Neuropathic pain and Trigeminal Neuralgia.

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Learning Objectives

- Highlight current hypotheses around mechanisms and aetiology of Neuropathic pain
- To provide up to date diagnostic criteria for neuropathic pain conditions in the trigeminal system
- To provide up to date assessment and management strategies to assist in assessment of neuropathic orofacial pain conditions with specific focus on PTPN and TN

Outline

- –Introduction
  - •The trigeminal system
  - •Definitions
- –Diagnosis
  - •**Trigeminal neuralgia (TN)**
  - •**Post traumatic painful trigeminal neuropathy (PTPN)**
    - –Mechanisms
    - –Assessment and prediction of outcome
- –Management;
  - **Trigeminal neuralgia (TN)**
    - –Medical
    - –Interventional
      - •Surgery
  - **Post traumatic painful neuropathy (PTPN)**
    - »Medical
    - »Interventional
      - •Surgery
      - •Advanced Stimulation, Peripheral, DBS
    - »Psychological
    - »Adjunctive
  - –The future

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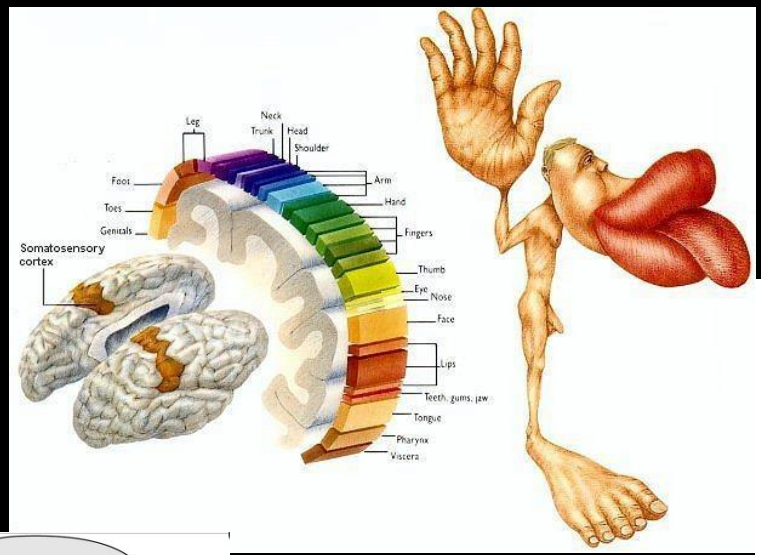
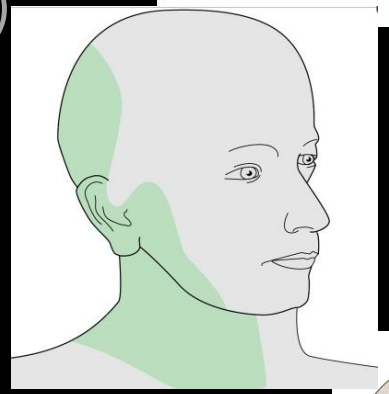
Why is Trigeminal pain unique?

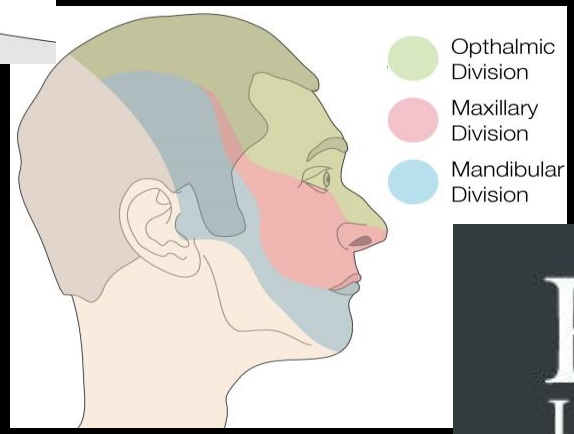
- Primordial brain - survival instincts
- Constant unavoidable activity
- C2,3 and vagal interaction (autonomic input)
- Underpins daily pleasure in health
  - Eating
  - Drinking
  - Speaking
  - Smiling
  - Sexual interaction
- **Bilateral cortical representation of pain**
- Thus any threat or actual harm to the V*th* nerve region comprises a massive threat to your very existence

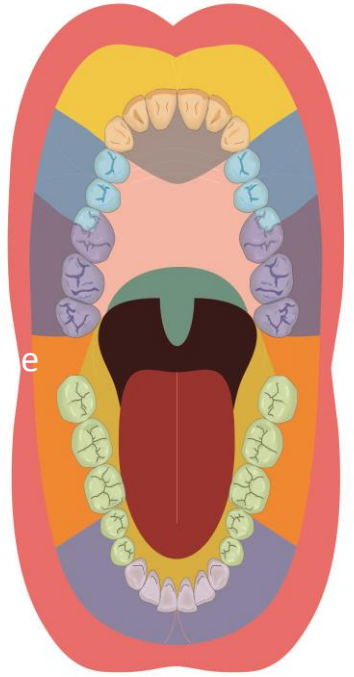
All patients are physiologically wired to run from the dentist!





The dermatomal distribution of C and C3 (Adapted from Foester O. e dermatomes in man [Schorstein Lecture, London, 1932]. Brain 1933;56:I-39.)





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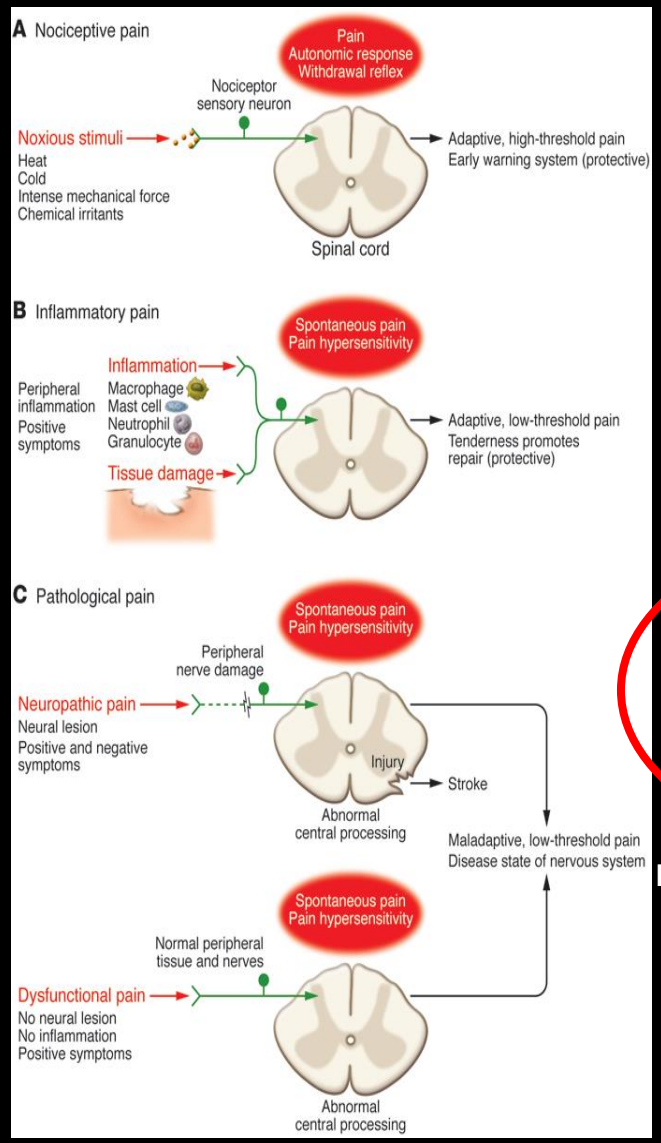
Definitions Neuropathic pain



Healthy acute pain

Nociceptive
healthy feeling pain 'pain'

Nociceptive pain

Inflammatory pain
healthy short lived after insult

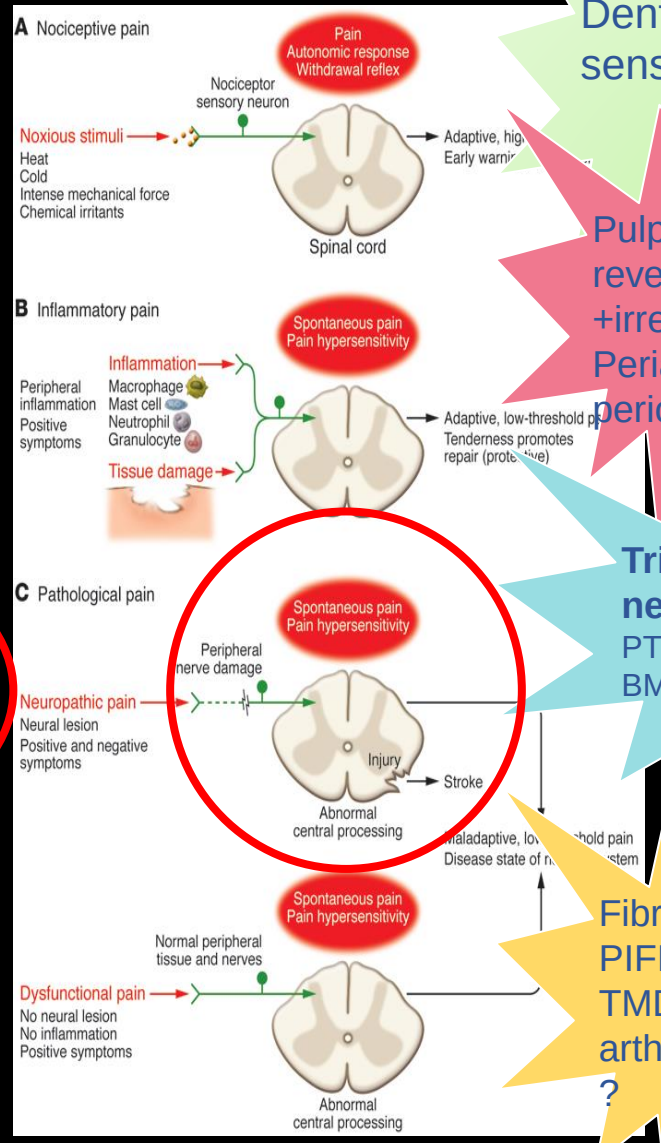
Chronic pain = disease of neuromatrix

Neuropathic pain
Associated with nerve lesion

Neuropathic pain

Dysfunctional or centralised pain
Unknown cause

Nociplastic pain



Dentine sensitivity

Pulpitis reversible +irreversible Periapical periodontitis

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*

Definition of neuropathic pain

Neuropathic pain (NP) is a pain caused by damage or disease affecting the somatosensory system.

Peripheral nervous system disorders include diseases of the spinal nerve roots, dorsal root ganglia, and peripheral nerves.

Classical examples include diabetic polyneuropathies, postherpetic neuralgia, and trigeminal neuralgia. **Post traumatic neuropathy**

Disorders of the CNS spinal cord can lead to “central pain,” such as that encountered in multiple sclerosis, after a stroke, and in spondylotic and posttraumatic myelopathy.

Incidence

- NP is estimated to afflict as much as 7%–8% of the general population in Europe.[
- An American study showed that 1/3 of patients affected by malignancies suffered from NP or a mix of NP and nociceptive pain.
- The Canadian Pain Society developed treatment guidelines of CPNP and estimated a 2%–3% prevalence.
- Buono M et al Postherpetic neuralgia, diabetic neuropathy, and trigeminal neuralgia – Chronic peripheral neuropathic pain in 58,480 rural Italian primary care patients. J Family Med Prim Care. 2017 Jan-Mar; 6(1): 110–114
- GMP applied DN4 questionnaire to 58,480 rural Italian primary care patients
- 0.82%, mean age 69 years
  - Diabetes (*n* = 179)
  - herpes zoster (*n* = 142)
  - trigeminal neuralgia (*n* = 41)
  - trauma (*n*= 27),
  - nerve entrapment (*n* = 27)
  - systemic diseases (*n* = 11), and unknown causes (*n* = 21) were the etiological determinants of CPNP in our study

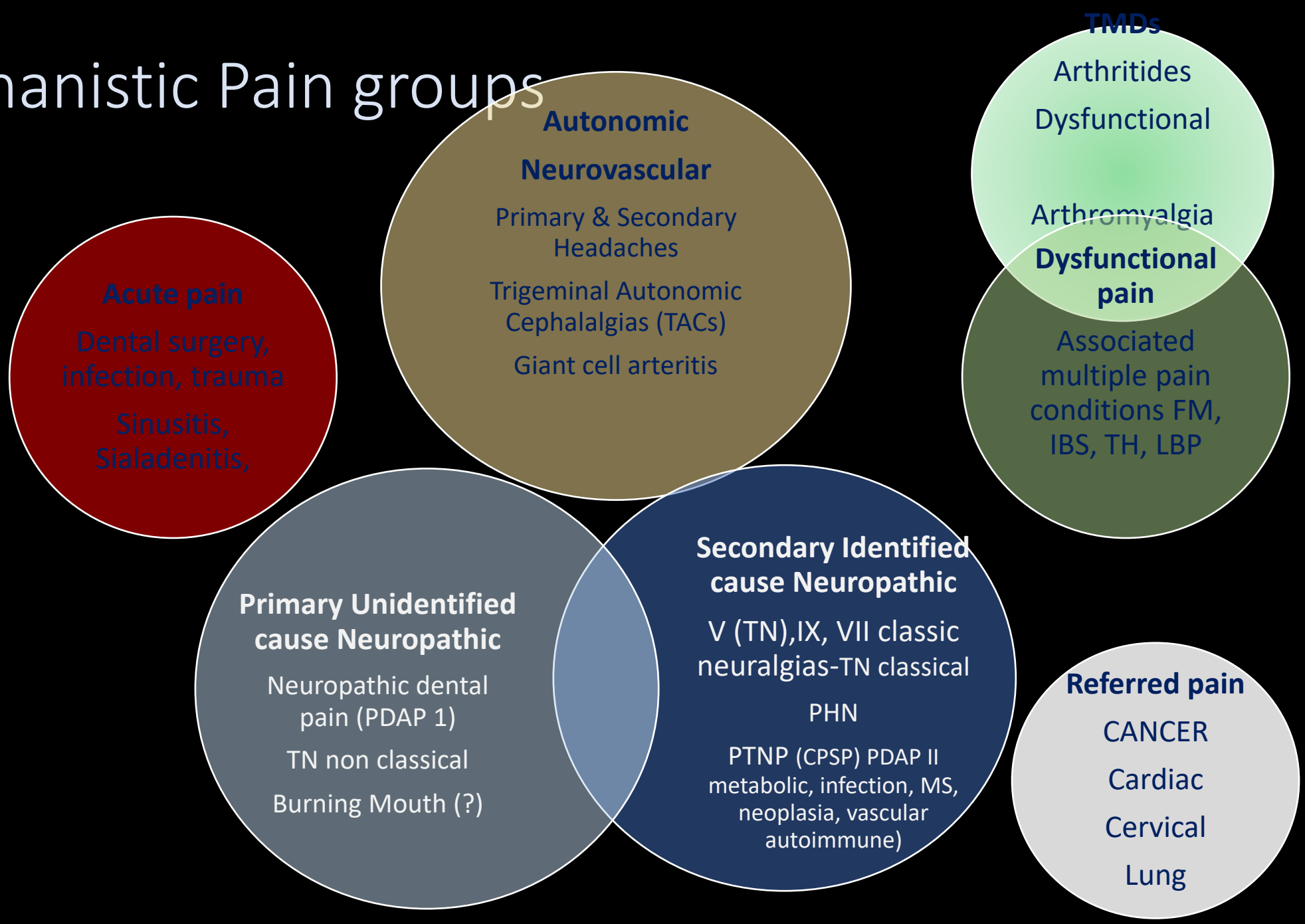
Definitions – do not confuse nomenclature

- **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)

ICD 2016 Disorders of trigeminal nerve G50- >

- Includes disorders of 5th cranial nerve
- Clinical Information A disorder characterized by involvement of the trigeminal nerve (fifth cranial nerve).
- A non-neoplastic or neoplastic disorder affecting the trigeminal nerve (fifth cranial nerve).
- Diseases of the trigeminal nerve or its nuclei, which are located in the pons and medulla. The nerve is composed of three divisions: ophthalmic, maxillary, and mandibular, which provide sensory innervation to structures of the face, sinuses, and portions of the cranial vault. The mandibular nerve also innervates muscles of mastication. Clinical features include loss of facial and intra-oral sensation and weakness of jaw closure. Common conditions affecting the nerve include brain stem ischemia, infratentorial neoplasms, and trigeminal neuralgia

Mechanistic Pain groups



Prevalence of OFP diagnoses
Common things happen commonly

- Toothache
  - The prevalence estimates for 5 case definitions identified were: 'toothache' 7-32%, 'pain in teeth with hot, cold or sweet things' **25-38%,** 'pain and discomfort needing medication or treatment' 7-9%, 'pain or discomfort in the mouth, teeth or gums' 19-66%, and 'oral and facial pain'40-44%. Pau AK, Croucher R, Marcenes W **Prevalence estimates and associated factors for dental pain: a review.** Oral Health Prev Dent.2003;1(3):209-20
- Migraines
  - **22.7%** in the National Health and Nutrition Examination Survey, 16.6% of adults 18 or older reported having migraine or other severe headaches in the last 3 months in the 2011 National Health Interview Survey. In contrast, the AMPP study found an overall prevalence of migraine of 11.7% and probable migraine of 4.5%, for a total of 16.2%. Smitherman TA, Burch R, Sheikh H, Loder E. **The prevalence, impact, and treatment of migraine and severe headaches in the United States: a review of statistics from national surveillance studies.** Headache. 2013 Mar;53(3):427-36. doi: 10.1111/head.12074. Epub 2013 Mar 7.
- Tension type headache
  - Episodic TTH,occurring on fewer than 15 days per month, is reported by more than **70% of some populations**. http://www.who.int/mediacentre/factsheets/fs277/en/
- Pain from TMD
  - Males / Females **6.7% / 12.4%** Johansson et al2002
- Chronic post surgical V pain
  - **0.01-20%** of patients undergoing third molar surgery
- Burning Mouth
  - ages 20 and 69 years. Fifty-three individuals (3.7%), 11 men (1.6%) and 42 women (5.5%) Bergdahl M Bergdahl J **Burning mouth syndrome: prevalence and associated factors.** J Oral Pathol Med. 1999 Sep;28(8):350-4.
- Trigeminal neuralgia
  - 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 http://www.iasp-pain.org/files/Content/ContentFolders/GlobalYearAgainstPain2/20132014OrofacialPain/FactSheets/Trigeminal_Neuralgia.pdf

Trigeminal Neuralgia

IASP defines trigeminal neuralgia as

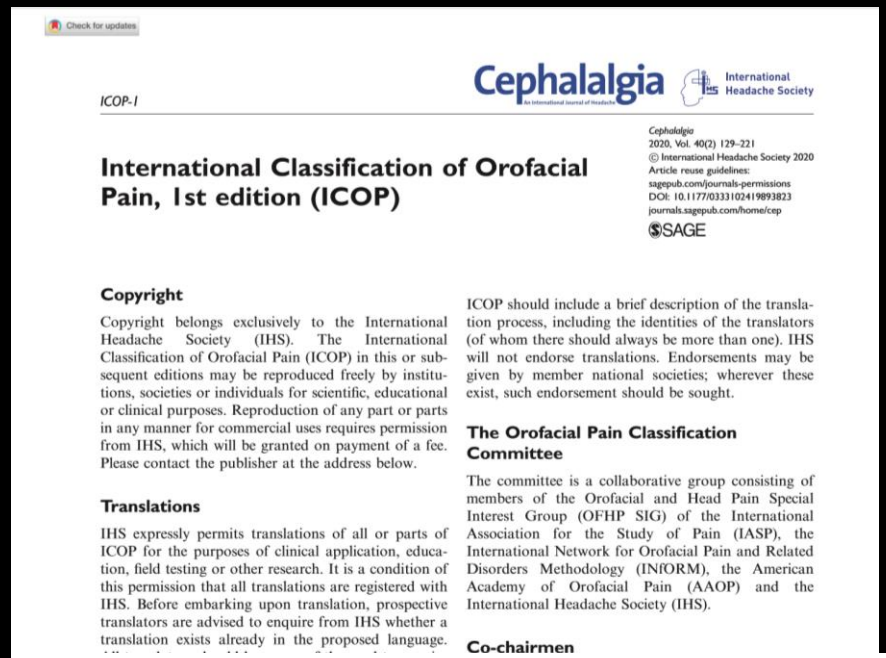
" a sudden, usually unilateral, severe, brief, stabbing, recurrent pain in the distribution of one or more branches of the fifth cranial nerve".

