Treatment Approach to Facial Pain and Patient Selection for Neuromodulation

Narayan R. Kissoon, MD

Assistant Professor of Neurology and Anesthesiology

Mayo Clinic

March 17-20th, 2022

AAPM 2022 38TH ANNUAL MEETING

DISCLOSURE

Relevant Financial Relationship(s)

SAB of Bright Minds Biosciences, Ltd

Investigator Initiated Study (IIS) grant with Nevro Corporation, but for an unrelated topic (Diabetic Peripheral Neuropathy)

Off Label Usage

Off-label use will be discussed in this presentation

Learning Objectives

- Discuss the evaluation for facial pain and initial management
- Review the different neuromodulation treatments available for facial pain
- Propose a treatment algorithm for when to incorporate neuromodulation in the treatment of facial pain and headache
- Identify patient factors that would guide selection of neuromodulation treatments

Outline

- Evaluation
- Medical management
- Treatment algorithm
- Neuromodulation Treatment Options

History and Physical Exam

Unilateral or bilateral
Dermatomal pattern or spans multiple nerve distributions
Characteristics – neuropathic or autonomic features
Anesthesia (sensory loss)
Episodic or constant pain
Cutaneous triggers, age, or triggered by eating
Pain with jaw movement +/- popping/clicking of jaw
SICCA symptoms
History of rash, trauma, surgery, or dental procedures
Neurological signs and/or symptoms

Differential Diagnosis for Facial Pain

- Trigeminal Neuralgia
- Trigeminal Neuropathy
- Sjogren's Syndrome +/- Trigeminal Neuropathy
- Post-Herpetic Neuralgia/Neuropathy
- SUNCT/SUNA Syndrome
- Great Auricular Neuralgia
- Temporomandibular Joint Disorder
- Burning Mouth Syndrome
- First Bite Syndrome
- Persistent Idiopathic Facial Pain
- Central Neuropathic Pain

Classical Trigeminal Neuralgia
(+/- concomitant persistent facial pain)

A. At least 3 attacks of unilateral facial pain

B. Trigeminal nerve distribution (typically V2/V3 distribution)

C. 3 of 4 characteristics:
   1. Paroxysmal attacks - fraction a second up to 2 minutes
   2. Severe intensity
   3. Electric shock-like, shooting, stabbing, or sharp in quality
   4. Precipitated by innocuous stimuli to the affected side of the face

D. No neurological deficits or alternative explanations to pain

Previously called tic douloureux = painful tic (muscle contraction)
Concomitant persistent facial pain is related to central sensitization

(IHS 2018)

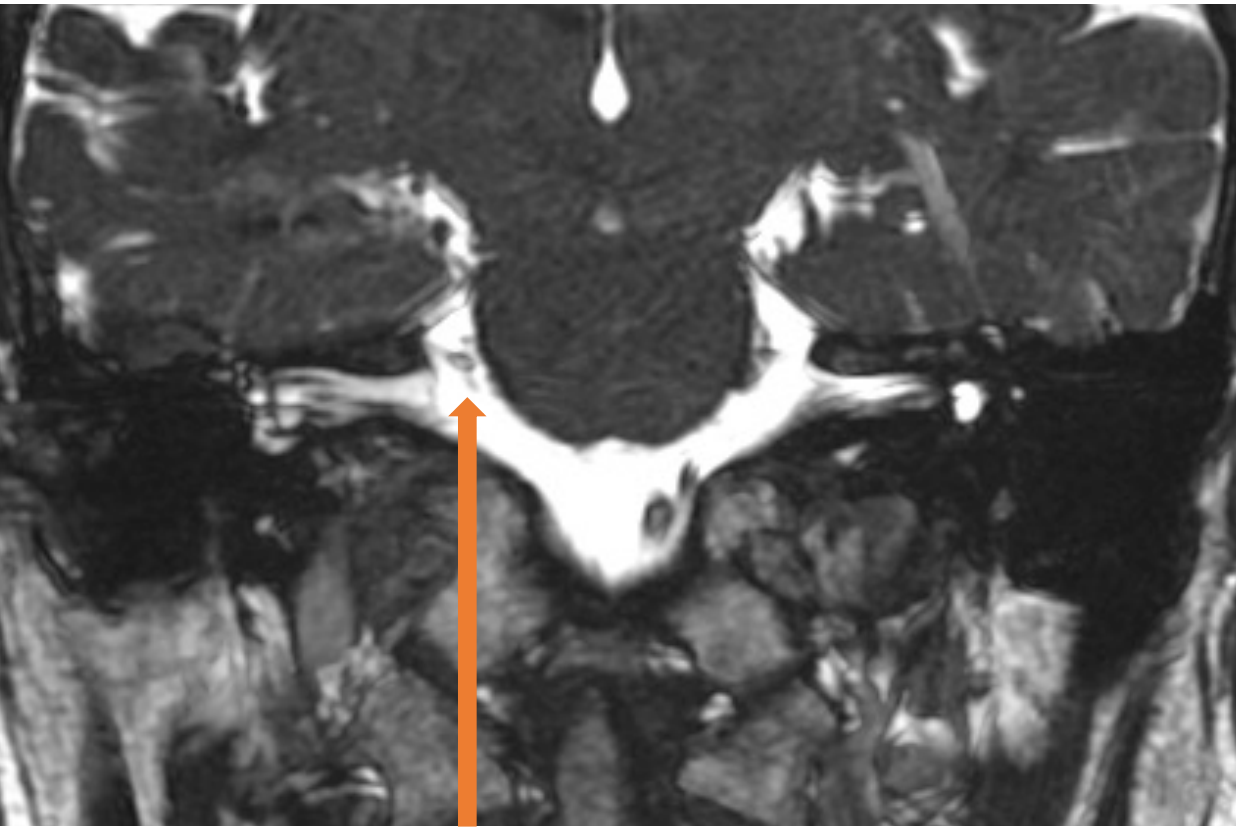
Trigeminal Neuralgia

1. Classical Trigeminal Neuralgia - Demonstration on MRI or during surgery of neurovascular compression
   - purely paroxysmal
   - with concomitant continuous pain
2. Secondary Trigeminal Neuralgia
   - Underlying disease known to cause or explain the neuralgia (e.g. multiple sclerosis, mass lesion)
   - Can be accompanied by sensory changes suggestive of a trigeminal neuropathy, but paroxysmal pain is predominant pain type
3. Idiopathic Trigeminal Neuralgia – No findings demonstrated for neurovascular compression or secondary cause

74 yo F with 10-year history of right V2-V3 distribution pain

- Onset of facial pain 10 years prior and started intermittent occurring up to 5 times a day lasting minutes in duration.
- Pain is in the right upper maxilla (teeth) and right mandible (teeth). The pain has 2 components 1 that is a dull constant pain and the other is a superimposed electric jabbing pain that is paroxysmal. The pain can occur multiple times a day for a week in duration and then stop. She can go periods of time up to months even a year without pain.
- Over the past year she has had daily episodes of pain with provoked while brushing her teeth and her ability to eat has been limited as swallowing and drinking can trigger her pain.
- Exam: Normal with intact trigeminal nerve distribution sensation.
- Management:
  - Oxcarbazepine 300 mg twice daily (dose limited by hyponatremia)
  - Gabapentin 600 mg twice daily (dose limited by side effect of sedation)

