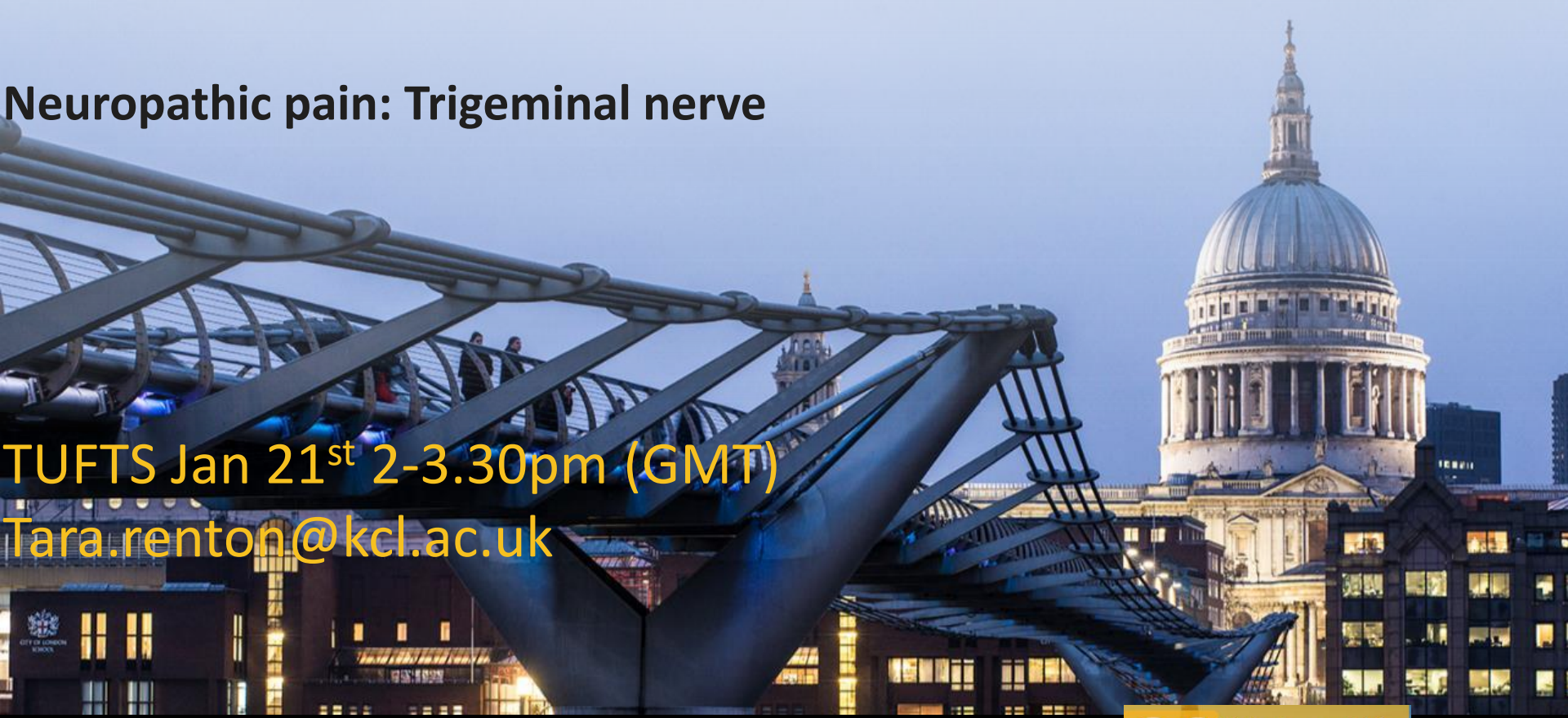
Neuropathic pain: Trigeminal nerve



TUFTS Jan 21st 2-3.30pm (GMT)

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Professor Oral Surgery Kings College London Past President British Association of Oral Surgeons

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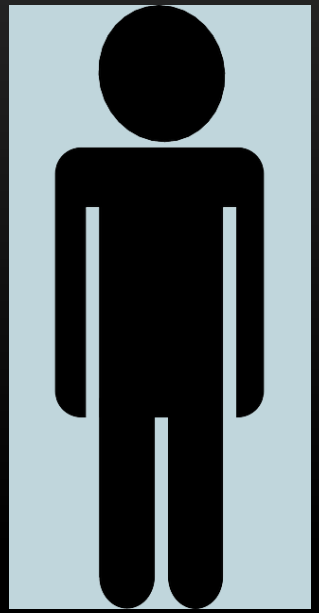
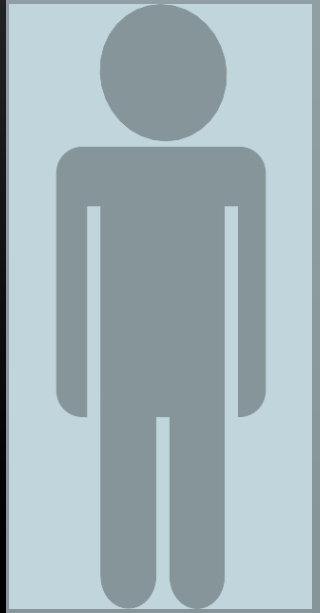
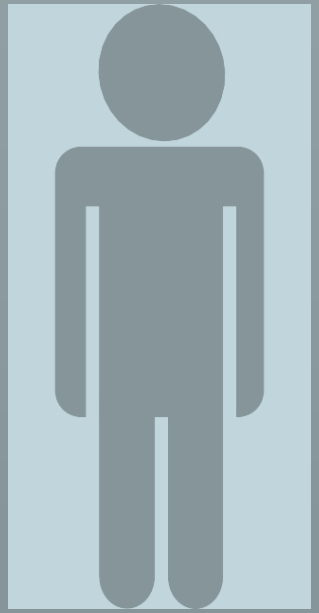
Part A Overview PTNP



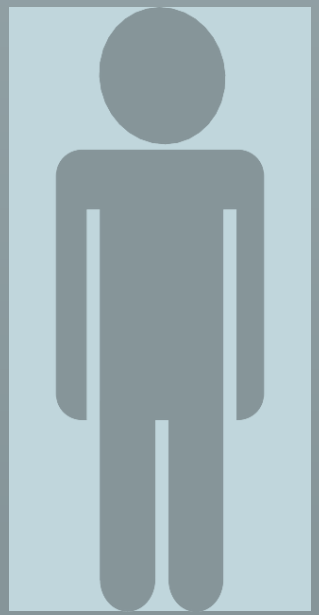
What is Neuropathic pain?



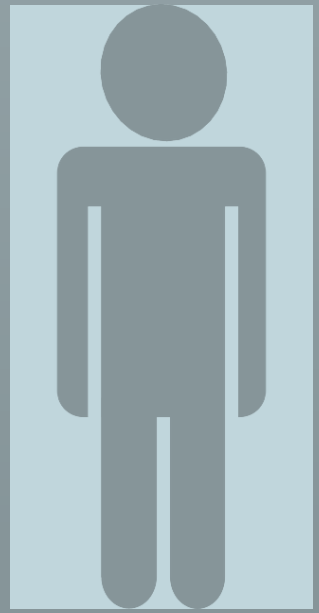
Who gets PTNP?



Why prevent PTNP?

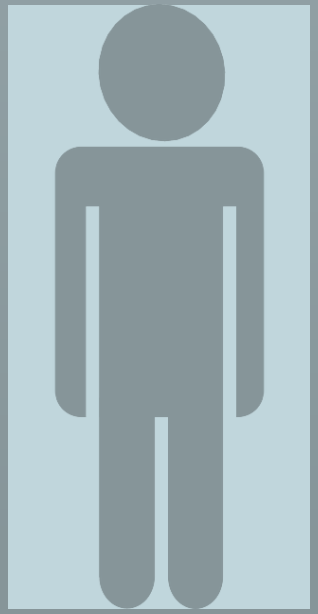


How to prevent these injuries?

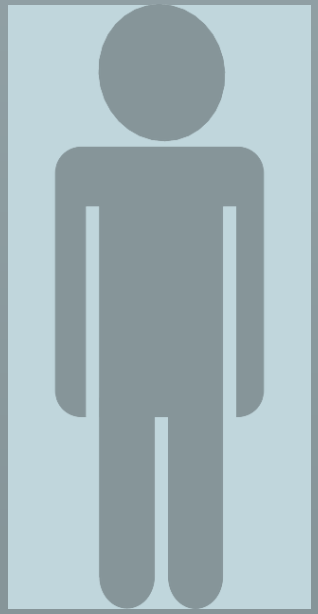


How to manage these injuries?

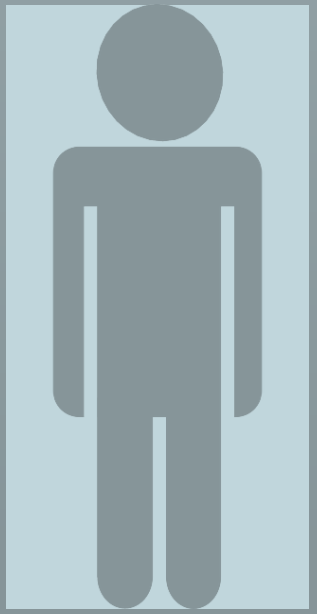
Part B Overview TN and other NPs



Diagnosis of TN?

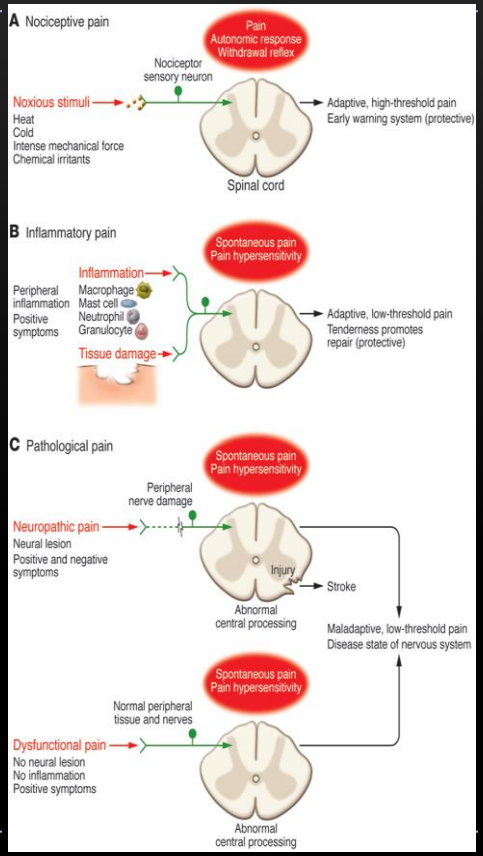


Who gets TN?



How to manage TN?

Types of pain



Types of pain
Healthy acute pain

Nociceptive
healthy feeling pain 'pain'

NOCICEPTIVE PAIN

Inflammatory pain
healthy short lived after insult

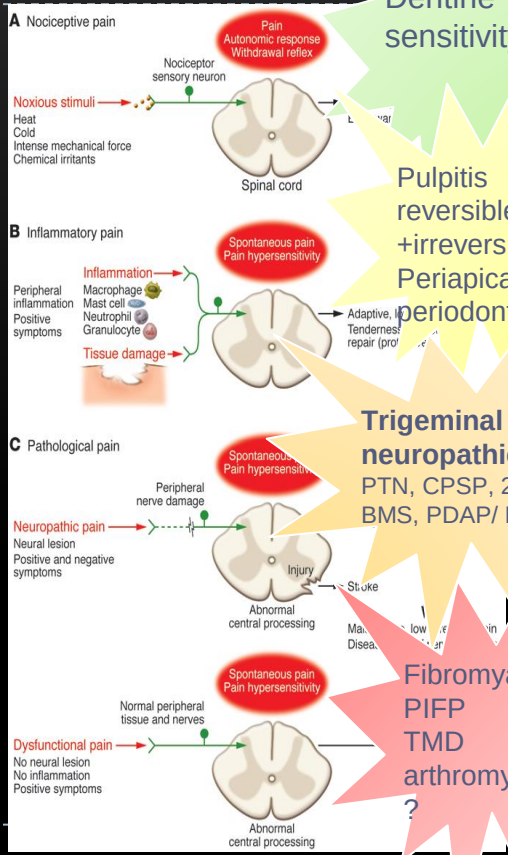
Chronic pain =
disease of neuromatrix

Neuropathic pain
Associated with nerve lesion

NEUROPATHIC PAIN

Dysfunctional or centralised pain
Unknown cause

NOCIPLASTIC PAIN



Dentine sensitivity

Pulpitis reversible +irreversible
Periapical periodontiti

Trigeminal neuropathic pain
PTN, CPSP, 2y TN, BMS, PDAP/ PHN

Fibromyalgia
PIFP
TMD
arthromyalgia
?

J Clin Invest. 2010 Nov 1; 120(11): 3742–3744. ***What is this thing called pain?*** *Clifford J. Woolf*

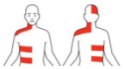
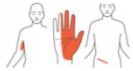
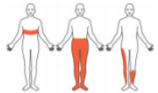
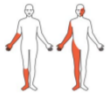
- Pain and stress-related cortical activity links to subcortical and cerebellar areas serving as a relay station for a feedforward neural network that may catalyse neuroimmune sensitization, neuroendocrine imbalance, sleep and circadian system alterations, and psychological comorbidities.
- Vice versa, dysregulation of these systems may facilitate pain generation and perpetuation.

Types of neuropathic pain

- In 1994, the International Association for the Study of Pain (IASP) defined neuropathic pain as "pain initiated or caused by a primary lesion or dysfunction in the nervous system."
- In 2008, a task force initiated by the IASP Special Interest Group on Neuropathic Pain (NeuPSIG) noted the need to distinguish neuropathic pain from nociceptive pain arising indirectly from neurological disorders and pain conditions with secondary neuroplastic changes occurring in the nociceptive system, and proposed a new definition that omitted the term "dysfunction":
- "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system."30
- A slightly modified version of this definition was proposed by the IASP Taxonomy Committee and accepted by the IASP: "**pain caused by a lesion or disease of the somatosensory nervous system."**

Table 1

Common neuropathic pain conditions and neuroanatomically plausible distribution of pain symptoms and sensory signs.

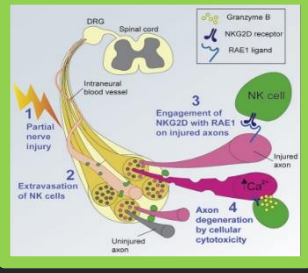
Neuropathic pain condition	Neuroanatomically plausible distribution of pain and sensory signs	Illustration of typical distribution
Trigeminal neuralgia	Within the facial or intraoral trigeminal territory.	
Postherpetic neuralgia	Unilateral distributed in one or more spinal dermatomes or the trigeminal ophthalmic division.	
Peripheral nerve injury pain	In the innervation territory of the lesioned nerve, typically distal to a trauma, surgery, or compression.	
Postamputation pain	In the missing body part and/or in the residual limb.	
Painful polyneuropathy	In feet, may extend to involve lower legs, thighs, and hands.	
Painful radiculopathy	Distribution consistent with the innervation territory of the nerve root.	
Neuropathic pain associated with spinal cord injury	At and/or below the level of the spinal cord lesion.	
Central poststroke pain	Contralateral to the stroke. In lateral medullary infarction, the distribution can also involve the ipsilateral side of the face.	
Central neuropathic pain associated with multiple sclerosis	Can be a combination of distributions seen in spinal cord injury and stroke.	

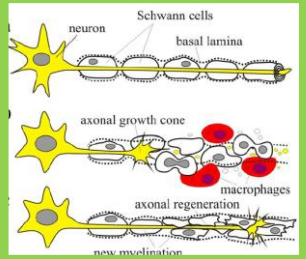
Classification of Neuropathic Pain:

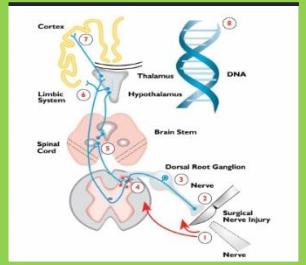
The type of damage or related pathophysiology causing a painful neuropathic disorder can be classified as the following [1, 2,]

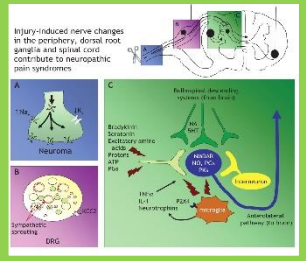
1. Mechanical nerve injury, e.g. carpal tunnel syndrome, vertebral disk herniation;
2. Metabolic disease, e.g. diabetic poly-neuropathy;
3. Neurotropic viral disease, e.g. herpes zoster, human immunodeficient virus (HIV) disease;
4. Neurotoxicity, e.g. by chemotherapy to treat cancer or tuberculosis;
5. Inflammatory and/or immunologic mechanisms, e.g. multiple sclerosis;
6. Nervous system focal ischemia. e.g. thalamic syndrome (anesthesia dolorosa);
7. Multiple neurotransmitter system dysfunction, e.g. complex regional pain syndrome (CGRP).

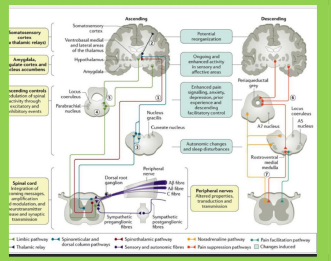
Evolution of neuropathic pain
Involves lesional damage to somatosensory nerve (PNS +/or CNS)

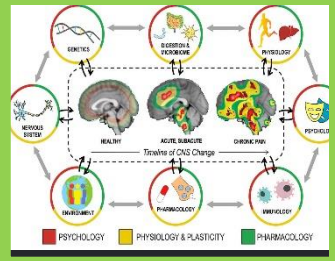












Initial insult to nerve
Trauma
Physical, chemical , thermal, radiation
Toxins
Infection, heavy metal poisoning, chemotherapy
Pressure ischaemia neoplasia

Peripheral sequelae
Inflammation
Growth cone
Wallerian degeneration
Macrophages and Schwann cells clean up myelin
Nerve sprouting regeneration

Central sequelae
Changes in gene expression
DRG
Spinal DH Altered activity and gene expression =central sensitisation loss inhibitory neurons and **microglial activation**
Changes in CPM
Limbic system and hypothalamus altered mood behaviour and autonomic

Peripheral pathophysiology
Spontaneous and Ectopic increased activity
Lowered thresholds
Upward facilitation
Neurotransmitter and receptor changes

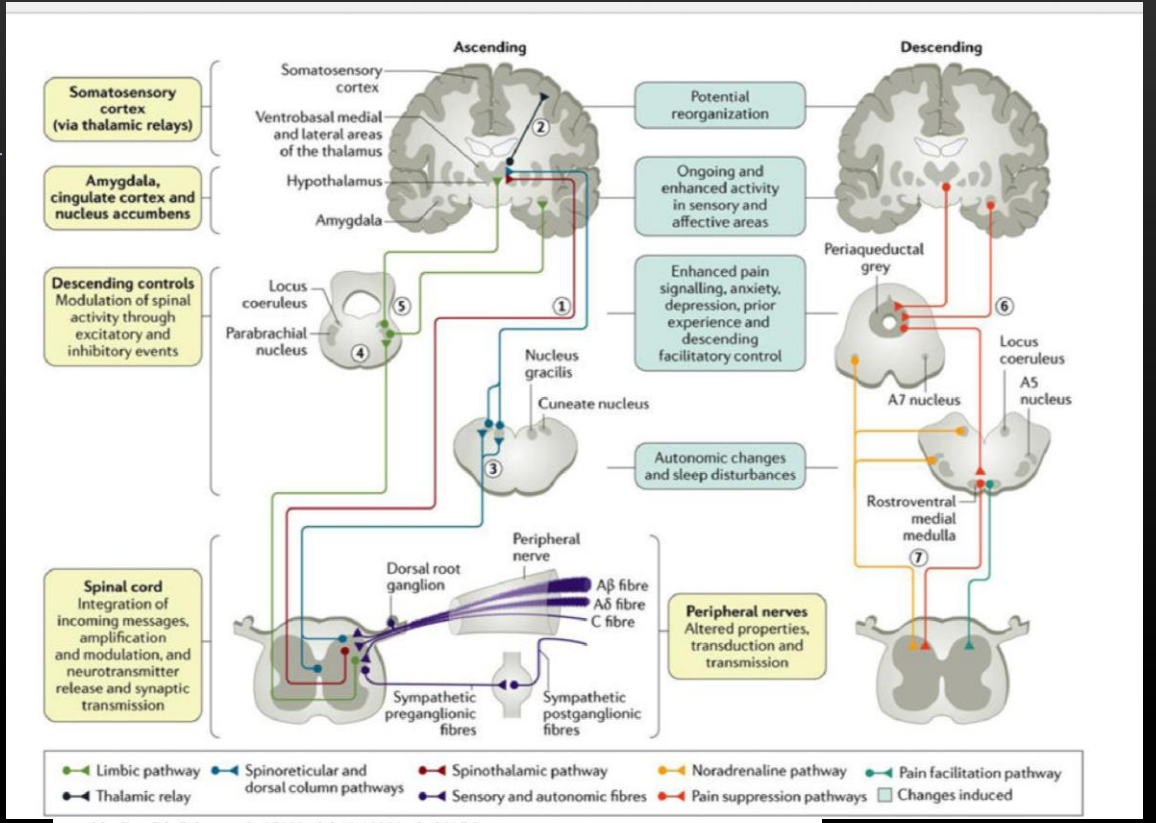
Central pathophysiology
Central reorganisation (plasticity)
Persistent and enhanced activity in sensory and affective regions (sensitisation)
Enhanced pain signalling and downward facilitation
Autonomic changes and sleep disorders

Endogenous and exogenous factors
Demographics
Genetics
Environment
Microbiome
Psychology
Cultural
Sleep

Physiology
Neurology

Pathophysiology

Figure 1. The peripheral and central changes induced by nerve injury or peripheral neuropathy Preclinical animal studies have shown that damage to all sensory peripheral fibres (namely, Aβ, Aδ and C fibres; BOX 1) alters transduction and transmission due to altered ion channel function. These alterations affect spinal cord activity, leading to an excess of excitation coupled with a loss of inhibition. In the ascending afferent pathways, the sensory components of pain are via the spinothalamic pathway to the ventrobasal medial and lateral areas (1), which then project to the somatosensory cortex allowing for the location and intensity of pain to be perceived (2). The spinal cord also has spinoreticular projections and the dorsal column pathway to the cuneate nucleus and nucleus gracilis (3). Other limbic projections relay in the parabrachial nucleus (4) before contacting the hypothalamus and amygdala, where central autonomic function, fear and «anxiety are altered (5). Descending efferent pathways from the amygdala and hypothalamus (6) drive the periaqueductal grey, the locus coeruleus, A5 and A7 nuclei and the rostroventral medial medulla. These brainstem areas then project to the spinal cord through descending noradrenaline (inhibition via α2 adrenoceptors), and, in neuropathy, there is a loss of this control and increased serotonin descending excitation via 5-HT3 receptors (7). The changes induced by peripheral neuropathy on peripheral and central functions are shown. Adapted with permission from REF. 38, Mechanisms and management of diabetic painful distal symmetrical polyneuropathy, American Diabetes Association, 2013. Copyright and all rights reserved. Material from this publication has been used with the permission of American Diabetes Association.



Nat Rev Dis Primers. ; 3: 17002. doi:10.1038/nrdp.2017.2.

Neuropathic pain

Luana Colloca[1], Taylor Ludman[1], Didier Bouhassira[2], Ralf Baron[3], Anthony H. Dickenson[4], David Yarnitsky[5], Roy Freeman[6], Andrea Truini[7], Nadine Attal[8], Nanna B. Finnerup[9], Christopher Eccleston[10,11], Eija Kalso[12], David L. Bennett[13], Robert H. Dworkin[14], and Srinivasa N. Raja[15]

About 413 physicians completed a total of 3,956 patient records forms. Total annual direct health-care costs per patient ranged from €1,939 (Italy) to €3,131 (Spain).

Annual professional caregiver costs ranged from €393 (France) to €1,242 (UK), but this only represented a small proportion of total care because much care is provided by family or friends. Sick leave costs ranged from €5,492 (UK) to €7,098 (France), with 10%–32% patients prevented from working at some point by NP.

Total cost (including **direct and indirect costs**) of NP per patient was €10,313 in France (69% of the total cost), €14,446 in Germany (78%), €9,305 in Italy (69%), €10,597 in Spain (67%), and **€9,685 in the UK (57%).**

Indirect costs (ie, sick leave) constituted the majority of costs in all five countries: €7,098 in France, €11,232 in Germany, €6,382 in Italy, €7,066 in Spain, and **€5,492 in the UK**. In the subgroup analysis, total annual direct costs per patient were highest for neuropathic back pain and radiculopathy, and lowest for fibromyalgia.
Mean WPAI score range was 34.4–56.1; BPI interference was 4.1–4.8; and EQ-5D was 0.57–0.74. The results suggest that a significant proportion of the patient's work time in the previous week was affected by NP, and these are relatively high compared with other diseases such as diabetes, respiratory conditions, and arthritis.

The wider costs appear significantly higher to patients, carers/families, and society as a whole than to the health system alone.

ClinicoEconomics and Outcomes Research

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ORIGINAL RESEARCH

A burden of illness study for neuropathic pain in Europe

This article was published in the following Dove Press journal:
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27 April 2016
Number of times this article has been viewed

Hiltrud Liedgens[1]
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Purpose: Neuropathic pain (NP) is often severe and represents a major humanistic and economic burden. This study aimed at providing insight on this burden across France, Germany, Italy, Spain, and the UK, considering direct and indirect costs, productivity loss, and humanistic impact on patients and their families.

Methods: Physician questionnaires provided data on patients presenting with NP covering demographics, sick leave and retirement, number of consultations, drug treatments, and surgical procedures. Patients provided further demographic and disease-related data and completed the Work Productivity and Activity Impairment (WPAI), the EuroQol 5-Dimension (EQ-5D), and the Brief Pain Inventory (BPI) questionnaires. All health-related direct unitary costs were collected from relevant country-specific sources and adjusted to 2012 prices (€) where necessary. A subgroup analysis of costs based on diabetic peripheral neuropathy (n=894), fibromyalgia (n=300), and low back pain (n=963) was performed.

Findings: About 413 physicians completed a total of 3,956 patient records forms. Total annual direct health-care costs per patient ranged from €1,939 (Italy) to €3,131 (Spain). Annual professional caregiver costs ranged from €393 (France) to €1,242 (UK), but this only represented a small proportion of total care because much care is provided by family or friends. Sick leave costs ranged from €5,492 (UK) to €7,098 (France), with 10%–32% patients prevented from working at some point by NP. Total cost (including direct and indirect costs) of NP per patient was €10,313 in France (69% of the total cost), €14,446 in Germany (78%), €9,305 in Italy (69%), €10,597 in Spain (67%), and €9,685 in the UK (57%). Indirect costs (ie, sick leave) constituted the majority of costs in all five countries: €7,098 in France, €11,232 in Germany, €6,382 in Italy, €7,066 in Spain, and €5,492 in the UK. In the subgroup analysis, total annual direct costs per patient were highest for neuropathic back pain and radiculopathy, and lowest for fibromyalgia. Mean WPAI score range was 34.4–56.1; BPI interference was 4.1–4.8; and EQ-5D was 0.57–0.74. The results suggest that a significant proportion of the patient's work time in the previous week was affected by NP, and these are relatively high compared with other diseases such as diabetes, respiratory conditions, and arthritis.

Implications: Despite differences in practice between countries, these findings suggest a high opportunity cost for society in terms of lost work and productivity due to NP. The wider costs appear significantly higher to patients, carers/families, and society as a whole than to the health system alone.

Keywords: neuropathic pain, burden of illness, chronic lower back pain, productivity

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Introduction

Chronic pain is a distinct and well-recognized condition ex
of the European adult population.[1] While the majority of c

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KING'S College LONDON

International Classification of OFP (ICOP) 2020

Cephalalgia
An International Journal of Headache
International Headache Society

Cephalalgia
2020, Vol. 40(2) 129–221

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International Classification of Orofacial Pain, 1st edition (ICOP)

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The Orofacial Pain Classification Committee

The committee is a collaborative group consisting of members of the Orofacial and Head Pain Special Interest Group (OFHP SIG) of the International Association for the Study of Pain (IASP), the International Network for Orofacial Pain and Related Disorders Methodology (INfORM), the American Academy of Orofacial Pain (AAOP) and the International Headache Society (IHS).

ICOP

1. *Orofacial pain attributed to disorders of dentoalveolar and anatomically related structures*
   - **1.1 Dental pain**
     - 1.1.1 Pulpal pain
     - 1.1.2 Periodontal pain
     - 1.1.3 Gingival pain
   - **1.2 Oral mucosal, salivary gland and jaw bone pains**
     - 1.2.1 Oral mucosal pain
     - 1.2.2 Salivary gland pain
     - 1.2.3 Jaw bone pain
   - **References**

Acute nociceptive pain

2. *Myofascial orofacial pain*
   - **2.1 Primary myofascial orofacial pain**
     - 2.1.1 Acute primary myofascial orofacial pain
     - 2.1.2 Chronic primary myofascial orofacial pain
   - **2.2 Secondary myofascial orofacial pain**
     - 2.2.1 Myofascial orofacial pain attributed to tendonitis
     - 2.2.2 Myofascial orofacial pain attributed to myositis
     - 2.2.3 Myofascial orofacial pain attributed to muscle spasm
   - **References**

Acute chronic Myogenous pain

3. *Temporomandibular joint (TMJ) pain*
   - **3.1 Primary temporomandibular joint pain**
     - 3.1.1 Acute primary temporomandibular joint pain
     - 3.1.2 Chronic primary temporomandibular joint pain
   - **3.2 Secondary temporomandibular joint pain**
     - 3.2.1 Temporomandibular joint pain attributed to arthritis
     - 3.2.2 Temporomandibular joint pain attributed to disc displacement
     - 3.2.3 Temporomandibular joint pain attributed to degenerative joint disease
     - 3.2.4 Temporomandibular joint pain attributed to subluxation
   - **References**

Acute chronic joint pain

4. *Orofacial pain attributed to lesion or disease of the cranial nerves*
   - **4.1 Pain attributed to lesion or disease of the trigeminal nerve**
     - 4.1.1 Trigeminal neuralgia
     - 4.1.2 Other trigeminal neuropathic pain
   - **4.2 Pain attributed to lesion or disease of the glossopharyngeal nerve**
     - 4.2.1 Glossopharyngeal neuralgia
     - 4.2.2 Glossopharyngeal neuropathic pain
   - **References**

Neuropathic pain

5. *Orofacial pains resembling presentations of primary headaches*
   - **Introduction**
   - **5.1 Orofacial migraine**
     - 5.1.1 Episodic orofacial migraine
     - 5.1.2 Chronic orofacial migraine
   - **5.2 Tension-type orofacial pain**
   - **5.3 Trigeminal autonomic orofacial pain**
     - 5.3.1 Orofacial cluster attacks
     - 5.3.2 Paroxysmal hemifacial pain
     - 5.3.3 Short-lasting unilateral neuralgiform facial pain attacks with cranial autonomic symptoms (SUNFA)
     - 5.3.4 Hemifacial continuous pain with autonomic symptoms
   - **5.4 Neurovascular orofacial pain**
     - 5.4.1 Short-lasting neurovascular orofacial pain
     - 5.4.2 Long-lasting neurovascular orofacial pain
   - **References**

Neurovascular pain

6. *Idiopathic orofacial pain*
   - **6.1 Burning mouth syndrome (BMS)**
     - 6.1.1 Burning mouth syndrome without somatosensory changes
     - 6.1.2 Burning mouth syndrome with somatosensory changes
     - 6.1.3 Probable burning mouth syndrome
   - **6.2 Persistent idiopathic facial pain (PIFP)**
     - 6.2.1 Persistent idiopathic facial pain without somatosensory changes
     - 6.2.2 Persistent idiopathic facial pain with somatosensory changes
     - 6.2.3 Probable persistent idiopathic facial pain
   - **6.3 Persistent idiopathic dentoalveolar pain**
     - 6.3.1 Persistent idiopathic dentoalveolar pain without somatosensory changes
     - 6.3.2 Persistent idiopathic dentoalveolar pain with somatosensory changes
     - 6.3.3 Probable persistent idiopathic dentoalveolar pain
   - **6.4 Constant unilateral facial pain with additional attacks (CUFPA)**
   - **References**

Nociplastic pain

7. *Psychosocial assessment of patients with orofacial pain*
   - **Introduction**
   - **Levels of psychosocial assessment**
   - **Pain- and function-related constructs and instruments for OFPs**
     - Extent of pain
     - Pain intensity and pain-related disability
     - Functional limitation
     - Over-use behaviours
   - **Psychosocial constructs and instruments for OFPs**
     - Depression and anxiety
     - Somatoform disorders
     - Catastrophizing
     - Fear avoidance

Definitions – do not confuse nomenclature!

- **Neuralgia –** nerve pain
- **Neuropathic pain (IASP)**
  Pain caused by a lesion or disease of the somatosensory nervous system.
- **Neuropathy (IASP)**
  A disturbance of function or pathological change in a nerve: in one nerve, mononeuropathy; in several nerves, mononeuropathy multiplex; if diffuse and bilateral, polyneuropathy.
- *Note:* **Neuritis** (q.v.) is a special case of neuropathy and is now reserved for inflammatory processes affecting nerves.
  - sensory (touch, heat, pain)
  - motor (movement)

Pain related to lesions of the cranial nerves
Neuropathic pain

4. *Orofacial pain attributed to lesion or disease of the cranial nerves*
4.1 Pain attributed to lesion or disease of the trigeminal nerve
4.1.1 Trigeminal neuralgia
4.1.2 Other trigeminal neuropathic pain
4.2 Pain attributed to lesion or disease of the glossopharyngeal nerve
4.2.1 Glossopharyngeal neuralgia
4.2.2 Glossopharyngeal neuropathic pain
References

- Trigeminal neuralgia
- Post traumatic neuropathic pain

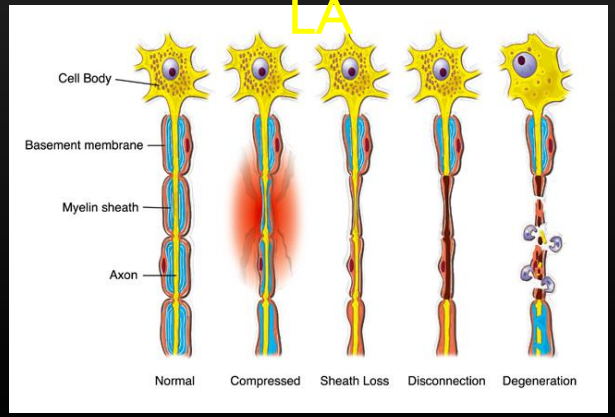
Neuropathic pain

SURGERY & LA

Viral
Herpes
Zoster
PHN
HIV

Chemotherapy

Diabetes



Alcoholism

Vitamin deficiency
B, E

Radiation, Burns

Demyelination
CTD, MS, GB

Peripheral sensory nerve injury

Pain related to lesions of the cranial nerves Neuropathic pain

4. *Orofacial pain attributed to lesion or disease of the cranial nerves*

4.1 Pain attributed to lesion or disease of the trigeminal nerve

4.1.1 Trigeminal neuralgia

4.1.2 Other trigeminal neuropathic pain

4.2 Pain attributed to lesion or disease of the glossopharyngeal nerve

4.2.1 Glossopharyngeal neuralgia

4.2.2 Glossopharyngeal neuropathic pain

References

- Trigeminal neuralgia
- Post traumatic neuropathic pain
- Damage due to
  - Local anaesthesia
  - Implants
  - Endodontics
  - Extractions especially third molar extractions
- Post viral
  - Post herpetic neuralgia

Post traumatic neuropathy

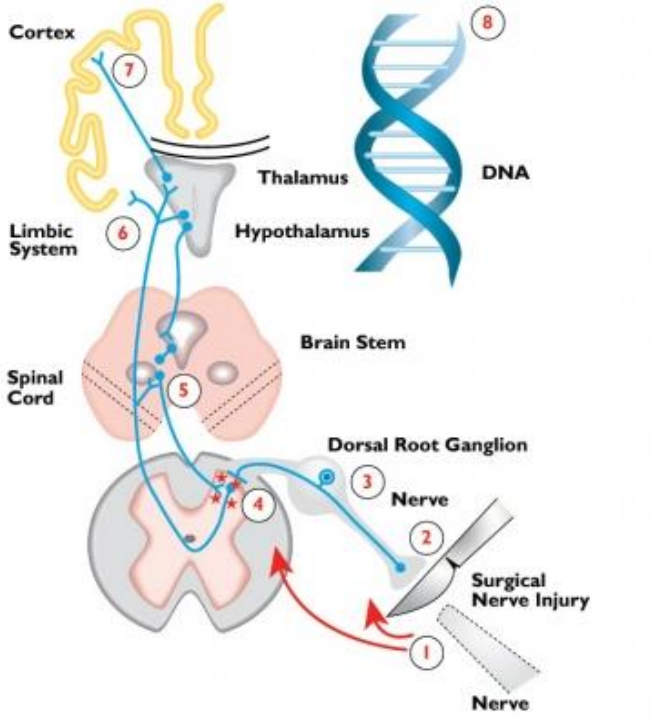


Figure 1. Sites and mechanisms of persistent postoperative pain.
Reprinted from *The Lancet*, Vol. 367, Kehlet H, et al. Persistent postsurgical pain: risk factors and prevention, pages 1618-1625, © 2006, with permission from Elsevier.

How Surgery (Wound) Can Lead to Chronic Pain

1. Denervated Schwann cells and infiltrating macrophages distal to nerve injury produce local and systemic chemicals that drive pain signaling.
2. Neuroma at site of injury is source of ectopic spontaneous excitability in sensory fibers.
3. Changes in gene expression in dorsal root ganglion after excitability, responsiveness, transmission, and survival of sensory neurons.
4. Dorsal horn is site of altered activity and gene expression, producing central sensitization, loss of inhibitory interneurons, and microglial activation, which together amplify sensory flow.
5. Brainstem descending controls modulate transmission in spinal cord.
6. Limbic system and hypothalamus contribute to altered mood, behavior, and autonomic reflexes.
7. Sensation of pain generated in cortex (past experiences, cultural inputs, and expectations converge to determine what patient feels).
8. Genomic DNA predispose (or not) patient to chronic pain and affect their reaction to treatment.

Post Traumatic neuropathic pain PTNP (ICOP)

4.1.2.3 Post-traumatic trigeminal neuropathic pain

- Previously used terms: Anaesthesia dolorosa; painful post-traumatic trigeminal neuropathy.
- Description: Unilateral or bilateral facial or oral pain following and caused by trauma to the trigeminal nerve(s), with other symptoms and/or clinical signs of trigeminal nerve dysfunction, and persisting or recurring for more than 3 months.
- *4.1.2.3.1 Probable post-traumatic trigeminal neuropathic pain*
- *Diagnostic criterion: A. Pain fulfilling all but criterion B2 for 4.1.2.3 Posttraumatic trigeminal neuropathic pain.*

4.1.2.4 Trigeminal neuropathic pain attributed to other disorder

4.1.2.5 Idiopathic trigeminal neuropathic pain

Description: Unilateral or bilateral facial pain in the distribution(s) of one or more branches of the trigeminal nerve

Diagnostic criteria:

A. Pain, in a neuroanatomically plausible area within the distribution(s) of one or both trigeminal nerve(s), persisting or recurring for >3 months and fulfilling criteria C and D

B. Both of the following:

1. history of a mechanical, thermal, radiation or chemical injury to the peripheral trigeminal nerve(s)
2. diagnostic test confirmation1 of a lesion of the peripheral trigeminal nerve(s) explaining the pain2

C. Onset within 6 months after the injury

D. Associated with somatosensory symptoms and/or signs4 in the same neuroanatomically plausible distribution

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

Diagnostic Criteria PTPN

Table 3. Core Diagnostic Criteria for Persistent Posttraumatic Neuropathic Pain

1. History of traumatic nerve injury or surgery associated with known risk of nerve injury.* Traumatic event = onset
2. Pain lasting ≥3 mo, with onset showing a temporal relation to known nerve injury (onset within days to weeks after the injury).†
3. Positive and/or negative signs of sensory disturbance in the innervation of the injured nerve as evidenced by ≥1 of the following:
   a. Mixed areas of hypo- and hypersensitivity to various sensory modalities Neuropathic area
   b. Hyposensitivity to nonpainful warmth (with or without changes in cold sensation) Allodynia / Hyperalgesia = hyperaesthesia
   c. Hypersensitivity to brush or pinprick in or around the painful area
4. No other condition (eg, inflammation, tumor) better explains the pattern of the clinical features (eg, radiculopathy) that could plausibly account for persisting pain in the affected dermatome or dermatomes. Anaesthesia/paraesthesia = hypoaesthesia

*This pain may occur even if there was a deliberate attempt to spare the large nerves crossing the surgical area (eg, in breast surgery).
†There is a spontaneous decline in reporting of pain >12 mo after surgery/trauma. Relevant citations in support of these diagnostic criteria are Bruehl,[34] Duffy et al,[77] Guo et al,[107] Haldar et al,[109] Pappagallo et al,[187] Teerijoki-Oksa

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Focus Article

AAPT Diagnostic Criteria for Peripheral Neuropathic Pain: Focal and Segmental Disorders

Roy Freeman,* Robert Edwards,† Ralf Baron,‡ Stephen Bruehl,§ Giorgio Cruccu,¶ Robert H. Dworkin,‖ and Simon Haroutounian**
*Center for Autonomic and Peripheral Nerve Disorders, Beth Israel Deaconess Medical Center, Boston, MA
†Department of Anesthesiology, Brigham & Women's Hospital, Harvard University School of Medicine, Boston, MA
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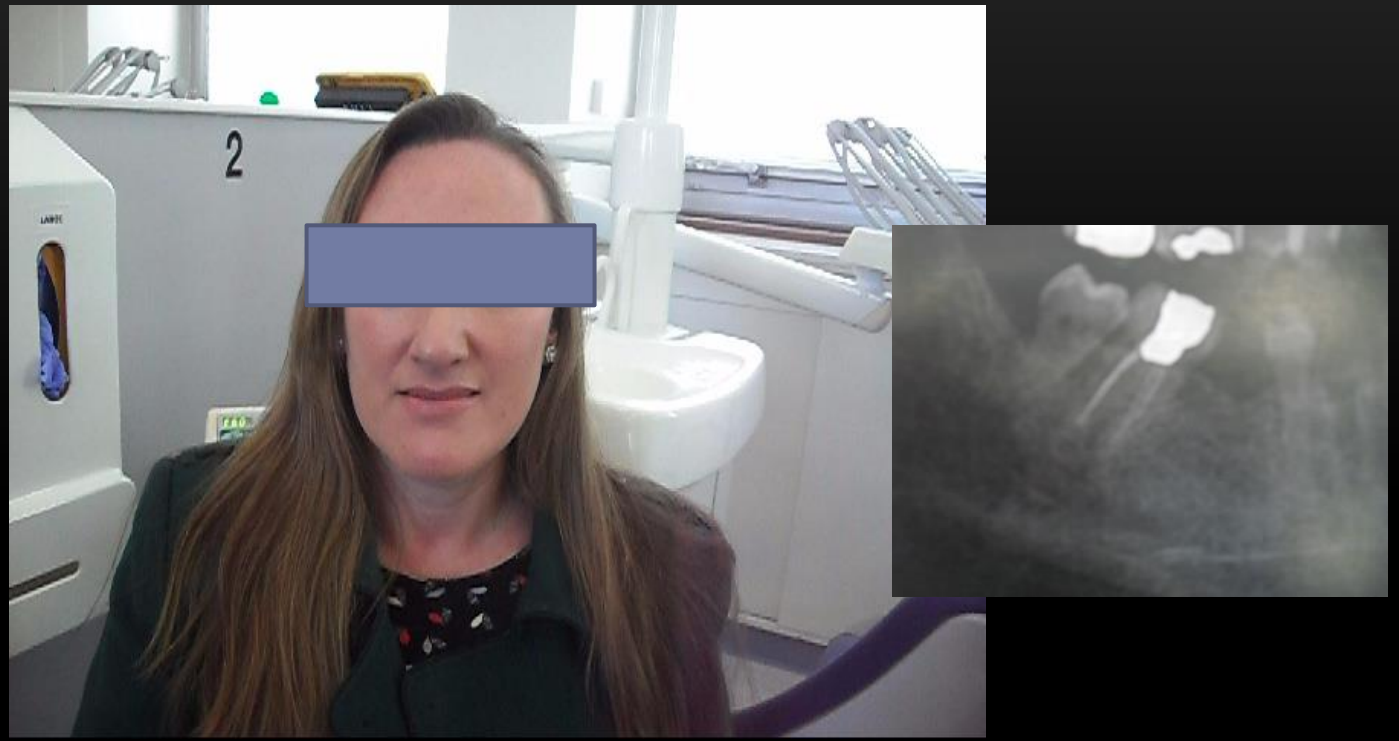
Late diagnosis of Endo PTN causing additional morbidity



Exclude other secondary non-traumatic causes of Neuropathic pain

Nutritional deficiencies

Fe, Ferritin, Zinc, Magnesium,

Vit B complex, D, E

Malignancy

Compression by a space occupying lesion centrally or peripherally NEOPLASIA

Metabolic Acromegaly, Hormonal neuropathy (Hypothyroidism, Diabetes),

Infarction (sickle cell hypoxic neural damage, giant cell arteritis)

Demyelination (Multiple sclerosis)

Infection Post viral neuropathy, Bacterial, Leprosy

Toxic Heavy metal poisoning (lead, mercury) radiation, thermal, chemotherapy, drugs

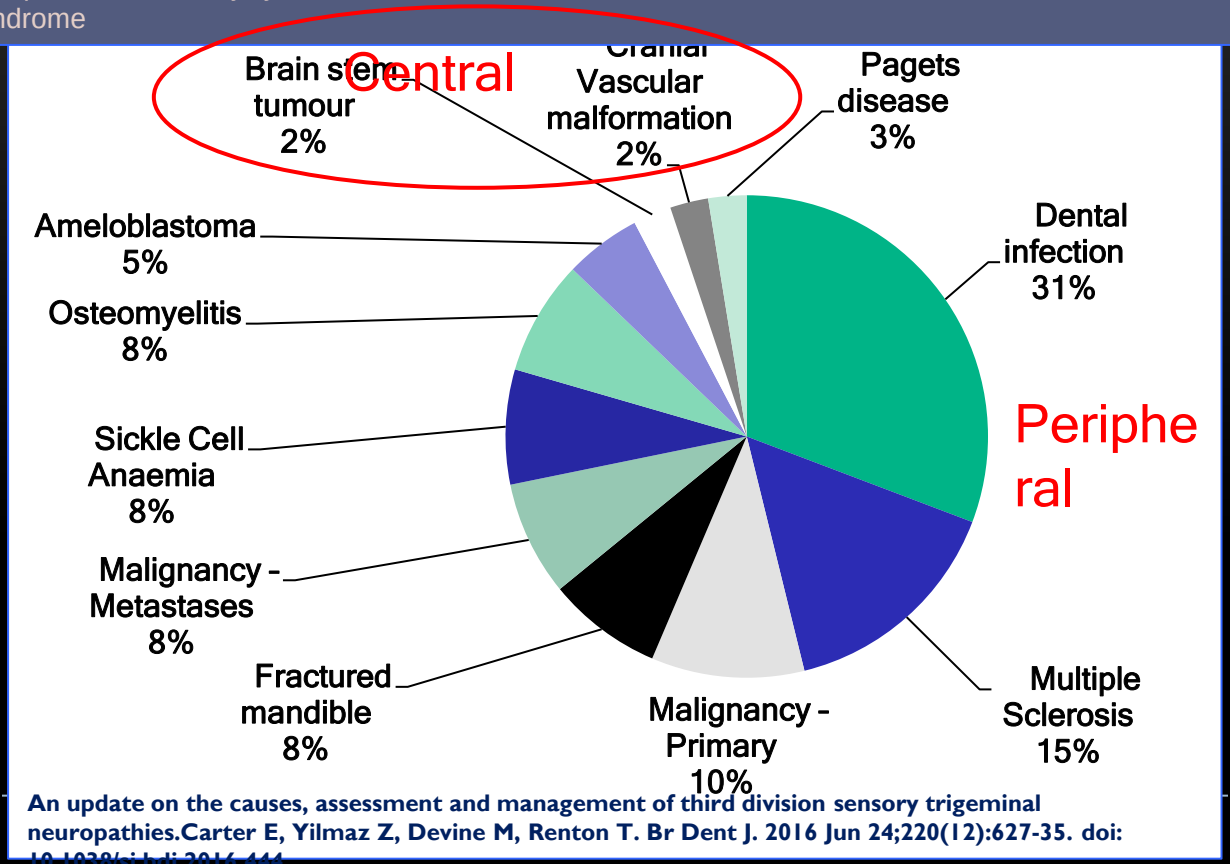
Auto immune problems: Lupus, Rheumatoid disease

Sarcoidosis and amyloidosis

Secondary Trigeminal neuropathic pain + neuropathy but NOT PTNP

Trigeminal neuropathy

Retrospective analysis of the case notes of 372 patients referred to the specialist nerve injury clinic between 2007 and 2014 was carried out to establish the cause of numb chin syndrome



An update on the causes, assessment and management of third division sensory trigeminal neuropathies.Carter E, Yilmaz Z, Devine M, Renton T. Br Dent J. 2016 Jun 24;220(12):627-35. doi: 10.1038/sj.bdj.2016.444

Chronic post surgical pain (CPSP) or NeP?

Haroutiunian S, Nikolajsen L, Finnerup NB, Jensen TS. The neuropathic component in persistent postsurgical pain: a systematic literature review. Pain. 2013 Jan;154(1):95-102. doi: 10.1016/j.pain.2012.09.010.

Persistent postsurgical pain (PPSP) is a frequent and often disabling complication of many surgical procedures.

Nerve injury-induced neuropathic pain (NeuP) has repeatedly been proposed as a major cause of PPSP. However, there is a lack of uniformity in NeuP assessment across studies, and the prevalence of NeuP may differ after various surgeries.

We performed a systematic search of the PubMed, CENTRAL, and Embase databases and assessed 281 studies that investigated PPSP after 11 types of surgery.

The prevalence of PPSP in each surgical group was examined. The prevalence of NeuP was determined by applying the recently published NeuP probability grading system. The prevalence of probable or definite NeuP was high in patients with persistent pain after thoracic and breast surgeries-66% and 68%, respectively. In patients with PPSP after groin hernia repair, the *prevalence of NeuP was 31%,* and after total hip or knee arthroplasty it was 6%.

The results suggest that the prevalence of NeuP among PPSP cases differs in various types of surgery, probably depending on the likelihood of surgical iatrogenic nerve injury. Because of large methodological variability across studies, a more uniform approach is desirable in future studies for evaluating persistent postsurgical NeuP.

	Estimated incidence of chronic pain	Estimated chronic severe (disabling) pain (>5 out of score of 10)	US surgical volumes (1000s)†
Amputation[2]	30–50%	5–10%	159 (lower limb only)
Breast surgery (lumpectomy and mastectomy)[3]	20–30%	5–10%	479
Thoracotomy[4–7]	30–40%	10%	Unknown
Inguinal hernia repair[8–10]	10%	2–4%	609
Coronary artery bypass surgery[11–13]	30–50%	5–10%	598
Caesarean section[14]	10%	4%	220

*Gall bladder surgery not included, since preoperative diagnosis of pain specifically from gall bladder is difficult and persistent postoperative pain could therefore be related to other intra-abdominal disorders. †National Center For Health Statistics, Ambulatory and Inpatients Procedures, USA, 1996.

Table 1: **Estimated incidence of chronic postoperative pain and disability after selected surgical procedures***

30% get persistent pain 10% are <u>severely</u> affected
Very few related to dentistry likely due to LA

Kehlet H *et al*, 2006 Lancet

Features of Neuropathic pain

- Multiple injuries or episodes of infection and pain
- Non respondent to anti inflammatory pain killers (NSAIDs Paracetamol)
- Better in mornings
- Does not disturb sleep
- Worsens during day
- Worsens with stress, tiredness and illness
- Pain presentation
  - Constant burning
  - Elicited neuralgic
  - Or combination

Table 2
Definitions of common features suggestive of neuropathic pain[29]

Paresthesia	An abnormal sensation, whether spontaneous or evoked
Dysesthesia	An unpleasant sensation, whether spontaneous or evoked
Hypoesthesia	Decreased sensitivity to stimulation (tactile or thermal; both are frequent)
Hyperesthesia	Increased sensitivity to stimulation (tactile or thermal; both are rare)
Hypoalgesia	Diminished pain response to a normally painful stimulus
Hyperalgesia	An increased response to a stimulus that is normally painful
Allodynia	Pain due to a stimulus that does not normally activate the nociceptive system

Table 3. Core Diagnostic Criteria for Persistent Posttraumatic Neuropathic Pain

1. History of traumatic nerve injury or surgery associated with known risk of nerve injury.*
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Diagnostic Criteria

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Post Traumatic neuropathic pain PTNP (ICOP)

4.1.2.3 Post-traumatic trigeminal neuropathic pain

- Previously used terms: Anaesthesia dolorosa; painful post-traumatic trigeminal neuropathy.
- Description: Unilateral or bilateral facial or oral pain following and caused by trauma to the trigeminal nerve(s), with other symptoms and/or clinical signs of trigeminal nerve dysfunction, and persisting or recurring for more than 3 months.
- *4.1.2.3.1 Probable post-traumatic trigeminal neuropathic pain*
- *Diagnostic criterion: A. Pain fulfilling all but criterion B2 for 4.1.2.3 Posttraumatic trigeminal neuropathic pain.*

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4.1.2.5 Idiopathic trigeminal neuropathic pain

Description: Unilateral or bilateral facial pain in the distribution(s) of one or more branches of the trigeminal nerve

Diagnostic criteria:

A. Pain, in a neuroanatomically plausible area within the distribution(s) of one or both trigeminal nerve(s), persisting or recurring for >3 months and fulfilling criteria C and D

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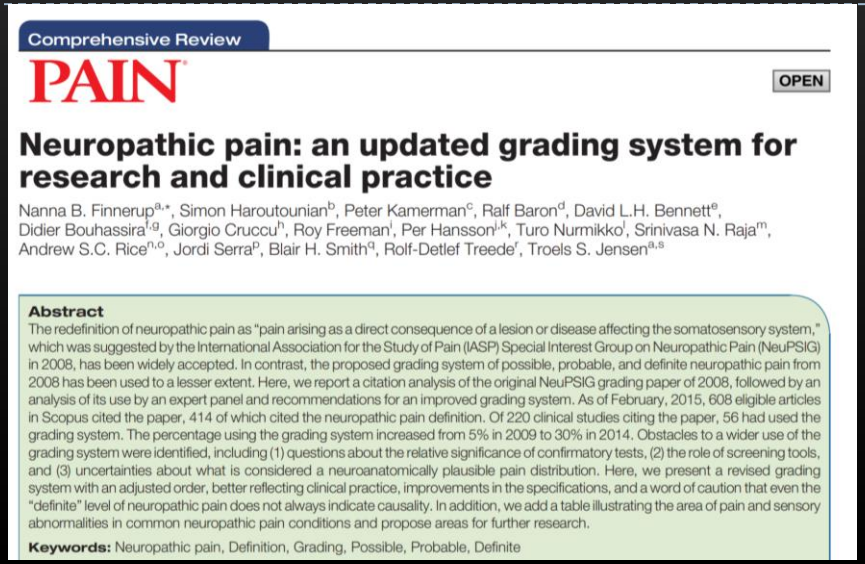
1. history of a mechanical, thermal, radiation or chemical injury to the peripheral trigeminal nerve(s)
2. diagnostic test confirmation1 of a lesion of the peripheral trigeminal nerve(s) explaining the pain2

C. Onset within 6 months after the injury

D. Associated with somatosensory symptoms and/or signs4 in the same neuroanatomically plausible distribution

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

Grading of neuropathic pain



Comprehensive Review

PAIN

OPEN

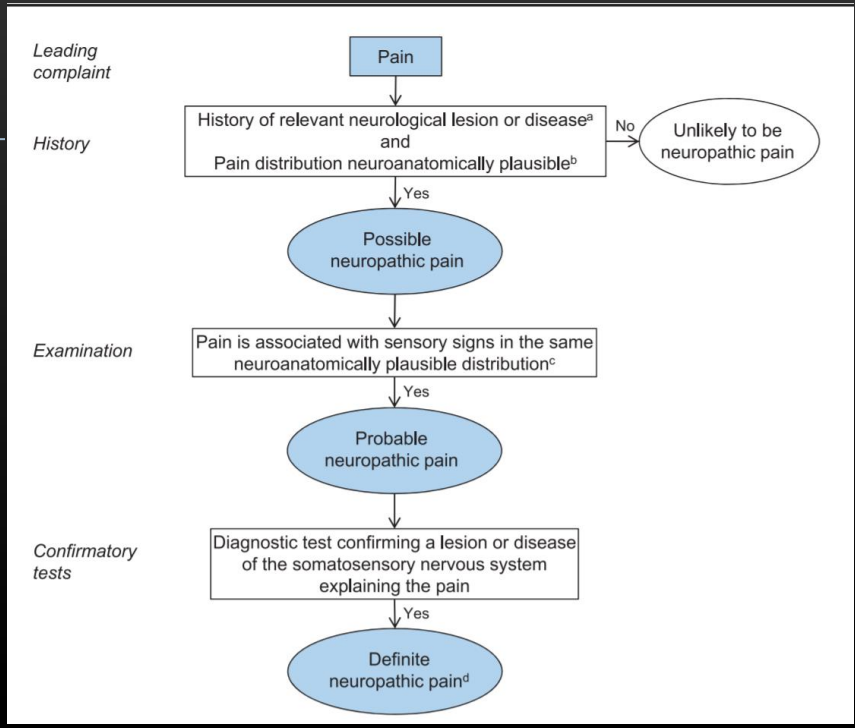
Neuropathic pain: an updated grading system for research and clinical practice

Nanna B. Finnerup[a,*], Simon Haroutounian[b], Peter Kamerman[c], Ralf Baron[d], David L.H. Bennett[e], Didier Bouhassira[f,g], Giorgio Cruccu[h], Roy Freeman[i], Per Hansson[j,k], Turo Nurmikko[l], Srinivasa N. Raja[m], Andrew S.C. Rice[n,o], Jordi Serra[p], Blair H. Smith[q], Rolf-Detlef Treede[r], Troels S. Jensen[a,s]

Abstract

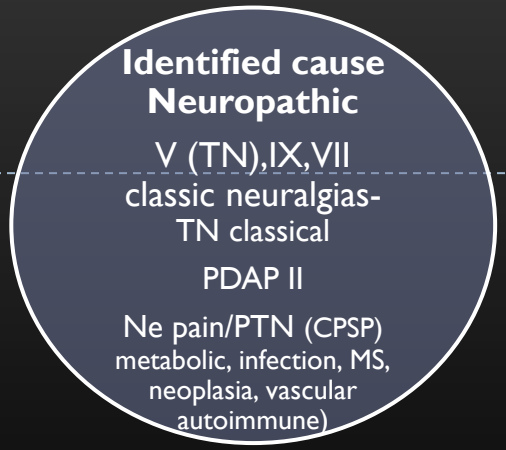
The redefinition of neuropathic pain as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system," which was suggested by the International Association for the Study of Pain (IASP) Special Interest Group on Neuropathic Pain (NeuPSIG) in 2008, has been widely accepted. In contrast, the proposed grading system of possible, probable, and definite neuropathic pain from 2008 has been used to a lesser extent. Here, we report a citation analysis of the original NeuPSIG grading paper of 2008, followed by an analysis of its use by an expert panel and recommendations for an improved grading system. As of February, 2015, 608 eligible articles in Scopus cited the paper, 414 of which cited the neuropathic pain definition. Of 220 clinical studies citing the paper, 56 had used the grading system. The percentage using the grading system increased from 5% in 2009 to 30% in 2014. Obstacles to a wider use of the grading system were identified, including (1) questions about the relative significance of confirmatory tests, (2) the role of screening tools, and (3) uncertainties about what is considered a neuroanatomically plausible pain distribution. Here, we present a revised grading system with an adjusted order, better reflecting clinical practice, improvements in the specifications, and a word of caution that even the "definite" level of neuropathic pain does not always indicate causality. In addition, we add a table illustrating the area of pain and sensory abnormalities in common neuropathic pain conditions and propose areas for further research.

