TMJ, Chronic Pain and Neurological Disorders

International Pain Foundation

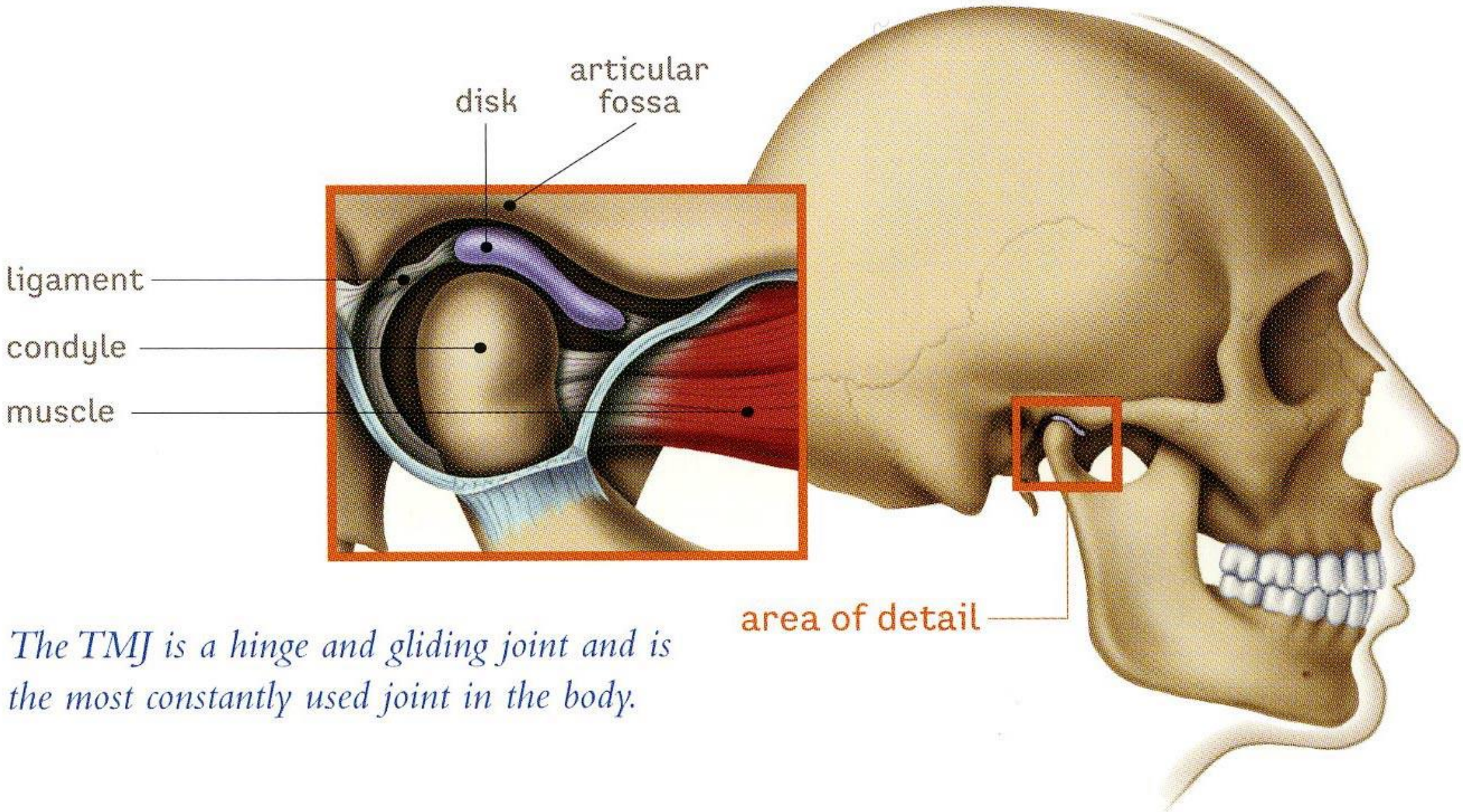
UCLA, November 16, 2019

G. Gary Demerjian DDS & Andre Barkhordarian M.S, Ph.D.

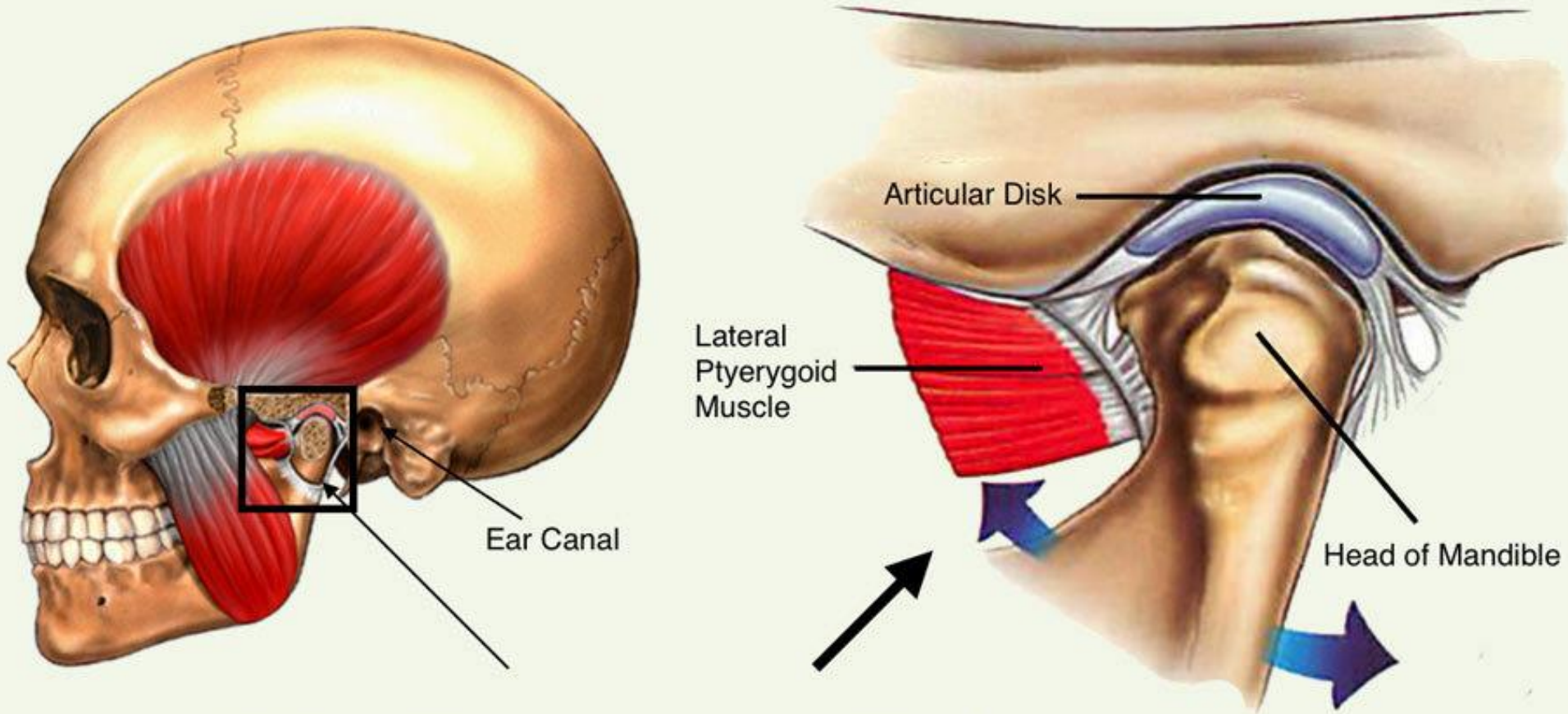
G. Gary Demerjian DDS

- Diplomate American Board of Craniofacial Pain
- Diplomate American Board of Dental Sleep Medicine
- Diplomate American Board of Craniofacial Dental Sleep Medicine
- Diplomate American Academy of Integrative Pain Management
- Diplomate American Academy of Forensic Examiners
- Diplomate American Academy of Dental Forensics
- Fellow International College of Craniomandibular Orthopedics
- Fellow American Academy of Craniofacial Pain
- Registered Polysomnographic Technologist
- Certified Forensics Consultant

- Pomona valley Medical Center Sleep Panel 2008-2014
- Kaiser Fontana Sleep Center 2014 - Present
- Project Scientist UCLA School of Dentistry, Department of Oral Biology and Medicine 2014-2018
- Published “Temporomandibular Joint and Airway Disorders, a Translational Perspective” Springer 2018



The TMJ is a hinge and gliding joint and is the most constantly used joint in the body.



TMJ - Temporomandibular Joint

Normal Temporomandibular Joint relationship and Movement

Anterior Disc Displacement with Reduction

Posteriorized Condyle

Anterior Disc Displacement non-reducing

Degenerative Arthritis

Posterior Displaced Condyle

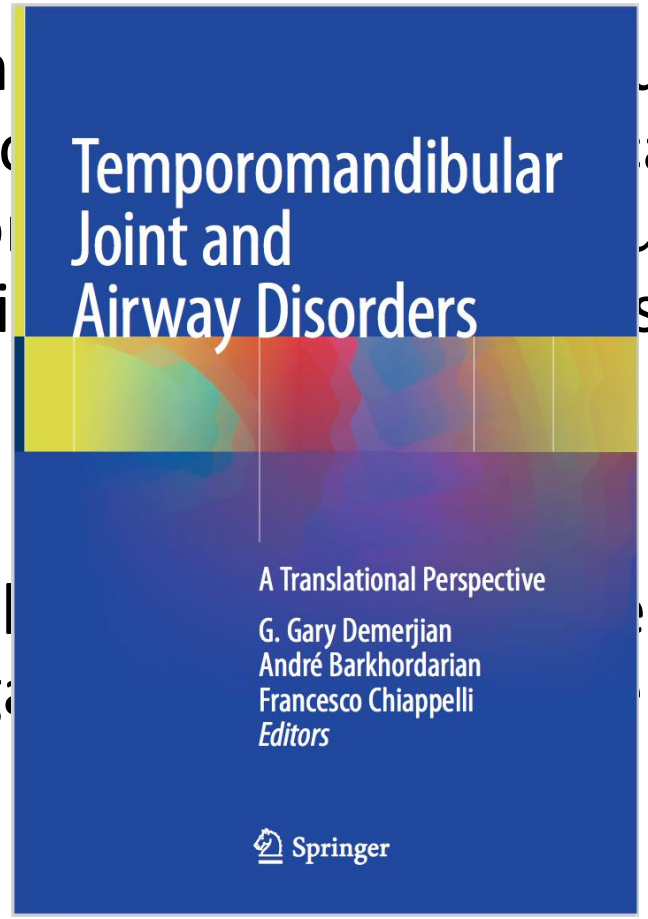
Arthokinetic Reflex

- Iceberg et al. described an **arthrokinetic reflex** in the muscles of mastication associated with disc displacements. Continuous muscle activity was provoked by disc displacements and ceased when the disc position was normalized on mouth opening, only to occur again every time the disc became displaced on mouth closure. These findings were in line with previously published on limb joints that indicated that joint derangements are a cause of muscle hyperactivity.

Isberg A, Widmalm SE, Ivarsson R. Clinical, Radiographic and Electromyographic Study of Patients with Internal Derangementsa of the Temporomandibular Joint. Am J. Orthodontics 1985; 88: 453-460

Arthokinetic Reflex

- Th upporting
  pr an cause
  co ular hype
  mi scial pain
- Wh s the gua
  lig nse and f

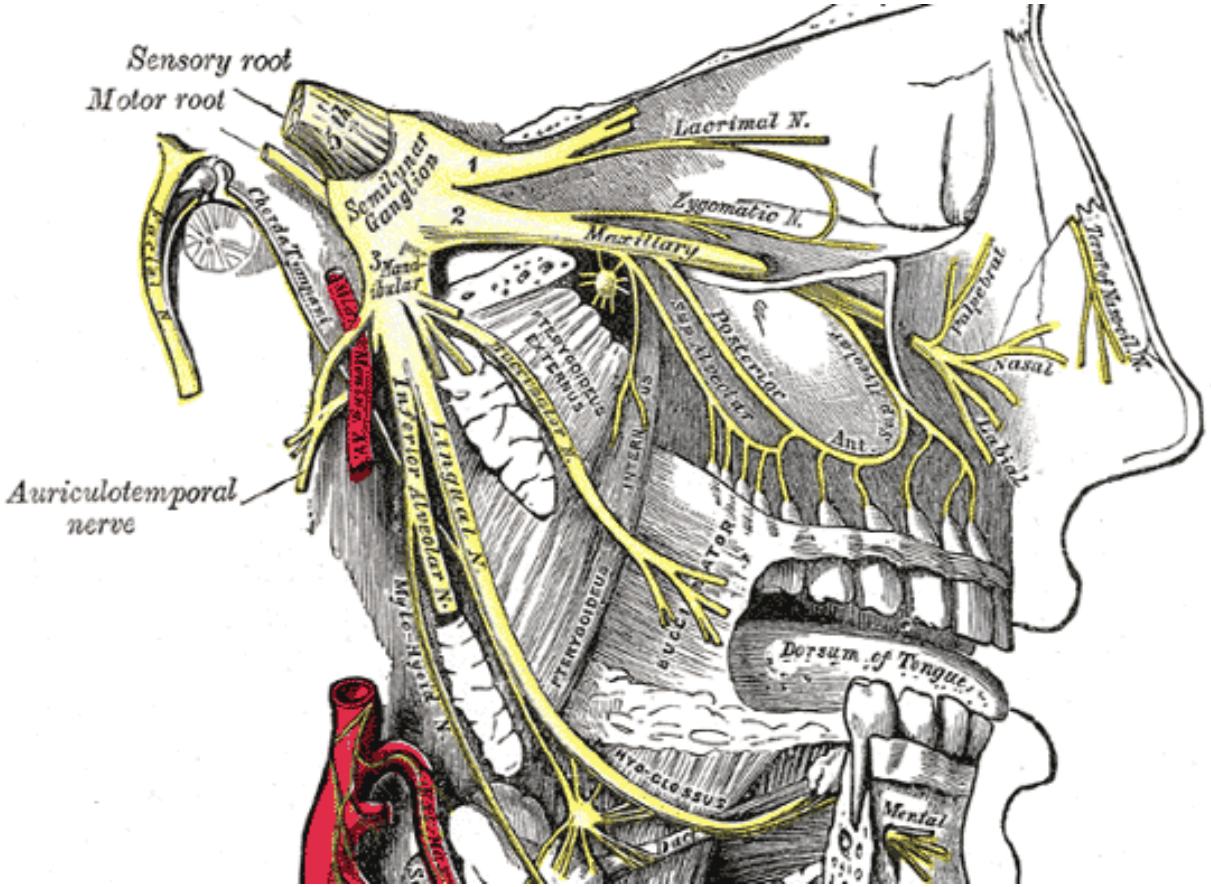


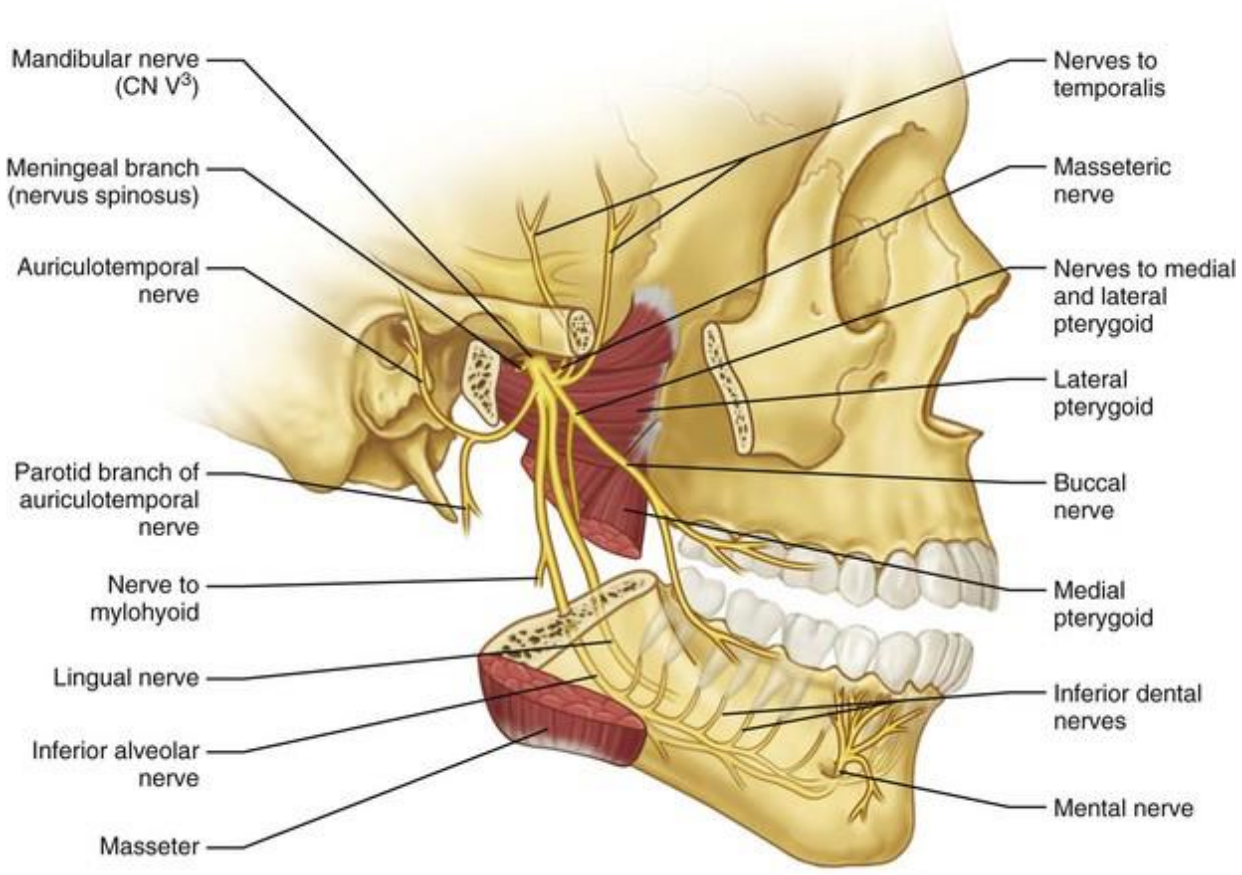
- **Demerjian GG**, Barkhordarian A, Chiappelli F. Testing patient targeted therapies in patients with Temporomandibular joint disorder with the arthrokinetic reflex: individual patient research. J Transl Med. 2016;14:231–5.
- **Demerjian GG**, Sims AB, Patel M, Balatgek TL, Sabal EB. Head and Neck Manifestations of Temporomandibular Joint Disorders. **Temporomandibular Joint and Airway Disorders, A Translational Perspective**. Springer 2018 Chapter 5, Pg 78.
- Chiappelli F, Barkhordarian A, **Demerjian GG**. Patient-Centered Outcomes Research and Collaborative Evidence-Based Medical and Dental Practice for Patients with Temporomandibular Joint Disorders. **Temporomandibular Joint and Airway Disorders, A Translational Perspective**. Springer 2018, Chapter 11, Pg 224.