Right Suboccipital Microvascular Decompression (MVD)



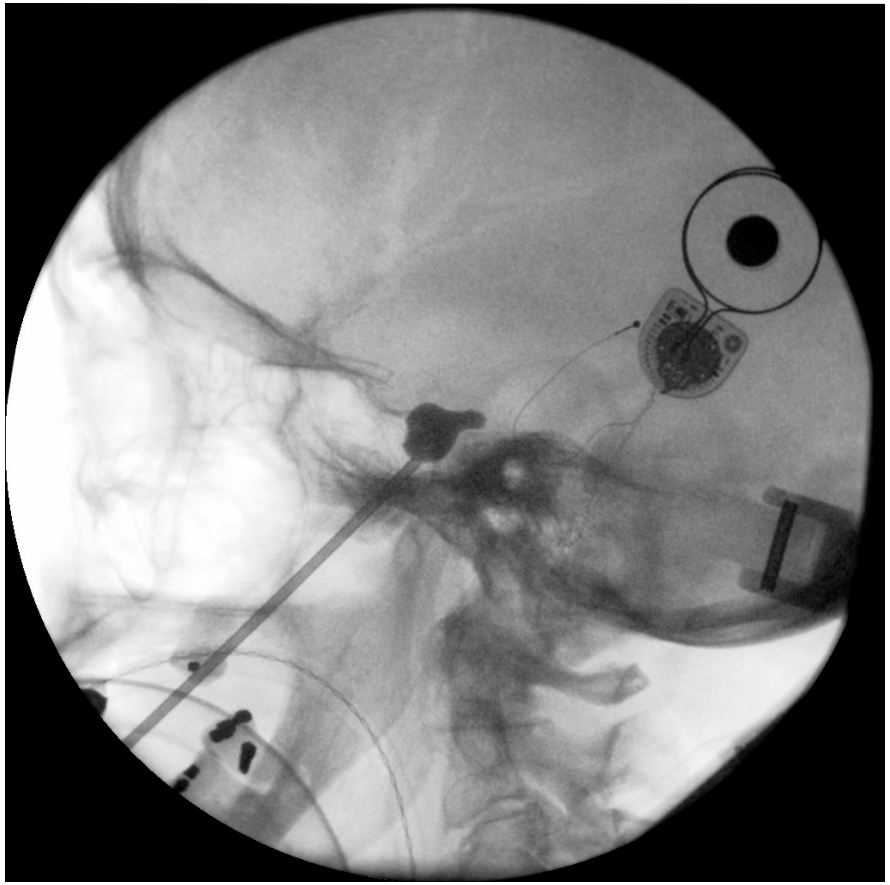
- Large superficial bridging cerebellar vein was cauterized
- Large vein along the underside of the 5th nerve was cauterized and divided.
- Small branch of the SCA artery was displaced
- Intraoperative compression of trigeminal nerve
- Six months following microvascular decompression, trigeminal neuropathic pain had resolved and she was tapered off anticonvulsants
- Right trigeminal distribution anesthesia was present and expected from intentional compression of trigeminal nerve

Vascular loop with compression of trigeminal nerve and probable demyelination

Diagnosis: Classical Trigeminal Neuralgia with concomitant continuous pain

Classical Trigeminal Neuralgia

- Demonstration on MRI or during surgery of neurovascular compression
- Severe electric shock-like, shooting, stabbing, or sharp pain
- Unilateral pain, cutaneous triggers, V2-3 distribution, older patients (age > 50), Paroxysmal attacks - fraction a second up to 2 minutes
- In medically refractory classical TN, MVD is treatment of choice
- Otherwise, RFA, glycerol rhizotomy, and percutaneous balloon compression are alternative options



(Data from: Gronseth et al 2008, ICHD)

Medications for Trigeminal Neuralgia

- Four times daily dosing as with neuralgias rarely have to worry about compliance.
- Trigeminal Neuralgia
    1. Carbamazepine: (Max 1200 mg total daily dose) – risk for hyponatremia, periodic lab monitoring.
    2. Oxcarbazepine: (Max 2400 mg total daily dose) – better tolerated, but more likely to have hyponatremia.
    3. Baclofen (at higher doses avoid abrupt cessation), Lamotrigine (slow titration to avoid Stevens-Johnson Syndrome), or Gabapentin (can titrate as high as 900 -1200 mg four times daily)
    4. Phenytoin – not ideal for long term use due to osteoporosis and gingival hyperplasia, periodic lab monitoring.
- Consider IV fosphenytoin or IV lidocaine (but not with concomitant phenytoin) for rescue.

27 yo F otherwise healthy presenting with left V2 distribution pain

- 4-month history of pain in left upper teeth/gums, severe stabbing/jabbing pain – "nerve being ripped out of face"
- Triggers: brushing her teeth, exposure to loud noises or suddenly bright light, eating cold or hot foods or beverages or drinking cold or cold or hot beverages, cold drafts on her cheek, and chewing can all cause severe volleys of pain lasting from a couple of minutes up to hours.
- Exam: Normal with intact sensation.
- Management:
  - Carbamazepine 1200 mg per day in divided doses
  - Gabapentin 300 mg three times daily
  - Prior trial of baclofen up to 20 mg three times daily
  - Left infraorbital nerve block worsened pain

Is this Trigeminal Neuralgia?

27 yo F otherwise healthy presenting with left V2 distribution pain

- MVD resolves pain for several months followed by recurrence.
- Percutaneous balloon compressions x 3 result in short improvements in pain, followed by recurrence.
- Now has constant dull achy pain with intermittent attacks of pain that resolve with IV fosphenytoin.
- 1 year later, the patient develops right sided pain similar to left. MRI shows atrophy of the left trigeminal nerve and no evidence of demyelinating lesions.
- Predictors of a response to MVD: Memorable onset, cutaneous triggers, and unilateral pain

Is this Trigeminal Neuralgia?

(Tyler-Kabara et al. 2002)

Medications for Facial Pain

Use characteristics of pain and comorbidities to determine medication

1. Gabapentin - (can titrate as high as 900 -1200 mg four times daily)
2. TCA – amitriptyline/nortriptyline (50 mg to 100 mg).
   - No higher than 50 mg if on concurrent SSRI/SNRI.
   - If sedating or weight gain, then consider protriptyline (10 mg twice daily during day).
   - Effective for burning type pain.
   - ECG for patients over age of 50.
3. Carbamazepine or Oxcarbazepine: risk for hyponatremia, and needs periodic lab monitoring
4. Lamotrigine (slow titration to avoid Stevens-Johnson Syndrome).

78 yo M presenting with facial pain after carotid endarterectomy

- Right V2-3 distribution pain with onset after right carotid endarterectomy
- Dysphagia after carotid endarterectomy and had feeding tube placed.
- When transitioned to an oral diet, that is when pain started.
- Specifically, citrus foods provoke his pain.
- Pain occurs with the first bite of food, but then improves with subsequent bites.

Diagnosis?