Keywords: Neuropathic pain, Definition, Grading, Possible, Probable, Definite



Compared to the grading system published in 2008, we have (1) changed the order of the grading criteria to better reflect clinical practice. (2) annotated the terms used to improve clarity. (3) recognized the role of screening tools (questionnaires) in neuropathic pain evaluation. (4) emphasized that reaching the final level of certainty (definite neuropathic pain) confirms clinically that a lesion or disease of the somatosensory nervous system can explain the pain but, as often in neurology, it does not establish causality (ie, there may still be other causes of the pain such as a diabetic ulcer). The main purpose of the grading system is to help in the classification of the pain as neuropathic.

Exclude non-traumatic Neuropathic pain



Nutritional deficiencies

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Vit B complex, D, E

Malignancy

Compression by a space occupying lesion centrally or peripherally NEOPLASIA

Metabolic Acromegaly, Hormonal neuropathy (Hypothyroidism, Diabetes),

Infarction (sickle cell hypoxic neural damage, giant cell arteritis)

Demyelination (Multiple sclerosis)

Infection Post viral neuropathy, Bacterial, Leprosy

Toxic Heavy metal poisoning (lead, mercury) radiation, thermal, chemotherapy, drugs

Auto immune problems: Lupus, Rheumatoid disease

Sarcoidosis and amyloidosis

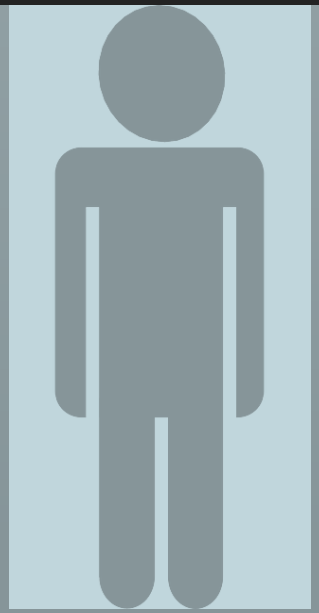
Any spontaneous neuropathy think Red flags of malignancy

- Over 50 years
- Previous history of Carcinoma
- Smoking /alcohol/ Betel nut/ Pan
- Night fevers
- Weight loss
- Blood loss/ aneamia

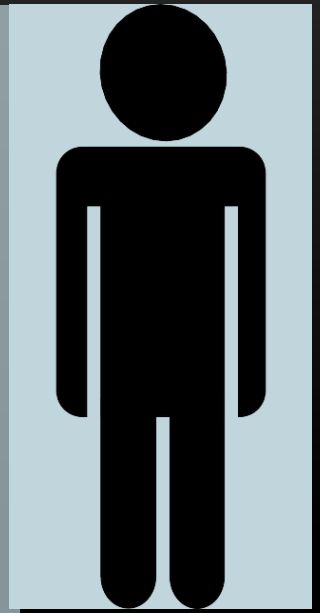
- Recent onset
- Rapid growth
- Neuropathy - sensory or motor
- Resorption of adjacent structures
- Localised mobility of teeth
- Progressive trismus
- Persistent painless ulcer
- Lymphadenopathy painless persistent
- Lack of response to conventional treatments:
  - Antibiotics
  - Endodontic surgery

NHS 2 (NICE 3) weeks Referral pathway

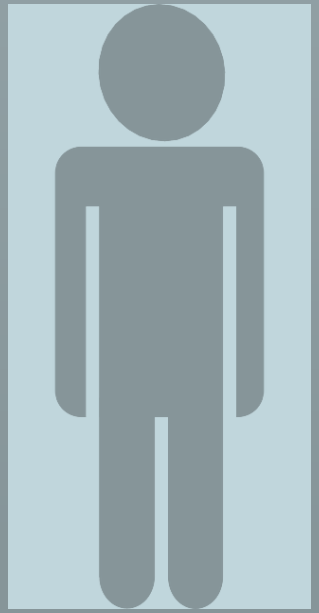
Overview



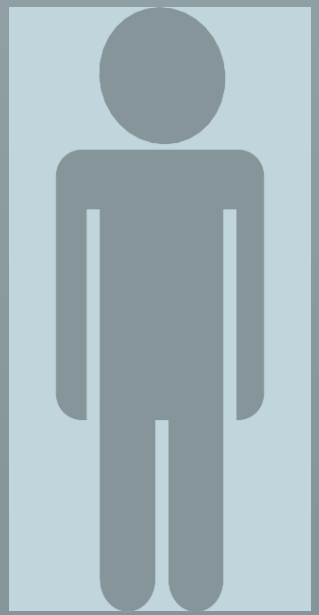
What is Neuropathic pain?



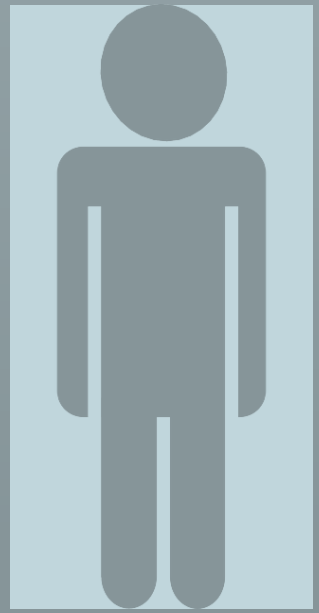
Who gets PTNP?



Why prevent PTNP?



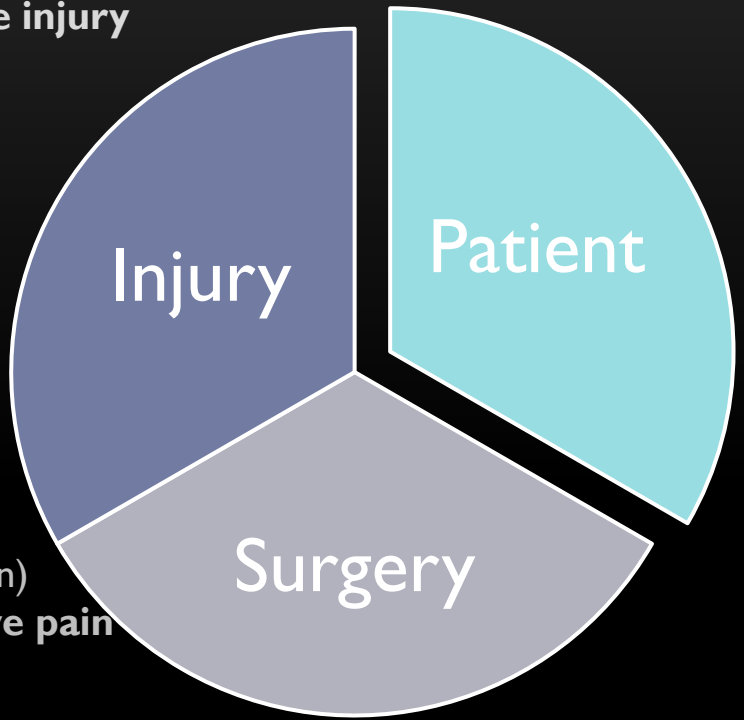
How to prevent these injuries?



How to manage these injuries?

Summary risk factors for PTPN /chronic post surgical pain

Resultant sensory nerve injury
Large neuropathic area
Thermal allodynia
Mechanical allodynia
Hyperalgesia



Age > 50 yrs
Female
Multiple pain conditions
Social Factors

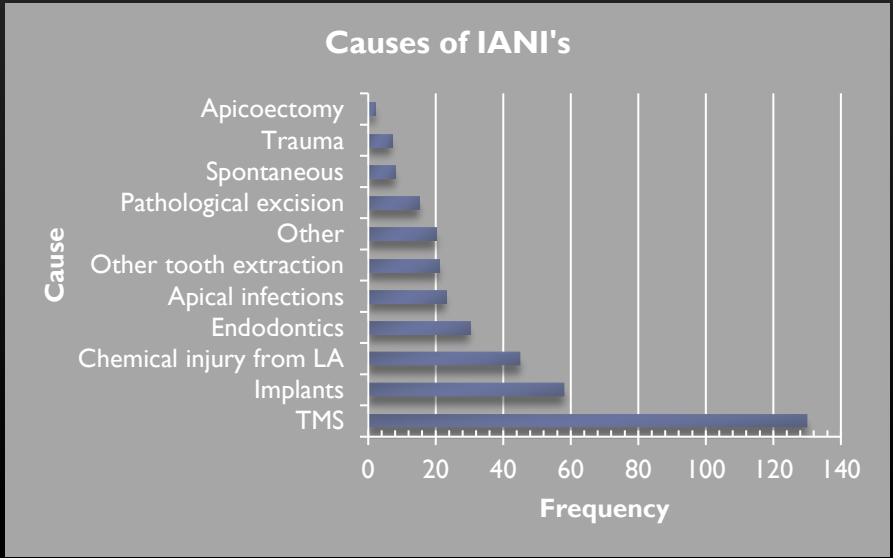
Axis II Psychological factors
Mood anxiety / depression
Introversion, neuroticism, hypervigilance, catastrophising
Fear of surgery
Fear of pain

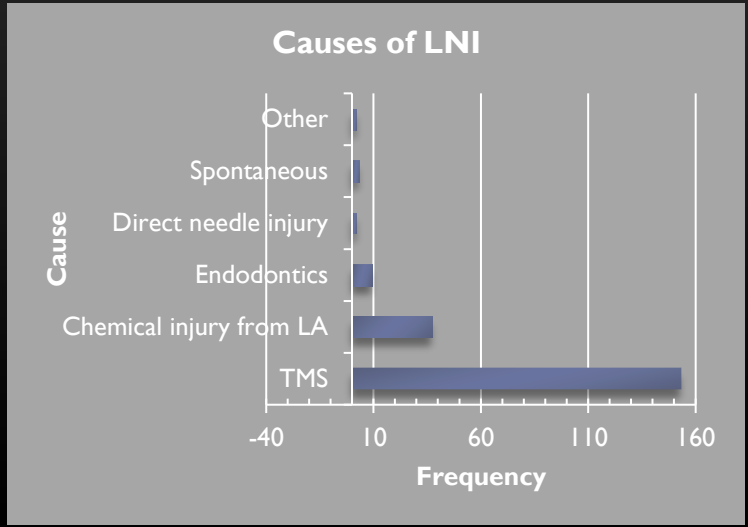
Poor pain modulation DNIC positive tests
Genetics
COMPT CA channels
Epigenetics
Prior abuse and neglect
OMICS ????

Surgical factors
Type of surgery
Site
Minimise nerve injury
(Tissue tension & Duration)
High level perioperative pain
(Lack of local anaesthesia)

Joel Katz & Ze'ev Seltzer Transition from acute to chronic postsurgical pain: risk factors and protective factors ▶ Expert Review of Neurotherapeutics Volume 9, 2009 - Issue 5

Dentistry causes of nerve injuries + neuropathic pain

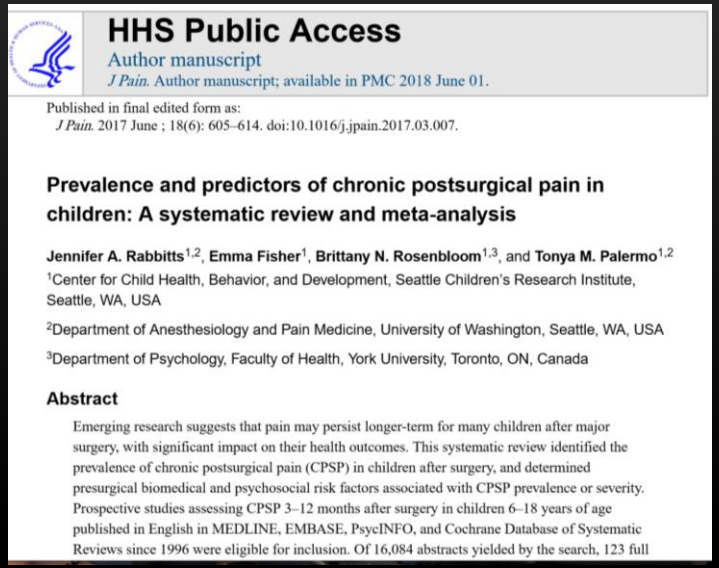




- **Summary of nerve injury patients** March 2008 –2016
- 400 IANI patients (73% F: 26.8% M; mean age = 46.5 years [range 18 – 85])
- 214 LNI patients (64.5% F: 34.6% M; mean age = 38.6 years [range 20 -73])

Predictive patient factors

- **Presurgical pain intensity, child anxiety, child pain coping efficacy, and parental pain catastrophizing** were the only presurgical factors identified as predictive of CPSP. Biological and medical factors assessed were not associated with CPSP in any study. Well-designed studies examining prevalence and predictors of CPSP are critically needed in children.
- The biopsychosocial model of pain is central to our understanding of factors involved in the development and maintenance of CPSP.
- **Several presurgical risk factors for CPSP have been consistently identified in adults undergoing surgery, including biological factors (older age, female sex), medical factors (greater presurgical pain), and psychosocial factors (higher levels of presurgical anxiety and pain catastrophizing)7–10.**



Published in final edited form as:
J Pain. 2017 June ; 18(6): 605–614. doi:10.1016/j.jpain.2017.03.007.

Prevalence and predictors of chronic postsurgical pain in children: A systematic review and meta-analysis

Jennifer A. Rabbitts[1,2], **Emma Fisher**[1], **Brittany N. Rosenbloom**[1,3], and **Tonya M. Palermo**[1,2]

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[2]Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, WA, USA

[3]Department of Psychology, Faculty of Health, York University, Toronto, ON, Canada

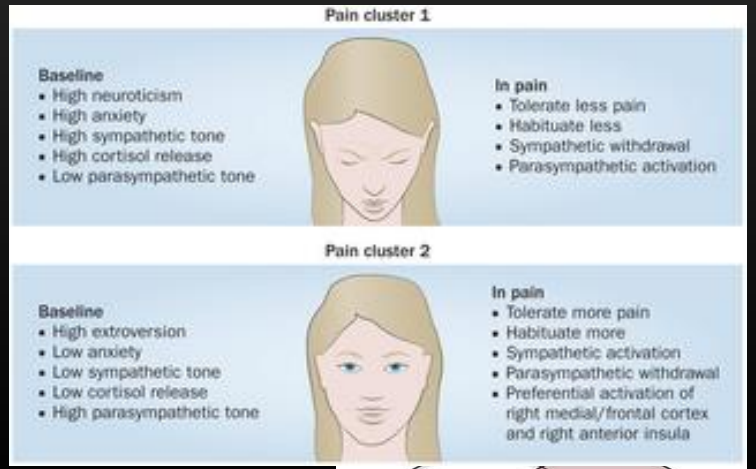
Abstract

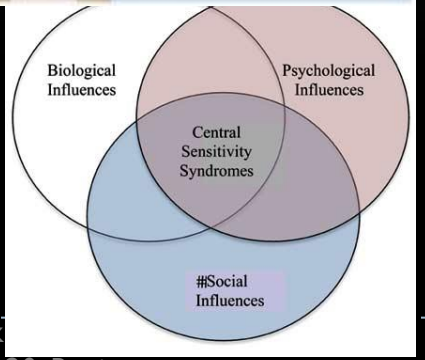
Emerging research suggests that pain may persist longer-term for many children after major surgery, with significant impact on their health outcomes. This systematic review identified the prevalence of chronic postsurgical pain (CPSP) in children after surgery, and determined presurgical biomedical and psychosocial risk factors associated with CPSP prevalence or severity. Prospective studies assessing CPSP 3–12 months after surgery in children 6–18 years of age published in English in MEDLINE, EMBASE, PsycINFO, and Cochrane Database of Systematic Reviews since 1996 were eligible for inclusion. Of 16,084 abstracts yielded by the search, 123 full

Hinrichs-Rocker A, Schulz K, Jarvinen I, Lefering R, Simanski C, Neugebauer EA. Psychosocial predictors and correlates for chronic post-surgical pain (CPSP) - a systematic review. Eur J Pain. 2009; 13:719–30. [PubMed: 18952472] 8. Katz J, Seltzer Z. Transition from acute to chronic postsurgical pain: risk factors and protective factors. Expert Rev Neurother. 2009; 9:723–44. [PubMed: 19402781] 9. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. Lancet. 2006; 367:1618–25. [PubMed: 16698416] 10. Kehlet, H., Edwards, RR., Brennan, T. Persistent Postsurgical Pain: Pathogenic Mechanisms and Preventive Strategies, Pain 2014. In: Srinivasa, RN., Sommer, CL., editors. Refresher Courses, 15th World Congress of Pain. Washington, D.C: IASP Press; 2014.

Psychosocial risk factors predictive of CPSP

- Cognitive
  - Fear of surgery and anxiety
  - Fear of pain
- Personality disorder
  - increased preoperative anxiety
  - Introverted personality
  - Catastrophizing
  - Poor coping skills
  - Hypervigilance state
- Psychological vulnerability – pain related fear
- Social support
- Solicitous responding
  - Empathetic spouse encouraging negative behaviour
  - Munchausen





Katz J, **Seltzer Z**. Transition from acute to chronic postsurgical pain: risk factors. Expert Rev Neurother. 2009 May;9(5):723-44. doi: 10.1586/ern.09.20. Review.

Type of patient

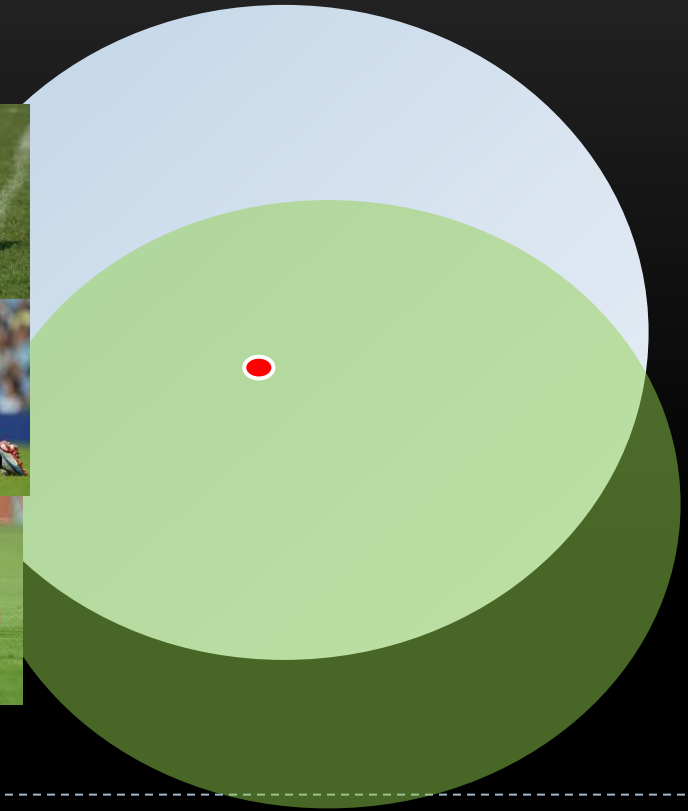
Nociception

Sensation

Behaviour

Suffering

Type of patient



W

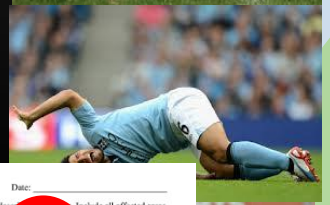
I

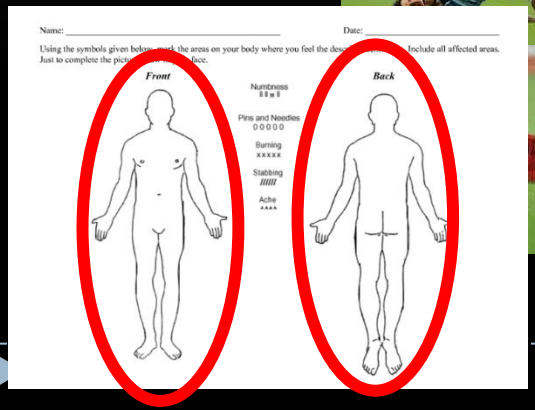
M

P

S

Type of patient





WW Women

~~GWAS~~

I I Injury- PTSD

Inhibition is poor with low pain modulation

M Mood disorders Anxiety & Stress

PP Personality disorders

introspective, catastrophiser and hypervigilance

Prior abuse and neglect

S Sleep deprivation

Stress

Determinants for onset and maintenance of chronic pain=AXIS

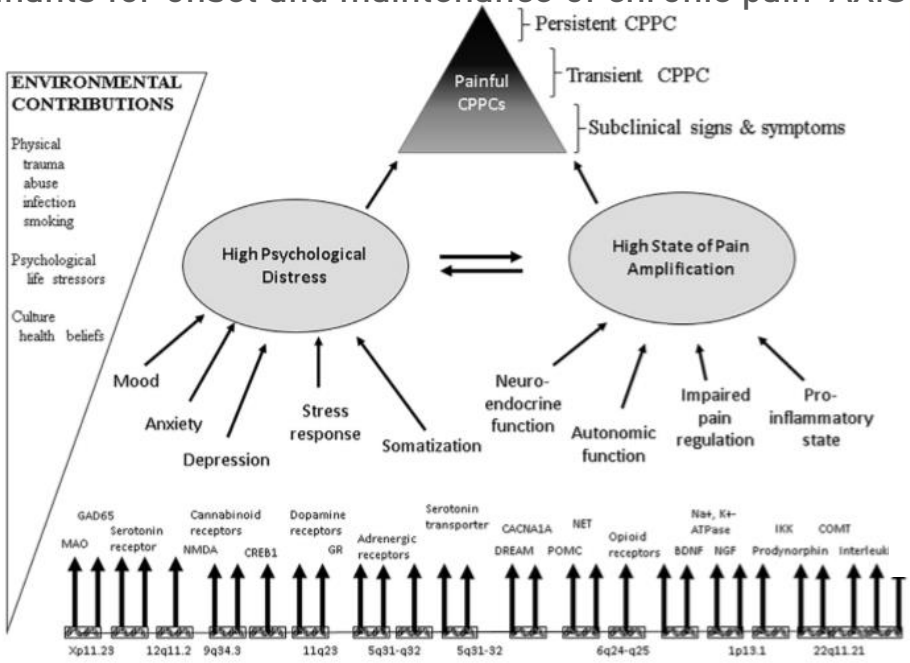


Figure 4. This model depicts likely determinants that contribute to the risk of onset and maintenance of common chronic overlapping pain conditions (COPCs). These factors are determined by genetic variability and environmental events that determine an individual's psychological profile and pain amplification status. These 2 primary domains are interactive and influence the risk of pain onset and persistence. Likely modifiers of the interaction between genetic and environmental factors include sex and ethnicity. Abbreviations: MAO, monoamine oxidase; GAD65, glutamate decarboxylase; NMDA, *N*-Methyl-D-aspartic acid; CREB1, CAMP responsive element binding protein 1; GR, glucocorticoid receptor; CACNA1, calcium channel, voltage-dependent, T type, alpha 1I subunit;

COMMENTARY

Check for updates

Pain chronification: what should a non-pain medicine specialist know?

Bart Morlion[a], Flaminia Coluzzi[b], Dominic Aldington[c], Magdalena Kocot-Kepska[d], Joseph Pergolizzi[e], Ana Cristina Mangas[f], Karsten Ahlbeck[g] and Eija Kalso[h]

[a]Leuven Centre for Algology & Pain Management, University Hospitals Leuven, KU Leuven, Belgium; [b]Department of Medical and Surgical Sciences and Biotechnologies Unit of Anaesthesia, Intensive Care and Pain Medicine, Sapienza University of Rome, Rome, Italy; [c]Royal Hampshire County Hospital, Winchester, UK; [d]Department of Pain Research and Treatment, Jagiellonian University Medical College, Kraków, Poland; [e]Global Pain Initiative, Golden, CO, USA and Naples Anesthesia and Pain Associates, Naples, FL, USA; [f]Hospital de Santo André, Leiria, Portugal; [g]Capio St Görans Hospital, Stockholm, Sweden; [h]Pain Clinic, Departments of Anaesthesiology, Intensive Care, and Pain Medicine, Helsinki University Central Hospital, Helsinki, Finland

ABSTRACT

Objective: Pain is one of the most common reasons for an individual to consult their primary care physician, with most chronic pain being treated in the primary care setting. However, many primary

ARTICLE HISTORY

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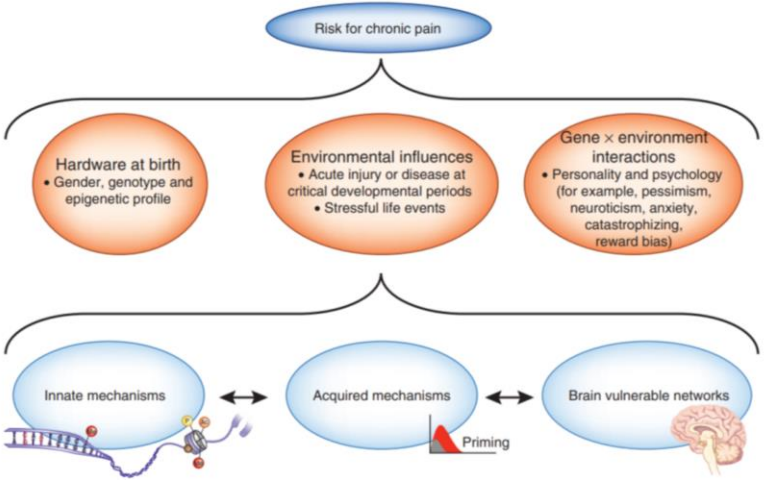

Den

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Neuron
Review

The Genetics of Neuropathic Pain from Model Organisms to Clinical Application

Margarita Calvo,[1,10] Alexander J. Davies,[2,10] Harry L. Hébert,[3,10] Greg A. Weir,[2,9,10] Elissa J. Chesler,[4] Nanna B. Fi
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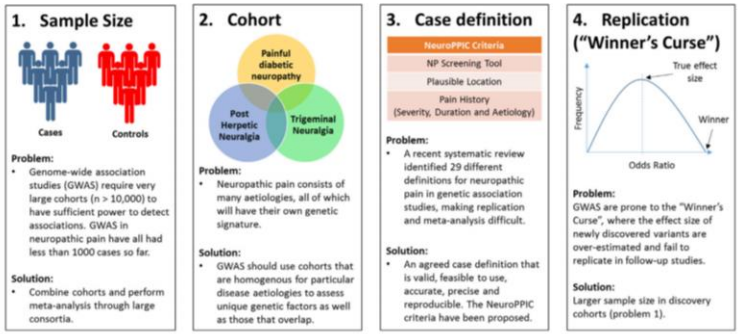
Glasgow, UK
[10]These authors contribu
*Correspondence: micha
https://doi.org/10.1016/j

Neuropathic pain (N
disabling, renderin
conservation of pai



2. The Challenges of Conducting Genome-wide Association Studies in NeuP

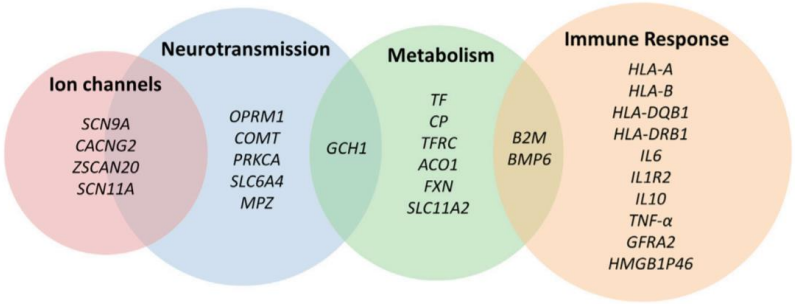
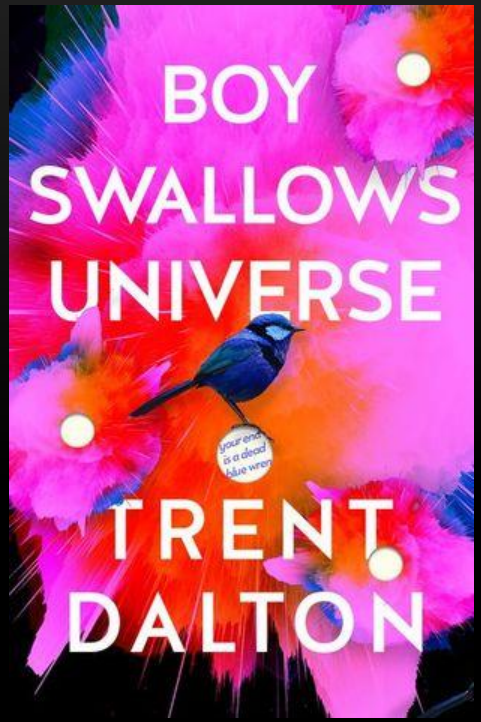


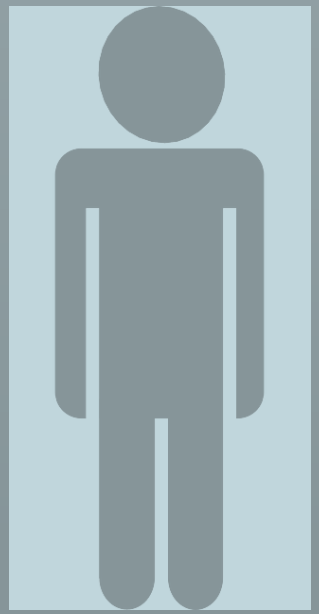
Figure 3. A Venn Diagram of Genes Reaching Study Specific or Suggestive Significance in Human Candidate Gene and Genome-wide Studies So Far in NeuP and the Overlap of Biological Pathways

These genes have been summarized in a recent systematic review of NeuP by Veluchamy et al. (2018), where the inclusion criteria were any study analyzing genetic variants in people with NeuP compared to people without NeuP. The number of genes and our understanding of their contribution within these pathways, in the context of NeuP, is likely to change as more studies are published.

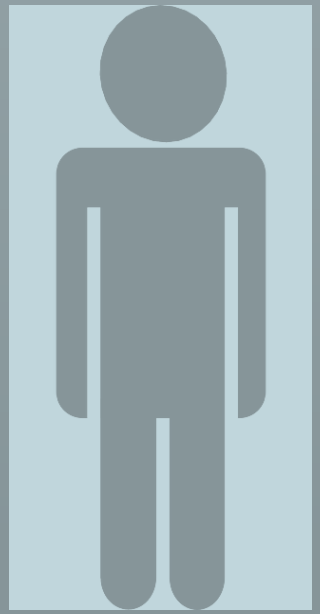
Past life events……



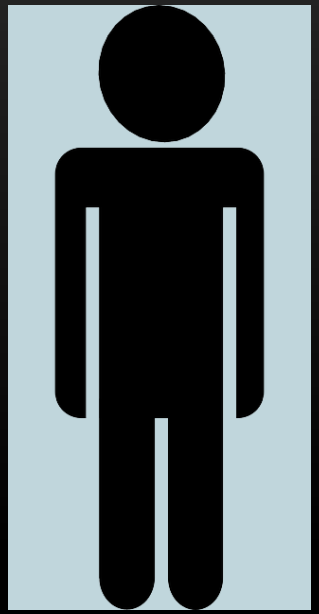
Overview



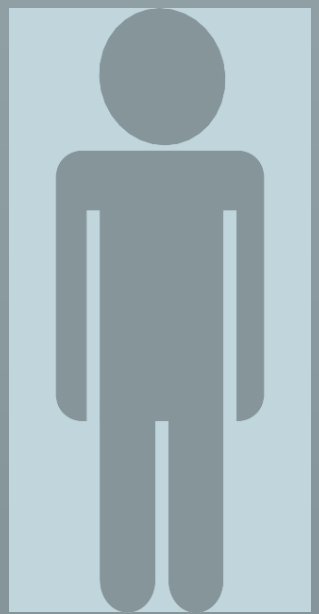
What is Neuropathic pain?



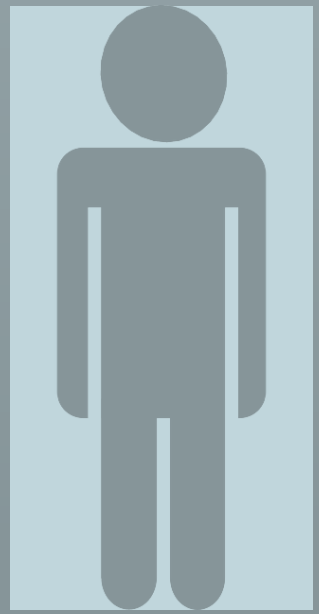
Who gets PTNP?



Why prevent PTNP?

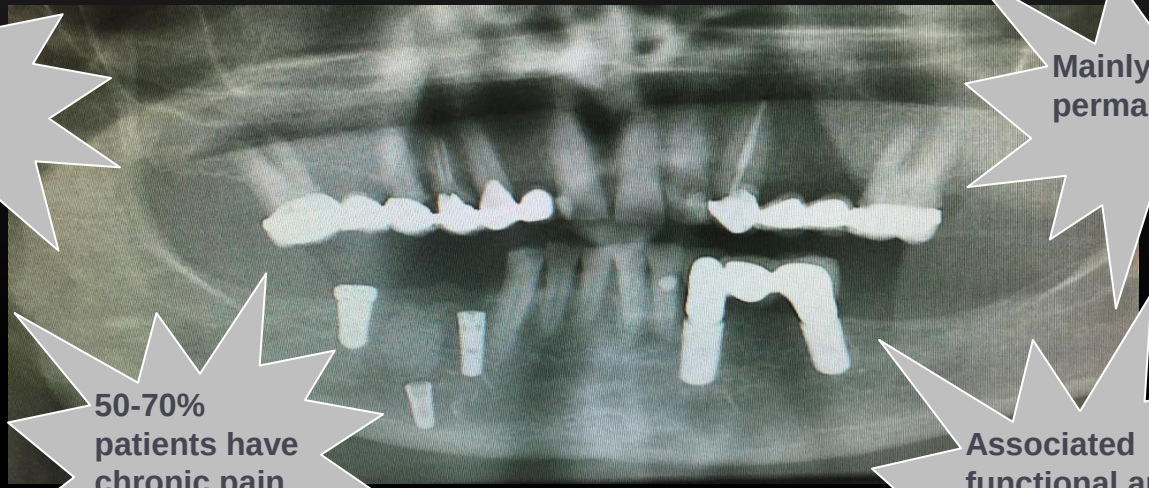


How to prevent these injuries?



How to manage these injuries?

Why are nerve injuries such a big deal ?



Avoidable / negligent

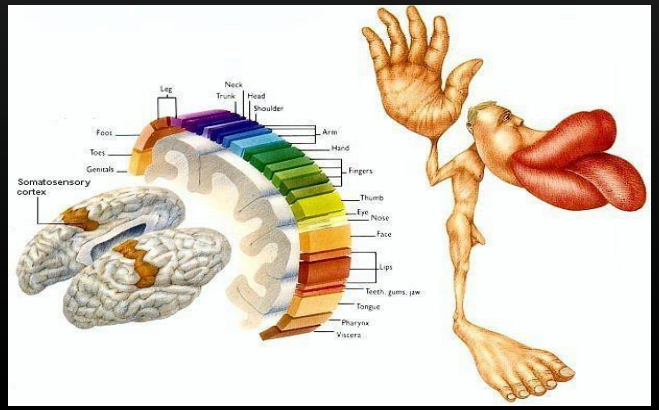
Mainly permanent

50-70% patients have chronic pain

Associated functional and psychological impact

Particular issues with Trigeminal pain?

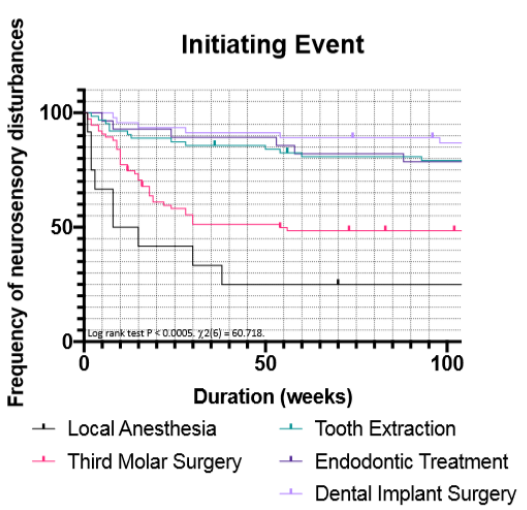
- Big part of our lives
- Underpins the primordial survival instincts
- Constant unavoidable activity
- Underpins daily pleasure in health
  - Eating
  - Drinking
  - Speaking
  - Smiling
  - Sexual interaction
- **Underpins our identity!**

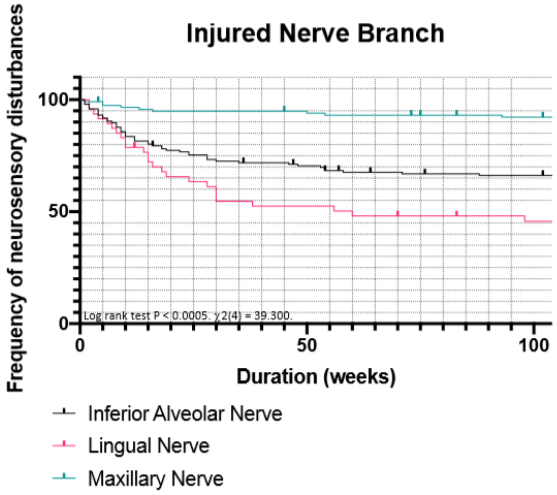


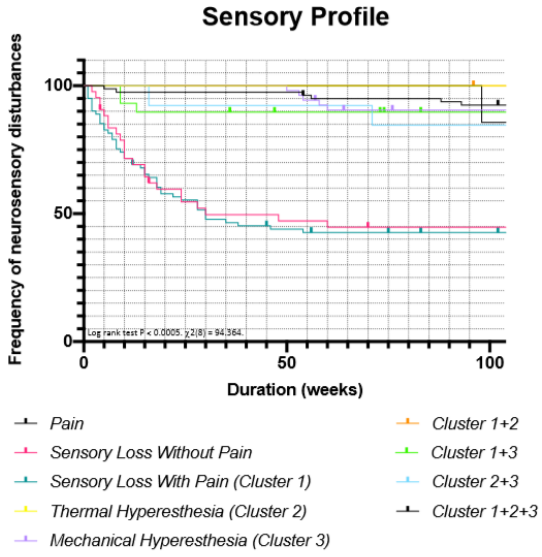
Most nerve injuries are permanent and cannot be fixed

Prognosis V Nerve injuries N=1331

Kaplan–Meier analysis of neurosensory disturbances over time comparing the injured nerve branch (A), initiating event (B), and sensory profile (C).

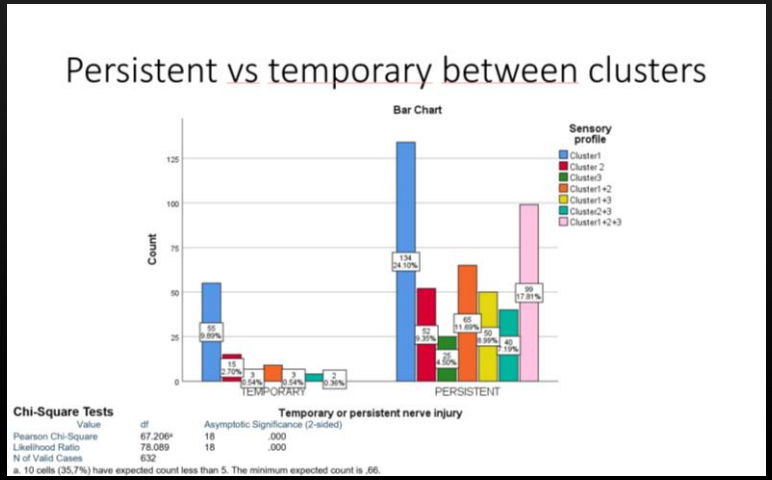






Van der Cruyssen F, Peeters F, De Laat A, Jacobs R, Politis C, Renton T. Factors affecting evolution of symptoms and quality of life in patients referred for iatrogenic post-traumatic trigeminal neuropathy: a longitudinal study in two tertiary referral centers in UK and Belgium. Pain 2020 in press.

Predictive prognosis by clustering n=1331



Positive factors for resolution

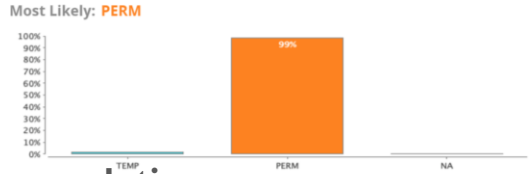
LA or M3M cause

EQ5D low pain

Lingual nerve

Sensory loss with or without pain

Prediction Model RapidMiner (generalized linear model)



Negative factors for resolution

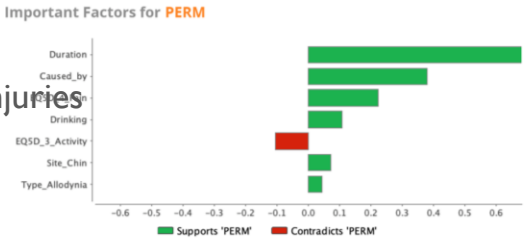
EQ5D poor activity

Allodynia

Endo Implant nerve injuries

Maxillary nerve

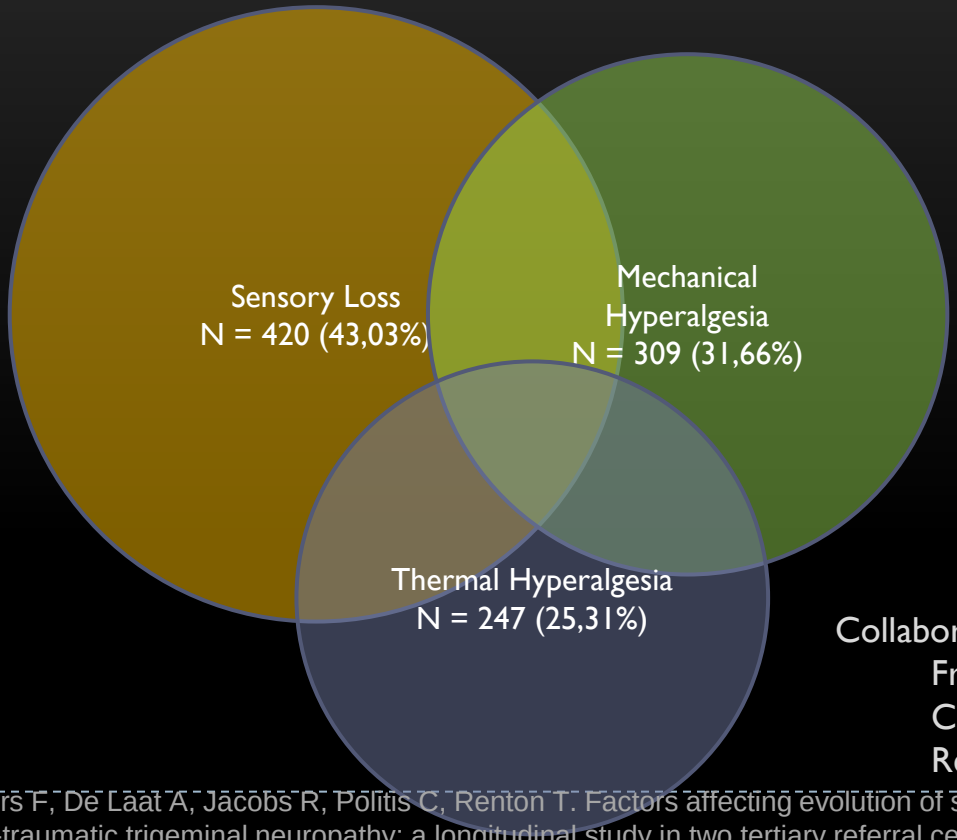
Duration of NI



Collaboration with University of Leuven

Fréderic Van de Cruyssen

Clustering of Sensory Profiles (N = 976) in press



Collaboration with University of Leuven
Fréderic Van der Cruyssen
Constantis Politis
Reinhilde Jacobs

Van der Cruyssen F, Peeters F, De Laat A, Jacobs R, Politis C, Renton T. Factors affecting evolution of symptoms and quality of life in patients referred for iatrogenic post-traumatic trigeminal neuropathy: a longitudinal study in two tertiary referral centers in UK and Belgium. Pain 2020 in press

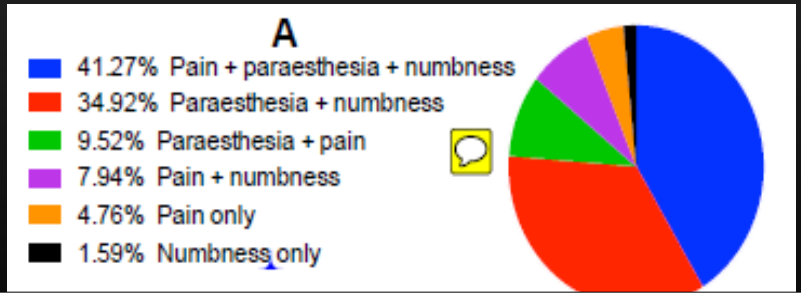
Consequences
Neuropathy causing functional problems

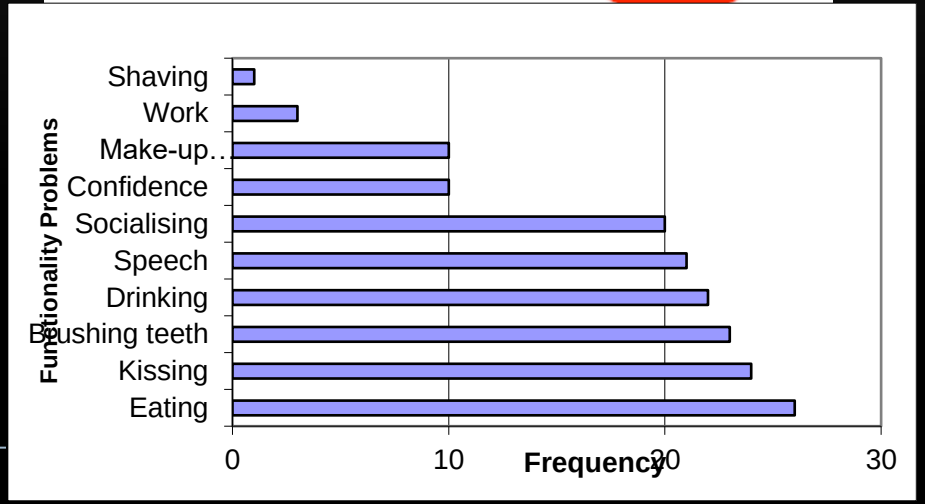
Recent study @ KCL on 100 implant nerve injury patients

95% of implant nerve injury neuropathic pain

92% permanent

Functional and psychological impact



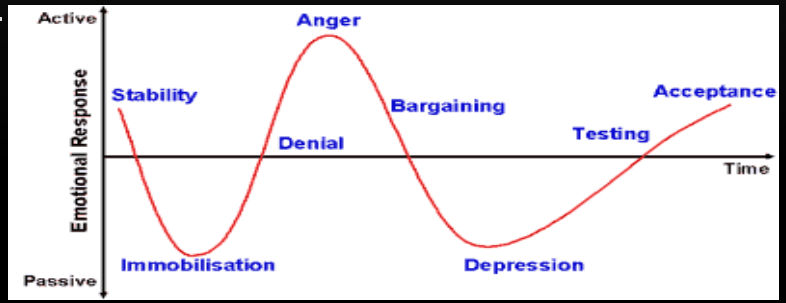


Renton T, Dawood A, Shah A, Searson L, Yilmaz Z. Post-implant neuropathy of the trigeminal nerve. A case series. Br Dent J. 2012 Jun 8;212(11):E17. doi: 10.1038/sj.bdj.2012.497

Psychological consequences

- Depression
- Anger
- Post traumatic stress disorder 68%
- Victim of abuse
- Loss of ability to trust

Kubler Ross

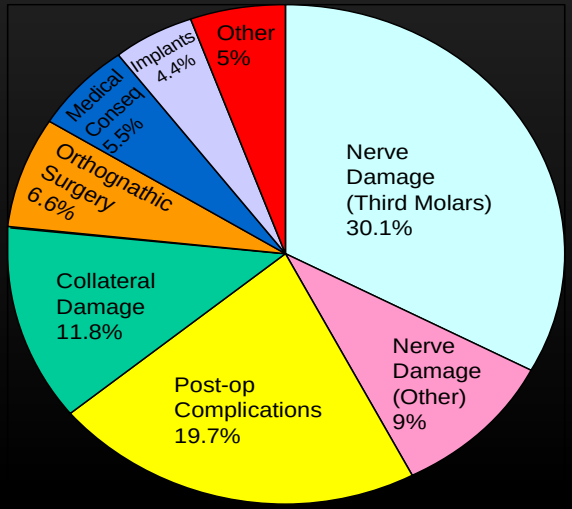


The psychosocial and affective burden of posttraumatic neuropathy following injuries to the trigeminal nerve. **Smith** JG, **Elias** LA, **Yilmaz** Z, Barker S, Shah K, Shah S, **Renton** T. J Orofac Pain. 2013 Fall;27(4):293-303. doi: 10.11607/jop.105 Sullivan MJ et al. Catastrophizing and perceived injustice: risk factors for the transition to chronicity after whiplash injury. Spine (Phila Pa 1976). 2011 Dec 1;36(25 Suppl):S244-9 Dec;92(12):2041-56. Review

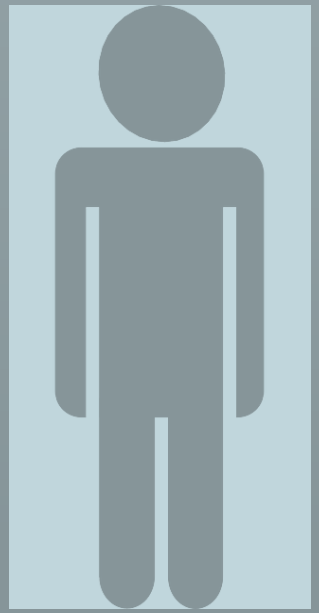
Medicolegal consequences

Nerve damage related to dental procedures are often NEGLIGENT as they are elective surgery and damage is avoidable.

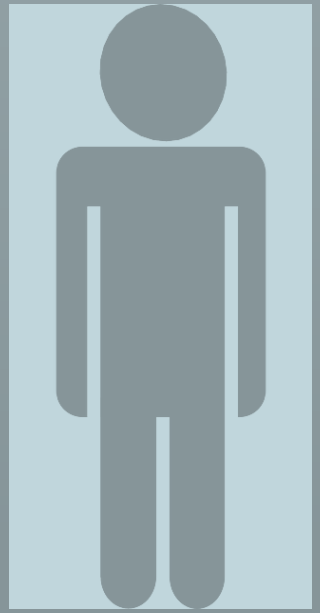
- This results in litigation and Settlements getting more expensive
  - Implant related cases settlements $1-3 million (2011)



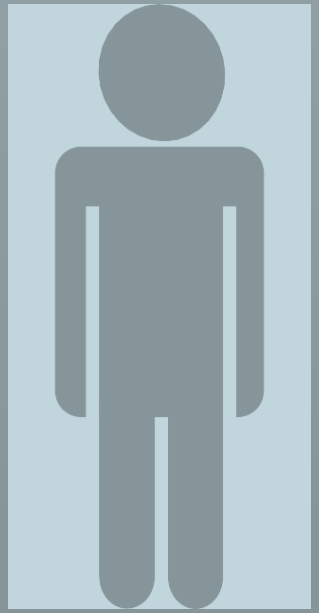
Overview



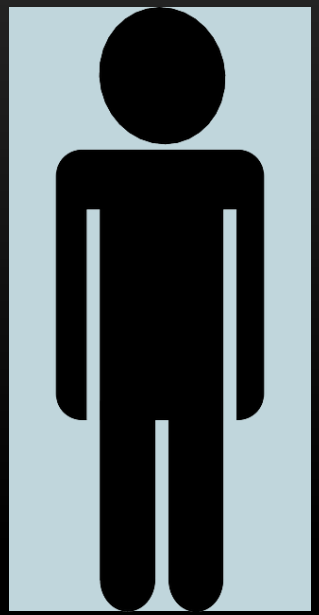
What is Neuropathic pain?



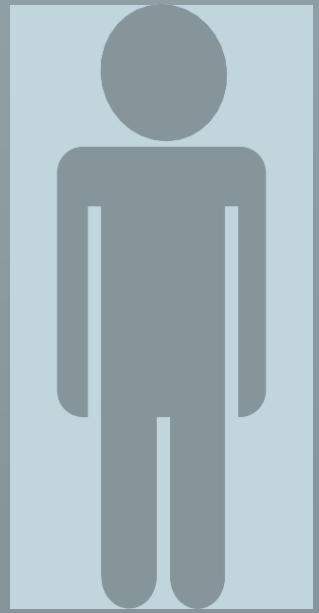
Who gets PTNP?



Why prevent PTNP?

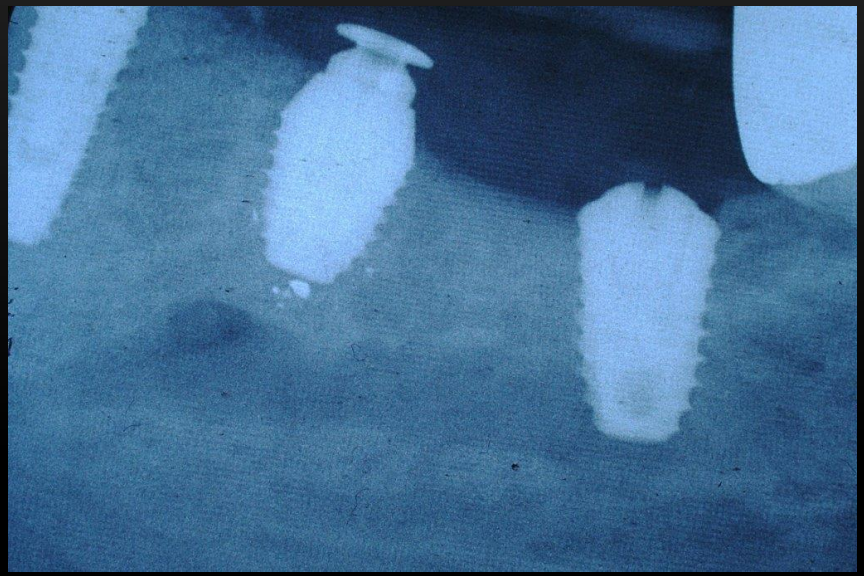


How to prevent these injuries and ~~how to manage~~ them?