noghue"
gement.
No3, July

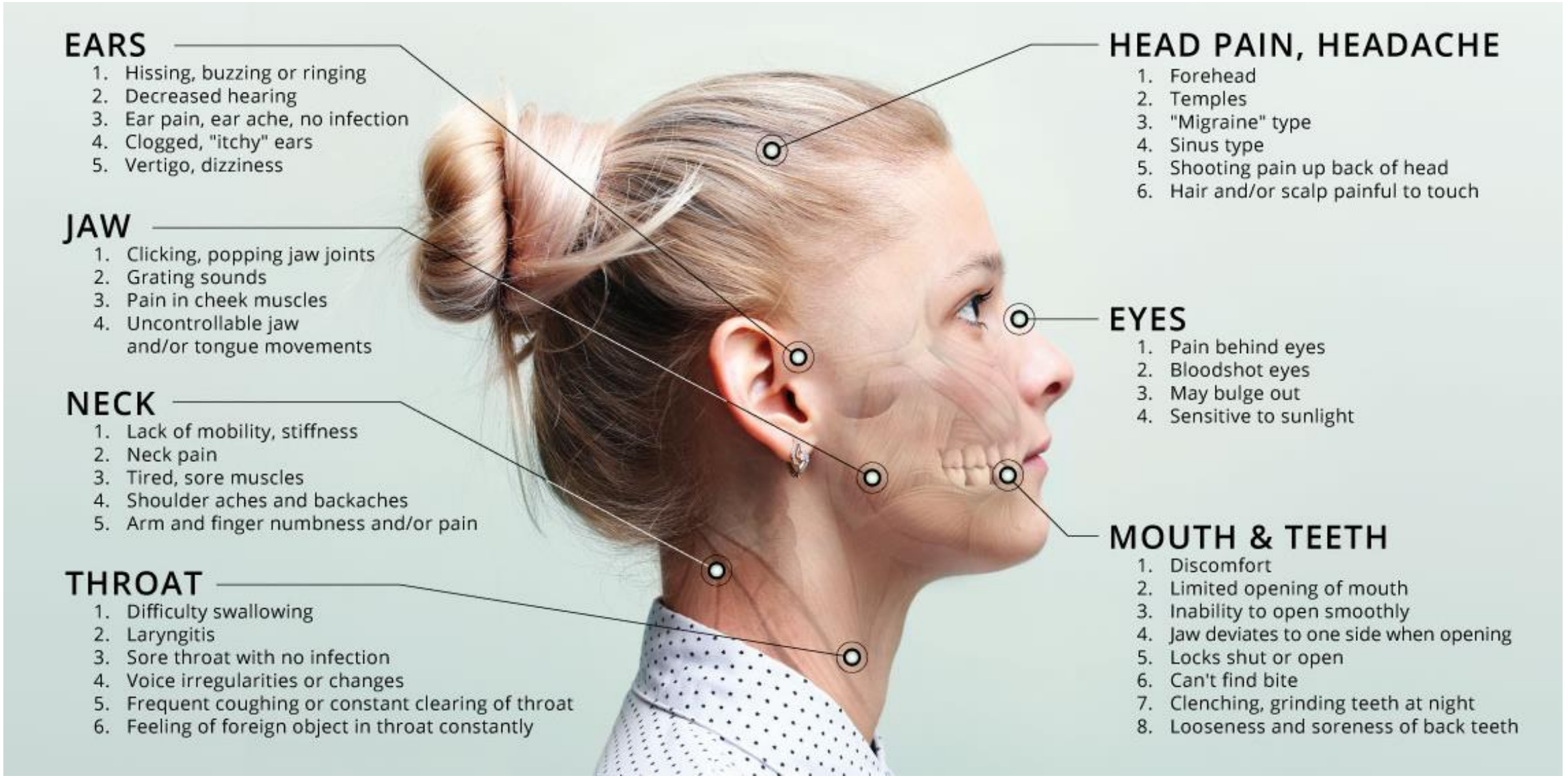
igament
erapy. 5th
5

Trigeminal Nerve

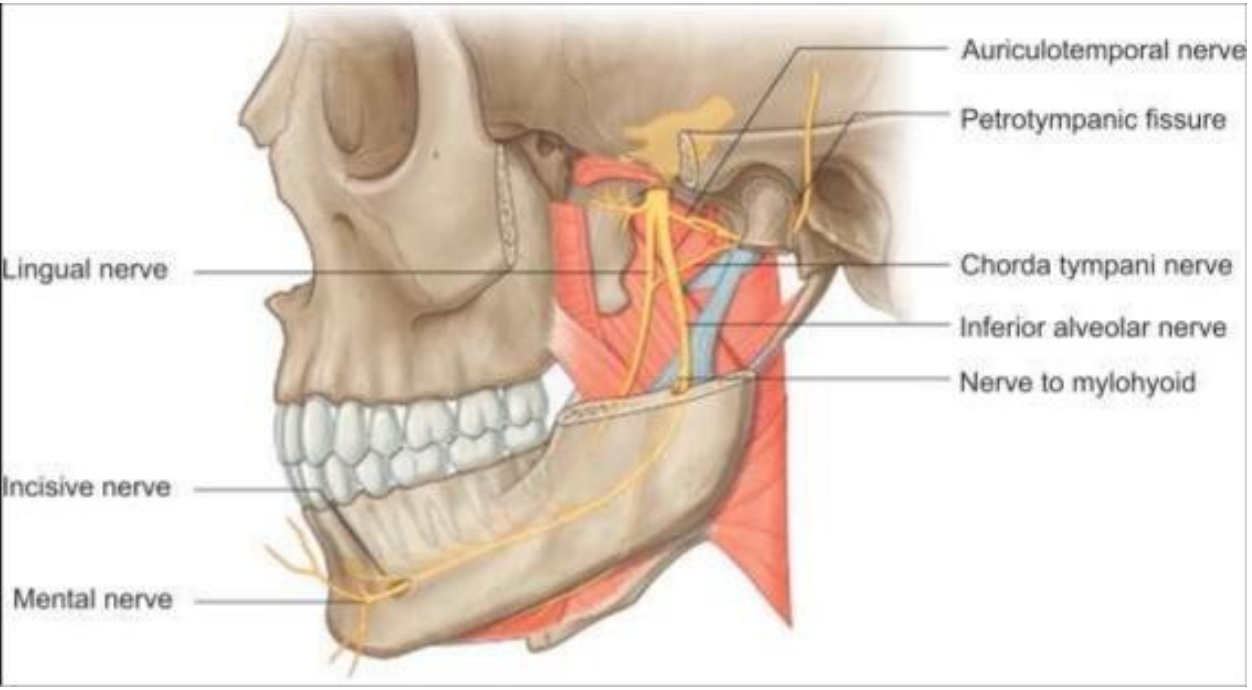


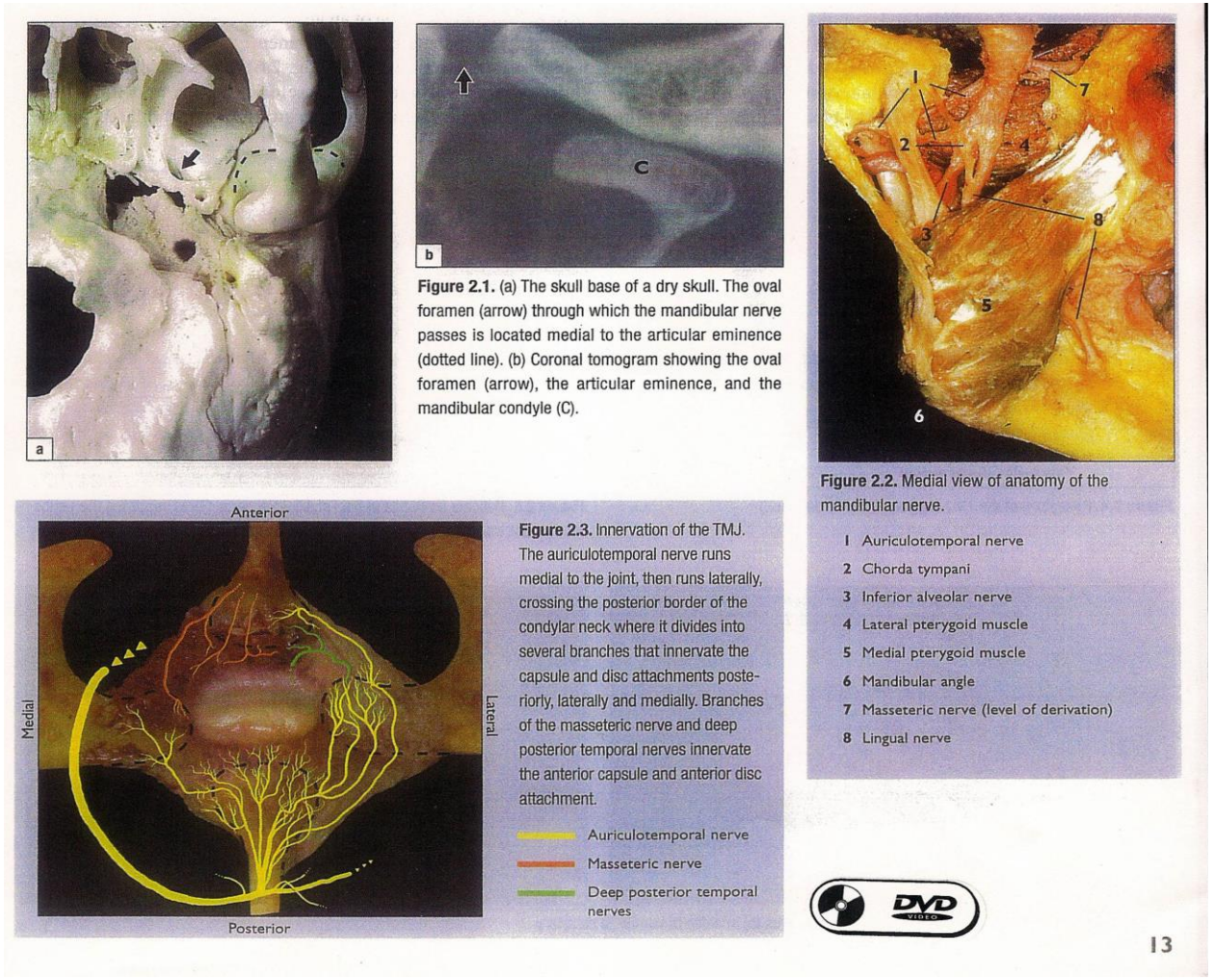


TMD Symptoms



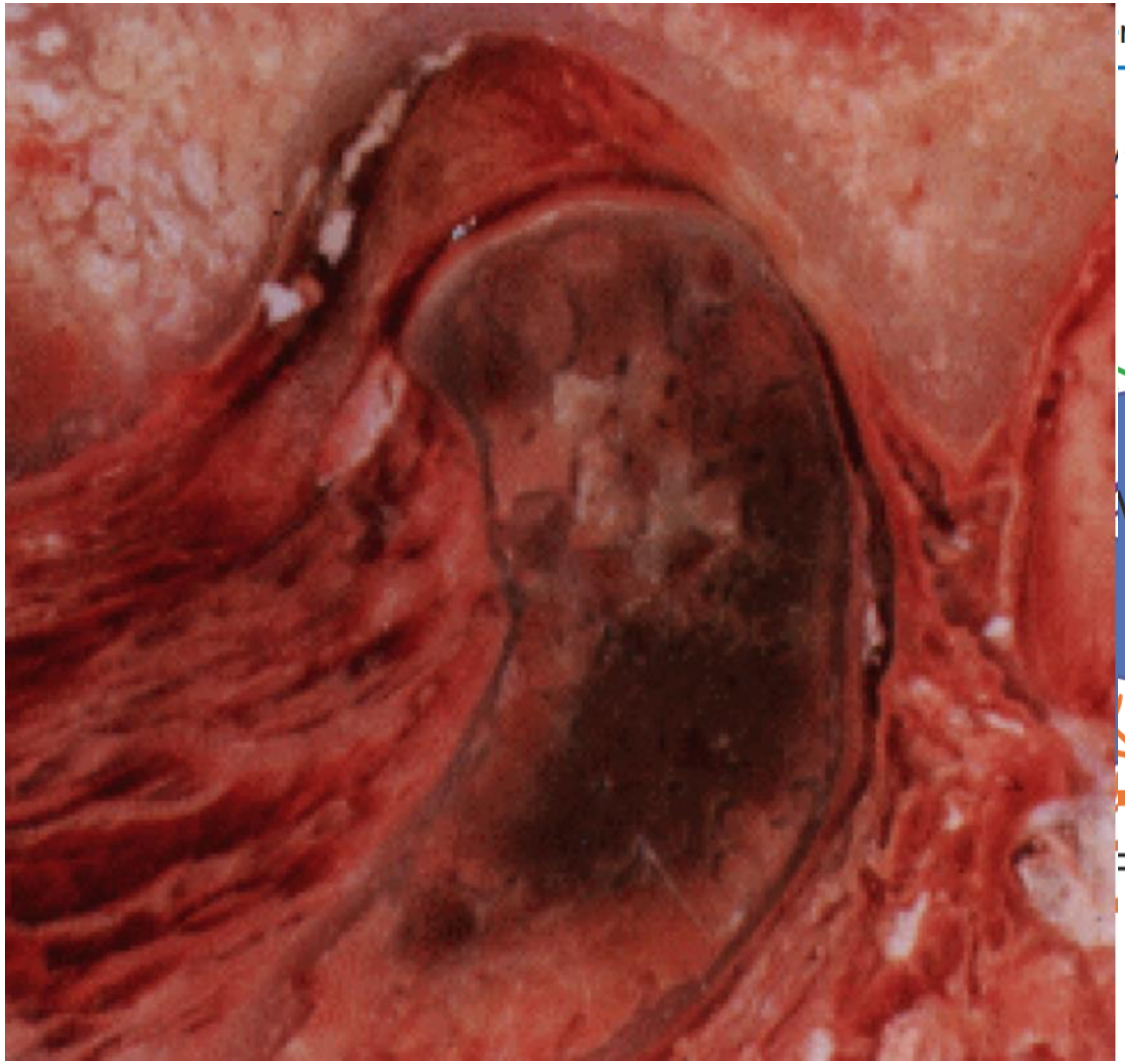
Auriculotemporal Nerve

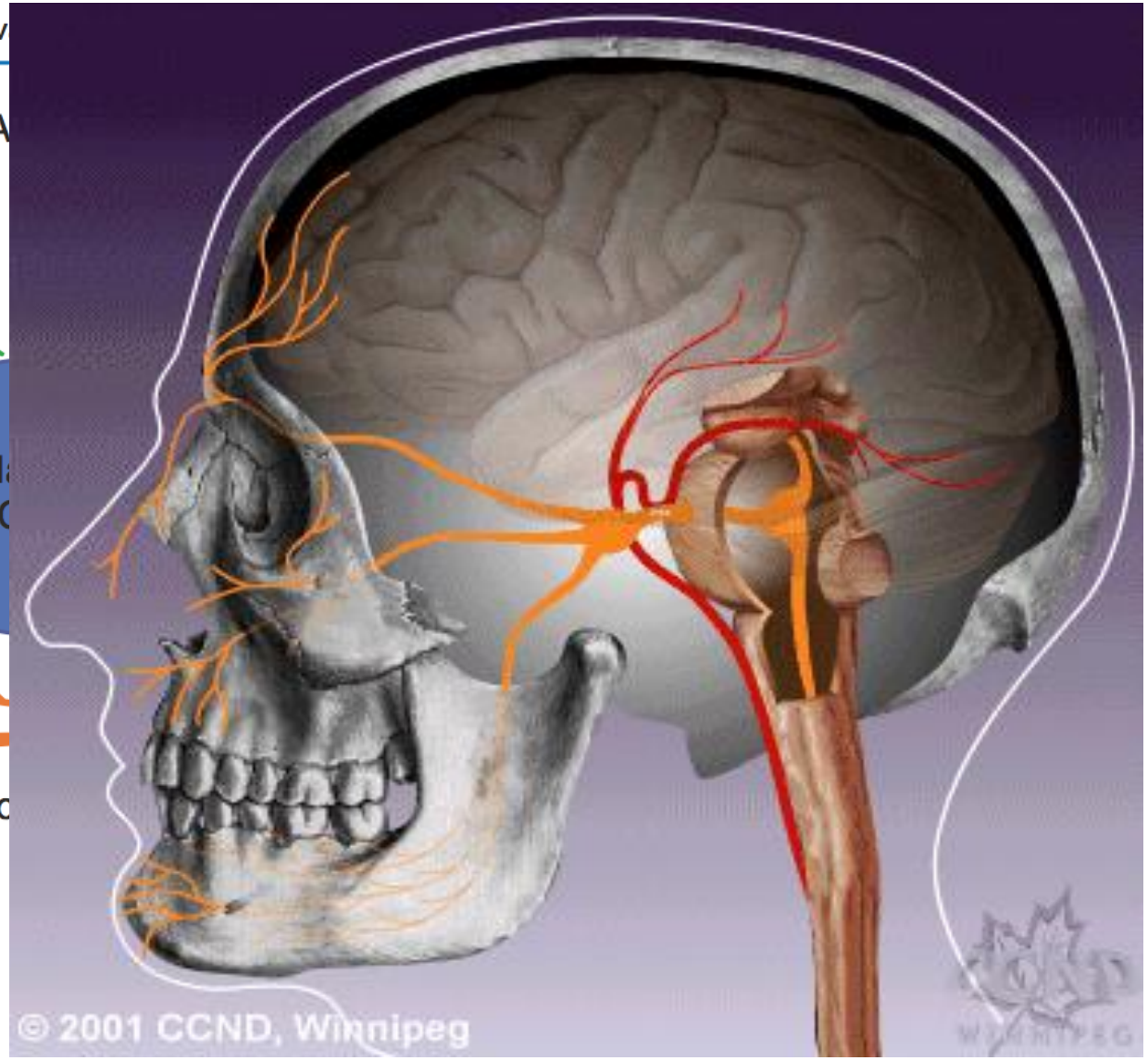




Isberg A, Widmalm SE, Ivarson R. Clinical Radiographic and Electromyographic Study of Patients with Internal Derangements of the Temporomandibular Joint. Am J. Orthodontics 1985;88:453-460

Peripheral Sensitization





- Compression of the AT nerve may result in a focal neuroinflammation.
- Nueroinflammation spreads from the site of nerve entrapment to the trigeminal ganglion via the mandibular nerve, then to the spinal trigeminal nucleus, as well as the reticular formation of the brainstem.
- Neuroinflammation in the brainstem centers could act as physiological drivers of aberrant reflexive behaviors, as well as supra brainstem changes within the nervous system.