First Bite Syndrome

Proposed Mechanism: Disruption of sympathetic innervation of the parotid gland after carotid endarterectomy

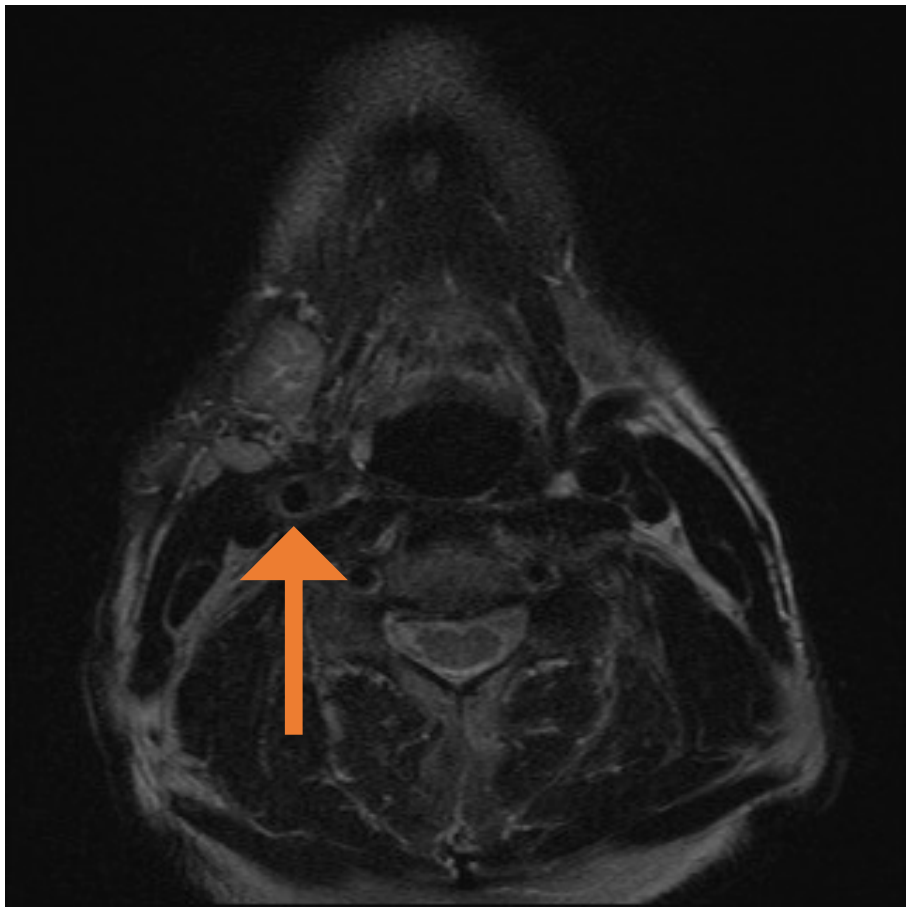
TCA (take advantage of anticholinergic properties)

If TCA ineffective, then consider parotid gland botulinum toxin injections

Important to image the neck if no history of neck surgery as a clear inciting incident

Management for our patient:

- Amitriptyline titrated up to 50 mg at night improved pain, but sedation, mental clouding, and dry mouth was not tolerated so the amitriptyline was tapered off.
- Proceeded with right parotid gland Botulinum toxin injections and he had 1.5 months of pain relief with the initial set of injections (1250 units of rimabotulinumtoxinB divided into two sites) and so with subsequent injection the dose was raised to 1500 units and he transitioned care locally.
- Plan was to add on nortriptyline in the future if monotherapy with botulinum toxin injections did not adequately treat pain.



Sluder's Neuralgia – more aptly named SUNCT/SUNA syndrome

(Short lasting unilateral neuralgiform headache with cranial autonomic symptoms)

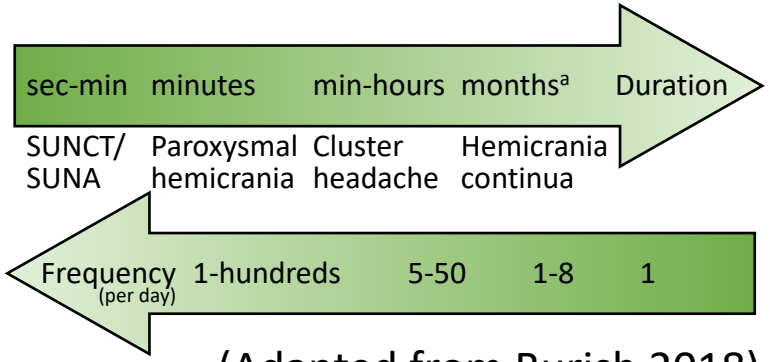
A. At least 20 attacks occurring with a frequency of at least one a day

B. Moderate or severe unilateral head pain, with orbital, supraorbital, temporal and/or other trigeminal distribution, lasting for 1–600 seconds and occurring as single stabs, series of stabs or in a saw-tooth pattern

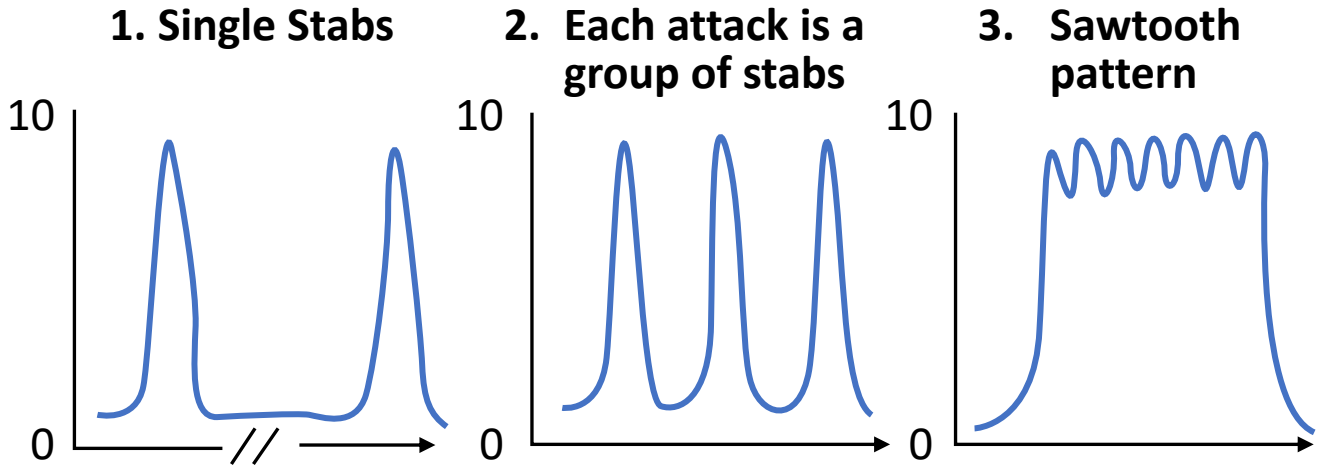
C. At least one of the following five cranial autonomic symptoms or signs, ipsilateral to the pain:
   1. conjunctival injection and/or lacrimation
   2. nasal congestion and/or rhinorrhea
   3. eyelid edema
   4. forehead and facial sweating
   5. miosis and/or ptosis

First line medications to treat are typically – lamotrigine, topiramate

(Data from: ICHD)



(Adapted from Burish 2018)



