivation, oversleeping, hunger, and prolonged sensory stimulation
- ✔ Migraineurs show hypersensitivity to sensory stimuli and abnormal processing of sensory information at period between attacks

Generally it is believed that migraine headache influenced by the activation and hypersensitization of the trigeminovascular pain pathway while cortical spreading depression is the neurophysiological correlate of migraine aura

Trigeminovascular pain pathway




Headache
Meninges
Glu
K+
5-HT
Thalamus
NA
PAG
Hypothalamus
DRN
LC
TNC
CSD
Cerebellum
CGRP
receptors
CGRP
Peripheral
neurogenic
inflammation
Trigeminal
neuron
Spinal cord
β-adrenergic blockers,
Antidepressant drugs

Pathogenesis of migraine

The pain phase is due to peripheral and central sensitization of the trigeminal system, as well as to the release of CGRP, both peripherally and centrally.

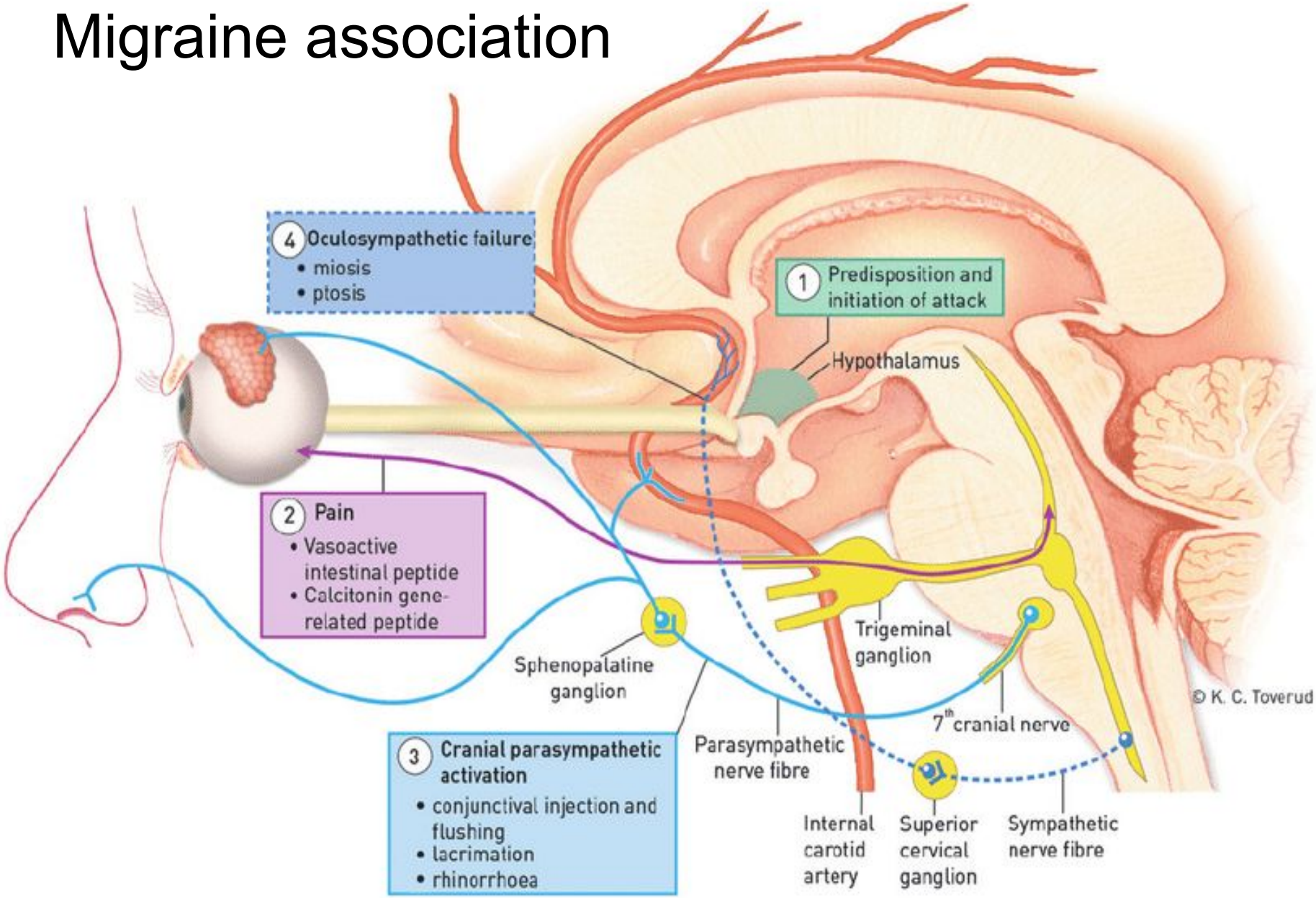
An initial activation of trigeminal nerve fibers activate trigeminospinal complex in brainstem (Periacqueduttal gray matter, locus coeruleus , nucleus of raphe magnum) which implicated in the processing of trigeminal pain. A dysfunction in brainstem pain-inhibiting circuitry may explain many headache phases.