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

ICOP Definitions and Diagnostic Criteria



Check for updates

ICOP-I

Cephalalgia International Headache Society

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

Cephalalgia
2020, Vol. 40(2) 129–221

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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).

Co-chairmen

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

Orofacial pain attributed to lesion or disease of the cranial nerves Lene Baad-Hansen, Denmark (chairman); Eli Eliav, USA;

4.1 Pain attributed to lesion or disease of the trigeminal nerve

4.1.1 Trigeminal neuralgia

Previously used term: Tic douloureux.

Description: A disorder characterized by recurrent unilateral brief electric shock-like pains, abrupt in onset and termination, limited to the distribution of one or more divisions of the trigeminal nerve and triggered by innocuous stimuli. It may develop without apparent cause or be a result of another disorder. Additionally, there may or may not be concomitant continuous pain of moderate intensity within the affected division(s).

Diagnostic criteria:

A. Recurrent paroxysms of unilateral facial pain in the distribution(s) of one or more divisions of the trigeminal nerve, with no radiation beyond,1 and fulfilling criteria B and C

B. The pain has all the following characteristics: 1. lasting from a fraction of a second to 2 minutes2 2. severe intensity3 3. electric shock-like, shooting, stabbing or sharp in quality C. Precipitated by innocuous stimuli within the affected trigeminal distribution4 D. Not better accounted for by another ICOP or ICHD-3 diagnosis.

ICOP classification

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.

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

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

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.
- 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 injury3 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.
- *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

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

ICHD3 diagnostic criteria for TN (ICHD3 and ICOP)

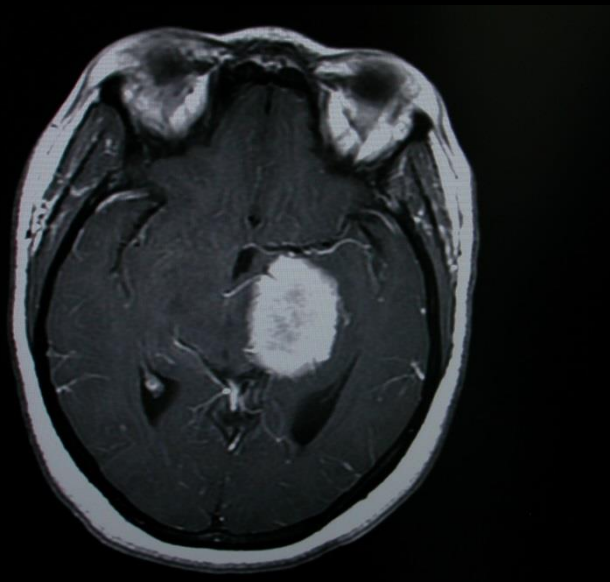
- Classical TN
  - Standard elicited ONLY pain in V” and V2, unilateral in patients over 60 years with Neurovascular conflict
  - Above with back ground pain and NVC conflict

- Secondary TN

  MS, SOL or other cause

  bilateral, neuropathy, younger age

- Idiopathic TN
  - Not secondary
  - No NVC

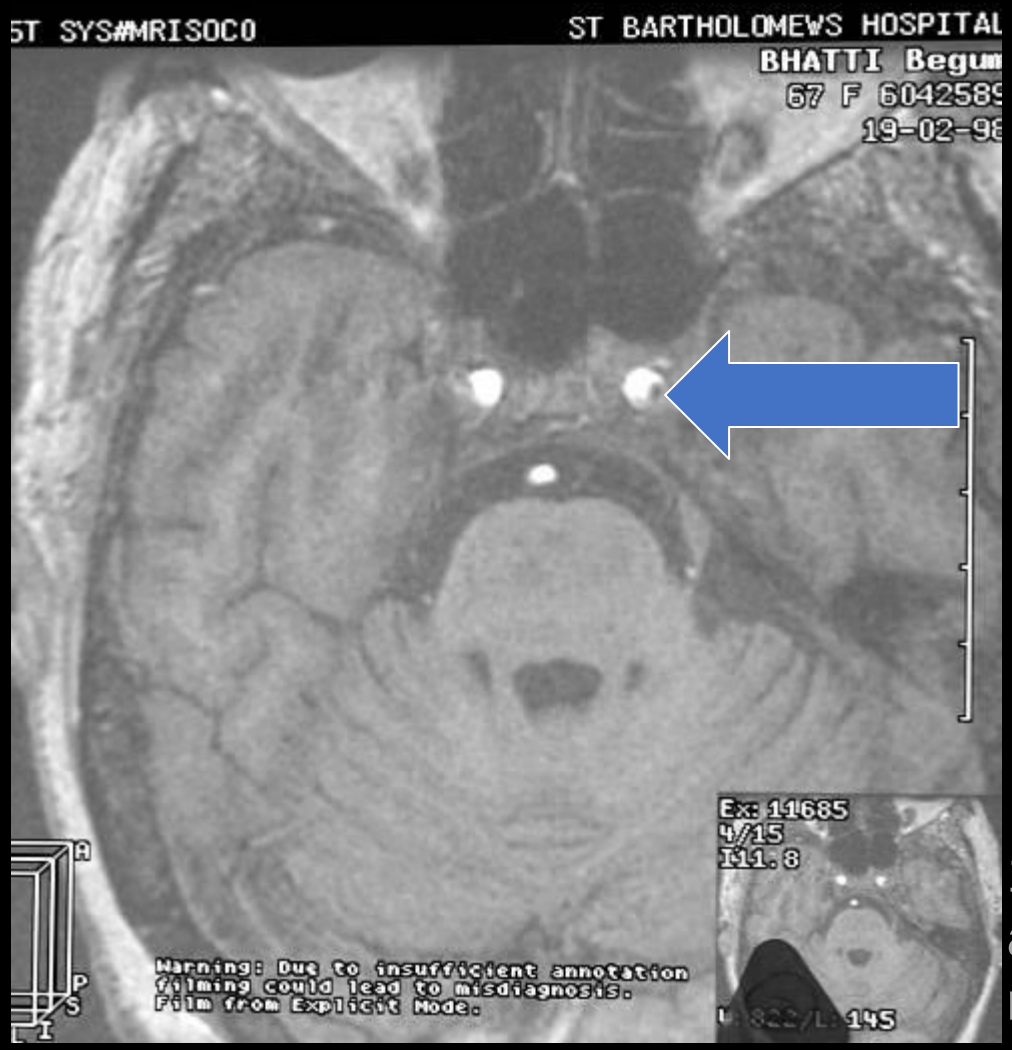


Trigeminal Neuralgia

- 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
- 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
- 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]

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
- Neurological – sensory testing and hearing



MRI scan

Diagnosis and differential diagnosis of trigeminal neuralgia

Zakrzewska JM.
Clin.J.Pain 2002;18:14–21

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)

Trigeminal Neuralgia

- Significant clinical challenge because the symptoms of PTN respond poorly, if at all, to AED or surgical therapies commonly used in TN.[1,2]
  - Neurolytic treatment may actually worsen pain in this subgroup
- More often associated with young, middle aged women and feelings of depression
- Motor cortex stimulation for trigeminal neuralgia seems promising – 70% success rate compared to 50% for central pain[5]
- May target trigeminal nerve at various sites with nerve blocks if unresponsive to medical therapy
  - Superficial V1/V2, gasserian ganglion
- If responsive to local anesthetic block, may pursue trigeminal neurolysis
  - Most common target is the gasserian ganglion via the foramen ovale[1]
  - Studies have all used patients w/classic trigeminal neuralgia
    - Less premorbid depression/anxiety, more satisfied w/outcome, fewer side effect complaints, more willing to repeat procedure[1]
  - Study by Taha and Tew in 1996 evaluated RF rhizotomy w/curved electrode, RF rhizotomy, glycerol rhizotomy, balloon compression, and posterior fossa exploration (microvascular decompression, partial trigeminal rhizotomy)[4]
    - Showed initial pain relief to be 91-98% with success of procedure in 85-98% and pain recurrence in 15-54%
      - Glycerol rhizotomy had lowest initial pain relief, lowest procedure success and highest pain recurrence
  - Complications of trigeminal neurolysis can be devastating and include anesthesia dolorosa, loss of corneal sensation, keratitis, dysesthesia[1]

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)	Discrete trigger zones
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	Sensory loss, subjective-objective, progressive, vasodilation and *swelling* may occur

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.

Post Traumatic Neuropathic Pain (PTNP)

- 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 injury3
- 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.
- *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*.

Diagnostic criteria PTNP What's the difference?

Condition	Classification	Diagnostic criteria:
Painful Post Traumatic Trigeminal Neuropathy **PPTTN** **PTN** **ICOP PTNP**	ICHD-3 Beta-2016 Part 3 (13.1.2.3) Description: Unilateral facial or oral pain following trauma to the trigeminal nerve, with other symptoms and/or clinical signs of trigeminal nerve dysfunction.	A. Unilateral facial and/or oral pain fulfilling criterion C B. History of an identifiable traumatic event[1] to the trigeminal nerve, with clinically evident positive (hyperalgesia, allodynia) and/or negative (hypoaesthesia, hypoalgesia) signs of trigeminal nerve dysfunction C. Evidence of causation demonstrated by both of the following: pain is located in the distribution of the same trigeminal nerve pain has developed within 3-6 months of the traumatic event D. Not better accounted for by another ICHD-3 diagnosis. Benoliel R, Zadik Y, Eliav E, Sharav Y. Peripheral painful traumatic trigeminal neuropathy: clinical features in 91 cases and proposal of novel diagnostic criteria. J Orofac Pain. 2012 Winter;26(1):49-58.
Persistent dento-alveolar pain (PDAP)	persistent (chronic) continuous pain symptom located in the dento-alveolar region and cannot be explained within the context of other diseases or disorders (Nixdorf et al, 2012). May include Phantom tooth pain, painful neuropathy (non-traumatic), atypical ontontalgia	A. Unilateral facial and/or oral pain fulfilling criterion C. B. History of an identifiable traumatic event to the trigeminal nerve, with clinically evident positive (hiperalgesia, allodynia), and/or negative (hypoaesthesia, hypoaelgesia) signs of trigeminal nerve dysfunction. C. Evidence of causation demonstrated by both of the following: 1. Pain is located in the distribution of the same trigeminal nerve. 2. Pain has developed within 3-6 months of the traumatic event. D. Not better accounted for by another ICHD-3 diagnosis. Donald Nixdorf & Estephan Moana-Filho Dento-Alveolar Pain Disorder (PDAP): Working towards a Better Understanding. Rev Pain. 2011 Dec; 5(4): 18–27.
Chronic post surgical pain **CPSP**	Other names include; **Surgically induced neuropathic pain SNPP, Post traumatic neuropathy PTN (with pain), Postoperative neuropathic pain PPNP or Phantom limb pain.**	A. Pain developed after surgery B. Minimum 2-month duration C. Other causes of pain have been excluded (infection, persistent malignancy, misdiagnosis) D. Excluded preoperative pain from other cause (80% display NePain features +/- neuropathic area)[4] Macrae WA. **Chronic post-surgical pain: 10 years on.** Br J Anaesth. 2008 Jul;101(1):77-86.

Diagnosis criteria for Ne Pain Guidelines for Ne Pain

American Medical Association

Geber C Baumgärtner U Schwab R Müller H Stoeter P Dieterich M, Sommer C, Birklein F, Treede RD. **Revised definition of neuropathic pain and its grading system: an open case series illustrating its use in clinical practice.** Am J Med. 2009 Oct;122(10 Suppl):S3-12. doi: 10.1016/j.amjmed.2009.04.005.

The definition of neuropathic pain has recently been revised by an expert committee of the Neuropathic Pain Special Interest Group of the International Association for the Study of Pain (NeuPSIG) as "**pain arising as direct consequence of a lesion or disease affecting the somatosensory system," and a grading system of "definite," "probable," and "possible" neuropathic pain has been introduced.** This open case series of 5 outpatients (3 men, 2 women; mean age 48 +/- 12 years) demonstrates how the grading system can be applied, in combination with appropriate confirmatory testing, to diagnosis neuropathic conditions in clinical practice. The proposed grading system includes a dynamic algorithm that enhances the physician's ability to determine with a greater level of certainty whether a pain condition is neuropathic. Its clinical use should be further validated in prospective studies

IASP neuropathic pain sig

Haanpää M attal N, backonja M, baron R, bennett M, bouhassira D, cruccu G, hansson P, haythornthwaite JA, iannetti GD, jensen TS, kauppila T, nurmikko TJ, rice AS, rowbotham M, serra J, sommer C, smith BH, treede RD. Pain. 2011 jan;152(1):14-27. Doi: 10.1016/j.Pain.2010.07.031. Epub 2010 sep 19. **Neupsig guidelines on neuropathic pain assessment.**

Abstract this is a revision of guidelines, originally published in 2004

Neuropathic pain is defined as pain arising as a direct consequence of a lesion or disease affecting the somatosensory system either at peripheral or central level. **Screening questionnaires are suitable for identifying potential patients with neuropathic pain**, but further validation of them is needed for epidemiological purposes. Clinical examination, including **accurate sensory examination, is the basis of neuropathic pain diagnosis. For more accurate sensory profiling, quantitative sensory testing is recommended for selected cases in clinic, including the diagnosis of small fiber neuropathies and for research purposes.** Measurement of trigeminal reflexes mediated by a-beta fibers can be used to differentiate symptomatic trigeminal neuralgia from classical trigeminal neuralgia. Measurement of laser-evoked potentials is useful for assessing function of the a-delta fiber pathways in patients with neuropathic pain. Functional brain imaging is not currently useful for individual patients in clinical practice, but is an interesting research tool. Skin biopsy to measure the intraepidermal nerve fiber density should be performed in patients with clinical signs of small fiber dysfunction. The intensity of pain and treatment effect (both in clinic and trials) should be assessed with numerical rating scale or visual analog scale. For future neuropathic pain trials, pain relief scales, patient and clinician global impression of change, the proportion of responders (50% and 30% pain relief), validated neuropathic pain quality measures and assessment of sleep, mood, functional capacity and quality of life are recommended.

Clarifying the diagnostic criteria for V Ne Pain

Vol. 125 No. 6 June 2018

Identifying criteria for diagnosis of post-traumatic pain and altered sensation of the maxillary and mandibular branches of the trigeminal nerve: a systematic review

Maria Devine, BDS, MFDS (RCS Ed), M Oral Surg, RCS, FHEA,[a] Murtaza
Justin Durham, BDS, MFDS (RCS Ed), PhD, FCS (OS) RCS,[b] Donald R. N
Tara Renton, PhD, MDSc, BDS, FDS, RCS, FRACDS (OMS), FHEA[a]

Objective. The aim of the study was to systematically identify criteria used to diag
Study Design. A systematic review of the literature registered in the PROSPERO
agnosed with nerve injury of the sensory divisions of the maxillary or mandibular br
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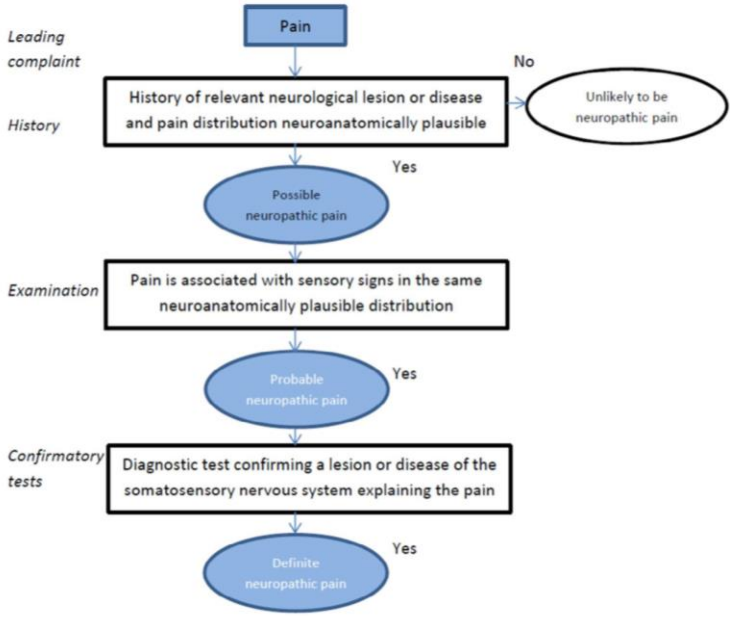


Proposed grading system for neuropathic pain (Finnerup et al 2016).