(Adapted from Cohen et al 2006)

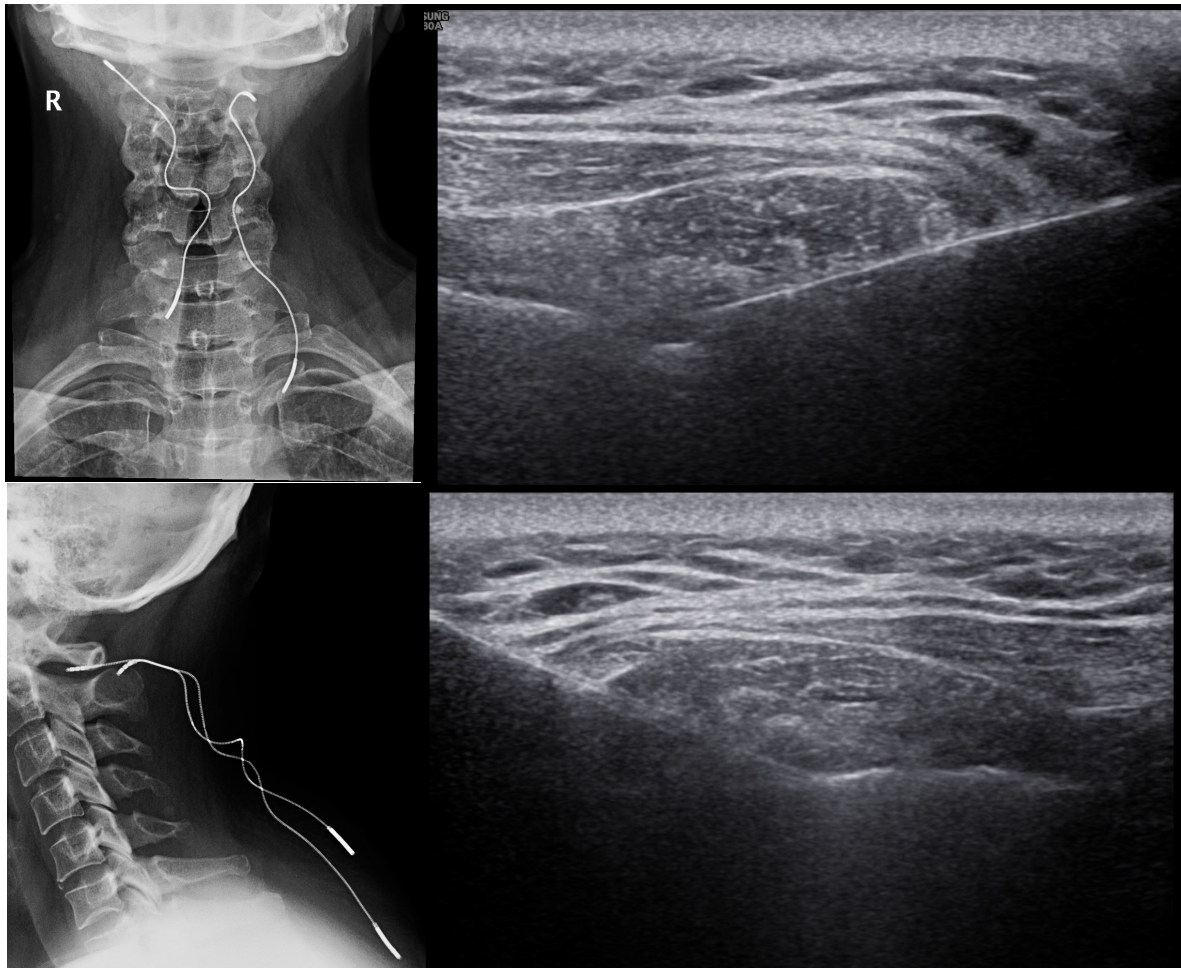
Interventional Treatment of Trigeminal Autonomic Cephalalgias

- SUNCT/SUNA - Short lasting unilateral neuralgiform headache with cranial autonomic symptoms (prospective studies)
- Cluster Headache (prospective studies)
- Limited evidence for ONS in Hemicrania continua and Paroxysmal Hemicranial (Case Series and Reports)

(Data from: Narouze 2009, Ornello 2020, Fontaine 2017)