Trigeminal neuralgia

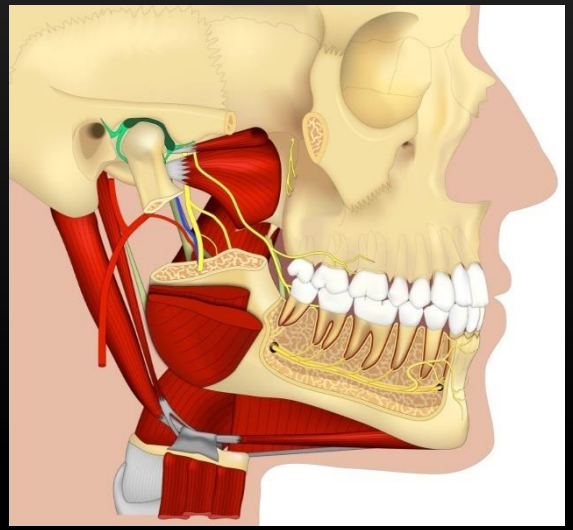
Preventing dentistry related nerve injury and PTNP

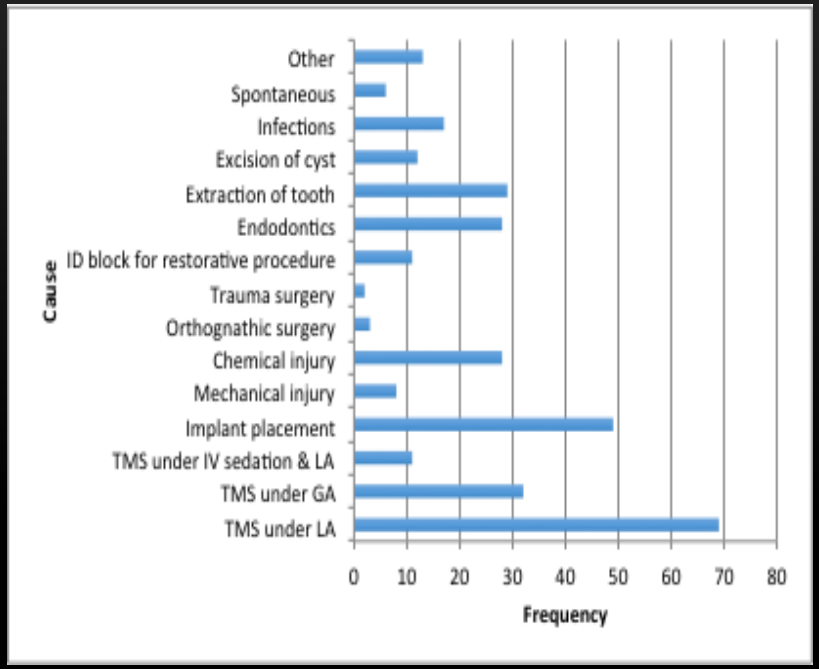


How do we prevent these injuries?

- Managing patients expectations
- Risk assessment and management
- Operative technique
- Post op follow up
- Recognition and early medical and or surgical intervention (if indicated)

Prevention of Trigeminal Post Traumatic Painful Neuropathy?





Local anaesthesia
Dental Implants
Endodontics
~~Third molar surgery~~

Risk factors for persistent neuropathy related to IDBs
In order to minimise complications related to dental LA you need to consider modifying the following risks;

- **Block anaesthesia** Nerve block injections should be undertaken without intent on direct 'hit' of the nerve. 60% of patients who experience the 'funny bone' neuralgia due to the IDB needle being placed too close t… lingual or inferior alveolar nerves experience persistent neuropathy (20)
- **Lingual nerve > IAN** Is this technique related or anatomically related (less fascicles in … or recovery). Perhaps the direct IDB approach may place the lingual nerve at increased … indirect technique. (14)
- **Concentration of LA** Any increased concentration of any agent leads to increased ne… eurot…
- **Volume of LA** There is no evidence to support this sugge… s are neu…otoxic, dependent upon the proximity, LA concentration, neural damage additi… add to potential neurotoxicity.
- **Multiple injections** Second or subsequent injections that impede direct… not be associated with the usual 'funny bone' neuralgic pain. Thus the patient does no… rendering the nerves more at risk of direct damage.
- **Severe pain on injection** 60% increased occurrence of persistent neuropathy after IDBs (…
- **Type of LA Agent** Bupivicaine most neurotoxic of all LA agents
- **Type of vasoconstrictor?** The role of vasoconstrictor in nerve damage is unknown
- **Sedated or anaesthetized patients?** There is no evidence to support unresponsive patie… s likely to pr…tect themselves when neuralgia (funny bone reaction) occurs as the IDB needle encr… nerve.
- **Lack of LA aspiration?** Again there is no evidence to support that aspiration dur… er persistent neuropathies but a pragmatic view may infer less chemical injected intra neu… mical nerve injury.

Block injections

Multiple injections

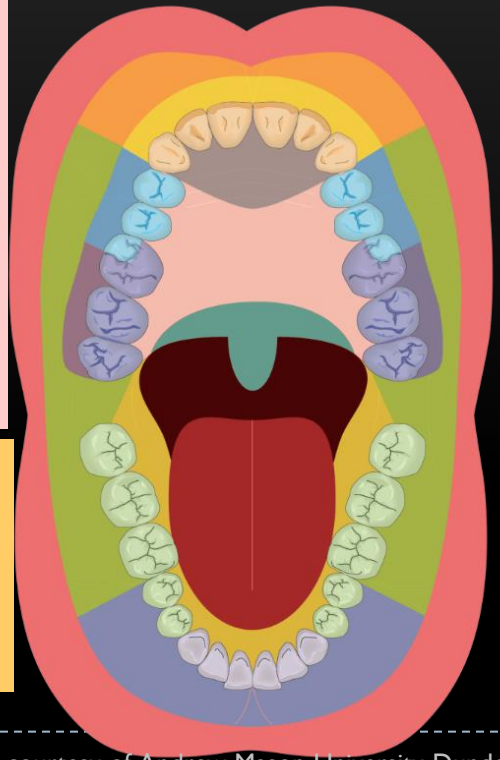
Type and concentration of LA agents

Extreme pain during injections

Infiltration dentistry is dependant upon the site and procedure

Maxillary dentistry can be performed entirely using Lidocaine 2% with adrenaline for all procedures
Buccal infiltration with intra-septal injections
No additional benefit using 4% Articaine
No palatal or incisal blocks are indicated

IDBS needed for
Posterior mandibular molar
Endodontic procedures may require IDBs or higher techniques (Gow Gates or Akinosi)



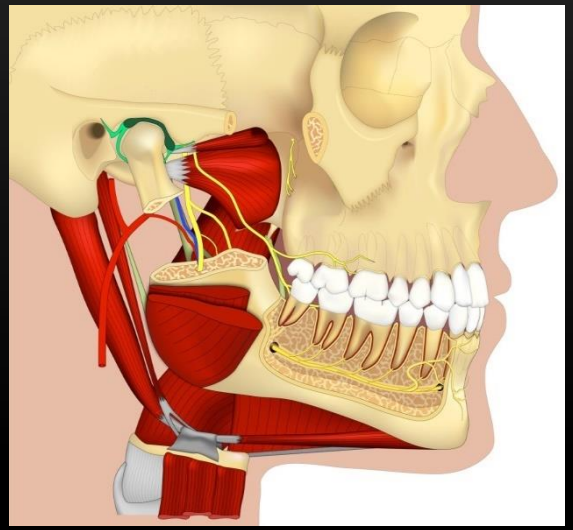
Mandibular 7s and 8s for **perio, restorations or implants**
Articaine 4% buccal infiltration and Lidocaine 2% lingual infiltrations OR for **extractions** intraligamental
If fails may need lidocaine IDB

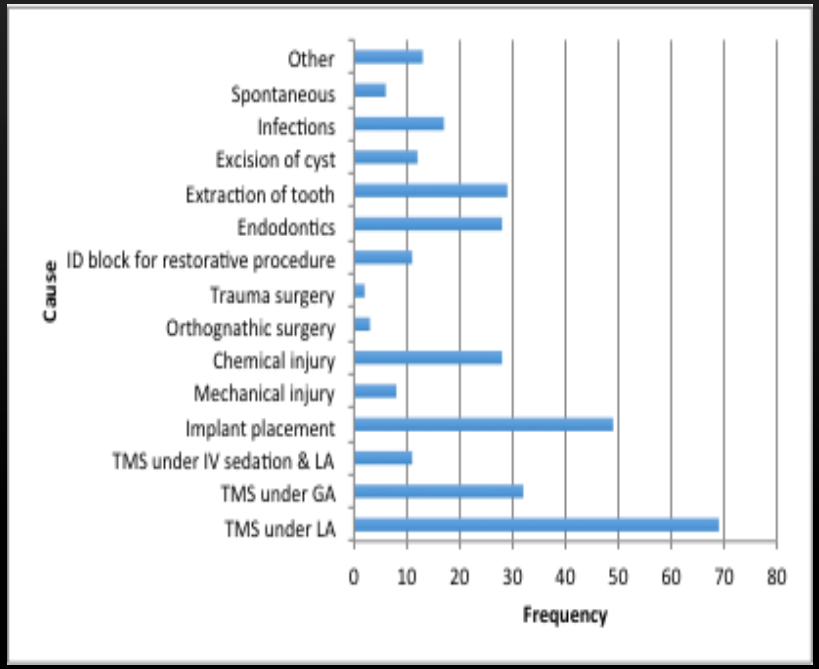
Mandibular 1st molars for **perio, restorations or implants**
Articaine 4% buccal +/- Lidocaine 2% crestal or lingual infiltration s OR for **extractions** add lidocaine lingual **of** intra-ligamental

Mandibular premolars, canines incisors for **perio, restorations or implants**
Articaine buccal infiltration (incisal nerve block using 30% cartridge) adjacent not in the mental foramen and massage over region. If fails repeat or add crestal or lingual infiltration OR for **extractions**, intra-ligamental

Illustration modified from figure courtesy of Andrew Mason University Dundee

Prevention of Trigeminal Post Traumatic Painful Neuropathy?



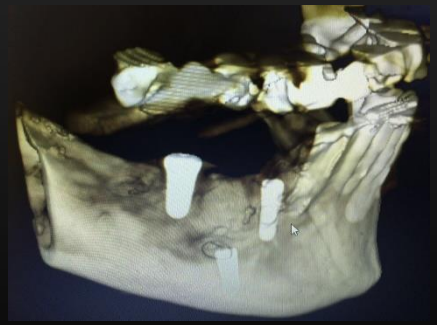


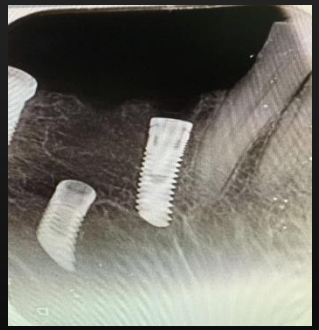
Local anaesthesia
Dental Implants
Endodontics
~~**Third molar surgery**~~

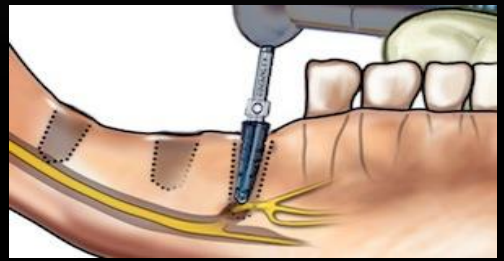
Prevention of Implant nerve injury
Risk factors

Most nerve injuries occur:

- **In patients over 47 years**
- **In the parasymphyseal region**
- **During preparation of implant bed**
- **Using Implants >10mm**
- **When the patient experiences severe pain**
  - during prep or implant placement
  - severe pain post surgery
  - Intraoperative bleed during prepping







Yilmaz Z, Ucer C, Scher E, Suzuki J, **Renton T**. A Survey of the Opinion and Experience of UK Dentists: Part 1: The Incidence and Cause of Iatrogenic Trigeminal Nerve Injuries Related to Dental Implant Surgery. Implant Dent. 2016 Oct;25(5):638-45.

Risk factors 1

A. Poor risk assessment - Inadequate preoperative assessment and planning due to;

Lack of knowledge/inexperience

Inadequate informed consent and management of patient expectations

Lack of identification of existing pre-surgical neuropathy.

Additional risk assessment of mandibular premolars and m

Poor planning

Know where the nerve is. Nerve localisation, risk factors when assessi
(Mental loop, characteristics of IAN position in various sites of mandible)

Parasymphyseal zone high risk.

The accuracy of estimating the position o
or CT scans is highlighted in the radiographi

Insufficient Safety zone- Risk perf
to the nerve.

Poor surgical technique

Poor recognition of intraoperative problems

Poor implant placement

Selection of implants 10mm plus

(evidence supports shorter implants **-**short impla
procedure and minimise morbidity**)**

Poor Planning

Insufficient Safety zone

Inappropriate radiographs

Inability to read CBCT

Using implants > 8mm

Operative

Poor technique reducing Safety zone/ lack use drill stops, guides/ intraoperative LCPAs

Lack of recognition risks bleeding/ drill sink

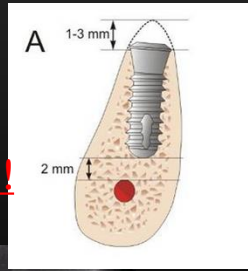
Post operative

Late recognition of nerve injury

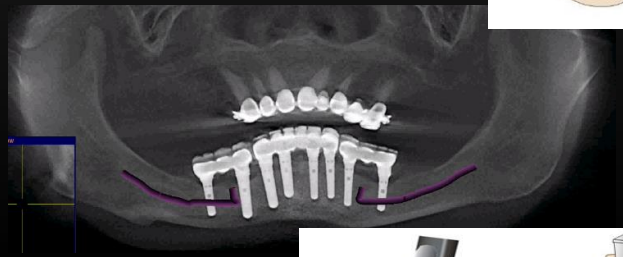
Lack removal implant within 30 hours

Evidence for prevention of implant related nerve injuries

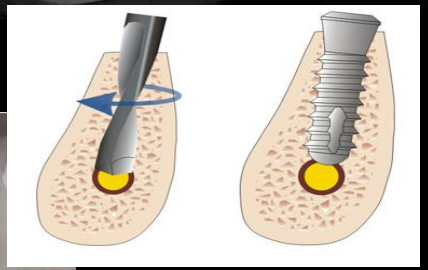
Safety zone of 2mm is insufficient with implant drills 1.5mm longer than the implants = resultant safety zone of 0.5mm!!!! 4mm!



- Computer guided surgery (**none**)
- Use surgical guides (**moderate**)
  - (Chan, Chik, Pow, & Chow, 2013; Van Assche et al., 2007).
- Drill stops stock or tailored **(none)**
- ITI recommendation **(moderate)**
  - PAUSE after 60% planned depth OR 6mm
  - Take LCPA and check position

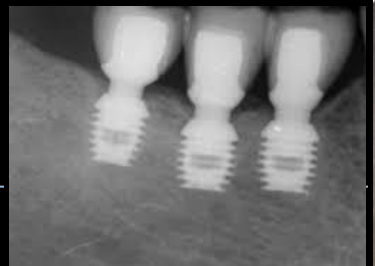


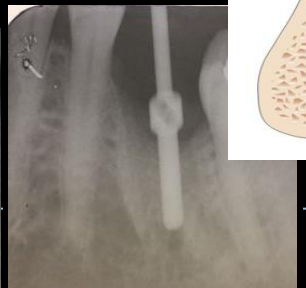
- **USE SHORT IMPLANTS** less than 10 mm for parasymphyseal region (**strong**) Implants should not need to be longer than 8 mm



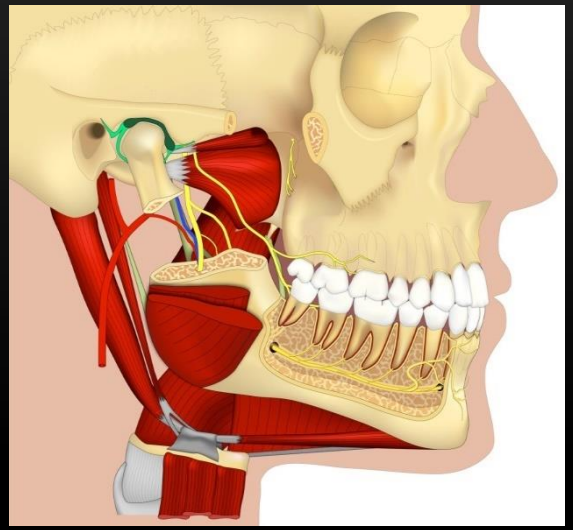
Short Implants (5 to 8 mm) Versus Longer Implants (>8 mm) with Sinus Lifting in Atrophic Posterior Maxilla: A Meta-Analysis of RCTs

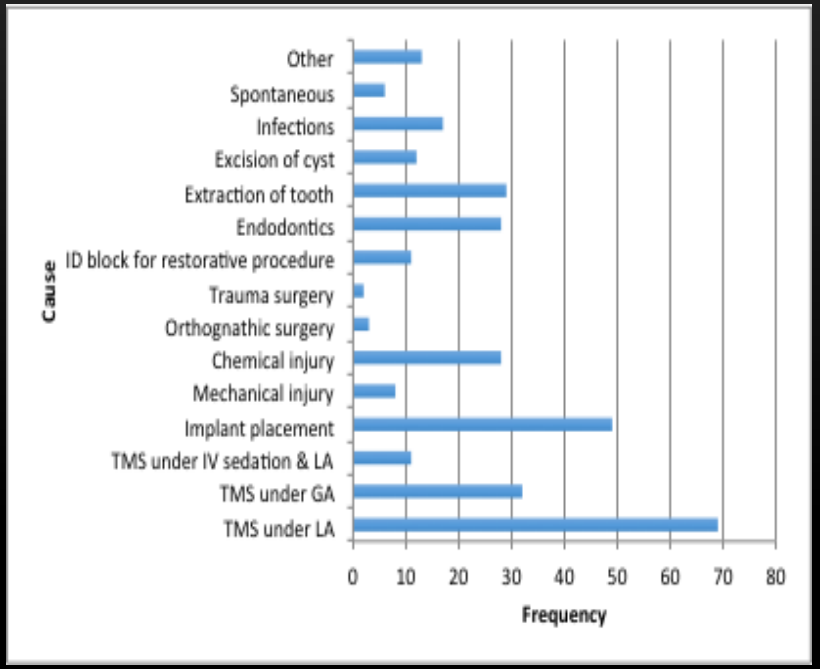
Tengfei Fan;* Yicun Li;* Wei-Wei Deng;* Tianfu Wu;* Wenfeng Zhang*,†





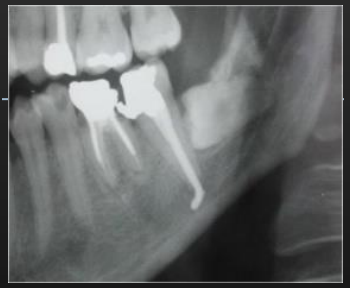
Prevention of Trigeminal Post Traumatic Painful Neuropathy?



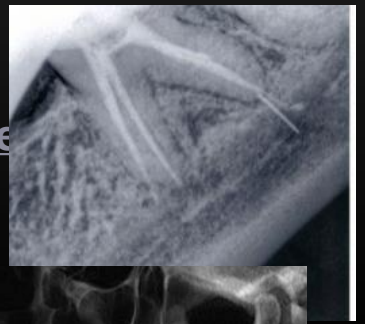


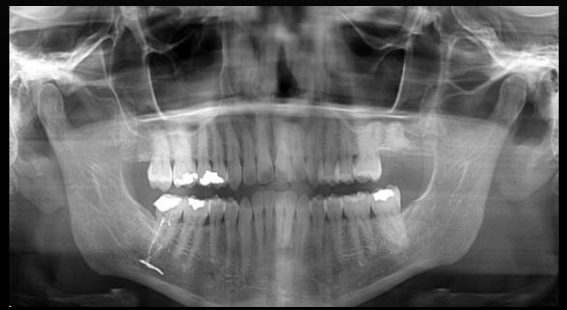
Local anaesthesia
Dental Implants
Endodontics
~~Third molar surgery~~

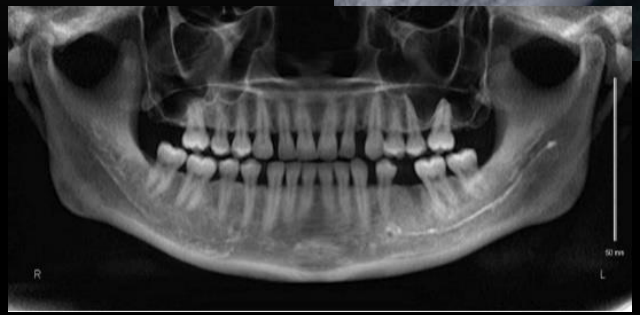
Endodontic related nerve injuries mechanisms



- Mechanical compression canal due to overfill
- Direct mechanical damage due to over instrumentation
- Haemorrhage with direct and indirect neural ischaemia
- **Loss of apical seal and CHEMICAL leakage and damage**
- Inflammation / infection







Fanibunda K, Whitworth J, Steele J (1998) The management of thermomechanically compacted gutta percha extrusion in the inferior dental canal. Br Dent J. 1998 Apr 11;184(7):330-2

Prevention of Endodontic related neuropathy: Risk factors

A. Inadequate preoperative assessment and planning due to;

- Lack of knowledge
  - GDP (80% of referrals) GDP endodontic success rates are significan… …vs 85%)
  - The American Association of Endodontists have made several recc… …ral of these patients
- Inability to read the radiographs or CBCT
- Inadequate informed consent-all options provided and related risk benef…
- Lack of identification of existing pre-surgical neuropathy (periapical lesions)

B. Premolar teeth & Proximity of tooth apex to IDC – 90% of the mandibular teeth in this series, were close to the IAN canal or premolars adjacent to the mental foramen. Proximity to the apex to the IAN/ breach a… seal and over chemical or instrumentation

- Tantanapornkul et al (33) reported the specificity and sensitivity of … …the IAN to the tooth roots in 161 mandibular third molars 161; for it was … …70% and 63% which were not significantly different.
- Patel et al (34) have reported on the use of CBCT in managi… cone periapicals.

C. Poor technique

- Breach of apex causing pain during surgery on irrigation or during instrumentati… …damage to periapical t…es
- Over instrumentation
- Overfill Detectable overfill occurred in 60% of cases and over instrumentation during preparation

D. Early recognition and intervention for Endodontic related nerve injuries

- ALWAYS undertake HOMECHECK , review patient and confirm neuropat…
- Neuropathy related to endodontics can be delayed and the patient must h… 3-4 days post treatment (Renton et al unpublished).
- If nerve injury is suspected, you will already be aware of the proximity of th… …was likely breach of apex, over instrumentation or deposition of endodontic material in…
- If there is suspected the material, the apex and or tooth must be removed within 4… …of placement in ord… …maximise recovery from nerve injury (9). If the patient is insistent on keeping the tooth urgent referral of the patient may be indicated for

Tooth apex position
Proximity to IDC
Related root morphology

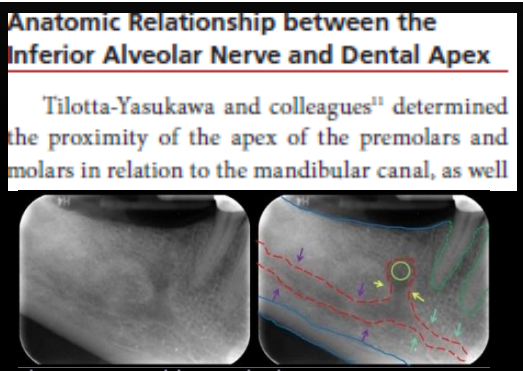
Poor technique
Lack apical seal
Over instrumentation
Over filling

Postoperative
Late recognition and late tooth or overfill removal

Risk assessment Radiographic Proximity to the Inferior dental canal (IDC)

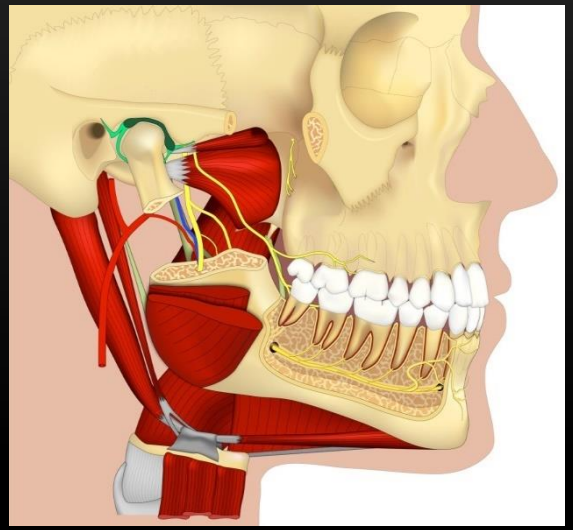
Mandibular teeth proximal to the IAN canal

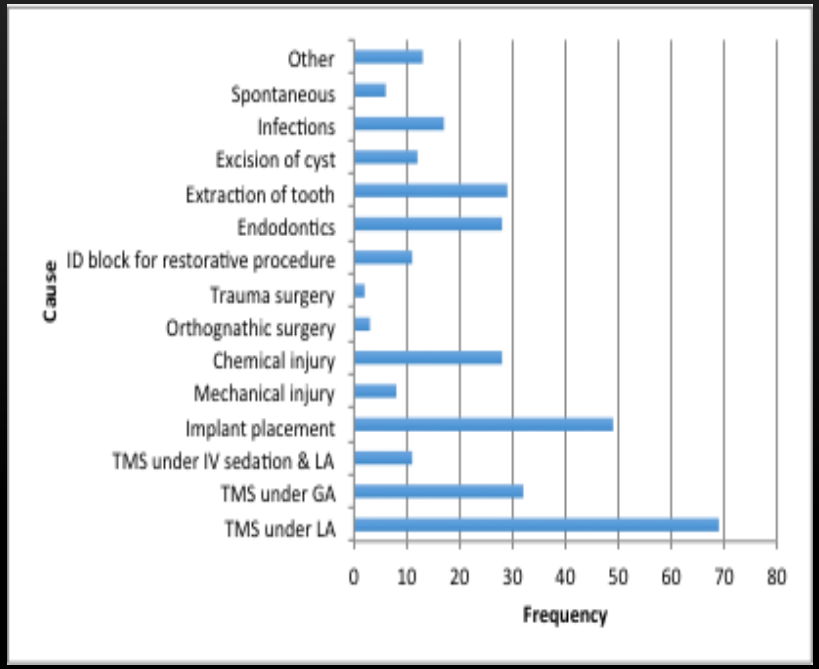
- Apex of the tooth may be adjacent or intruding into the IDC canal and any small degree of leakage or overfilling may compromise the IAN.
- Assessment of the proximity of the tooth apex to the IAN canal has become significantly improved with Cone Beam CT scanning (CBCT) with the attendant risk of additional radiation and may not provide significantly more information than a plane long cone radiograph.
- Most of CBCT assessment of tooth positioning relation to the IAN canal is based on M3M prior to extraction



Tilotta-Yasukawa F, Millot S, El Haddioui A, Bravetti P, Gaudy JF.Labiomandibular paresthesia caused by endodontic treatment: an anatomic and clinical study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Oct;102(4):e47-59.

Prevention of Trigeminal Post Traumatic Painful Neuropathy?





Local anaesthesia
Dental Implants
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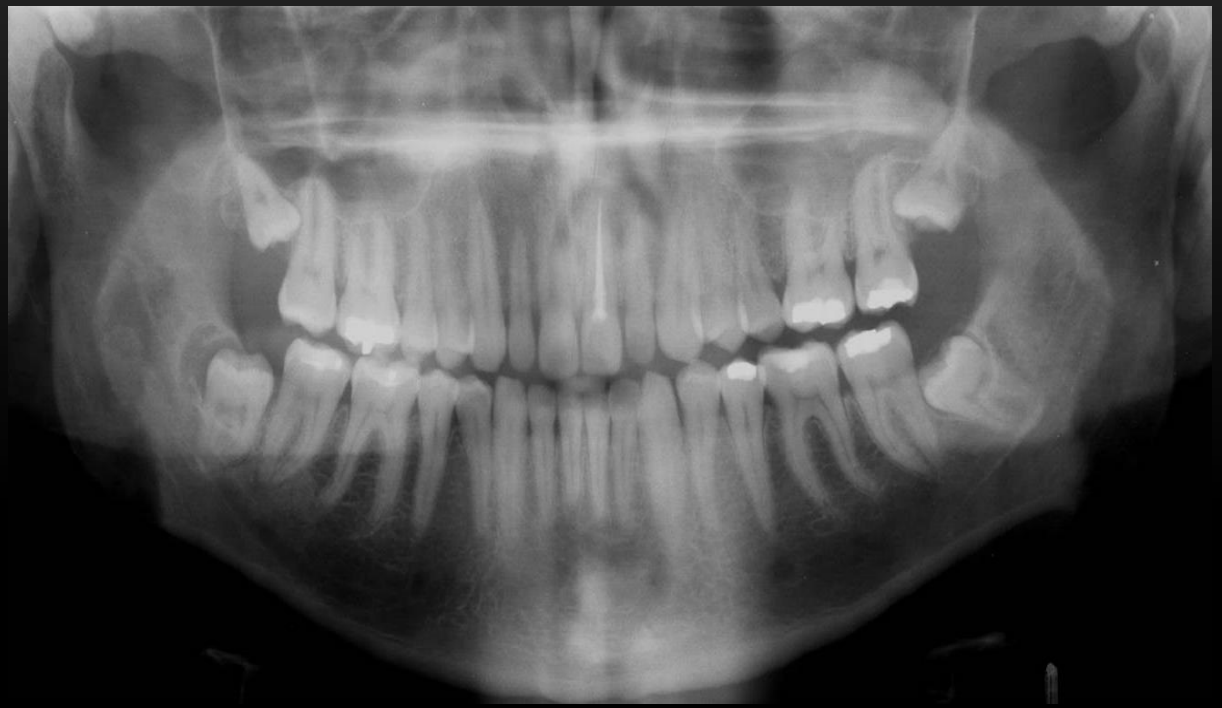
Third molar surgery

Preventing M3M surgery related PTPN



Lingual nerve
Age of the patient
Poor surgical technique
- Junior surgeons
- Duration of surgery
- Lingual access surgery
- Distal bone removal and lingual nerve injury
  - Use Buccal approach
  - Minimal access
- 'aberrant' Lingual nerve anatomy
  - 11-18% of lingual nerve above alveolar crest distal to M3Ms

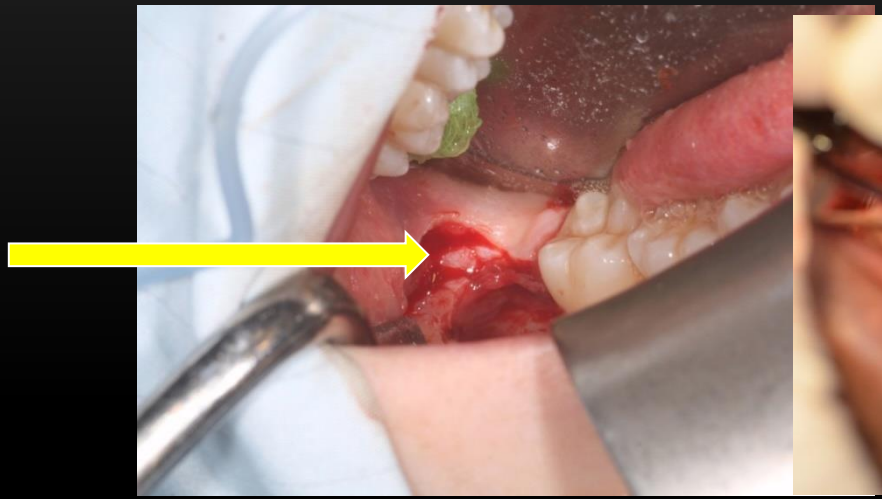
Inferior alveolar nerve
Age of the patient
- Intra-operatory exposure of the nerve
- Un-erupted tooth

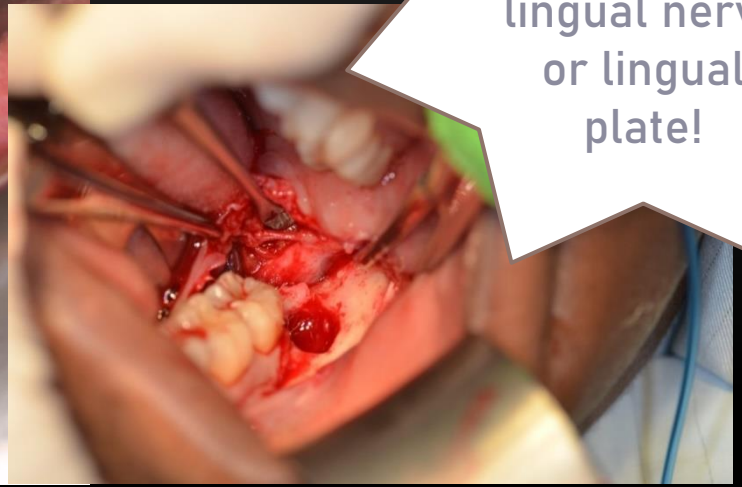
Poor Radiographic risk assessment
- Perforation of tooth roots by IDC
- Proximity of tooth roots to inferior dental canal (IDC)
- Plain film
  - IDC loss LD
  - Darkening of roots
  - Deviation of IDC
- CBCT lack cortication, distortion of canal.
- Lingual IDC

Acta Odontol Scand. 2013 Jul 4. The importance of a good evaluation in order to prevent oral nerve injuries: A review.Céspedes-Sánchez JM, Ayuso-Montero R, Marí-Roig A, Arranz-Obispo C, López-López J. 662 were obtained from the search, from which 25 were selected accomplishing the inclusion criteria. Moreover, seven important articles were selected from the references of the ones mentioned, obtaining a total of 32 articles for the review.
Renton T, McGurk M. Brit J Oral Maxillofac Surg 2001; 39: 423-428 Acta Odontol Scand. 2013 Jul 4. [Epub ahead of print]

The importance of a good evaluation in order to prevent oral nerve injuries: A review.Céspedes-Sánchez JM, Ayuso-Montero R, Marí-Roig A, Arranz-Obispo C, López-López J. 662 were obtained from the search, from which 25 were selected accomplishing the inclusion criteria. Moreover, seven important articles were selected from the references of the ones mentioned, obtaining a total of 32 articles for the review.

Prevention
Lingual nerve Injury in M3M surgery



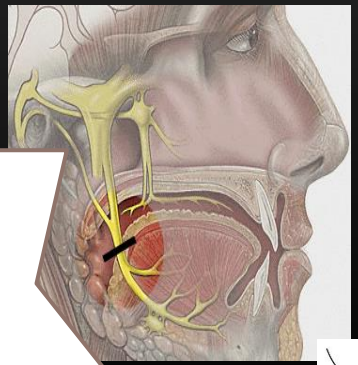


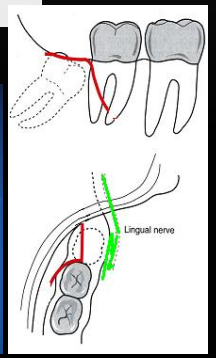
Avoid going anywhere near the lingual nerve or lingual plate!

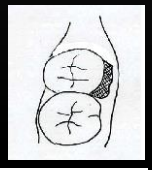
Spot the lingual nerve!

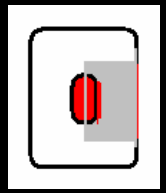
Minimal access prevents LNI

NEVER Remove distal bone OR section through the tooth

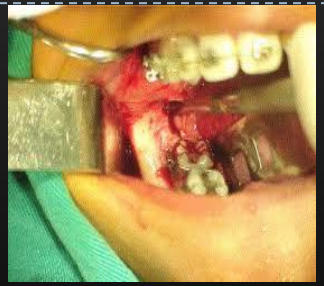


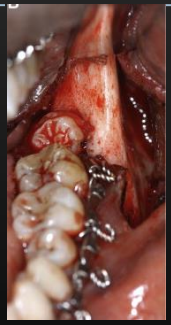




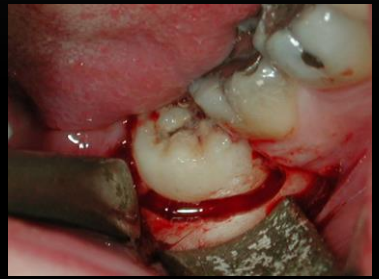


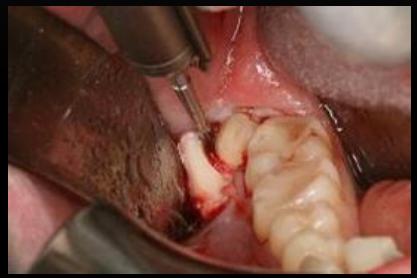
Old Technique 'Explode the patient'





New technique minimal access

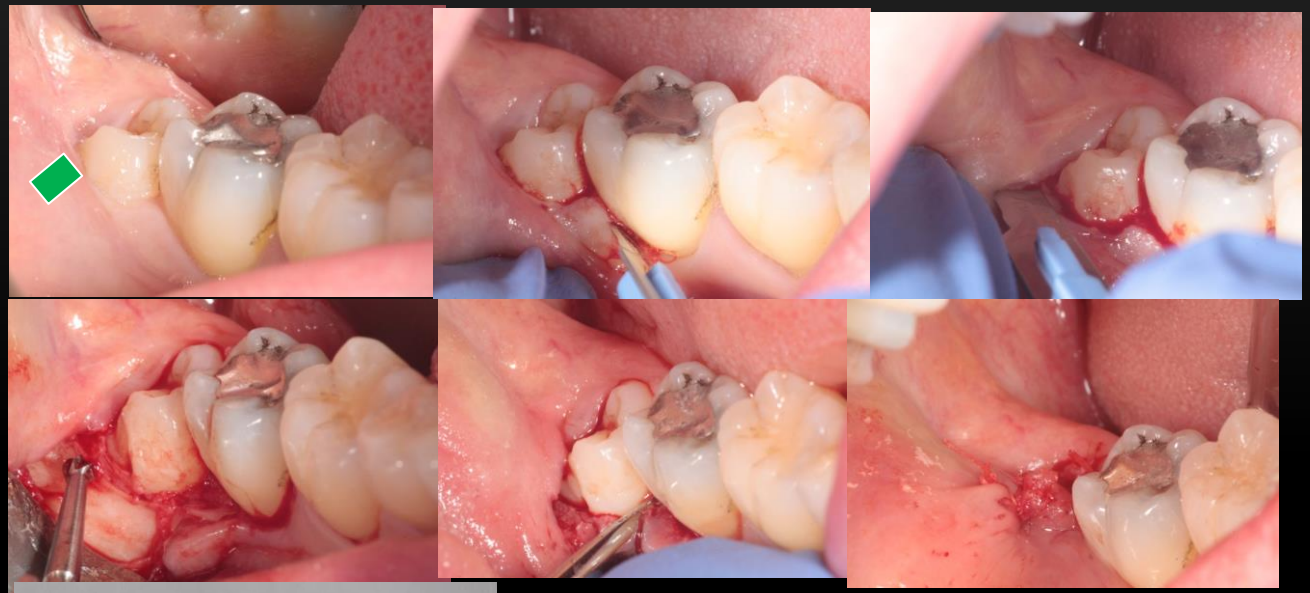




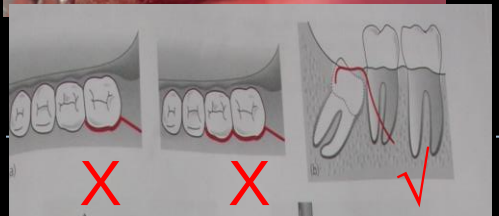
Evaluation of trigeminal nerve injuries in relation to third molar surgery in a prospective patient cohort. Recommendations for prevention. **Renton T**, Yilmaz Z, Gaballah K. Int J Oral Maxillofac Surg. 2012 Dec;41(12):1509-18.

Prevention LNI related to M3M surgery

Buccal minimal access surgery



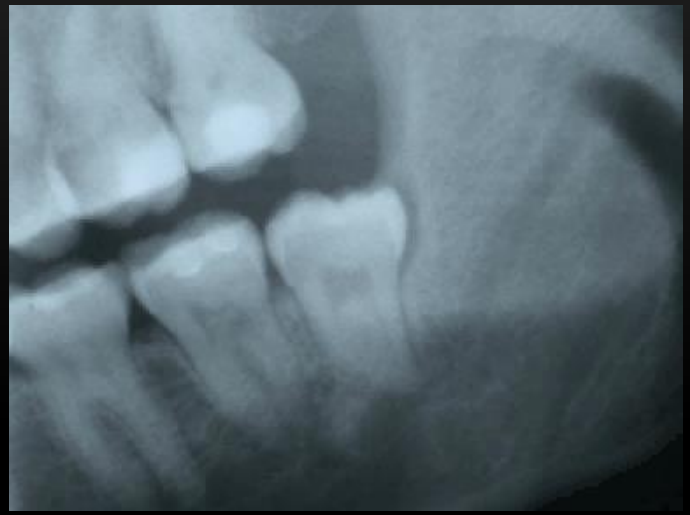
Fissure bur not rose head bur to get more accurate and minimal bone removal and tooth section



Triangular flap ensures minimal access and no exposure of distal bone behind M3M

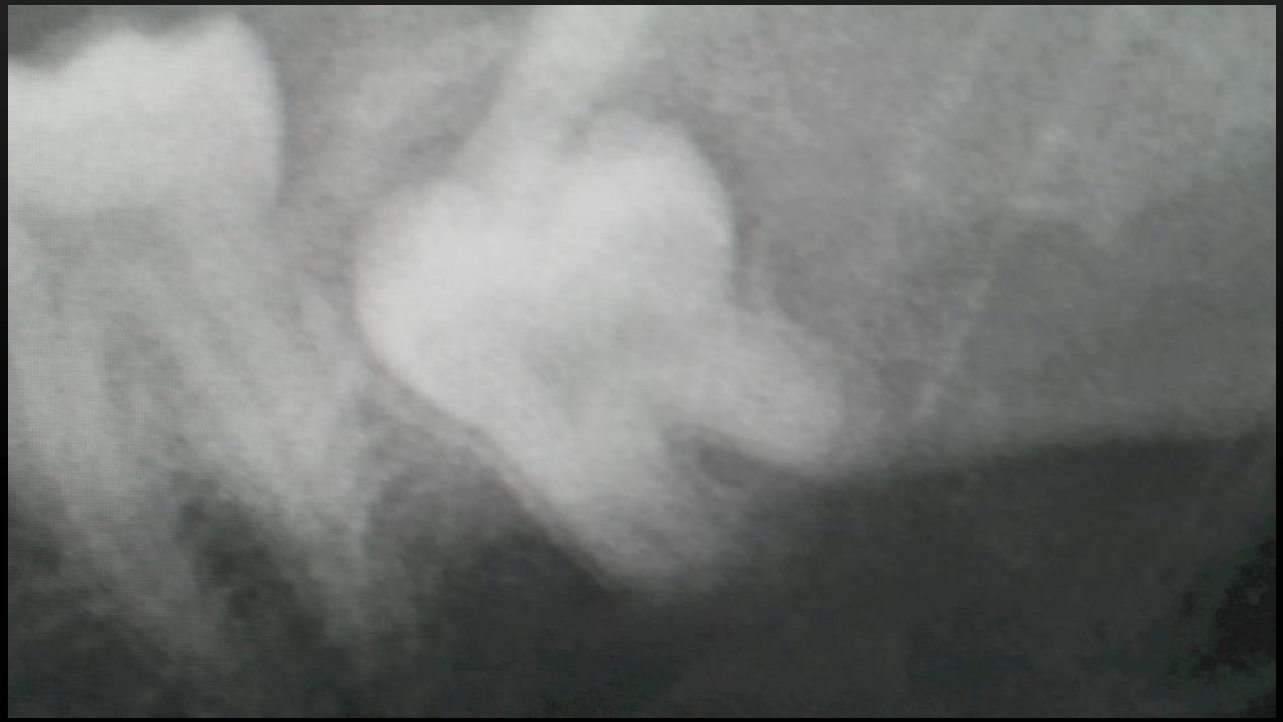
Envelope flap increases trismus too

Prevention of lingual nerve injury

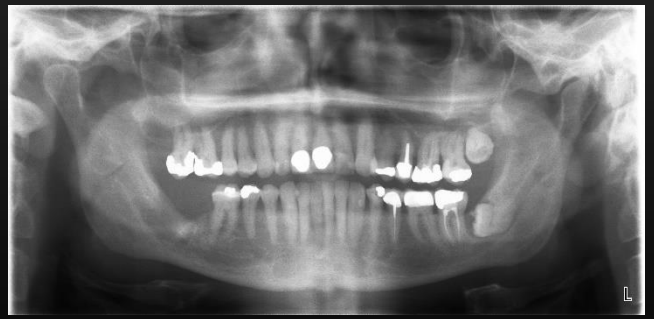


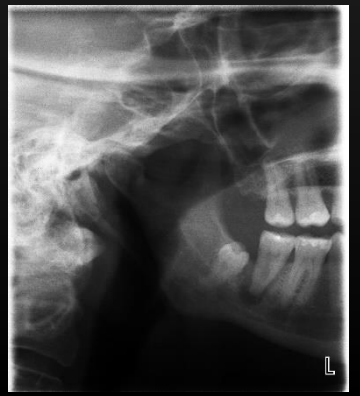
Use the buccal approach with No distal bone removal

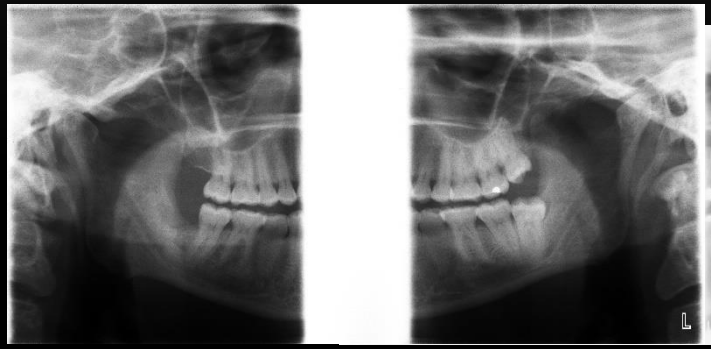
The buccal approach

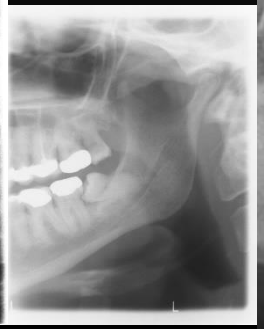


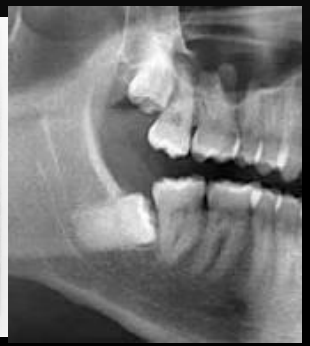
Preventing inferior alveolar nerve injury
Risk assessment











Céspedes-Sánchez JM, Ayuso-Montero R, Marí-Roig A, Arranz-Obispo C, López-López J The importance of a good evaluation in order to prevent oral nerve injuries: A review. Acta Odontol Scand.2013 Jul 4.

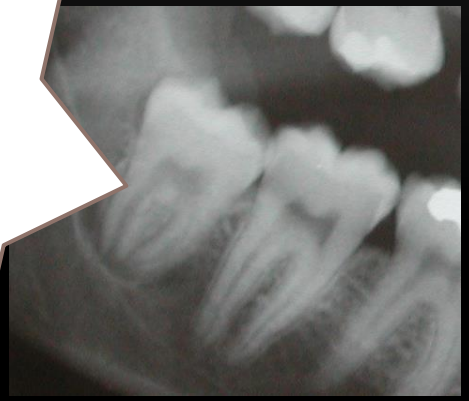
Factors that are associated with injury to the IAN in high-risk patients after removal of third Molars. Selvi, Dodson, Nattestad, Robertson, Tolstunov. BJOMS 51 (2013) 868–873. with permission.

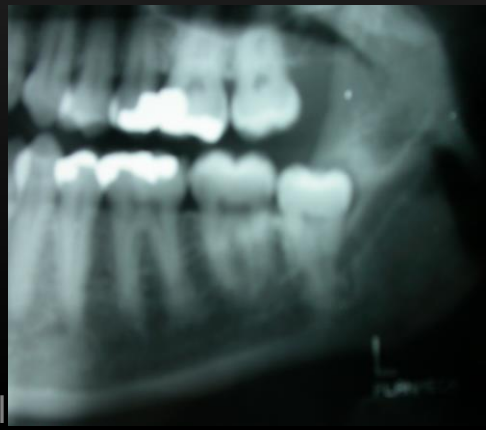
Risk assessment using plain films

Radiographic factors

- Diversion of the canal
- Darkening of the root
- Interruption of the canal LD

Recognise plain film risk factors
If high risk - CBCT





NEW

- Juxta-apical area
- Deviation of canal
- Narrowing / darkening of roots

Renton T, Hankins M, Sproate C, McGurk M. A randomised controlled clinical trial to compare the incidence of injury to the inferior alveolar nerve as a result of coronectomy and removal of mandibular third molars. Br J Oral Maxillofac Surg. 2005 Feb;43(1):7-12 Rood JP, Shehab BA.The radiological prediction of inferior alveolar nerve injury during third molar surgery.Br J Oral Maxillofac Surg. 1990 Feb;28(1):20-5 Rud J.Third molar surgery: perforation of the inferior dental nerve through the root. Tandlaegebladet. 1983 Oct;87(19):659-67. No abstract available.

Risk assessment using plain films

Risk

- 0.5% of cases permanently
- 2% of cases temporarily

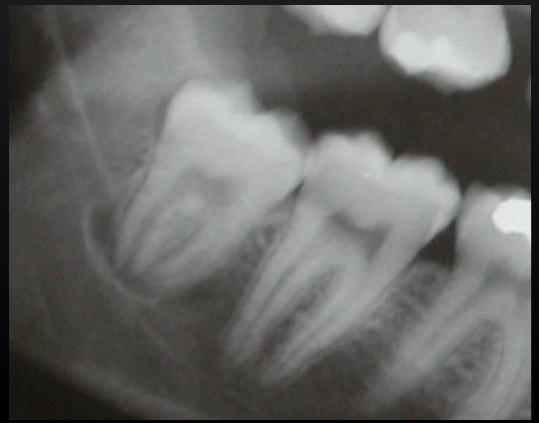
BUT if the teeth are superimposed on the IAN canal

- 20% temporary
- 2% permanent

Risk factors

- increased age
- difficulty of surgery
- proximity to the IAN canal

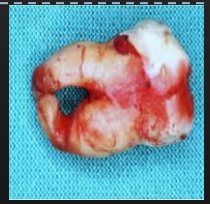
10 x

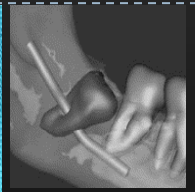


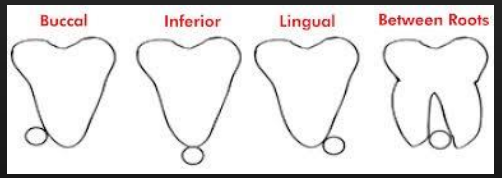
- Renton T, Hankins M, Sproate C, McGurk M. A randomised controlled clinical trial to compare the incidence of injury to the inferior alveolar nerve as a result of coronectomy and removal of mandibular third molars. Br J Oral Maxillofac Surg. 2005 Feb;43(1):7-12
- Rood JP, Shehab BA.The radiological prediction of inferior alveolar nerve injury during third molar surgery.Br J Oral Maxillofac Surg. 1990 Feb;28(1):20-5
- Rud J.Third molar surgery: perforation of the inferior dental nerve through the root. Tandlaegebladet. 1983 Oct;87(19):659-67. No abstract available.

CBCT Risk assessment to IANI
Proximity to IDC and perforation

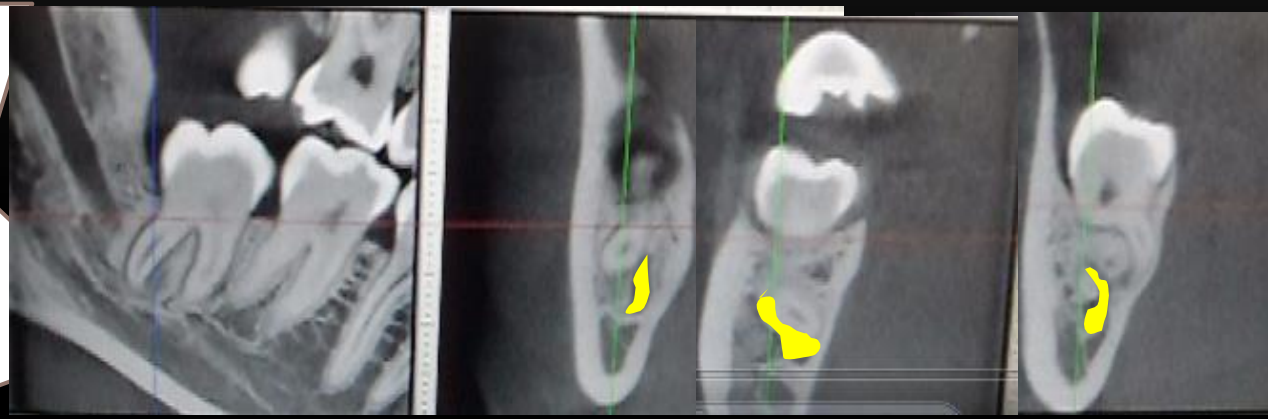
Perforation is very rare
How close does the nerve have to be?
The nerve doesn't have to 'perforate' tooth…







IAN at risk CBCT
Distortion of IDC
Lingual position IDC
Loss of cortication IDC
Bifid IDC
Inter proximal
IDC/perforation tooth root by IDC



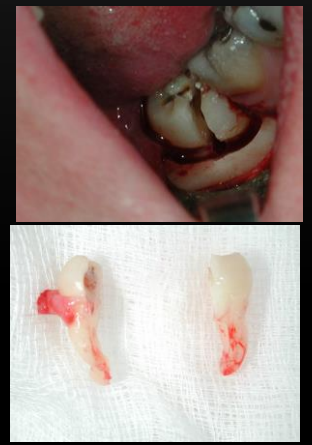
ison between cone beam computed tomography and panoramic radiography in the assessment of the
and impacted class C mandibular third molars. Dent Res J. 2011;8:203
trapment. J Oral Maxillofac Surg 68:1173-1178, 2010

M3M Removal or Coronectomy?

- Patient healthy?
- Patient reliable?
- Tooth vital?
- Tooth high risk- confirmed on CBCT inter radicular IAN?

Yes to all → Coronectomy

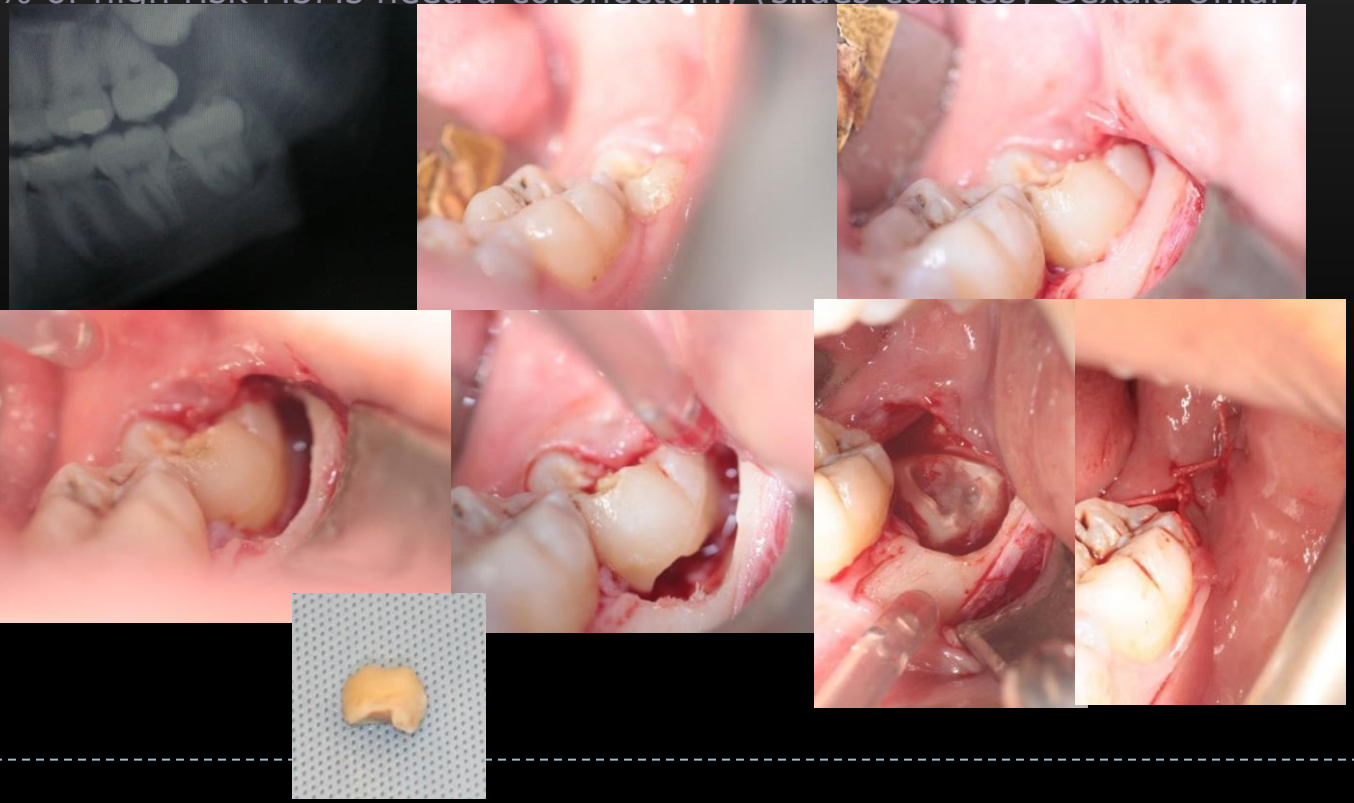
No to any → Removal with sectioning



Guerrero ME, Botetano R, Beltran J, Horner K, Jacobs R Can preoperative imaging help to predict postoperative outcome after wisdom tooth removal? A randomized controlled trial using panoramic radiography versus cone-beam CT. Clin Oral Investig. 2014 Jan;18(1):335-42. doi: 10.1007/s00784-013-0971-x. Epub 2013 Mar 15.