Table VI. Proposed diagnostic criteria for PPTTN

Diagnostic criteria	*Notes*
A Spontaneous or touch-evoked (stimulus dependent) pain predominantly affecting the receptive field of one or more divisions of the trigeminal nerve.	Pain tends to spread with time and is mostly unilateral without crossing the midline. Paroxysmal pain patients may also have constant background pain. Time pattern may change over the course of the disease.
Duration ranges widely from episodic (minutes to days) and may also be constant	
B Develops within 3 months of an identifiable traumatic event to the painful area or relevant innervation.	Trauma, surgery, invasive dental treatment.
Continues for >3 months.	*Usually localized pain †Likely to cause dermatomal pain, may spread due to central mechanisms
C At least one clinically evident neurologic dysfunction:	Must be a constant feature and reproducible. Nonvital tooth is evidence of nerve damage.
Positive sign	Clinical examination may be suitable.
- Hyperalgesia	If area is amenable, quantitative sensory testing may reveal changes.
- Allodynia	Advanced neurophysiologic testing is not always available but certainly valuable (e.g., nerve conduction studies, electromyography, laser-evoked potentials, blink reflex, masseter inhibitory reflex). Convincing data from C may be considered sufficient.
- Swelling or flushing	
And/or negative sign	
- Anesthesia	
- Hypoesthesia	
D Imaging or neurophysiology demonstrating a neurologic lesion and its location	Imaging may often be historical, e.g., zygomatic fractures affecting the infraorbital nerve that have been decompressed, dental implants that impinged on nerve bundles but may have been removed. Root canal therapy is considered evidence of nerve damage. Neurophysiology (see above)
E Not attributed to another disorder	Other causes are ruled out by history, physical examination, and special investigations, if necessary
Diagnostic level	Possible NP
Fulfils criteria A, B, and E	Probable NP

Mechanisms Neuropathic pain

Pain

Neuropathic pain: aetiology, symptoms, mechanisms, and management

Clifford J Woolf, Richard J Mannion

We highlight current theories about peripheral neuropathic pain and show that progress in management is contingent on targeting treatment not at the aetiological factors or the symptoms but at the mechanisms that operate to produce the symptoms. This approach will require substantial progress in our understanding of the pathophysiology of neuropathic pain, the development of accurate diagnostic tools to discover what mechanisms contribute to the pain syndrome in an individual, and effective treatments aimed specifically at the mechanisms.

Neuropathic pain is a pathological pain

The capacity to experience pain has a protective role: it warns us of imminent or actual tissue damage and elicits coordinated reflex and behavioural responses to keep such damage to a minimum. If tissue damage is unavoidable, a set of excitability changes in the peripheral and central nervous system establish a profound but reversible pain hypersensitivity in the inflamed and surrounding tissue. This process assists wound repair because any contact with the damaged part is avoided until healing has occurred. By contrast, persistent pain syndromes offer no biological advantage and cause suffering and distress. Such maladaptive pain typically results from damage to the nervous system—the peripheral nerve, the dorsal root ganglion or dorsal root, or the central nervous system—and is known as neuropathic pain. Such syndromes comprise a complex combination of negative symptoms or sensory deficits, such as partial or complete loss of sensation, and positive symptoms that include dysaesthesia, paraesthesia, and pain.

Apart from trigeminal neuralgia, which responds well to carbamazepine,[1] pharmacotherapy for neuropathic pain has been disappointing. Patients with neuropathic pain do not respond to non-steroidal anti-inflammatory drugs and resistance or insensitivity to opiates is common. Patients are usually treated empirically with tricyclic or serotonin and norepinephrine uptake inhibitors, antidepressants, and anticonvulsants that all have limited efficacy and undesirable side-effects.[2] Neurosurgical lesions have a negligible role and functional neurosurgery, including dorsal column or brain stimulation, is controversial, although transcutaneous nerve stimulation may provide some relief. Local anaesthetic blocks targeted at trigger points, peripheral nerves, plexi, dorsal roots, and the sympathetic nervous system have useful but short-lived effects; longer lasting blocks by phenol injection or cryotherapy risk irreversible functional impairment and have not been tested in placebo-controlled trials. Chronic epidural administration of drugs such as clonidine, steroids, opioids, or midazolam is invasive, has side-effects, and the efficacy of these drugs has not been adequately assessed.

There is no treatment to prevent the development of neuropathic pain,[3] nor to adequately, predictably, and specifically control established neuropathic pain.[2,4] The aim of treatment, therefore, is often just to help the patient cope by means of psychological or occupational therapy, rather than to eliminate the pain. Thus, there is an unmet clinical need and a challenge to develop more effective therapy can be achieved only if the relation between the aetiology, mechanisms, and symptoms of neuropathic pain are understood.

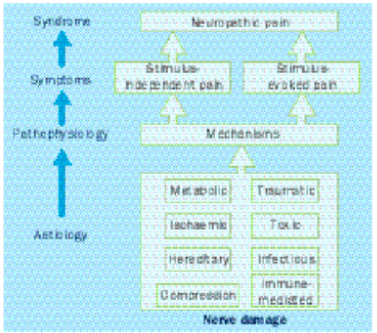


Figure 1: **Aetiology, mechanisms, and symptoms**

Aetiology of neuropathic pain

Neuropathic pain is currently classified on the basis of the aetiology of the insult to the nervous system or the anatomical distribution of the pain. Although this classification has some use for the differential diagnosis of the neuropathy, and for disease-modifying treatment if available, it offers no framework for clinical management of the pain. The relation between aetiology, mechanisms, and symptoms in this condition is complex (figure 1). The pain that manifests in diverse diseases may operate through common mechanisms. No pain mechanism is an inevitable consequence of a particular disease process; only a few patients are affected and there are no predictors to indicate which patient will develop neuropathic pain. One mechanism could be responsible for many different symptoms. Furthermore, the same symptom in two patients may be caused by different mechanisms. Finally, more than one mechanism can operate in a single patient,

Lancet 1999; **353:** 1959–64

Neural Plasticity Research Group, Department of Anesthesia and Critical Care, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA 02129, USA (Prof C J Woolf MRCP, R J Mannion PhD)

Drug treatment of neuropathic pain and new agents under development

Mechanism	Symptom	Target	Drug
Sodium-channel accumulation, redistribution, altered expression	Spontaneous pain, paraesthesia, neuroma sign	Sodium channels sensitive to tetrodotoxin Sodium channels resistant to tetrodotoxin	Sodium-channel blockers Antiepileptic agents (carbamazipine lamotrigine) Antiarrhythmic agents (mexilitine tricyclic antidepressants) Blockers with greater analgesic than anticonvulsant index* Ion-channel selective blockers†
Central sensitisation	Tactile (dynamic) hyperalgesia Cold hyperalgesia Pin-prick hyperalgesia	NMDA-R Neurokinin 1-R Neuronal nitric oxide synthase Protein kinase γ	NMDA antagonists Ketamine, dextramethorphan, amantidin Glycine site antagonists* Subunit specific antagonists† Neurokinin-1-R antagonists* Neuronal nitric oxide synthase, protein kinase C inhibitors
Peripheral sensitisation	Pressure (static) hyperalgesia Thermal hyperalgesia Spontaneous pain Neurogenic inflammation	Vanilloid receptor-1-desensitisation Neurokinin 1 Sodium channels resistant to tetrodotoxin Nerve growth factor	Capsaicin Neurokinin-1-R antagonists* Blockers of sodium channels resistant t tetrodotoxin† Nerve growth factors
α-receptor expression Sympathetic sprouting	Spontaneous pain	α-receptor antagonists Nerve growth factor/trKA	Phentolamine Guanethidine Nerve growth factor antagonists†
Increased transmision Reduced inhibition	Spontaneous pain Hyperalgesia	N-type calcium channels Receptors (MOR, α_2, GABA, neurokinin 1 adenosine, $P2X_3$, kainate, mGluR, CCK, nAChR)	Conotoxin Opiates Gabapentin Clonidine Tricyclic antidepressants SNRIs

*In clinical development. †In preclinical development.

Risk factors predictive of chronic pain after surgery CPSP

PAIN: Clinical Updates

OPEN

PAIN REPORTS

Risk stratification for the development of chronic postsurgical pain

Stephan A. Schug[a,*], Julie Bruce[b]

Keywords: Chronic postsurgical pain, Persistent postsurgical pain, Risk stratification, Genetics, Psychosocial, Surgery

The past 20 years have seen an increasing recognition of the burden of chronic pain after surgery and other trauma. There is now good evidence that chronic postsurgical pain (CPSP) is by far more common and more severe than previously thought with far-reaching consequences for quality of life and function of those affected. There are also significant implications and costs for health care systems and society as a whole.[14] **Table 1** highlights this by showing the incidence of chronic pain after a number of surgical interventions, as well as the proportion of patients who experience severe pain and the contribution of neuropathic pain features to this presentation. The wide variability of these numbers is largely due to methodological differences, caused by the use of variable definitions for chronicity, in particular regarding the time frame applied for measurement (between 2 and 12 months). Other factors include differences in study design (eg, cross-sectional, prevalence surveys or prospective surgical cohort studies), as well as variable assessment of preoperative chronic pain and measurement of postoperative pain. Attempts to standardise a definition have been based on the initial proposal by Macrae

Key Points

1. Chronic postsurgical pain (CPSP) is a common complication of surgery with important consequences for the individual patient and society as a whole.
2. Risk stratification is best defined as the grouping of patients based on factors measured at baseline (in this context before surgery), to determine an individual's risk of suffering a particular condition and thereby the likely level of need for preventive interventions.
3. Risk factors for CPSP have been identified in the preoperative, intraoperative, and postoperative periods and cover 6 broad domains: genetic, demographic, psychosocial, pain, clinical, and surgical factors.
4. Risk stratification for CPSP enables clinicians to address these risk factors before surgery, to discuss the necessity of surgery or to change the surgical and anaesthetic/analgesic planning.

Risk factors for CPSP have been identified in the; Preoperative
Intraoperative
Postoperative periods

6 broad domains:

Genetic
Demographic
Psychosocial
Pain
Clinical
Surgical factors.

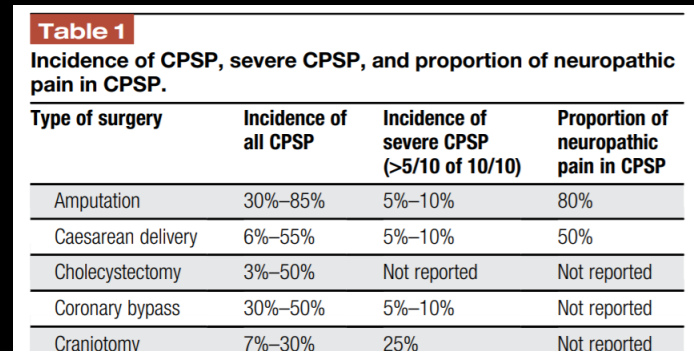
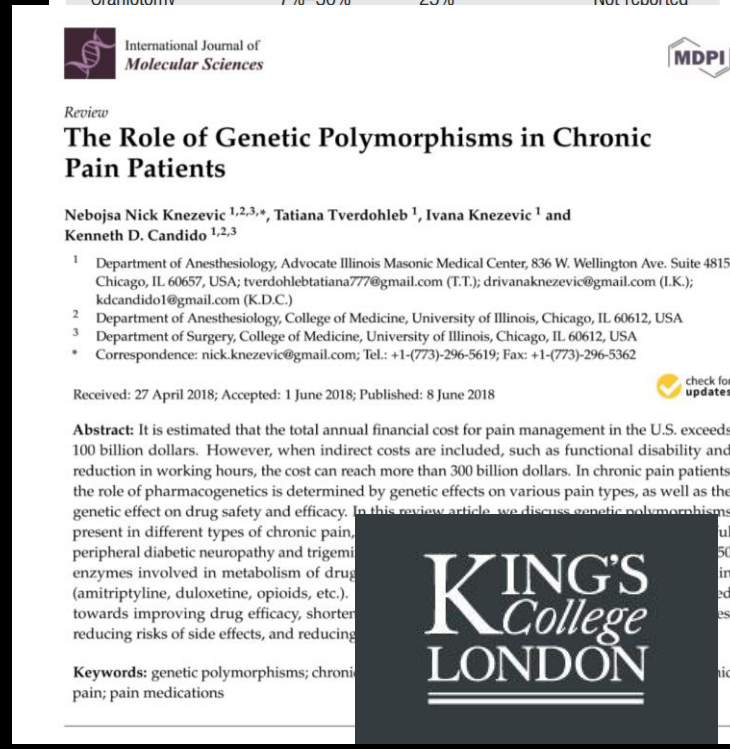


Table 1

Incidence of CPSP, severe CPSP, and proportion of neuropathic pain in CPSP.

Type of surgery	Incidence of all CPSP	Incidence of severe CPSP (>5/10 of 10/10)	Proportion of neuropathic pain in CPSP
Amputation	30%–85%	5%–10%	80%
Caesarean delivery	6%–55%	5%–10%	50%
Cholecystectomy	3%–50%	Not reported	Not reported
Coronary bypass	30%–50%	5%–10%	Not reported
Craniotomy	7%–30%	25%	Not reported



International Journal of *Molecular Sciences*

MDPI

Review

The Role of Genetic Polymorphisms in Chronic Pain Patients

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Abstract: It is estimated that the total annual financial cost for pain management in the U.S. exceeds 100 billion dollars. However, when indirect costs are included, such as functional disability and reduction in working hours, the cost can reach more than 300 billion dollars. In chronic pain patients the role of pharmacogenetics is determined by genetic effects on various pain types, as well as the genetic effect on drug safety and efficacy. In this review article, we discuss genetic polymorphisms present in different types of chronic pain, peripheral diabetic neuropathy and trigemi enzymes involved in metabolism of drug (amitriptyline, duloxetine, opioids, etc.). towards improving drug efficacy, shorter reducing risks of side effects, and reducing

Keywords: genetic polymorphisms; chroni pain; pain medications

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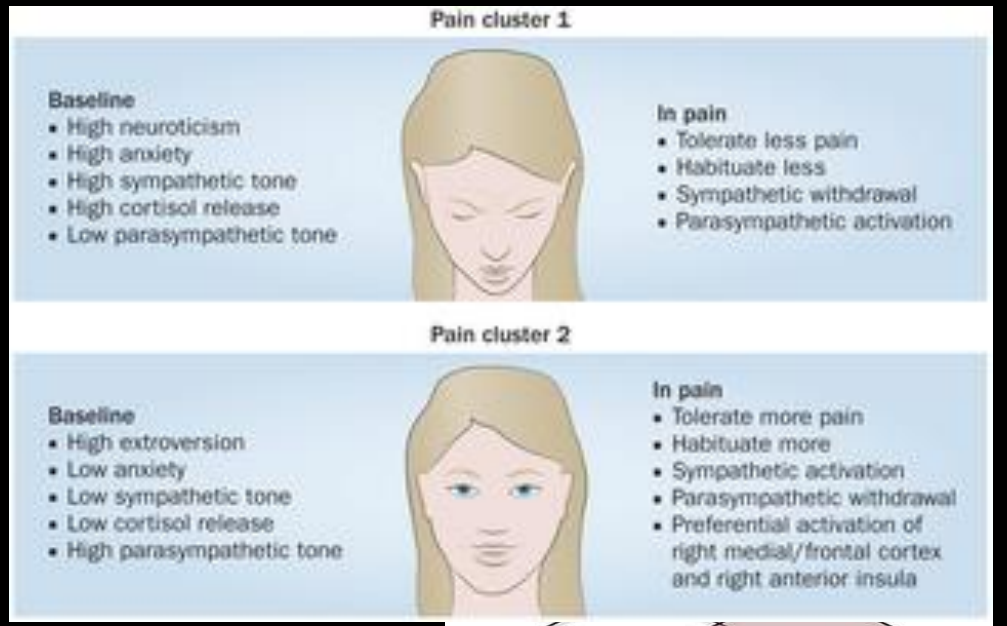
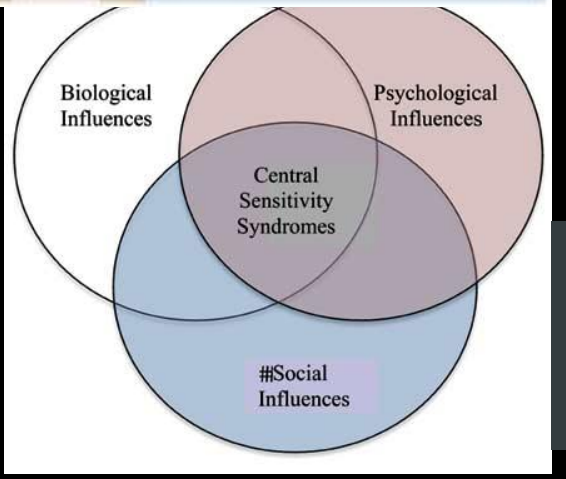
Risk factors predictive of CPSP
Psychosocial

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

- 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





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Axis 2
Assessment of preceding and injury related psychological problems

- NEW
- All patients:
  - **GAD7 generalised anxiety disorder**
  - **PHQ9 Patient Health Questionnaire**
  - **PHQ 15 MULTIDIMENSIONAL SCALE OF PERCEIVED SOCIAL SUPPORT**
  - **GCPS**
  - SF-MPQ-2 Short-form McGill Pain Questionnaire-2
  - PAIN DETECT PAIN QUESTIONNAIRE Ne pain
  - BPI Facial pain
  - CPSI (sleep)
  - ES-R (abuse)

- Dash board with red flags suicidal thoughts/ depression, anxiety and somatic disorders