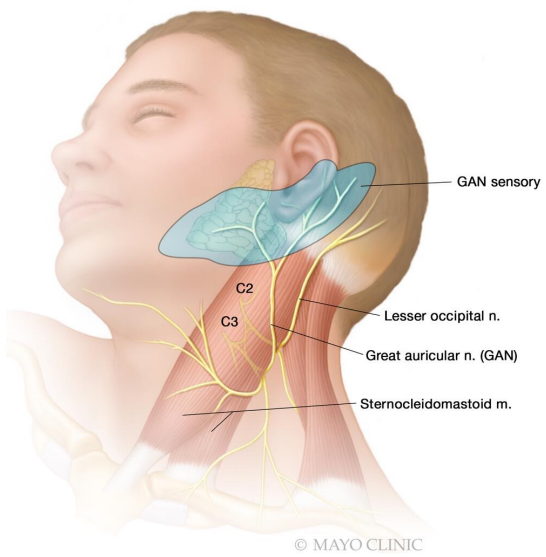
RF treatment of the SPG

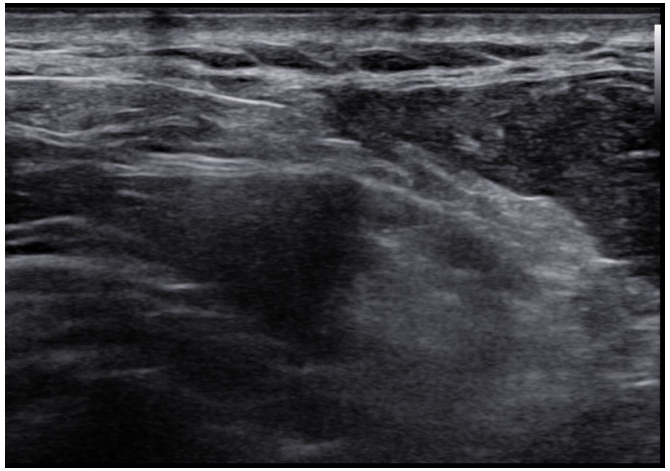
Occipital Nerve Stimulation



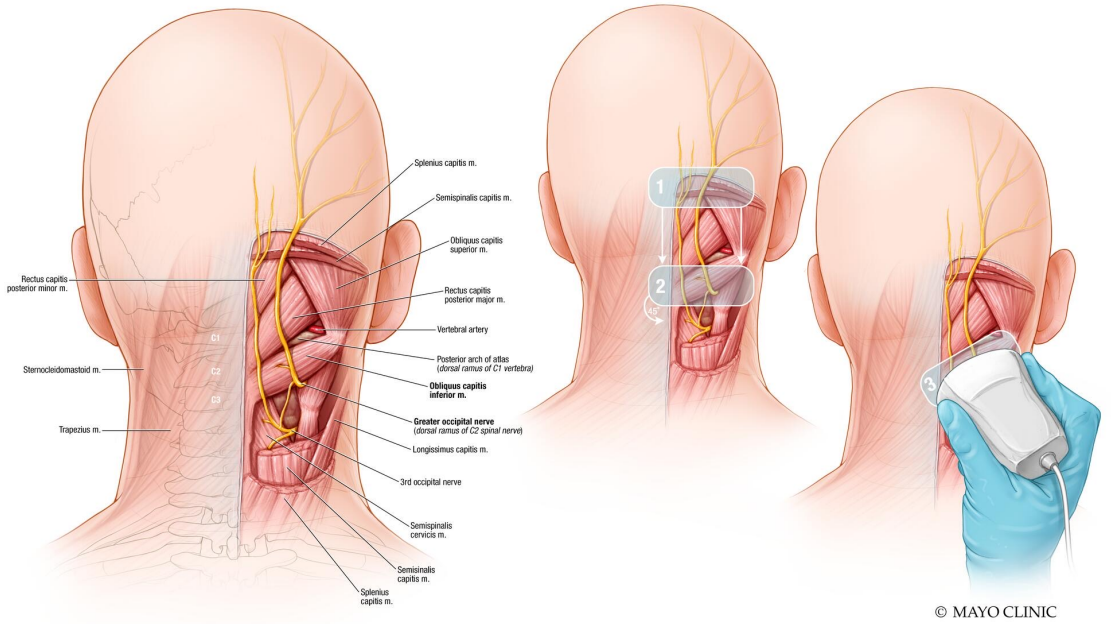
Peripheral Nerve Stimulation – some devices cleared for use in areas of the head and neck

Great Auricular Nerve Stimulation:
Case series showing benefit in Great Auricular Neuralgia





Occipital Nerve Stimulation:
Case series showing benefit in for Occipital Neuralgia



(Duvall et al 2020, Salmasi et al 2020, Pingree et al 2017)

Facial Pain of Central Origin

Conditions

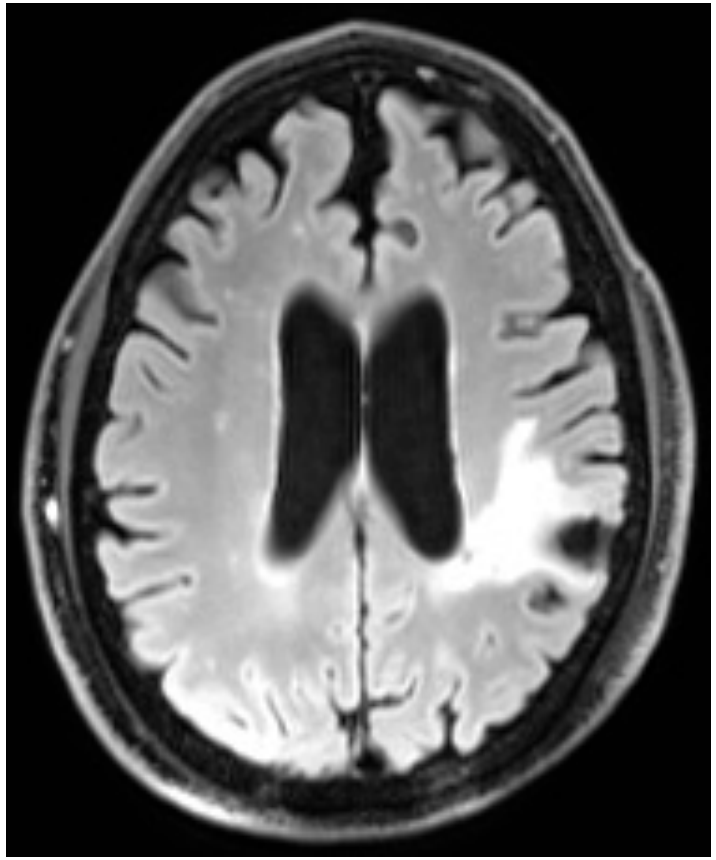
- Trigeminal Neuropathy – Deafferentation pain
- Central Pain Syndrome (e.g. post-stroke pain, demyelinating disease)

Transcranial Magnetic Stimulation (rTMS) with MRI localization

- Contralateral low frequency (e.g. < 5 Hz) rTMS of motor cortex ineffective
- Contralateral high frequency (e.g. 10-20 Hz) rTMS of motor cortex effective

Motor Cortex Stimulation (MCS)

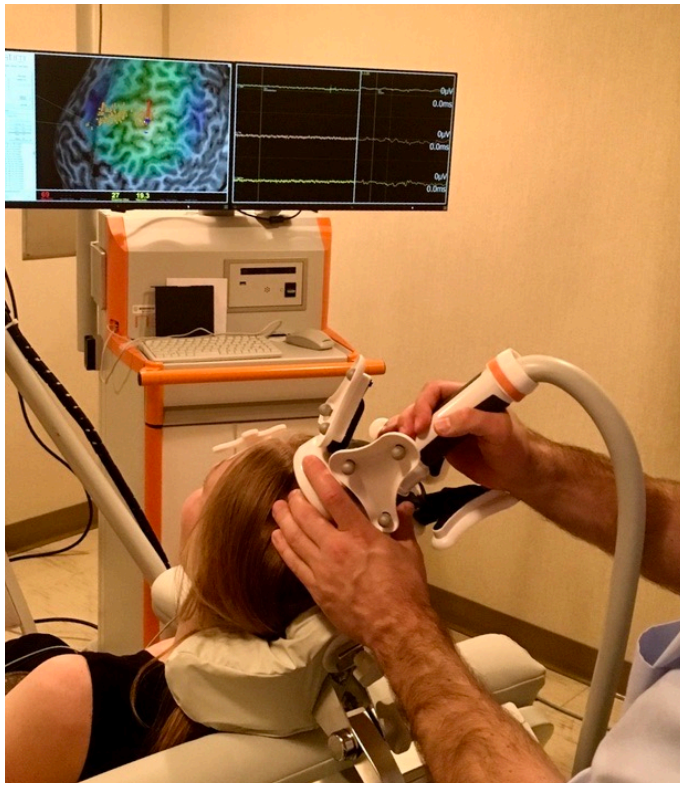
- rTMS suggested as method to identify patients who will benefit from MCS
- Trial stimulation for 2-4 days with goal of 50% improvement followed by permanent implant
- Case series show 63-75% pain relief at 10-12 months
- Epidural stimulation vs subdural stimulation (typically 40 Hz or greater)



(Data from: Thomas et al 2009)

Transcranial Magnetic Stimulation (TMS)