Sims et al 2011
Demerjian et al 2011

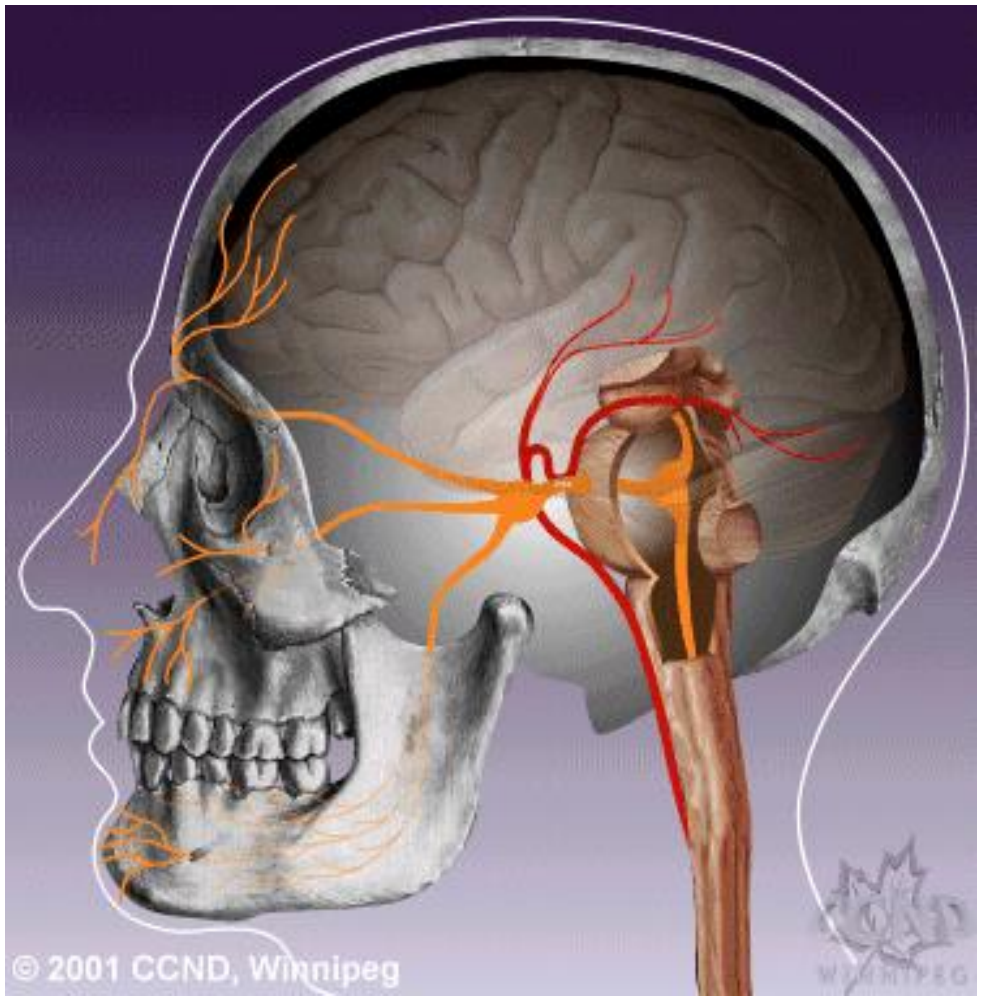
Central Sensitization

- Central sensitization is a condition of the nervous system that is associated with the development and maintenance of chronic pain. When central sensitization occurs, the nervous system goes through a process called *wind-up* and gets regulated in a persistent state of high reactivity. This persistent or regulated, state of reactivity lowers the threshold for what causes pain and subsequently comes to maintain pain even after the initial injury might have healed.

- Pain
- CNS Changes

Central Sensitization

- exaggerated response of the CNS
- changes following tissue injury and/or nerve damage
- increase in noxious stimulation
- sensory input from a site of peripheral trauma into the CNS



- "Clinical Management of Temporomandibular Disorders and Orofacial Pain" by Richard Pertes