The activation of trigeminospinal complex resulting release of vasoactive neuropeptides (calcitonin gene–related peptide, Serotonin, Neurokinin A, substance B and glutamate) with subsequent sterile inflammation of dura and cerebral vasodilatation with propagation of migraine headache.

CGRP is considered a key mediator in migraine, together with NO resulting in vasodilation and neurogenic inflammation in the dura and brainstem.

Functional and structural PAG abnormalities occurring in migraineurs, contribute to the hyper-excitability of trigeminal nociceptive pathways. Functional alteration of noradrenergic nuclei of the LC are believed to be involved in cortical vasomotor instability.

Migraine association



Pathophysiology

Cortical spreading depression

Its cortical neuronal discharges followed by cortical depression that begins in the occipital lobe spreads frontally over the cortex at a rate of about 3 mm/minute, corresponding to the aura's symptomatic spread.

Initiation and propagation of Cortical Spreading Depression are determined by massive increases in extracellular potassium ion concentration and excitatory glutamate in the cortex.

Clinical features

- A prodromal period (few hours) of fatigue, anorexia irritability or behavioral change before headache
- 20% experience an Aura characterized by a mix of positive and negative features (Not motors) , gradual development (> 5 min), duration no longer than 1 hour with complete reversibility.
  - Visual (fortification spectra)
  - Sensory (tingling followed by numbness, spreading over 20–30 minutes, from one part of the body to another.
  - Speech disturbance (Dominant hemisphere)

migraine aura (fortification spectra)