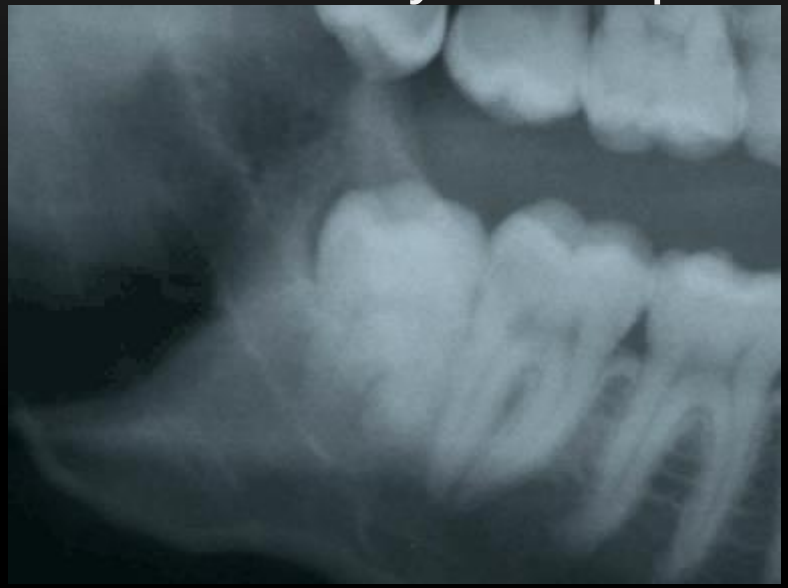
Prevention of M3M IANI
Technique decision Coronectomy

Less than 4% of high risk M3Ms need a coronectomy (slides courtesy Gexala Umar)



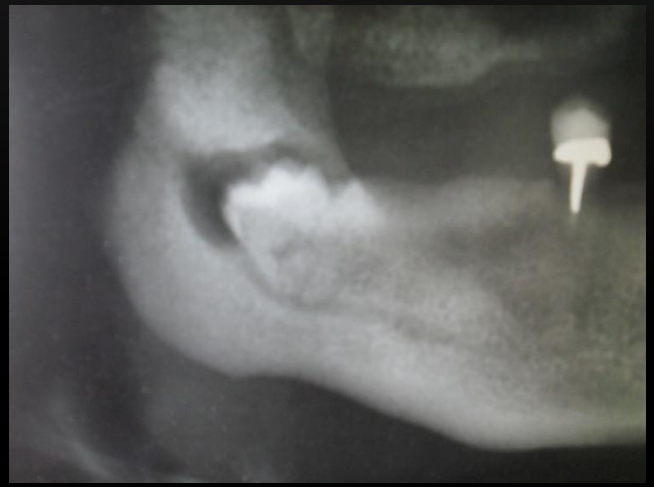
Prevention of IAN injury

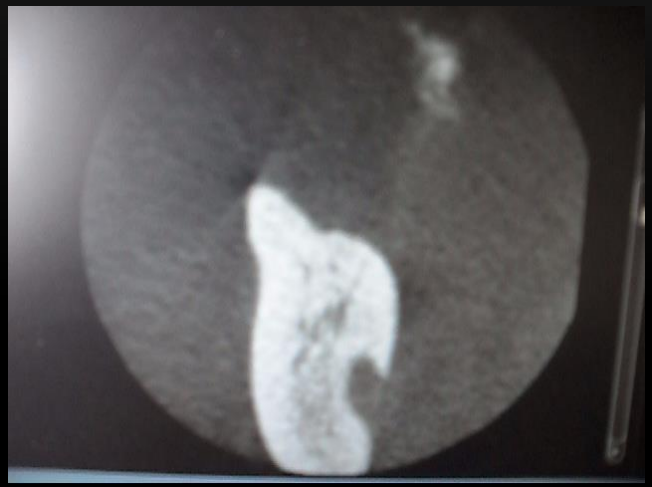
Coronectomy technique



Coronectomy does prevent nerve injury in selected cases

Unfortunate case:
Booked for coronectomy but had M3M removal
Now patient has a permanent painful IANI





Management of dentistry related nerve injury

- **Treat the patient with the nerve injury!**
- **Prevention is best!**
- **Treatment must depend upon the mechanism and duration of nerve injury**
- **Holistic approach**

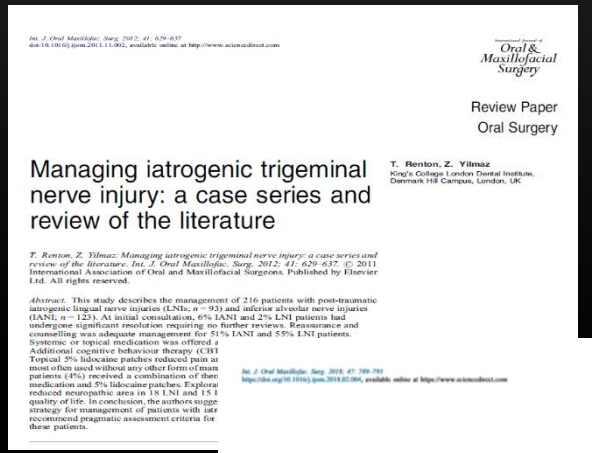
•Treat
  - *Pain*
  - *Functional disability*
  - *Psychological impact*

•Counselling
  - *Reaffirm nerve injury is permanent*
  - *Be honest with the patient*
  - *Reassurance and explanation*

•Medical for pain +/- depression
  - *Topical*
  - *Systemic*

•Surgical

•**Remove implant or Endo within 30 hours**



Int. J. Oral Maxillofac. Surg. 2012; 41: 629–637
doi:10.1016/j.ijom.2011.11.002, available online at http://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

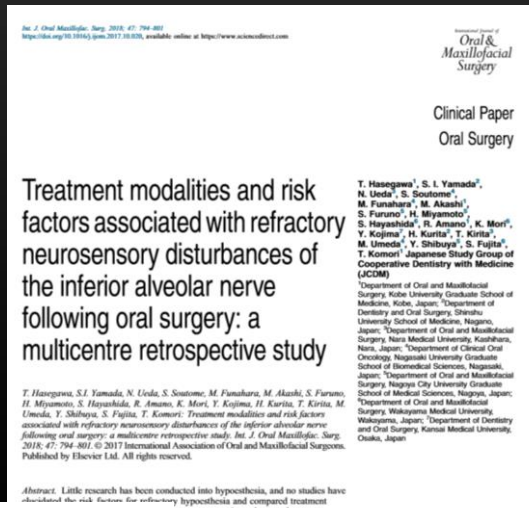
Review Paper
Oral Surgery

Managing iatrogenic trigeminal nerve injury: a case series and review of the literature

T. Renton, Z. Yilmaz
King's College London Dental Institute, Denmark Hill Campus, London, UK

T. Renton, Z. Yilmaz; Managing iatrogenic trigeminal nerve injury: a case series and review of the literature. Int. J. Oral Maxillofac. Surg. 2012; 41: 629–637. © 2011 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Abstract. This study describes the management of 216 patients with post-traumatic iatrogenic lingual nerve injuries (LNIs; $n = 93$) and inferior alveolar nerve injuries (IANI; $n = 123$). At initial consultation, 6% IANI and 2% LNI patients had undergone significant resolution requiring no further reviews. Reassurance and counselling was adequate management for 51% IANI and 55% LNI patients. Systemic or topical medication was offered a
Additional cognitive behaviour therapy (CBT
Topical 5% lidocaine patches reduced pain a
most often used without any other form of man
patients (4%) received a combination of ther
medication and 5% lidocaine patches. Explora
reduced neuropathic area in 18 LNI and 15 I
quality of life. In conclusion, the authors sugge
strategy for management of patients with late
recommend pragmatic assessment criteria for
these patients.



Int. J. Oral Maxillofac. Surg. 2018; 47: 794–801
https://doi.org/10.1016/j.ijom.2017.10.020, available online at https://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical Paper
Oral Surgery

Treatment modalities and risk factors associated with refractory neurosensory disturbances of the inferior alveolar nerve following oral surgery: a multicentre retrospective study

T. Hasegawa[1], S. I. Yamada[2], N. Ueda[3], S. Soutome[4], M. Funahara[5], M. Akashi[1], S. Furuno[6], H. Miyamoto[7], S. Hayashida[8], R. Amano[1], K. Mori[9], Y. Kojima[1], H. Kurita[2], T. Kirita[3], M. Umeda[4], Y. Shibuya[5], S. Fujita[6], T. Komori[1] Japanese Study Group of Cooperative Dentistry with Medicine (JCDM)
[1]Department of Oral and Maxillofacial Surgery, Kobe University Graduate School of Medicine, Kobe, Japan; [2]Department of Dentistry and Oral Surgery, Shinshu University School of Medicine, Nagano, Japan; [3]Department of Oral and Maxillofacial Surgery, Nara Medical University, Kashihara, Nara, Japan; [4]Department of Clinical Oral Oncology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan; [5]Department of Oral and Maxillofacial Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; [6]Department of Oral and Maxillofacial Surgery, Wakayama Medical University, Wakayama, Japan; [7]Department of Dentistry and Oral Surgery, Kansai Medical University, Osaka, Japan

T. Hasegawa, S.I. Yamada, N. Ueda, S. Soutome, M. Funahara, M. Akashi, S. Furuno, H. Miyamoto, S. Hayashida, R. Amano, K. Mori, Y. Kojima, H. Kurita, T. Kirita, M. Umeda, Y. Shibuya, S. Fujita, T. Komori: Treatment modalities and risk factors associated with refractory neurosensory disturbances of the inferior alveolar nerve following oral surgery: a multicentre retrospective study. Int. J. Oral Maxillofac. Surg. 2018; 47: 794–801. © 2017 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Abstract. Little research has been conducted into hypoesthesia, and no studies have
ntre retrospective cohort study was to
ious risk factors, treatment modalities, and
r refractory hypoesthesia after oral surgery
ultivariate analysis. To minimize the
ective data analysis, a propensity score
edication and non-medication groups
ere hypoesthesia (odds ratio 13.42) and no
B12 (odds ratio 2.28) were significantly
. In the propensity score analysis, the
a in the medication group was lower than
0.001). This study demonstrated the
ous risk factors, treatment modalities, and
vere hypoesthesia and no or late
re significantly associated with refractory
ld consider these risk factors and initiate
n B12 in cases of hypoesthesia.

Key words: neurosensory deficit; extraction; treatment; hypoesthesia.
Accepted for publication 3 October 2017
Available online 5 January 2018

Int. J. Oral Maxillofac. Surg. 2018; 47: 789–793
https://doi.org/10.1016/j.ijom.2018.02.004, available online at https://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical Paper
Oral Surgery

Iatrogenic trigeminal post-traumatic neuropathy: a retrospective two-year cohort study

Y. Klazen[1,2], F. Van der Cruyssen[1,2], M. Vranckx[1,2], M. Van Vlierberghe[1,2], C. Politis[1,2,3], T. Renton[4], R. Jacobs[1,2,3,4]
[1]OMFS-IMPATH Research Group, Department of Imaging and Pathology, Faculty of Medicine, University of Leuven, Leuven, Belgium; [2]Department of Oral and Maxillofacial Surgery, University Hospitals Leuven, Leuven, Belgium; [3]Department Oral Surgery, King's College London, London, UK; [4]Department of Dental Medicine, Karolinska Institutet, Stockholm, Sweden

Y. Klazen, F. Van der Cruyssen, M. Vranckx, M. Van Vlierberghe, C. Politis, T. Renton, R. Jacobs: Iatrogenic trigeminal post-traumatic neuropathy: a retrospective two-year cohort study. Int. J. Oral Maxillofac. Surg. 2018; 47: 789–793. © 2018 The Author(s). Published by Elsevier Ltd on behalf of International Association of Oral and Maxillofacial Surgeons. This is an open access article under the CC BY-NC-ND

KING'S College LONDON

We do know that
Surgery alone is not enough for neuropathic pain!

Zuniga JR, Renton T. J Neurol Neuromed (2016) 1(7): 10-14
www.jneurology.com

Journal of Neurology & Neuromedicine

Mini Review Open Access

Managing post-traumatic trigeminal neuropathic pain: is surgery enough?

John R. Zuniga[1], Tara F. Renton[2]

[1]Departments of Surgery and Neurology and Neurotherapeutics, The University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA
[2]Department of Oral Surgery, Kings College London Dental Institute, Denmark Hill Campus, London SE5 9RS, UK

Article Info

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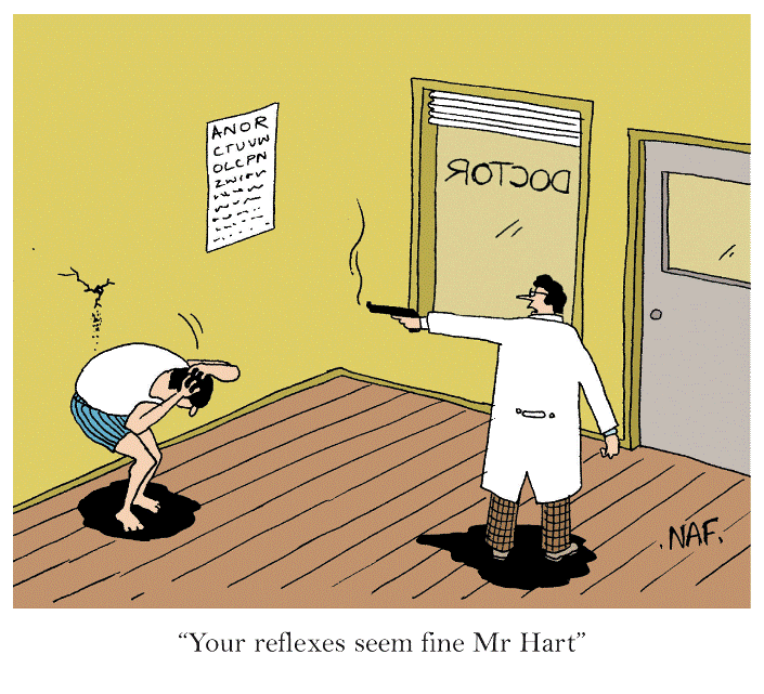
Keywords:
Trigeminal Nerve
Neuropathic Pain
Trigeminal Nerve Microsurgery

ABSTRACT

In the absence of effective non-surgical methods to permanently resolve neuropathic pain involving the lip, chin, or tongue following inferior alveolar and/or lingual nerve injury, microsurgery of these nerves has been a recommended modality. In two ambispective clinical trials, we demonstrated that phenotypic differences exist between individuals with neuropathic pain and those without neuropathic pain of the trigeminal nerve. In those without neuropathic pain before microsurgery there was a 2% incidence of neuropathic pain after microsurgery whereas there was a 67% incidence of neuropathic pain after microsurgery, some reporting an increase in pain levels, when neuropathic pain was present before microsurgery. The recurrence of neuropathic pain after trigeminal microsurgery is likely multifactorial and might not depend on factors that normally affect useful or functional sensory recovery in those who have no neuropathic pain. These results indicate that the understanding of post-traumatic trigeminal neuropathic pain is incomplete. Predictive outcomes of treatment will probably improve when the etiology is better defined to allow mechanistic or target-/site-specific treatment. Until then, non-surgical treatment for post-traumatic trigeminal neuropathic pain remains a safer option. Risk factors have been identified for patients developing chronic post -surgical pain due to post-traumatic neuropathy. These include psychological, medical, and age related factors. The best management may lie in preoperative screening and avoidance of elective surgery for high risk

CLINICAL ASSESSMENT
Mechanosensory assessment



"Your reflexes seem fine Mr Hart"

The purpose of this study was to determine the statistical efficacy of the clinical neurosensory test using surgical findings as the "gold" standard, and to determine whether a correlation existed between the sensory impairment score obtained by preoperative testing and the degree of nerve injury found at surgery.

The positive predictive and negative predictive values for LN-injured patients were 95% and 100%, respectively. The positive predictive and negative predictive values for IAN patients were 77% and 60%, respectively.

There were statistically **significant differences in the distribution of age, duration of injury, cause of injury, presence of neuropathic pain, presence of trigger pain, and degree of injury between the IAN and LN patient populations**.

There was a statistically significant positive relationship found between the sensory impairment score and the degree of nerve injury.

No complicated tests!

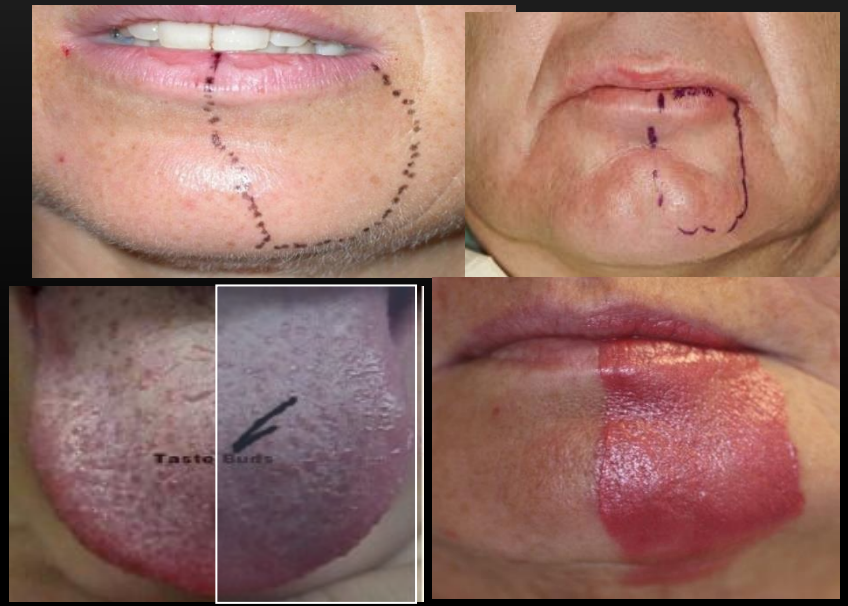
Zuniga JR, Meyer RA, Gregg JM, Miloro M, Davis LF. The accuracy of clinical neurosensory testing for nerve injury diagnosis. J Oral Maxillofac Surg. 1998 Jan;56(1):2-8.

Management of Implant nerve injury

Confirm Nerve injury

Temporary or permanent?

- **Mechanism**
- **Duration**
- Identify the extent of injury
  - Size neuropathic area
  - Subjective function
  - Mechanosensory function
  - Disability
  - Pain / discomfort
    - Allodynia
    - Hyperalgesia
    - Spontaneous or elicited?



Patient's story and expectations?

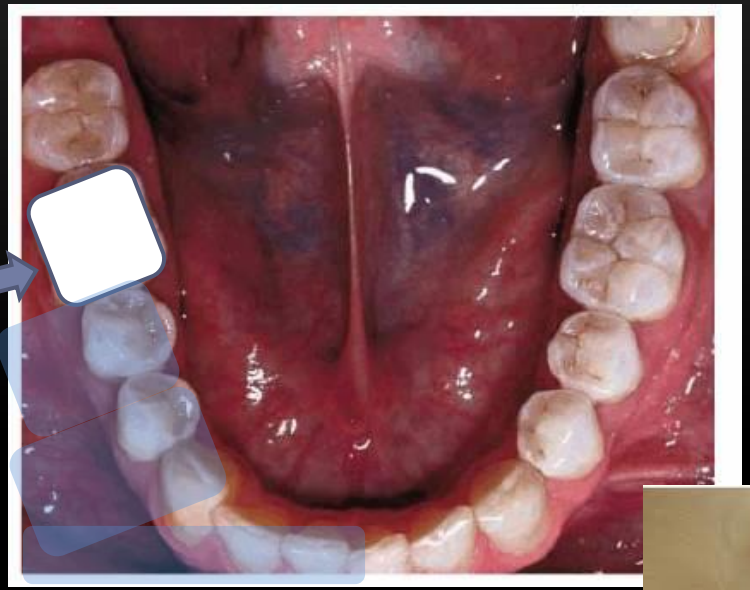
Renton T, Thexton A, SJ Crean, Hankins M. Simplifying assessment of recovery of the lingual nerve from injury. BDJ 2006 10:569-573 **Renton T**, Thexton A, Mcgurk M. New method for the objective evaluation of injury to the lingual nerve after operation on third molars.Br J Oral Maxillofac

Assessment of neuropathic area
Know your anatomy!

Implant extraction or endodontic procedure undertaken with resultant numbness of mouth& lip with pain

Neuropathic area should affect 'DISTAL' domain of dermatome

In some cases only socket area can be affected with localised hypersensitivity



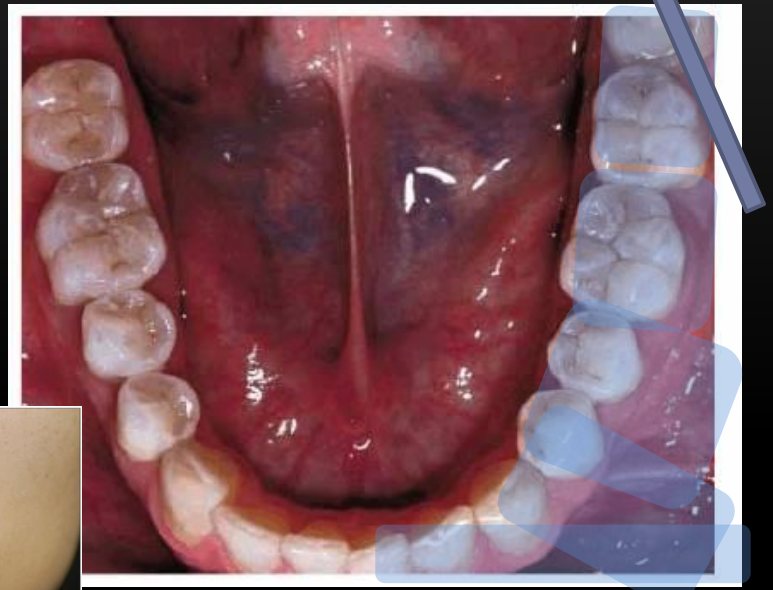
Neuropathic area you can use dental vitality tests but not very reliable

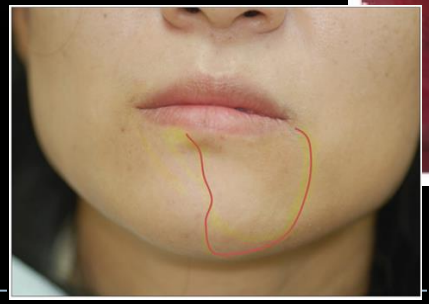
Extraoral area may be complete **or partial Below illustrates 40% affected**

Assessment of neuropathic area
Know your anatomy!

Neuropathic area you can use dental vitality tests but not very reliable

Extraoral neuropathy affecting 9 of area0%





Inferior dental block undertaken with resultant numbness of mouth&lip with pain

Neuropathic area should affect ‘DISTAL’ domain of dermatome

Presentation of persistent PTNP (n=525) Renton et al unpublished

- **Onset of neuropathy +/- pain correlates with intervention surgery or local anaesthetic**
  - LNI patients (mean age 38.4 years [range 20-64]
    Male:Female ratio 37:63%
  - IANI patients (mean age 43.2 years [range 22-85];
    Male:Female ratio 27:70%

  Referral from:
  - General dental practitioner LNI = 40%/IANI = 51%
  - Specialist
    LNI = 50% IANI = 32%
- **Reported extreme pain during surgery 4**
- **Reported high level pain post surgically 56**
- IANI related to;
  - Third molar surgery 60%
  - Implant
  - LA 16%
  - Endo 8%
  - Periapical infections 1%
  - Facial electrolysis 1%
- LNIs related to;

Pain descriptors

Presenting with neuropathic pain 70%

Functionality

Significantly daily functional impact 65% with pain

Psychologically (PTSD in 68% of patients) impact especially with pain 62%

Neuropathy 100%

Dermatome: The neuropathic area varied between 5-100% of the affected dermatome (intra- and/or extra-orally).

Hypoeasthetic or **Hyperaesthetic**

Mechanical allodynia	**70%**
Mechanical Hyperalgesia	**48%**
Cold allodynia in IANI pts	**87%**

CBT			
		Subjective Function	
	Neuropathic Area (%)	Min	Max
Extraorally	70 (2-100)	3.1 (0-10)	8.8 (1-30)
Intraorally	66 (0-100)	2.3 (0-5)	10.5 (6-12)
Versatis			
		Subjective Function	
	Neuropathic Area (%)	Min	Max
Extraorally	68 (8-100)	1.75 (1-2)	9.6 (4-12)
Intraorally	69 (0-100)	4.0 (4)	10.0 (6-12)

Table 1: Summary of Neuropathic Area Affected and Subjective Function (SF). Hypersensitivity to touch is indicated by a subjective function (SF) value of above 10, as a value of 10 indicates

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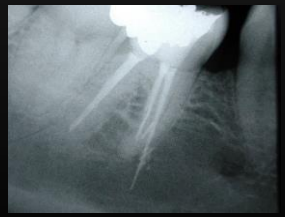
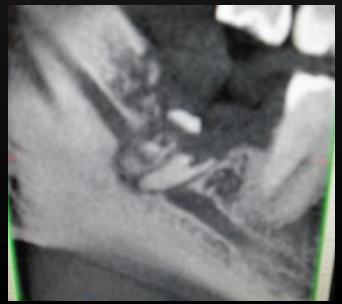
You cannot ‘see’ nerves on radiographs just the canals and foramina……

but CBCT may be useful for post wisdom tooth surgery and confirmed nerve injury

ADDITIONAL INVESTIGATIONS POSSIBLE BIOMARKERS?

Radiology Post surgical radiographs (panoral for wisdom teeth and LCPA for endo Nis) are required to confirm causality though mainly a clinical diagnosis





Post surgical CBCTs only required for M3M Inferior alveolar nerve injury

Use plain film only
CBCT -unnecessary irradiation of the patient
Provides no further information and does not change treatment unless M3M nerve injury to exclude roots displaced into submandibular or sublingual space

Additional tests
Neurosensory
- **Mechanosensory**
- **QST**
- **Blink reflex**

Diagnostic Lidocaine blocks
Psychological

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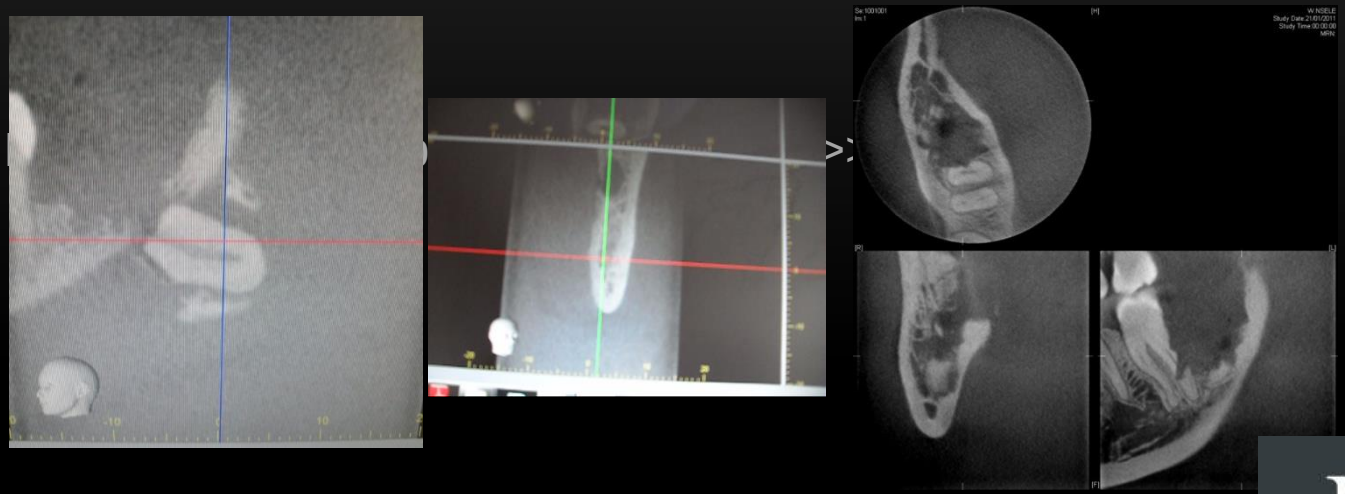
IMAGING Inferior alveolar nerve injury (IANI)

WHEN IS CBCT INIDICATED POST NERVE INJURY?



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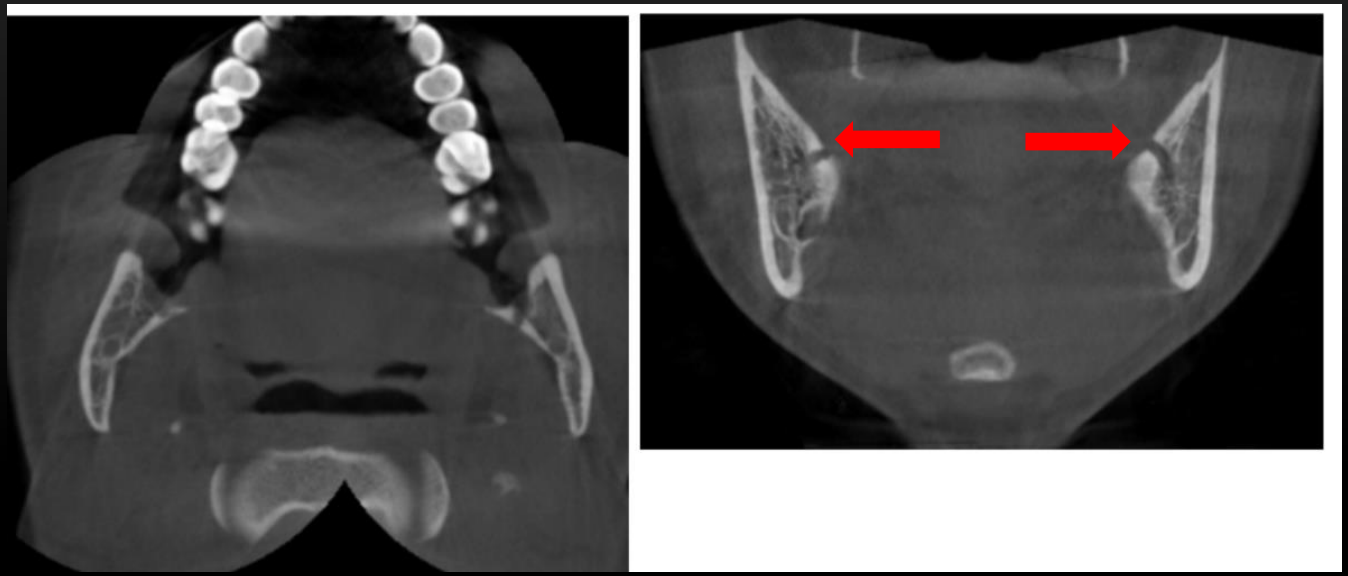
IMAGING Lingual nerve injury (LNI)
CBCT early post op detection of Lingual plate damage



CBCT MAY BE USEFUL WITH CLINICAL CONFIRMATION OF LINGUAL NEUROPATHY USEFUL TO ESTABLISH IF LINGUAL PLATE DAMAGE INDICATES URGENT NEED FOR LINGUAL NERVE EXPLORATION AND REPAIR CBCT DEMONSTRATING BILATERAL BUR PERFORATION OF LINGUAL PLATE POST TMS (COURTESY OF TONY POGREL)

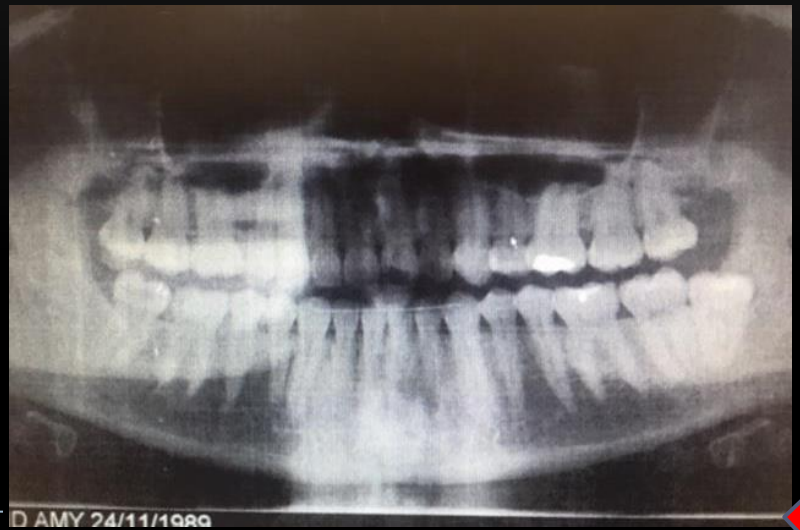
Recent Case Pre op findings

Dense left sided hypoaesthetic neuropathy LN (M3M surgery 3 weeks ago)

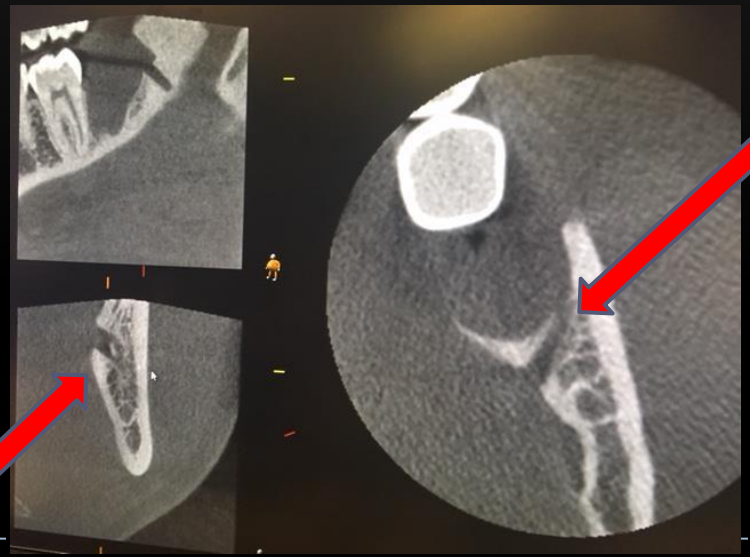
c/o numbness with occ spontaneous paraesthesia, functional difficulty speaking and eating.

mechanosensory sf 2/10, no SB detection or LT

Preop DPT



CBCT taken 14/08/18



Management of trigeminal nerve injuries

Management of trigeminal nerve injuries

Treat the patient with the nerve injury

Cochrane

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Informed decisions.
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Treatments for accidental damage during surgery to the nerves supplying sensation to the tongue, lower lip and chin

Published:
16 April 2014

Authors:
Coulthard P, Kushnerev E, Yates JM, Walsh T, Patel N, Bailey E, Renton TF

Primary Review Group:
Oral Health Group

Review question

The main question addressed by this review is how effective are different treatments and what are the best timings for these treatments following accidental damage during surgery to the nerves that supply sensation to the tongue, lower lip and chin.

Background

The nerves (alveolar and lingual) supplying sensation to the tongue, lower lip and chin, may be injured as a result of surgical treatments to the mouth and face, including surgery to remove lower wisdom teeth. The vast majority (90%) of these

Who is talking about this article?

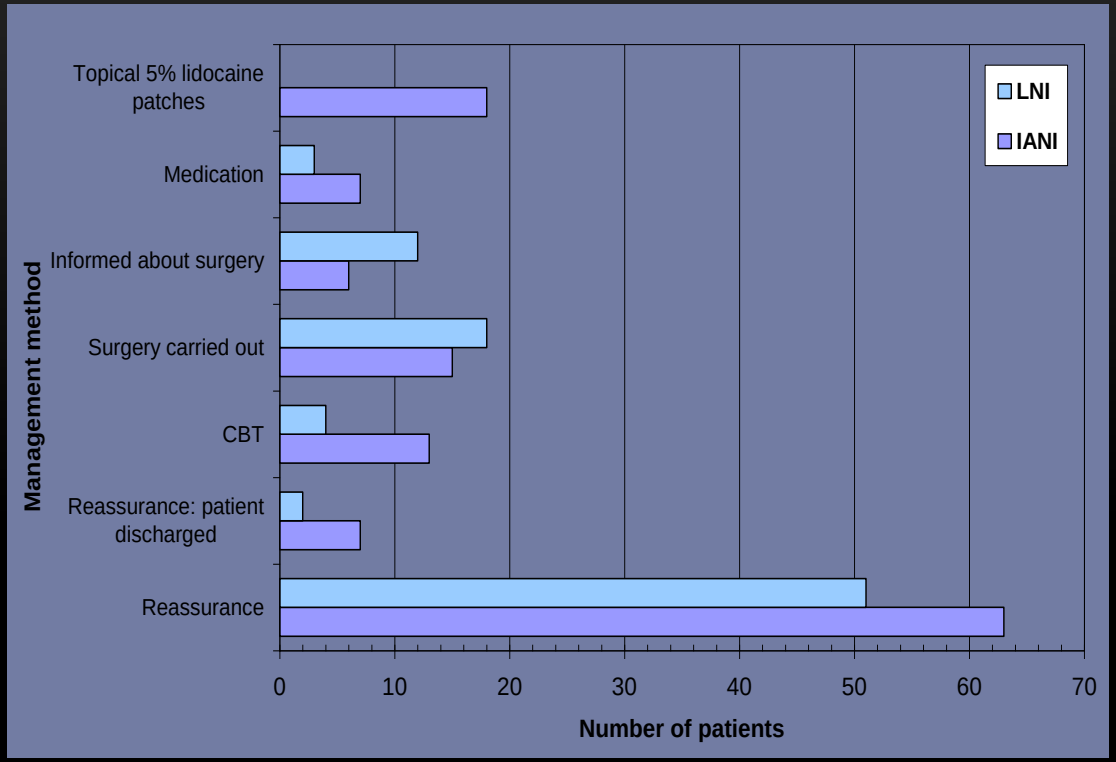
Authors' conclusions:

There is clearly a need for randomised controlled clinical trials to investigate the effectiveness of surgical, medical and psychological interventions for iatrogenic inferior alveolar and lingual nerve injuries. Primary outcomes of this research should include: patient-focused morbidity measures including altered sensation and pain, pain, quantitative sensory testing and the effects of delayed treatment.

What are we trying to treat?

- The patient with the nerve injury
- Impact of nerve injury include;
  - Pain, numbness and or altered sensation
  - Functional difficulties
  - Psychological impact
- These result in changed behaviours, anxiety depression, anger, frustration and PTSD
- Management Strategies
  - Understanding and acknowledging their problem. Providing realistic prognosis and possible management strategies
  - Pain ‘relief’
  - Behavioural techniques to assist the patient in adapting to new self (both functional and psychological)

Maximising response to treatment requires a multi modal approach



A small percentage of IANI patients (4%) received a combination of therapies involving CBT, surgery, medication and 5% lidoc

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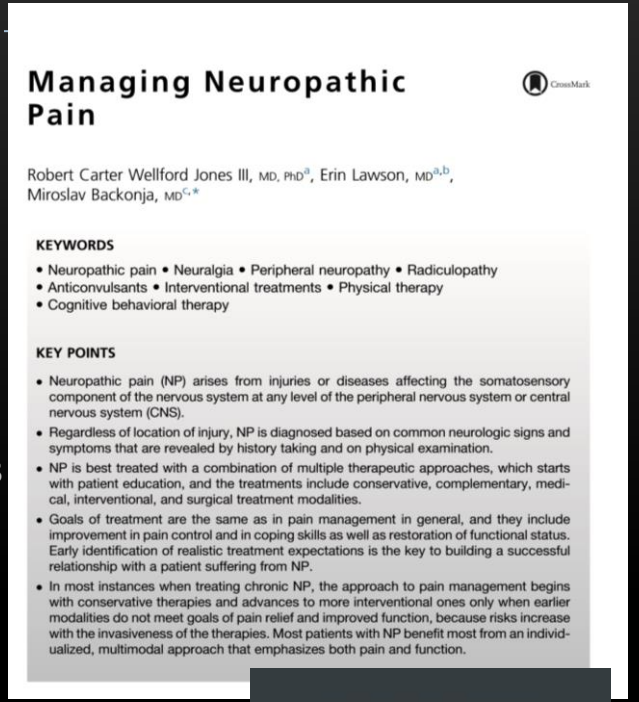
Multidisciplinary management

Regardless of location of injury, NP is diagnosed based on common neurologic signs and symptoms that are revealed by history taking and on physical examination.

NP is best treated with a combination of multiple therapeutic approaches, which starts with patient education, and the treatments include conservative, complementary, medical, interventional, and surgical treatment modalities.

Goals of treatment include improvement in **pain control and in coping skills as well as restoration of functional status.** Early identification of realistic treatment expectations is the key to building a successful relationship with a patient suffering from NP.

In most instances when treating chronic NP, the approach to pain management begins with conservative therapies and advances to more interventional ones only when earlier modalities do not meet goals of pain relief and improved function, because risks increase with the invasiveness of the therapies. Most patients with NP benefit most from an individualized, multimodal approach that emphasizes both pain and function.



Managing Neuropathic Pain

Robert Carter Wellford Jones III, MD, PhD[a], Erin Lawson, MD[a,b], Miroslav Backonja, MD[c,*]

KEYWORDS

• Neuropathic pain • Neuralgia • Peripheral neuropathy • Radiculopathy
• Anticonvulsants • Interventional treatments • Physical therapy
• Cognitive behavioral therapy

KEY POINTS

- Neuropathic pain (NP) arises from injuries or diseases affecting the somatosensory component of the nervous system at any level of the peripheral nervous system or central nervous system (CNS).
- Regardless of location of injury, NP is diagnosed based on common neurologic signs and symptoms that are revealed by history taking and on physical examination.
- NP is best treated with a combination of multiple therapeutic approaches, which starts with patient education, and the treatments include conservative, complementary, medical, interventional, and surgical treatment modalities.
- Goals of treatment are the same as in pain management in general, and they include improvement in pain control and in coping skills as well as restoration of functional status. Early identification of realistic treatment expectations is the key to building a successful relationship with a patient suffering from NP.
- In most instances when treating chronic NP, the approach to pain management begins with conservative therapies and advances to more interventional ones only when earlier modalities do not meet goals of pain relief and improved function, because risks increase with the invasiveness of the therapies. Most patients with NP benefit most from an individualized, multimodal approach that emphasizes both pain and function.

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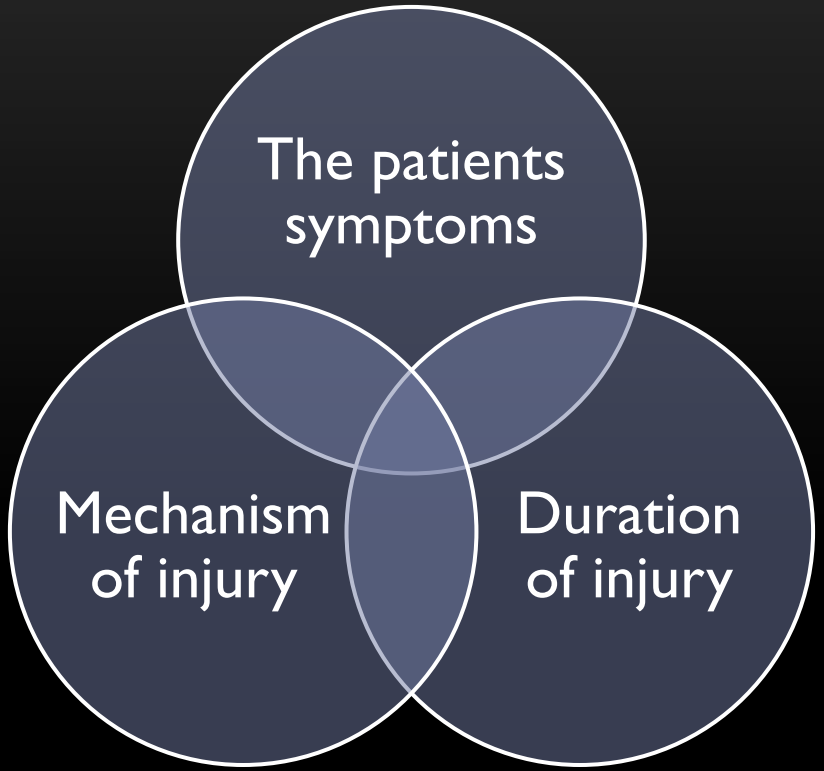
Management of trigeminal nerve injuries will depend upon....



MANAGEMENT OF TRIGEMINAL NERVE INJURIESRELTED TO DENTAL PROCEDURES

Timeline	During surgery	Post surgery 2 -6 weeks	12 weeks	> 12 weeks
		Psychological intervention		

Medical intervention

High risk nerve injury/ or patient high risk of developing neuropathic pain consider pre-emptive Amitriptyline or Pregabalin	Reported neuropathy immediate post-surgery • NSAIDs Ibuprofen 6—mg TDS 5 days (MH permitting) • step down Prednisolone 50-10mg over 5 days (exclude known risk of DU and or PU) • Vitamin B complex (long term during recovery)	If required: Psychological support (for PTSD and sleep disorders) and Therapeutic management of neuropathic pain (NICE Guidance Ne Pain in adults) • Step 1 Amitriptyline or Nortriptyline • Adjunctive topical agents (Lidocaine, Capsaicin) • Step II Gabapentin or Pregabalin

Surgical intervention

Known or suspected nerve Inferior alveolar or lingual injury **Duty of candour inform patient immediately** **Repair nerve immediately Or refer for immediate repair** to a specialist centre	Post Local anaesthesia or orthognathic surgery or trauma **Duty of candour inform patient immediately** **Surgery not indicated** **Medical and psychological therapies**	Post Implant or endodontic surgery Patient presents with nerve injury early postoperatively Confirm extensive dermatome affected, anaesthesia, +/- paraesthesia, +/- neuropathic pain **Within 30 hours** **Remove implant or endodontically treated tooth** and reassess patient combined with medical intervention above	Post M3M surgery Patient presents with nerve injury early postoperatively Confirm extensive dermatome affected, anaesthesia, +/- paraesthesia, +/- neuropathic pain **Inferior alveolar nerve** DPT confirms retained roots or bony defect of IDC **Lingual nerve (buccal approach)** DPT confirms retained roots CBCT confirms lingual plate defect due to M3M surgery **Consider early exploration (IAN via M3M socket) +/- nerve repair dependent upon surgical findings**	Patient presents with persistent non-resolving **LINGUAL nerve injury** after lingual access (lingual retraction +/- lingual split) surgery Confirm extensive dermatome affected, anaesthesia, +/- paraesthesia, +/- neuropathic pain **Consider exploration @ 12 weeks +/- nerve repair dependent upon surgical findings**	Patient presents with persistent non-resolving **Inferior alveolar nerve injury** OR **LINGUAL nerve injury** after M3M surgery Confirm extensive dermatome affected, anaesthesia, +/- paraesthesia, +/- neuropathic pain Consider medical and psychological therapeutic measures. **N.B Surgical repair DOES NOT IMPROVE neuropathic pain**

- *New developments*
- *MRI micro neurography may assist in confirmation of damage to IAN and LN (currently available in US under development London).*
- *Larger IAN defects can be optimally repaired using Axogen cadaveric nerve graft (currently NICE approved for hand surgery in UK)*

Management of PTPN
Cause and duration

URGENT treatment < 30 hours

- Any known or Suspected nerve trauma
- Implants
- Endodontics (neuropathy may develop 2-3 days post treatment)

- **Within 2 weeks**
- Buccal approach causing Lingual nerve
- Inferior alveolar nerve injuries related to third molar surgery

- **> 2 weeks**
- Not ideal

Consent patient properly…forearmed is for warned
Risk assessment in planning
Check on patients post operatively HOMECHECK
Acknowledge problem
No sit and WAIT !!!!!
You MUST reassure your patient but don't give them false expectations!
Seek advice- Trigeminalnerve.org.uk- Medication and REFERRAL

Wait for resolution

- Lingual nerve injuries related to LINGUAL ACCESS third molar surgery (consider explore @ 12 weeks)
- LA
- Trauma
- Orthognathic

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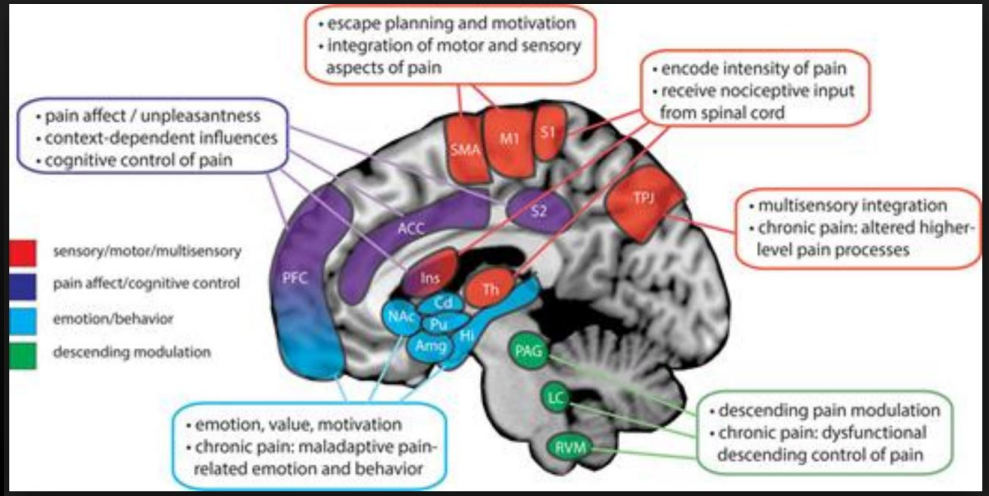
Why is timing of intervention do crucial?

Pain
Central changes after peripheral nerve injury

- CPSP likely due to biological and psychological factors. Here, we tested the hypotheses that
- **high Pain Catastrophizing Scale (PCS) scores at the time of injury and repair are associated with pain**
- cold sensitivity after 1-year recovery
- **insula gray matter changes reflect the course of injury and improvements over time.**
- **pain catastrophizing trended toward predicting cold pain thresholds at time 2, and at time 1 cortical thickness of the right insula was reduced**.
- At time 2, chronic pain was related to the time 1 pain-PCS relationship and cold sensitivity, pain catastrophizing correlated with cold pain threshold, and insula thickness reversed to control levels.
- This study highlights the interplay between **personality, sensory function, and pain in patients following PNI and repair**. The PCS-pain association suggests that a focus on affective or negative components of pain could render patients vulnerable to chronic pain. Cold sensitivity and structural insula changes may reflect altered thermosensory or sensorimotor awareness representations.



Goswami R Anastakis DJ Katz J, Davis KD. A longitudinal study of pain, personality, and brain plasticity following peripheral nerve injury. Pain. 2016 Mar;157(3):729-39.

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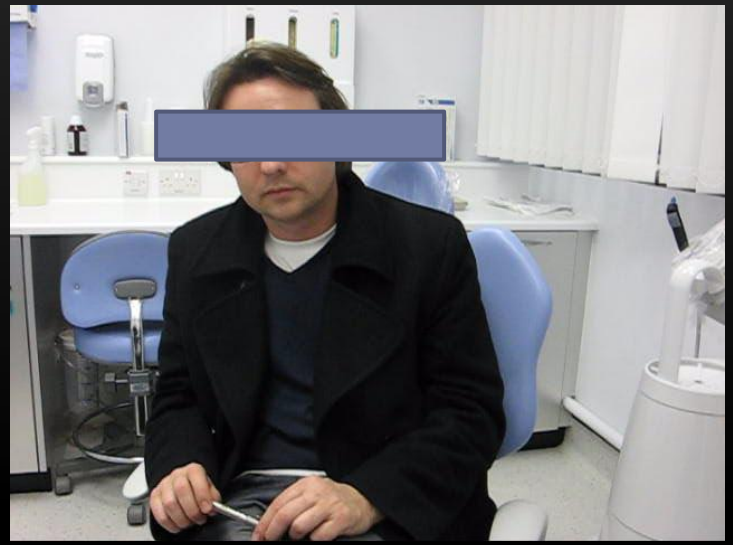
Psychological and functional consequences



Patients with severe pain showed particularly elevated levels of depression and pain catastrophizing, as well as substantially reduced HRQoL and coping efficacy levels.

Pain intensity level was a significant predictor in all models except anxiety, uniquely contributing between 17% and 26% of variance to the prediction of pain catastrophizing, depression, coping efficacy, and generic and oral HRQoL.

40% of patients display PTSD

J Orofac Pain. 2013 Fall;27(4):293-303. doi: 10.11607/jop.1056.

The psychosocial and affective burden of posttraumatic neuropathy following injuries to the trigeminal nerve.

Smith JG, Elias LA, Yilmaz Z, Barker S, Shah K, Shah S, Renton T.

Abstract

AIMS: To explore the impact of trigeminal nerve injuries on quality of life, including the effect of pain on psychological and affective function.

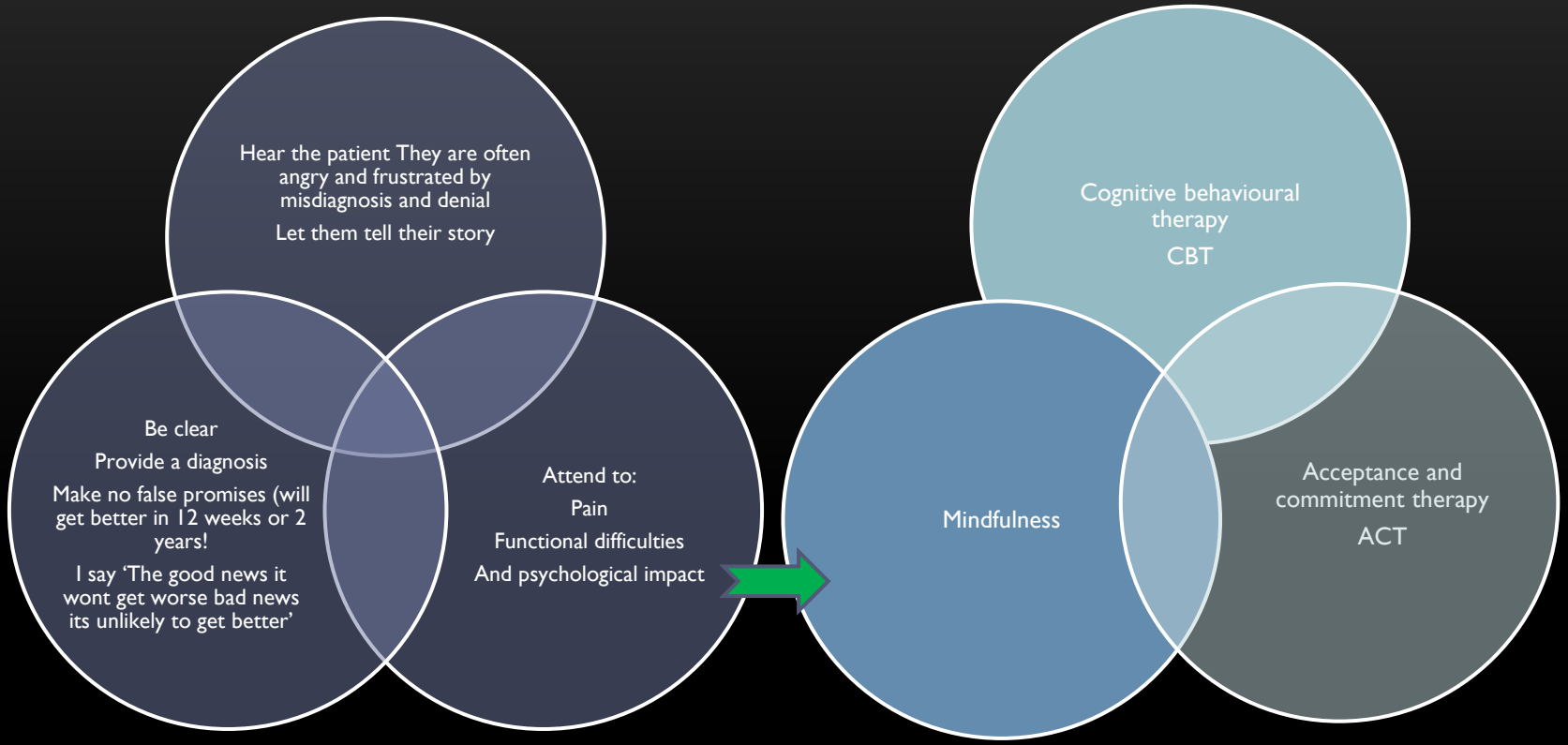
METHODS: An observational, cross-sectional survey design was employed. Fifty-six patients with inferior alveolar nerve injury (IANI) and 33 patients with lingual nerve injury (LNI) completed standardized self-report measures of pain intensity, pain catastrophizing, self-efficacy to cope with pain, and mood, in addition to generic and oral health-related quality of life (HRQoL) indicators. The impact of pain severity on these aspects of psychosocial function was examined. Summary statistics were calculated for all measures and compared with norms or values of other relevant studies, when available, using t tests. The impact of pain severity on these aspects of psychosocial function was examined using analysis of variance and hierarchical multivariate regression models.

RESULTS: The majority of patients reported pain associated with their nerve injury (86%). Nerve injury had a significant impact on all investigated domains, and this was closely linked with reported pain levels. Patients with severe pain showed particularly elevated levels of depression and pain catastrophizing, as well as substantially reduced HRQoL and coping efficacy levels. Pain intensity level was a significant predictor in all models except anxiety, uniquely contributing between 17% and 26% of variance to the prediction of pain catastrophizing, depression, coping efficacy, and generic and oral HRQoL.

CONCLUSION: Traumatic injury to the trigeminal nerve is associated with a substantial patient burden, particularly in patients who experience severe neuropathic pain as part of their condition. These findings highlight the need to identify, develop, and evaluate more effective treatments for neuropathic pain in trigeminal nerve injury that will not only provide clinically meaningful reductions in pain but also improve patients' quality of life.