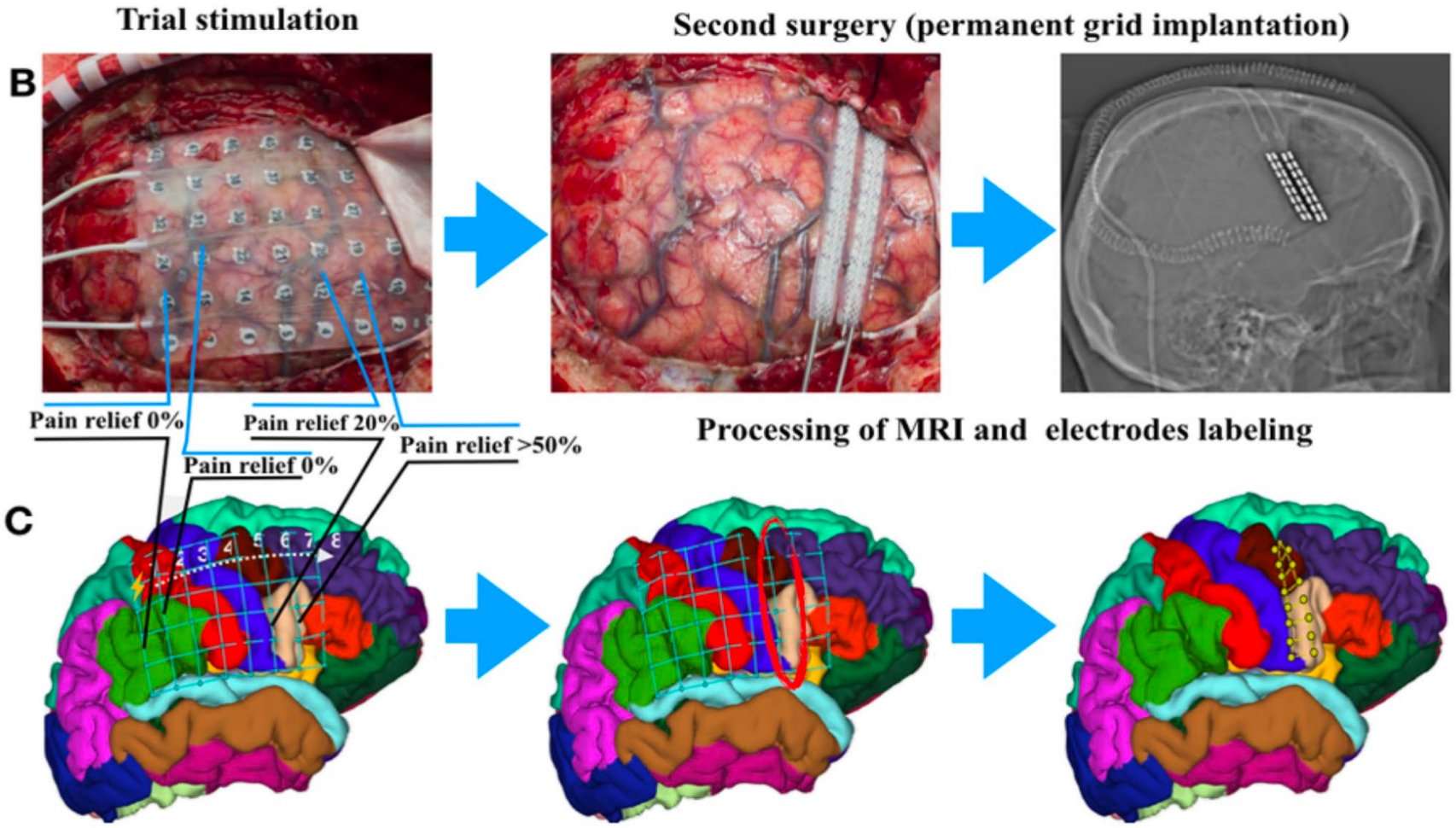
- Level A evidence for high frequency rTMS for neuropathic pain
  - Contralateral primary motor cortex
  - Lefaucheur et al, Clin Neurophysiol, 2020
- Predictive of epidural MCS
  - Andre-Obadia et al, Clin Neurophysiol 2006
  - Andre-Obadia et al, Pain Physician 2014
- Experience with 3 patients
  - 5 sessions, 10-20 Hz stim, 2000-3000 pulses, 10-15 min
  - Stereotactic TMS
  - 2/3 transient (3-4 weeks) response