Clinical features

Headache

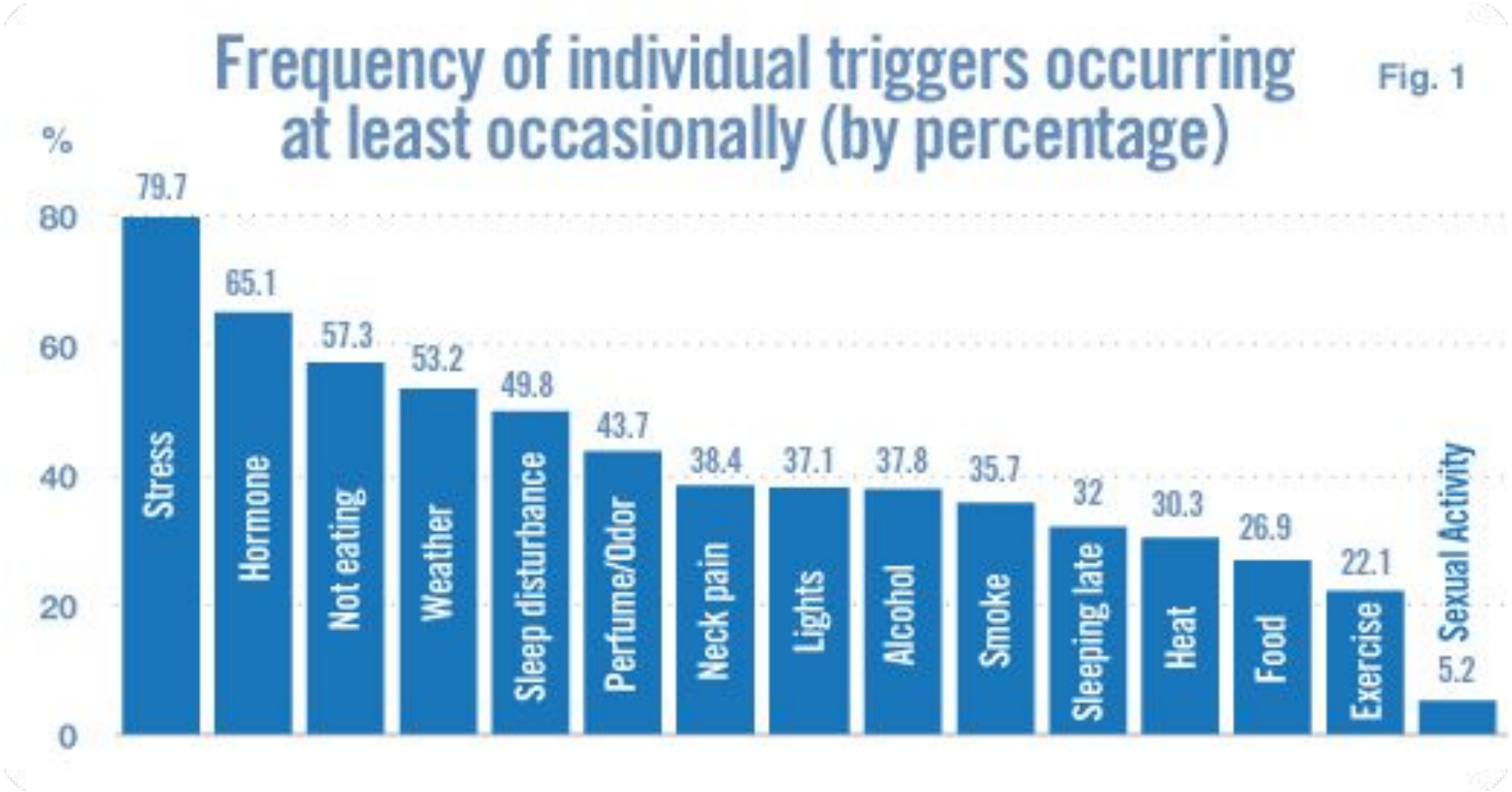
- ✔ Usually unilateral
- ✔ Gradual in onset
- ✔ Lasting hours to several days.
- ✔ Throbbing in quality
- ✔ Severity may be mild to debilitating
- ✔ Can be aggravated by routine activities, light, sound, and smells.

Migraine is more prevalent among women and is strongly influenced by hormonal cycles. More in the days before menses. The stability of estrogen levels during pregnancy and after menopause leads to reduction migraine for the majority of women

symptoms accompanying severe migraine

Symptoms	%	Symptoms	%
Nausea	87	Vertigo	33
Photophobia	82	Alteration of consciousness	18
Allodynia	65	Diarrhea	16
Vomiting	56	Syncope	10
Visual disturbances	36	Seizure	4
Paresthesia	33	Confusion	4

Trigger factors



Diagnostic Criteria:

A. At least 5 attacks fulfilling criteria B through D

B. Headache attacks lasting 4 to 72 hours (untreated or unsuccessfully treated)

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 (walking or climbing stairs)

D. During headache at least one of the following:

1. Nausea and/or vomiting
2. Photophobia and phonophobia

E. Not attributed to another disorder

Migraine with aura

At least two attacks fulfilling criteria B and C

B: Having one or more of these fully reversible aura symptoms: brainstem, motor, retinal, sensory, speech and/or language, visual

C: Having at least two of these characteristics:

- at least one aura symptom spreads gradually over at least 5 minutes and/or two or more symptoms occur in succession
- aura symptom lasts 5 to 60 minutes;
- one aura symptom is unilateral
- the aura is accompanied or followed within 60 minutes by headache