PMID: 24171179 [PubMed - indexed for MEDLINE]

Psychological intervention for PTNP



Medical intervention- Acute and chronic Pain medication

- **Acute phase**
  - Step down steroids prednisolone 50/40/30/20/10 mg over 5 days
  - Vitamin B complex including Riboflavin 300mg daily 3 months
  - NSAIDs
- **Late phase**
- **Neuralgic pain**
  - Neurontin (Lyrica) Pregabalin
  - Gabapentin
  - Oxcarbazepine
- **Burning chronic pain**
  - SNRIs
  - TCAs Nortriptyline > Amitriptyline
- 15% Pts persisted with systemic meds
- 18% IANI used topical medication

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Summary Background—Neuropathic pain is difficult to treat. New treatments, clinical trials and standards of quality for assessing evidence justify an update of evidence-based recommendations for its pharmacological treatment.

- **a strong GRADE recommendation for use and proposal as first line for TCAs, SNRIs, pregabalin, gabapentin and gabapentin ER/enacarbil in neuropathic pain** :
  - NNTs were 3 ·6 (95 % CI 3 ·0–4 ·4) for **tricyclic antidepressants** (TCAs), 6 ·4 (95 % CI 5 ·2–8 ·4)
  - for **serotonin- noradrenaline reuptake inbibitor (SNRI)** antidepressants duloxetine and venlafaxine, 7 ·7 (95 % CI 6 ·5–9 ·4)
  - for **pregabalin** and 6 ·3 (95 % CI 5 ·0–8 ·3)
  - for gabapentin. NNTs were higher for **gabapentin** ER/enacarbi
  - For **capsaicin high concentration patches**,
- **a weak recommendation for use and proposal as second line for lidocaine patches, capsaicin patches and tramadol,**
  - opioids
  - Final quality of evidence was lower for lidocaine patches and BTX-A. Tolerability/safety and values/preferences were high for lidocaine patches and lower for opioids and TCAs.

Finnerup et al. Lancet Neurol. Author manuscript; available in PMC 201

HHS Public Access
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Pharmacotherapy for neuropathic pain in adults: systematic review, meta-analysis and updated NeuPSIG recommendations

Nanna B Finnerup, MD[*,a], **Nadine Attal, MD**[*,b,c,1], **Simon Haroutounian, PhD**[d], **Ewan McNicol, MS**[e], **Ralf Baron, MD**[f], **Robert H Dworkin, PhD**[g], **Ian Gilron, MD**[h], **Maija Haanpaa, MD**[i], **Per Hansson, MD**[j], **Troels S Jensen, MD**[a,k], **Peter R Kamerman, PhD**[l], **Karen Lund, MD**[a], **Andrew Moore, DSc**[m], **Srinivasa N Raja, MD**[n], **Andrew SC Rice, MD**[o], **Michael Rowbotham, MD**[p], **Emily Sena, PhD**[q], **Philip Siddall, MD**[r], **Blair H Smith, MD**[s], and **Mark Wallace, MD**[t]

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[*]N Attal and NB Finnerup contributed equally to this work.

Conflicts of interest

NA has served on the advisory boards or speakers panels of Astellas Pharma, Adir Servier, Eli Lilly, Grunenthal, Johnson and Johnson, Sanofi Pasteur Merieux and Pfizer and has been investigator of studies sponsored by Astellas, Grunenthal and Astra Zeneca. RB has received grant/research support from Pfizer, Genzyme, Grünenthal, German Federal Ministry of Education and Research (BMBF): German Research Network on Neuropathic Pain, NoPain system biology and German Research Foundation (DFG). He has received speaker honorarium from Pfizer, Genzyme, Grünenthal, Mundipharma, Sanofi Pasteur, Medtronic, Eisai, Lilly, Boehringer Ingelheim, Astellas, Desitin, Teva Pharma, Bayer-Schering, MSD and served as consultant for Pfizer, Genzyme, Grünenthal, Mundipharma, Allergan, Sanofi Pasteur, Medtronic, Eisai, Lilly, Boehringer Ingelheim, Astellas, Novartis, Bristol-Myers Squibb, Biogenidec, AstraZeneca, Merck, Abbvie. RHD has received research grants from US Food and Drug Administration and US National Institutes of Health, and compensation for activities involving clinical trial research methods from Acorda, Adynxx, Allergan, Analgesic Solutions, Anika, Astellas, AstraZeneca, Avanir, Axsome, Bayer, Biogen, Bioness, Bristol-Myers Squibb, Cardiome, Centrexion, Charleston, Chromocell, Collegium, Concert, Daiichi Sankyo, Depomed, Depuy, Eli Lilly, Epicept, Flexion, Genzyme, Glenmark, Inhibitex, Johnson & Johnson, Lpath, Medicinova, Merck, Metys, MMS Holdings, Nektar, Neura, NeurogesX, Olatec, Ono, Periphagen, Pfizer, Phillips, Phosphagenics, Prolong, Q-Med, QRx Pharma, Regenesis, Relmada, Sanofi-Aventis, Salix, Smith & Nephew, Sorrento, Spinifex, Takeda, Taris, Teva, Theravance, and Xenon. NBF has received speaker's honorarium from Pfizer, Grunenthal, and Norpharma, research grant from Grünenthal, and consultancy fee from Astellas. MH has received honoraria from Eli Lilly, Janssen-Cilag, MSD, Mundipharma, Orion, Sanofi-Aventis for lecture, honoraria from Pfizer, Allergan, Astellas for lecture and consulting and honoraria from Abbvie for consulting TSJ have received honoraria from Pfizer, Grünenthal, Astellas, Orion and Sanofi Pasteur as speaker, advisory Board participant or grant. PK has served on advisory board for Reckitt Benckizer, and received speakers' honoraria from Pfizer. KL has received travel grants from Pfizer and Astellas. EM reports grants from Richard Saltonstall Charitable Foundation, USA, during the conduct of the study. AM has received speaker's honorarium from Pfizer, speaker's honorarium and consultancy fees from Eli Lilly and Grünental and research grant from Grünenthal. SNR has served on the advisory boards of Purdue Pharma, QRx pharma, Salix Pharmaceuticals, and Shionogi. ASCR has share options in Spinifex Pharmaceuticals. He undertakes consulting for Imperial College Consultants, and has received fees from Spinifex Pharmaceuticals, Astellas, Servier, Allergan, Asahi Kasei, and Medivir. Through EuroPain, ASCR's laboratory has received funding for research studentships from Pfizer and Astellas. Other recent or current grant/studentship funding for ASCR's laboratory are: Wellcome Trust (London Pain Consortium), Dunhill Medical Trust, NC3Rs, Westminster Medical School Research Trust, International Association for the Study of Pain, National Institute of Academic Anaesthesia, Derek Butler Trust, Medical Research Council Industrial, Biotechnology and Biological Sciences Research Council and Pfizer/Christian-Albrechts University of Kiel (Neuropain). ASCR is a member of the England and Wales Joint Committee on Vaccinati
and other from Afferent Pharmaceuticals, Centrexion, Nektar Th
Biogen IDEC outside the submitted work. PS has a patent Systen
resonance spectroscopy, US Patent 08755862 issued. BHS has co
grants from Pfizer to support epidemiological research. MW repo
Modulations, Depomed and Inergetics. RB, NBF, KL, TSJ and A
industry members of this are: Astra Zeneca, Pfizer, Esteve, UCB-
Ingelheim, Astellas, Abbott and Lundbeck. The other authors hav

Contributors

NA, NF, SH, KL, and EM did the search and extracted data. NF
NA and NF drafted the manuscript and the tables. PH, MR, PS a
members contributed to the guidelines in formulating the recomm
external reviewers contributed to the final text version.

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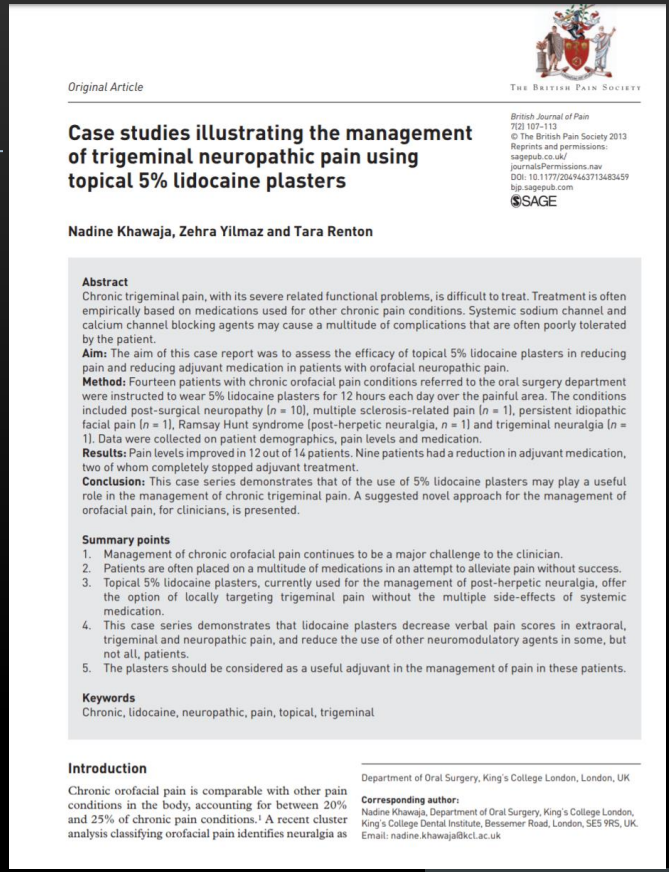
Lidocaine patches

- Prevent cold allodynia
- For outdoor sports, cycling, tennis, golf, swimming
- Prevent sleep interruption at night
- Improve quality and quantity of sleep

Medical Management- topical 5% Lidocaine Versatis patches

- Excellent in minimising elicited pain due to:
- Cold allodynia caused by sport and winter activity
- Mechanical allodynia interfering sleep



Original Article

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SAGE

Case studies illustrating the management of trigeminal neuropathic pain using topical 5% lidocaine plasters

Nadine Khawaja, Zehra Yilmaz and Tara Renton

Abstract

Chronic trigeminal pain, with its severe related functional problems, is difficult to treat. Treatment is often empirically based on medications used for other chronic pain conditions. Systemic sodium channel and calcium channel blocking agents may cause a multitude of complications that are often poorly tolerated by the patient.

Aim: The aim of this case report was to assess the efficacy of topical 5% lidocaine plasters in reducing pain and reducing adjuvant medication in patients with orofacial neuropathic pain.

Method: Fourteen patients with chronic orofacial pain conditions referred to the oral surgery department were instructed to wear 5% lidocaine plasters for 12 hours each day over the painful area. The conditions included post-surgical neuropathy (n = 10), multiple sclerosis-related pain (n = 1), persistent idiopathic facial pain (n = 1), Ramsay Hunt syndrome (post-herpetic neuralgia, n = 1) and trigeminal neuralgia (n = 1). Data were collected on patient demographics, pain levels and medication.

Results: Pain levels improved in 12 out of 14 patients. Nine patients had a reduction in adjuvant medication, two of whom completely stopped adjuvant treatment.

Conclusion: This case series demonstrates that of the use of 5% lidocaine plasters may play a useful role in the management of chronic trigeminal pain. A suggested novel approach for the management of orofacial pain, for clinicians, is presented.

Summary points

1. Management of chronic orofacial pain continues to be a major challenge to the clinician.
2. Patients are often placed on a multitude of medications in an attempt to alleviate pain without success.
3. Topical 5% lidocaine plasters, currently used for the management of post-herpetic neuralgia, offer the option of locally targeting trigeminal pain without the multiple side-effects of systemic medication.
4. This case series demonstrates that lidocaine plasters decrease verbal pain scores in extraoral, trigeminal and neuropathic pain, and reduce the use of other neuromodulatory agents in some, but not all, patients.
5. The plasters should be considered as a useful adjuvant in the management of pain in these patients.

Keywords
Chronic, lidocaine, neuropathic, pain, topical, trigeminal

Introduction

Chronic orofacial pain is comparable with other pain conditions in the body, accounting for between 20% and 25% of chronic pain conditions.[1] A recent cluster analysis classifying orofacial pain identifies neuralgia as

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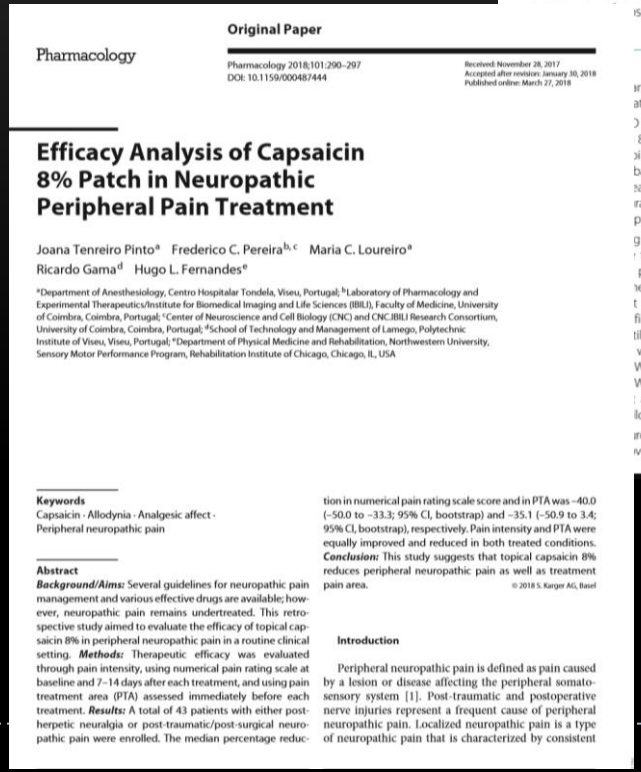
Capsaicin patches

- Grade evidence for other PTNs
- Low evidence for PPTTN



Original Paper

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Efficacy Analysis of Capsaicin 8% Patch in Neuropathic Peripheral Pain Treatment

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Keywords
Capsaicin · Allodynia · Analgesic affect · Peripheral neuropathic pain

Abstract
Background/Aims: Several guidelines for neuropathic pain management and various effective drugs are available; however, neuropathic pain remains undertreated. This retrospective study aimed to evaluate the efficacy of topical capsaicin 8% in peripheral neuropathic pain in a routine clinical setting. ***Methods:*** Therapeutic efficacy was evaluated through pain intensity, using numerical pain rating scale at baseline and 7–14 days after each treatment, and using pain treatment area (PTA) assessed immediately before each treatment. ***Results:*** A total of 43 patients with either postherpetic neuralgia or post-traumatic/post-surgical neuropathic pain were enrolled. The median percentage reduction in numerical pain rating scale score and in PTA was −40.0 (−50.0 to −33.3; 95% CI, bootstrap) and −35.1 (−50.9 to 3.4; 95% CI, bootstrap), respectively. Pain intensity and PTA were equally improved and reduced in both treated conditions. ***Conclusion:*** This study suggests that topical capsaicin 8% reduces peripheral neuropathic pain as well as treatment pain area.

Introduction

Peripheral neuropathic pain is defined as pain caused by a lesion or disease affecting the peripheral somatosensory system [1]. Post-traumatic and postoperative nerve injuries represent a frequent cause of peripheral neuropathic pain. Localized neuropathic pain is a type of neuropathic pain that is characterized by consistent

RESEARCH ARTICLE Open Access

Effectiveness of the capsaicin 8% patch in the management of peripheral neuropathic pain in European clinical practice: the ASCEND study

Colette Mankowski[1], Chris D. Poole[1], Etienne Ernault[2*], Roger Thomas[3], Ellen Berni[3], Craig J. Currie[4], ...sé I. Calvo[5], Christina Plastira[6], Eirini Zafeiropoulou[6] and Isaac Odeyemi[1]

...ndomised studies, the capsaicin 8% patch has demonstrated effective pain relief in patients with ...athic pain (PNP) arising from different aetiologies.

...) was an open-label, non-interventional study of patients with non-diabetes-related PNP who ... 8% patch treatment, according to usual clinical practice, and were followed for ≤52 weeks. ...oints were percentage change in the mean numeric pain rating scale (NPRS) 'average daily ...baseline to the average of Weeks 2 and 8 following first treatment; and median time from ...eatment. The primary analysis was intended to assess analgesic equivalence between ...uralgia (PHN) and other PNP aetiologies. Health-related quality of life (HRQoL, using EQ-5D), ...pression of Change (PGIC) and tolerability were also assessed.

...g first application, patients experienced a 26.6% (95% CI: 23.6, 29.62; $n = 412$) reduction in ... from baseline to Weeks 2 and 8. Equivalence was demonstrated between PHN and the ... pain, post-operative and post-traumatic neuropathic pain and 'other' PNP aetiology ...edian time from first to second treatment was 191 days (95% CI: 147, 235; $n = 181$). ...t of all patients were responders (≥30% reduction in NPRS score from baseline to Weeks 2 ...first treatment, and 86.9% ($n = 159/183$) remained so at Week 12. A sustained pain response ...til Week 52, with a 37.0% (95% CI: 31.3, 42.7; $n = 176$) reduction in mean NPRS score from ... with the shortest duration of pain (0–0.72 years) experienced the highest pain response ...Weeks 2 and 8. Mean EQ-5D index score improved by 0.199 utils (responders: 0.292 utils) ...Week 2 and was maintained until Week 52. Most patients reported improvements in PGIC ... all follow-up assessments regardless of number of treatments received. Adverse events ...ld or moderate reversible application site reactions.

...ropean clinical practice, the capsaicin 8% patch provided effective and sustained pain relief, ...ved HRQoL, improved overall health status and was generally well tolerated in a heterogeneous

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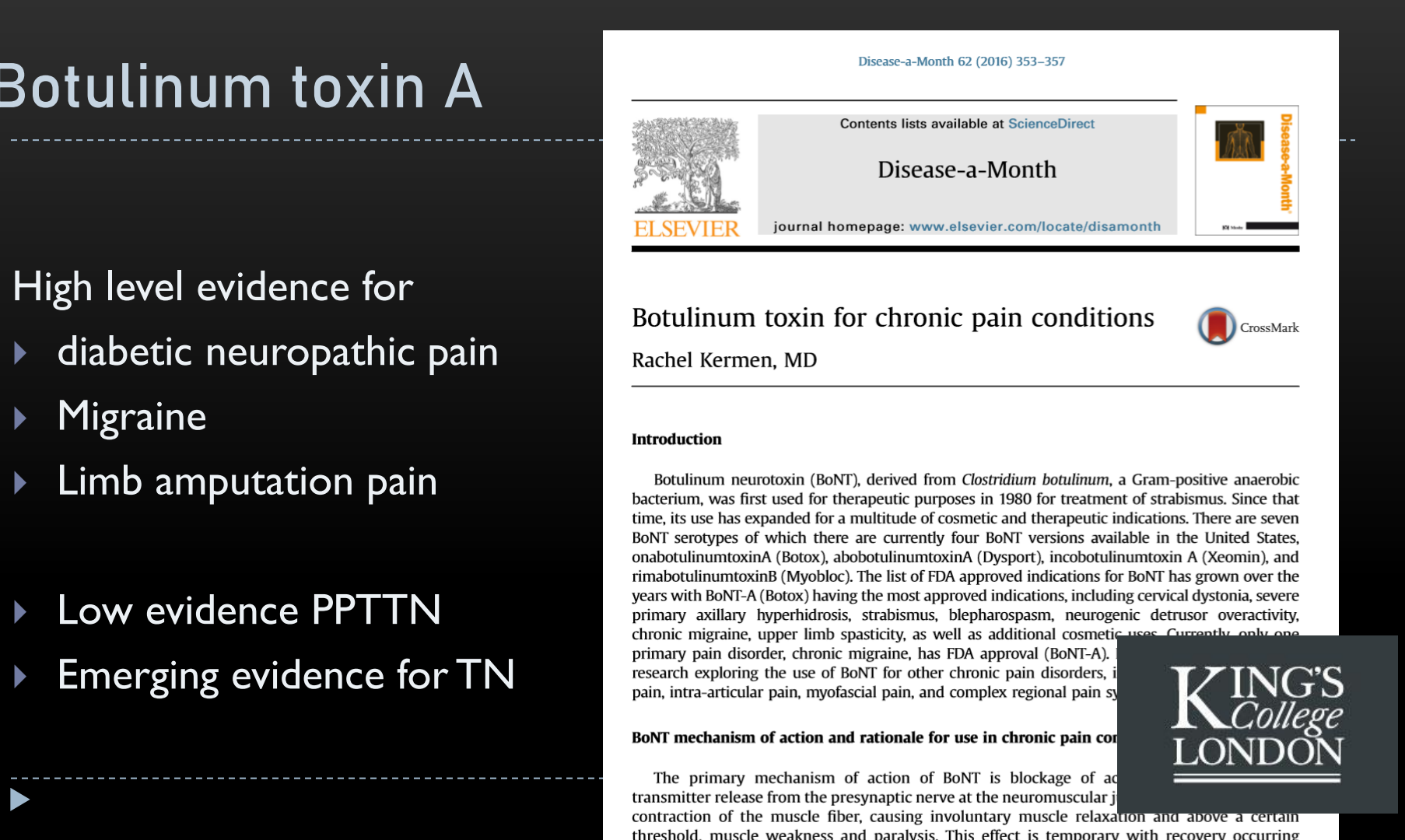
Botulinum toxin A

High level evidence for

- diabetic neuropathic pain
- Migraine
- Limb amputation pain

- Low evidence PPTTN
- Emerging evidence for TN



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Botulinum toxin for chronic pain conditions

Rachel Kermen, MD

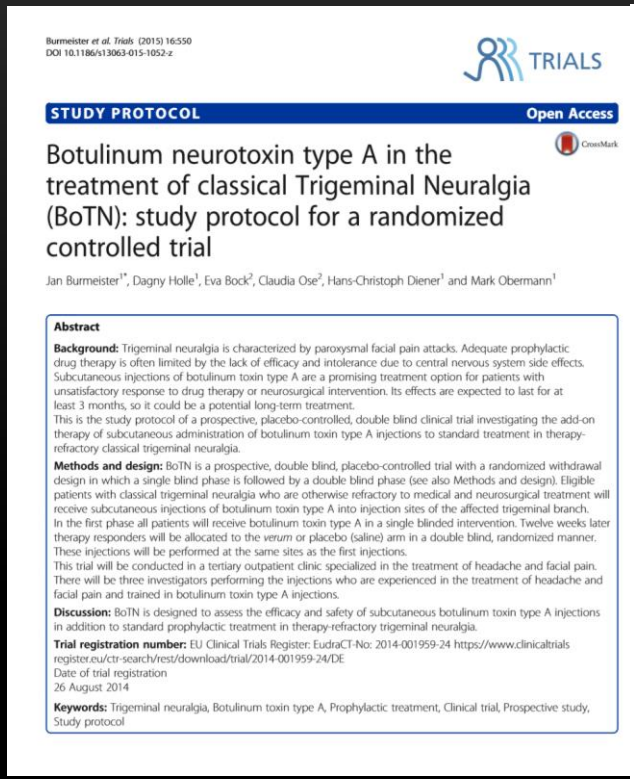
Introduction

Botulinum neurotoxin (BoNT), derived from *Clostridium botulinum*, a Gram-positive anaerobic bacterium, was first used for therapeutic purposes in 1980 for treatment of strabismus. Since that time, its use has expanded for a multitude of cosmetic and therapeutic indications. There are seven BoNT serotypes of which there are currently four BoNT versions available in the United States, onabotulinumtoxinA (Botox), abobotulinumtoxinA (Dysport), incobotulinumtoxin A (Xeomin), and rimabotulinumtoxinB (Myobloc). The list of FDA approved indications for BoNT has grown over the years with BoNT-A (Botox) having the most approved indications, including cervical dystonia, severe primary axillary hyperhidrosis, strabismus, blepharospasm, neurogenic detrusor overactivity, chronic migraine, upper limb spasticity, as well as additional cosmetic uses. Currently only one primary pain disorder, chronic migraine, has FDA approval (BoNT-A). research exploring the use of BoNT for other chronic pain disorders, i pain, intra-articular pain, myofascial pain, and complex regional pain sy

BoNT mechanism of action and rationale for use in chronic pain cor

The primary mechanism of action of BoNT is blockage of ac transmitter release from the presynaptic nerve at the neuromuscular j contraction of the muscle fiber, causing involuntary muscle relaxation and above a certain threshold, muscle weakness and paralysis. This effect is temporary with recovery occurring

Botoxin A



Burmeister et al. Trials (2015) 16:550
DOI 10.1186/s13063-015-1052-z

TRIALS

STUDY PROTOCOL Open Access

Botulinum neurotoxin type A in the treatment of classical Trigeminal Neuralgia (BoTN): study protocol for a randomized controlled trial

Jan Burmeister[1*], Dagny Holle[1], Eva Bock[2], Claudia Ose[2], Hans-Christoph Diener[1] and Mark Obermann[1]

Abstract

Background: Trigeminal neuralgia is characterized by paroxysmal facial pain attacks. Adequate prophylactic drug therapy is often limited by the lack of efficacy and intolerance due to central nervous system side effects. Subcutaneous injections of botulinum toxin type A are a promising treatment option for patients with unsatisfactory response to drug therapy or neurosurgical intervention. Its effects are expected to last for at least 3 months, so it could be a potential long-term treatment.
This is the study protocol of a prospective, placebo-controlled, double blind clinical trial investigating the add-on therapy of subcutaneous administration of botulinum toxin type A injections to standard treatment in therapy-refractory classical trigeminal neuralgia.

Methods and design: BoTN is a prospective, double blind, placebo-controlled trial with a randomized withdrawal design in which a single blind phase is followed by a double blind phase (see also Methods and design). Eligible patients with classical trigeminal neuralgia who are otherwise refractory to medical and neurosurgical treatment will receive subcutaneous injections of botulinum toxin type A into injection sites of the affected trigeminal branch. In the first phase all patients will receive botulinum toxin type A in a single blinded intervention. Twelve weeks later therapy responders will be allocated to the *verum* or placebo (saline) arm in a double blind, randomized manner. These injections will be performed at the same sites as the first injections.
This trial will be conducted in a tertiary outpatient clinic specialized in the treatment of headache and facial pain. There will be three investigators performing the injections who are experienced in the treatment of headache and facial pain and trained in botulinum toxin type A injections.

Discussion: BoTN is designed to assess the efficacy and safety of subcutaneous botulinum toxin type A injections in addition to standard prophylactic treatment in therapy-refractory trigeminal neuralgia.

Trial registration number: EU Clinical Trials Register: EudraCT-No: 2014-001959-24 https://www.clinicaltrials register.eu/ctr-search/rest/download/trial/2014-001959-24/DE
Date of trial registration
26 August 2014

Keywords: Trigeminal neuralgia, Botulinum toxin type A, Prophylactic treatment, Clinical trial, Prospective study, Study protocol

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The efficacy of botulinum toxin for the treatment of trigeminal and postherpetic neuralgia: a systematic review with meta-analyses

Thomas Shackleton, DDS, MS,[a] Saravanan Ram, DDS, MS,[b] Misty Black, DDS, MS,[c] Jon Ryder, DDS, MS,[c] Glenn T. Clark, DDS, MS,[c] and Reyes Enciso, PhD[d]

Objective. To evaluate the efficacy of a botulinum toxin type A (BoTN-A) in treating trigeminal neuralgia (TN) and postherpetic neuralgia (PHN).
Study Design. Three databases were searched: Medline, Web of Science, and Cochrane Library. The search was restricted to English-language randomized, placebo-controlled trials. Three review authors evaluated the cases for risk of bias.
Results. Six studies were eligible for inclusion. Pooled results showed a difference in post-treatment pain intensity of −3.009 (95% confidence interval −4.566 to −1.453; $P < .001$) in favor of BoTN-A compared with placebo in managing TN or PHN. Of the six studies, five had unclear risk of bias, and one showed high risk.
Conclusions. Although the studies had unclear or high risk of bias, moderate evidence regarding the efficacy of BoTN-A in treating TN and PHN was found. BoTN-A might be an alternative treatment to those patients who are either unable to manage their pain medically or would like adjunct therapy. (Oral Surg Oral Med Oral Pathol Oral Radiol 2016;122:61-71)

Neuralgia is described as pain extending along the course of one or more nerves. Many varieties of neuralgia are distinguished according to the nerves affected, such as the trigeminal, brachial, occipital, and supraorbital nerves, or to the cause, such as postherpetic, anemic, diabetic, gouty, malarial, or syphilitic factors.[1] Pain from neuralgias is often debilitating to those who suffer from it. These patients often suffer for extended periods before any sort of beneficial therapy is suggested.[2] There are two major treatment strategies for neuralgias: pharmacotherapy and neurosurgery. Medical management is the mainstay treatment for most neuralgias, since it generally carries a lower risk compared with major surgical procedures and is suitable for medically compromised patients who are unfit for such surgery.[3] However, side effects from systemic medications, such as ataxia, dizziness, nausea, fatigue, rash, and somnolence, can be problematic and debilitating.

Botulinum toxin type A (BoTN-A) is a potent neurotoxin that blocks acetylcholine release from presynaptic nerve endings by interfering with the activity of SNARE (soluble *N*-ethylamide-sensitive-factor attachment protein receptors) proteins. BoTN-A has been reported to have analgesic effects independent of its action on muscle tone.[4] The most significant results have been observed in patients with neuropathic pain. Neuropathic pain caused by peripheral lesions has been the most widely studied. BoTN-A has shown its efficacy on pain and allodynia in various animal models of inflammatory neuropathic pain.[4] The objective of this review was to determine the efficacy of BoTN-A when used as a treatment in patients suffering from trigeminal neuralgia (TN) or postherpetic neuralgia (PHN).

MATERIALS AND METHODS

This systematic review followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.[5]

Eligibility criteria

Studies were limited to randomized controlled trials (RCTs) on the efficacy of BoTN-A compared with

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2212-4403/$ - see front matter
http://dx.doi.org/10.1016/j.oooo.2016.03.003

Statement of Clinical Relevance

In this systematic review, the number of eligible studies was small, and the authors found unclear or high risk of bias in the included studies. However, moderate evidence regarding the efficacy of botulinum toxin A in treating trigeminal and postherpetic neuralgia was found; this evidence provides hope that this may be an alternative treatment for those patients who are either unable to manage their pain medically or would like an adjunct therapy.

Morra et al. The Journal of Headache and Pain (2016) 17:63
DOI 10.1186/s10194-016-0651-8

The Journal of Headache and Pain

REVIEW ARTICLE Open Access

Therapeutic efficacy and safety of *Botulinum Toxin A Therapy* in *Trigeminal Neuralgia*: a systematic review and meta-analysis of randomized controlled trials

Mostafa Ebraheem Morra[1†], Ahmed Elgebaly[1†], Ahmed Elmaraezy[1†], Adham M. Khalil[2†], Ahmed M. A. Altibi[3], Tran Le-Huy Vu[4], Mostafa Reda Mostafa[5], Nguyen Tien Huy[6,7*] and Kenji Hirayama[8*]

Abstract

Background: Several different interventions have been examined to alleviate pain and reduce frequency of trigeminal neuralgia (TN) paroxysms. However, some patients continue to have persistent or recurrent painful attacks. Using a systematic review and meta-analysis approach, we aimed to synthesize evidence from published randomized controlled trials (RCTs) regarding safety and efficacy of botulinum toxin type A (BTX-A) as a possible emerging choice of treatment for TN.

Methods: We conducted an electronic search in 10 databases/electronic search engines to access relevant publications. All articles in all languages reporting RCTs on the efficacy and safety of BTX-A in the treatment of TN were included for systematic review and meta-analysis.

Results: A total of four RCTs (n = 178) were identified for final meta-analysis. The overall effect favored BTX-A versus placebo in terms of proportion of responders (risk ratio RR = 2.87, 95 % confidence interval CI [1.76, 4.69], p <0.0001) with no significant detected heterogeneity (p = 0.31; I^2 = 4 %). Paroxysms frequency per day was significantly lower for BTX-A group (mean difference MD = -29.79, 95 % CI [-38.50,–21.08], p <0.00001) with no significant heterogeneity (p = 0.21; I^2 = 36 %).

Conclusion: Despite limited data, our results suggest that BTX-A may be an effective and safe treatment option for patients with TN. Further larger and well-designed RCTs are encouraged to translate these findings into better clinical outcome and better quality of life for TN patients.

Keywords: Botulinum, BTX-A, Trigeminal neuralgia, Clinical trials, Systematic review, Meta-analysis

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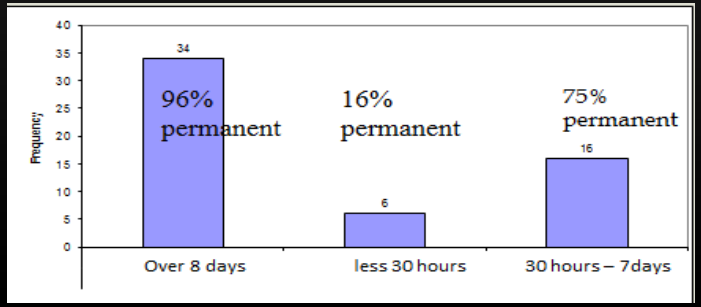
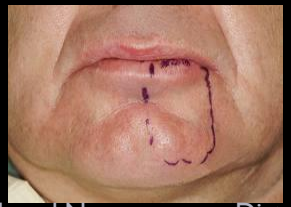
Acute surgical intervention – removal implant / endo tooth

- **Acute management < 30 hours (delayed onset neuropathy)**
  - (LA IDB lasts 3 hours and 25minutes)
  - Check on Patient after 6 hours (Home check)
  - IAN NEUROPATHY? (extreme pain/ mixed symptoms large neuropathic area)
    - Yes
      - Consult patient, check for area of neuropathy and signs of nerve injury
        - Confirmed
          - **Remove IMPLANT OR Endo / tooth < 30 hours with neuropathy**
            - + High dose oral NSAIDs (600-800mgs Ibuprofen PO QDS)
            - Prednisolone 5 day step down does 50-40-30-20-10mg PO
            - Vitamin B Complex?
            - (check medical history!)
            - Review

Only use plain films

Removing implant or endo filled tooth < 30 hours does Improve NI resolution



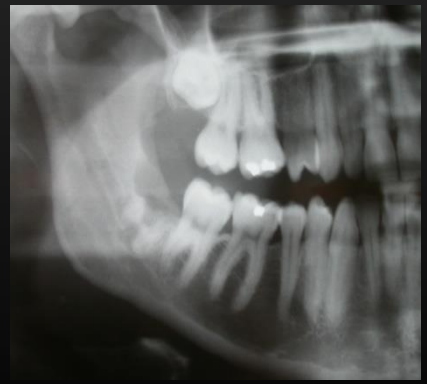


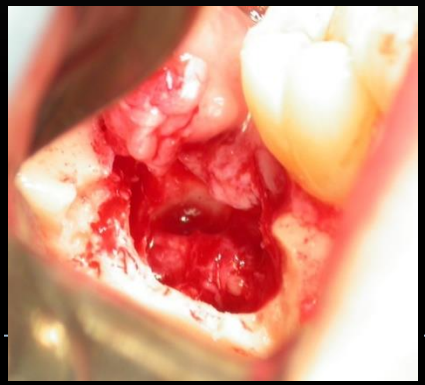
~~Bhavsar I, Khalaf M, Ferrin J, Al-Sabbagh M. Resolution of Implant-Induced Neurosensory Disturbance: A Procedural Failure. Implant Dent. 2015 Dec;24(6):735-41.~~

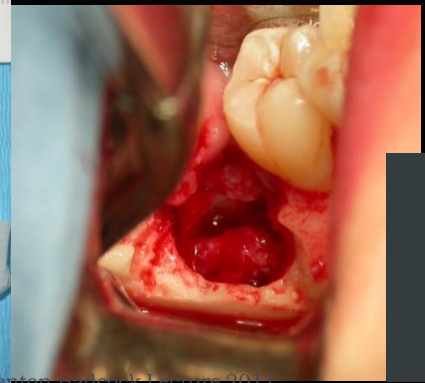
Khawaja N, Renton T. Case studies on **implant removal** influencing the resolution of inferior alveolar **nerve injury**. Br Dent J. 2009 Apr 11;206(7):365-70

Acute surgical intervention for patients IANI (< 2 weeks)

Procedure	Number of patients
Exploration and debridement	1
Exploration and decompression	8
Exploration and removal of roots and decompression	12
Excision of neuroma and reanastamosis of the nerve	3
Extraction of infected retained root and re-anastomosis of the nerve,	1







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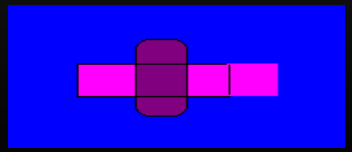
Nerve exploration what do we find?

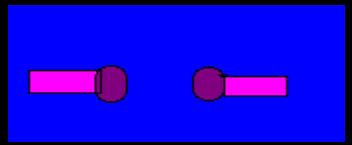
- Exploration

- Decompression

- Neuroma in continuity (NIC) excision and re-approximation

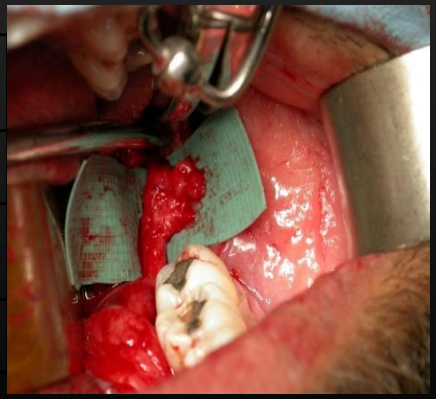


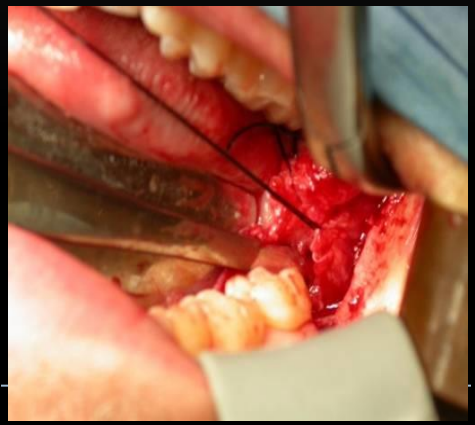
- End neuromata EN) excision and re-approximation with minimal tension

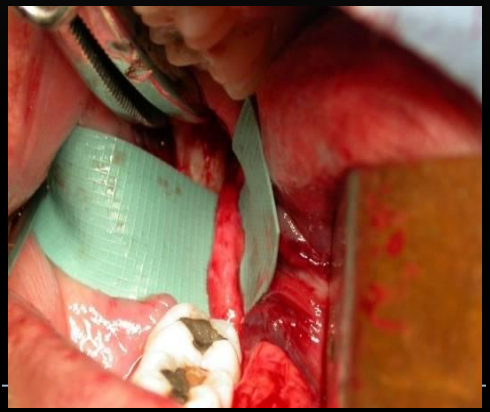


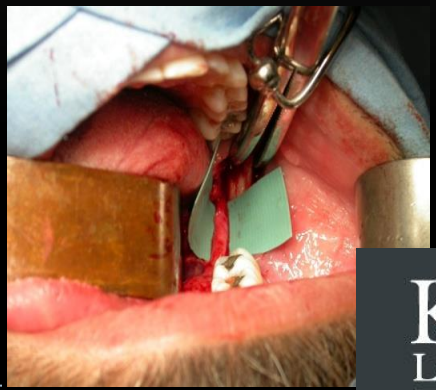
Key surgical procedures carried out for LNI patients

Procedure	Number of patients
Exploration and decompression	28
Release of scar tissue, excision of neuroma and re-anastimosis of the nerve	7
Nerve appears normal	2

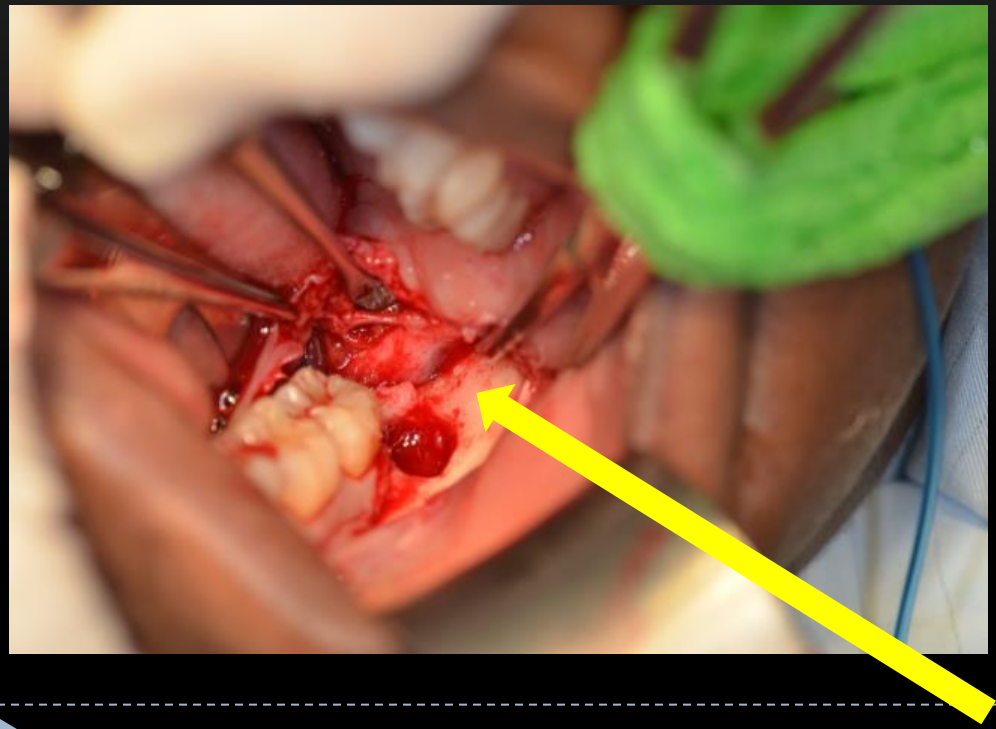








Findings during lingual nerve exploration ……we can see damaged lingual plates

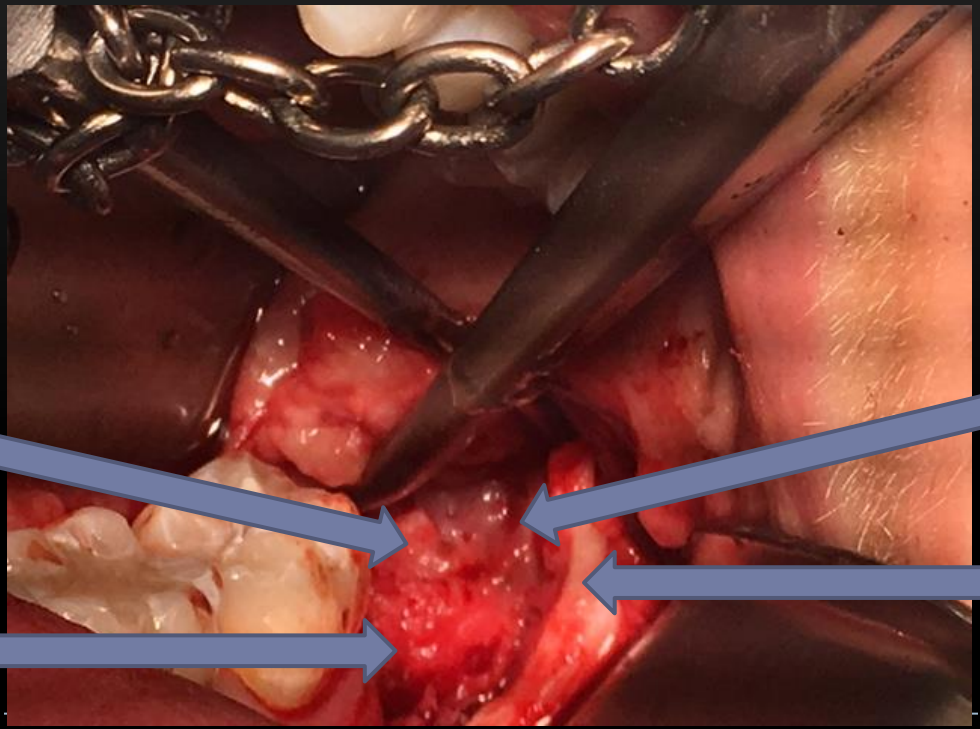


Damaged Lingual plate can be detected by CBCT scanning early post surgically

Allowing for earlier lingual nerve exploration and repair if necessary

ONLY wait for 12 weeks for resolution associated ONLY with lingual access surgery NOT Buccal access surgery

Operative findings lingual nerve injury



Sharp ledge bone with defect caused by previous surgery into lingual space

Nerve tissue pulled into socket

Granulation tissue in healing socket

Exposed buccal bone illustrating healing socket margin

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Edorium J Surg 2015;2:12–15.
www.edoriumjournalofsurgery.com

EDITORIAL OPEN ACCESS

Inferior alveolar nerve injuries and impacted lower third molars: The importance of third dimension

József Szalma

One of the most frequent oral surgical intervention is the removal of impacted wisdom-teeth. Inferior alveolar nerve (IAN) injury is a possible and unpleasing complication of surgical removal of impacted lower third molars. The incidence of irreversible injuries according to literature is usually below 1%, but reversible injuries are reported between 0.4–8.4% [1].

Anesthesia or paresthesia of the lower lip (consequent mental nerve sensory function disturbance) can significantly change patients' quality of life. Missing or reduced sensory innervation of the lower lip causes difficulties during eating and drinking, and uncontrolled bite trauma of the soft tissues is more frequent.

To predict "high-risk" cases more accurately or to try to avoid nerve injuries, several diagnostic and

as the neurovascular bundle can "vibrate together" with piezoelectric-tips avoiding irreversible injury) when bone removal is necessary near to the IAN at the apical region of third molars.

Diagnostic efforts include the analysis of two dimensional (panoramic radiography, periapical-, occlusal radiographs, vertical tube shifting technique) and three dimensional imaging methods such as computed tomography (CT) scan, cone beam CT magnetic resonance imaging (MRI) sc and limitations of specific and non-spe signs indicating intimate connections molar and the IAN are well investigat panoramic radiography, however the can carry several times important additi

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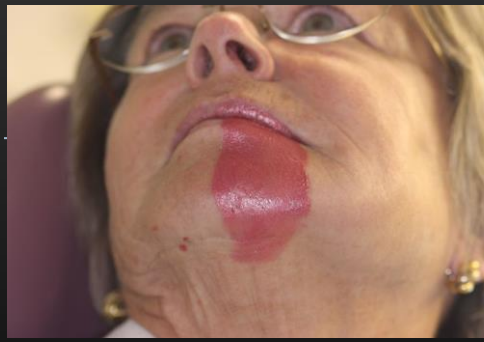
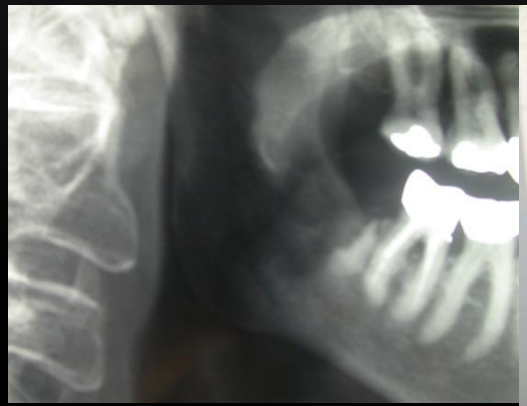
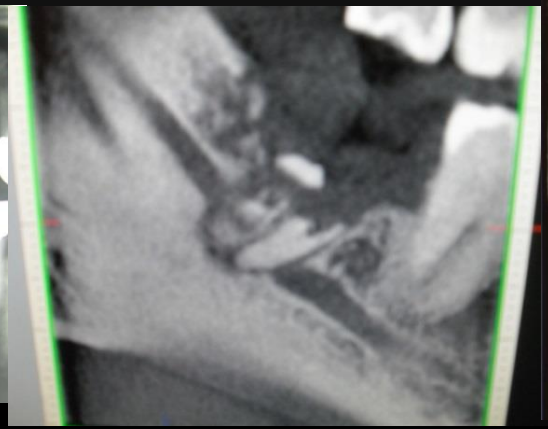
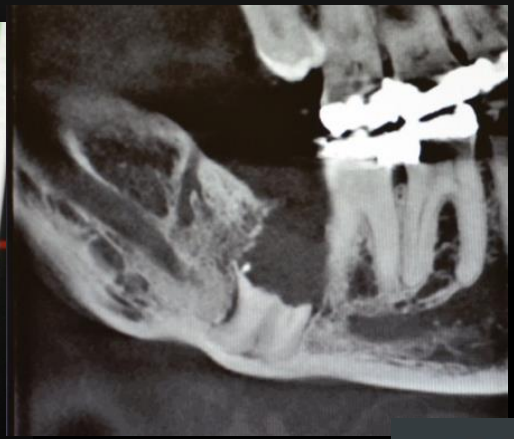
Inferior alveolar nerve injury



If DPT illustrates retained roots or compressed inferior dental canal (IDC) the CBCT useful to assess root position/ displacement and IDC structure **consider early exploration**







A Survey of the Opinion and Experience of UK Dentists: Part 2: Risk Assessment Strategies and the Management of Iatrogenic Trigeminal Nerve Injuries Related to Dental Implant **Surgery**.
Yilmaz Z, Ucer C, Scher E, Suzuki J, Renton T. Implant Dent. 2017 Apr;26(2):256-262. doi: 10.1097/ID.0000000000000545

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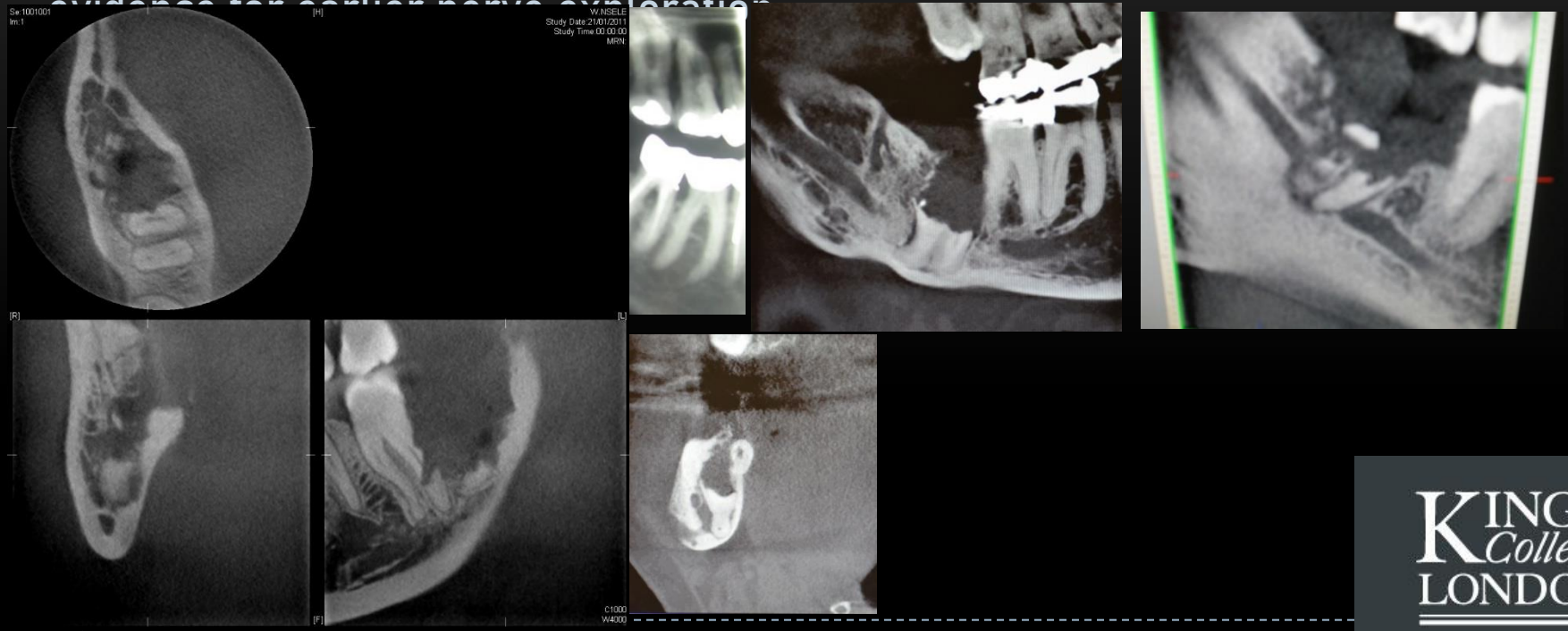
Inferior alveolar nerve injury with root retention
early surgical intervention < 2 weeks

CBCT useful for risk assessment of nerve injury on removing roots and provides evidence for earlier nerve exploration



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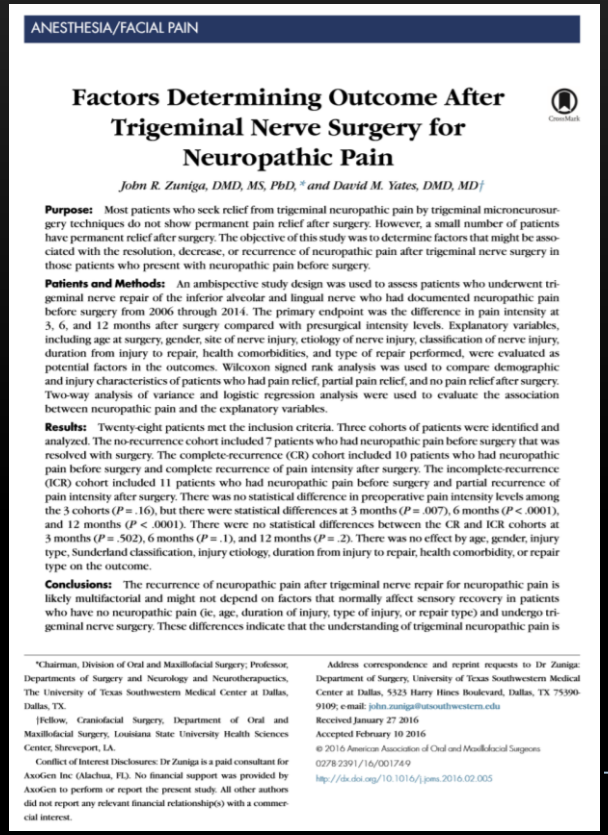
However Neuropathic pain does not respond to surgery

Surgical impact on NP

~~**Lingual nerve repair** and recurrence of neuropathic pain~~

27 patients Various procedures



ANESTHESIA/FACIAL PAIN

Factors Determining Outcome After Trigeminal Nerve Surgery for Neuropathic Pain

John R. Zuniga, DMD, MS, PhD, and David M. Yates, DMD, MD†*

Purpose: Most patients who seek relief from trigeminal neuropathic pain by trigeminal microneurosurgery techniques do not show permanent pain relief after surgery. However, a small number of patients have permanent relief after surgery. The objective of this study was to determine factors that might be associated with the resolution, decrease, or recurrence of neuropathic pain after trigeminal nerve surgery in those patients who present with neuropathic pain before surgery.

Patients and Methods: An ambispective study design was used to assess patients who underwent trigeminal nerve repair of the inferior alveolar and lingual nerve who had documented neuropathic pain before surgery from 2006 through 2014. The primary endpoint was the difference in pain intensity at 3, 6, and 12 months after surgery compared with presurgical intensity levels. Explanatory variables, including age at surgery, gender, site of nerve injury, etiology of nerve injury, classification of nerve injury, duration from injury to repair, health comorbidities, and type of repair performed, were evaluated as potential factors in the outcomes. Wilcoxon signed rank analysis was used to compare demographic and injury characteristics of patients who had pain relief, partial pain relief, and no pain relief after surgery. Two-way analysis of variance and logistic regression analysis were used to evaluate the association between neuropathic pain and the explanatory variables.

Results: Twenty-eight patients met the inclusion criteria. Three cohorts of patients were identified and analyzed. The no-recurrence cohort included 7 patients who had neuropathic pain before surgery that was resolved with surgery. The complete-recurrence (CR) cohort included 10 patients who had neuropathic pain before surgery and complete recurrence of pain intensity after surgery. The incomplete-recurrence (ICR) cohort included 11 patients who had neuropathic pain before surgery and partial recurrence of pain intensity after surgery. There was no statistical difference in preoperative pain intensity levels among the 3 cohorts ($P = .16$), but there were statistical differences at 3 months ($P = .007$), 6 months ($P < .0001$), and 12 months ($P < .0001$). There were no statistical differences between the CR and ICR cohorts at 3 months ($P = .502$), 6 months ($P = .1$), and 12 months ($P = .2$). There was no effect by age, gender, injury type, Sunderland classification, injury etiology, duration from injury to repair, health comorbidity, or repair type on the outcome.

Conclusions: The recurrence of neuropathic pain after trigeminal nerve repair for neuropathic pain is likely multifactorial and might not depend on factors that normally affect sensory recovery in patients who have no neuropathic pain (ie, age, duration of injury, type of injury, or repair type) and undergo trigeminal nerve surgery. These differences indicate that the understanding of trigeminal neuropathic pain is

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†Fellow, Craniofacial Surgery, Department of Oral and Maxillofacial Surgery, Louisiana State University Health Sciences Center, Shreveport, LA.

Conflict of Interest Disclosures: Dr Zuniga is a paid consultant for AxoGen Inc (Alachua, FL). No financial support was provided by AxoGen to perform or report the present study. All other authors did not report any relevant financial relationship(s) with a commercial interest.