Slide and Photo courtesy of Dr. Brian Lundstrom

Motor Cortex Stimulation

Trial stimulation and subdural lead implantation

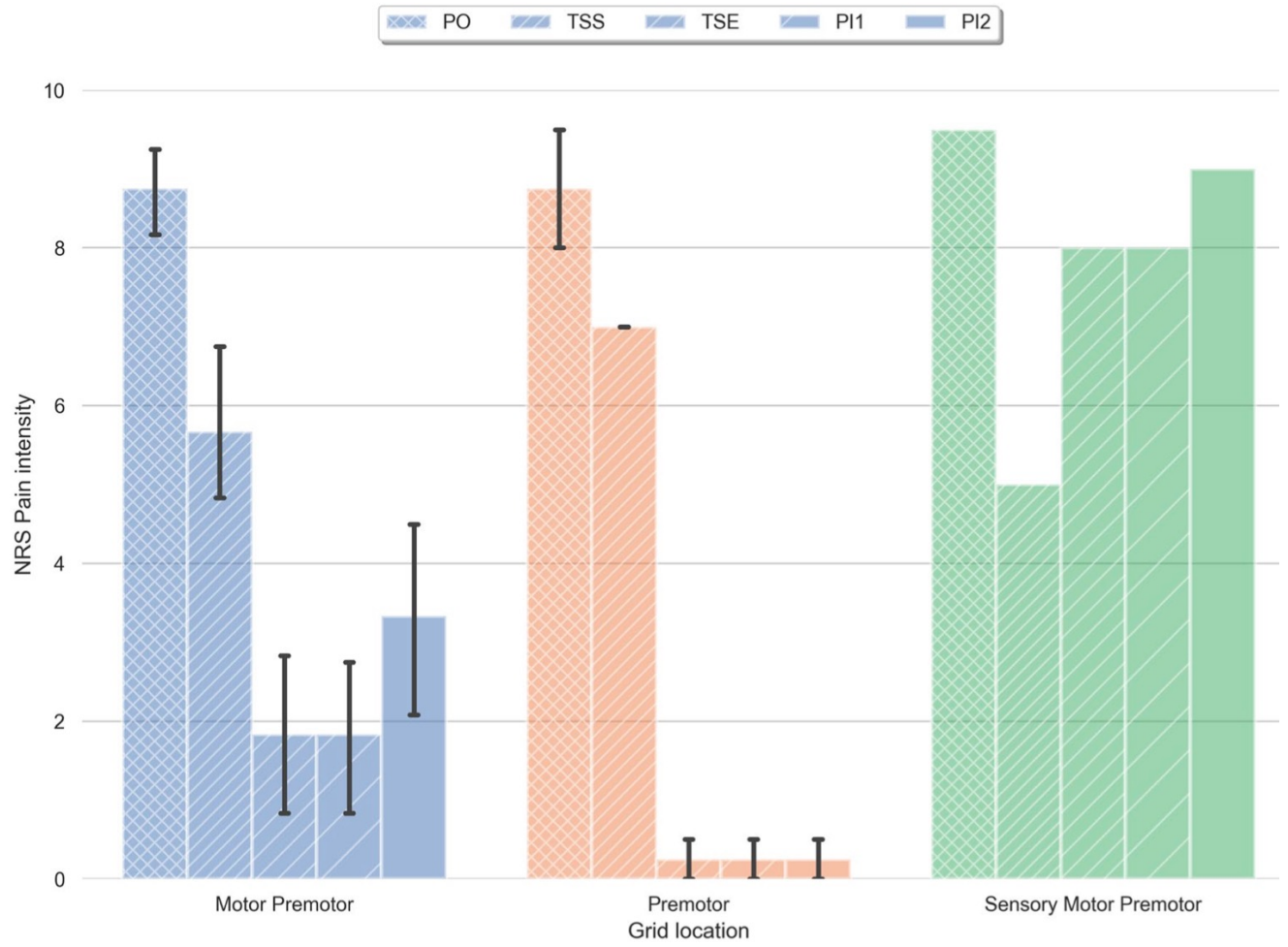


Lavrov et al, Sci Rep, 2021

Slide courtesy of Dr. Brian Lundstrom

Premotor vs Motor Cortex Stimulation

Premotor Stimulation More Effective



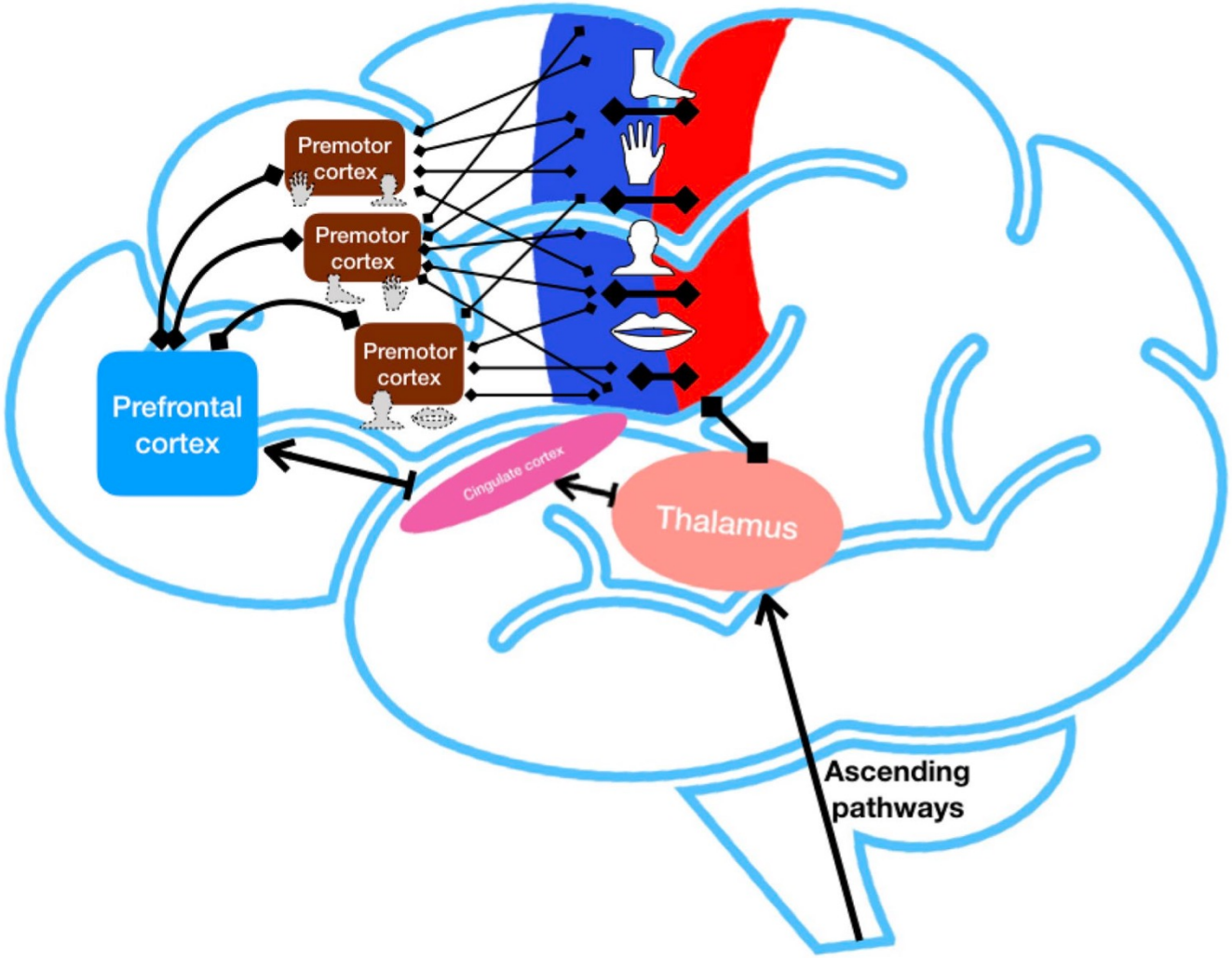
Lavrov et al, Sci Rep, 2021

Slide courtesy of Dr. Brian Lundstrom

n = 6, 2, 1

AAPM 2022 38TH ANNUAL MEETING

Premotor Areas Influence Pain Processing



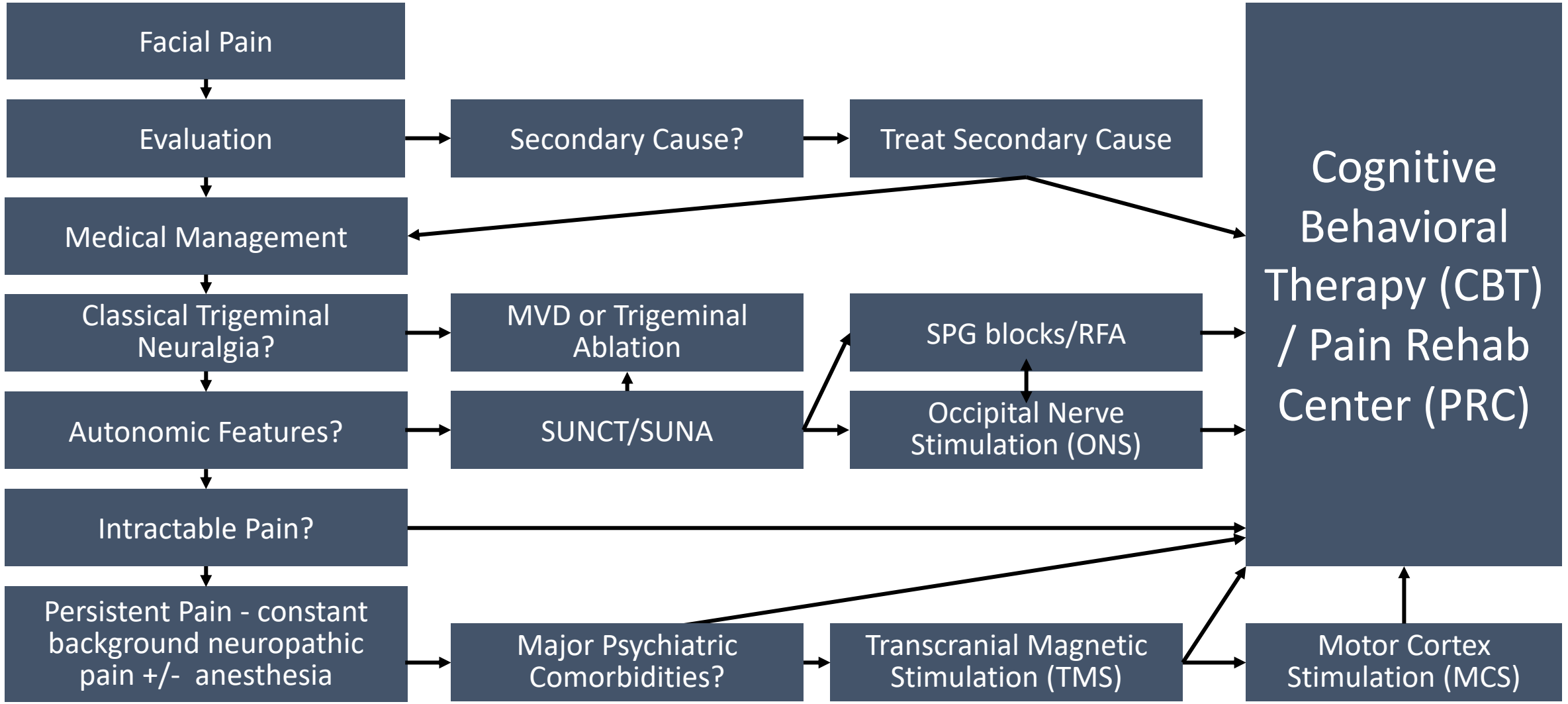
Lavrov et al, Sci Rep, 2021

Slide and Diagram courtesy of Dr. Brian Lundstrom

Other Neuromodulation Treatment Options for Facial Pain

- Deep Brain Stimulation
  - Neuropathic Facial Pain – VPL/VPM of thalamus or Periventricular Grey (PVG)
  - Two negative multicenter trials for chronic pain
- C2 Spinal Cord Stimulation – case series showing benefit in facial pain, but high rate of lead migration
- Peripheral Nerve Stimulation (PIFP, Supraorbital Neuralgia) – SON, ION, Gasserian Ganglion
  - Case series showing wide range of benefit (14%-100%) and high rates of complications due to device malfunction and infection

(Data from: Coffee 2001, Chivukula et al 2014, Rasskazoff et al 2013)


Facial Pain
Evaluation
Secondary Cause?
Treat Secondary Cause
Medical Management
Classical Trigeminal Neuralgia?
MVD or Trigeminal Ablation
SPG blocks/RFA
Autonomic Features?
SUNCT/SUNA
Occipital Nerve Stimulation (ONS)
Intractable Pain?
Persistent Pain - constant background neuropathic pain +/- anesthesia
Major Psychiatric Comorbidities?
Transcranial Magnetic Stimulation (TMS)
Motor Cortex Stimulation (MCS)
Cognitive Behavioral Therapy (CBT) / Pain Rehab Center (PRC)

Summary

- Screen and evaluate for secondary causes of persistent facial pain
- Good history is critical to successful treatment of facial pain
- Maximize medical therapy as neuromodulation alone is not enough to treat headache and facial pain
- Characterize the pain and use clinical features to guide treatment when neuromodulation is indicated
- With intractable facial pain, most patients benefit from multimodal therapy with inclusion of cognitive behavioral therapy

References

Gronseth G, Cruccu G, Alksne J, Argoff C, Brainin M, Burchiel K, et al. Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. Neurology. 2008;71(15):1183-90.

Fontaine et al. Occipital nerve stimulation improves the quality of life in medically-intractable chronic cluster headache: Results of an observational prospective study. Cephalalgia. 2017 Oct;37(12):1173-1179. doi: 10.1177/0333102416673206. Epub 2016 Oct 3.

Schoenen, J. et al. Stimulation of the sphenopalatine ganglion (SPG) for cluster headache treatment. Pathway CH-1: a randomized, sham-controlled study. Cephalalgia 2013; 33: 10.

Burish, M., *Cluster Headache and Other Trigeminal Autonomic Cephalalgias.* Continuum (Minneap Minn), 2018. 24(4, Headache): p. 1137-1156.