- QLD

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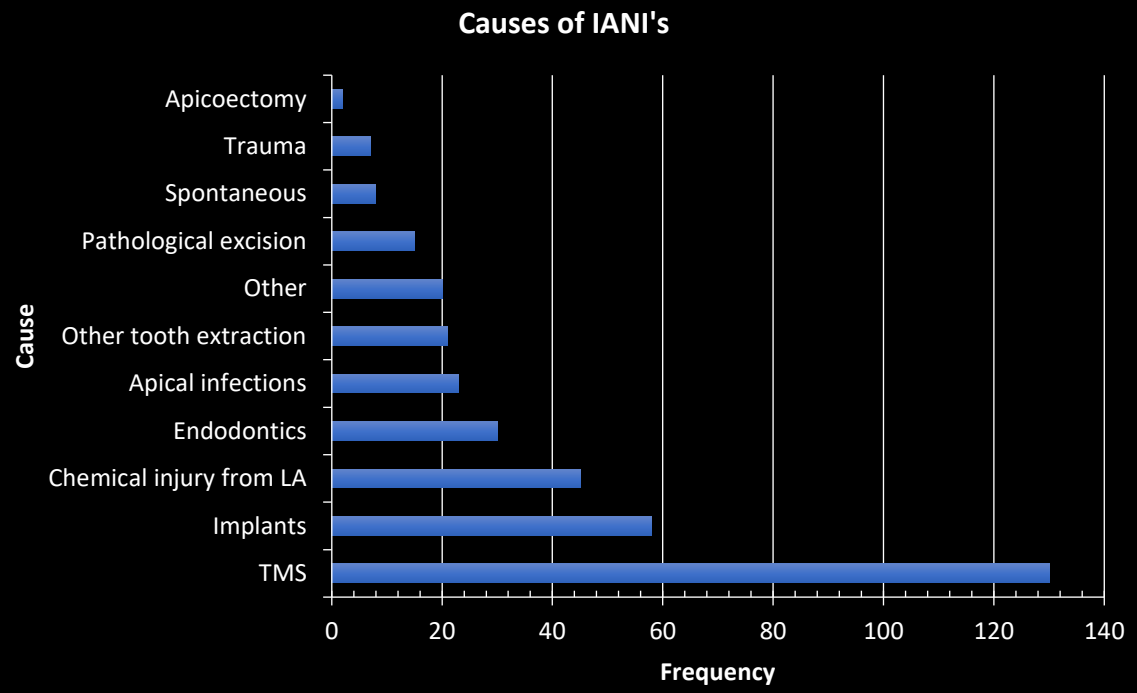
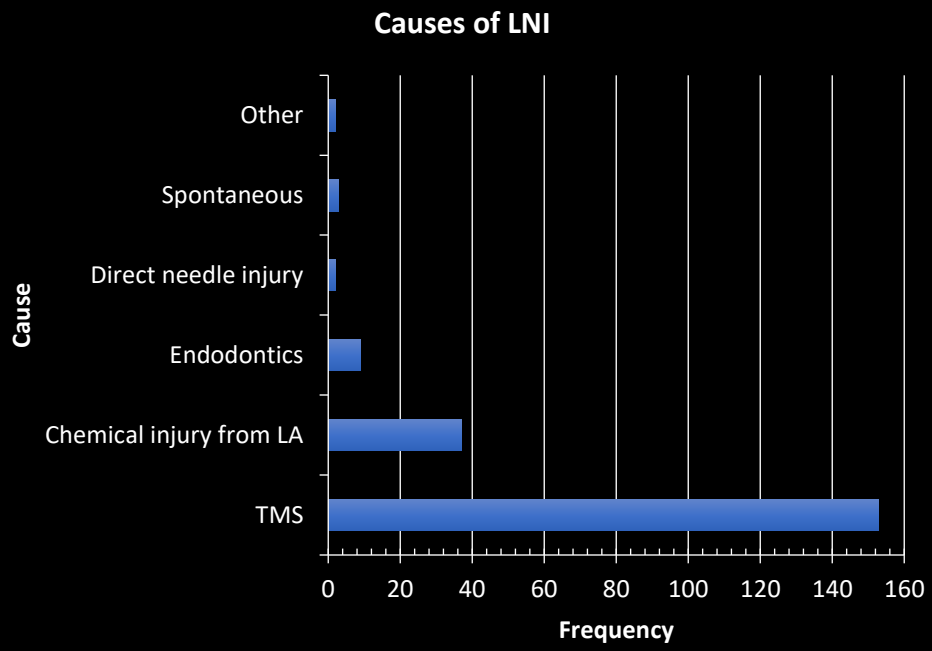
Causes of nerve injuries related to dentistry





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

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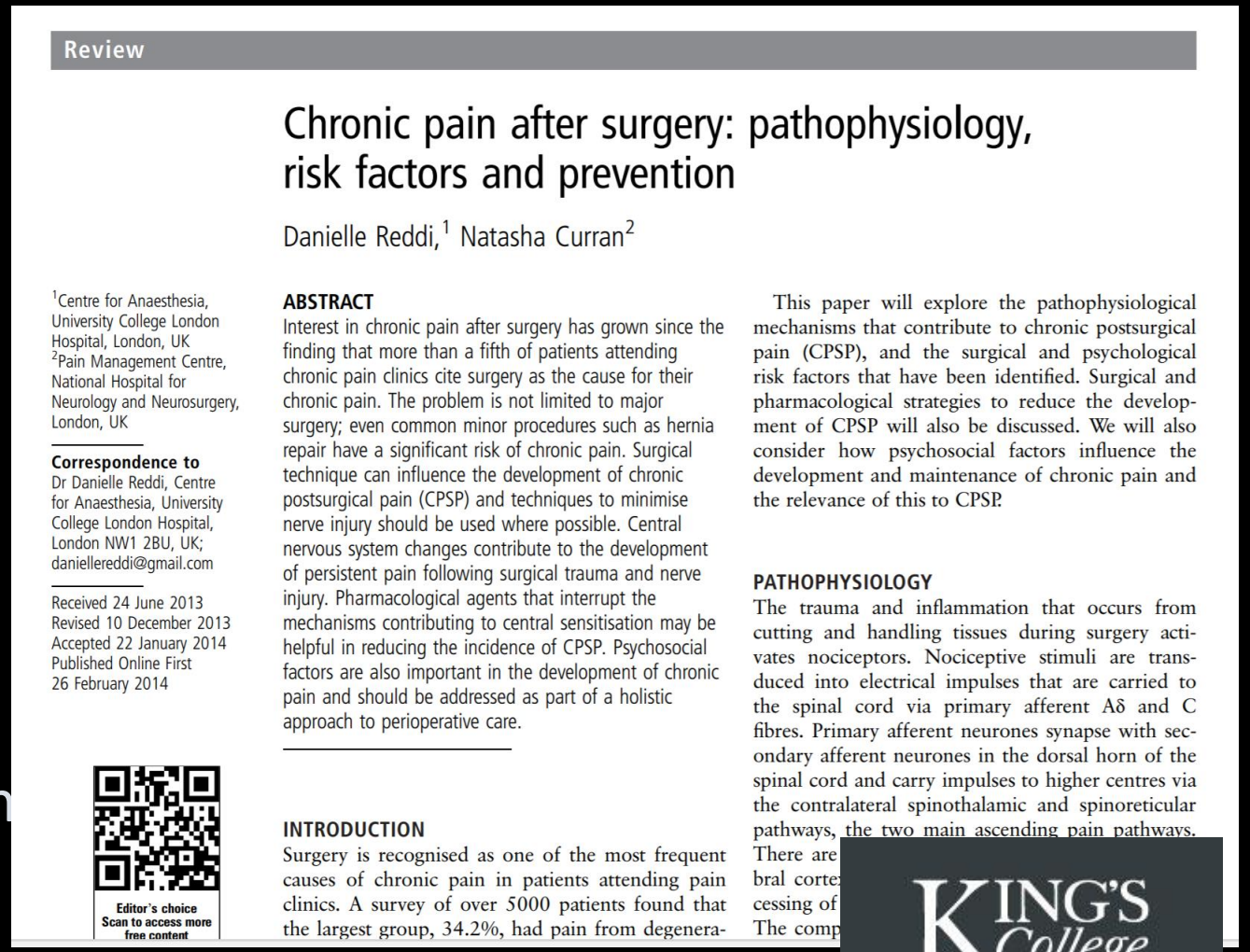
Risk factors predictive of CPSP
SURGICAL

Minimise Surgical risks

- **Patient younger age**
- minimal access
- Duration
- Site
- Use of Local anaesthesia
- Perioperative pain managemen



Review

Chronic pain after surgery: pathophysiology, risk factors and prevention

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ABSTRACT
Interest in chronic pain after surgery has grown since the finding that more than a fifth of patients attending chronic pain clinics cite surgery as the cause for their chronic pain. The problem is not limited to major surgery; even common minor procedures such as hernia repair have a significant risk of chronic pain. Surgical technique can influence the development of chronic postsurgical pain (CPSP) and techniques to minimise nerve injury should be used where possible. Central nervous system changes contribute to the development of persistent pain following surgical trauma and nerve injury. Pharmacological agents that interrupt the mechanisms contributing to central sensitisation may be helpful in reducing the incidence of CPSP. Psychosocial factors are also important in the development of chronic pain and should be addressed as part of a holistic approach to perioperative care.

INTRODUCTION
Surgery is recognised as one of the most frequent causes of chronic pain in patients attending pain clinics. A survey of over 5000 patients found that the largest group, 34.2%, had pain from degenera-

This paper will explore the pathophysiological mechanisms that contribute to chronic postsurgical pain (CPSP), and the surgical and psychological risk factors that have been identified. Surgical and pharmacological strategies to reduce the development of CPSP will also be discussed. We will also consider how psychosocial factors influence the development and maintenance of chronic pain and the relevance of this to CPSP.

PATHOPHYSIOLOGY
The trauma and inflammation that occurs from cutting and handling tissues during surgery activates nociceptors. Nociceptive stimuli are transduced into electrical impulses that are carried to the spinal cord via primary afferent Aδ and C fibres. Primary afferent neurones synapse with secondary afferent neurones in the dorsal horn of the spinal cord and carry impulses to higher centres via the contralateral spinothalamic and spinoreticular pathways, the two main ascending pain pathways. There are
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Australian Endodontic Journal
The Journal of the Australian Society of Endodontology Inc., the Australian and New Zealand Academy of Endodontists and the Asian Pacific Endodontic Confederation

Aust Endod J 2017; 43: 56–65

ORIGINAL RESEARCH

Mandibular division trigeminal nerve injuries following primary endodontic treatment. A case series

Maria Devine, BDS, MFDS (RCS Ed), M Oral Surg, FHEA*; Omesh Modgill, BDS, MFDS (RCS Ed); and Tara Renton, PhD, MDSc, BDS, FDS, RCS, FRACDS (OMS), FHEA

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Keywords
injury, neurogenic, neuropathy, neurosensory, paraesthesia, trigeminal nerve.

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doi: 10.1111/aej.12209

(Accepted for publication 29 May 2017.)

Abstract

The aim of this study is to report a series of patients with mandibular division trigeminal nerve (V_3) injuries secondary to endodontic treatment, evaluate presentation characteristics and identify prevention strategies. This article describes a retrospective review of patients referred to a tertiary clinic 2007–2015 with V_3 injury following endodontic treatment. The sample in male and 16 female patients with a mean age of 41.5 years. Sixteen sented following endodontic treatment of the first and second molar teeth in eight cases and canine in two cases. Fifteen patients reporte ate post-operative symptoms, in eleven cases there was a 24–48 tomatic period. The average referral delay was 23.1 months. Twen had permanent neuropathy. Four patients experienced resolution of within 8 weeks. V_3 injury following endodontic treatment is rar result in permanent neuropathy and functional impairment. Th avoided through comprehensive pre-operative radiographic exa identification and referral of high-risk cases.

Introduction

Injury to the mandibular division of the trigeminal nerve (V_3) is a rare but serious complication of endodontic treatment of mandibular teeth. Endodontic treatment success depends on a number of factors including pre-operative vitality of the tooth, presence and size of a peri-apical lesion, over or under filling of the root canal and provision of an adequate coronal sealing restoration (1). The success rate of primary endodontic treatment in published research is reported to range from 68% to 85% and in United Kingdom general dental services is estimated to be 74% (2).

The inferior alveolar nerve (IAN) is at risk from a variety of dental procedures, in that the IAN is contained within a bony canal; predisposing it to both direct trauma and ischaemia. IAN injury can be caused by many dental and maxillofacial procedures including extraction of mandibular third molar teeth, mandibular local anaesthetic block administration, mandibular implant placement, mandibular fracture fixation and orthognathic surgery (3). Endodontic therapy is one of the rarer causes of IAN injury, however, there have been a number of case reports and case series of this complica lished. In teeth in close proximity to the IA mental foramen, there is a risk of direct inju nerve due to instrumentation beyond the apex injury through leakage of endodontic medica sealants through the apex of the tooth into th indirect injury due to compression of the nerv ration materials (4). Most cases have been r connection with the lower second molars, related to the first molars and the premolars been reported (5).

Many authors recommend referral of nerv after 6 months (6), however, this may be to now understand that after 3 months, permane changes occur within the nervous system sub injury, which are unlikely to respond to surg vention (7).

We undertook evaluation of the V_3 injury ca by endodontic treatment in a sample of patie the nerve injury clinic at Kings College Lond Institute. We aimed to evaluate their presenta acteristics and identify possible strategies for and management.

Clin Oral Invest (2015) 19:149–157
DOI 10.1007/s00784-014-1222-5

ORIGINAL ARTICLE

Trigeminal nerve injuries after mandibular oral surgery in a university outpatient setting—a retrospective analysis of 1,559 cases

Herbert Deppe · Thomas Mücke · Stefan Wagenpfeil · Marco Kesting · Eva Linsenmeyer · Thomas Tölle

Received: 11 March 2013 / Accepted: 3 March 2014 / Published online: 16 March 2014

Abstract

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evaluated by the authors and 12 were interviewed by phone and observed by their dentist without any problems. Persistence of sensory disturbance was found in 5 of the 21 patients (0.32 %), and four of these five lesions were in the lingual nerve (0.25 %). Related to the type of surgery, most sensory disturbances were seen following periradicular surgery.

Discussion Within the limitations of this study, it may be stated that oral surgery in an outpatient setting of a teaching university hospital resulted in very low rates of trigeminal nerve injuries. It may be concluded that adequately surveyed trainees can perform mandibular surgery without an increased risk of trigeminal sensorial disturbance.

Keywords Oral surgery · Nerve injury · Sensory disturbance

Introduction

ID

Neurosensory Disturbance of the Inferior Alveolar Nerve After 3025 Implant Placements

Antonio Scarano, MD, DDS,* Bruna Sinjari, DDS,† Giovanna Murmura, DDS,‡ and Felice Lorusso, DDS†

Purpose: *The aim of this retrospective study was to evaluate the incidence of inferior alveolar nerve (IAN) lesion and duration of sensitivity disturbances after the insertion of dental implants.*

Methods: *One thousand sixty-five patients (mean age: 58.9 years) enrolled between February 2004 and July 2015 with partial or full mandibular edentulism were selected to receive dental implants for oral rehabilitation. A total of 3025 implants were placed. After surgical procedures, controls were scheduled at suture removal, that is, 10 days after surgery, and repeated at intervals of 1, 3, and 6 months, and comprised patient interview, clinical examination, and sensitivity tests.*

Results: *Only 23 (2.2%) of the 1065 patients presented sensitivity disturbances 1 month after implant insertion, and only 2 (0.19%) after 6 months, though a complete recovery was observed in these patients within 13 months.*

Conclusions: *Considering the debilitating effects resulting from IAN lesion and the complexity of the therapeutic diagnostic protocols, all patients undergoing oral rehabilitation through dental implants should be evaluated with CBCT imaging. (Implant Dent 2017;26:735–743)*

Key Words: dental implants, peripheral nerve injuries, iatrogenic lesion, sensitivity disorders

The loss or functional insufficiency of bone tissue represents one of the most frequent problems in implant prosthetic rehabilitation in the posterior mandible. To avoid these problems, different regenerative surgical techniques have been developed: conventional onlay/inlay grafts, interpositional sandwich osteotomies, guided bone regeneration with semipermeable membranes, piezoelectric stimulation, and alveolar distraction osteogenesis procedures.[1–3] Mandibular bone atrophy makes it more susceptible to invasion of the inferior alveolar nerve (IAN) during implant site preparation and during implant placement.[4,5] Iatrogenic injury to the IAN is an important clinical eventuality that may occur during implantology, with postoperative dysesthesia in a range between 1.7% and 43.5%, and permanent sensory disturbance (after more than 1 year) of 5% to 15%.[6,7]

*Professor, Department of Medical, Oral and Biotechnological Sciences, CeSI-Met University "G. D'Annunzio" of Chieti-Pescara, Chieti, Italy.
†Resident, Department of Medical, Oral and Biotechnological Sciences, University "G. D'Annunzio" of Chieti-Pescara, Chieti,

The IAN lesion in implantology can be related to direct and indirect different pathogenetic mechanisms that may overlap:

1. direct compression determined by the dental implant penetrating into
5. stretching due to mishandling of the mental nerve (with elongation greater than 20%) during flap dissection or maneuvering of IAN transposition in edentulous mandibular saddles with strong alveolar bone resorption.

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Diagnosis PTNP

- 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.
- 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 pain
- 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

- 1. Tests that confirm a relevant lesion or disease affecting the trigeminal nerve may, for example, be surgical or radiological confirmation of nerve compression or lesion, nerve conduction study, laser-evoked potentials, blink reflex or skin biopsy confirmation of reduced nerve fibre terminals. Positive findings in these investigations may provide important diagnostic hints at the source of pain. However, all clinical and diagnostic aspects of the pain need to be considered.
- 2. The severity of nerve injuries may range from mild to severe. They include external trauma and iatrogenic injuries from dental treatments such as local anaesthetic injections, root canal therapies, extractions, oral surgery, dental implants, orthognathic surgery and other invasive procedures.
- 3. Specifically following radiation-induced postganglionic injury, neuropathic pain may appear after >3 months.
- 4. Somatosensory symptoms or signs may be negative (e.g. hypaesthesia and/or hyperalgesia) and/or positive (e.g. hyperalgesia and/or allodynia). Note that positive somatosensory signs are not specific to neuropathy. Negative or positive somatosensory signs consistent with the distribution of the pain may be sufficient to indicate the presence of a lesion of the trigeminal nerve. The clinical examination is supplemented by laboratory tests.

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

Treatment not working?