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http://dx.doi.org/10.1016/j.joms.2016.02.005

If surgical reconstruction is used to treat allodynia, this often results in a decrease of complaints but symptoms almost never completely resolve.[10] Zuniga[26] reported only 3% of patients with neuropathic pain before surgery will completely recover following surgery. Occasionally, reconstruction can worsen complaints.[9,26]

9. Pogrel MA. The results of microneurosurgery of the inferior alveolar and lingual nerve. *J Oral Maxillofac Surg* 2002;60:485–489
10. Coulthard P, Kushnerev E, Yates JM, et al. Interventions for iatrogenic inferior alveolar and lingual nerve injury. *Cochrane Database Syst Rev* 2014:4:CD005293
26. Zuniga JR. Sensory outcomes after reconstruction of lingual and inferior alveolar nerve discontinuities using processed nerve allograft—a case series. *J Oral Maxillofac Surg* 2015;73:734–744

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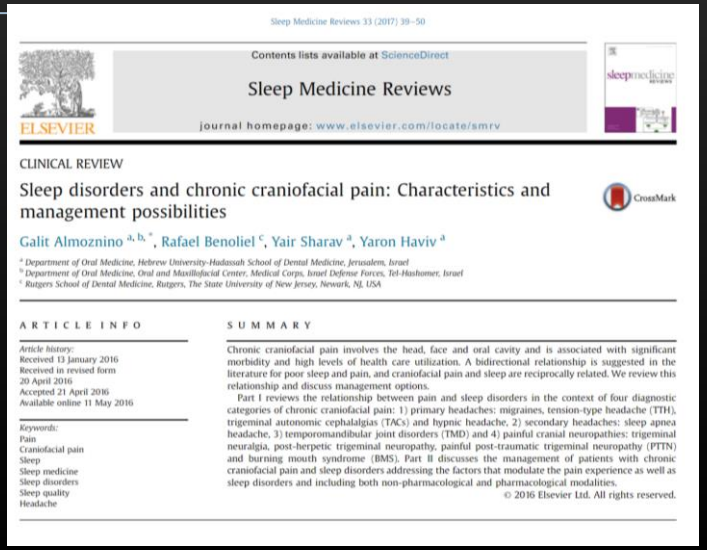
Conclusions: The recurrence of neuropathic pain after trigeminal nerve repair for neuropathic pain is likely multifactorial and might not depend on factors that normally affect sensory recovery in patients who have no neuropathic pain (ie, age, duration of injury, type of injury, or repair type) and undergo tri-

Adjunctive therapies

- Homeopathic
  - Arnica reduces bruising and swelling
- Hypnotherapy
  - self hypnosis
  - induced hypnosis
- Counselling
  - Chronic pain patients may need counselling to improve their coping strategies
- CBT
- Sleep
- Biofeedback
  - training in changing function to reduce pain
- Tens shown to reduce the discomfort of ID blocks
- Pet therapy
- Mirror therapy



Sleep Medicine Reviews 33 (2017) 39–50

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

Sleep disorders and chronic craniofacial pain: Characteristics and management possibilities

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[b] Department of Oral Medicine, Oral and Maxillofacial Center, Medical Corps, Israel Defense Forces, Tel-Hashomer, Israel
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SUMMARY

Chronic craniofacial pain involves the head, face and oral cavity and is associated with significant morbidity and high levels of health care utilization. A bidirectional relationship is suggested in the literature for poor sleep and pain, and craniofacial pain and sleep are reciprocally related. We review this relationship and discuss management options.

Part I reviews the relationship between pain and sleep disorders in the context of four diagnostic categories of chronic craniofacial pain: 1) primary headaches: migraines, tension-type headache (TTH), trigeminal autonomic cephalalgias (TACs) and hypnic headache, 2) secondary headaches: sleep apnea headache, 3) temporomandibular joint disorders (TMD) and 4) painful cranial neuropathies: trigeminal neuralgia, post-herpetic trigeminal neuropathy, painful post-traumatic trigeminal neuropathy (PTTN) and burning mouth syndrome (BMS). Part II discusses the management of patients with chronic craniofacial pain and sleep disorders addressing the factors that modulate the pain experience as well as sleep disorders and including both non-pharmacological and pharmacological modalities.

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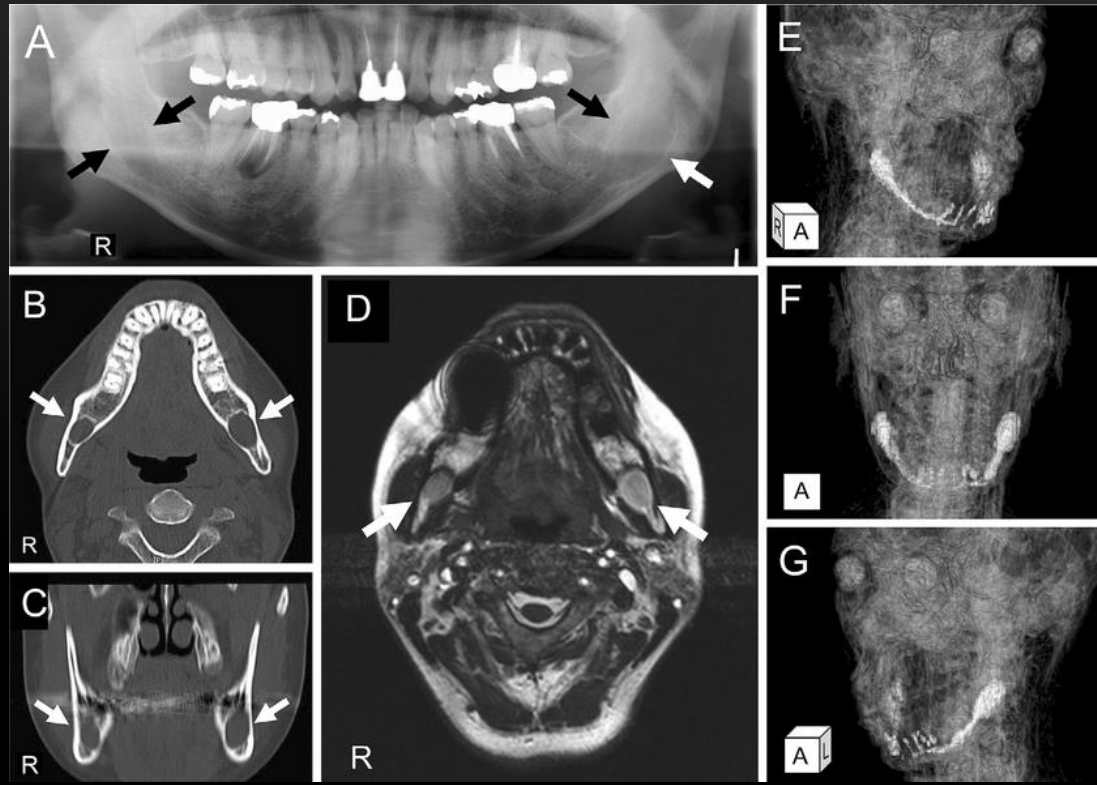
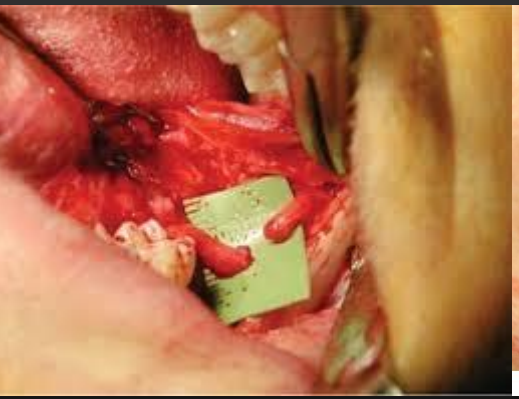
New developments

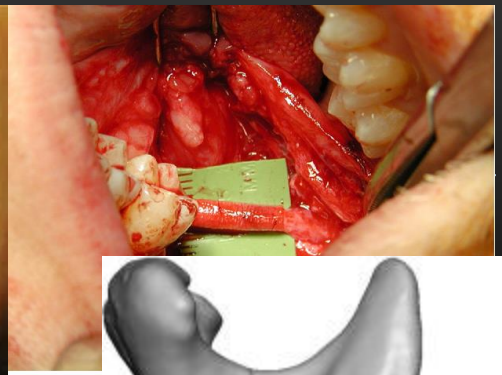
Zuniga JR, Mistry C, Tikhonov I, Dessouky R, **Chhabra** A Magnetic Resonance Neurography of Traumatic and Nontraumatic Peripheral Trigeminal Neuropathies. J Oral Maxillofac Surg. 2018 Apr;76(4):725-736. doi: 10.1016/j.joms.2017.11.007. Epub 2017 Nov 16.

Dessouky R, Xi Y, **Zuniga J**, **Chhabra** A. Role of MR Neurography for the Diagnosis of Peripheral Trigeminal Nerve Injuries in Patients with Prior Molar Tooth Extraction. AJNR Am J Neuroradiol. 2018 Jan;39(1):162-169.

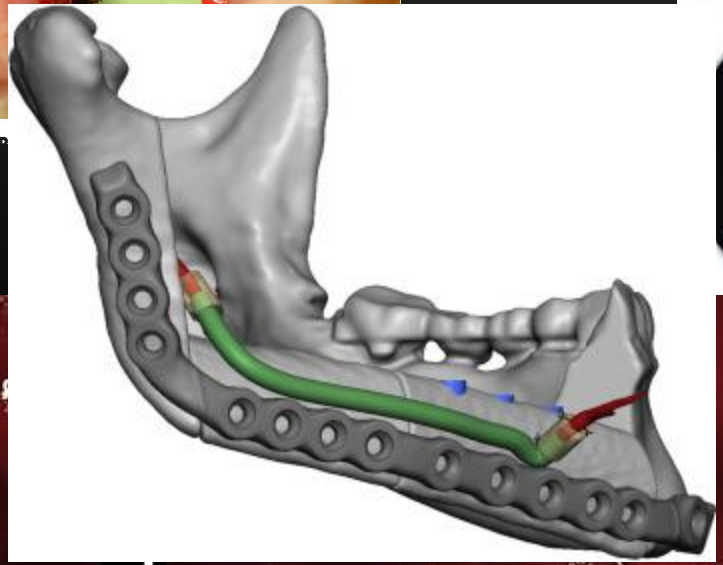
Cox B, Zuniga JR, Panchal N, Cheng J, **Chhabra** A. Magnetic resonance neurography in the management of peripheral trigeminal neuropathy: experience in a tertiary care centre. Eur Radiol. 2016 Oct;26(10):3392-400. doi: 10.1007/s00330-015-4182-5. Epub 2016 Jan 21

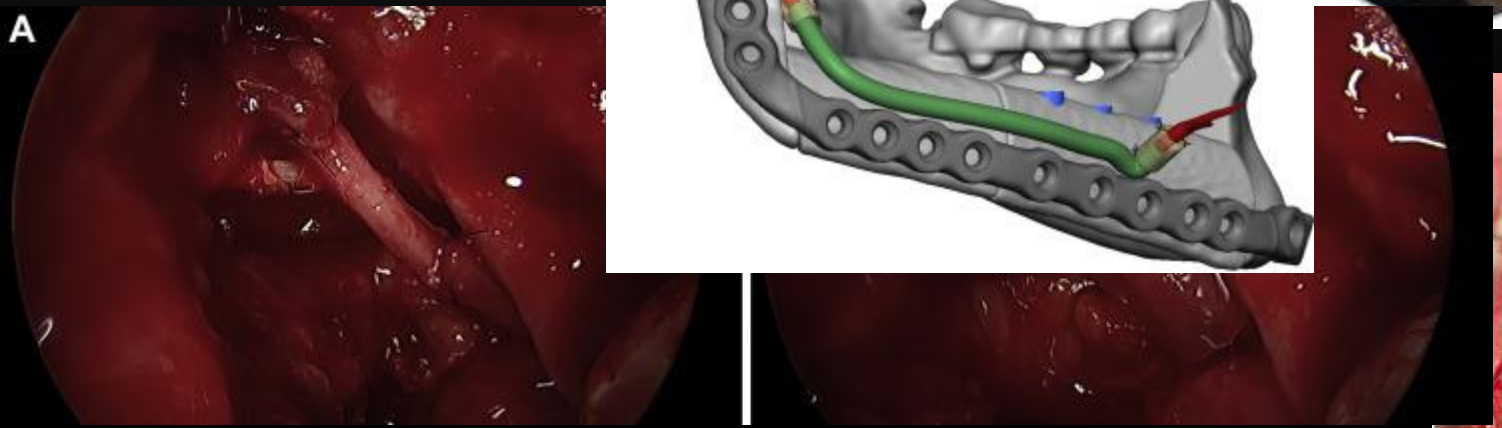


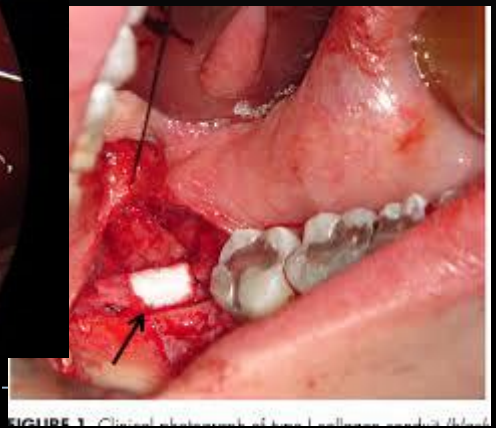




John Zuniga







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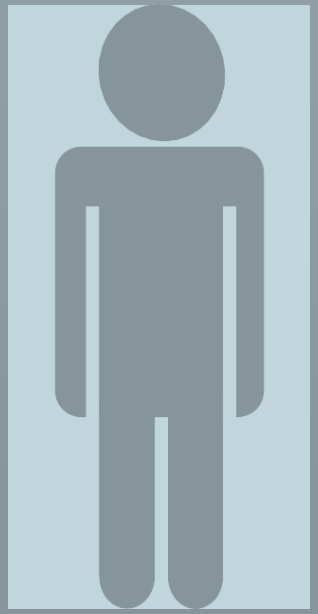
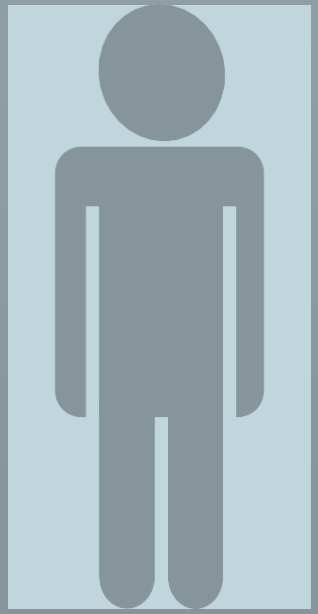
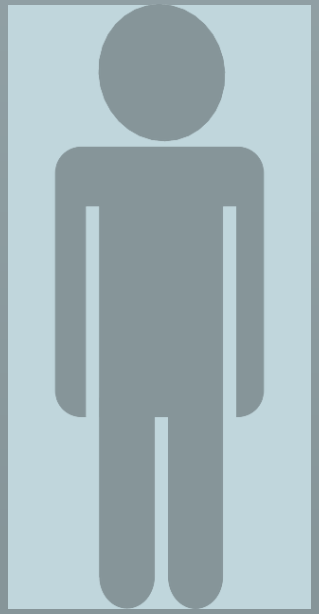
Part B Overview TN and other NP



Diagnosis of TN?



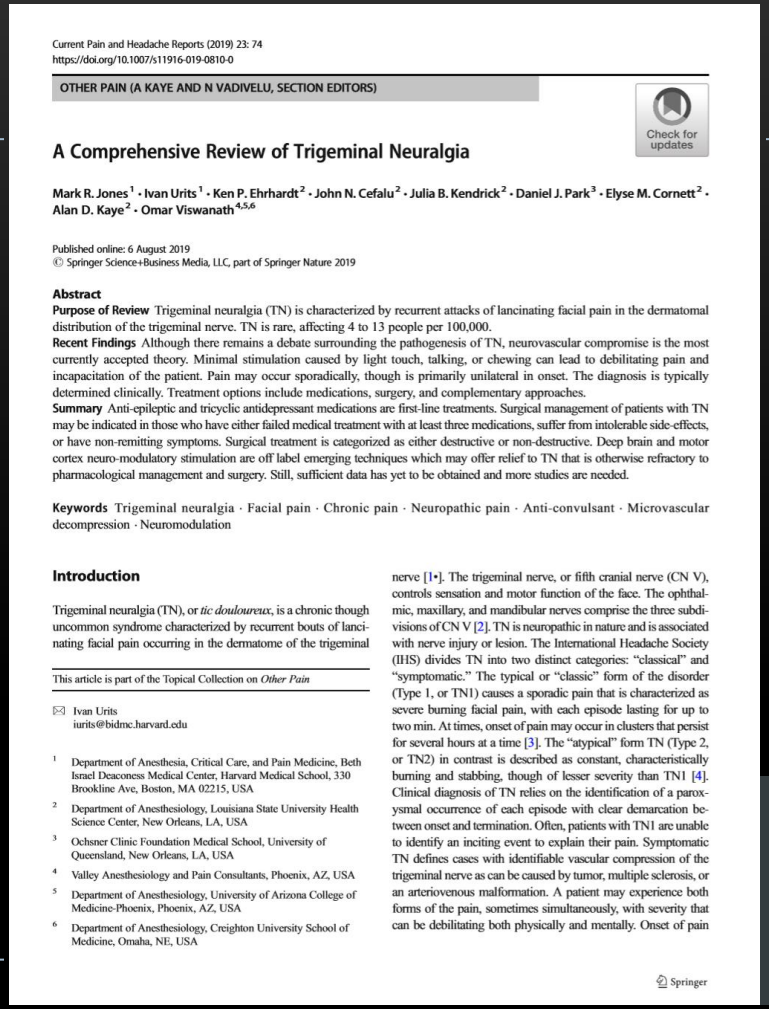
Who gets TN?



How to manage TN?

Outline

- –Introduction
  - •The trigeminal system
  - •Definitions neuropathic pain
  - •Trigeminal neuralgia
- –Diagnostic criteria TN
- –Aetiology TN
- –Assessment TN and PTNP
- –Management;
  - **Trigeminal neuralgia (TN)**
    - –Medical
    - –Interventional
    - –Surgery
  - –The future



Current Pain and Headache Reports (2019) 23: 74
https://doi.org/10.1007/s11916-019-0810-0

OTHER PAIN (A KAYE AND N VADIVELU, SECTION EDITORS)

Check for updates

A Comprehensive Review of Trigeminal Neuralgia

Mark R. Jones[1] · Ivan Urits[1] · Ken P. Ehrhardt[2] · John N. Cefalu[2] · Julia B. Kendrick[2] · Daniel J. Park[3] · Elyse M. Cornett[2] · Alan D. Kaye[2] · Omar Viswanath[4,5,6]

Published online: 6 August 2019

Abstract
Purpose of Review Trigeminal neuralgia (TN) is characterized by recurrent attacks of lancinating facial pain in the dermatomal distribution of the trigeminal nerve. TN is rare, affecting 4 to 13 people per 100,000.
Recent Findings Although there remains a debate surrounding the pathogenesis of TN, neurovascular compromise is the most currently accepted theory. Minimal stimulation caused by light touch, talking, or chewing can lead to debilitating pain and incapacitation of the patient. Pain may occur sporadically, though is primarily unilateral in onset. The diagnosis is typically determined clinically. Treatment options include medications, surgery, and complementary approaches.
Summary Anti-epileptic and tricyclic antidepressant medications are first-line treatments. Surgical management of patients with TN may be indicated in those who have either failed medical treatment with at least three medications, suffer from intolerable side-effects, or have non-remitting symptoms. Surgical treatment is categorized as either destructive or non-destructive. Deep brain and motor cortex neuro-modulatory stimulation are off label emerging techniques which may offer relief to TN that is otherwise refractory to pharmacological management and surgery. Still, sufficient data has yet to be obtained and more studies are needed.

Keywords Trigeminal neuralgia · Facial pain · Chronic pain · Neuropathic pain · Anti-convulsant · Microvascular decompression · Neuromodulation

Introduction

Trigeminal neuralgia (TN), or *tic douloureux*, is a chronic though uncommon syndrome characterized by recurrent bouts of lancinating facial pain occurring in the dermatome of the trigeminal nerve [1•]. The trigeminal nerve, or fifth cranial nerve (CN V), controls sensation and motor function of the face. The ophthalmic, maxillary, and mandibular nerves comprise the three subdivisions of CN V [2]. TN is neuropathic in nature and is associated with nerve injury or lesion. The International Headache Society (IHS) divides TN into two distinct categories: "classical" and "symptomatic." The typical or "classic" form of the disorder (Type 1, or TN1) causes a sporadic pain that is characterized as severe burning facial pain, with each episode lasting for up to two min. At times, onset of pain may occur in clusters that persist for several hours at a time [3]. The "atypical" form TN (Type 2, or TN2) in contrast is described as constant, characteristically burning and stabbing, though of lesser severity than TN1 [4]. Clinical diagnosis of TN relies on the identification of a paroxysmal occurrence of each episode with clear demarcation between onset and termination. Often, patients with TN1 are unable to identify an inciting event to explain their pain. Symptomatic TN defines cases with identifiable vascular compression of the trigeminal nerve as can be caused by tumor, multiple sclerosis, or an arteriovenous malformation. A patient may experience both forms of the pain, sometimes simultaneously, with severity that can be debilitating both physically and mentally. Onset of pain

This article is part of the Topical Collection on *Other Pain*

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Trigeminal neuralgia History

TN was first described in the writings of Galen, Aretaeus of Cappadocia, and Avicenna as early as the first century, although the first accurate descriptions were not officially documented until the 1700s .

In 1756, Nicholas André coined the term “tic douloureux” because of the distinctive facial spasms that accompany the attacks.

An English physician named John Fothergill is creditedas the first to give a full and accurate description of the disorder in a submission to the Medical Society of London in 1773, titled “On a Painful Affliction of the Face.” As such, the disease is also known as “Fothergill’s Disease.

Trigeminal Neuralgia

IASP defines trigeminal neuralgia as

" a sudden, usually unilateral, severe, brief, stabbing, recurrent pain in the distribution of one or more branches of the fifth cranial nerve".

TN in the general population might be between 0.01% and 0.3%, although studies carried out in primary care settings suggest that it may be much higher, around 12% per 100,000 persons per year

- Does it meet the White and Sweet criteria:[2]
  - The pain is paroxysmal.
  - The pain is confined to the trigeminal distribution.
  - The pain is unilateral.
  - The bedside clinical sensory examination is normal.
  - The pain may be provoked by light touch to the face (trigger zones)

- http://www.iasp-pain.org/files/Content/ContentFolders/GlobalYearAgainstPain2/20132014OrofacialPain/FactSheets/Trigeminal_Neuralgia.pdf

Trigeminal Neuralgia

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ICOP diagnostic criteria

4.1.1.1 Classical trigeminal neuralgia
Previously used term: Primary trigeminal neuralgia.
192 Cephalalgia 40(2) International Headache Society 2020

Description: Trigeminal neuralgia developing without apparent cause other than neurovascular compression.
Diagnostic criteria:

A. Recurrent paroxysms of unilateral pain fulfilling criteria for 4.1.1 Trigeminal neuralgia
B. B. Demonstration on magnetic resonance imaging (MRI) or during surgery of neurovascular compression (not simply contact), with morphological changes1 in the trigeminal nerve root.

4.1.1.1.1 Classical trigeminal neuralgia, purely paroxysmal
Description: Classical trigeminal neuralgia without persistent background pain.

4.1.1.1.2 Classical trigeminal neuralgia with concomitant continuous pain
Previously used terms: Atypical trigeminal neuralgia; trigeminal neuralgia type 2.

ICOP classification for TN

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Previously used terms: Atypical trigeminal neuralgia; trigeminal neuralgia type 2.

Types of TN

4.1.1.2 Secondary trigeminal neuralgia
Description: Trigeminal neuralgia caused by an underlying disease. Clinical examination shows sensory changes in a substantial percentage of these patients.

4.1.1.2.1 Trigeminal neuralgia attributed to multiple sclerosis
Description: Trigeminal neuralgia caused by a multiple sclerosis (MS) plaque or plaques in the pons or trigeminal root entry zone, and associated with other symptoms and/or clinical or laboratory findings of MS
4.1.1.2.2 Trigeminal neuralgia attributed to space-occupying lesion
Description: Trigeminal neuralgia caused by contact between the affected trigeminal nerve and a space-occupying lesion
4.1.1.2.3 Trigeminal neuralgia attributed to other cause
Description: Trigeminal neuralgia caused by an underlying disease other than those described above.

4.1.1.3 Idiopathic trigeminal neuralgia
Description: Trigeminal neuralgia with neither electrophysiological tests nor MRI showing significant abnormalities

4.1.1.3.1 Idiopathic trigeminal neuralgia, purely paroxysmal
Diagnostic criteria: A. Recurrent paroxysms of unilateral facial pain fulfilling criteria for 4.1.1.3 Idiopathic trigeminal neuralgia B. Pain-free between attacks in the affected trigeminal distribution.

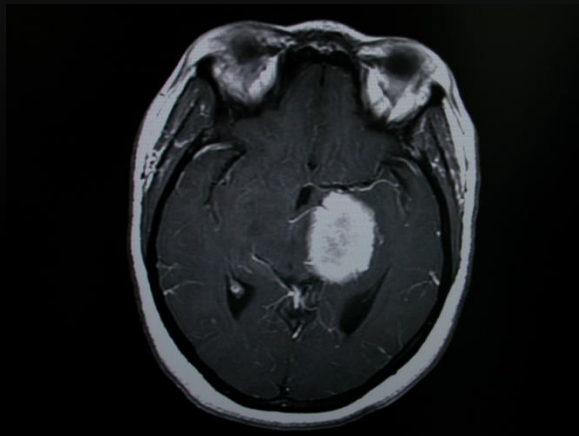
4.1.1.3.2 Idiopathic trigeminal neuralgia with concomitant continuous pain

ICHD3 diagnostic criteria for TN (IASP, ICHD3 and ICOP)

- Classical TN
  - Paroxysmal pain ONLY pain in V" and V2, unilateral in patients over 60 years with Neurovascular conflict
  - Above with back ground pain and NVC conflict
- Secondary TN

  MS, SOL or other cause

  bilateral, neuropathy, younger age
- Idiopathic TN
  - Not secondary
  - No NVC



TN is rare, affecting 4 to 13 people per 100,000.

TN is rare, affecting 4 to 13 people per 100,000.

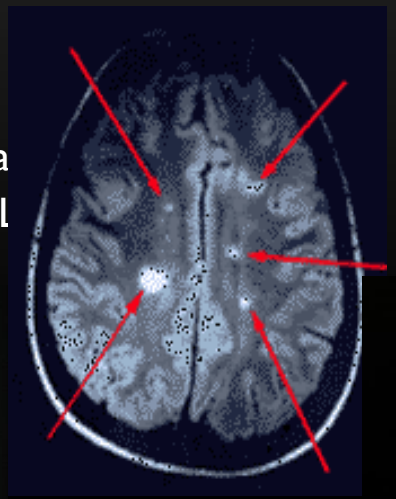
- Classical TN
  - Paroxysmal pain ONLY pain in V" and V2, unilateral in patients over 60 years with Neurovascular conflict
  - Above with back ground pain and Neurovascular conflict (NVC) conflict
- Secondary TN

  Multiple sclerosis (MS)

  bilateral, neuropa

  Space occupying lesions (SOL

  Stroke



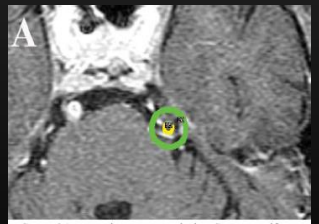
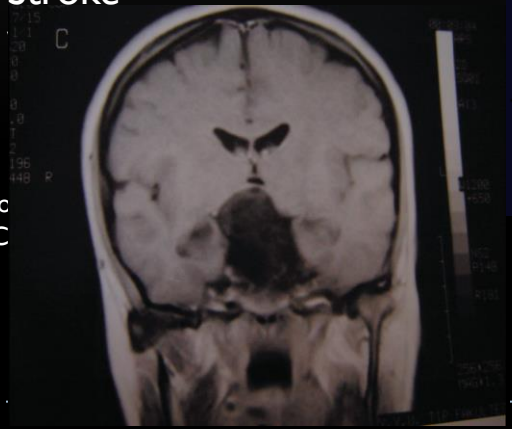
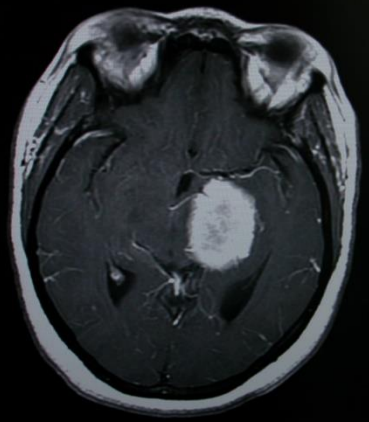


FIGURE 2A: Targeting MR scan during Gamma Knife stereotactic radiosurgery showing the radiation focus spot targeted on the trigeminal nerve root. The yellow line is the 85% dose prescription line and the green line shows the





- Idiopathic TN
  - Not secc
  - No NVC

Diagnosis and differential diagnosis of trigeminal neuralgia Zakrzewska JM. Clin J Pain 2002;18:14–21

Trigeminal Neuralgia

- Patient characteristics
- Older patients 5th-6th decade
- Spontaneous onset
- V2 and V3 most commonly affected
- Often starts as pain on brushing teeth 'dental pain'

- Familial TN
- ? Nav1.7 and Nav1.8 sodium channel genetic mutation

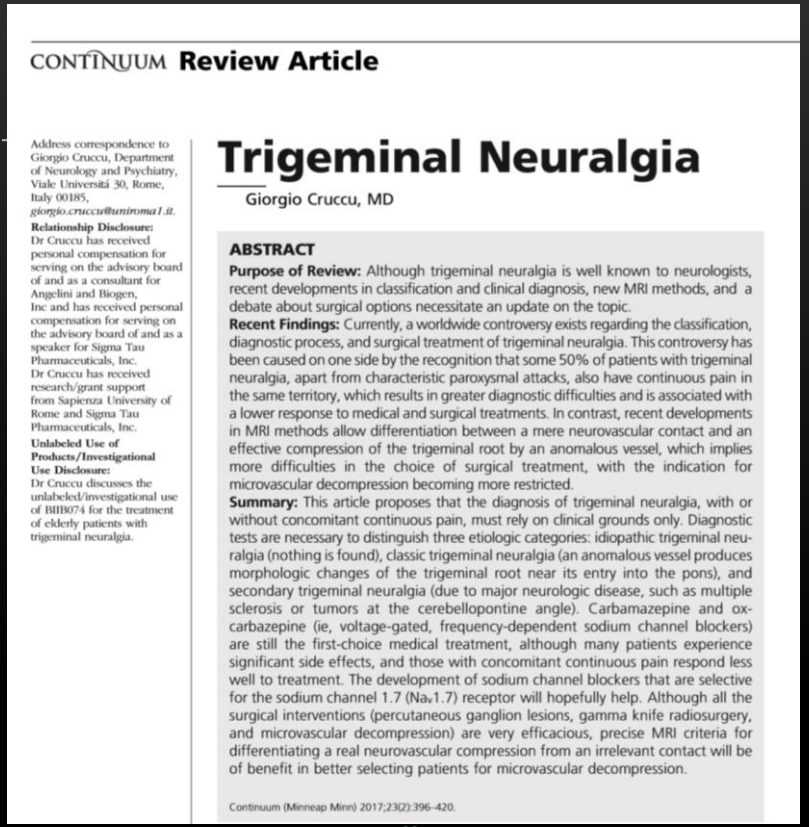
- Pain Characteristics
  - Flashing, shooting, sharp, unbearable
- Severity
  - Moderate to severe
- Site, radiation
  - Distribution of trigeminal nerve
- Duration, periodicity
  - Bouts last for seconds, pain free periods
- Refractory period
- Less pain at Night
- Elicited pain
  - Light touch, eating, talking
- Relieving factors
  - Avoid touch, anticonvulsants
- Associated factors
  - Trigger areas, weight loss

Trigeminal Neuralgia clinical features

- Most common pain syndrome referable to a cranial nerve.[1]
- Most common in adults > 50 y/o, women slightly more than men[2]
- Classically, pain is described as an electric shock–like, stabbing, unilateral pain with abrupt onset and termination in distribution of trigeminal nerve – usually V2/3.[2,3]
  - Intervals between attacks are pain free
  - Minimal or no sensory loss in the region of pain
  - Although the duration of trigeminal neuralgia paroxysms may last up to 2 minutes, in most patients they are only a few seconds long
- Precipitation from trigger areas or by certain daily activities, such as eating, talking, washing the face, or cleaning the teeth[3]
- Diagnosis is typically made by the history
- Unlike other neuropathic pains, trigeminal neuralgia may enter into periods of complete pain remission in up to 63% of patients
- Imaging is often pursued to r/o other causes of facial pain &/or to evaluate for MS, vascular compression of the trigeminal nerve etc.
- Typically, 80% of patients respond to medical therapy[3]
  - 1st line therapy is carbamazepine[2,3,5]

Aetiology of TN

Several studies suggest that compression-induced microstructural changes may be estimated using diffusion-tensor imaging (DTI) and tractography to measure focal demyelination and edema.



CONTINUUM **Review Article**

Address correspondence to Giorgio Cruccu, Department of Neurology and Psychiatry, Viale Università 30, Rome, Italy 00185, *giorgio.cruccu@uniroma1.it.*

Relationship Disclosure: Dr Cruccu has received personal compensation for serving on the advisory board of and as a consultant for Angelini and Biogen, Inc and has received personal compensation for serving on the advisory board of and as a speaker for Sigma Tau Pharmaceuticals, Inc. Dr Cruccu has received research/grant support from Sapienza University of Rome and Sigma Tau Pharmaceuticals, Inc.

Unlabeled Use of Products/Investigational Use Disclosure: Dr Cruccu discusses the unlabeled/investigational use of BIIB074 for the treatment of elderly patients with trigeminal neuralgia.

Trigeminal Neuralgia

Giorgio Cruccu, MD

ABSTRACT

Purpose of Review: Although trigeminal neuralgia is well known to neurologists, recent developments in classification and clinical diagnosis, new MRI methods, and a debate about surgical options necessitate an update on the topic.

Recent Findings: Currently, a worldwide controversy exists regarding the classification, diagnostic process, and surgical treatment of trigeminal neuralgia. This controversy has been caused on one side by the recognition that some 50% of patients with trigeminal neuralgia, apart from characteristic paroxysmal attacks, also have continuous pain in the same territory, which results in greater diagnostic difficulties and is associated with a lower response to medical and surgical treatments. In contrast, recent developments in MRI methods allow differentiation between a mere neurovascular contact and an effective compression of the trigeminal root by an anomalous vessel, which implies more difficulties in the choice of surgical treatment, with the indication for microvascular decompression becoming more restricted.

Summary: This article proposes that the diagnosis of trigeminal neuralgia, with or without concomitant continuous pain, must rely on clinical grounds only. Diagnostic tests are necessary to distinguish three etiologic categories: idiopathic trigeminal neuralgia (nothing is found), classic trigeminal neuralgia (an anomalous vessel produces morphologic changes of the trigeminal root near its entry into the pons), and secondary trigeminal neuralgia (due to major neurologic disease, such as multiple sclerosis or tumors at the cerebellopontine angle). Carbamazepine and oxcarbazepine (ie, voltage-gated, frequency-dependent sodium channel blockers) are still the first-choice medical treatment, although many patients experience significant side effects, and those with concomitant continuous pain respond less well to treatment. The development of sodium channel blockers that are selective for the sodium channel 1.7 ($Na_v1.7$) receptor will hopefully help. Although all the surgical interventions (percutaneous ganglion lesions, gamma knife radiosurgery, and microvascular decompression) are very efficacious, precise MRI criteria for differentiating a real neurovascular compression from an irrelevant contact will be of benefit in better selecting patients for microvascular decompression.

Continuum (Minneap Minn) 2017;23(2):396–420.

Leal PR, Roch JA, Hermier M, et al. Structural abnormalities of the trigeminal root revealed by diffusion tensor imaging in patients with trigeminal neuralgia caused by neurovascular compression: a prospective, double-blind, controlled study. Pain 2011;152(10): 2357-2364. doi:10.1016/j.pain.2011.06.029.

Desouza DD, Davis KD, Hodaie M. Reversal of insular and microstructural nerve abnormalities following effective surgical treatment for trigeminal neuralgia. Pain 2015;156(6):1112-1123. doi:10.1097/ j.pain.0000000000000156.

NVC Focal neuropathy Pathogenesis of TN

- The primary mechanism is focal demyelination of primary afferents near the entry (extra-axial or intra-axial) of the trigeminal root into the pons.
  - Some investigators believe this area represents a locus minoris resistentiae (a site of lower resistance or higher susceptibility to damage) because it is the site where Schwann cells are substituted by oligodendroglia in providing the myelin sheath.
- A second pathophysiologic theory, admittedly more debatable, is that the damaged primary afferents in the area of focal demyelination become a source of ectopic generation of impulses.
  - Cruccu proposes that, because mitochondria and the energetic apparatus necessary to pump sodium off are physiologically concentrated at the level of the nodes of Ranvier, when the demyelinating process allows the passage of ions in and out of the axon, then the axons do not have enough energy to promptly re-establish the resting potential.
  - Hence, the axons tend toward a depolarization level, which makes them hyperexcitable
- A third potential pathophysiologic theory, with almost no sound evidence at all at this time, is that the hyperactivity of primary afferents secondarily induces central sensitization of wide dynamic range neurons in the spinal trigeminal nucleus or even more central changes

New theories of Pathogenesis TN

- NAV 1.7 ongoing trial Nav 1.7 blocker
  - A new, better tolerated, Nav1.7 selective state-dependent, sodium channel blocker (vixotrigine) is under development.
  - Future trials testing the effect of combination therapy in patients with TN are needed, especially in patients with concomitant continuous pain and in TN secondary to multiple sclerosis
- NaV 1.6
- Familial TN

Molecular Medicine

A Gain-of-Function Mutation in Nav1.6 in a Case of Trigeminal Neuralgia

Brian S Tanaka,[1,2,3] Peng Zhao,[1,2,3] Fadia B Dib-Hajj,[1,2,3] Valerie Morisset,[4] Simon Tate,[4] Stephen G Waxman,[1,2,3] and Sulayman D Dib-Hajj[1,2,3]

[1]Department of Neurology; [2]Center for Neuroscience and Regeneration Research, Yale University School of Medicine, New Haven, Connecticut, United States of America; [3]Rehabilitation Research Center, Veterans Affairs Connecticut Healthcare System, West Haven; and [4]Convergence Pharmaceuticals Ltd, Cambridge, United Kingdom

Idiopathic trigeminal neuralgia (TN) is a debilitating pain disorder characterized by episodic unilateral facial pain along the territory of branches of the trigeminal nerve. Human pain disorders, but not TN, have been linked to gain-of-function mutations

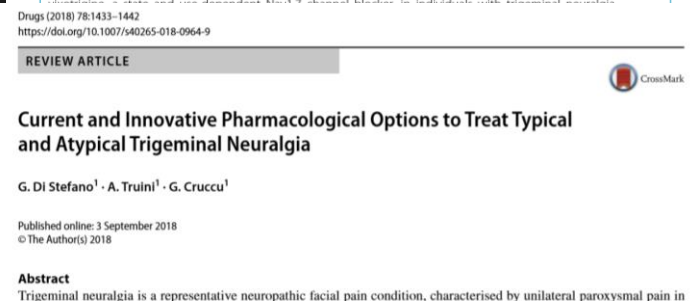
RESEARCH Open Access

Challenges recruiting to a proof-of-concept pharmaceutical trial for a rare disease: the trigeminal neuralgia experience

Joanna M. Zakrzewska[1,9,10*], Joanne Palmer[2], Lars Bendtsen[3], Giulia Di Stefano[4], Dominik A. Ettlin[5], Stine Maarbjerg[3], Mark Obermann[6,7], Valerie Morisset[2], Deb Steiner[8], Simon Tate[2] and Giorgio Cruccu[4]

Abstract

Background: This study aimed to describe recruitment challenges encountered during a phase IIa study of



Drugs (2018) 78:1433–1442
https://doi.org/10.1007/s40265-018-0964-9

REVIEW ARTICLE

Current and Innovative Pharmacological Options to Treat Typical and Atypical Trigeminal Neuralgia

G. Di Stefano[1] · A. Truini[1] · G. Cruccu[1]

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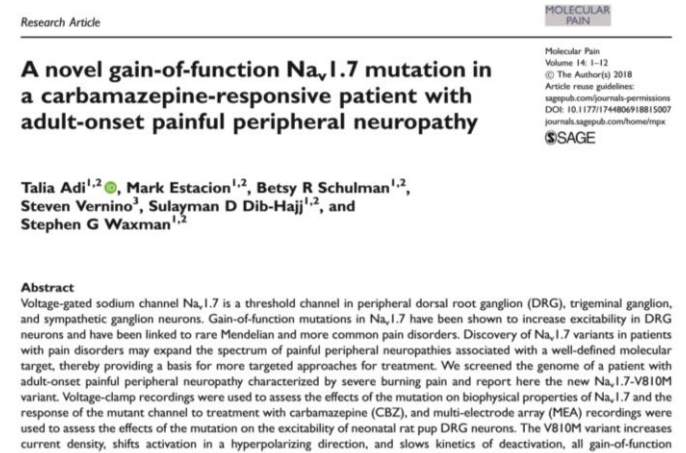
Abstract

Trigeminal neuralgia is a representative neuropathic facial pain condition, characterised by unilateral paroxysmal pain in



Research Article

MOLECULAR PAIN

A novel gain-of-function $Na_v1.7$ mutation in a carbamazepine-responsive patient with adult-onset painful peripheral neuropathy

Molecular Pain
Volume 14: 1–12
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DOI: 10.1177/1744806918815007
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Talia Adi[1,2], Mark Estacion[1,2], Betsy R Schulman[1,2], Steven Vernino[3], Sulayman D Dib-Hajj[1,2], and Stephen G Waxman[1,2]

Abstract

Voltage-gated sodium channel $Na_v1.7$ is a threshold channel in peripheral dorsal root ganglion (DRG), trigeminal ganglion, and sympathetic ganglion neurons. Gain-of-function mutations in $Na_v1.7$ have been shown to increase excitability in DRG neurons and have been linked to rare Mendelian and more common pain disorders. Discovery of $Na_v1.7$ variants in patients with pain disorders may expand the spectrum of painful peripheral neuropathies associated with a well-defined molecular target, thereby providing a basis for more targeted approaches for treatment. We screened the genome of a patient with adult-onset painful peripheral neuropathy characterized by severe burning pain and report here the new $Na_v1.7$-V810M variant. Voltage-clamp recordings were used to assess the effects of the mutation on biophysical properties of $Na_v1.7$ and the response of the mutant channel to treatment with carbamazepine (CBZ), and multi-electrode array (MEA) recordings were used to assess the effects of the mutation on the excitability of neonatal rat pup DRG neurons. The V810M variant increases current density, shifts activation in a hyperpolarizing direction, and slows kinetics of deactivation, all gain-of-function

Familial TN

- 12 out of 88 pts had a family history of TN
- In patients with familial trigeminal neuralgia, pain was more often located in the right, second division. All patients reported triggers. Four patients experienced concomitant continuous pain
- Whole genome sequencing
- We concentrated on the genetic variants within a 173-gene panel, comprising channel genes encoding sodium, potassium, calcium, chloride, transient receptor potential channels, and gap junction channels. Gene expression profiles were based on published RNA sequencing datasets of rodent/human trigeminal ganglia tissues, with a focus on genes related to neuronal excitability
- 41 rare variants in ion channels, consisting of variants in sodium channels (6), potassium channels (10), chloride channels (5), calcium channels (7), transient receptor potential channels (12), and gap junction channels (1). In one patient, a previously profiled gain-of-function mutation **in SCN10A (Nav1.8p.**Ala1304Thr), previously reported in painful neuropathy, was found; this variant was not present in unaffected siblings.

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Cephalalgia
International Headache Society

Original Article

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Familial trigeminal neuralgia – a systematic clinical study with a genomic screen of the neuronal electrogenisome

Giulia Di Stefano*[,1], Jun-Hui Yuan[2,3,4,*], Giorgio Cruccu[1], Stephen G Waxman[2,3,4], Sulayman D Dib-Hajj[2,3,4] and Andrea Truini[1]

Abstract

Objective: This cross-sectional study examined, for the first time, a large cohort of patients with trigeminal neuralgia, to ascertain the occurrence of familial cases, providing a systematic description of clinical features of familial disease. Since there is evidence linking hyperexcitability of trigeminal ganglion neurons to trigeminal neuralgia, we also carried out an exploratory genetic analysis of the neuronal electrogenisome in these patients.

Methods: We recorded familial occurrence by systematically interviewing all patients with a definite diagnosis of classical or idiopathic trigeminal neuralgia. We found 12 occurrences of trigeminal neuralgia with positive family history out of 88 enrolled patients. Whole-exome sequencing was carried out in 11 patients. We concentrated on the genetic variants within a 173-gene panel, comprising channel genes encoding sodium, potassium, calcium, chloride, transient receptor potential channels, and gap junction channels. Gene expression profiles were based on published RNA sequencing datasets of rodent/human trigeminal ganglia tissues, with a focus on genes related to neuronal excitability.

Results: In patients with familial trigeminal neuralgia, pain was more often located in the right, second division. All patients reported triggers. Four patients experienced concomitant continuous pain. Whole-exome sequencing analysis within the trigeminal ganglion electrogenisome identified 41 rare variants in ion channels, consisting of variants in sodium channels (6), potassium channels (10), chloride channels (5), calcium channels (7), transient receptor potential channels (12), and gap junction channels (1). In one patient, a previously profiled gain-of-function mutation in *SCN10A*

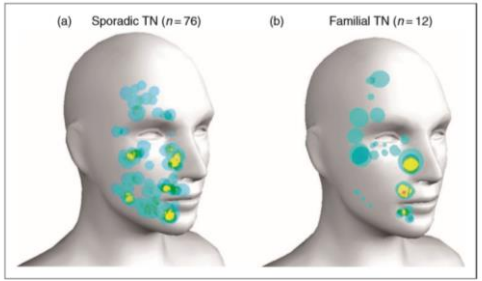
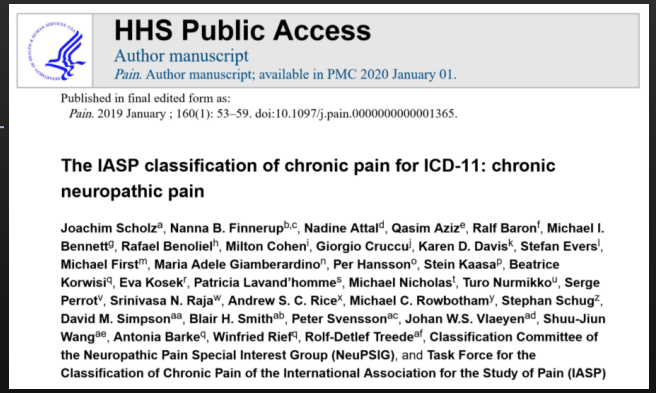


Figure 1. Trigger zones overlap profiling in patients with sporadic (a) and familial (b) TN. The number of superimpositions ranged from 2 (dark cyan) to 15 (dark orange), in sporadic forms, and between 2 (dark cyan) and 7 (dark orange) in familial forms.

Trigeminal neuralgia

- Trigeminal neuralgia is a manifestation of orofacial neuropathic pain restricted to one or more divisions of the trigeminal nerve.
- The pain is recurrent, abrupt in onset and termination, triggered by innocuous stimuli and typically compared to an electric shock or described as shooting or stabbing.
- Some patients experience continuous pain between these painful paroxysms (50%).
- The diagnosis comprises
  - Idiopathic trigeminal neuralgia,
  - Classical neuralgia produced by vascular compression of the trigeminal nerve
  - Secondary neuralgias caused by a tumor or cyst at the cerebellopontine angle, or multiple sclerosis.6 As for other conditions of chronic neuropathic pain, the detailed content model will include a discussion of the etiology.



Published in final edited form as:
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The IASP classification of chronic pain for ICD-11: chronic neuropathic pain

Joachim Scholz[a], Nanna B. Finnerup[b,c], Nadine Attal[d], Qasim Aziz[e], Ralf Baron[f], Michael I. Bennett[g], Rafael Benoliel[h], Milton Cohen[i], Giorgio Cruccu[j], Karen D. Davis[k], Stefan Evers[l], Michael First[m], Maria Adele Giamberardino[n], Per Hansson[o], Stein Kaasa[p], Beatrice Korwisi[q], Eva Kosek[r], Patricia Lavand'homme[s], Michael Nicholas[t], Turo Nurmikko[u], Serge Perrot[v], Srinivasa N. Raja[w], Andrew S. C. Rice[x], Michael C. Rowbotham[y], Stephan Schug[z], David M. Simpson[aa], Blair H. Smith[ab], Peter Svensson[ac], Johan W.S. Vlaeyen[ad], Shuu-Jiun Wang[ae], Antonia Barke[q], Winfried Rief[q], Rolf-Detlef Treede[af], Classification Committee of the Neuropathic Pain Special Interest Group (NeuPSIG), and Task Force for the Classification of Chronic Pain of the International Association for the Study of Pain (IASP)

All three types of TN ay present with continuous pain
The mechanisms underlying continuous as opposed to paroxysmal pain are not fully understood.

Continuous pain may develop as a result of progressive root damage after prolonged compression or reflect central mechanisms.

Several authors have suggested that continuous pain is associated with poorer outcome after surgical intervention

TN Diagnostic algorithm

CONTINUUM **Review Article**

Address correspondence to Giorgio Cruccu, Department of Neurology and Psychiatry, Viale Università 30, Rome, Italy 00185, *giorgio.cruccu@uniroma1.it.*

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Trigeminal Neuralgia

Giorgio Cruccu, MD

ABSTRACT

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Recent Findings: Currently, a worldwide controversy exists regarding the classification, diagnostic process, and surgical treatment of trigeminal neuralgia. This controversy has been caused on one side by the recognition that some 50% of patients with trigeminal neuralgia, apart from characteristic paroxysmal attacks, also have continuous pain in the same territory, which results in greater diagnostic difficulties and is associated with a lower response to medical and surgical treatments. In contrast, recent developments in MRI methods allow differentiation between a mere neurovascular contact and an effective compression of the trigeminal root by an anomalous vessel, which implies more difficulties in the choice of surgical treatment, with the indication for microvascular decompression becoming more restricted.

Summary: This article proposes that the diagnosis of trigeminal neuralgia, with or without concomitant continuous pain, must rely on clinical grounds only. Diagnostic tests are necessary to distinguish three etiologic categories: idiopathic trigeminal neuralgia (nothing is found), classic trigeminal neuralgia (an anomalous vessel produces morphologic changes of the trigeminal root near its entry into the pons), and secondary trigeminal neuralgia (due to major neurologic disease, such as multiple sclerosis or tumors at the cerebellopontine angle). Carbamazepine and oxcarbazepine (ie, voltage-gated, frequency-dependent sodium channel blockers) are still the first-choice medical treatment, although many patients experience significant side effects, and those with concomitant continuous pain respond less well to treatment. The development of sodium channel blockers that are selective for the sodium channel 1.7 ($Na_v1.7$) receptor will hopefully help. Although all the surgical interventions (percutaneous ganglion lesions, gamma knife radiosurgery, and microvascular decompression) are very efficacious, precise MRI criteria for differentiating a real neurovascular compression from an irrelevant contact will be of benefit in better selecting patients for microvascular decompression.

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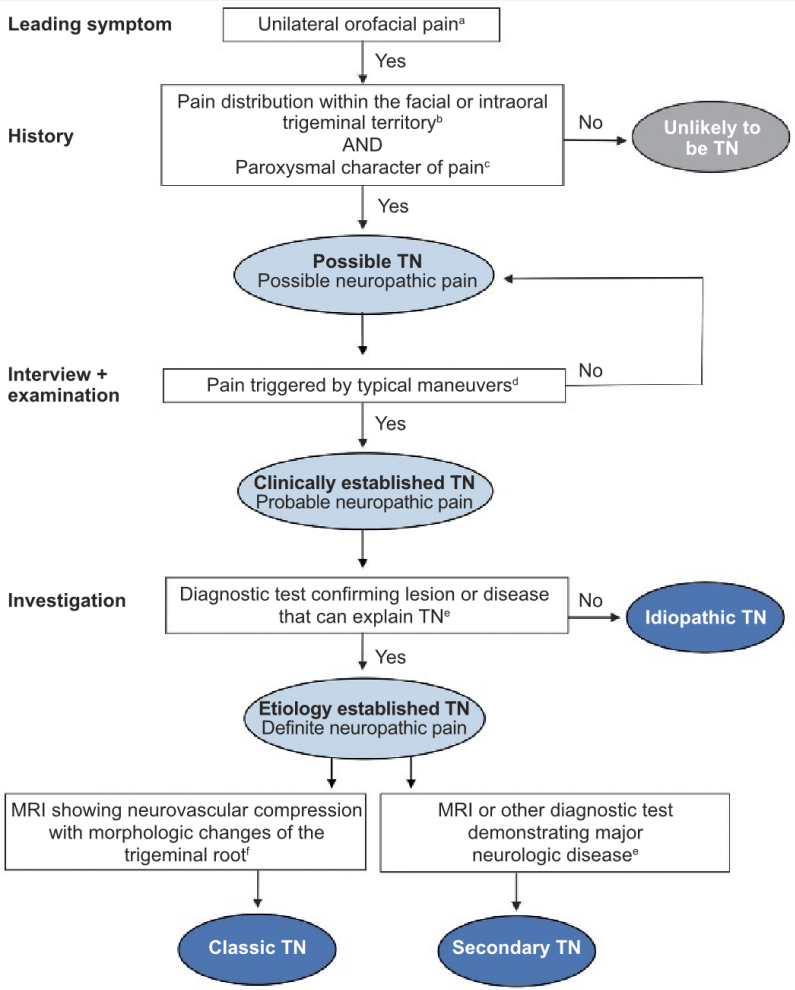

Diagnosis of TN

Review

Cephalalgia
An International Journal of Headache
International Headache Society

Cephalalgia
2017, Vol. 37(7) 648–657

DOI: 10.1177/0333102416687280
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Trigeminal neuralgia – diagnosis and treatment

Stine Maarbjerg[1], Giulia Di Stefano[2], Lars Bendtsen[1]

Work up

History: onset (trauma or herpes?), quality, intensity, duration and localization of pain, autonomic ipsilateral symptoms, other neurological or medical complaints

Exam: general clinical and neurological examination focusing on trigeminal sensory function and signs of multiple sclerosis or cerebellopontine tumor

Paraclinical work up: ECG, blood tests (electrolytes, liver and kidney function) and MRI of the brain and brainstem are mandatory

Diagnosis

Differential diagnosis: is there another diagnosis that is more likely? Has the patient consulted a dentist?

Diagnostic criteria: are the diagnostic criteria fulfilled?* Is it primary or secondary trigeminal neuralgia?

Information: provide thorough patient information on medical and surgical treatment options and their expected rate of success, side effects and complications

Second line surgical treatment

oxysmal pain in
ave continuous

try zone is the
topic impulses
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Differential Diagnosis TN PTPN

Trigeminal neuralgia **Type 1 or 3 classic (+NVC or idiopathic)**	Rare Spontaneous onset Older patients	***Trigeminal region*** *Unilateral can be bilateral* Intraoral or extraoral	Elicited pain Allodynia Each episode of pain lasts for seconds to minutes; refractory periods, and long periods of no pain *+/- spontaneous pain*	No neuropathic area (May be neuropathy in Type 2 TN)	Light touch provoked (e.g., eating, washing, talking) May have background intermittent or continuous pain	Discrete trigger zones Refractory period Remission periods
Secondary TN	Identifiable cause	same	*same*	*Identifiable neuropathic area*	same	Same as below
PTNP **History of surgery or trauma**	Onset related to trauma 5% after endo 0,2-2% after M3M surgery Younger patients	***Trigeminal region***, unilateral Dermatome where treatment took place Intraoral or extraoral	*Elicited pain Allodynia to mechanical and thermal stimuli* *+/- hyperalgesia* *+/- hyperpathia* *+/- spontaneous pain* *No refractory period*	*Identifiable neuropathic area*	Areas of allodynia, light touch, function, cold and warm changes May have continuous and elicited pain	Sensory changes subjective qualitative and quantitative sensory tests Rare autonomic signs No refractory period No remission

Adapted from Essentials of physical medicine and rehabilitation: musculoskeletal disorders, pain, and rehabilitation/ [edited by] Walter R. Frontera, Julie K. Silver, Thomas D. Rizzo Jr.—2nd ed. Chapter 90.

Exclude Trigeminal autonomic cephalalgias and Migraine?

- Exclude migrainous symptoms
  - Nausea
  - Vertigo
  - Cold and touch sensitivity
  - Photo phobia
  - Phono phobia
  - Aura

Behaviour…retire to dark room and lie down

TREAT Migraine

- Exclude autonomic symptoms
  - Red eye conjunctival irritation
  - Tearing
  - Nasal congestion
  - Facial flushing
  - Drooping eyelid (Ptosis)
  - Enlarged pupil (Meiosis)

Behaviour…aggressive irritated restless

TREAT TAC

Trigger zones

Because triggered pain paroxysms are a unique somatosensory phenomenon, it also increases the diagnostic certainty of neuropathic pain so that it should also be considered probable neuropathic pain.