Chivukula, S., et al., *Cervical and cervicomedullary spinal cord stimulation for chronic pain: efficacy and outcomes.* Clin Neurol Neurosurg, 2014. 127: p. 33-41.

Coffey, R.J., *Deep brain stimulation for chronic pain: results of two multicenter trials and a structured review.* Pain Med, 2001. 2(3): p. 183-92.

Cohen, A.S., M.S. Matharu, and P.J. Goadsby, *Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) or cranial autonomic features (SUNA)--a prospective clinical study of SUNCT and SUNA.* Brain, 2006. 129(Pt 10): p. 2746-60.
Duvall, J.R., et al., *Great Auricular Neuralgia: Case Series.* Headache, 2020. 60(1): p. 247-258.

Narouze, S., et al., *Sphenopalatine ganglion radiofrequency ablation for the management of chronic cluster headache.* Headache, 2009. **49**(4): p. 571-7.
Lambru, G., et al., *Occipital nerve stimulation in the treatment of medically intractable SUNCT and SUNA.* Pain Physician, 2014. 17(1): p. 29-41.

Ornello, R., et al., *Sphenopalatine Ganglion Pulsed Radiofrequency for the Treatment of Refractory Chronic SUNCT and SUNA: A Prospective Case Series.* Headache, 2020. 60(5): p. 938-945.

Salmasi, V., et al., *Peripheral Nerve Stimulation for Occipital Neuralgia.* Pain Med, 2020. 21(Suppl 1): p. S13-S17.

Silberstein, S.D., et al., *Safety and efficacy of peripheral nerve stimulation of the occipital nerves for the management of chronic migraine: results from a randomized, multicenter, double-blinded, controlled study.* Cephalalgia, 2012. 32(16): p. 1165-79.

Thomas, L., et al., *Motor cortex and deep brain stimulation for the treatment of intractable neuropathic face pain.* Curr Neurol Neurosci Rep, 2009. 9(2): p. 120-6.

Lefaucheur JP, Aleman A, Baeken C, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): An update (2014-2018). *Clin Neurophysiol* 2020;131(2):474-528. doi: 10.1016/j.clinph.2019.11.002 [published Online First: 2020/01/07]

Lefaucheur JP, Andre-Obadia N, Antal A, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). *Clin Neurophysiol* 2014;125(11):2150-206. doi: 10.1016/j.clinph.2014.05.021 [published Online First: 2014/07/19]

Andre-Obadia N, Peyron R, Mertens P, et al. Transcranial magnetic stimulation for pain control. Double-blind study of different frequencies against placebo, and correlation with motor cortex stimulation efficacy. *Clin Neurophysiol* 2006;117(7):1536-44. doi: 10.1016/j.clinph.2006.03.025 [published Online First: 2006/06/07]

Andre-Obadia N, Mertens P, Lelekov-Boissard T, et al. Is Life better after motor cortex stimulation for pain control? Results at long-term and their prediction by preoperative rTMS. *Pain Physician* 2014;17(1):53-62. [published Online First: 2014/01/24]

Lavrov I, Latypov T, Mukhametova E, et al. Pre-motor versus motor cerebral cortex neuromodulation for chronic neuropathic pain. *Sci Rep* 2021;11(1):12688. doi: 10.1038/s41598-021-91872-2 [published Online First: 2021/06/18]

Rasskazoff SY, Slavin KV. Neuromodulation for cephalgias. Surg Neurol Int. 2013;4(Suppl 3):S136-50.

AAPM 2022 38TH ANNUAL MEETING