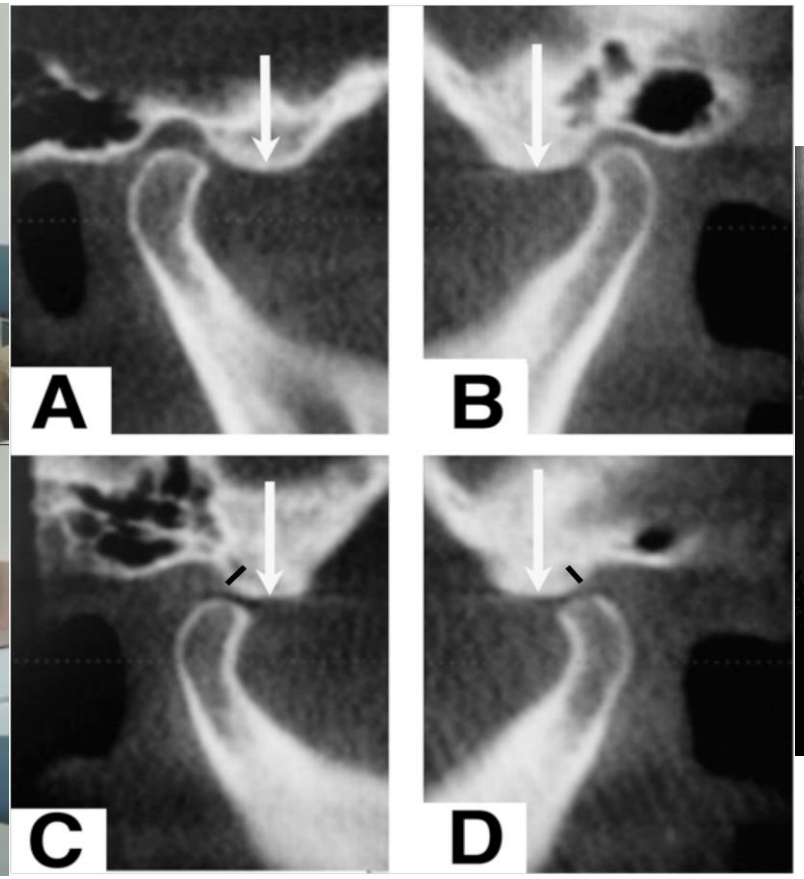



SYMMETRICAL POSTURE CHART

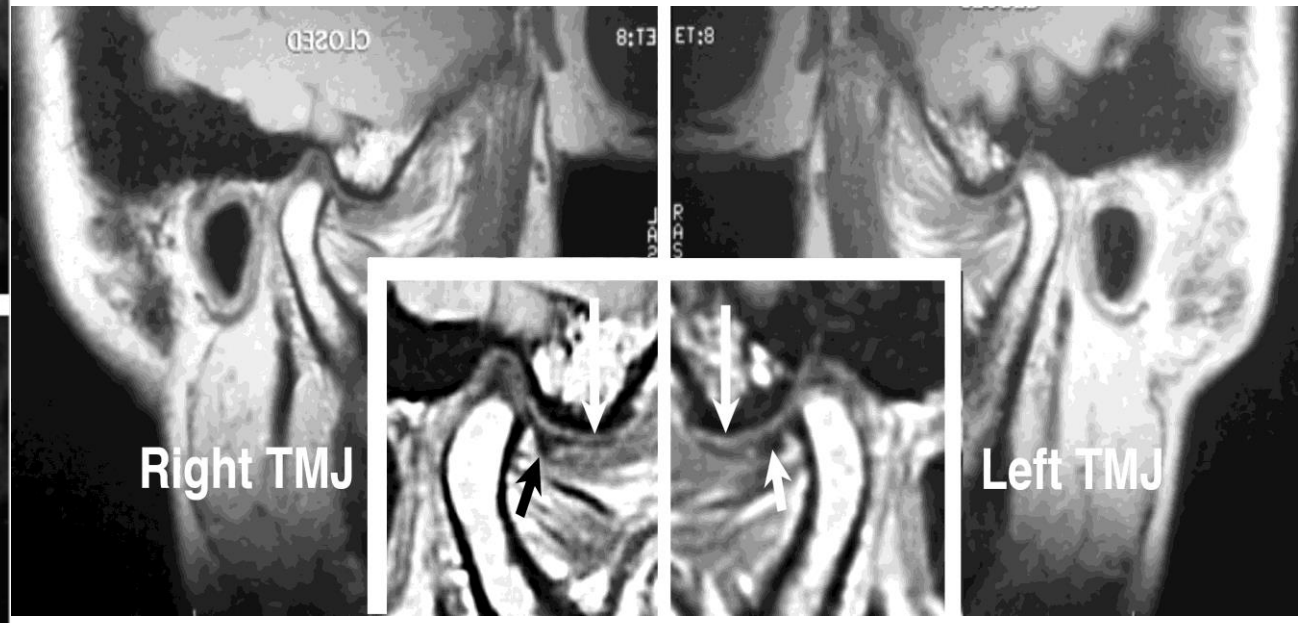
SYMMETRICAL POSTURE CHART

Blepharospasm

CBCT of TMJ

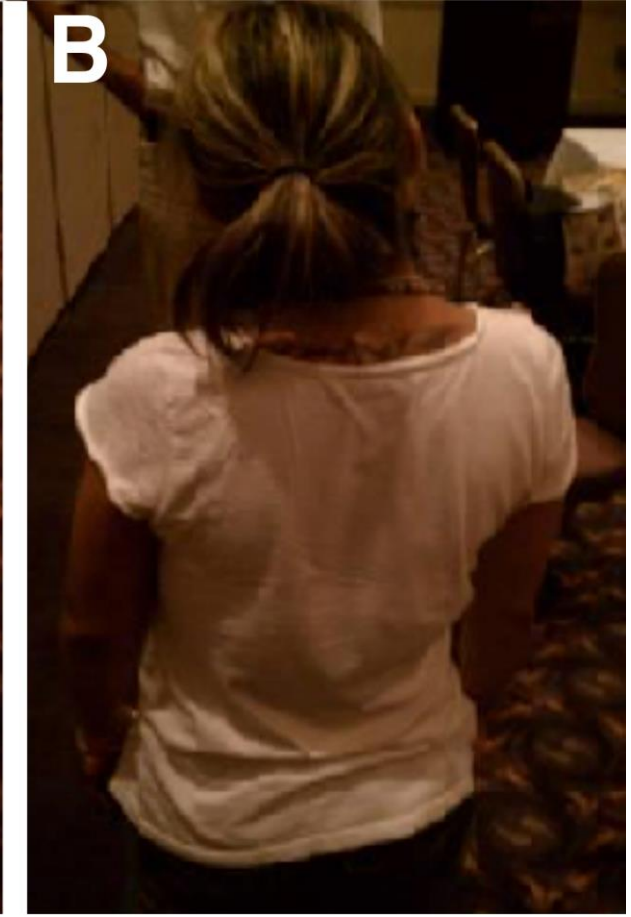


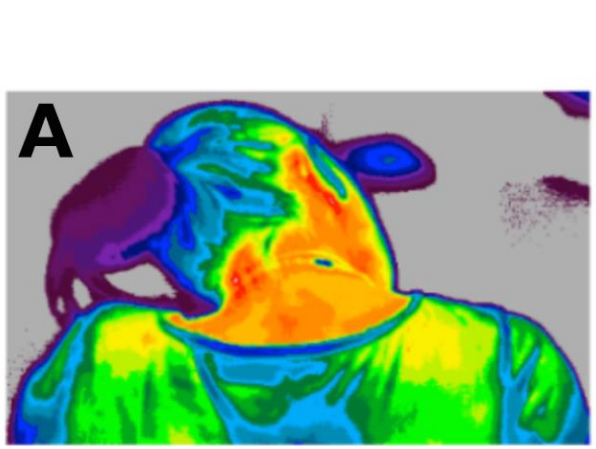
MRI of TMJ

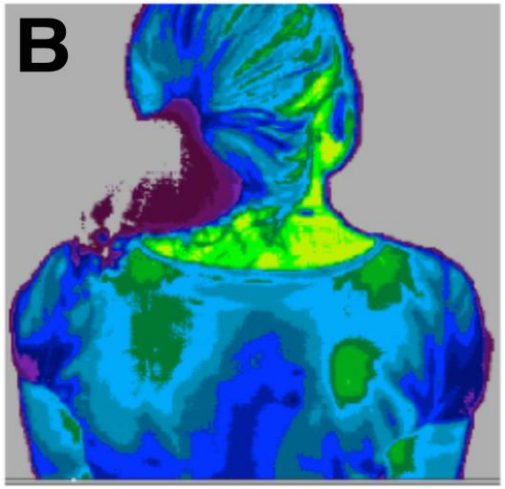


Cervical dystonia

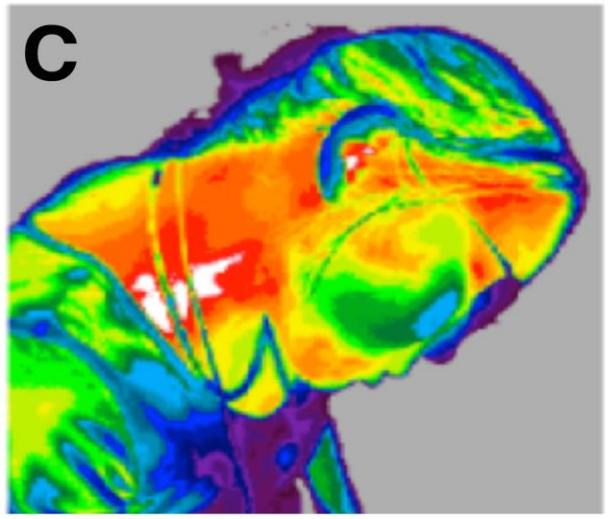

A

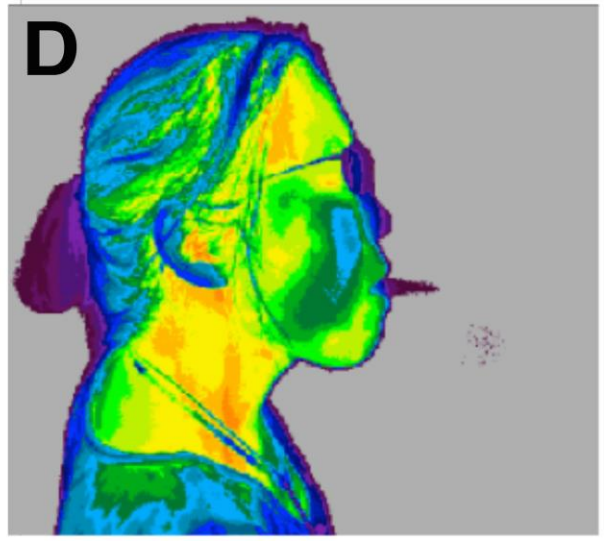

B


A

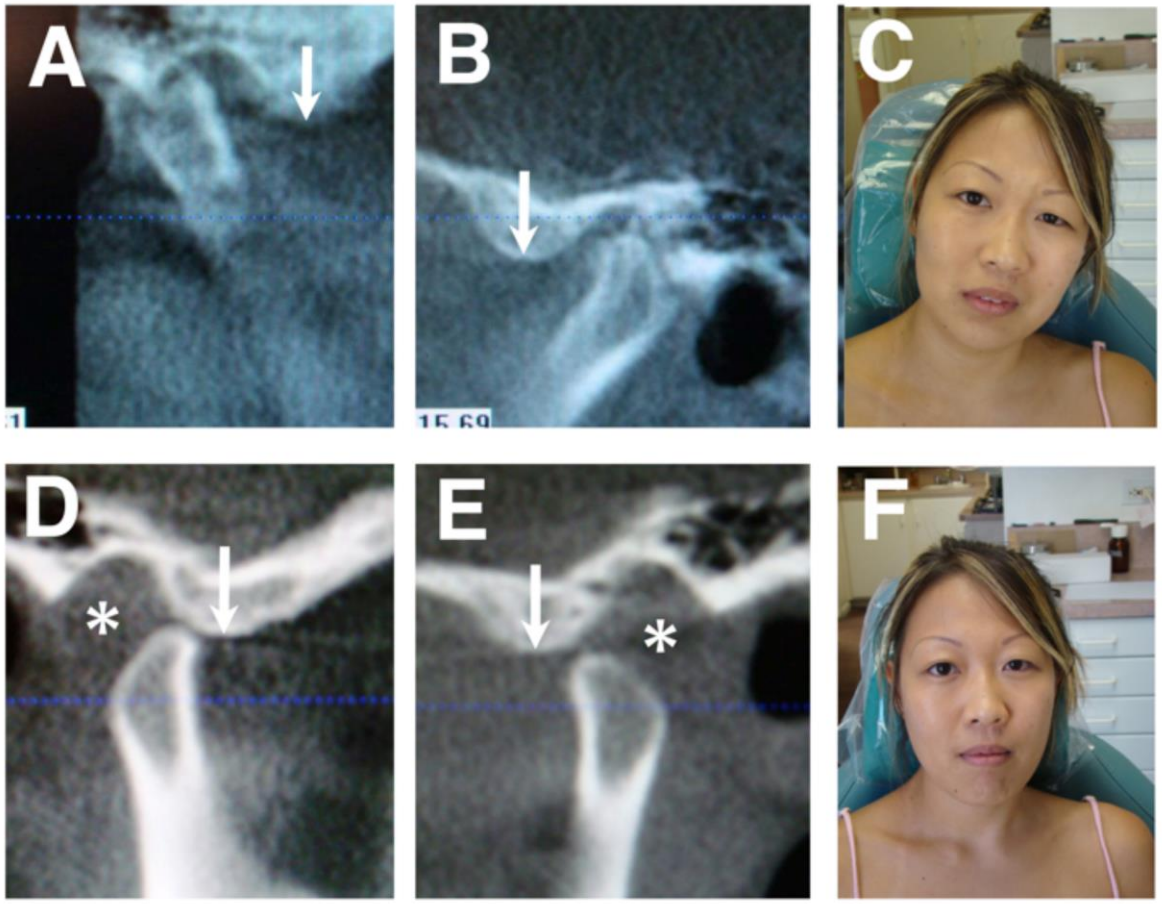

B


37 C
26 C

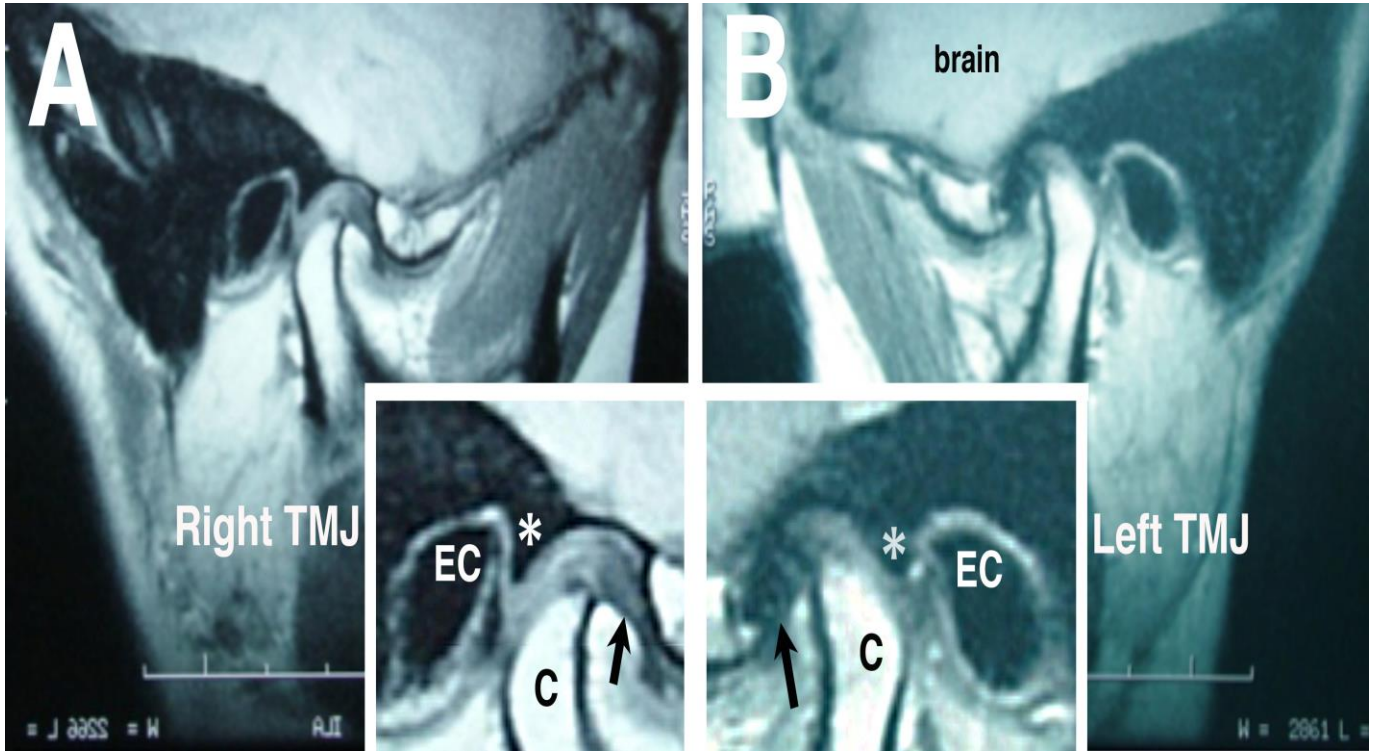

C


D

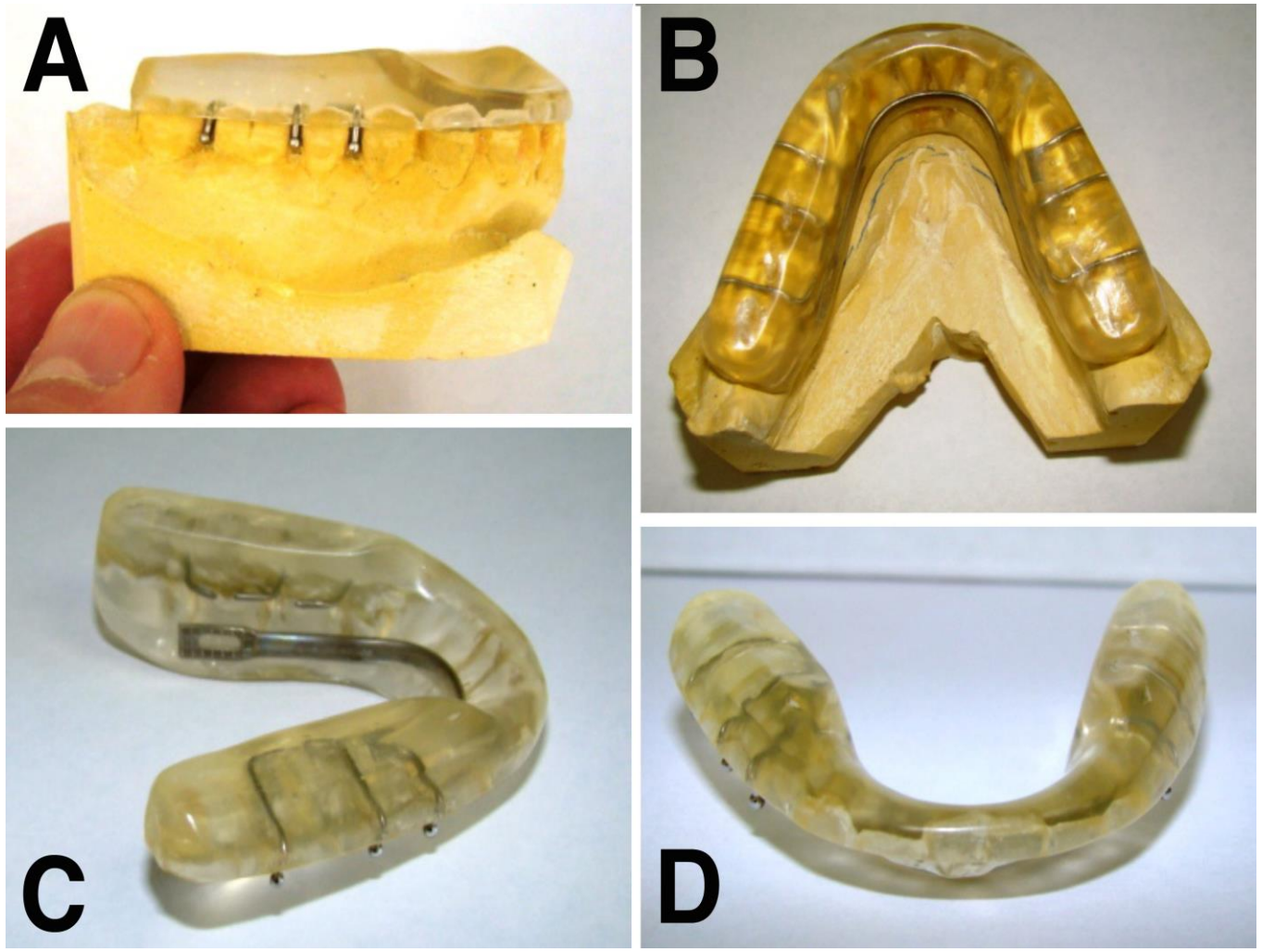
CBCT of TMJ



MRI of TMJ



Non-invasive orthopedic treatment



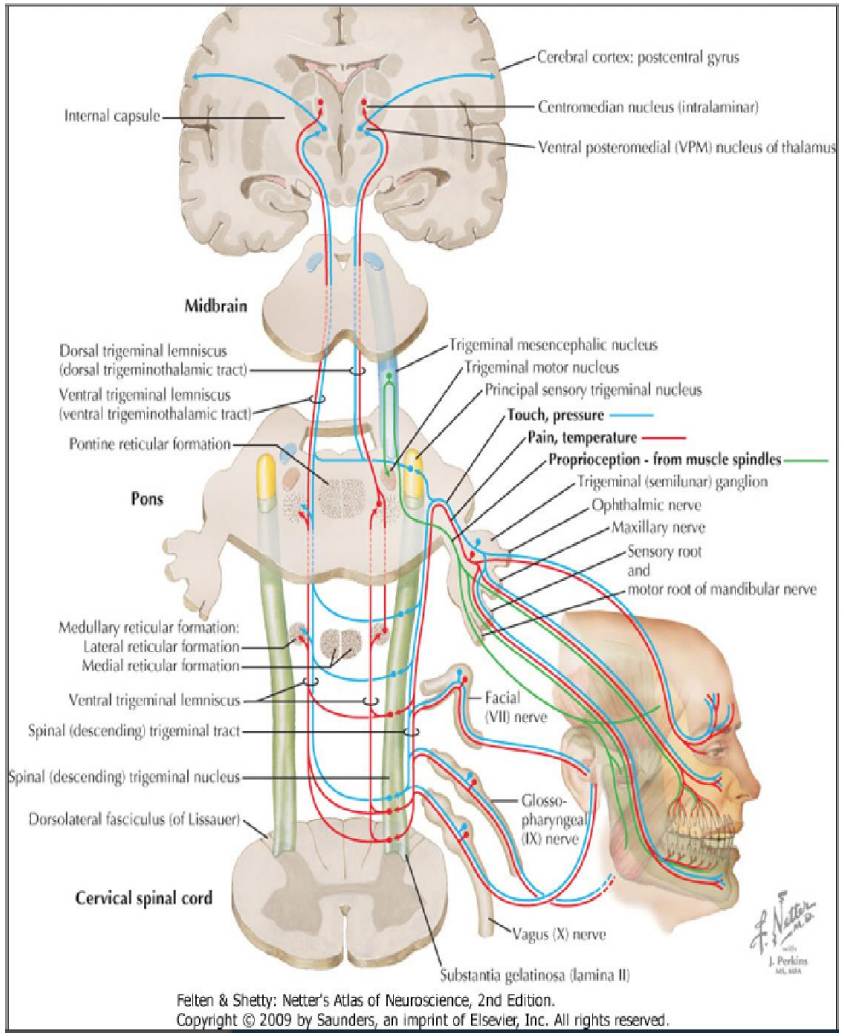
Symptoms of Comorbid Conditions clinically effected by orthopedic TMJ treatment

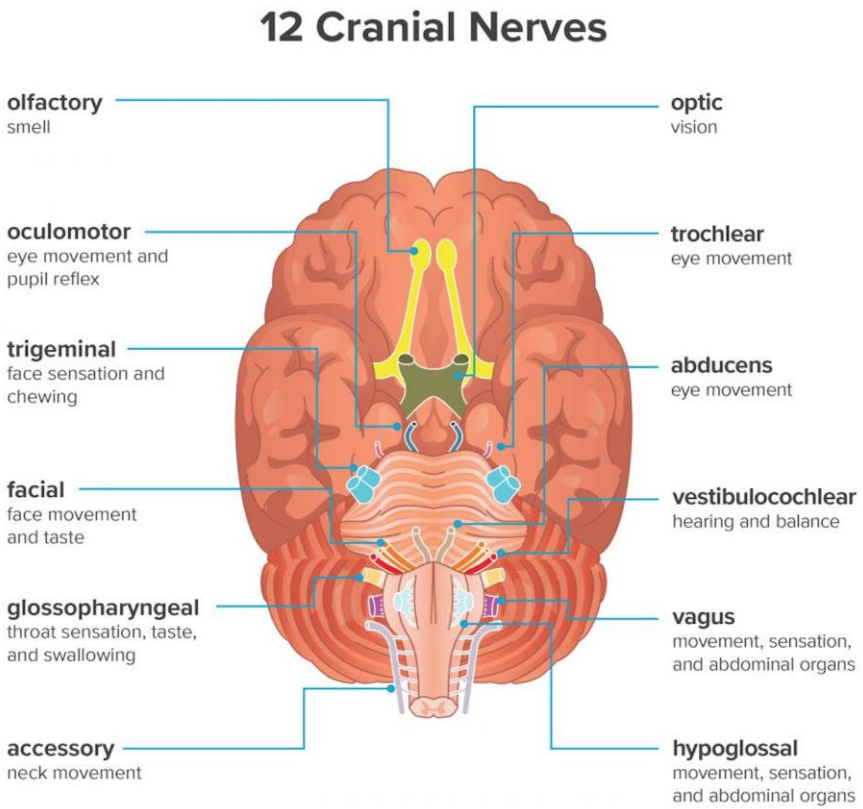
- Spasmodic Torticollis/Cervical Dystonia
- Parkinson’s Disease (Balance, Gait, Posture)
- Tourette's
- Blepharospasm
- Strabismus
- Functional Tremor
- Complex Regional Pain Syndrome/ Reflex Sympathetic Dystrophy
- Fibromyalgia
- Multiple Sclerosis
- Trigeminal Neuralgia
- Hemi-facial Spasm
- Chiari Malformation

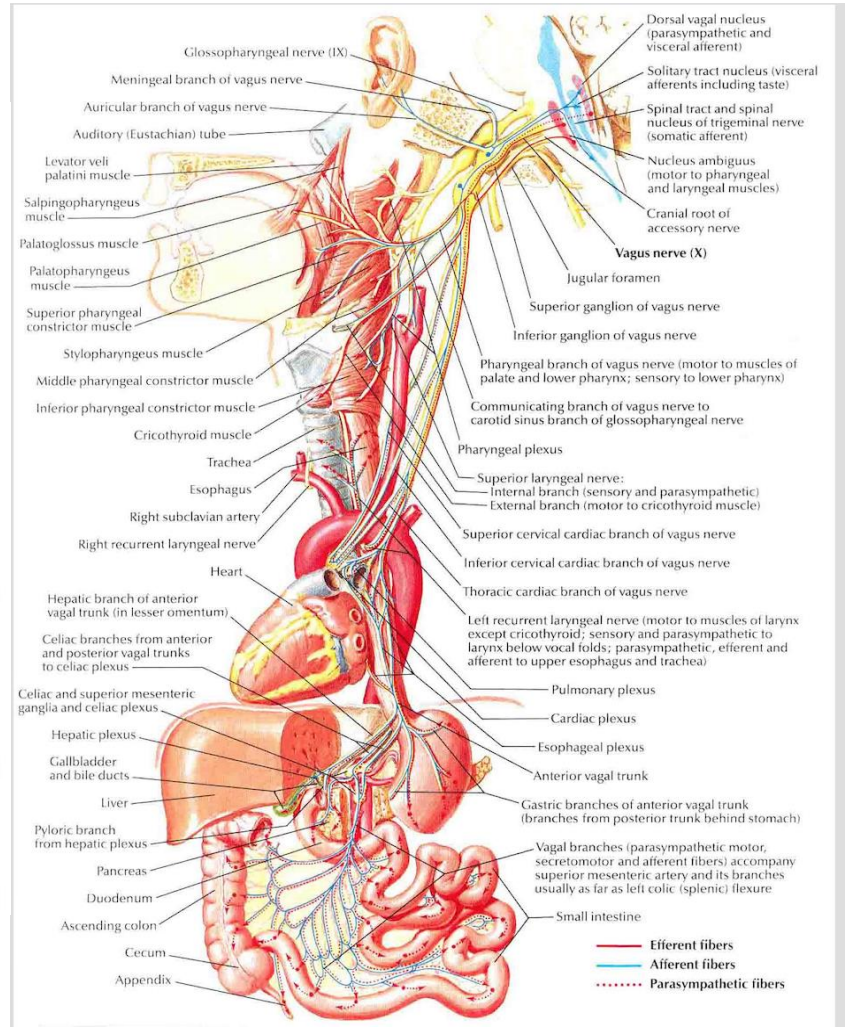
Biomarkers and local responses to Temporomandibular Joint Disorders and Related Neurological Pathologies

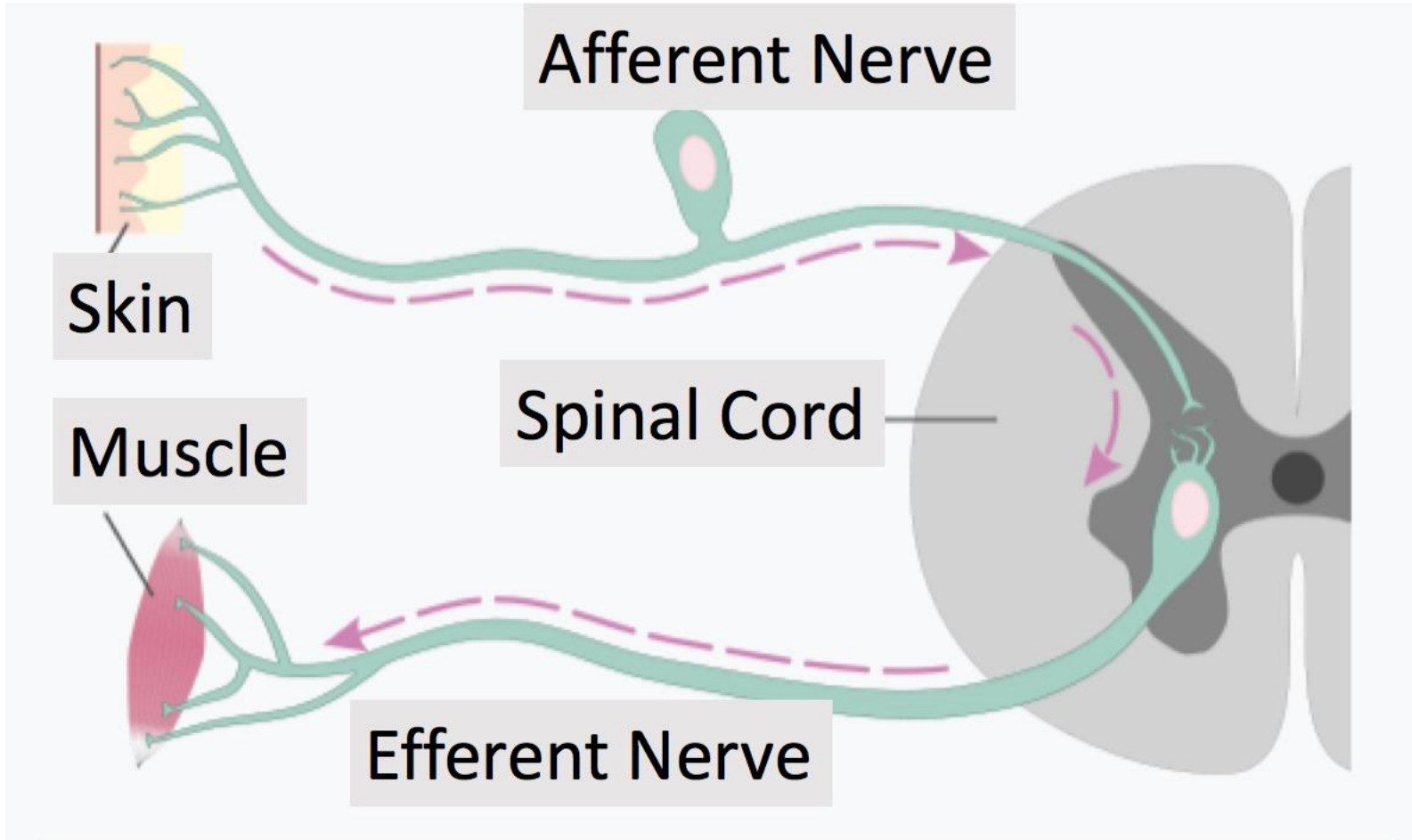
International Pain Foundation
UCLA, November 16, 2019
Andre Barkhordarian M.S, Ph.D.
UCLA School of Dentistry