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

Behaviour…retire to dark room and lie down

TREAT Migraine

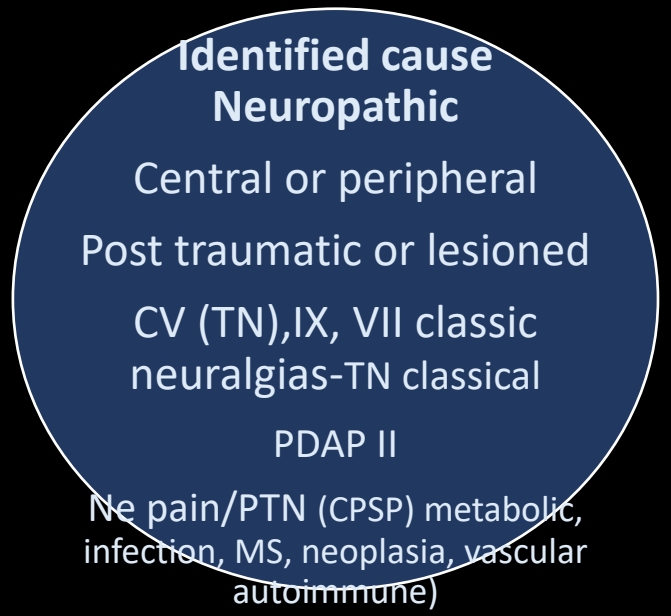
- Exclude autonomic symptoms
  - Red eye conjunctival irritation
  - Tearing
  - Nasal congestion
  - Facial flushing
  - Drooping eyelid (Ptosis)
  - Enlarged pupil (Meiosis)

Behaviour…aggressive irritated restless

TREAT TAC

Secondary Neuropathic pain

- Central
  - TN classical or non classical
    - Vascular compromise, MS, SOL
    - Stroke, IC bleed
- Peripheral -Disease / Lesioned
  - Traumatic
    - *Chemical – chemotherapy, Endodontic treatments*
    - *Thermal*
    - *Radiation p-ost irradiation*
    - *Mechanical trauma*
      - *Chronic post surgical pain, Phantom limb pain, spinal cord injury, trauma and postoperative neuropathic pain,*
      - *Post Traumatic pain Complex regional pain syndromes (CRPSs) (principally type 1)*
      - *PDAP II*

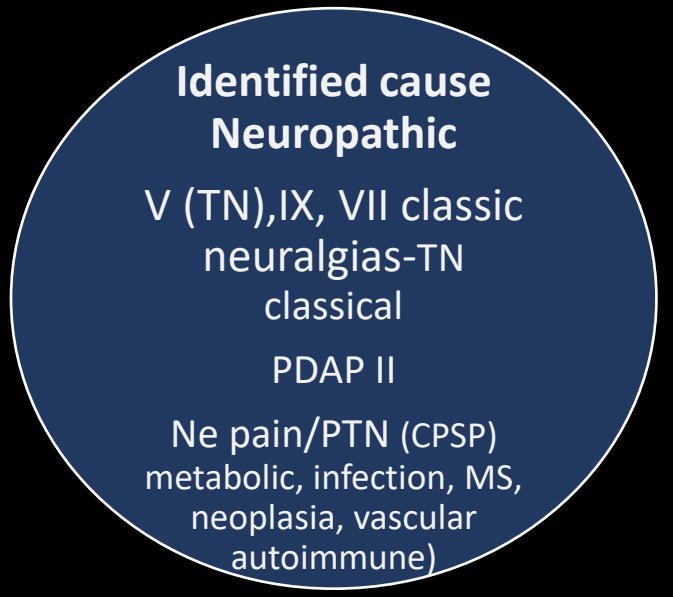


Neoplasia
- benign or malignant

Systemic disease
- DM
- Hypothyroid
- MS, sickle cell

Infection
- Herpes
- Periapical infection
- OM, ORN and ON

Secondary neuropathic pain peripheral lesional

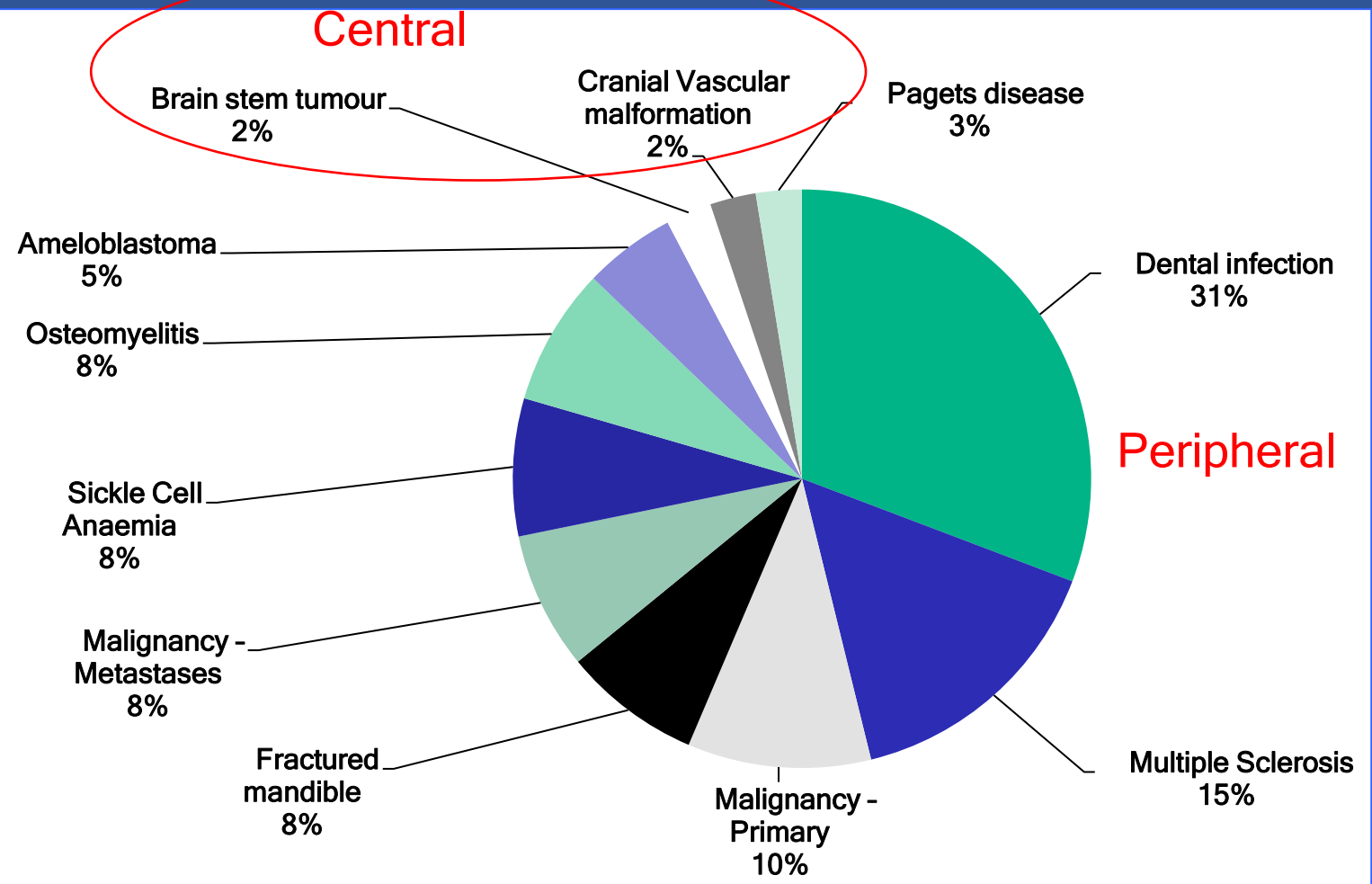


Nutritional deficiencies
Fe, Ferritin, Zinc, Magnesium,
Vit B complex, D, E
Malignancy
Compression by a space occupying lesion centrally or peripherally NEOPLASIA
Metabolic Acromegaly, Hormonal neuropathy (Hypothyroidism, Diabetes),
Infarction (sickle cell hypoxic neural damage, giant cell arteritis)
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

Non Traumatic TNP

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



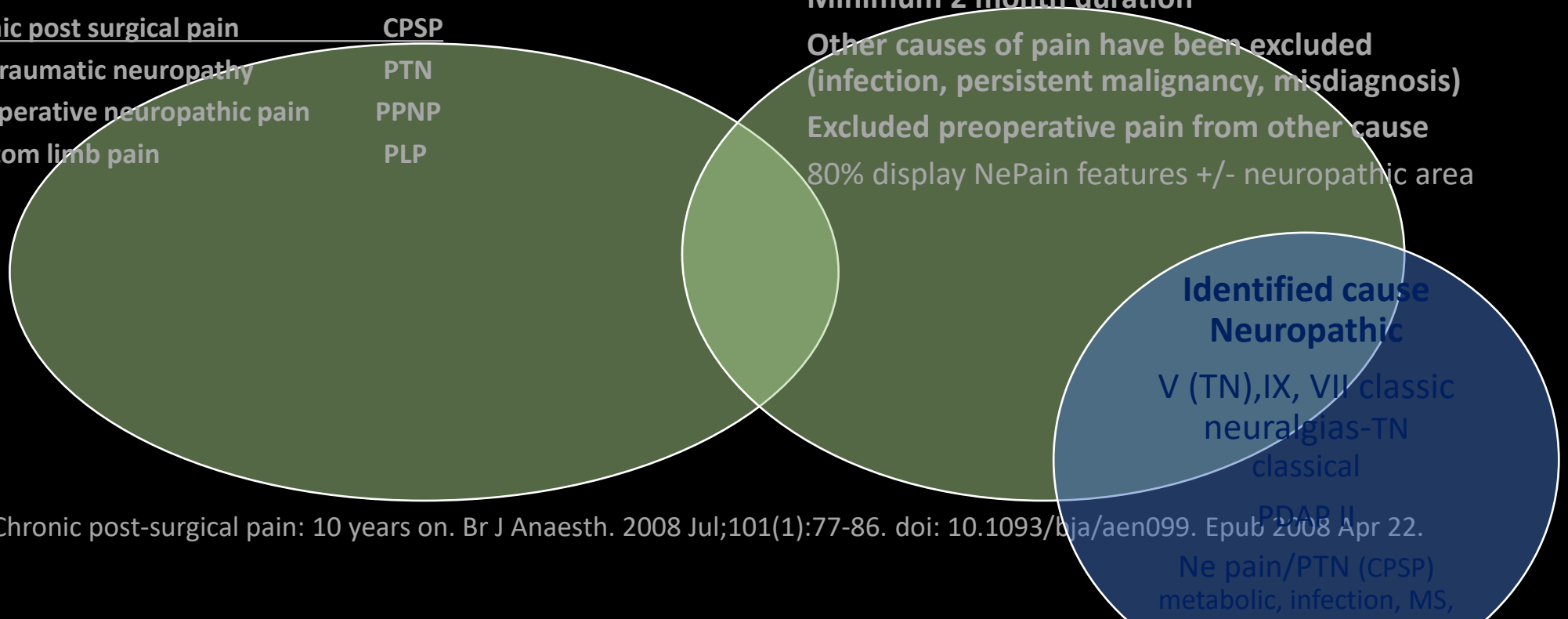
An update on the causes, assessment and management of third division sensory trigeminal neuropathies.Carter E, Yilmaz Z, Devine M, Renton T. Br Dent J. 2016 Jun 24;220(12):627-35. doi: 10.1038/sj.bdj.2016.444

Chronic post surgical pain?

- Chronic pain after surgery is a well recognised problem and affects upwards of 20-30% of patients undergoing limb amputation, thoracotomy and breast surgery.
- There is confusing nomenclature for surgical induced pain without identifiable neuropathy and nerve damage these include:

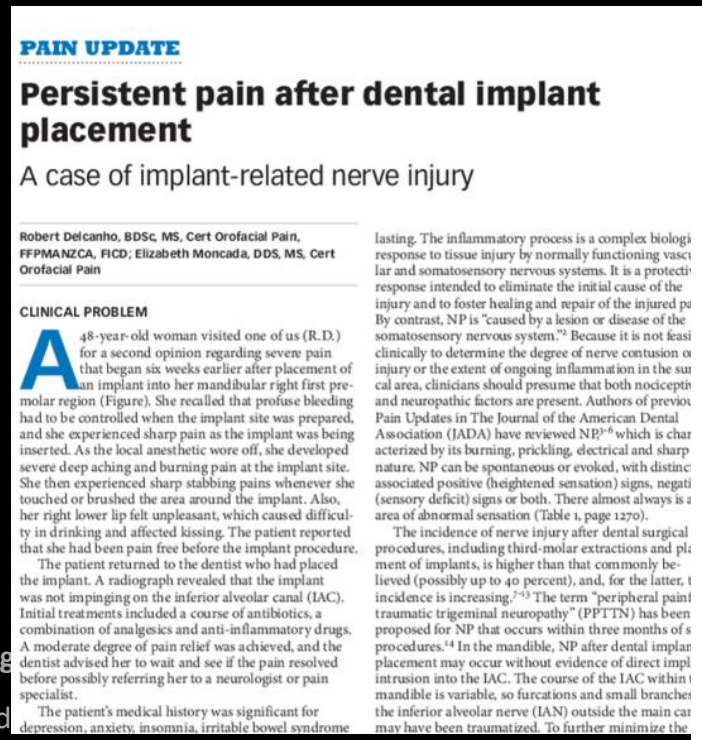
Surgically induced neuropathic pain	**SNPP**
Chronic post surgical pain	**CPSP**
Post traumatic neuropathy	**PTN**
Postoperative neuropathic pain	**PPNP**
Phantom limb pain	**PLP**

- Over the last 10 years it has become evident that significant numbers of patients suffer from chronic pain as a result of routine surgery with over 30-40% of patients presenting in chronic pain clinics being diagnosed with CPSP. Macrae (2008) suggested a definition including;
  - **Pain developed after surgery**
  - **Minimum 2 month duration**
  - **Other causes of pain have been excluded (infection, persistent malignancy, misdiagnosis)**
  - **Excluded preoperative pain from other cause**
  - 80% display NePain features +/- neuropathic area



Macrae WA1 Chronic post-surgical pain: 10 years on. Br J Anaesth. 2008 Jul;101(1):77-86. doi: 10.1093/bja/aen099. Epub 2008 Apr 22.

CPSP after Dentistry



PAIN UPDATE

Persistent pain after dental implant placement

A case of implant-related nerve injury

Robert Delcanho, BDSc, MS, Cert Orofacial Pain, FFPMANZCA, FICD; Elizabeth Moncada, DDS, MS, Cert Orofacial Pain

CLINICAL PROBLEM

A 48-year-old woman visited one of us (R.D.) for a second opinion regarding severe pain that began six weeks earlier after placement of an implant into her mandibular right first premolar region (Figure). She recalled that profuse bleeding had to be controlled when the implant site was prepared, and she experienced sharp pain as the implant was being inserted. As the local anesthetic wore off, she developed severe deep aching and burning pain at the implant site. She then experienced sharp stabbing pains whenever she touched or brushed the area around the implant. Also, her right lower lip felt unpleasant, which caused difficulty in drinking and affected kissing. The patient reported that she had been pain free before the implant procedure.

The patient returned to the dentist who had placed the implant. A radiograph revealed that the implant was not impinging on the inferior alveolar canal (IAC). Initial treatments included a course of antibiotics, a combination of analgesics and anti-inflammatory drugs. A moderate degree of pain relief was achieved, and the dentist advised her to wait and see if the pain resolved before possibly referring her to a neurologist or pain specialist.

The patient's medical history was significant for depression, anxiety, insomnia, irritable bowel syndrome

lasting. The inflammatory process is a complex biologi response to tissue injury by normally functioning vascu lar and somatosensory nervous systems. It is a protecti response intended to eliminate the initial cause of the injury and to foster healing and repair of the injured pa By contrast, NP is "caused by a lesion or disease of the somatosensory nervous system."[2] Because it is not feasi clinically to determine the degree of nerve contusion o injury or the extent of ongoing inflammation in the su cal area, clinicians should presume that both nociceptiv and neuropathic factors are present. Authors of previou Pain Updates in The Journal of the American Dental Association (JADA) have reviewed NP,[3–6] which is char acterized by its burning, prickling, electrical and sharp nature. NP can be spontaneous or evoked, with distinc associated positive (heightened sensation) signs, negati (sensory deficit) signs or both. There almost always is a area of abnormal sensation (Table 1, page 1270).

The incidence of nerve injury after dental surgical procedures, including third-molar extractions and pla ment of implants, is higher than that commonly be- lieved (possibly up to 40 percent), and, for the latter, t incidence is increasing.[7–13] The term "peripheral painf traumatic trigeminal neuropathy" (PPTTN) has been proposed for NP that occurs within three months of s procedures.[14] In the mandible, NP after dental implan placement may occur without evidence of direct impl intrusion into the IAC. The course of the IAC within t mandible is variable, so furcations and small branches the inferior alveolar nerve (IAN) outside the main can may have been traumatized. To further minimize the

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Persistent Pain after Dental Surgery

Tara Renton, BDS MDSc PhD FDS RCS FRACDS (OMS) ILTM, Professor in Oral Surgery[1]

Journal List › Rev Pain › v.5(1); 2011 Mar › PMC4590080

REVIEWS IN PAIN

Rev Pain. 2011 Mar; 5(1): 8–17. PMCID: PMC4590080
doi: 10.1177/204946371100500103

Persistent Pain after Dental Surgery

Tara Renton, BDS MDSc PhD FDS RCS FRACDS (OMS) ILTM

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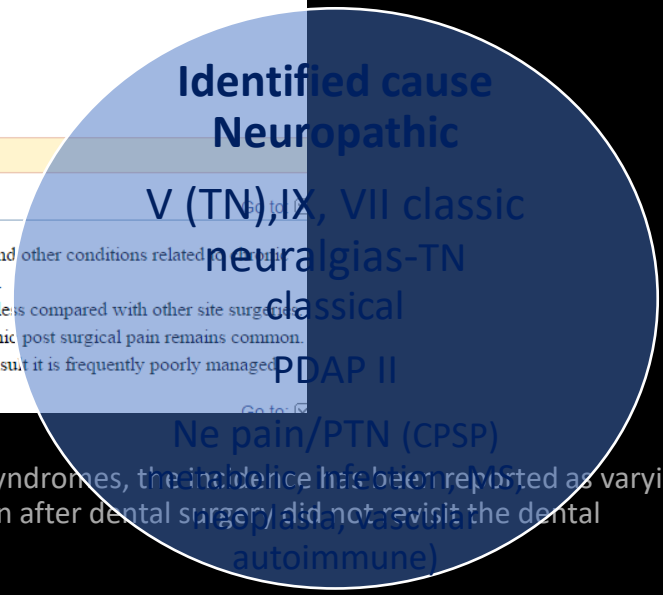
Abstract

- This article aims to cover post surgical trigeminal neuropathy and other conditions related to orofa trigeminal pain not specifically covered elsewhere in this series.
- Is estimated to occur in 4–5% of patients overall, considerably le s compared with other site surgeries
- Due to the high volume surgery undertaken in this region chronic post surgical pain remains common.
- Relatively few clinicians are aware of this condition and as a resu t it is frequently poorly managed

Introduction

Go to: ☒

Rev Pain



Identified cause Neuropathic

V (TN), IX, VII classic neuralgias-TN classical

PDAP II

Ne pain/PTN (CPSP)

metabolic, infection, MS, neoplasia, vascular, autoimmune)

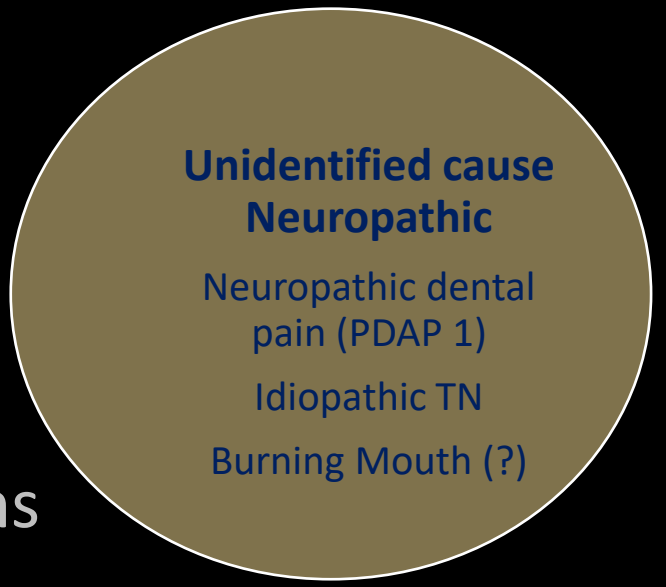
Chronic pain after dental surg

Two distinct chronic pain synd

- Persistent dentoalveolar pain =post-traumatic dysaesthesia
- Phantom tooth pain. The incidence of phantom tooth pain after endodontic therapy has been reported as 3%. For other pain syndromes, the incidence has been reported as varying from 5% to 13%. An interesting finding from the study by Lobb and colleagues was that most patients who suffered chronic pain after dental surgery did not revisit the dental surgeon. This does suggest that many dental surgeons will be underestimating the morbidity of the procedures.