CONTINUUM **Review Article**

Address correspondence to Giorgio Cruccu, Department of Neurology and Psychiatry, Viale Università 30, Rome, Italy 00185, *giorgio.cruccu@uniroma1.it.*

Trigeminal Neuralgia

Giorgio Cruccu, MD

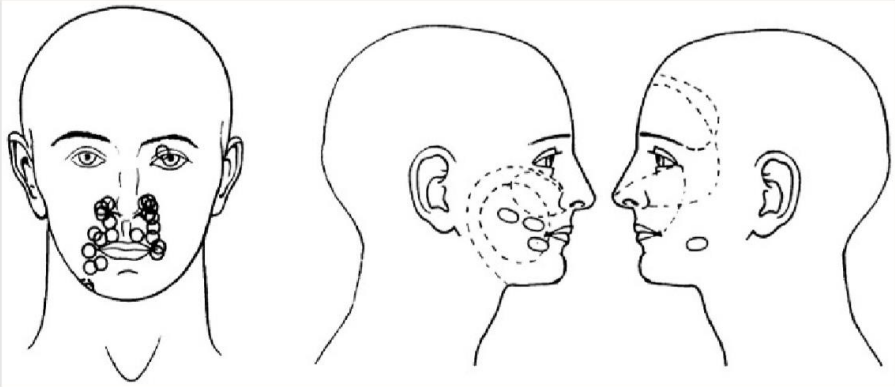


FIGURE 3-3 Mechanism of pain in trigeminal neuralgia. Distribution of 31 trigger zones in 30 patients. *Circles* denote the typically small areas where light touch or other innocuous mechanical stimuli trigger the pain paroxysms. In some patients, the trigger zones are larger (*dashed areas*) or intraoral (*ovals*).

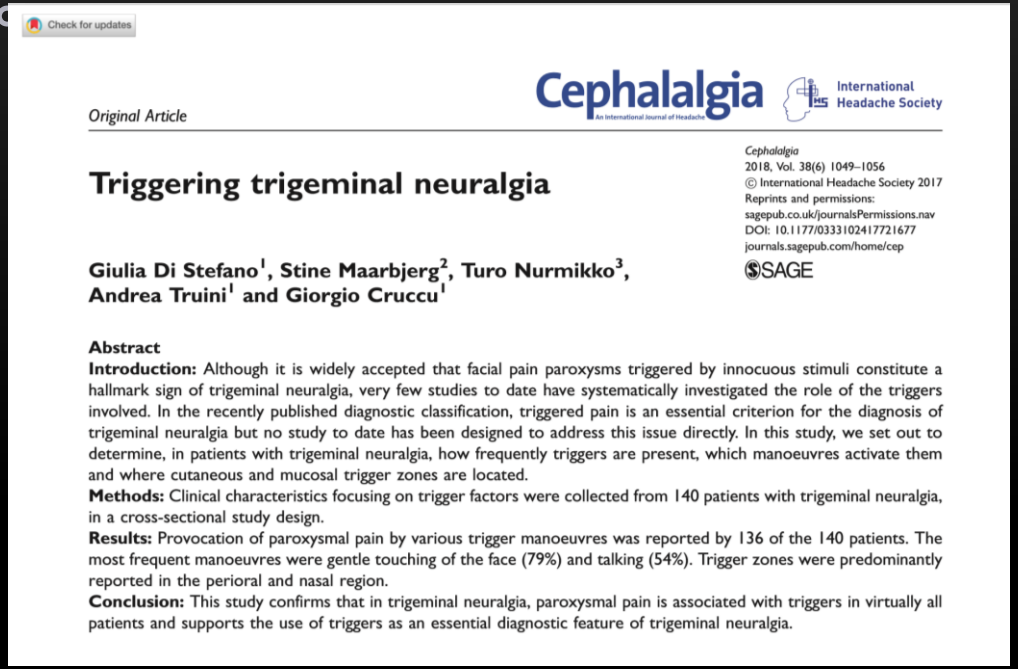
Treede RD, Jensen TS, Campbell JN, et al. Neuropathic pain: redefinition and a grading system for clinical and research purposes. Neurology 2008;70(18):1630-1635. doi:10.1212/01.wnl.0000282763.29778.59.

Most common triggers

- Gentle touching face 79%

And

- Talking 54%



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Original Article

Cephalalgia
An International Journal of Headache
International Headache Society

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DOI: 10.1177/0333102417721677
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Triggering trigeminal neuralgia

Giulia Di Stefano[1], Stine Maarbjerg[2], Turo Nurmikko[3], Andrea Truini[1] and Giorgio Cruccu[1]

Abstract

Introduction: Although it is widely accepted that facial pain paroxysms triggered by innocuous stimuli constitute a hallmark sign of trigeminal neuralgia, very few studies to date have systematically investigated the role of the triggers involved. In the recently published diagnostic classification, triggered pain is an essential criterion for the diagnosis of trigeminal neuralgia but no study to date has been designed to address this issue directly. In this study, we set out to determine, in patients with trigeminal neuralgia, how frequently triggers are present, which manoeuvres activate them and where cutaneous and mucosal trigger zones are located.

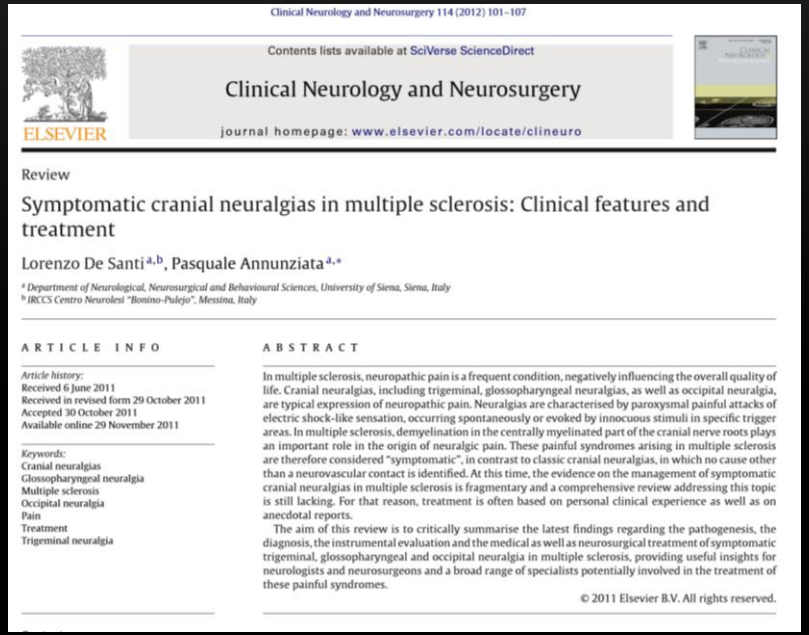
Methods: Clinical characteristics focusing on trigger factors were collected from 140 patients with trigeminal neuralgia, in a cross-sectional study design.

Results: Provocation of paroxysmal pain by various trigger manoeuvres was reported by 136 of the 140 patients. The most frequent manoeuvres were gentle touching of the face (79%) and talking (54%). Trigger zones were predominantly reported in the perioral and nasal region.

Conclusion: This study confirms that in trigeminal neuralgia, paroxysmal pain is associated with triggers in virtually all patients and supports the use of triggers as an essential diagnostic feature of trigeminal neuralgia.

TN Investigations

- MRI – patients under 40 years to exclude
  - multiple sclerosis
  - assess if micro vascular compression
  - Space occupying lesions (Devor 2010)
- CT - tumours of posterior fossa
- Haematological tests
- Biochemical tests
- ECG prior to prescribing Tegretol
- Neurological
  - sensory testing and hearing



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journal homepage: www.elsevier.com/locate/clineuro

Review

Symptomatic cranial neuralgias in multiple sclerosis: Clinical features and treatment

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Treatment
Trigeminal neuralgia

ABSTRACT

In multiple sclerosis, neuropathic pain is a frequent condition, negatively influencing the overall quality of life. Cranial neuralgias, including trigeminal, glossopharyngeal neuralgias, as well as occipital neuralgia, are typical expression of neuropathic pain. Neuralgias are characterised by paroxysmal painful attacks of electric shock-like sensation, occurring spontaneously or evoked by innocuous stimuli in specific trigger areas. In multiple sclerosis, demyelination in the centrally myelinated part of the cranial nerve roots plays an important role in the origin of neuralgic pain. These painful syndromes arising in multiple sclerosis are therefore considered "symptomatic", in contrast to classic cranial neuralgias, in which no cause other than a neurovascular contact is identified. At this time, the evidence on the management of symptomatic cranial neuralgias in multiple sclerosis is fragmentary and a comprehensive review addressing this topic is still lacking. For that reason, treatment is often based on personal clinical experience as well as on anecdotal reports.

The aim of this review is to critically summarise the latest findings regarding the pathogenesis, the diagnosis, the instrumental evaluation and the medical as well as neurosurgical treatment of symptomatic trigeminal, glossopharyngeal and occipital neuralgia in multiple sclerosis, providing useful insights for neurologists and neurosurgeons and a broad range of specialists potentially involved in the treatment of these painful syndromes.

Cruccu and colleagues reviewed studies of MS associated with trigeminal neuralgia and identified a total of 24 cases of bilateral trigeminal neuralgia out of 252 MS patients with trigeminal neuralgia (ie, a frequency of slightly less than 10%).

For patients with TN without non-trigeminal neurological symptoms, routine imaging may be considered to identify STN (Level C).

Younger age of onset, involvement of the first division of the trigeminal nerve, unresponsiveness to treatment, and abnormal trigeminal evoked potentials should be disregarded as useful for disclosing STN (Level B).

Determining the presence of trigeminal sensory deficits or bilateral involvement of the trigeminal nerves should be considered useful to distinguish STN from CTN. However, the absence of these features should be disregarded as useful for distinguishing STN from CTN. (Level B).

Measuring

Trigeminal reflexes in a qualified electrophysiogical laboratory should be considered useful for distinguishing STN form CTN (Level B).

There is insufficient evidence to support or refute the usefulness of MRI to identify CTN patients who are more likely to respond to MVD.

European Journal of Neurology 2008, **15**: 1013–1028 doi:10.1111/j.1468-1331.2008.02185.x

EFNS GUIDELINES/CME ARTICLE

AAN-EFNS guidelines on trigeminal neuralgia management

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Key words:
trigeminal neuralgia, diagnosis, neurovascular contact, MRI, trigeminal reflex, treatment, anti-epileptic drugs, Gasserian ganglion surgery, micro-vascular decompression, gamma knife

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Several issues regarding diagnosis, pharmacological treatment, and surgical treatment of trigeminal neuralgia (TN) are still unsettled. The American Academy of Neurology and the European Federation of Neurological Societies launched a joint Task Force to prepare general guidelines for the management of this condition. After systematic review of the literature the Task Force came to a series of evidence-based recommendations. In patients with TN MRI may be considered to identify patients with structural causes. The presence of trigeminal sensory deficits, bilateral involvement, and abnormal trigeminal reflexes should be considered useful to disclose symptomatic TN, whereas younger age of onset, involvement of the first division, unresponsiveness to treatment and abnormal trigeminal evoked potentials are not useful in distinguishing symptomatic from classic TN. Carbamazepine (stronger evidence) or oxcarbazepine (better tolerability) should be offered as first-line treatment for pain control. For patients with TN refractory to medical therapy early surgical therapy may be considered. Gasserian ganglion percutaneous techniques, gamma knife and microvascular decompression may be considered. Microvascular decompression may be considered over other surgical techniques to provide the longest duration of pain freedom. The role of surgery versus pharmacotherapy in the management of TN in patients with multiple sclerosis remains uncertain.

Introduction

The American Academy of Neurology (AAN) and the European Federation of Neurological Societies (EFNS) decided to develop scientifically sound, clinically relevant guidelines to aid specialists and non-specialists in the management of trigeminal neuralgia (TN), by addressing its diagnosis, pharmacological treatment, and surgical treatment.

The International Association for the Study of Pain (IASP) defines TN as sudden, usually unilateral, severe, brief, stabbing, recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve.[54] The annual incidence of TN is 4 to 5/100,000.[34] TN is the most common neuralgia. In the latest classification of the International Headache Society,[29] a distinction is made between *classical* and *symptomatic* TN: classical TN (CTN) includes all cases without an established etiology, i.e. idiopathic, as well as those with potential vascular compression of the fifth cranial nerve, whereas the diagnosis of symptomatic TN (STN) is made in cases secondary to tumour, MS, structural abnormalities of the skull base, and the like. It should be noted that categorization of TN into *typical* and *atypical* forms is based on symptom constellation, and not etiology, and will not be discussed further in this review.

The first issue facing the clinician caring for a patient with TN is accurately distinguishing symptomatic from classical TN. The diagnostic portion of this parameter addresses the following questions:

1. How often does routine neuroimaging (CT, MRI) identify a cause (excluding vascular contact) of TN?
2. Which clinical or laboratory features accurately identify patients with STN?
3. For patients with classical TN does high resolution MRI accurately identify patients with neurovascular compression?

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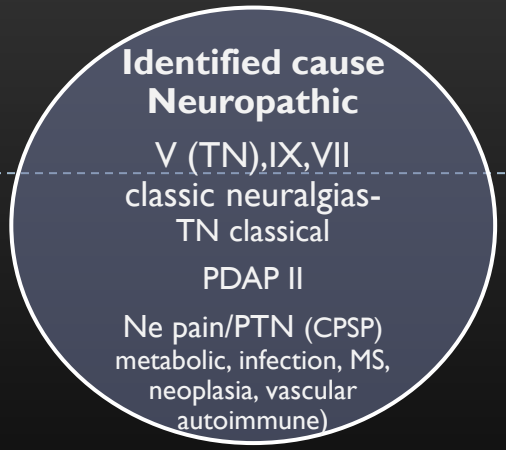
This is a Continuing Medical Education article and can be found with corresponding questions on the internet at http://www.efns.org/content.php?pid=132. Certificates for correctly answering the questions will be issued by the EFNS.

Secondary neuropathic pain



Nutritional deficiencies

Fe, Ferritin, Zinc, Magnesium,

Vit B complex, D, E

Malignancy

Compression by a space occupying lesion centrally or peripherally NEOPLASIA

Metabolic Acromegaly, Hormonal neuropathy (Hypothyroidism, Diabetes),

Infarction (sickle cell hypoxic neural damage, giant cell arteritis)

Demyelination (Multiple sclerosis)

Infection Post viral neuropathy, Bacterial, Leprosy

Toxic Heavy metal poisoning (lead, mercury) radiation, thermal, chemotherapy, drugs

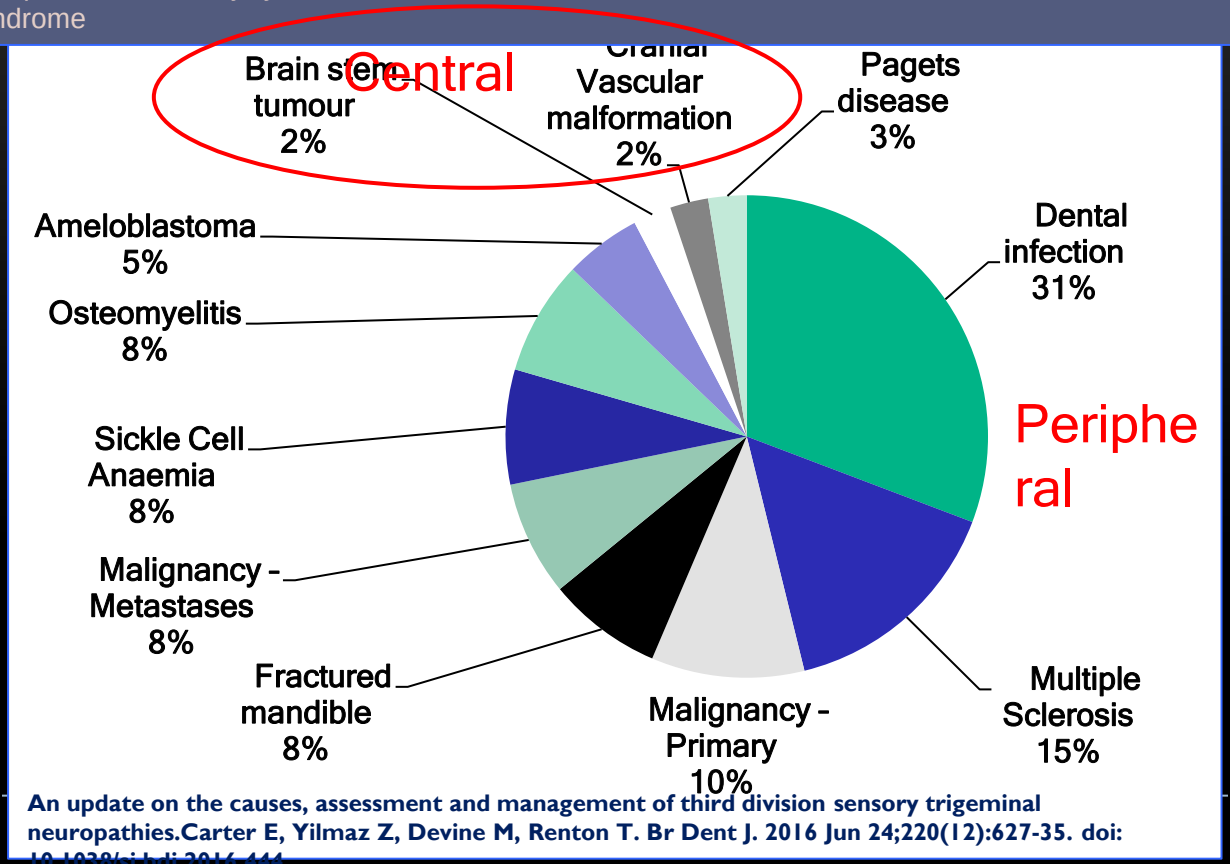
Auto immune problems: Lupus, Rheumatoid disease

Sarcoidosis and amyloidosis

Secondary Trigeminal neuropathic pain + neuropathy but NOT PTNP

Trigeminal neuropathy

Retrospective analysis of the case notes of 372 patients referred to the specialist nerve injury clinic between 2007 and 2014 was carried out to establish the cause of numb chin syndrome



An update on the causes, assessment and management of third division sensory trigeminal neuropathies.Carter E, Yilmaz Z, Devine M, Renton T. Br Dent J. 2016 Jun 24;220(12):627-35. doi: 10.1038/sj.bdj.2016.444

Classic or symptomatic TN?

Younger age (one Class I, three Class II studies) and abnormal trigeminal nerve evoked potentials (two class II and two Class III studies) are probably associated with an increased risk of STN. However, there is too much overlap in patients with CTN and STN for these predictors to be considered clinically useful

The presence of trigeminal sensory deficits or bilateral involvement of the trigeminal nerves probably increases the risk of STN. However, the absence of these features does not "rule out" STN. (One Class I, two Class II). Because of a high specificity (94%) and sensitivity (87%) abnormal trigeminal reflexes are probably useful in distinguishing STN from CTN (one Class I and two Class II studies).

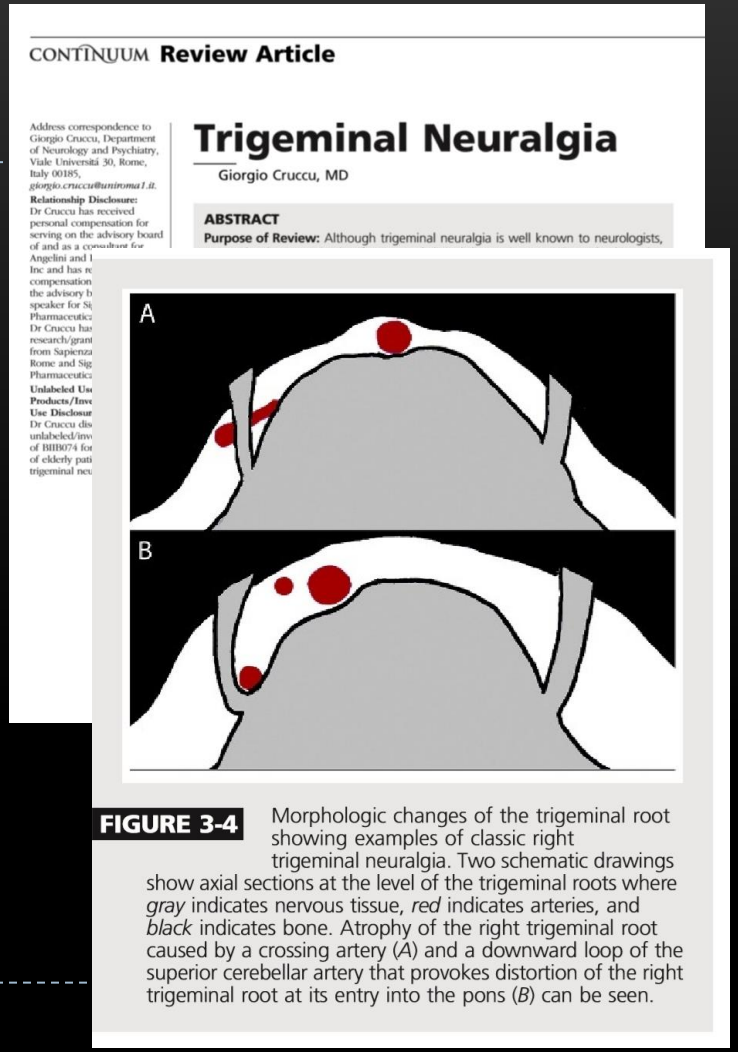
Table 1 Diagnosis: frequency at which neuroimaging identified patients with symptomatic TN

First Author Year	Class	Sampling	Population	Data collection	TN criteria	Modality	Total TN Patients	STN Patients (CI)
Cruccu 2006 [16]	III	Consecutive pts with TN	Referral centre	prospective	IHS	MRI	120	16 MS 6 tumours
Sato 2004 [69]	III	Consecutive patients with TN	University	retrospective	IASP	MRI or CT	61	7 tumours
Goh 2001 [27]	III	Consecutive patients with TN and MRI	National dental centre	retrospective	Not stated	MRI	40[a]	4 masses
Majoie 1998 [50]	III	Consecutive patients with TN and MRI	University	retrospective	Not stated	MRI	22	3 tumours 1 aneurysm
Nomura 1994 [59]	IV	Consecutive patients with TN	University	retrospective	Not stated (non-TN neurological signs)	MRI or CT	164	22 masses
Pooled Class III							37/243 Yield	15% (11 to 20)

[a]Patients with non-trigeminal symptoms or signs eliminated. CI: 95% confidence interval.

Neurovascular contact (NVC)

- Recent studies have emphasized the importance of differentiating the type of contact and its physical impact on the nerve, to the point that Cruccu and colleagues became convinced that the reintroduction of the term idiopathic trigeminal neuralgia was needed.
- The degree of morphologic trigeminal root changes is therapeutically relevant. The long-term outcome after surgical correction of simple neurovascular contacts is poorer compared to the decompression of dislocated, distorted, or flattened nerve roots
- Advanced MRI techniques now allow radiologic verification of morphologic changes of the compressed trigeminal root. These changes of symptomatic nerve roots are highly suggestive of physical alteration and have a high predictive value for pain relief after decompression.
- In a recent meta-analysis of nine high-quality blinded and controlled studies, mere neurovascular contact was found in 471 out of 531 symptomatic nerves and in 244 out of 681 asymptomatic nerves, indicating high sensitivity but low specificity.



CONTINUUM **Review Article**

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Relationship Disclosure: Dr Cruccu has received personal compensation for serving on the advisory board of and as a consultant for Angelini and I... Inc and has re... compensation... the advisory b... speaker for Si... Pharmaceutic... Dr Cruccu has... research/grant... from Sapienza... Rome and Sig... Pharmaceutic...

Unlabeled Use... Products/Inve... Use Disclosur... Dr Cruccu dis... unlabeled/inv... of BIIB074 for... of elderly pati... trigeminal neu...

Trigeminal Neuralgia

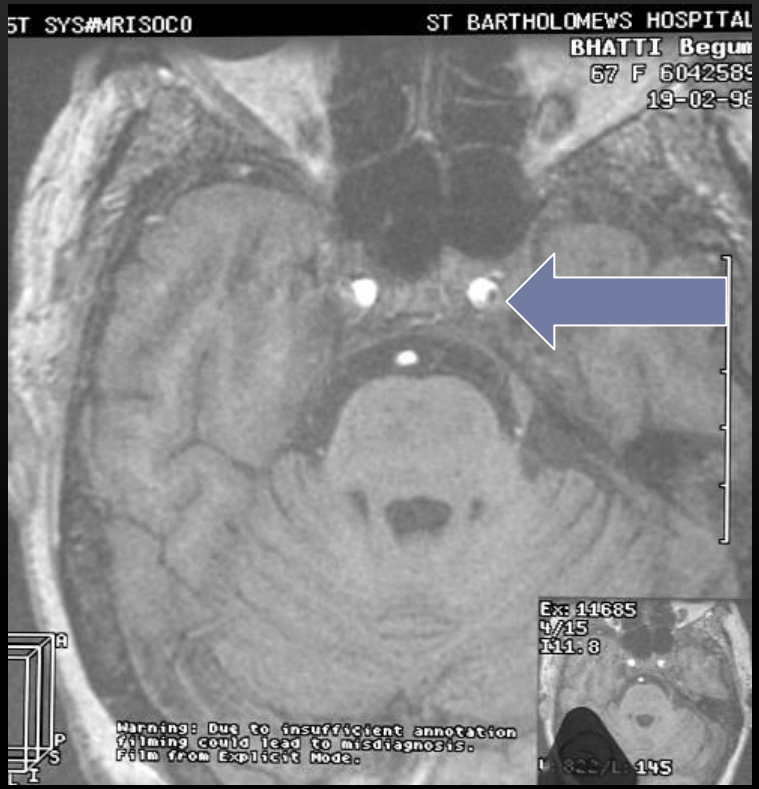
Giorgio Cruccu, MD

ABSTRACT

Purpose of Review: Although trigeminal neuralgia is well known to neurologists,

FIGURE 3-4 Morphologic changes of the trigeminal root showing examples of classic right trigeminal neuralgia. Two schematic drawings show axial sections at the level of the trigeminal roots where *gray* indicates nervous tissue, *red* indicates arteries, and *black* indicates bone. Atrophy of the right trigeminal root caused by a crossing artery (*A*) and a downward loop of the superior cerebellar artery that provokes distortion of the right trigeminal root at its entry into the pons (*B*) can be seen.

+/- Neurovascular contact NVC?



MRI scan to;
Exclude MS
Space occupying lesions
Evaluate Neurovascular conflict

Typical imaging paradigms include sequences for three-dimensional T2-weighted MRI (eg, constructive interference in steady state [CISS]) for a detailed examination of the cisternal and cavernous segments of the nerve and three dimensional time-of-flight magnetic resonance angiography (MRA) for visualization of arteries

15-88% MRI+ superior cerebellar artery vascular compromise+ve results
25-49% people with NO TN have MRI +ve signs!!!!!
(Kakizawa et al 2008,Adamczyk et al 2007)

~~Diagnosis and differential diagnosis of trigeminal neuralgia~~
Zakrzewska JM. Clin.J.Pain 2002;18:14-21

Type of MRI sequence will affect sensitivity and specificity of NVC detection

We suggest patients considered suitable for MVD undergo high-resolution MRI.

Table 5 Diagnostic accuracy of MRI for identifying abnormal vascular contact in classic TN

Author year	Class	Method	Design	Spectrum	Masked	Ref. Standard	Symptomatic NVC/T	Asymptomatic NVC/T	P assoc	Sen (CI)	Spe (CI)
Korogi 1995 [40]	I	3D-TOF	CO P	broad	yes	Symptomatic side	12/16	4/16	<0.012	75%	75%
Masur 1995 [52]	I	3D-FLASH	CO P	broad	yes	Symptomatic side	12/18	10/18	NS	67%	44%
Majoie 1997 [51]	III	3D-FISP MP-RAGE	CC P	narrow	yes	clinical	10/13	8/113	<0.0001	77%	93%
Yamakami 2000 [79]	I	CISS-3D-TOF	CO P	broad	yes	Symptomatic side	14/14	7/30	<0.0001	100%	77%
Benes 2005 [6]	I	3D-Fiesta 3D-FSPGR	CO P	broad	yes	Symptomatic side	11/21	10/21	NS	52%	52%
Anderson 2006 [1]	I	3D-TOF 3D-Gad	CO P	broad	yes	Symptomatic side	42/48	34/48	NS	88%	29%
Erbay 2006 [23]	III	CISS-MPR	CO R	broad	yes	Symptomatic side	30/40	10/40	<0.0001	75%	75%
Pooled	I,III						131/170	83/286	<0.0001	77% (70–83)	71% (65–76)

NVC/T: neurovascular contact/total. CO: cohort survey. CC: case control. P: Prospective data collection. R: Retrospective or not described data collection. CI: 95% confidence intervals. P assoc: probability of statistically significant association between the presence of the characteristic and the presence of TN. Sen: sensitivity. Spe: specificity. Sensitivities calculated for presence of neurovascular contact on the symptomatic side. Specificities calculated for absence of neurovascular contact on the asymptomatic side.

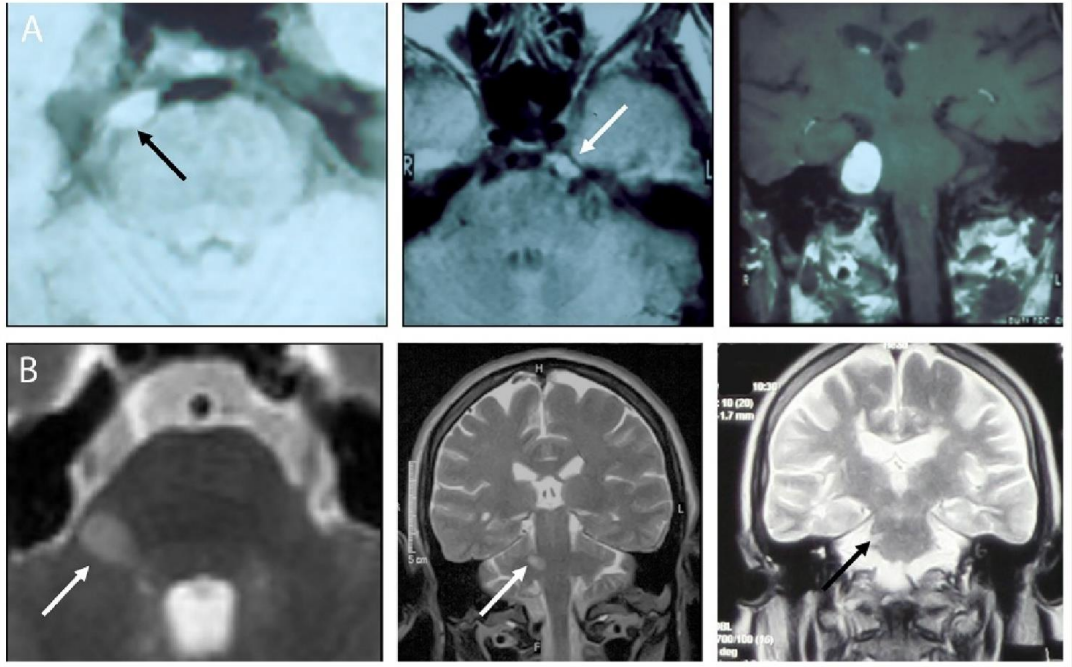


FIGURE 3-6 Common causes of symptomatic trigeminal neuralgia. *A*, Benign tumors along the extraaxial course of the trigeminal root (*arrows*). *B*, Demyelinating plaques along the intraaxial course of the trigeminal afferents (*arrows*).

Reprinted with permission from Cruccu G, et al, Handb Clin Neurol.[42] © 2010 Elsevier. *sciencedirect.com/science/article/pii/S0072975210970565*.

CONTINUUM **Review Article**

Trigeminal Neuralgia

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Unlabeled Use of Products/Investigational Use Disclosure: Dr Cruccu discusses the unlabeled/investigational use of BIIB074 for the treatment of elderly patients with trigeminal neuralgia.

ABSTRACT

Purpose of Review: Although trigeminal neuralgia is well known to neurologists, recent developments in classification and clinical diagnosis, new MRI methods, and a debate about surgical options necessitate an update on the topic.

Recent Findings: Currently, a worldwide controversy exists regarding the classification, diagnostic process, and surgical treatment of trigeminal neuralgia. This controversy has been caused on one side by the recognition that some 50% of patients with trigeminal neuralgia, apart from characteristic paroxysmal attacks, also have continuous pain in the same territory, which results in greater diagnostic difficulties and is associated with a lower response to medical and surgical treatments. In contrast, recent developments in MRI methods allow differentiation between a mere neurovascular contact and an effective compression of the trigeminal root by an anomalous vessel, which implies more difficulties in the choice of surgical treatment, with the indication for microvascular decompression becoming more restricted.

Summary: This article proposes that the diagnosis of trigeminal neuralgia, with or without concomitant continuous pain, must rely on clinical grounds only. Diagnostic tests are necessary to distinguish three etiologic categories: idiopathic trigeminal neuralgia (nothing is found), classic trigeminal neuralgia (an anomalous vessel produces morphologic changes of the trigeminal root near its entry into the pons), and secondary trigeminal neuralgia (due to major neurologic disease, such as multiple sclerosis or tumors at the cerebellopontine angle). Carbamazepine and oxcarbazepine (ie, voltage-gated, frequency-dependent sodium channel blockers) are still the first-choice medical treatment, although many patients experience significant side effects, and those with concomitant continuous pain respond less well to treatment. The development of sodium channel blockers that are selective for the sodium channel 1.7 ($Na_v1.7$) receptor will hopefully help. Although all the surgical interventions (percutaneous ganglion lesions, gamma knife radiosurgery, and microvascular decompression) are very efficacious, precise MRI criteria for differentiating a real neurovascular compression from an irrelevant contact will be of benefit in better selecting patients for microvascular decompression.

Continuum (Minneap Minn) 2017;23(2):396–420.

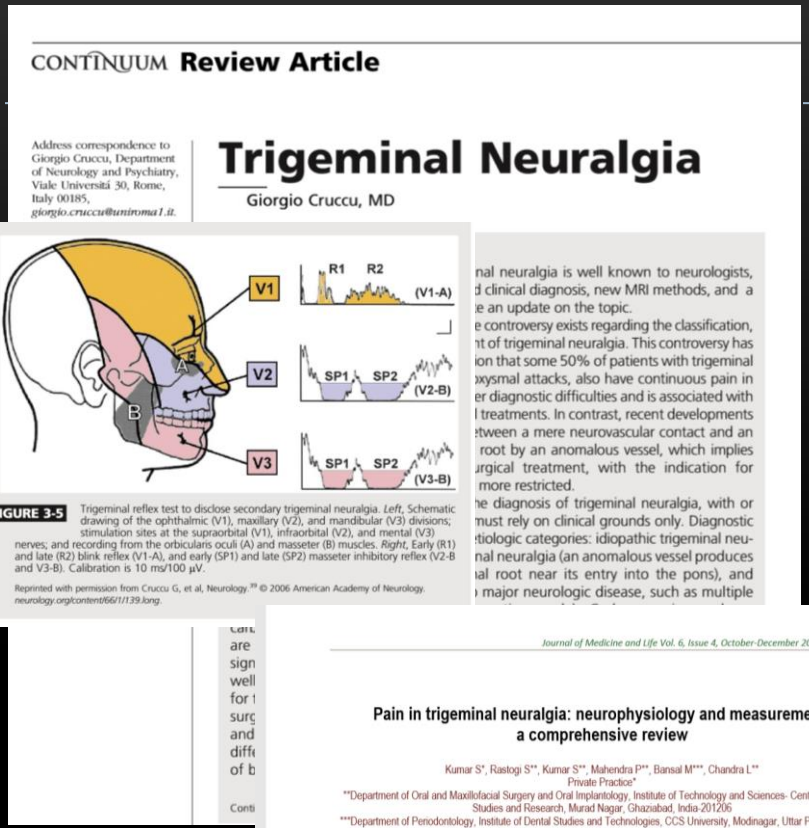
Patients with MS have a 20-fold increased risk of trigeminal neuralgia.

The prevalence of trigeminal neuralgia in MS is 2% to 5%

Sensory testing for TN

- Exclude neuropathic area
- Probable neuropathic pain (check patient not in remission)
  - Mechanical and or thermal allodynia
  - Hyperalgesia
  - Hyperpathia
  - Refractory period
- Trigeminal reflex testing is an established neurophysiologic assessment of nerve function (Figure 3-539). Trigeminal reflex testing requires only standard nerve conduction study equipment
- Evoked potentials after electric or thermal stimuli have been studied in trigeminal neuralgia. In contrast to trigeminal reflex testing, which is normal in idiopathic or classic trigeminal neuralgia, evoked potentials may be altered, but their mean specificity of 64% is low

TN has No Neuropathy



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Trigeminal Neuralgia

Giorgio Cruccu, MD

FIGURE 3-5 Trigeminal reflex test to disclose secondary trigeminal neuralgia. *Left*, Schematic drawing of the ophthalmic (V1), maxillary (V2), and mandibular (V3) divisions; stimulation sites at the supraorbital (V1), infraorbital (V2), and mental (V3) nerves; and recording from the orbicularis oculi (A) and masseter (B) muscles. *Right*, Early (R1) and late (R2) blink reflex (V1-A), and early (SP1) and late (SP2) masseter inhibitory reflex (V2-B and V3-B). Calibration is 10 ms/100 μV.

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Pain in trigeminal neuralgia: neurophysiology and measurement: a comprehensive review

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Abstract

Trigeminal neuralgia (TN) is defined as sudden, usually unilateral, severe, brief, stabbing recurrent episodes of pain within the distribution of one or more branches of the trigeminal nerve. It is the most frequent cranial neuralgia, the incidence being 1 per 1,000.00 persons per year. Pain attacks start abruptly and last several seconds but may persist 1 to 2 minutes. The attacks are initiated by non painful physical stimulation of specific areas (trigger points or zones) that are located ipsilateral to the pain. After

Outline

- –Introduction
  - •The trigeminal system
  - •Definitions neuropathic pain
  - •Trigeminal neuralgia
- –Diagnostic criteria TN
- –Aetiology TN
- –Assessment TN
- –Management;
  - **Trigeminal neuralgia (TN)**
    - –Medical
    - –Interventional
    - –Surgery
- –The future

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EFNS GUIDELINES/CME ARTICLE

AAN-EFNS guidelines on trigeminal neuralgia management

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Key words:
trigeminal neuralgia, diagnosis, neurovascular contact, MRI, trigeminal reflex, treatment, anti-epileptic drugs, Gasserian ganglion surgery, micro-vascular decompression, gamma knife

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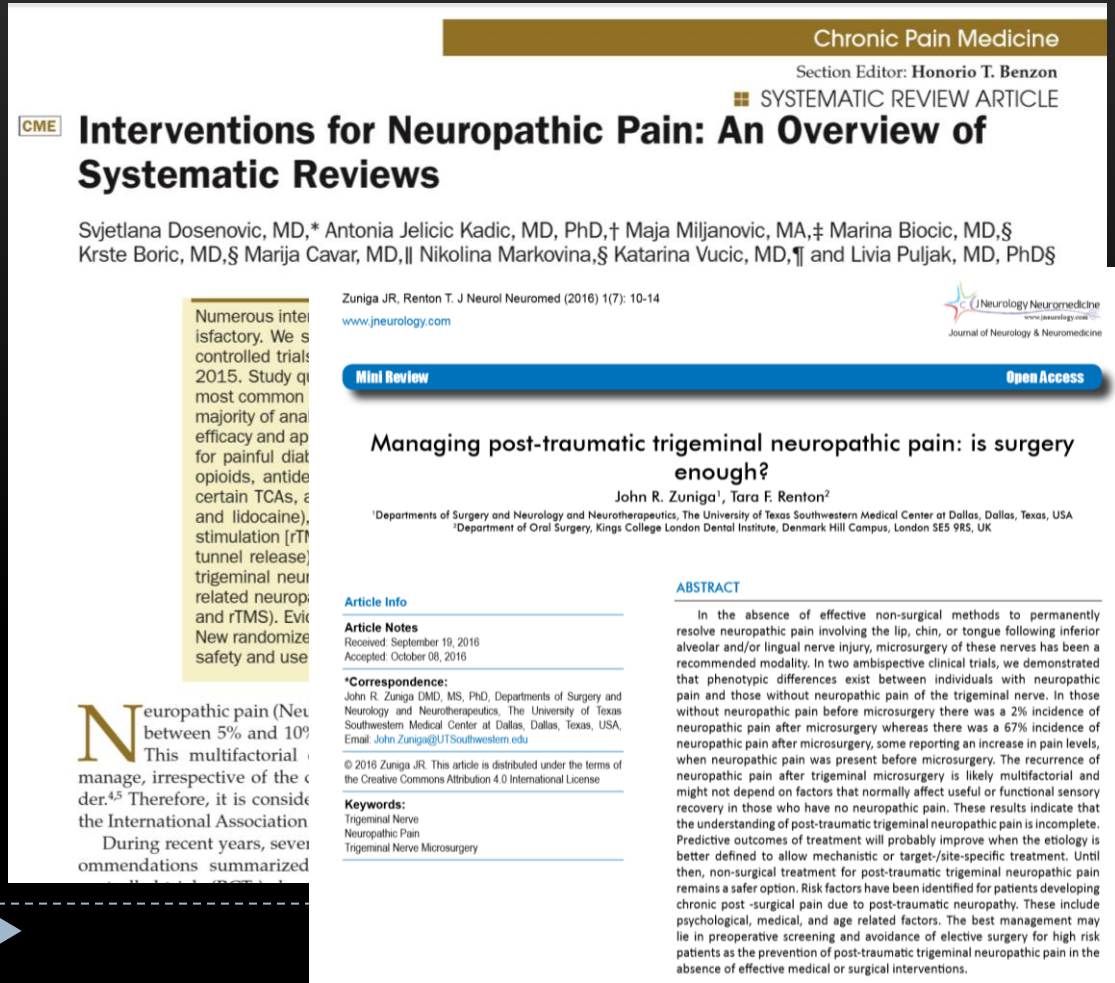
The International Association for the Study of Pain latest classification of the International Headache Society,[29] a distinction is made between *classical* and *symptomatic* TN: classical TN (CTN) includes all cases without an established etiology, i.e. idiopathic, as well as those with potential vascular compression of the fifth cranial nerve, whereas the diagnosis of symptomatic TN (STN) is made in cases secondary to tumour, MS, structural abnormalities of the skull base, and the like. It should be noted that categorization of TN into *typical* and *atypical* forms is based on symptom constel-



Chronic Pain Medicine

Section Editor: **Honorio T. Benzon**

SYSTEMATIC REVIEW ARTICLE

CME

Interventions for Neuropathic Pain: An Overview of Systematic Reviews

Svjetlana Dosenovic, MD,* Antonia Jelicic Kadic, MD, PhD,† Maja Miljanovic, MA,‡ Marina Biocic, MD,§ Krste Boric, MD,§ Marija Cavar, MD,‖ Nikolina Markovina,§ Katarina Vucic, MD,¶ and Livia Puljak, MD, PhD§

Numerous inte
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and lidocaine),
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tunnel release)
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and rTMS). Evi
New randomize
safety and use

Neuropathic pain (Neu
between 5% and 10%
This multifactorial
manage, irrespective of the c
der.[4,5] Therefore, it is conside
the International Association

During recent years, sever
ommendations summarized

Zuniga JR, Renton T. J Neurol Neuromed (2016) 1(7): 10-14

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Journal of Neurology & Neuromedicine

Mini Review Open Access

Managing post-traumatic trigeminal neuropathic pain: is surgery enough?

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Keywords:
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Neuropathic Pain
Trigeminal Nerve Microsurgery

ABSTRACT

In the absence of effective non-surgical methods to permanently resolve neuropathic pain involving the lip, chin, or tongue following inferior alveolar and/or lingual nerve injury, microsurgery of these nerves has been a recommended modality. In two ambispective clinical trials, we demonstrated that phenotypic differences exist between individuals with neuropathic pain and those without neuropathic pain of the trigeminal nerve. In those without neuropathic pain before microsurgery there was a 2% incidence of neuropathic pain after microsurgery whereas there was a 67% incidence of neuropathic pain after microsurgery, some reporting an increase in pain levels, when neuropathic pain was present before microsurgery. The recurrence of neuropathic pain after trigeminal microsurgery is likely multifactorial and might not depend on factors that normally affect useful or functional sensory recovery in those who have no neuropathic pain. These results indicate that the understanding of post-traumatic trigeminal neuropathic pain is incomplete. Predictive outcomes of treatment will probably improve when the etiology is better defined to allow mechanistic or target-/site-specific treatment. Until then, non-surgical treatment for post-traumatic trigeminal neuropathic pain remains a safer option. Risk factors have been identified for patients developing chronic post -surgical pain due to post-traumatic neuropathy. These include psychological, medical, and age related factors. The best management may lie in preoperative screening and avoidance of elective surgery for high risk patients as the prevention of post-traumatic trigeminal neuropathic pain in the absence of effective medical or surgical interventions.

Evidence about interventions for NeuP is frequently inconclusive or completely lacking.

New randomized controlled trials about interventions for NeuP are necessary; they should address safety and use clear diagnostic criteria. (Anesth Analg 2017;125:643–52)

KING'S College LONDON

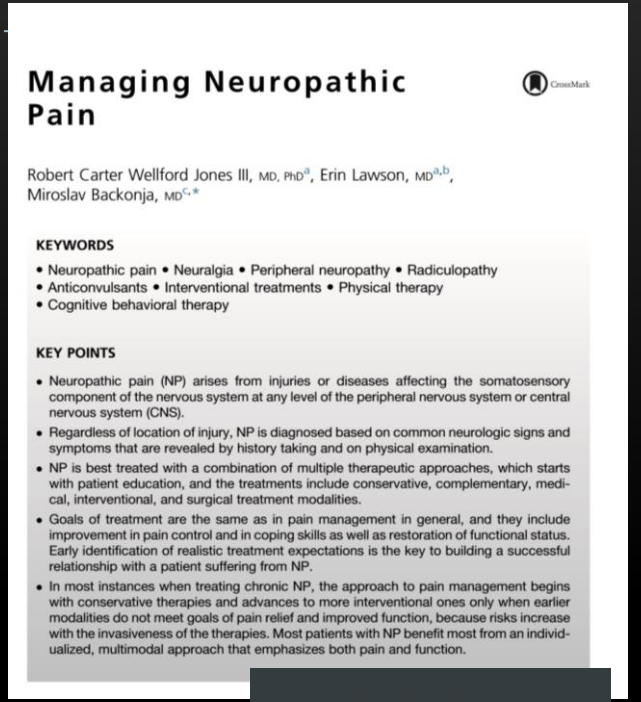
NEUROPATHIC PAIN (NP) ARISES FROM INJURIES OR DISEASES OF THE NERVOUS SYSTEM AT ANY LEVEL OF THE PERIPHERAL NERVOUS SYSTEM OR CENTRAL NERVOUS SYSTEM (CNS).

Regardless of location of injury, NP is diagnosed based on common neurologic signs and symptoms that are revealed by history taking and on physical examination.

NP is best treated with a combination of multiple therapeutic approaches

- **Start with patient education**
- **Treatments include**
  - **Conservative**
  - **Complementary**
  - **Medical**
  - **Interventional**
  - **and surgical treatment modalities.**

Goals of treatment include improvement in **pain control and in coping skills as well as restoration of functional status.** Early identification of realistic treatment expectations is the key to building a successful relationship with a



Managing Neuropathic Pain

Robert Carter Wellford Jones III, MD, PhD[a], Erin Lawson, MD[a,b], Miroslav Backonja, MD[c,*]

KEYWORDS

- Neuropathic pain • Neuralgia • Peripheral neuropathy • Radiculopathy
- Anticonvulsants • Interventional treatments • Physical therapy
- Cognitive behavioral therapy

KEY POINTS

- Neuropathic pain (NP) arises from injuries or diseases affecting the somatosensory component of the nervous system at any level of the peripheral nervous system or central nervous system (CNS).
- Regardless of location of injury, NP is diagnosed based on common neurologic signs and symptoms that are revealed by history taking and on physical examination.
- NP is best treated with a combination of multiple therapeutic approaches, which starts with patient education, and the treatments include conservative, complementary, medical, interventional, and surgical treatment modalities.
- Goals of treatment are the same as in pain management in general, and they include improvement in pain control and in coping skills as well as restoration of functional status. Early identification of realistic treatment expectations is the key to building a successful relationship with a patient suffering from NP.
- In most instances when treating chronic NP, the approach to pain management begins with conservative therapies and advances to more interventional ones only when earlier modalities do not meet goals of pain relief and improved function, because risks increase with the invasiveness of the therapies. Most patients with NP benefit most from an individualized, multimodal approach that emphasizes both pain and function.

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Management of TN

Cephalalgia
International Headache Society
Review
Cephalalgia
2017, Vol. 37(7) 648–657

DOI: 10.1177/0333102416687280
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SAGE

Trigeminal neuralgia – diagnosis and treatment

Stine Maarbjerg[1], Giulia Di Stefano[2], Lars Bendtsen[1] and Giorgio Cruccu[2]

Abstract

Introduction: Trigeminal neuralgia (TN) is characterized by touch-evoked unilateral brief shock-like paroxysmal pain in

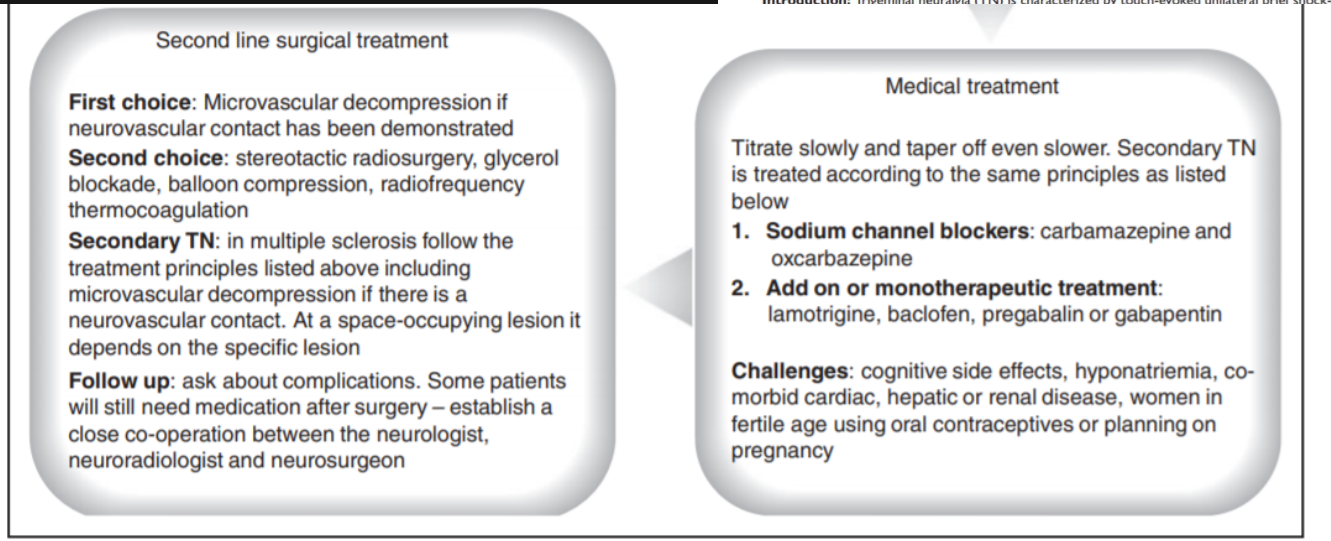

Figure 3. Work up and treatment algorithm in trigeminal neuralgia (TN) – presented in short. Diagnostic criteria of TN are outlined in Table 1.

Medical Management TN

- Carbamazepine is established as effective (level A) and oxcarbazepine is probably effective (level B) for controlling pain in CTN.
- Baclofen, lamotrigine, and pimozide may be considered to control pain in patients with CTN (level C).
- Topical ophthalmic anesthesia is probably ineffective in controlling pain in patients with CTN (Level B).
- There is insufficient evidence to support or refute the efficacy of other medications in CTN, of any medication in STN, and of any intravenous medication for the acute treatment of pain form TN.

European Journal of Neurology 2008, **15:** 1013–1028 doi:10.1111/j.1468-1331.2008.02185.x

EFNS GUIDELINES/CME ARTICLE

AAN-EFNS guidelines on trigeminal neuralgia management

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Key words:
trigeminal neuralgia, diagnosis, neurovascular contact, MRI, trigeminal reflex, treatment, anti-epileptic drugs, Gasserian ganglion surgery, micro-vascular decompression, gamma knife

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Several issues regarding diagnosis, pharmacological treatment, and surgical treatment of trigeminal neuralgia (TN) are still unsettled. The American Academy of Neurology and the European Federation of Neurological Societies launched a joint Task Force to prepare general guidelines for the management of this condition. After systematic review of the literature the Task Force came to a series of evidence-based recommendations. In patients with TN MRI may be considered to identify patients with structural causes. The presence of trigeminal sensory deficits, bilateral involvement, and abnormal trigeminal reflexes should be considered useful to disclose symptomatic TN, whereas younger age of onset, involvement of the first division, unresponsiveness to treatment and abnormal trigeminal evoked potentials are not useful in distinguishing symptomatic from classic TN. Carbamazepine (stronger evidence) or oxcarbazepine (better tolerability) should be offered as first-line treatment for pain control. For patients with TN refractory to medical therapy early surgical therapy may be considered. Gasserian ganglion percutaneous techniques, gamma knife and microvascular decompression may be considered. Microvascular decompression may be considered over other surgical techniques to provide the longest duration of pain freedom. The role of surgery versus pharmacotherapy in the management of TN in patients with multiple sclerosis remains uncertain.

Introduction

The American Academy of Neurology (AAN) and the European Federation of Neurological Societies (EFNS) decided to develop scientifically sound, clinically relevant guidelines to aid specialists and non-specialists in the management of trigeminal neuralgia (TN), by addressing its diagnosis, pharmacological treatment, and surgical treatment.

The International Association for the Study of Pain (IASP) defines TN as sudden, usually unilateral, severe, brief, stabbing, recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve.[54] The annual incidence of TN is 4 to 5/100,000.[34] TN is the most common neuralgia. In the latest classification of the International Headache Society,[29] a distinction is made between *classical* and *symptomatic* TN: classical TN (CTN) includes all cases without an established etiology, i.e. idiopathic, as well as those with potential vascular compression of the fifth cranial nerve, whereas the diagnosis of symptomatic TN (STN) is made in cases secondary to tumour, MS, structural abnormalities of the skull base, and the like. It should be noted that categorization of TN into *typical* and *atypical* forms is based on symptom constellation, and not etiology, and will not be discussed further in this review.

The first issue facing the clinician caring for a patient with TN is accurately distinguishing symptomatic from classical TN. The diagnostic portion of this parameter addresses the following questions:

1. How often does routine neuroimaging (CT, MRI) identify a cause (excluding vascular contact) of TN?
2. Which clinical or laboratory features accurately identify patients with STN?
3. For patients with classical TN does high resolution MRI accurately identify patients with neurovascular compression?

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This is a Continuing Medical Education article and can be found with corresponding questions on the internet at http://www.efns.org/content.php?pid=132. Certificates for correctly answering the questions will be issued by the EFNS.

Medical regimes for TN

Table 1 Summary of medical therapies for the treatment of trigeminal neuralgia [24]

	Medication	Dose	Features
First line	Carbamazepine	200–300 mg/day	Gold standard treatment. As with most anticonvulsants, the most common side-effects include drowsiness, dizziness, and nausea
	Oxcarbazepine	1200–2400 mg/day	Another first-line treatment typically used if carbamazepine is not tolerated
Second line	Baclofen	60–80 mg/day	Sudden discontinuation can cause seizures and hallucinations
	Lamotrigine	200–400 mg/day	Associated with skin rash if titrated too quickly and 1:10,000 chance to develop Steven-Johnsons syndrome
Third line	Levetiracetam	1000–4000 mg/day	Advantages include no need for routine blood tests and less drug interactions
	Topiramate	100–400 mg/day	Binds to non-benzodiazepine GABA receptors and blocks voltage-gated calcium channels
	Gabapentin	300–1800 mg/day	Advantages include no known drug interactions, no known skin reactions, and a mild side-effect profile
	Pregabalin	150–600 mg/day	Analog of GABA that is structurally related to gabapentin
	Botulinum toxin A	20–75 U	Causes local release of anti-nociceptive neuropeptides

Evidence based Treatment algorithm for TN

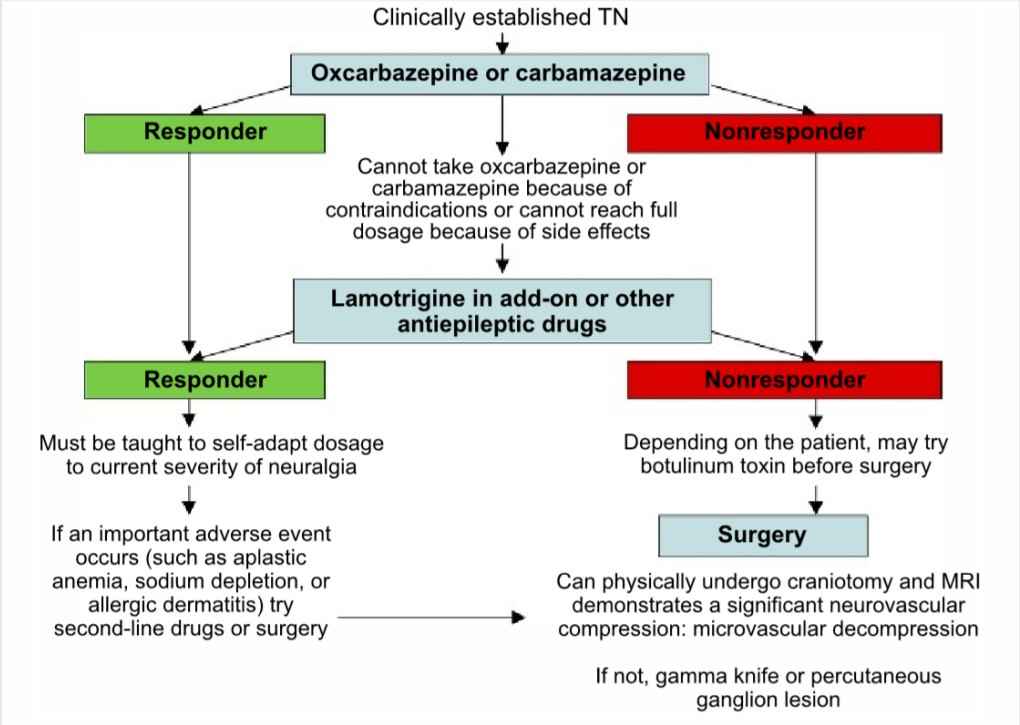
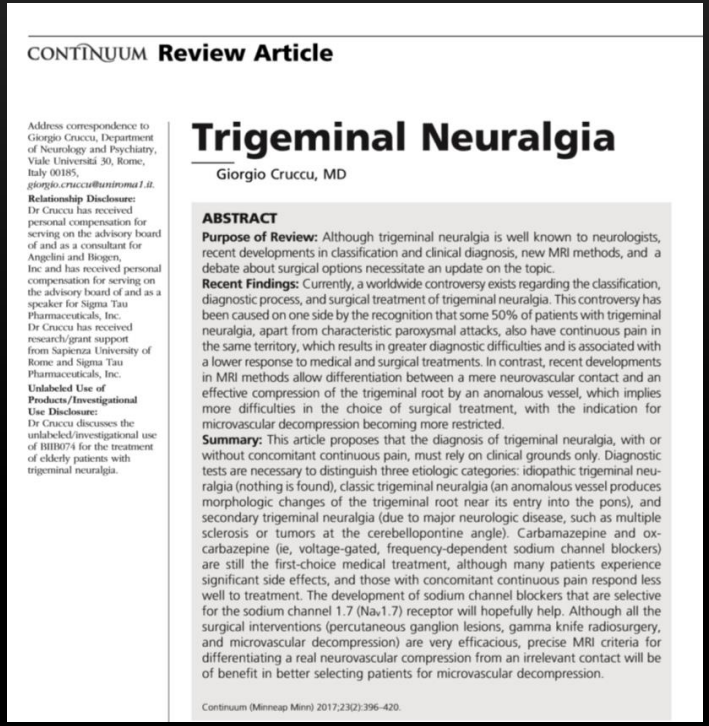


FIGURE 3-7 Trigeminal neuralgia (TN) treatment algorithm.