Cranial Nerves








Afferent Nerve
Skin
Muscle
Spinal Cord
Efferent Nerve

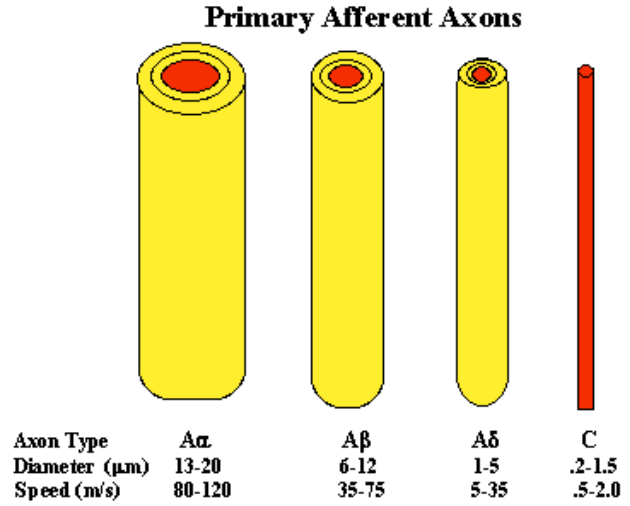
Nerve Fibers

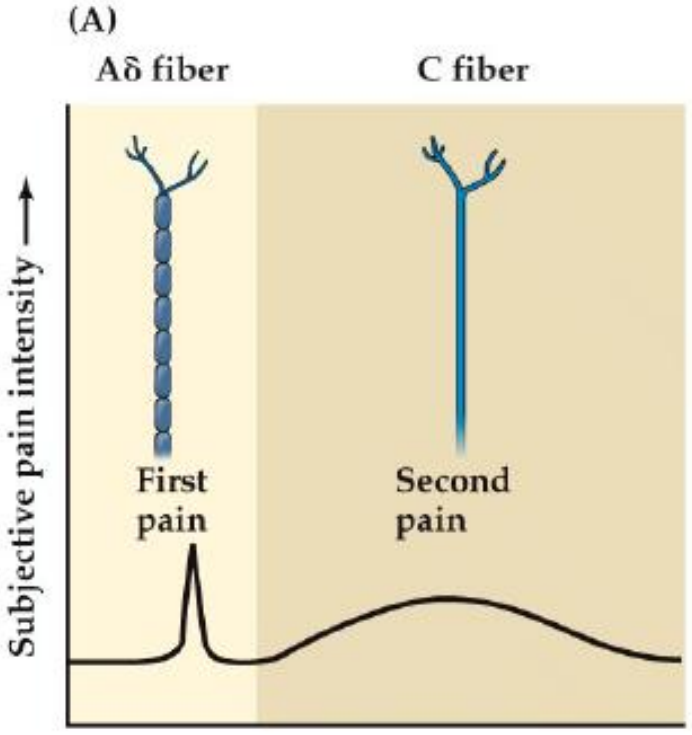
Motor fiber types

Type	Erlanger-Gasser Classification	Diameter	Myelin	Conduction velocity	Associated muscle fibers
α	Aα	13–20 μm	Yes	80–120 m/s	Extrafusal muscle fibers
γ	Aγ	5–8 μm	Yes	4–24 m/s [2][3]	Intrafusal muscle fibers

Sensory fiber types

Type	Erlanger-Gasser Classification	Diameter	Myelin	Conduction velocity	Associated sensory receptors
Ia	Aα	13–20 μm	Yes	80–120 m/s[4]	Responsible for proprioception
Ib	Aα	13–20 μm	Yes	80–120 m/s	Golgi tendon organ
II	Aβ	6–12 μm	Yes	33–75 m/s	Secondary receptors of muscle spindle All cutaneous mechanoreceptors Some Nociceptors [5]
III	Aδ	1–5 μm	Thin	3–30 m/s	Free nerve endings of touch and pressure Nociceptors of neospinothalamic tract Cold thermoreceptors
IV	C	0.2–1.5 μm	No	0.5–2.0 m/s	Nociceptors of paleospinothalamic tract Warmth receptors





Somatosensory Receptors

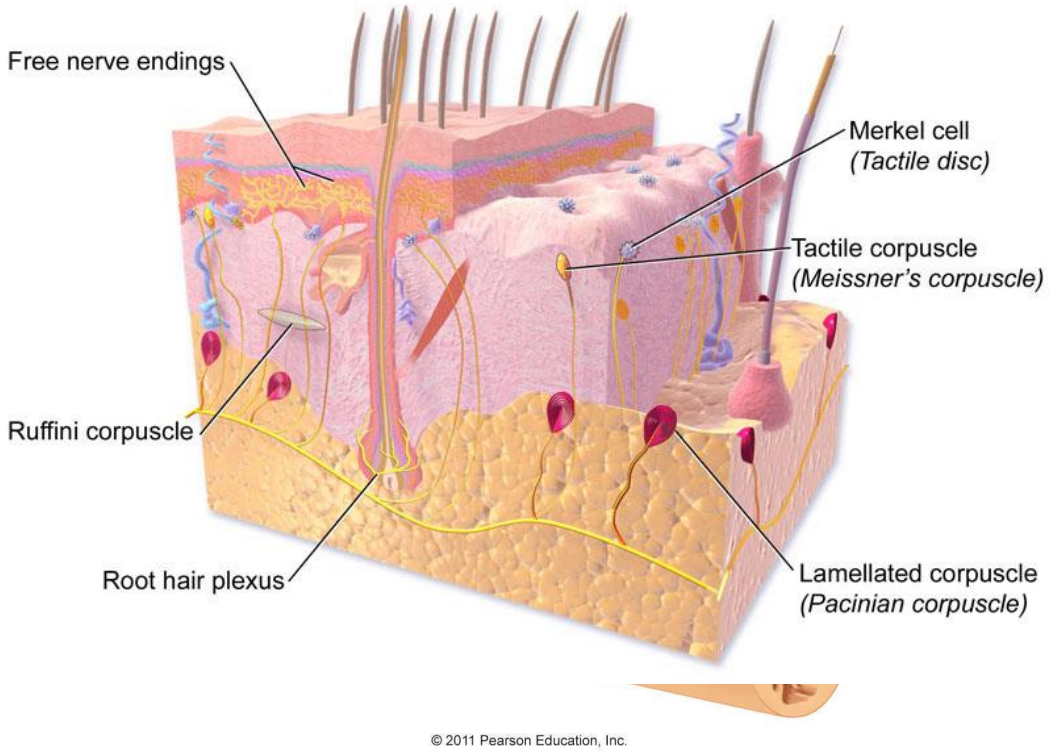
Sensory receptors are classified into five categories: mechanoreceptors, thermoreceptors, proprioceptors, pain receptors, and chemoreceptors.

Somatosensory receptors of the oral tissues are generally divided into mechanoreceptors, nociceptors, and thermoreceptors.

- There are four principal types of mechanoreceptors:
- Meissner corpuscles, rapidly adapting type I, respond to light touch and adapt rapidly to changes in texture.
- Ruffini endings, slowly adapting type II, detect tension deep in the skin and fascia.
- Merkel discs, slowly adapting type I, detect sustained pressure.
- Pacinian corpuscles, rapidly adapting type II, in the skin and fascia detect rapid vibrations.

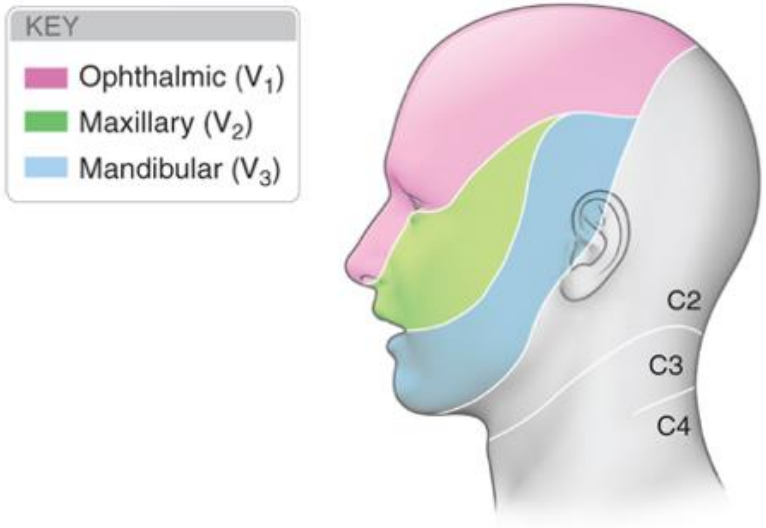
Proprioceptors:

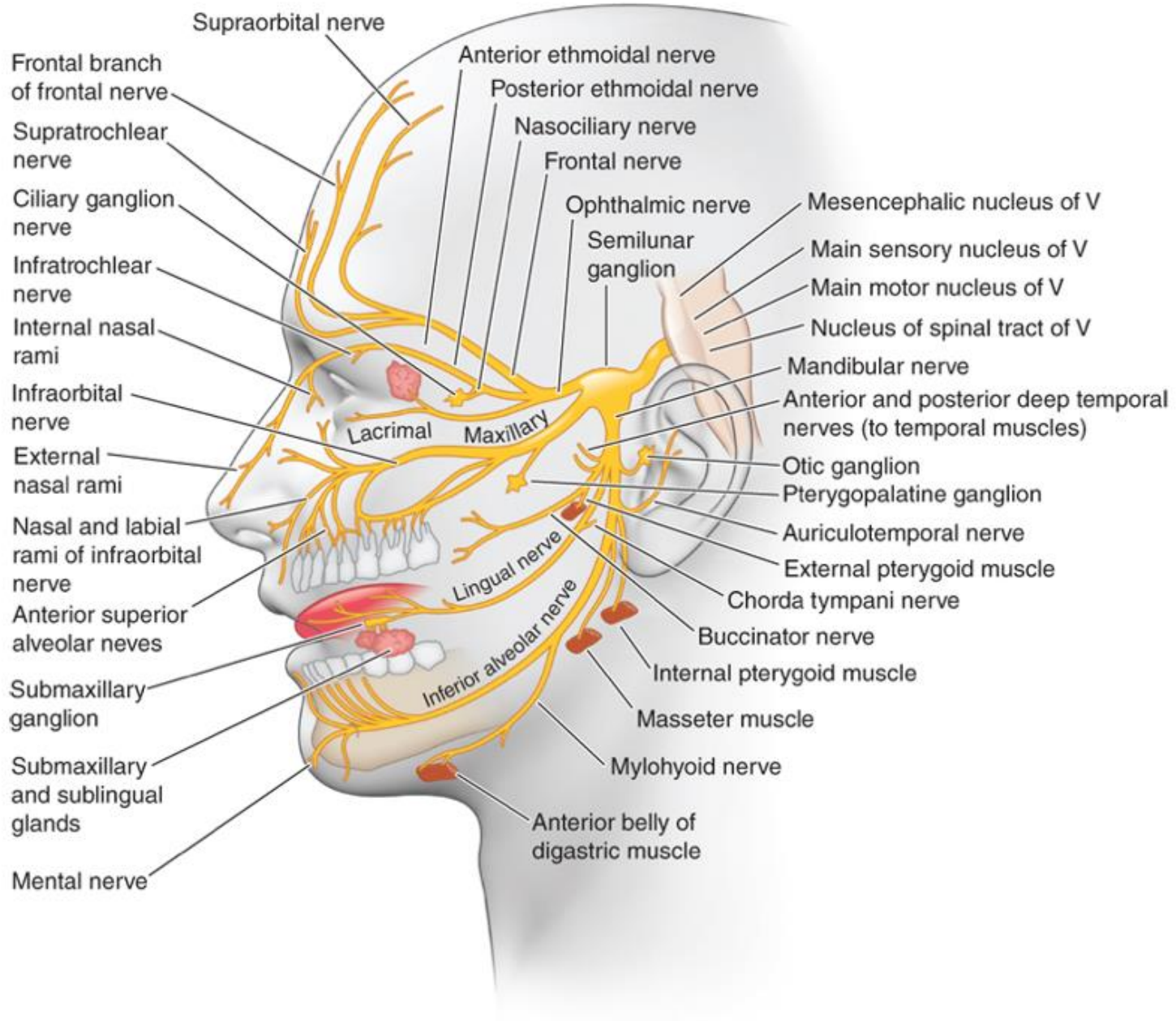
- Muscle Spindles: mechanoreceptors between muscle fibers
- Golgi Tendon Organs: mechanoreceptor