Lobb WK, Zakariasen KL, McGrath PJ. Endodontic treatment outcomes: do patients perceive problems? J Am Dent Assoc 1996; 127: 597–600: Marbach JJ, Hulbrook J, Hohn C, Segal AG. Incidence of phantom tooth pain: an atypical facial neuralgia. Oral Surg Oral Med Oral Pathol 1982; 53: 190–3: Campbell RL, Parks KW, Dodds RN. Chronic facial pain associated with endodontic therapy. Oral Surg Oral Med Oral Pathol 1990; 69: 287–90: Gay-Escoda C[1], Párraga-Manzol G[2], Sánchez-Torres A[2], Moreno-Arias G[3]. Chronic neuropathic facial pain after intense pulsed light hair removal. Clinical features and pharmacological management.J Clin Exp Dent. 2015 Oct 1;7(4):e544-7. doi: 10.4317/jced.52520. eCollection 2015.

Neuropathic pain or toothache?
Idiopathic neuropathic pain



- Congenital neuropathic pain conditions
- Persistent idiopathic orofacial pain?
- Burning Mouth Syndrome
- Idiopathic Trigeminal neuralgia
- Primary neuropathic pain in intraoral region =
  - Pre TN
  - Pre Tic
  - Persistent dentoalveolar pain
    - PDAP 1
    - = Atypical odontalgia

Pain history SOCRATES

- Site - Where is the pain? Or the maximal site of the pain.
- **Onset - When did the pain start, and was it sudden or gradual?** Include also whether if it is progressive or regressive.
- **C**haracter - What is the pain like? An ache? Stabbing?
- **R**adiation - Does the pain radiate anywhere? (See also Radiation.)
- **A**ssociations - Any other signs or symptoms associated with the pain?
- **T**ime course - Does the pain follow any pattern?
- **E**xacerbating/Relieving factors - Does anything change the pain?
- Severity - How bad is the pain?

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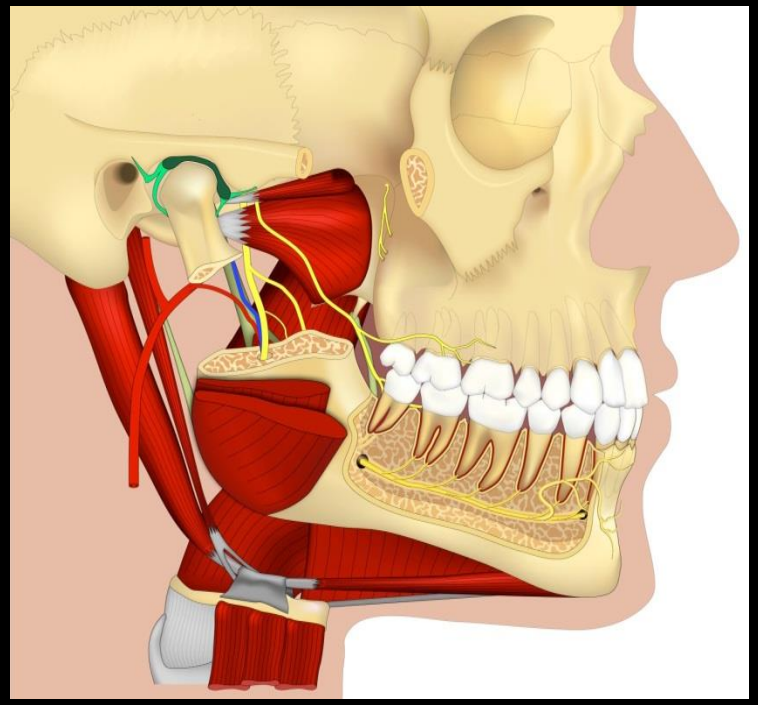
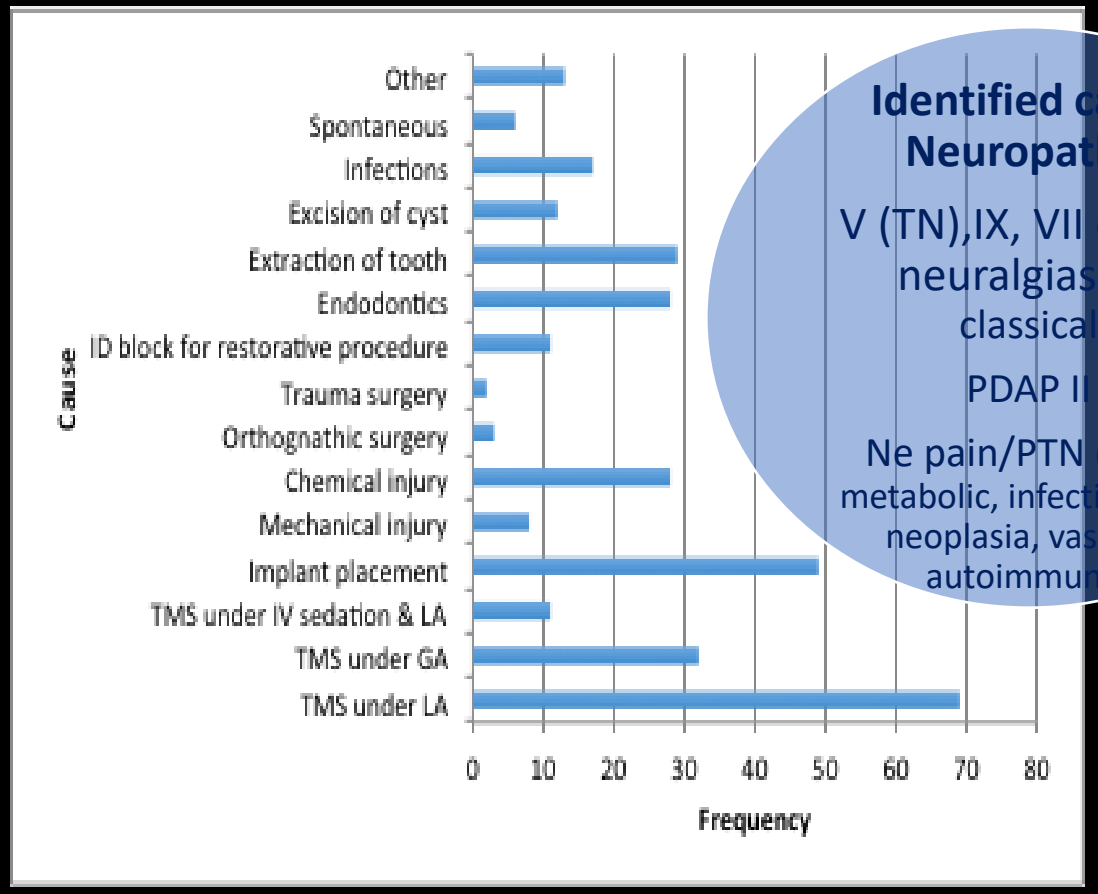
Dental causes of Trigeminal Post Traumatic Neuropathy (+/- pain)



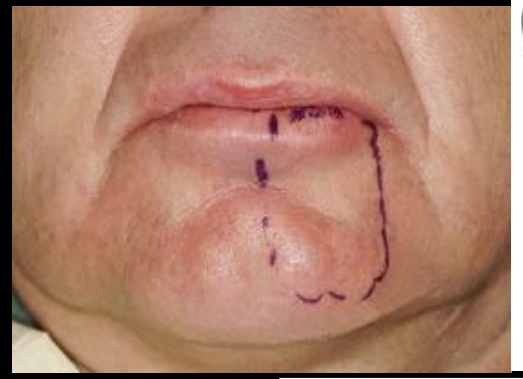


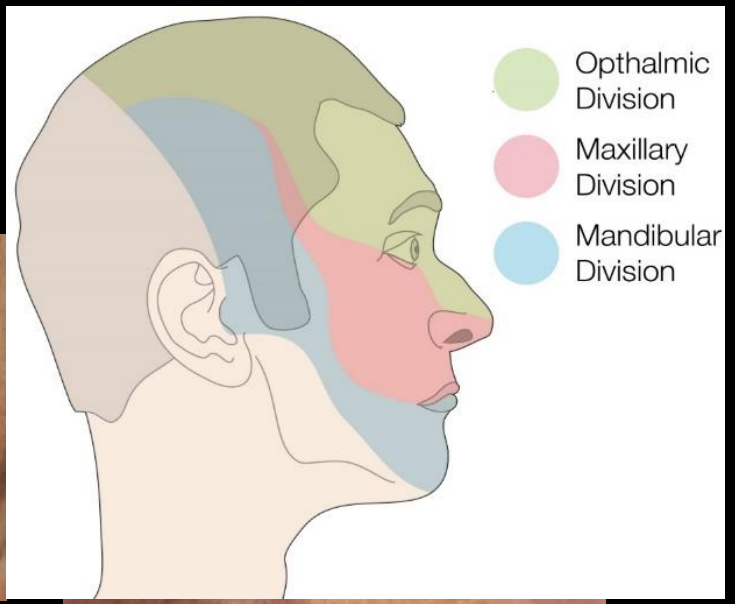
Summary of 535 TNIs assessed by TR 2016

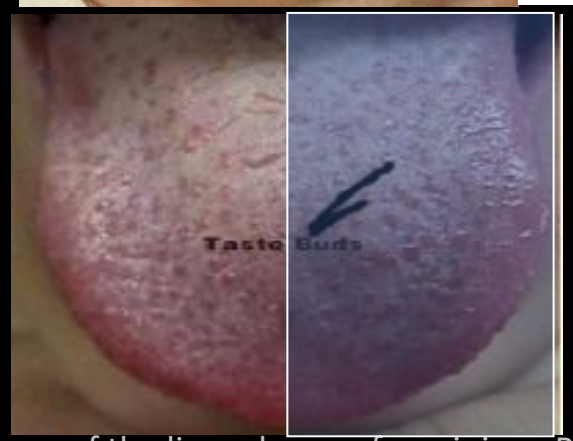
Management of nerve injury

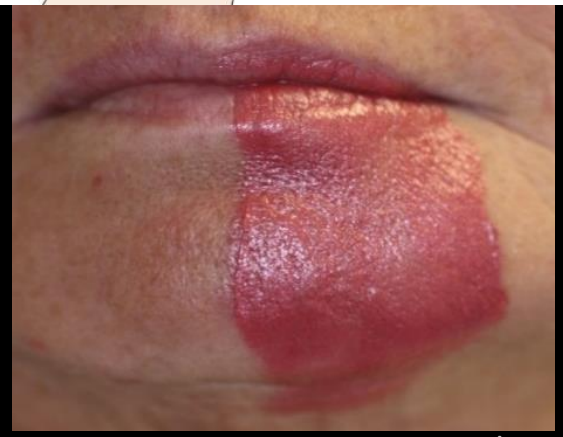
Confirm Nerve injury / Neuropathy

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









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 Surg. 2005 Jun;43(3):238-45. **Renton T**, Thexton A, Mcgurk M. Objective evaluation of iatrogenic lingual nerve injuries using the jaw-opening reflex. Br J Oral Maxillofac Surg. 2005 Jun;43(3):232-8

Consequences

Presentation Features of neuropathic pain

Neuropathic area with

Pain

Allodynia pain with non noxious stimulus

pain on touch/cold/hot

- **70% mechanical allodynia**
- **Cold allodynia a particular feature of extra oral dermatome in patients with IANIs**
- **Some LNI patients report tastent and warm allodynia**

Hyperpathia

pain continues when stimulus removed **54% patients**

Hyperalgesia (mechanical +/- thermal)

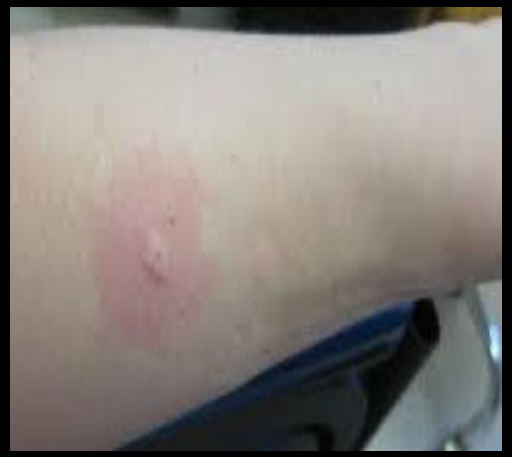
increased pain to painful stimulus **48% of patients**

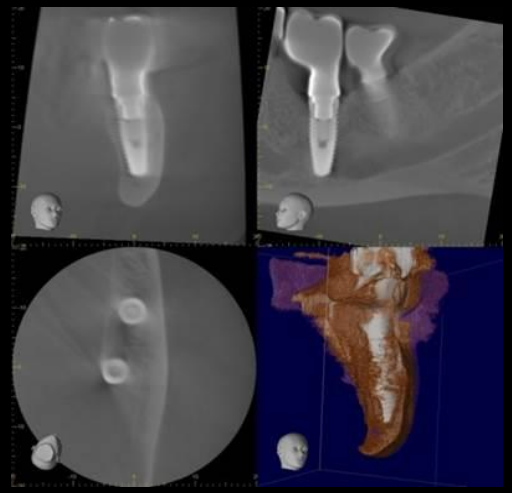
Altered sensation -Hyperaesthesia

- Paraesthesia –pins and needles, formication, many descriptions
- Dysaesthesia – uncomfortable sensations often burning

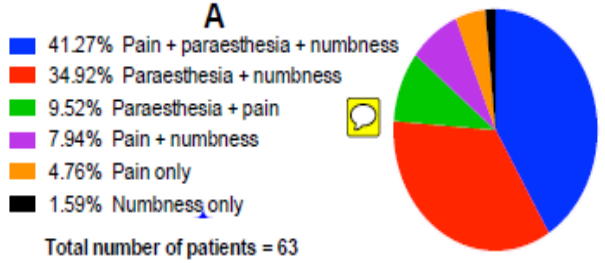
Anaesthesia -Numbness- **hypo aesthesia**

Wheal and flare





Neuropathic pain in 60 patients post implant nerve injury



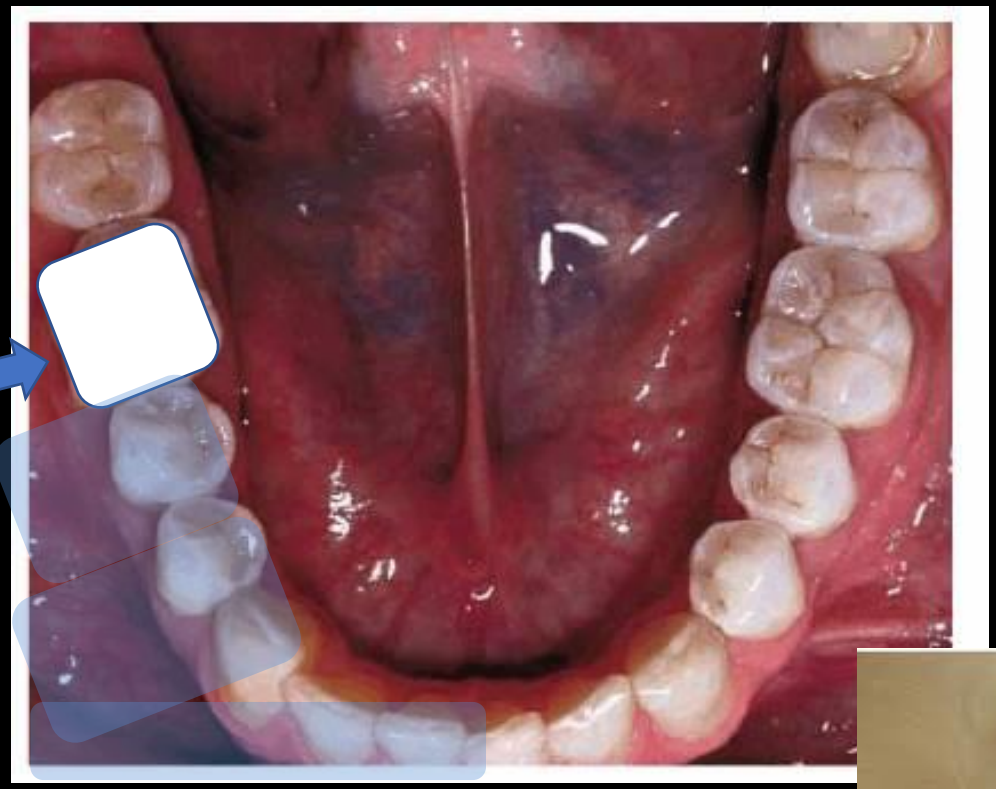
Neuropathic pain in;
95% of implant patients
92% of endodontic nerve injuries
57% of wisdom tooth surgery
IANI> LNI

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

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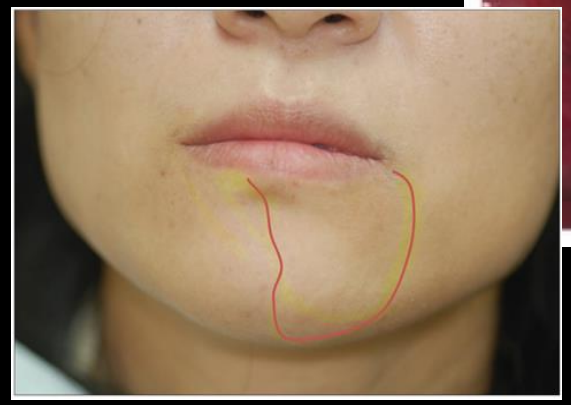
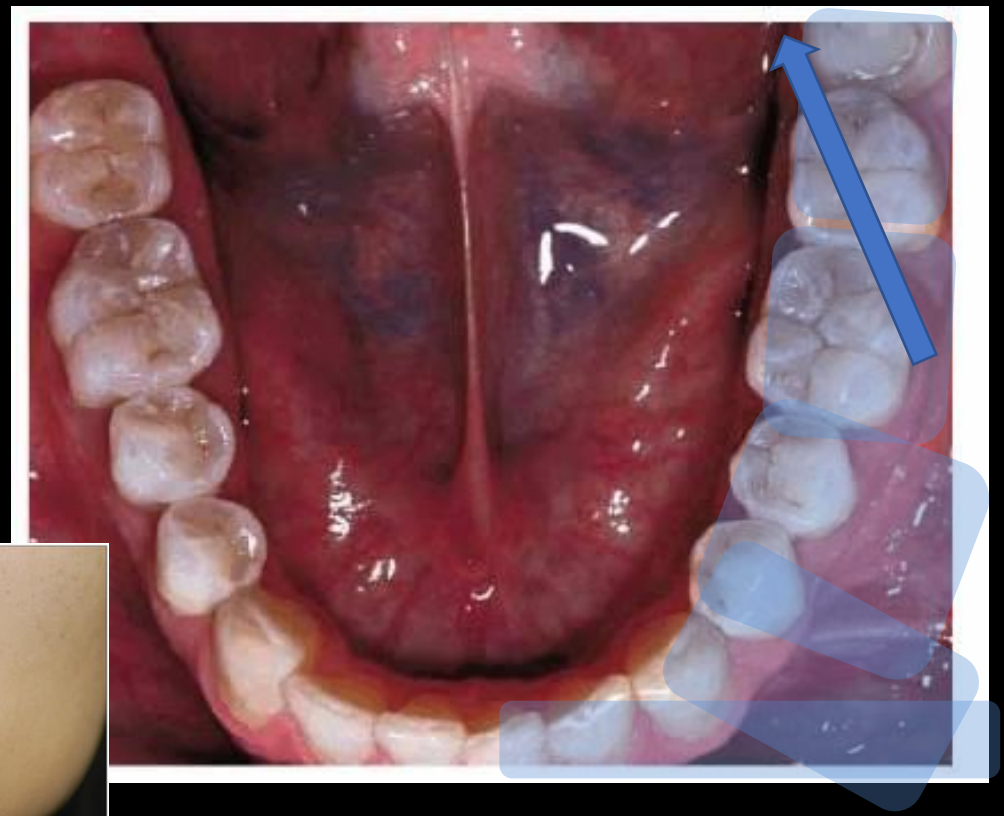
Assessment of neuropathic area
Know your anatomy!