MRI = magnetic resonance imaging.



CONTINUUM **Review Article**

Trigeminal Neuralgia

Giorgio Cruccu, MD

Address correspondence to Giorgio Cruccu, Department of Neurology and Psychiatry, Viale Università 30, Rome, Italy 00185, *giorgio.cruccu@uniroma1.it.*

Relationship Disclosure: Dr Cruccu has received personal compensation for serving on the advisory board of and as a consultant for Angelini and Biogen, Inc and has received personal compensation for serving on the advisory board of and as a speaker for Sigma Tau Pharmaceuticals, Inc. Dr Cruccu has received research/grant support from Sapienza University of Rome and Sigma Tau Pharmaceuticals, Inc.

Unlabeled Use of Products/Investigational Use Disclosure: Dr Cruccu discusses the unlabeled/investigational use of BIIB074 for the treatment of elderly patients with trigeminal neuralgia.

ABSTRACT

Purpose of Review: Although trigeminal neuralgia is well known to neurologists, recent developments in classification and clinical diagnosis, new MRI methods, and a debate about surgical options necessitate an update on the topic.

Recent Findings: Currently, a worldwide controversy exists regarding the classification, diagnostic process, and surgical treatment of trigeminal neuralgia. This controversy has been caused on one side by the recognition that some 50% of patients with trigeminal neuralgia, apart from characteristic paroxysmal attacks, also have continuous pain in the same territory, which results in greater diagnostic difficulties and is associated with a lower response to medical and surgical treatments. In contrast, recent developments in MRI methods allow differentiation between a mere neurovascular contact and an effective compression of the trigeminal root by an anomalous vessel, which implies more difficulties in the choice of surgical treatment, with the indication for microvascular decompression becoming more restricted.

Summary: This article proposes that the diagnosis of trigeminal neuralgia, with or without concomitant continuous pain, must rely on clinical grounds only. Diagnostic tests are necessary to distinguish three etiologic categories: idiopathic trigeminal neuralgia (nothing is found), classic trigeminal neuralgia (an anomalous vessel produces morphologic changes of the trigeminal root near its entry into the pons), and secondary trigeminal neuralgia (due to major neurologic disease, such as multiple sclerosis or tumors at the cerebellopontine angle). Carbamazepine and oxcarbazepine (ie, voltage-gated, frequency-dependent sodium channel blockers) are still the first-choice medical treatment, although many patients experience significant side effects, and those with concomitant continuous pain respond less well to treatment. The development of sodium channel blockers that are selective for the sodium channel 1.7 ($Na_v1.7$) receptor will hopefully help. Although all the surgical interventions (percutaneous ganglion lesions, gamma knife radiosurgery, and microvascular decompression) are very efficacious, precise MRI criteria for differentiating a real neurovascular compression from an irrelevant contact will be of benefit in better selecting patients for microvascular decompression.

Continuum (Minneap Minn) 2017;23(2):396-420.

Issues with drug compliance in TN

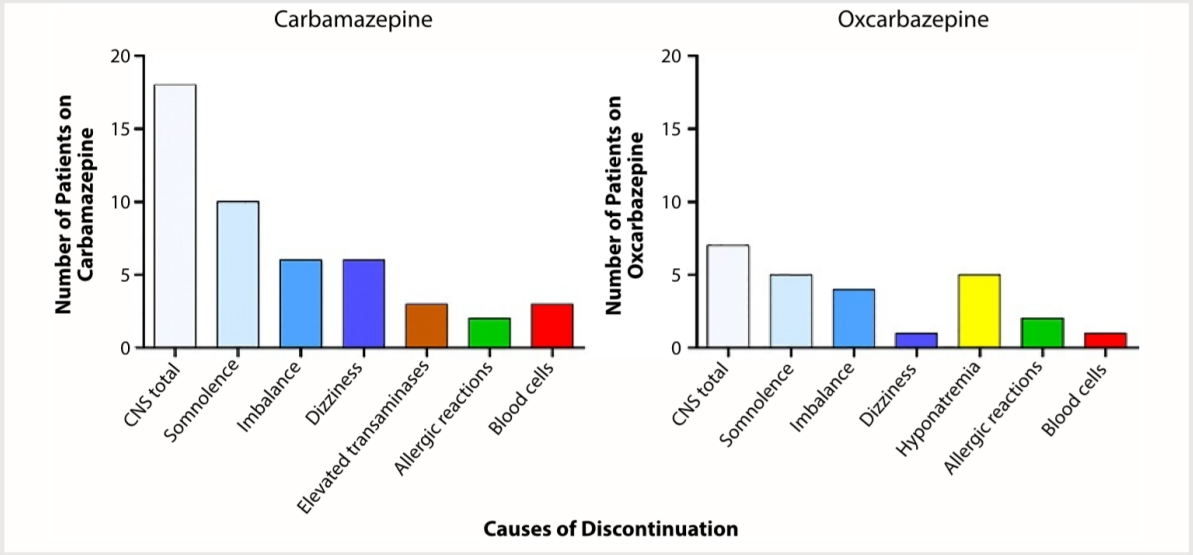


FIGURE 3-8 Dropouts due to adverse events in 100 patients on carbamazepine and 100 patients on oxcarbazepine. Note that central nervous system (CNS) disturbances affected patients on carbamazepine far more frequently than patients on oxcarbazepine, whereas hyponatremia only affected patients on oxcarbazepine.

Blood cells = white cells, red cells, or thrombocytes.

CONTINUUM **Review Article**

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Surgical Management TN

Our literature search on surgical procedures revealed three Class I prospective RCTs, one Class II prospective cohort study, and a handful of Class III studies where the outcome was independently assessed (explicitly stated).

The vast majority of the evidence was Class IV.

For patients with TN refractory to medical therapy early surgical therapy may be considered (Level C).

Percutaneous procedures on the Gasserian ganglion, gamma knife and microvascular decompression may be considered (Level C).

Microvascular decompression may be considered over other surgical techniques to provide the longest duration of pain freedom (Level C).

Although the evidence regarding the surgical management of TN in patients with MS is insufficient, we recommend that before surgical intervention pharmacological avenues be thoroughly explored (Clinical good practice point).

European Journal of Neurology 2008, **15:** 1013–1028 doi:10.1111/j.1468-1331.2008.02185.x

EFNS GUIDELINES/CME ARTICLE

AAN-EFNS guidelines on trigeminal neuralgia management

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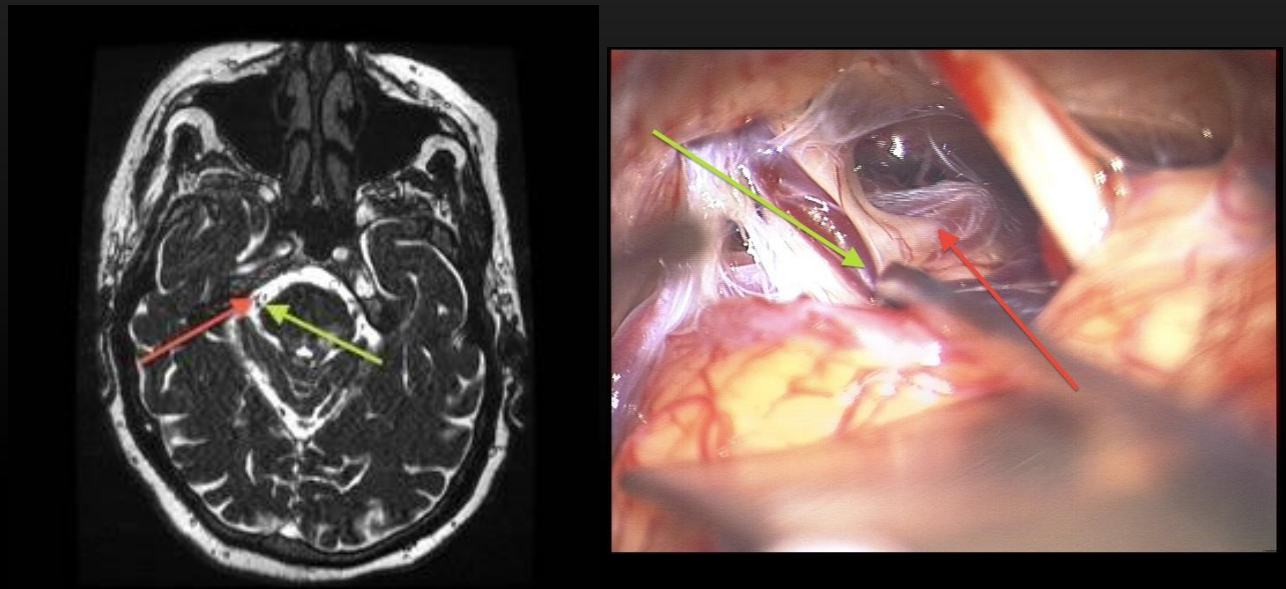
Surgical management TN
Microvascular decompression

- Although microvascular decompression is the only causal cure and huge numbers of patients have undergone this procedure, no reported trial meets the minimal criteria of evidence to be considered in a Cochrane Review!
- Allowing for the lack of evidence based data, still the meta-analyses of the largest studies make microvascular decompression the most efficacious of the surgical interventions for classic trigeminal neuralgia: according to the AAN/EFNS guidelines, 90% of patients obtain pain relief.
- More than 80% of patients will still be pain free at 1 year, 75% at 3 years, and 73% at 5 years. The average mortality associated with the operation is 0.2%. Up to 4% of patients incur major problems such as CSF leaks, infarctions, or hematomas. Aseptic meningitis is the most common complication (11%). Diplopia is usually transient, and facial palsy is rare. Sensory loss occurs in 7% of patients. The major long-term complication is ipsilateral hearing loss

MVD
Sup cerebellar artery vascular compromise



Green arrow shows retraction of trigeminal vein in contact with but not compressing V; red arrow shows a branch of the superior cerebellar artery passing medial to and severely compressing V at the root entry zone

Courtesy Mr Sinan Barazi Neurosurgeon KCH

Surgical Management TN
Gamma knife

According to the 2008 AAN/EFNS guidelines on trigeminal neuralgia,6 at 1 year after gamma knife therapy, complete pain relief with no medication occurs in up to 69% of patients. This falls to 52% at 3 years. Facial numbness is reported in 9% to 37% of patients (although it tends to improve with time), and troublesome sensory loss or paresthesia is reported in 6% to 13%, whereas anesthesia dolorosa is practically absent

A recent metaanalysis of gamma knife interventions, however, found that, because about 34% of patients do not reach 1 year of pain relief, repeated administration of radiations were necessary. With the increasing number of interventions, the rate of success and the pain-free time increase significantly Unfortunately, toxicity also increases, with facial hypesthesia persisting in 50% of patients at 1-year follow-up.82

Other emerging Rx

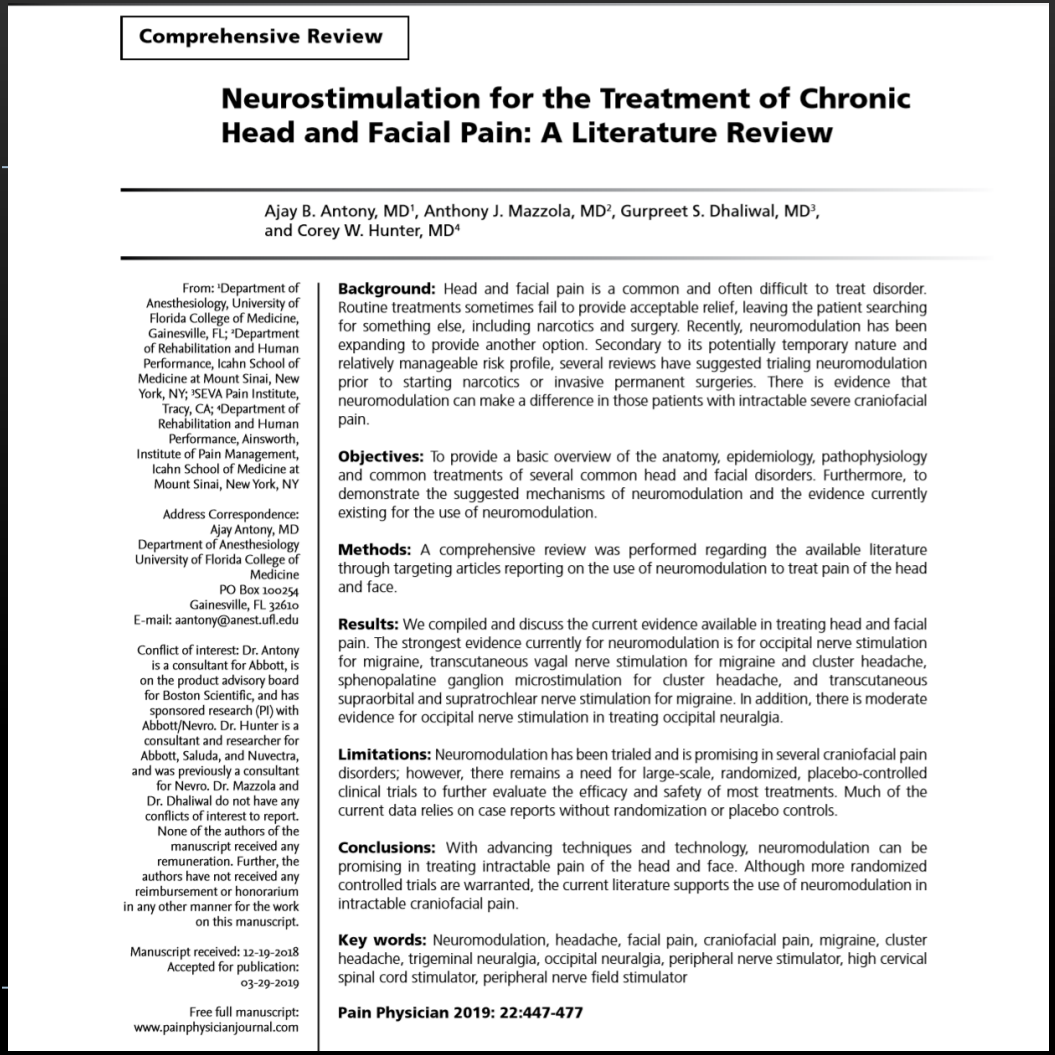
- Peripheral stimulation

Jakobs M[1], Unterberg A[2], Treede RD[3], Schuh-Hofer S[3], Ahmadi R[4]. Subcutaneous trigeminal nerve field stimulation for refractory trigeminal pain: a cohort analysis. Acta Neurochir (Wien). 2016 Sep;158(9):1767-74. doi: 10.1007/s00701-016-2881-6. Epub 2016 Jul 2.

Klein J[1], Sandi-Gahun S[2], Schackert G[2], Juratli TA[2]. Peripheral nerve field stimulation for trigeminal neuralgia, trigeminal neuropathic pain, and persistent idiopathic facial pain. Cephalalgia. 2016 Apr;36(5):445-53. doi: 10.1177/0333102415597526. Epub 2015 Jul 24.

- Repeated Local anaesthetic injections
- Botulinum toxin
- Deep brain stimulation

Jones MR[1], Urits I[2], Ehrhardt KP[3], Cefalu JN[3], Kendrick JB[3], Park DJ[4], Cornett EM[3], Kaye AD[3], Viswanath O[5,6,7].**A Comprehensive Review of Trigeminal Neuralgia.** Curr Pain Headache Rep. 2019 Aug 6;23(10):74. doi: 10.1007/s11916-019-0810-0.



Comprehensive Review

Neurostimulation for the Treatment of Chronic Head and Facial Pain: A Literature Review

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Conflict of interest: Dr. Antony is a consultant for Abbott, is on the product advisory board for Boston Scientific, and has sponsored research (PI) with Abbott/Nevro. Dr. Hunter is a consultant and researcher for Abbott, Saluda, and Nuvectra, and was previously a consultant for Nevro. Dr. Mazzola and Dr. Dhaliwal do not have any conflicts of interest to report. None of the authors of the manuscript received any remuneration. Further, the authors have not received any reimbursement or honorarium in any other manner for the work on this manuscript.

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Free full manuscript: www.painphysicianjournal.com

Background: Head and facial pain is a common and often difficult to treat disorder. Routine treatments sometimes fail to provide acceptable relief, leaving the patient searching for something else, including narcotics and surgery. Recently, neuromodulation has been expanding to provide another option. Secondary to its potentially temporary nature and relatively manageable risk profile, several reviews have suggested trialing neuromodulation prior to starting narcotics or invasive permanent surgeries. There is evidence that neuromodulation can make a difference in those patients with intractable severe craniofacial pain.

Objectives: To provide a basic overview of the anatomy, epidemiology, pathophysiology and common treatments of several common head and facial disorders. Furthermore, to demonstrate the suggested mechanisms of neuromodulation and the evidence currently existing for the use of neuromodulation.

Methods: A comprehensive review was performed regarding the available literature through targeting articles reporting on the use of neuromodulation to treat pain of the head and face.

Results: We compiled and discuss the current evidence available in treating head and facial pain. The strongest evidence currently for neuromodulation is for occipital nerve stimulation for migraine, transcutaneous vagal nerve stimulation for migraine and cluster headache, sphenopalatine ganglion microstimulation for cluster headache, and transcutaneous supraorbital and supratrochlear nerve stimulation for migraine. In addition, there is moderate evidence for occipital nerve stimulation in treating occipital neuralgia.

Limitations: Neuromodulation has been trialed and is promising in several craniofacial pain disorders; however, there remains a need for large-scale, randomized, placebo-controlled clinical trials to further evaluate the efficacy and safety of most treatments. Much of the current data relies on case reports without randomization or placebo controls.

Conclusions: With advancing techniques and technology, neuromodulation can be promising in treating intractable pain of the head and face. Although more randomized controlled trials are warranted, the current literature supports the use of neuromodulation in intractable craniofacial pain.

Key words: Neuromodulation, headache, facial pain, craniofacial pain, migraine, cluster headache, trigeminal neuralgia, occipital neuralgia, peripheral nerve stimulator, high cervical spinal cord stimulator, peripheral nerve field stimulator

Pain Physician 2019: 22:447-477

TN single diagnostic = ‘therapeutic’ block

The study evaluated the therapeutic effect of combination of pharmacotherapy and lidocaine block.

Thirteen patients with CTN managed with pharmacotherapy were recruited and assigned either to no additional treatment (Group I) or to additional analgesic block (Group II).

The primary endpoint was the reduction in the frequency of pain episodes in a month assessed at 30 and 90 days.

- Comparisons of measurements of pain, general health and depression scales were secondary endpoints.
- The results from the follow-up visits at 30 and 90 days showed the Group II to have larger reduction in the frequency of pain and exhibited a bigger improvement in the scores of the pain, general health and depression scales.
- The results from this preliminary study suggest a clinical benefit of the combination of pharmacotherapy and lidocaine block.

Di Stani F Ojango C, Dugoni D, Di Lorenzo L, Masala S, Delfini R, Bruti G, Simonetti G, Piovesan EJ, Ruggeri AG. Combination of pharmacotherapy and lidocaine analgesic block of the peripheral trigeminal branches for trigeminal neuralgia: a pilot study. Arq Neuropsiquiatr. 2015 Aug;73(8):660-4. doi: 10.1590/0004-282X20150077.

LA infiltrations or NB for TN

DOI: 10.1590/0004-282X20150077

ARTICLE

Combination of pharmacotherapy and lidocaine analgesic block of the peripheral trigeminal branches for trigeminal neuralgia: a pilot study

Combinação de farmacoterapia e bloqueio analgésico com lidocaína sobre os ramos periféricos trigeminais no tratamento da neuralgia do trigêmeo: um estudo piloto

Fabrizio Di Stani[1], Christine Ojango[2], Demo Dugoni[1], Luigi Di Lorenzo[3], Salvatore Masala[2], Roberto Delfini[1], Gianluca Bruti[1], Giovanni Simonetti[2], Elcio Juliato Piovesan[4], Andrea Gennaro Ruggeri[1]

ABSTRACT

Classical trigeminal neuralgia (CT
study was carried out to evaluate t
managed with pharmacotherapy
(Group II). The primary endpoint w
of measurements of pain, gener
30 and 90 days showed the Grou
of the pain, general health and de
pharmacotherapy and lidocaine b

curs. The current
patients with CTN
l analgesic block
ys. Comparisons
llow-up visits at
ent in the scores
e combination of

Keywords: analgesic block, class

RESUMO

A neuralgia clássica do trigêmio (
Avaliamos o efeito terapêutico
portadores de NTC tratados com
medicamentos e Grupo II paciente
30 e 90 dias após o bloqueio. Secu
uma redução significativa na freq

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Treze pacientes
iente tratamento
reqüência da dor
da. O grupo II teve
ão. Os resultados

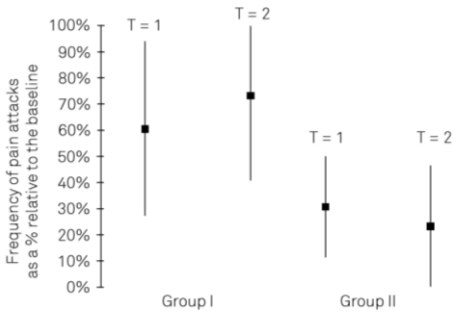

Figure 2. The average frequency of pain attacks in a month measured at T = 1 and T = 2 and expressed as a percentage relative to the baseline (0%- free from attacks; 100%- same frequency of attacks as at baseline) in both groups.

Demographic characteristics of study patients.

		Group I		Group II	
Age (years)	Mean ± SD	63.0	11.8	68.2	10.8
Gender	Women n %	4	57.1	4	66.7
Duration of symtoms (years)	Mean ± SD	5.0	2.90	16.8	9.20
Symtomatic facial side	Right n %	2	28.6	3	50
	Left n %	5	71.4	3	50
Pain location (trigeminal branches)	V2 or V3 n %	3	42.9	3	50
	V1 + V2 or V2 + V3 n %	4	57.1	2	33.3
	V1 + V2 + V3 n %	0		1	16.7
Frequency of pain attacks	dd/month	30		28.3	

SD: standard deviation; n: number of patients; dd/month: days per month.

	Group I		Group II	
	Mean ± SD		Mean ± SD	
SF-36 physical functioning	50.7	35.76	66.7	26.3
SF-36 physical role functioning	25.7	36.56	25	38.7
SF-36 bodily pain	25.9	14.38	39.8	21.1
SF-36 general health perceptions	38.6	19.32	46	11.8
SF-36 vitality	43.1	18.37	50	14.8
SF-36 social role functioning	39.2	25.45	52	14.7
SF-36 mental health	34.3	25.81	60.7	19.6
SF-36 emotional role functioning	19.6	26.59	38.9	49.0
BDI	26.7	16.18	14	11.2
BPI severity index	5.1	1.999	5.3	2.55
BPI interferference index	4.3	1.599	3.4	3.35

Baseline assessment of The Medical Outcomes Trust 36-Item; SF-36®: Short Form, Health Survey; BDI: Beck Depression Inventory; BPI: Brief Pain Inventory scales.

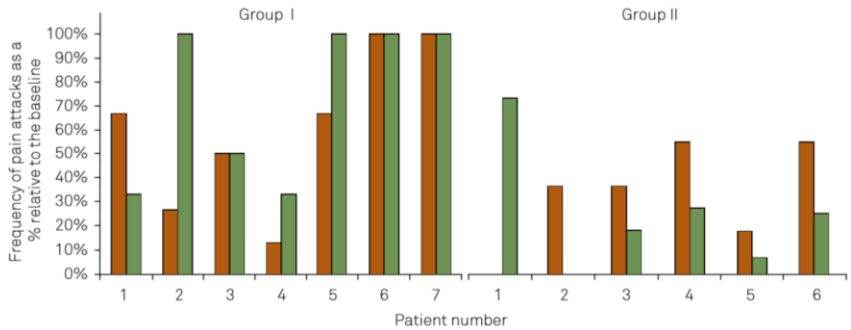

Figure 1. Frequency of pain attacks in a month measured at T = 1 and T = 2 expressed as a percentage relative to the baseline (0%- free from attacks; 100% same frequency of attacks as at baseline) in all patients. Brown: follow-up visit T = 1; Green: follow-up visit T = 2.

Botulinum Toxin for TN

The effect of BTX-A was sustained throughout the initial 6 month
of the follow up and was demonstrated to persist for as long as 2
rse and high injection dose
r long-term VAS scores.
-(50-70 units) or high-do

Journal of Pain Research

Dovepress

ORIGINAL RESEARCH

Botulinum Toxin Type A for refractory trigeminal neuralgia in older patients: a better therapeutic effect

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Yajun Lian[1]
Haifeng Zhang[1]
Yuan Chen[1]
Chuanjie Wu[2]
Shuang Li[1]
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Background: Some studies have indicated th
(BTX-A) is a promising therapy for trigemin
is still ineffective for approximately 10–43%
factors are associated with the therapeutic effe
classical TN.
Methods: We performed a retrospective coh
receiving BTX-A injection for medically refr
October 2016. A VAS score, pain attack fr
response to treatment and side effects were
receiving BTX-A.
Results: A total of 87 patients reported su
completely controlled while 46 reported adequa
that treatment success was higher in patients
Univariate and multivariate analyses demonst
associated with treatment outcome (OR=1.72,
significant predictor of pain relief (P=0.020
(16.3%) reported mild side effects.
Conclusion: A local injection of BTX-A ma
TN which lasts for several months. BTX-A
trying for particularly middle-aged and elderly
and may be afraid of serious complications fr

Keywords: trigeminal neuralgia, Botulinum effect

Introduction

Trigeminal neuralgia (TN) is characterize
like paroxysmal pain in one or more divis
the paroxysmal pain, some patients exp
ment is typically sodium channel blocker
However, as a result of intolerable side
treatment microvascular decompression
neurovascular contact has been demons
tions may occur, such as cranial nerve d
Botulinum Toxin Type A (BTX-A) is a
positive bacterium Clostridium botulinum.

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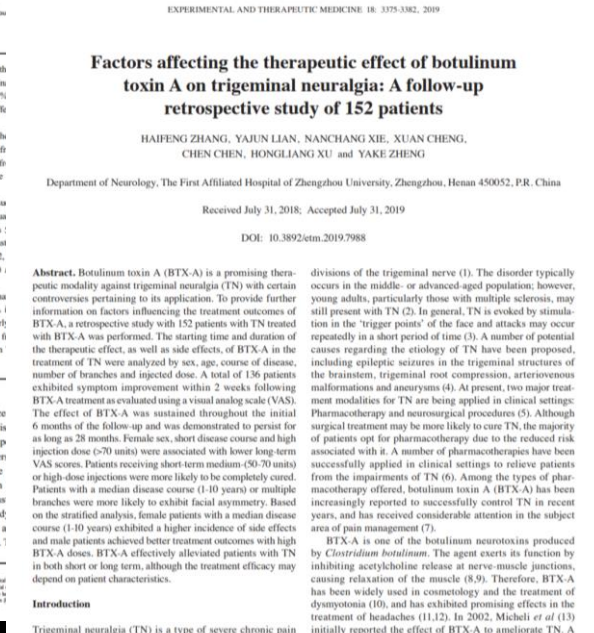

EXPERIMENTAL AND THERAPEUTIC MEDICINE 18: 3375-3382, 2019

Factors affecting the therapeutic effect of botulinum toxin A on trigeminal neuralgia: A follow-up retrospective study of 152 patients

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Abstract. Botulinum toxin A (BTX-A) is a promising therapeutic modality against trigeminal neuralgia (TN) with certain controversies pertaining to its application. To provide further information on factors influencing the treatment outcomes of BTX-A, a retrospective study with 152 patients with TN treated with BTX-A was performed. The starting time and duration of the therapeutic effect, as well as side effects, of BTX-A in the treatment of TN were analyzed by sex, age, course of disease, number of branches and injected dose. A total of 136 patients exhibited symptom improvement within 2 weeks following BTX-A treatment as evaluated using a visual analog scale (VAS). The effect of BTX-A was sustained throughout the initial 6 months of the follow-up and was demonstrated to persist for as long as 28 months. Female sex, short disease course and high injection dose (>70 units) were associated with lower long-term VAS scores. Patients receiving short-term medium-(50-70 units) or high-dose injections were more likely to be completely cured. Patients with a median disease course (1-10 years) or multiple branches were more likely to exhibit facial asymmetry. Based on the stratified analysis, female patients with a median disease course (1-10 years) exhibited a higher incidence of side effects and male patients achieved better treatment outcomes with high BTX-A doses. BTX-A effectively alleviated patients with TN in both short or long term, although the treatment efficacy may depend on patient characteristics.

Introduction

Trigeminal neuralgia (TN) is a type of severe chronic pain divisions of the trigeminal nerve (1). The disorder typically occurs in the middle- or advanced-aged population; however, young adults, particularly those with multiple sclerosis, may still present with TN (2). In general, TN is evoked by stimulation in the 'trigger points' of the face and attacks may occur repeatedly in a short period of time (3). A number of potential causes regarding the etiology of TN have been proposed, including epileptic seizures in the trigeminal structures of the brainstem, trigeminal root compression, arteriovenous malformations and aneurysms (4). At present, two major treatment modalities for TN are being applied in clinical settings: Pharmacotherapy and neurosurgical procedures (5). Although surgical treatment may be more likely to cure TN, the majority of patients opt for pharmacotherapy due to the reduced risk associated with it. A number of pharmacotherapies have been successfully applied in clinical settings to relieve patients from the impairments of TN (6). Among the types of pharmacotherapy offered, botulinum toxin A (BTX-A) has been increasingly reported to successfully control TN in recent years, and has received considerable attention in the subject area of pain management (7).

BTX-A is one of the botulinum neurotoxins produced by *Clostridium botulinum*. The agent exerts its function by inhibiting acetylcholine release at nerve-muscle junctions, causing relaxation of the muscle (8,9). Therefore, BTX-A has been widely used in cosmetology and the treatment of dysmyotonia (10), and has exhibited promising effects in the treatment of headaches (11,12). In 2002, Micheli *et al* (13) initially reported the effect of BTX-A to ameliorate TN. A

DOI: 10.1002/brb3.1409

ORIGINAL RESEARCH

Brain and Behavior WILEY

The efficacy and safety of botulinum toxin type A in treatment of trigeminal neuralgia and peripheral neuropathic pain: A meta-analysis of randomized controlled trials

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Abstract

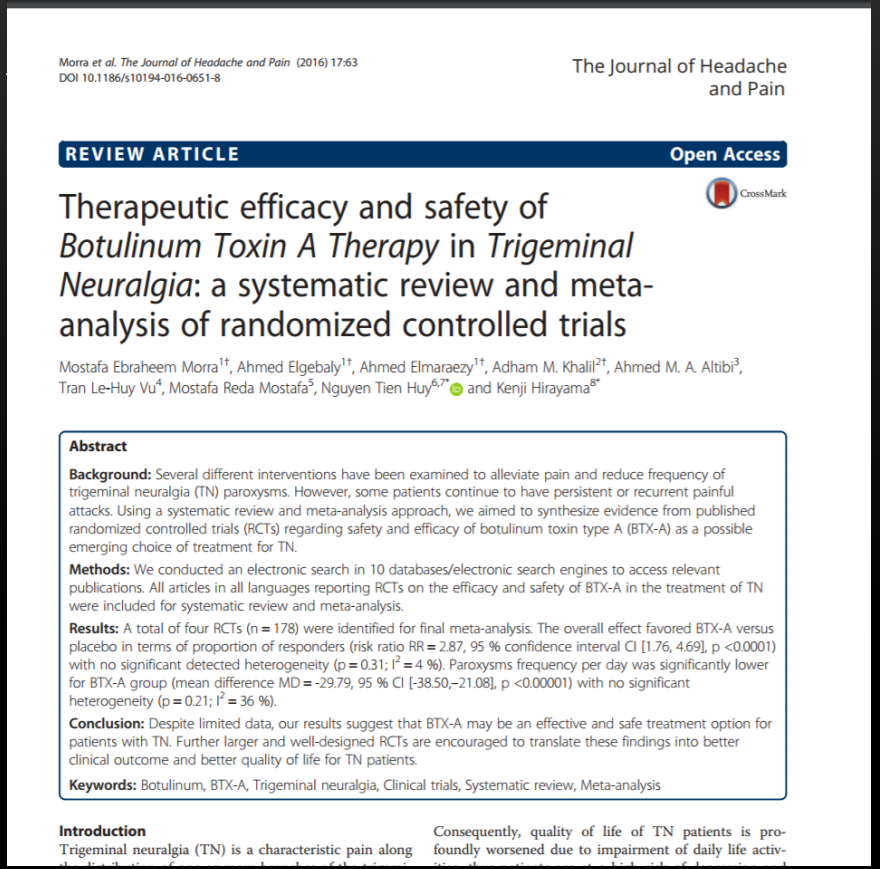
Background: Although recent studies have shown that botulinum toxin-A (BTX-A) has a good analgesic effect on trigeminal neuralgia (TN) and peripheral neuropathic pain (PNP), the quality of evidence is low due to limited data. This meta-analysis is used

assessing the efficacy of botulinum toxin from the estimates of three randomized clinical trials[4,5,6] with the methodology described similarly elsewhere.[7] Relative risk (95% confidence intervals) of patients with pain relief was the outcome variable, and one study[7] did not report this outcome. We observed statistically significant pooled estimates (2.86 [1.82, 4.48]) favoring botulinum toxin [Figure 1], and the trial sequential analysis confirmed the existence of adequate evidence for therapeutic utility of botulinum toxin. Although there is no expert consensus on using botulinum toxin in refractory TN due to lack of robust and long-term follow-up studies and cost-effectiveness data, the agent looks promising to use based on trial sequential analysis principles.

BTX
TN -Systematic Review 2017

4 PRCTS

- Several different interventions have been examined to alleviate pain and reduce frequency of trigeminal neuralgia (TN) paroxysms. However, some patients continue to have persistent or recurrent painful attacks. Using a systematic review and meta-analysis approach, we aimed to synthesize evidence from published randomized controlled trials (RCTs) regarding safety and efficacy of botulinum toxin type A (BTX-A) as a possible emerging choice of treatment for TN.
- **METHODS:** We conducted an electronic search in 10 databases/electronic search engines to access relevant publications. All articles in all languages reporting RCTs on the efficacy and safety of BTX-A in the treatment of TN were included for systematic review and meta-analysis.
- **RESULTS:** A total of four RCTs (n = 178) were identified for final meta-analysis. The overall effect favored BTX-A versus placebo in terms of proportion of responders (risk ratio RR = 2.87, 95 % confidence interval CI [1.76, 4.69], p <0.0001) with no significant detected heterogeneity (p = 0.31; I(2) = 4 %). Paroxysms frequency per day was significantly lower for BTX-A group (mean difference MD = -29.79, 95 % CI [-38.50,-21.08], p <0.00001) with no significant heterogeneity (p = 0.21; I(2) = 36 %).
- CONCLUSION: Despite limited data, our results suggest that BTX-A may be an effective and safe treatment option for patients with TN. Further larger and well-designed RCTs are encouraged to translate these findings into better clinical outcome and better quality of life for TN patients.



Morra et al. The Journal of Headache and Pain (2016) 17:63
DOI 10.1186/s10194-016-0651-8

The Journal of Headache and Pain

REVIEW ARTICLE Open Access

Therapeutic efficacy and safety of *Botulinum Toxin A Therapy* in *Trigeminal Neuralgia*: a systematic review and meta-analysis of randomized controlled trials

Mostafa Ebraheem Morra[1†], Ahmed Elgebaly[1†], Ahmed Elmaraezy[1†], Adham M. Khalil[2†], Ahmed M. A. Altibi[3], Tran Le-Huy Vu[4], Mostafa Reda Mostafa[5], Nguyen Tien Huy[6,7*] and Kenji Hirayama[8*]

Abstract

Background: Several different interventions have been examined to alleviate pain and reduce frequency of trigeminal neuralgia (TN) paroxysms. However, some patients continue to have persistent or recurrent painful attacks. Using a systematic review and meta-analysis approach, we aimed to synthesize evidence from published randomized controlled trials (RCTs) regarding safety and efficacy of botulinum toxin type A (BTX-A) as a possible emerging choice of treatment for TN.

Methods: We conducted an electronic search in 10 databases/electronic search engines to access relevant publications. All articles in all languages reporting RCTs on the efficacy and safety of BTX-A in the treatment of TN were included for systematic review and meta-analysis.

Results: A total of four RCTs (n = 178) were identified for final meta-analysis. The overall effect favored BTX-A versus placebo in terms of proportion of responders (risk ratio RR = 2.87, 95 % confidence interval CI [1.76, 4.69], p <0.0001) with no significant detected heterogeneity (p = 0.31; I^2 = 4 %). Paroxysms frequency per day was significantly lower for BTX-A group (mean difference MD = -29.79, 95 % CI [-38.50,–21.08], p <0.00001) with no significant heterogeneity (p = 0.21; I^2 = 36 %).

Conclusion: Despite limited data, our results suggest that BTX-A may be an effective and safe treatment option for patients with TN. Further larger and well-designed RCTs are encouraged to translate these findings into better clinical outcome and better quality of life for TN patients.

Keywords: Botulinum, BTX-A, Trigeminal neuralgia, Clinical trials, Systematic review, Meta-analysis

Introduction

Trigeminal neuralgia (TN) is a characteristic pain along

Consequently, quality of life of TN patients is pro-foundly worsened due to impairment of daily life activ-

Morra ME, Elgebaly A, Elmaraezy A, Khalil AM, Altibi AM, Vu TL, Mostafa MR, Huy NT, Hirayama K. Therapeutic efficacy and safety of Botulinum Toxin A Therapy in Trigeminal Neuralgia: a systematic review and meta-analysis of randomized controlled trials. J Headache Pain. 2016 Dec;17(1):63. doi: 10.1186/s10194-016-0651-8. Epub 2016 Jul 5.

Grade B evidence

Less favoured neuro ablative techniques

- Rhizotomy
- Glycerol injections
- Thermocoagulation
- Cryotherapy

Eighty-two percutaneous rhizotomies and 33 microvascular decompressions were performed in 99 trigeminal neuralgia patients. Of 92 patients contacted, 51 were alive and willing to participate. Two thirds reported being pain-free. Forty-one patients (82%) initially consulted their dentist; of these, 27 patients received invasive dental treatment for the pain syndrome, including extractions, root canal treatments, and implants.
Of 98 local dentists contacted, 51 responded, with three quarters feeling competent in evaluating trigeminal neuralgia.
A high percentage of patients that are surgically treated for trigeminal neuralgia consult their dentist first and receive possibly unjustified dental treatment. Differential diagnoses include odontogenic pain syndromes as well as atypical orofacial pain. The present literature acknowledges difficulties in correctly diagnosing trigeminal neuralgia, but seems to underestimate the extent

von Eckardstein KL[1], Keil M, Rohde V. **Unnecessary dental procedures as a consequence of trigeminal neuralgia.** Neurosurg Rev. 2015 Apr;38(2):355-60; discussion 360. doi: 10.1007/s10143-014-0591-1. Epub 2014 Nov 25.

Issues with TN

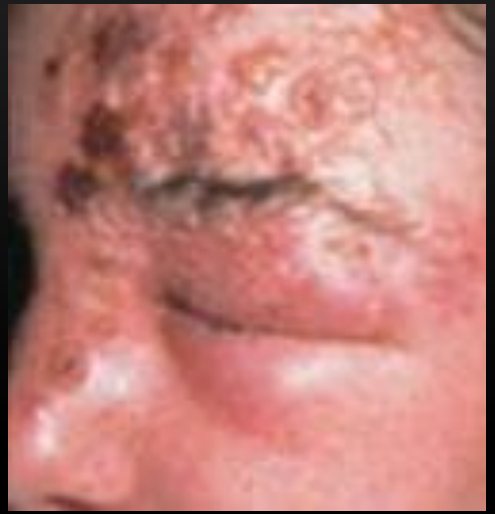
- Wrong diagnosis
  - GMPs diagnose TN raher than much more common toothache
  - Mis diagnosis SUNCT/SUNA
- Pre TN mimics 'toothache' exactly in older patients with heavily restored dentition
- Early MRI beneficial?
- Stevens-Johnson syndrome (SJS) has Genetic link skin reaction in HLA-B*1502 gene in Han Chinese and Thai population.

Hung SI et al. **Genetic susceptibility to carbamazepine-induced cutaneous adverse drug reactions.** Pharmacogenet Genomics. 2006 Apr;16(4):297-306.

Trigeminal neuropathic pain NOT TN (ICOP)

4.1.2.1 Trigeminal neuropathic pain attributed to herpes zoster

- Description: Unilateral facial pain of less than 3 months' duration in the distribution of one or more branches of the trigeminal nerve, caused by, and associated with other symptoms and/or clinical signs of, acute herpes zoster.
- Diagnostic criteria:
- A. Unilateral facial pain in the distribution(s) of a trigeminal nerve branch or branches, lasting <3 months B. One or more of the following: 1. herpetic eruption has occurred in the same trigeminal distribution (as the pain) 2. Varicella-zoster virus (VZV) has been detected in the cerebrospinal fluid (CSF) by polymerase chain reaction (PCR) 3. direct immunofluorescence assay for VZV antigen or PCR assay for VZV DNA is positive in cells obtained from the base of lesions C. Not better accounted for by another ICOP or ICHD-3 diagnosis



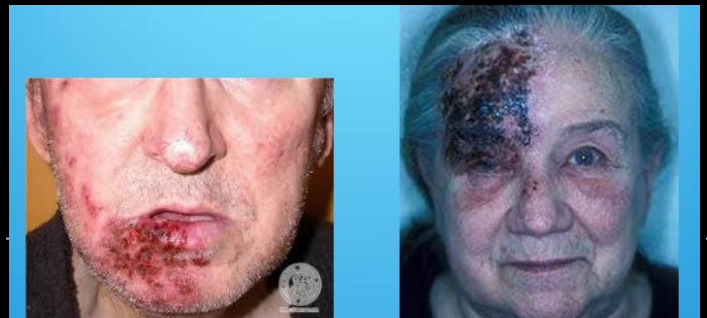
4.1.2.2 Trigeminal postherpetic neuralgia

Previously used term: Postherpetic trigeminal neuropathy

Post Herpetic Neuralgia

- 20% of patients (60%>50yrs) progress to neuropathic pain after Shingles caused by a reactivation of the varicella-zoster virus (VZV).
- In the trigeminal system most commonly V1 and V2
- If patient is <40 years check immunostatus (15 times higher in HIV-infected patients)
  - If caught early treat with high dose antifungals
    - Acyclovir (Zovirax)†800 mg orally five times daily for 7 to 10 day 10 mg per kg IV every 8 hours for 7 t 10 days
    - Prednisone 30 mg orally twice daily on days 1 through 7; then 15 mg twice daily on days 8 through 14 then 7.5 mg twice daily on days 15 through 21

  Ramsay hunt syndrome HZ of geniculate ganglion (facial nerve, CT)



IXth Cranial Nerve

- 4.2 Pain attributed to lesion or disease of the glossopharyngeal nerve 4.2.1 Glossopharyngeal neuralgia
- 4.2.1.1 Glossopharyngeal neuralgia
- Diagnostic criteria:
- A. Recurrent paroxysms of unilateral pain fulfilling criteria for
- 4.2.1.2 Secondary glossopharyngeal neuralgia
- 4.2.2.1 Glossopharyngeal neuropathic pain attributed to a known cause
- 4.2.2.2 Idiopathic glossopharyngeal neuropathic pain

Key messages on prevention and management…

Prevention of nerve injuries and related neuropathic pain is essential and possible

- Patient selection – preoperative psych assessment / pain comorbidity /age/ gender
- Good planning and risk assessment - Awareness of intraoperative risk factors
- Good surgical technique –minimal access avoid nerve injury and minimise pain

Manage the patients expectations

- **Surgery does not fix neuropathic pain**
- Most patients have pain with related functional, social and psychological sequelae
- We cannot 'fix' the patients with nerve injuries

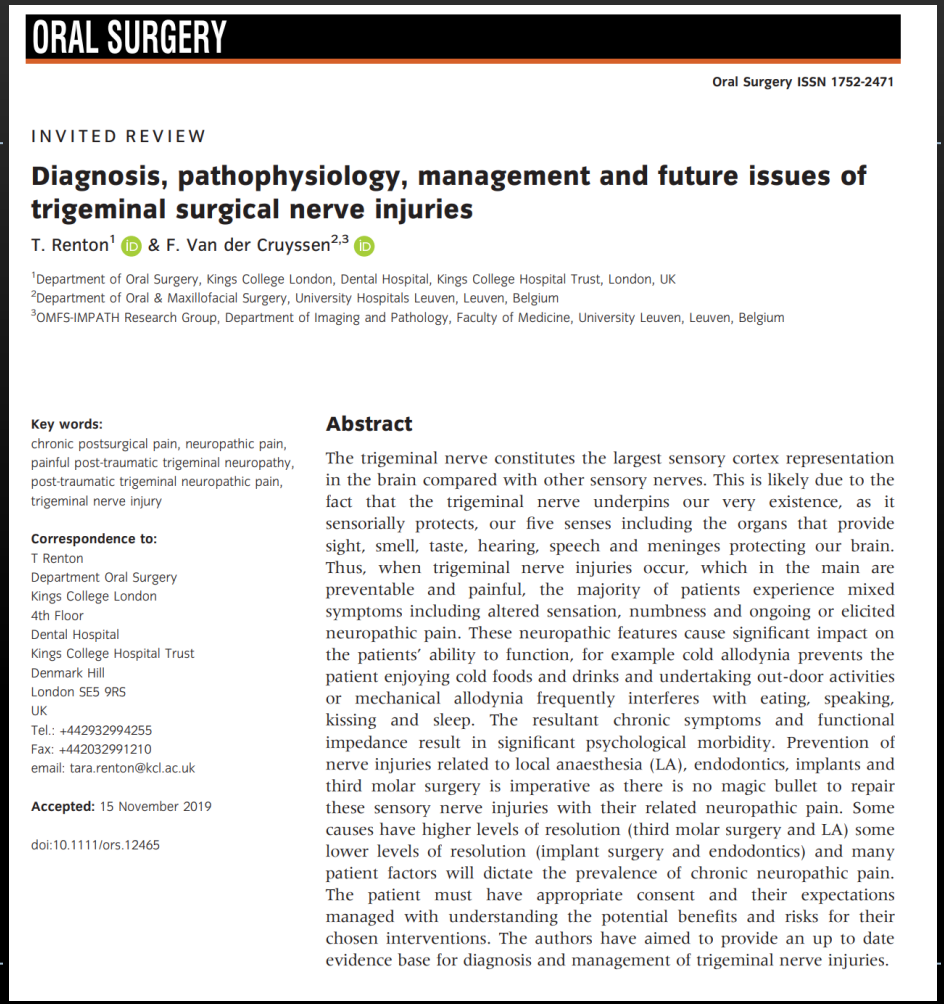
DO NOT SIT AND WAIT for resolution

- Home check will facilitate timely urgent intervention < 24-30 hours
- Refer to resources at **Trigeminalnerve.org.uk**

Dedicated Journal Oral Surgery to OFP

- Ed Justin Durham

https://onlinelibrary.wiley.com/journal/1752248x



ORAL SURGERY

Oral Surgery ISSN 1752-2471

INVITED REVIEW

Diagnosis, pathophysiology, management and future issues of trigeminal surgical nerve injuries

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[2]Department of Oral & Maxillofacial Surgery, University Hospitals Leuven, Leuven, Belgium
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Key words:
chronic postsurgical pain, neuropathic pain, painful post-traumatic trigeminal neuropathy, post-traumatic trigeminal neuropathic pain, trigeminal nerve injury

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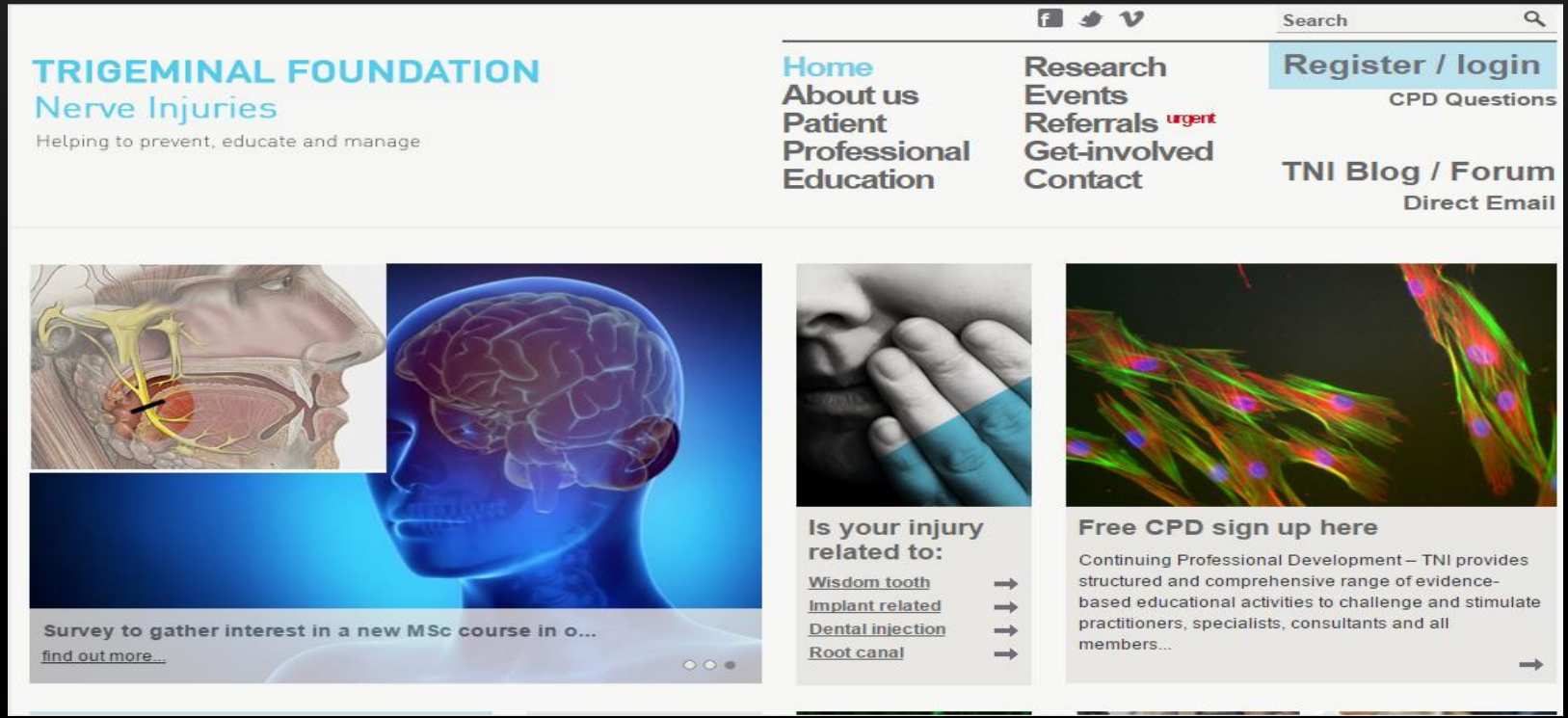
Accepted: 15 November 2019

doi:10.1111/ors.12465

Abstract

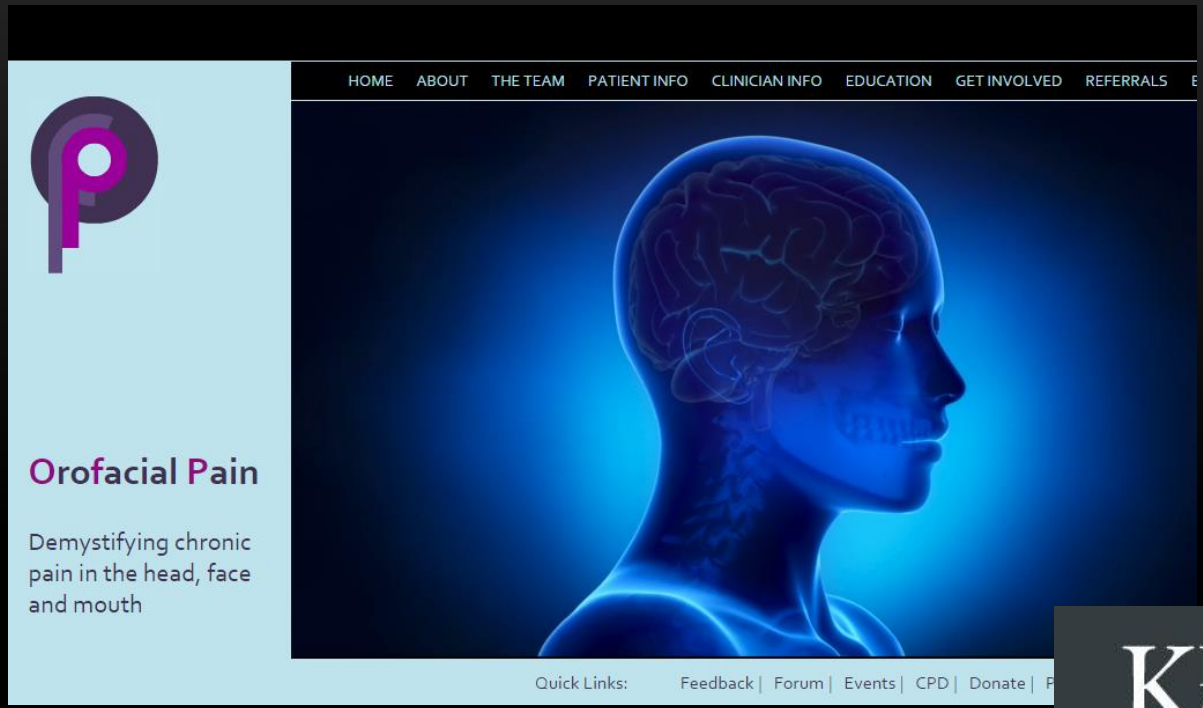
The trigeminal nerve constitutes the largest sensory cortex representation in the brain compared with other sensory nerves. This is likely due to the fact that the trigeminal nerve underpins our very existence, as it sensorially protects, our five senses including the organs that provide sight, smell, taste, hearing, speech and meninges protecting our brain. Thus, when trigeminal nerve injuries occur, which in the main are preventable and painful, the majority of patients experience mixed symptoms including altered sensation, numbness and ongoing or elicited neuropathic pain. These neuropathic features cause significant impact on the patients' ability to function, for example cold allodynia prevents the patient enjoying cold foods and drinks and undertaking out-door activities or mechanical allodynia frequently interferes with eating, speaking, kissing and sleep. The resultant chronic symptoms and functional impedance result in significant psychological morbidity. Prevention of nerve injuries related to local anaesthesia (LA), endodontics, implants and third molar surgery is imperative as there is no magic bullet to repair these sensory nerve injuries with their related neuropathic pain. Some causes have higher levels of resolution (third molar surgery and LA) some lower levels of resolution (implant surgery and endodontics) and many patient factors will dictate the prevalence of chronic neuropathic pain. The patient must have appropriate consent and their expectations managed with understanding the potential benefits and risks for their chosen interventions. The authors have aimed to provide an up to date evidence base for diagnosis and management of trigeminal nerve injuries.

Trigeminalnerve.org.uk



THANK YOU

http://www.orofacialpain.org.uk



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KING'S College LONDON

Thank you

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