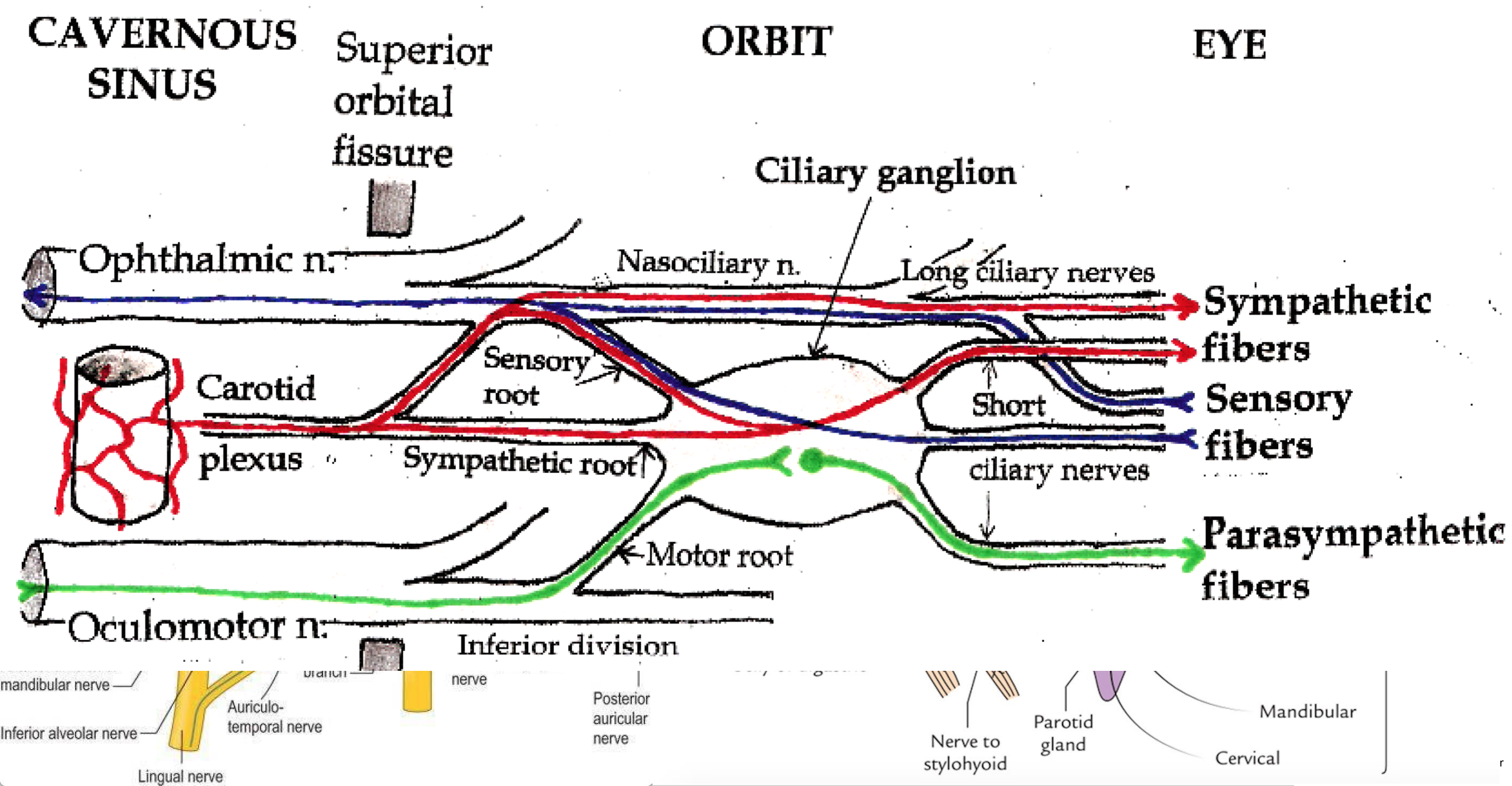


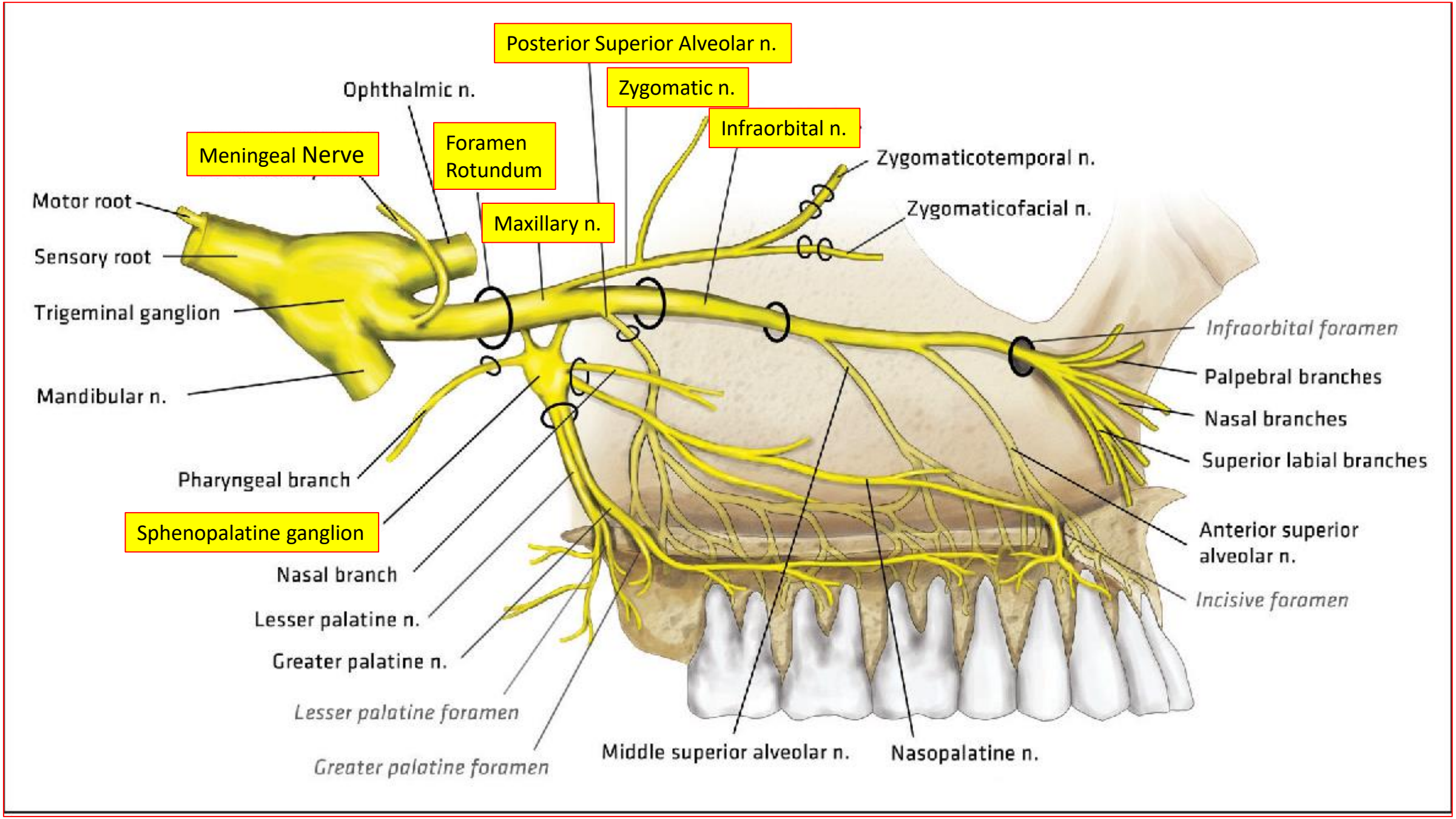
- Free nerve endings detect temperature, mechanical stimuli (touch, pressure, stretch), or nociception (polymodal receptors)
- Most A-delta and C fibers end as free nerve endings.

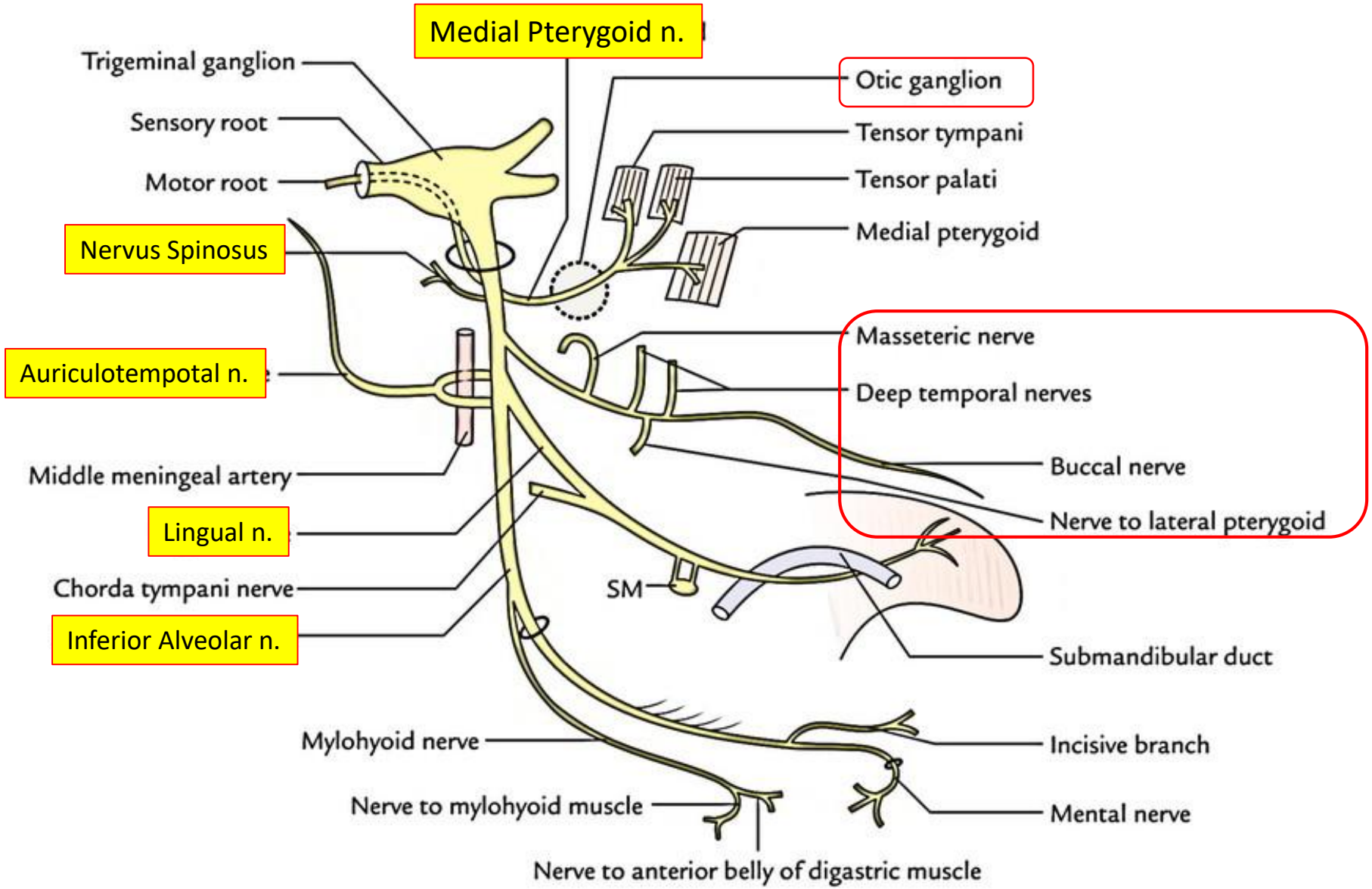
Trigeminal Nerve



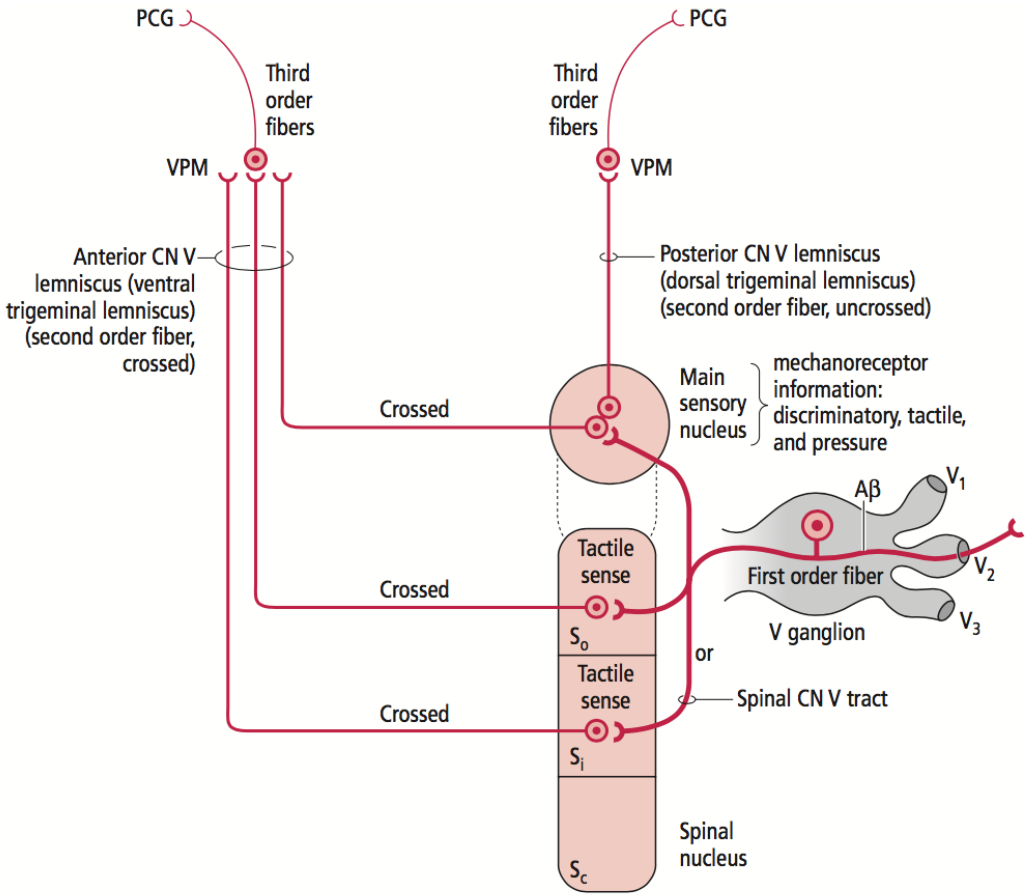



CAVERNOUS SINUS
Superior orbital fissure
ORBIT
EYE
Ciliary ganglion
Ophthalmic n.
Nasociliary n.
Long ciliary nerves
Sympathetic fibers
Sensory fibers
Carotid plexus
Sensory root
Short ciliary nerves
Sympathetic root
Motor root
Parasympathetic fibers
Oculomotor n.
Inferior division
mandibular nerve
Inferior alveolar nerve
Auriculo-temporal nerve
Lingual nerve
nerve
Posterior auricular nerve
Nerve to stylohyoid
Parotid gland
Mandibular
Cervical


Posterior Superior Alveolar n.
Ophthalmic n.
Zygomatic n.
Infraorbital n.
Meningeal Nerve
Foramen Rotundum
Zygomaticotemporal n.
Motor root
Maxillary n.
Zygomaticofacial n.
Sensory root
Trigeminal ganglion
Infraorbital foramen
Palpebral branches
Mandibular n.
Nasal branches
Superior labial branches
Pharyngeal branch
Sphenopalatine ganglion
Anterior superior alveolar n.
Nasal branch
Incisive foramen
Lesser palatine n.
Greater palatine n.
Lesser palatine foramen
Middle superior alveolar n.
Nasopalatine n.
Greater palatine foramen

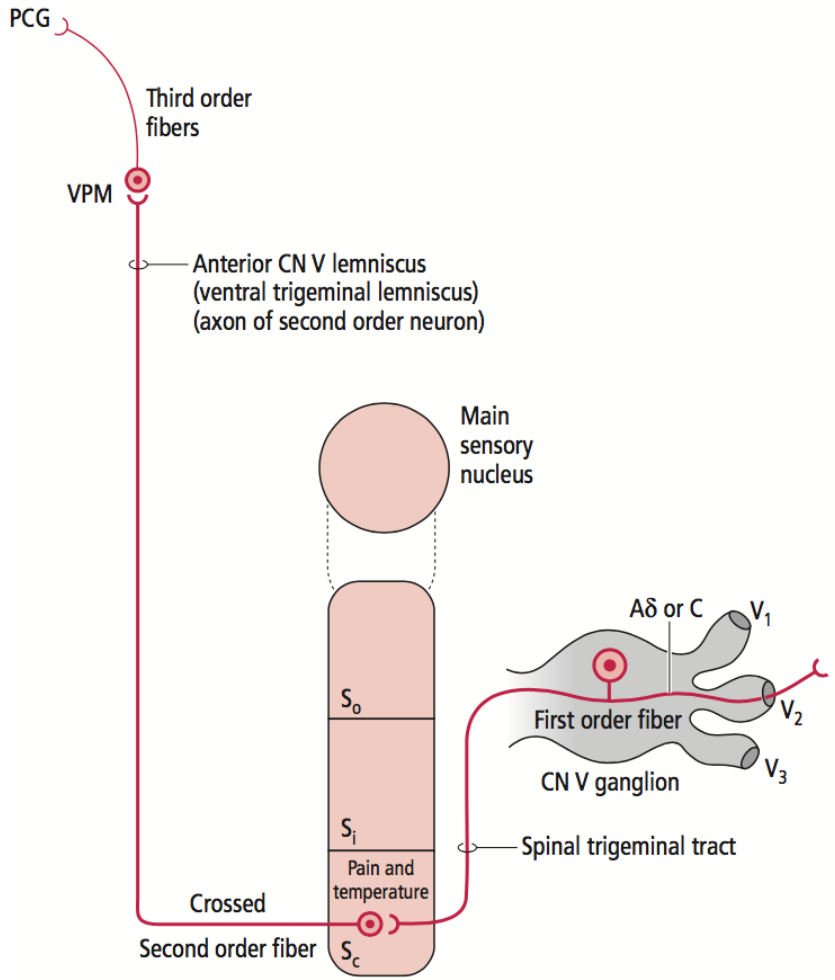

Medial Pterygoid n.
Trigeminal ganglion
Sensory root
Motor root
Nervus Spinosus
Auriculotempotal n.
Middle meningeal artery
Lingual n.
Chorda tympani nerve
Inferior Alveolar n.
Otic ganglion
Tensor tympani
Tensor palati
Medial pterygoid
Masseteric nerve
Deep temporal nerves
Buccal nerve
Nerve to lateral pterygoid
SM
Submandibular duct
Mylohyoid nerve
Incisive branch
Nerve to mylohyoid muscle
Mental nerve
Nerve to anterior belly of digastric muscle