Management

It is helpful to the patients to understand that migraine is an inherited tendency to headache, it can be modified and controlled by lifestyle adjustments and medications, but it cannot be eradicated.

lifestyle adjustments

- Avoid specific headache triggers (contraceptive pill)
- A regulated lifestyle
  - ✔ Healthy diet
  - ✔ Regular exercise
  - ✔ Regular sleep patterns
  - ✔ Avoid excess of caffeine and alcohol
  - ✔ Avoid acute changes in stress levels

Migraine-Inducing Foods

Caffeine

Nitrates

Tyramine

Phenylethylamine

Histamine

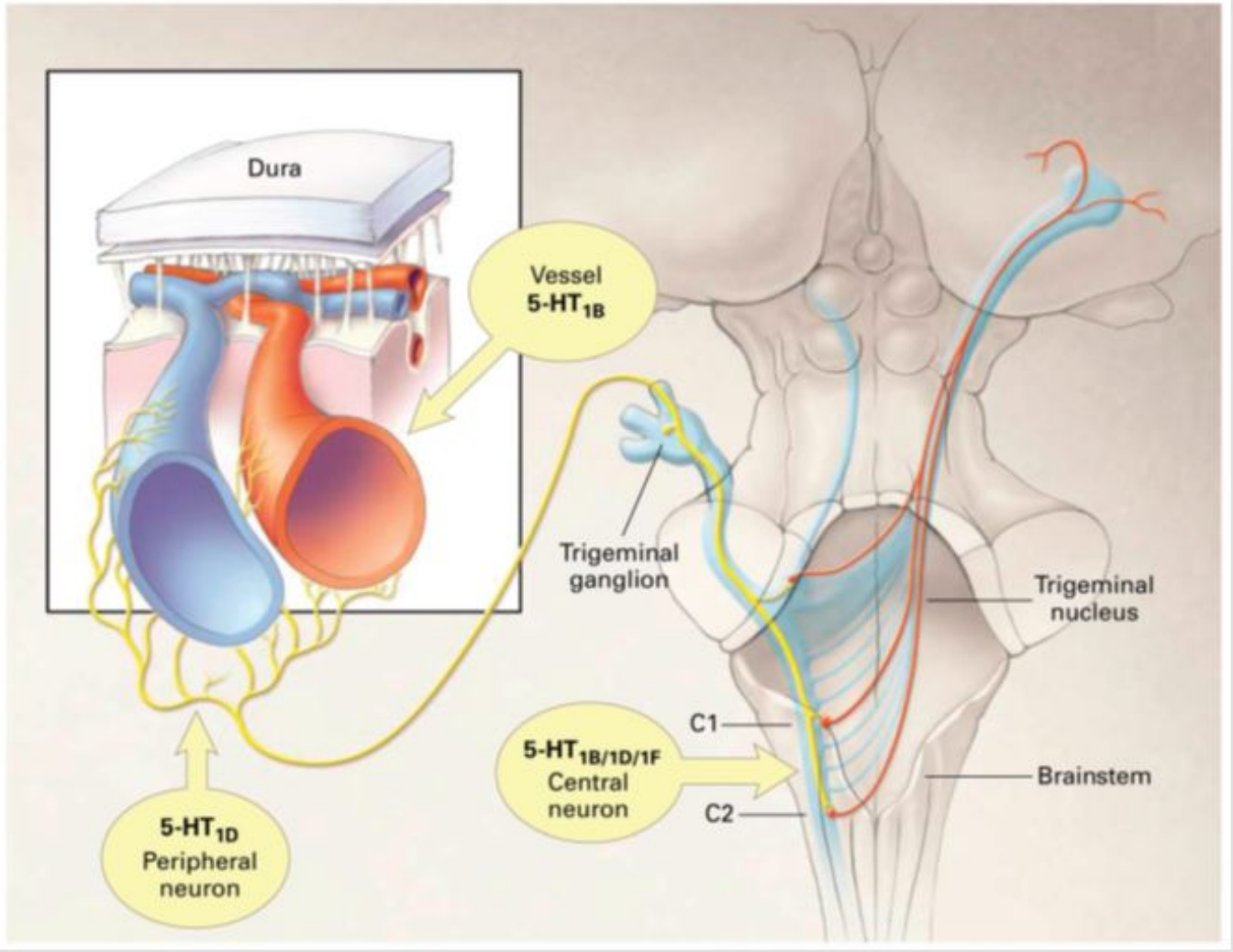
Management

Acute attack treatment

- Acetaminophen, aspirin, caffeine (Excedrin)
- NSAIDs (Naproxen, Ibuprofen, Diclofenac)
- serotonin 1A receptor ($5\text{-}HT_{1A}$) agonist
  - Triptans (Naratriptan, Rizatriptan, Sumatriptan, Frovatriptan, Almotriptan, Eletriptan & Zolmitriptan)
  - Ergotamine 1 mg + caffeine 100 mg (Cafergot)
- Dopamine Receptor Antagonists
  - Chlorpromazine
  - Metoclopramide
  - Prochlorperazine
- Opioids

Triptans

is activate serotonin receptor in the brain lead to hyperpolarisation and reduction of firing rate of the postsynaptic neuron.



Emergency treatment

- Sumatriptan 4 mg to 6 mg subcutaneously
- Antiemetics plus dihydroergotamine (0.5 mg to 1 mg IV, repeat in 1 hour)
- Neuroleptics
  - Chlorpromazine (0.1 mg/kg) 12.5 mg to 37.5 mg IV/IM
  - Prochlorperazine 5 mg to 10 mg IM, 25 mg per rectum
  - Haloperidol 5 mg IV infusion in normal saline over 20 to 30 minutes
- Valproate 300 mg to 500 mg IV; open-label trials
- Corticosteroids (eg, dexamethasone 10 mg to 24 mg IV)

Preventive treatment

Indications

1. Three or more headache episodes per month
2. Significant interference with daily activity
3. Acute medications are ineffective, contraindicated or overused
4. Adverse effects from acute medications
5. Patient preference for prevention
6. Special circumstances: elderly, pregnant, and pediatric populations

Preventive treatment

The goals of migraine preventive therapy are to:

- ✔ Reduce frequency, severity, and duration of attacks.
- ✔ Improve responsiveness to treatment of acute attacks
- ✔ Reduce level of disability.
- ✔ Maintain cost of care for migraine treatments.
- ✔ Reduce excessive overuse of acute medications

The choice of medication depends on many factors such as co-existing conditions (high blood pressure, asthma, diabetes, or pregnancy) or personal individual needs (depression, obesity& anxiety)

The probability of success is 50–75%. Once effective stabilization is achieved, the drug is continued for ~6 months and then slowly tapered to assess the continued need.

Preventive medications

- Antiepileptic (valproate, topiramate).
- Antidepressant drugs(amitriptyline, Nortriptyline, dosulepin)
- Beta-adrenergic blockers (Propranolol, Atenolol, Metoprolol, Timolol)
- Calcium channel blockers (Verapamil, Diltiazem, Nimodipine)
- Flunarizine, Pizotifen
- SSRI (Fluoxetine, Paroxetine, Sertraline)
- Candesartan
- Vitamins (Riboflavin)
- Serotonin antagonists (Methysergide, Methylergonovine)

Low doses are used at first and gradually increased to higher doses as needed. Therefore, you may need to increase medication dose until the desired response is achieved

It may take two to three months before you notice a decrease in the frequency or severity of attacks even after reaching “the beneficial dose.” Treatment may be required for six to twelve months or longer.

Chronic migraine

headaches on at least 15 days of every month, at least 8 days of which are migraine.

- Neurotoxins (botulinum toxin A) recommended when failure of response to at least 3 previous preventative medical treatments.
- Monoclonal antibodies (fremanezumab, galcenezumab and erenumab) If patient have frequent migraines and other treatments have not helped

Migraine complications

- *Status Migrainosus*

  severe migraine with aura lasts for longer than 72 hours.

- *Migralepsy*
- *Stroke*

  migraines have about twice the risk of having a stroke & higher in smoker women who taken oral contraceptives