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

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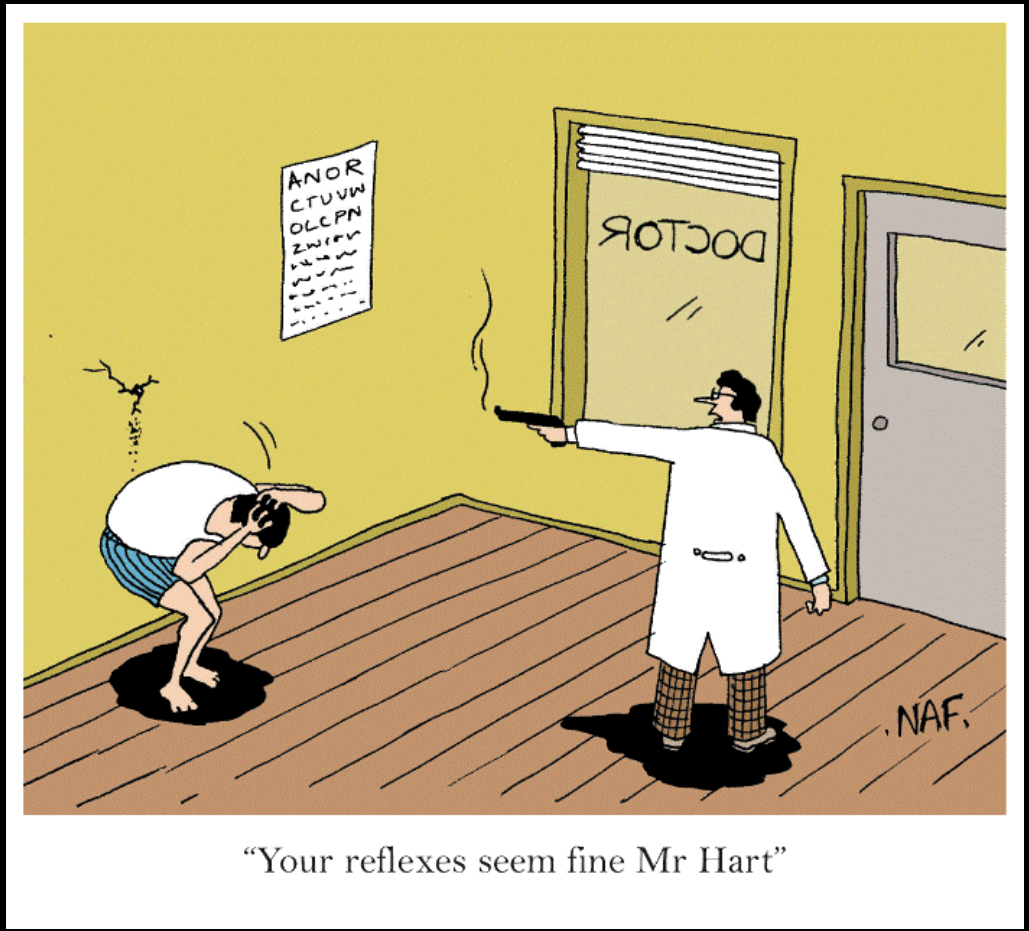
CLINICAL ASSESSMENT
Mechanosensory assessment



"Your reflexes seem fine Mr Hart"

No complicated tests!

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.

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.

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 48%**
- **Reported high level pain post surgically 56%**
- IANI related to;
  - Third molar surgery 60%
  - Implant 14%
  - LA 16%
  - Endo 8%
  - Periapical infections 1%
  - Facial electrolysis 1%
- LNIs related to;
  - TMS 75%
  - LA 21%

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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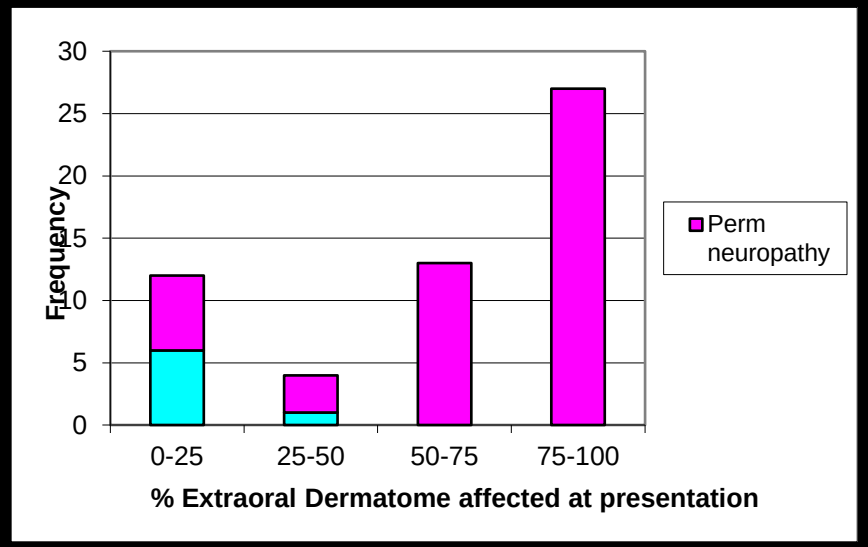
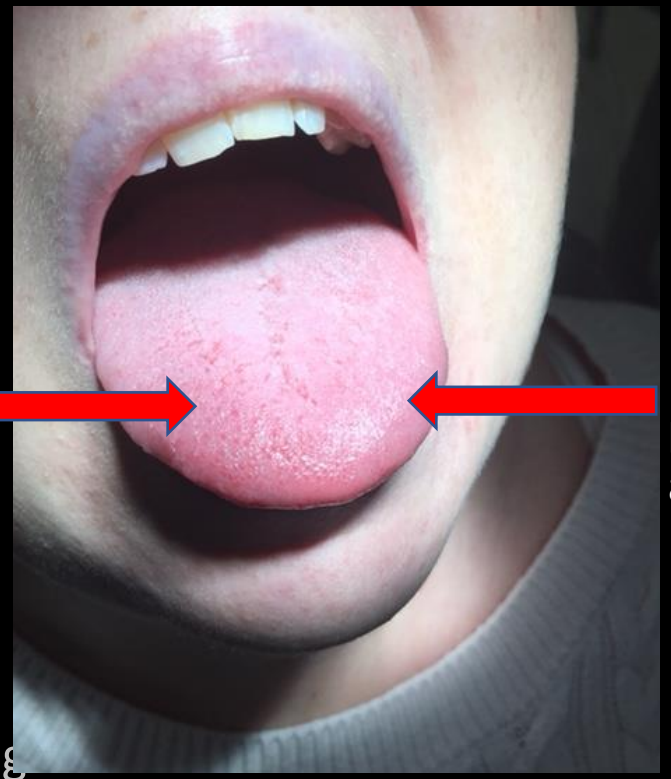
Predictors resolution of nerve injury

Mechanosensory testing is NOT predictive of outcome





At 2-4 weeks post Lingual nerve injury
Small size of neuropathic area (<50% of dermatome) and hig
subjective function (>4/10) may be predictive of resolution in
lingual nerve injuries at 12 weeks

Significant loss fungi form papillae at 2 weeks
Renton et al un published

Renton T, Thexton A, Crean SJ, Hankins M. Simplifying the assessment of the recovery from surgical injury to the lingual nerve. Br Dent J. 2006 May 27;200(10):569-73; discussion 565.

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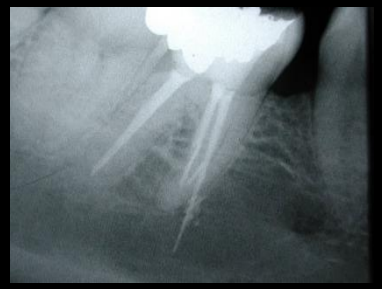
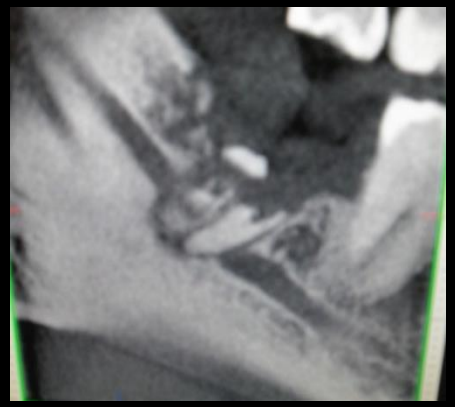
You cannot ‘see’ nerves on radiographs just the canals and foramina……

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





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

Post surgical CBCTs only required for M3M Inferior alveolar nerve injury

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

Diagnostic Lidocaine blocks
Psychological

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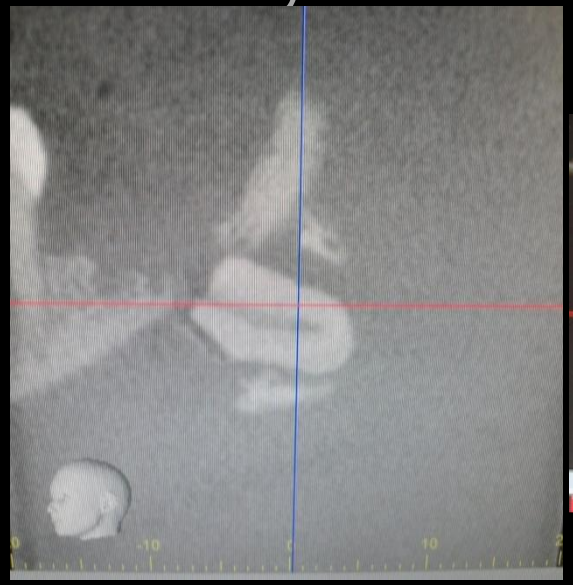
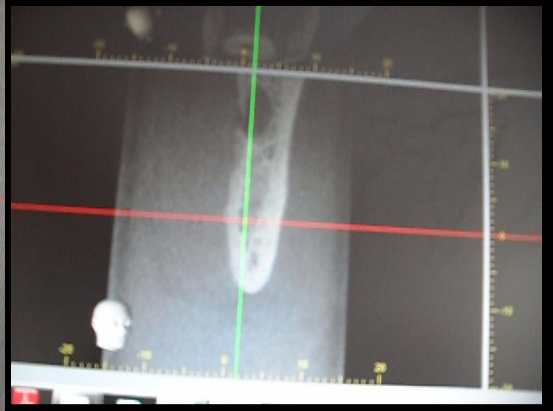
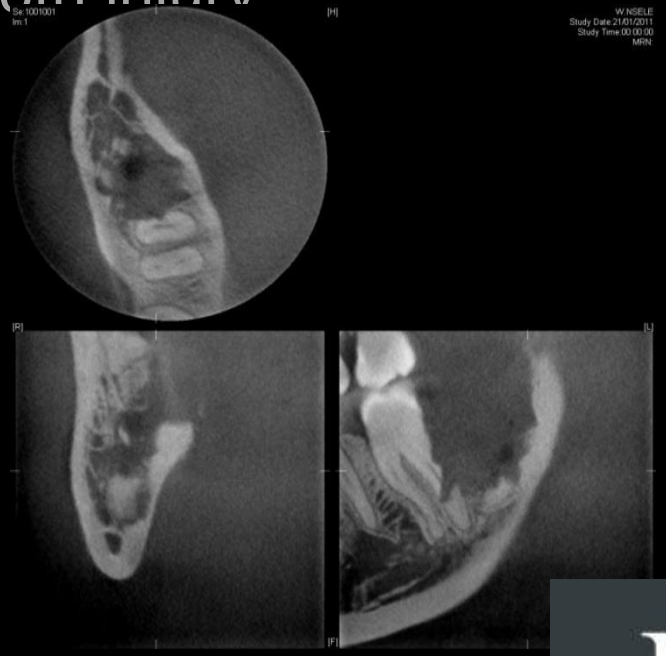
IMAGING Inferior alveolar nerve injury (IANI)

WHEN IS CBCT INIDICATED POST NERVE INJURY?

Retained roots? In submandibular space?
CBCT may be useful for post wisdom tooth injury







MRI neuroradiography>>>>>>>>>>>>>>>>>>>

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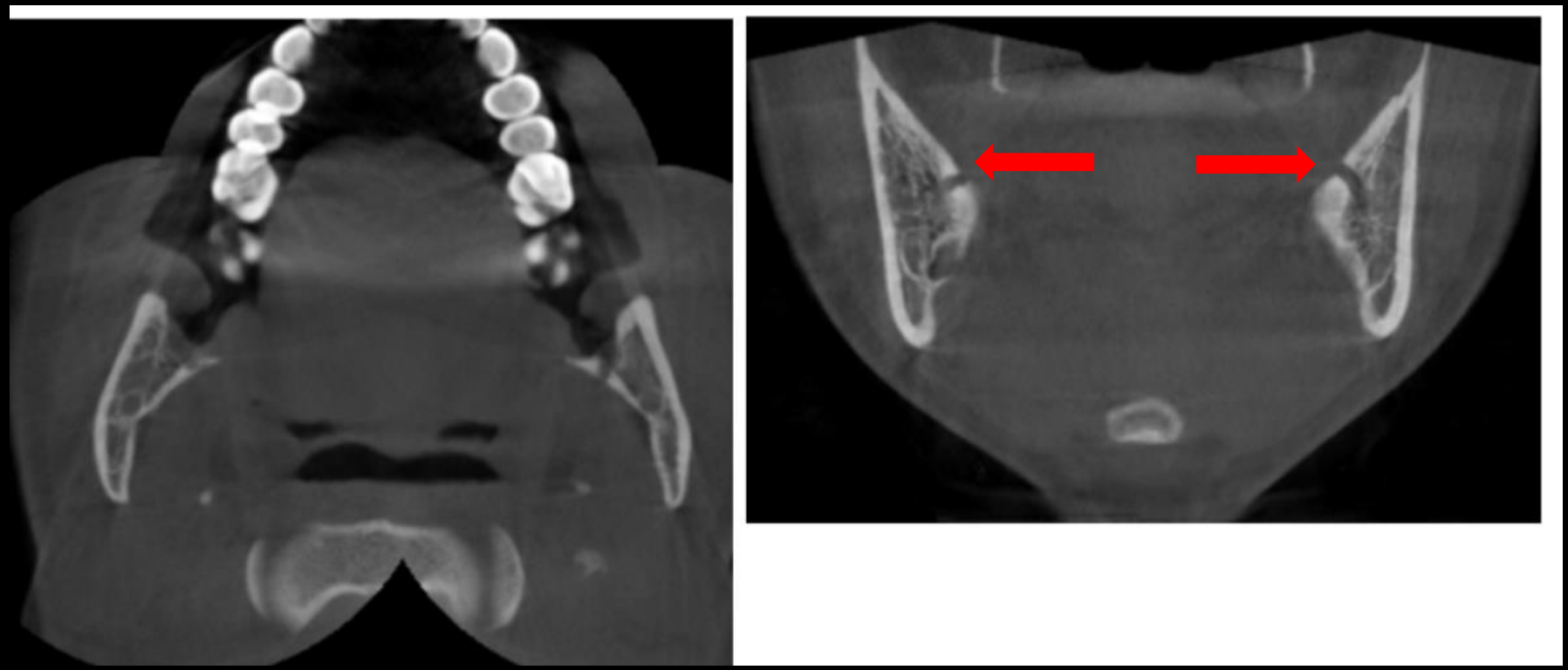
IMAGING Lingual nerve injury (LNI)
CBCT early post op detection of Lingual plate damage



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)

Outline

- –Introduction
  - •The trigeminal system
  - •Definitions
  - •Painful Post traumatic trigeminal neuropathy (PPTTN)
    - –Mechanisms
    - –Assessment and prediction of outcome
- –Management;
  - •Medical
  - •Interventional
    - –Surgery
    - –Advanced Stimulation, Peripheral, DBS
  - •Psychological
  - •Adjunctive
  - •The future

Zuniga JR, Renton T. J Neurol Neuromed (2016) 1(7): 10-14
www.jneurology.com
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Managing post-traumatic trigeminal neuropathic pain: is surgery enough?

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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 patients as the prevention of post-traumatic trigeminal neuropathic pain in the absence of effective medical or surgical interventions.