Trigeminal Pathway for Touch & Pressure

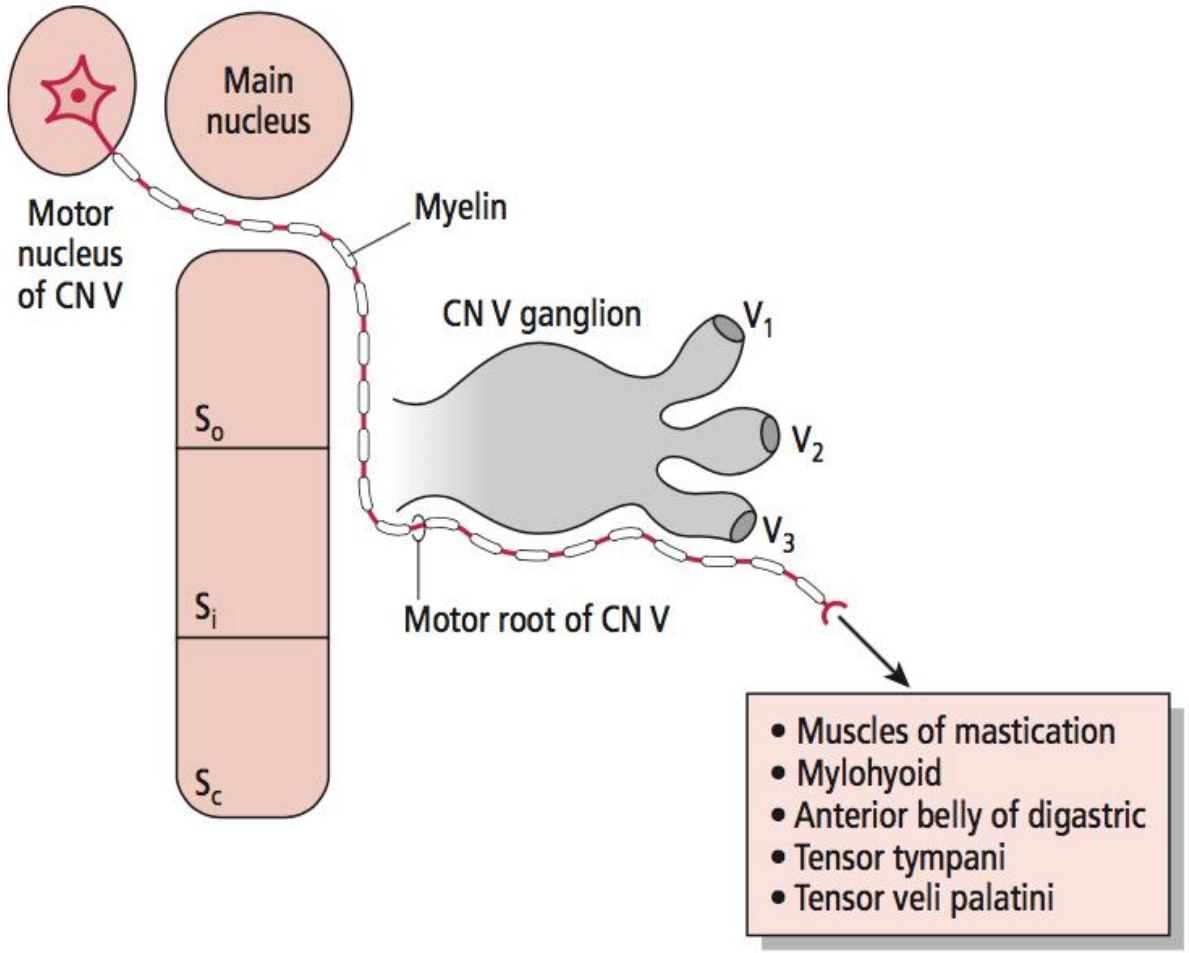


A

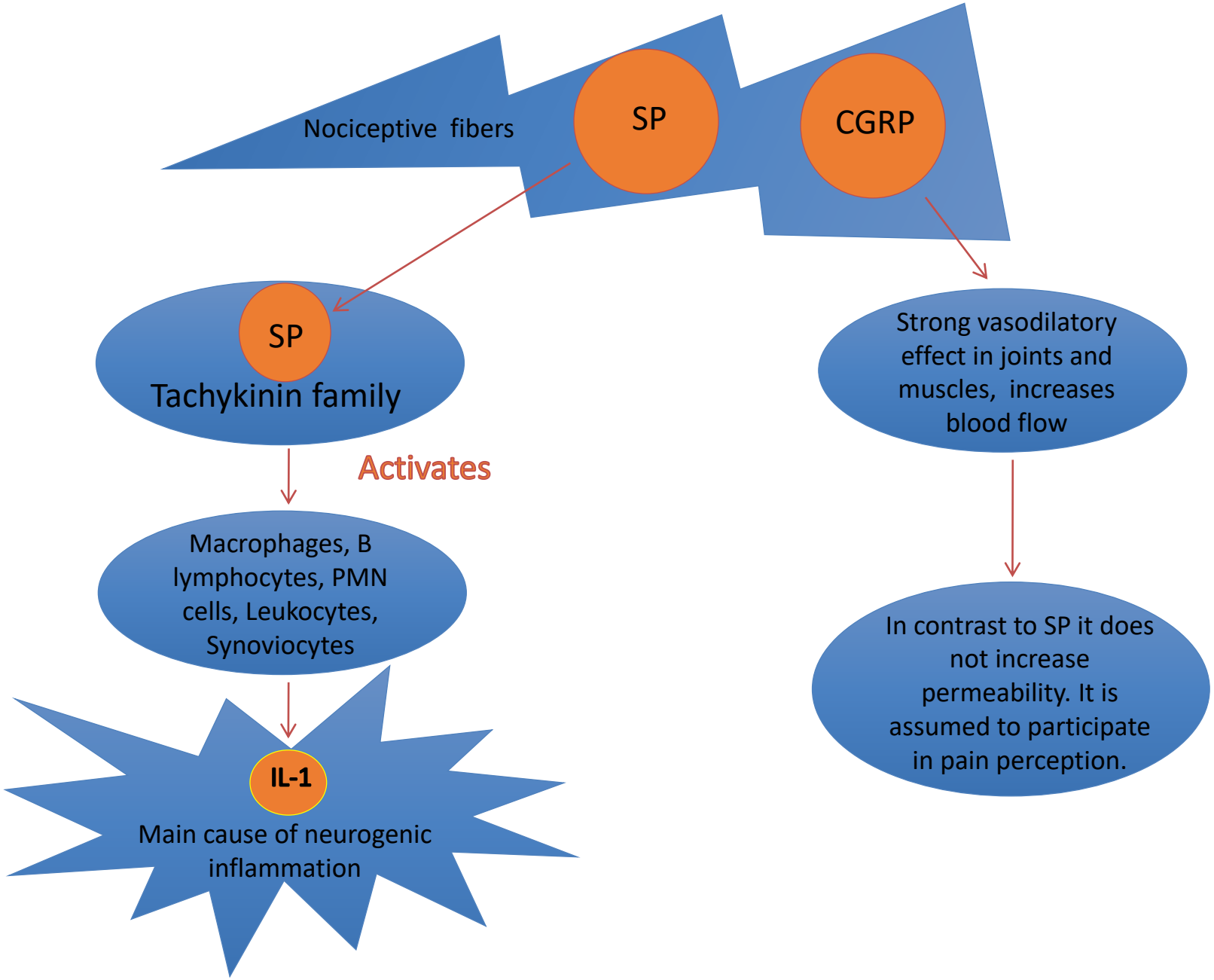
Trigeminal Pathway for Pain & Temperature



Branchiomotor Innervation Trigeminal Nerve



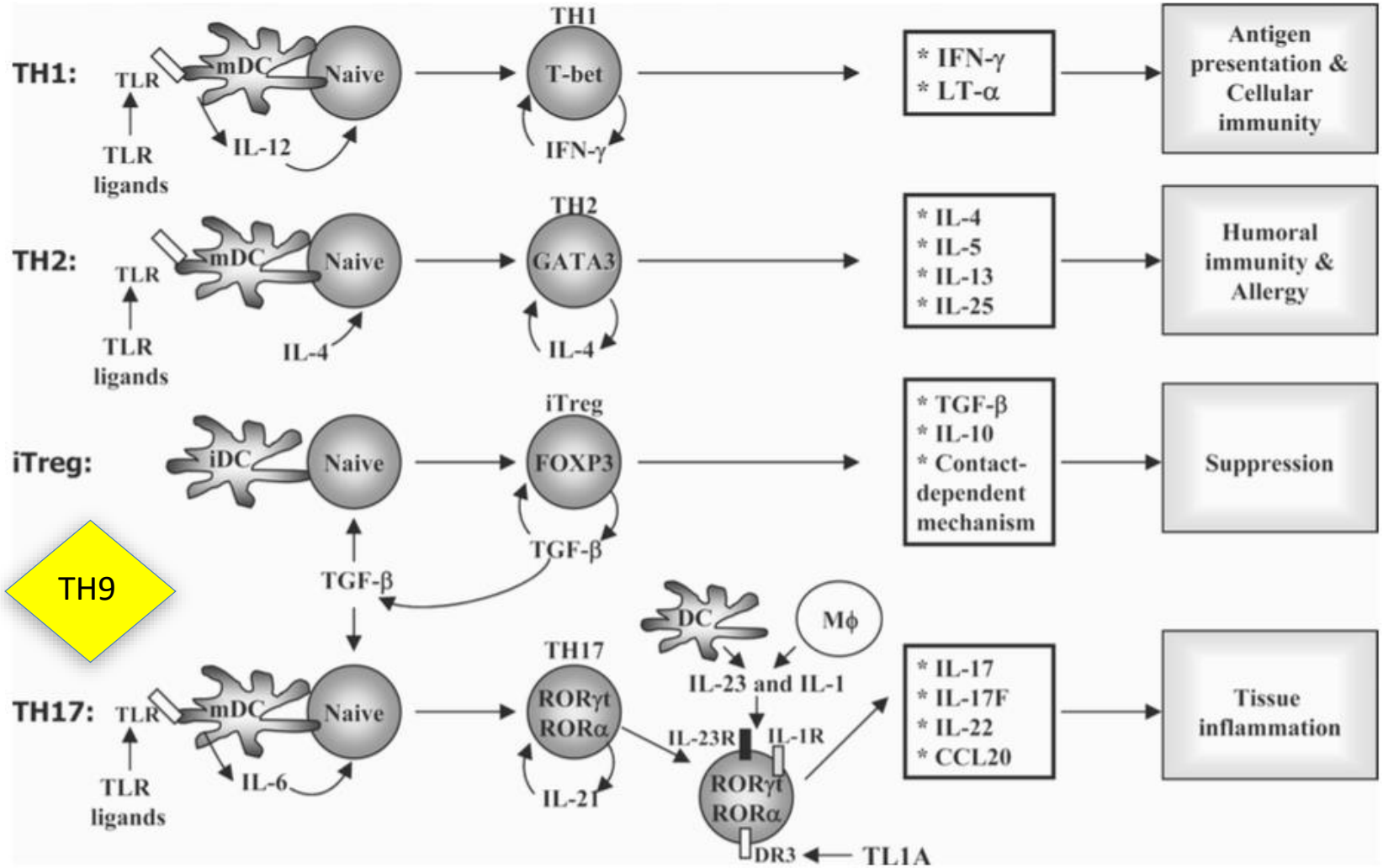
Neuropeptides



Regulation and Function of inflammatory TH Cells

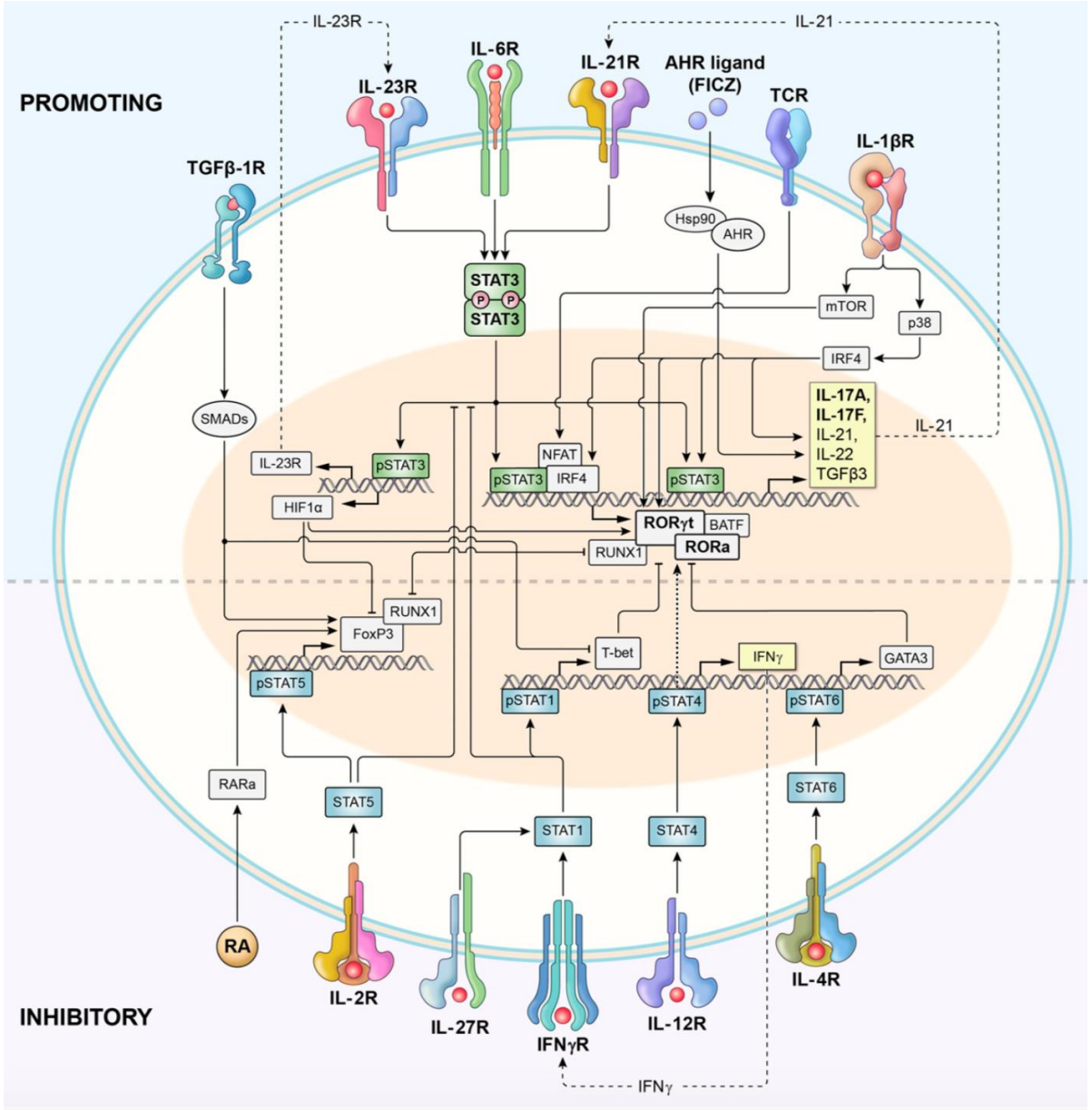
PAMPs

DAMPs



Gustavo J, et al. **Regulation and Function of Proinflammatory TH17 Cells.** Ann. N.Y. Acad. Sci. 1143: 188–211 (2008)

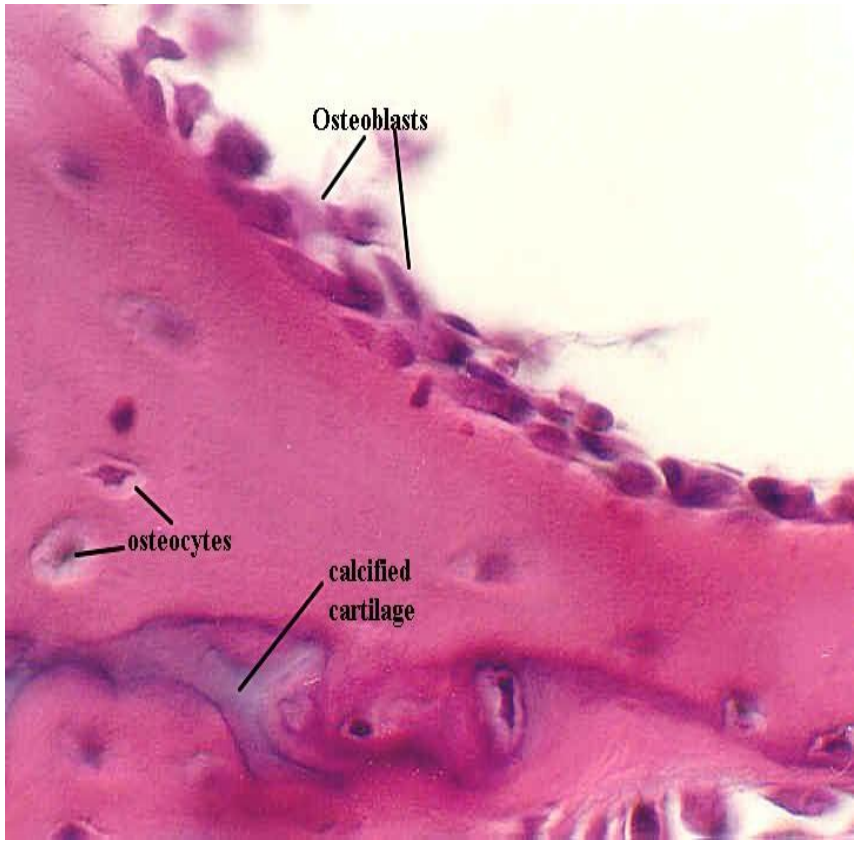
The Signaling and Transcriptional Regulation of Th17 Polarization

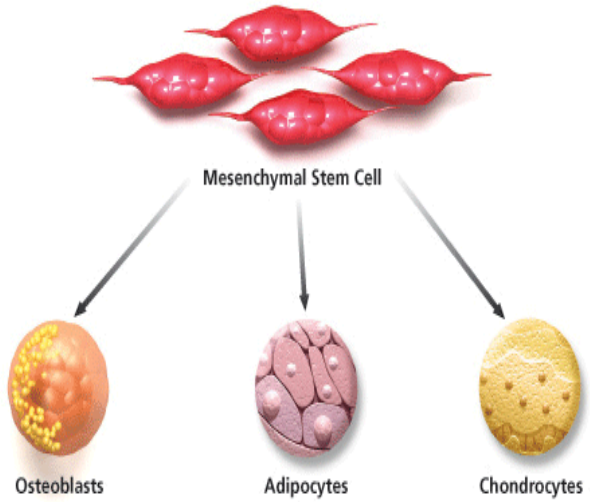


Muranski P, Restifo N. Essentials of Th17 cell commitment and plasticity. BLOOD, 28 MARCH 2013 Vol. 121, No. 13

Osteoblasts

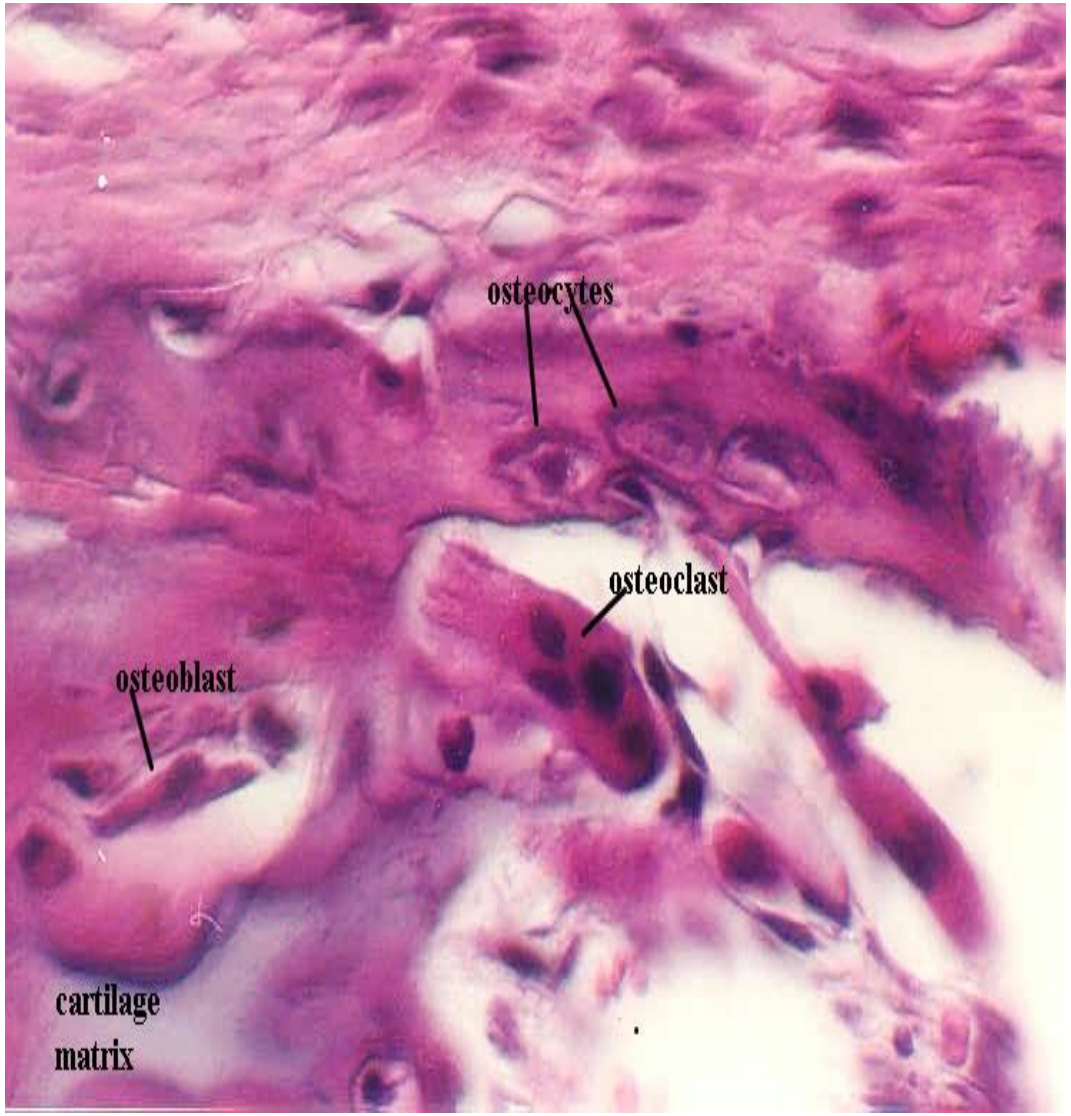
- Mononucleated cells derived form terminally differentiated MSCs
- Line surface of the bone and produce osteoid
- Become bone cells or osteocytes



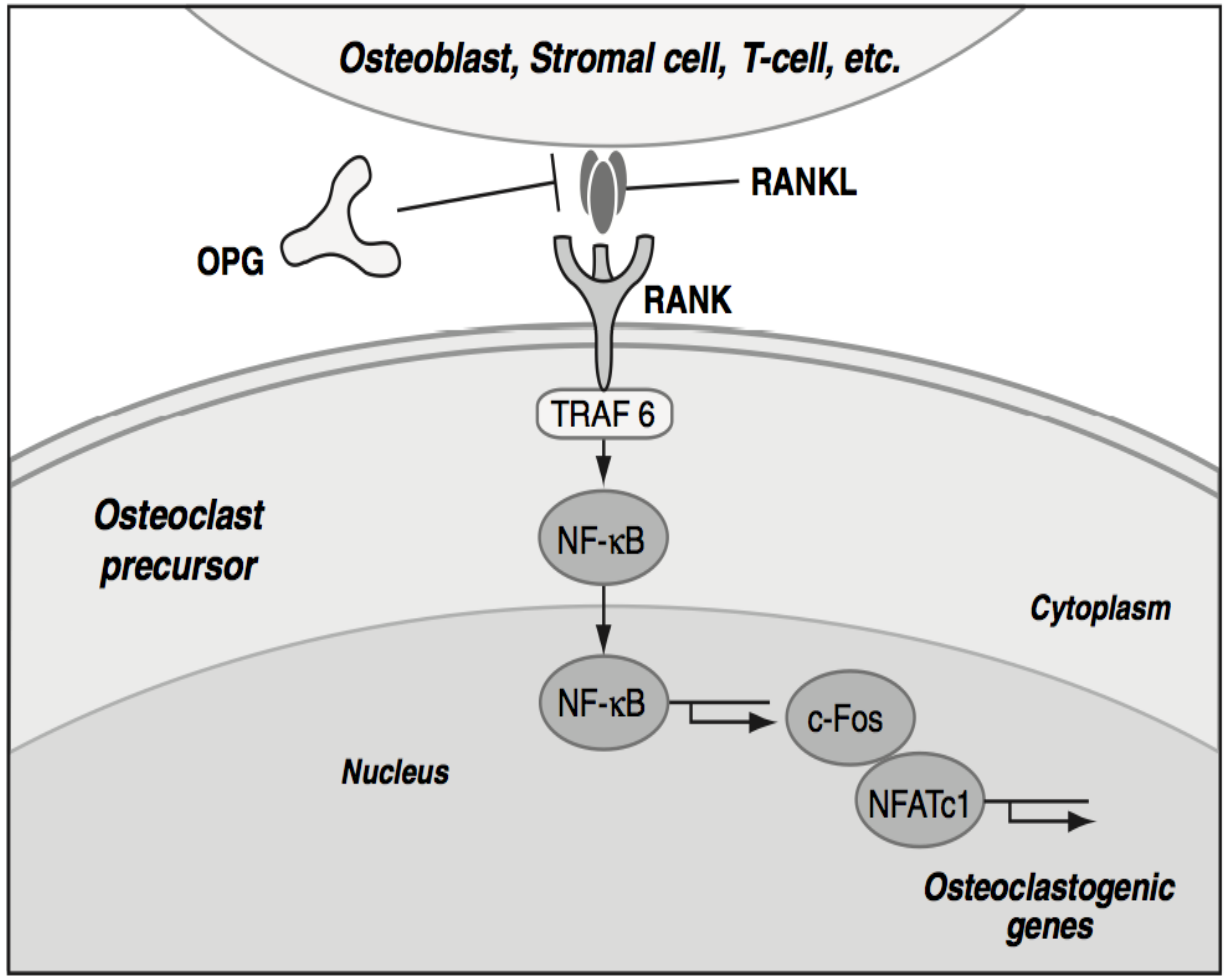


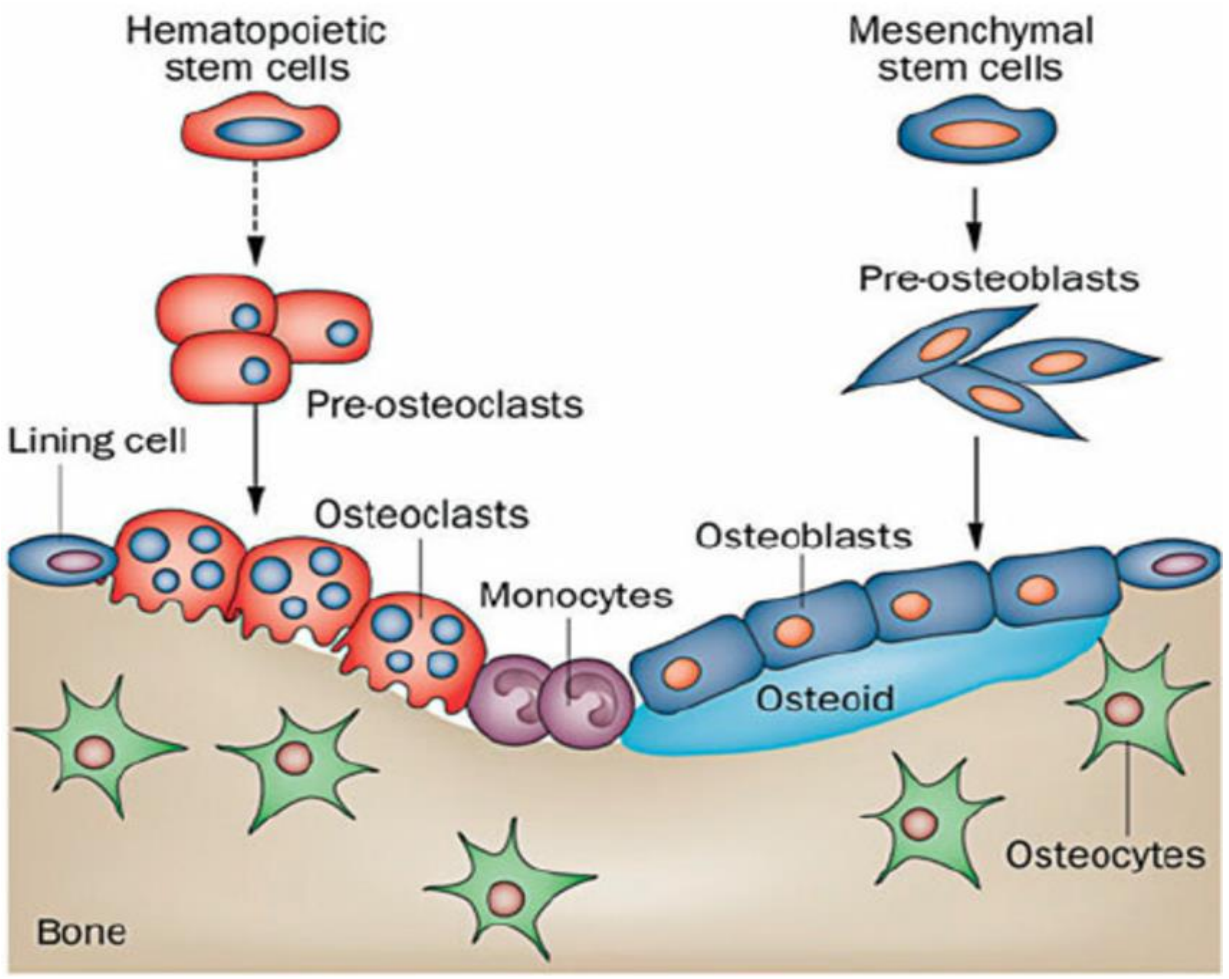
Osteoclasts

- Derived from hematopoietic stem cells (myeloid-monocyte and macrophage precursor cells)
- Multinucleated cells responsible for bone resorption
- Release lysosomes, organic acids and hydrolytic enzymes and beak down bone matrix
- Two parts: ruffled border, clear zone



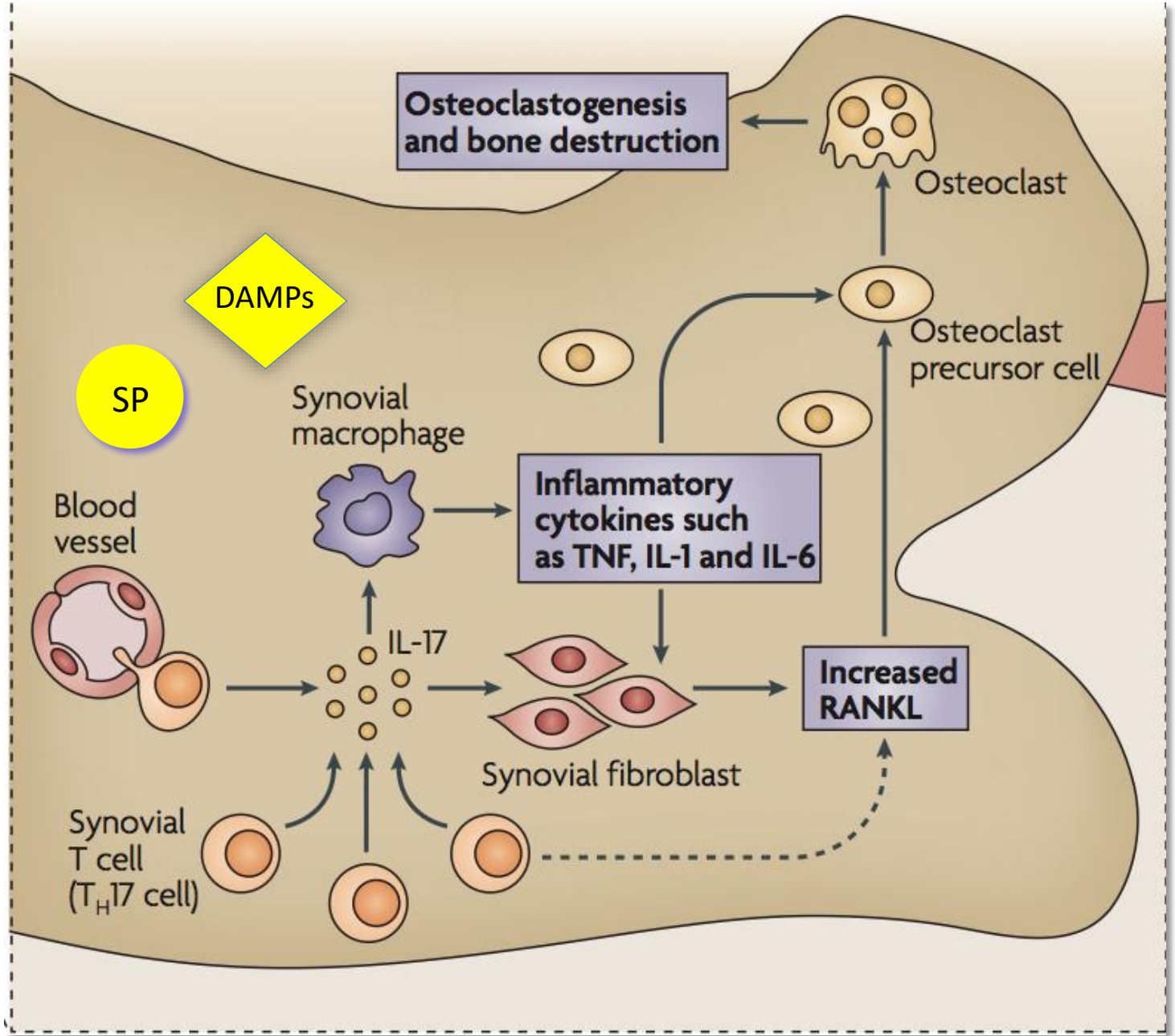
RANK, RANKL and OPG

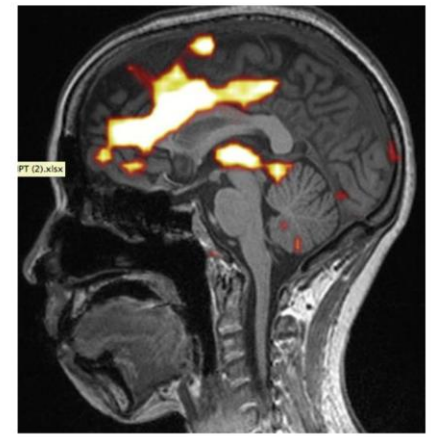




Alghazali KM, et al. **Bone-tissue engineering: complex tunable structural and biological responses to injury, drug delivery, and cell-based therapies. Drug Matabolism Rev. vol. 47, 2015**

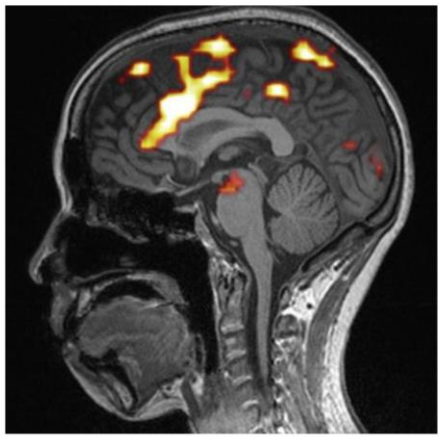
At Molecular Level





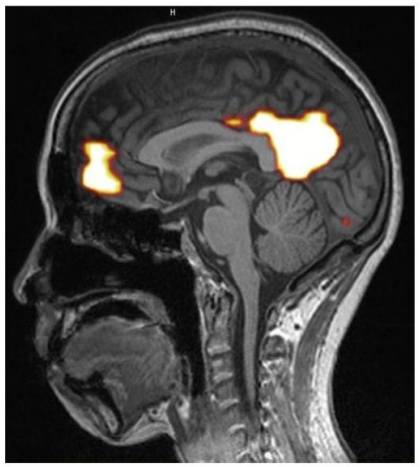
SAG Salience without Retainer

Patient #2



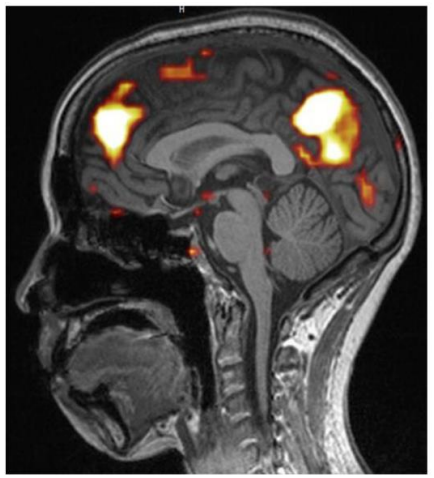
SAG Salience with Retainer

Patient #2



SAG DMN without Retainer

Patient #2



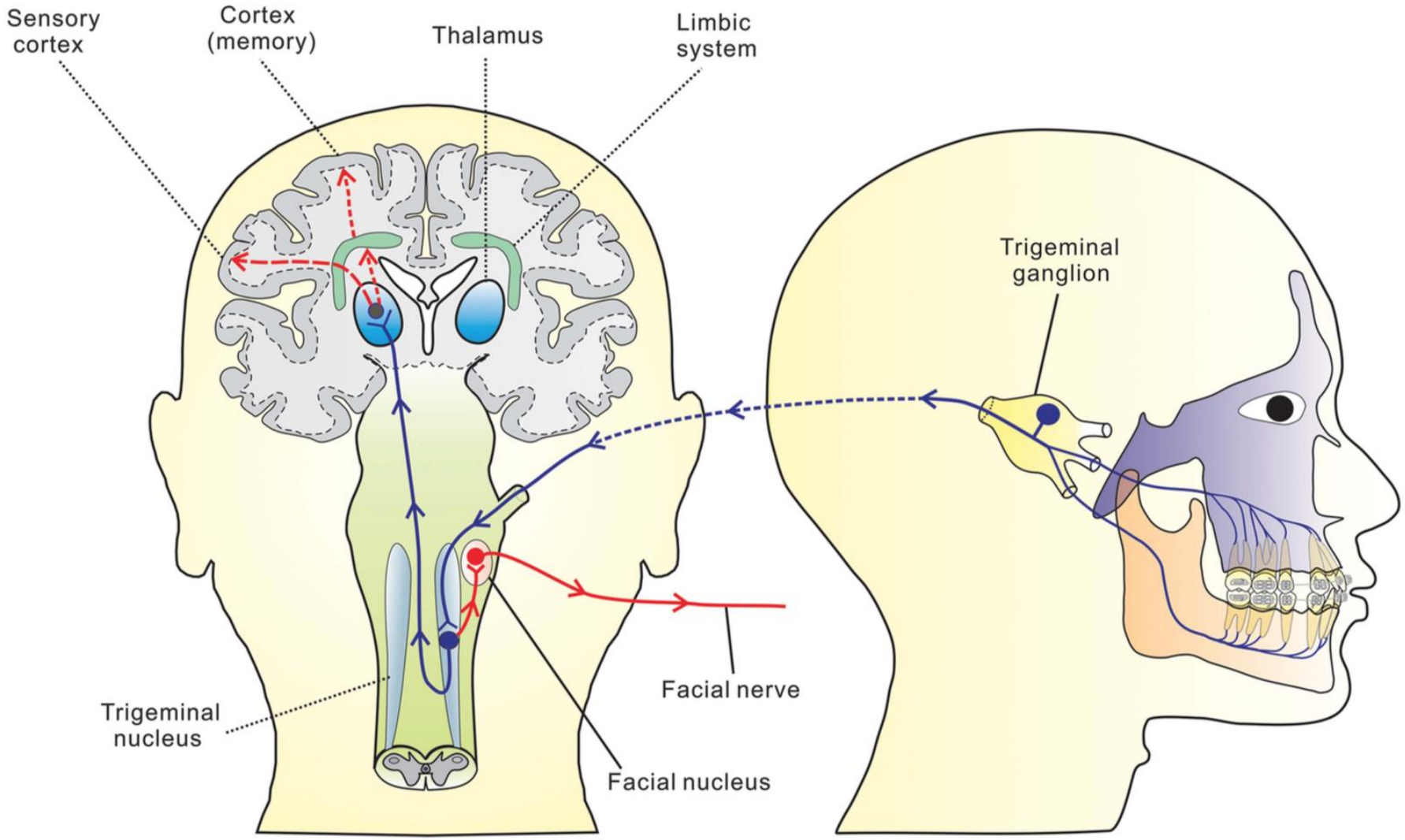
SAG DMN with Retainer

Patient #2

- MPRAGE.
- Resting state network was studied using BOLD. Scans were then post processed on a 3D workstation and the (ICA) was performed separating out the various networks.
- Arterial Spin Labeling.
- Tractography and fractional anisotropy.

Cervical Dystonia

Tourettes



Hu Long, Yan Wang, Fan Jian, Li-Na Liao, Xin Yang and Wen-Li Lai, Current advances in orthodontic pain. International Journal of Oral Science (2016) 8, 67–75.

Hemi-facial spasm

Thank you