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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 interventions for neuropathic pain (NeuP) are available, but its treatment remains unsatisfactory. We systematically summarized evidence from systematic reviews (SRs) of randomized controlled trials on interventions for NeuP. Five electronic databases were searched up to March 2015. Study quality was analyzed using A Measurement Tool to Assess Systematic Reviews. The most common interventions in 97 included SRs were pharmacologic (59%) and surgical (15%). The majority of analyzed SRs were of medium quality. More than 50% of conclusions from abstracts on efficacy and approximately 80% on safety were inconclusive. Effective interventions were described for painful diabetic neuropathy (pregabalin, gabapentin, certain tricyclic antidepressants [TCAs], opioids, antidepressants, and anticonvulsants), postherpetic neuralgia (gabapentin, pregabalin, certain TCAs, antidepressants and anticonvulsants, opioids, sodium valproate, topical capsaicin, and lidocaine), lumbar radicular pain (epidural corticosteroids, repetitive transcranial magnetic stimulation [rTMS], and discectomy), cervical radicular pain (rTMS), carpal tunnel syndrome (carpal tunnel release), cubital tunnel syndrome (simple decompression and ulnar nerve transposition), trigeminal neuralgia (carbamazepine, lamotrigine, and pimozide for refractory cases, rTMS), HIV-related neuropathy (topical capsaicin), and central NeuP (certain TCAs, pregabalin, cannabinoids, and rTMS). 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)

Neuropathic pain (NeuP) has been estimated to affect between 5% and 10% of the general population.[1–3] This multifactorial condition can be difficult to manage, irrespective of the cause of the underlying disorder.[4,5] Therefore, it is considered a priority health issue by the International Association for the Study of Pain (IASP).[5]

During recent years, several evidence-based clinical recommendations summarized evidence from randomized

the interventional management of NeuP published in 2013 by the IASP Neuropathic Pain Special Interest Group indicated that many interventions used to treat refractory NeuP are supported by weak evidence.[11] There is an increasing number of systematic reviews (SRs) that have investigated different treatment modalities of NeuP. However, their findings can be difficult to interpret, and their conclusions are often discordant and limited by the quality of the included

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)

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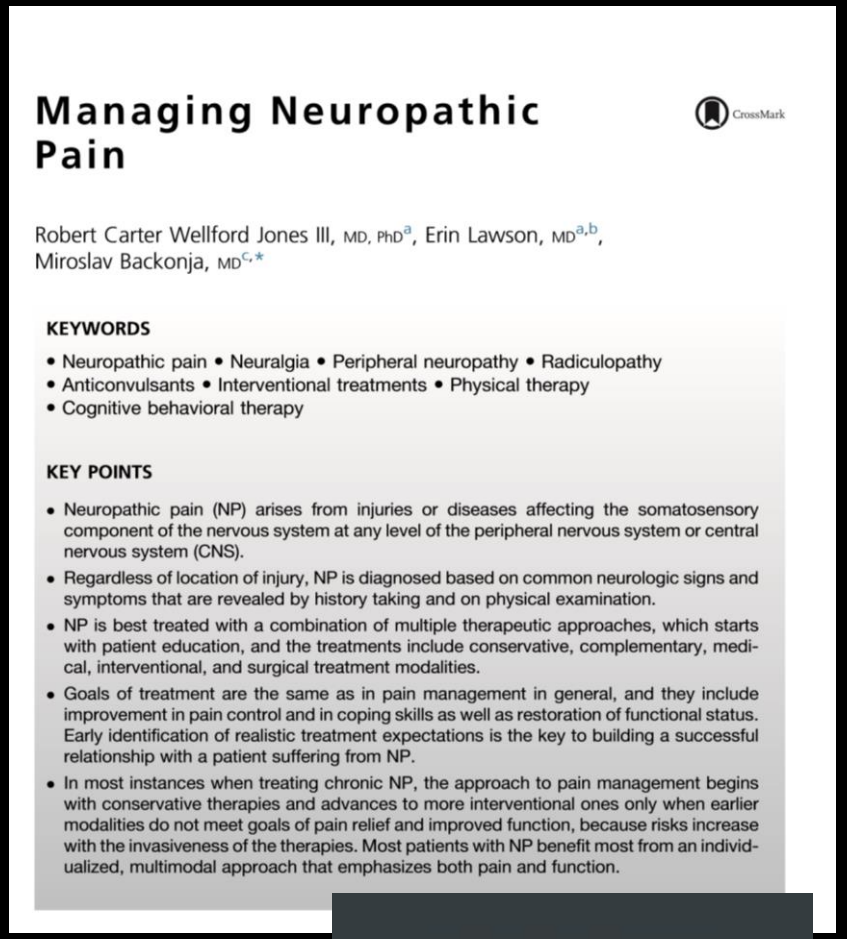
NEUROPATHIC PAIN (NP) ARISES FROM INJURIES OR DISEASES OF THE NERVOUS SYSTEM AT ANY LEVEL OF THE PERIPHERAL NERVOUS SYSTEM OR CENTRAL NERVOUS SYSTEM (CNS).

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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We do know that
Surgery alone is not enough!

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]

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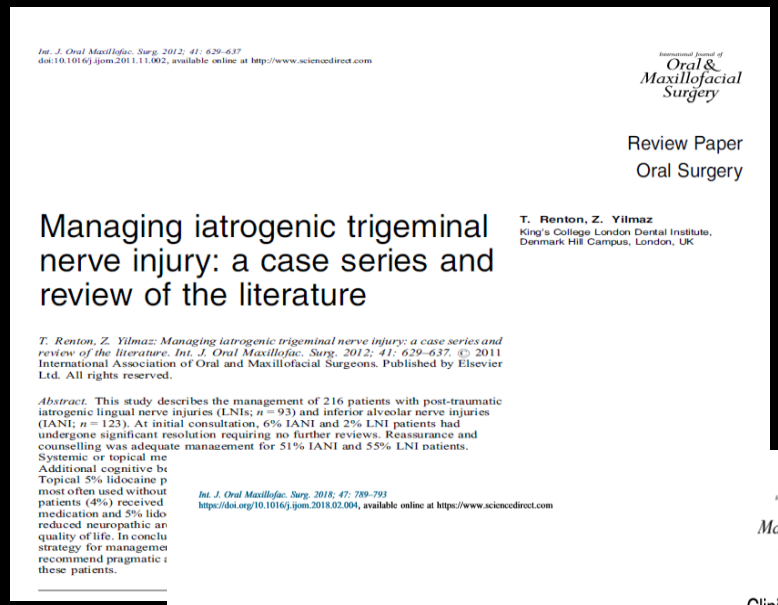
Introduction

Management of dentistry related 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

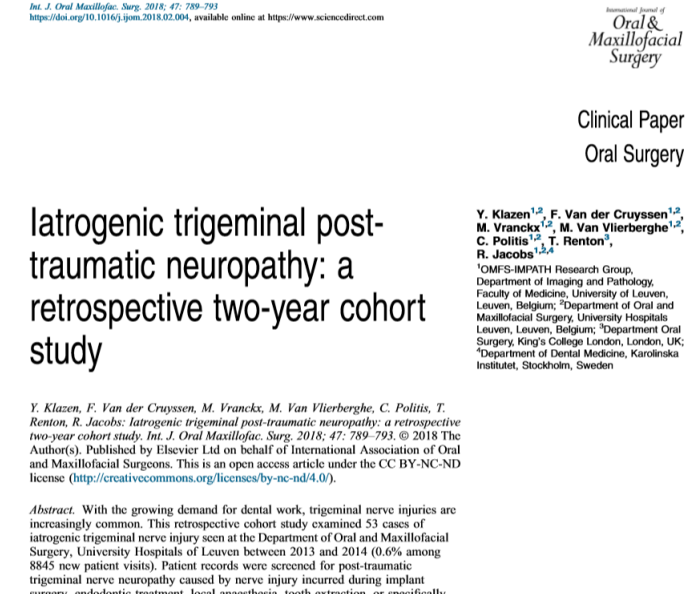
Review Paper
Oral Surgery

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 me
Additional cognitive be
Topical 5% lidocaine p
most often used without
patients (4%) received
medication and 5% lido
reduced neuropathic an
quality of life. In conclu
strategy for managemer
recommend pragmatic
these patients.



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], T. Renton[3], R. Jacobs[1,2,4]
[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 license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Abstract. With the growing demand for dental work, trigeminal nerve injuries are increasingly common. This retrospective cohort study examined 53 cases of iatrogenic trigeminal nerve injury seen at the Department of Oral and Maxillofacial Surgery, University Hospitals of Leuven between 2013 and 2014 (0.6% among 8845 new patient visits). Patient records were screened for post-traumatic trigeminal nerve neuropathy caused by nerve injury incurred during implant

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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[2], M. Akashi[1], S. Furuno[5], H. Miyamoto[6], S. Hayashida[2], R. Amano[7], K. Mori[6], Y. Kojima[7], H. Kurita[2], T. Kirita[3], M. Umeda[4], Y. Shibuya[3], 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. buya, S. Fujita, T. Komori: Treatment modalities and risk factors refractory neurosensory disturbances of the inferior alveolar nerve urgery: a multicentre retrospective study. Int. J. Oral Maxillofac. Surg. 801. © 2017 International Association of Oral and Maxillofacial Surgeons. lsevier Ltd. All rights reserved.

e research has been conducted into hypoesthesia, and no studies have risk factors for refractory hypoesthesia and compared treatment e purpose of this multicentre retrospective cohort study was to relationships between various risk factors, treatment modalities, and oesthesia. Risk factors for refractory hypoesthesia after oral surgery l using univariate and multivariate analysis. To minimize the associated with a retrospective data analysis, a propensity score erformed between the medication and non-medication groups h group). Moderate or severe hypoesthesia (odds ratio 13.42) and no tration of ATP/vitamin B12 (odds ratio 2.28) were significantly refractory hypoesthesia. In the propensity score analysis, the of refractory hypoesthesia in the medication group was lower than -medication group ($P < 0.001$). This study demonstrated the lationships between various risk factors, treatment modalities, and oesthesia. Moderate or severe hypoesthesia and no or late of ATP/vitamin B12 were significantly associated with refractory Therefore, clinicians should consider these risk factors and initiate inistration of ATP/vitamin B12 in cases of hypoesthesia.

Key words: neurosensory deficit; extraction; treatment; hypoesthesia.

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Most important questions are based upon your Assessment to predict NI outcome

To surgerise or to wait?

- **Pain, altered sensation or / and numbness**
- **Functional problems**
- **Psychological impact**

Patient understanding of their condition and realistic expectations underpins their compliance with treatment and optimises the outcomes

Dependent upon the patient's presentation

Cause, duration and impact on patient

- Patient reassurance and education imperative
- Realistic expectations
- Management of pain
- Management of functional limitations
- Management of psychological issues

  (pre-existing and sequelae)

Assess & treat the patient with the nerve injury

Not the nerve injury alone!!!

King's College London

Management

Treatment depends on the Types of pain and types of patient

Healthy acute pain

Nociceptive
healthy feeling pain 'pain'

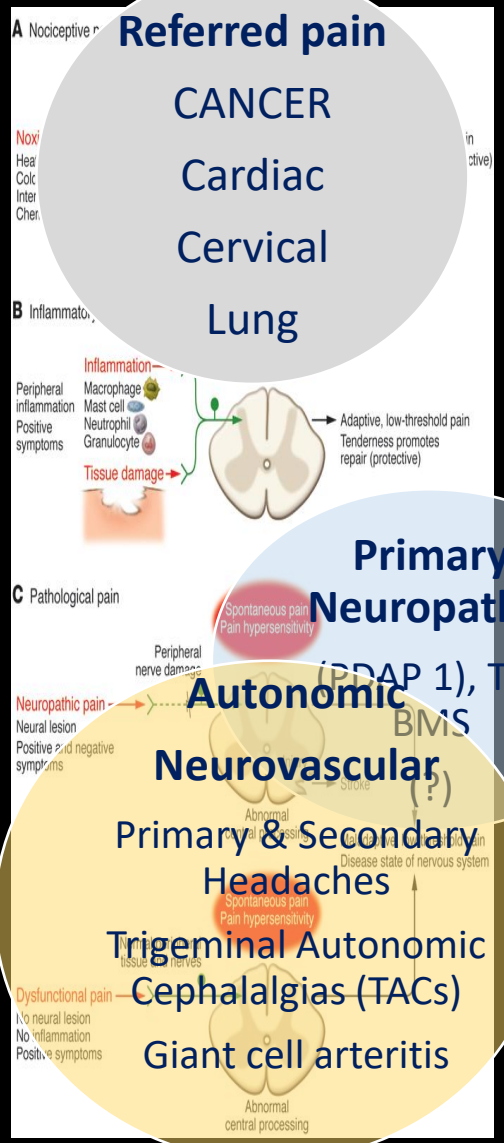
Inflammatory pain
healthy short lived after insult

Chronic pain = disease of neuromatrix

Neuropathic pain
Associated with nerve lesion

Plus autonomic / migrainious assocaited factors

Dysfunctional or centralised pain
Unknown cause



Referred pain
CANCER
Cardiac
Cervical
Lung

TMDs
Arthritides
Dysfunctional
Arthromyalgia

Acute pain
Dental infection, trauma, surgery sinusitis, salivary infections

Primary Neuropathic
(PDAP 1), TN, BMS

Secondary Neuropathic
neuralgias-TN I Ne
pain/PTN/PDAP (CPSP)

Autonomic Neurovascular
Primary & Secondary Headaches
Trigeminal Autonomic Cephalalgias (TACs)
Giant cell arteritis

Dysfunctional pain
Associated multiple pain conditions FM, IBS, TH, LBP

Dentine sensitivity

Pulpitis reversible +irreversible
Periapical periodontitis

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*

Type of pain	Condition	Guidance	Medical Management
Nociceptive pain	Dentine sensitivity	SDCEP prescribing guidance	Topical agents
Inflammatory pain	Irreversible pulpitis Dental abscess	SDCEP prescribing guidance FGDP AMS guidance	Extirpate RCT or extraction NO antibiotics
Inflammatory pain +/- Mixed Ne centralised	TMD Arthromaylagia Arthritides	TMD RDC guidance FDS RCS TMD guidance	Non interventional Analgesia Paracetamol ibuprofen Bite Guard
Neurovascular pain	Headaches Migraine	NICE Guidance Adult headaches	TCAs, Triptans< GON Block or Botox
Neurovascular pain	Trigeminal Autonomic Cephalalgias	NICE Guidance Adult headaches	CH GON block SUNCT Lamotrogine PH Indomethacin trial
Neuropathic pain	Primary PDAP 1 or post traumatic	NICE neuropathic guidance adults	TCAs, Gabanoids, SSRIs
Neuropathic pain	Burning mouth syndrome	AAOP	TCAs, topical clonazepine, SSRIs
Centralised pain	PIFP	AAOP	TCAs, Gabanoids, SSRIs

Management of TN

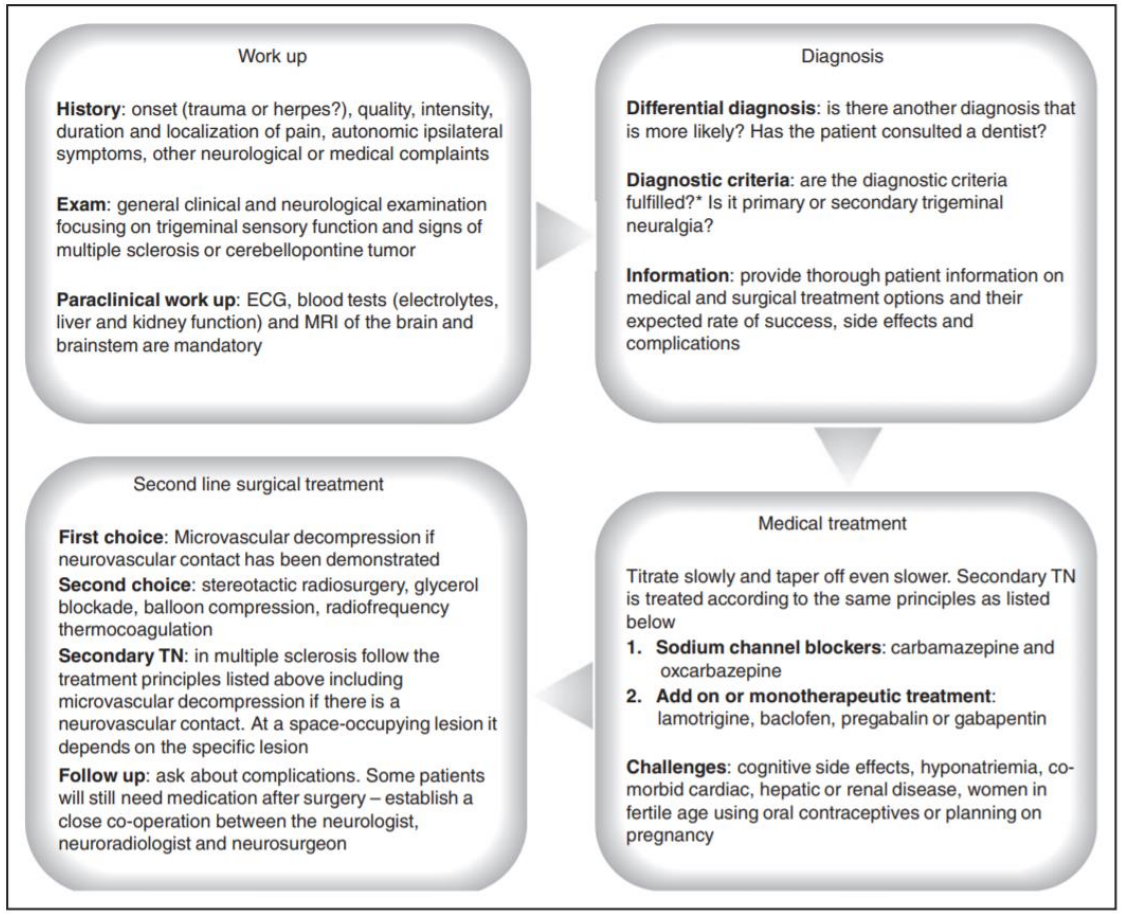


Figure 3. Work up and treatment algorithm in trigeminal neuralgia (TN) – presented in short. Diagnostic criteria of TN are outlined in Table 1.

Review

Cephalalgia
An International Journal of Headache
International Headache Society

Cephalalgia
2017, Vol. 37(7) 648–657

DOI: 10.1177/0333102416687280
journals.sagepub.com/home/cep
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 one or more divisions of the trigeminal nerve. In addition to the paroxysmal pain, some patients also have continuous pain. TN is divided into classical TN (CTN) and secondary TN (STN).

Etiology and pathophysiology: Demyelination of primary sensory trigeminal afferents in the root entry zone is the predominant pathophysiological mechanism. Most likely, demyelination paves the way for generation of ectopic impulses and ephaptic crosstalk. In a significant proportion of the patients, the demyelination is caused by a neurovascular conflict with morphological changes such as compression of the trigeminal root. However, there are also other unknown etiological factors, as only half of the CTN patients have morphological changes. STN is caused by multiple sclerosis or a space-occupying lesion affecting the trigeminal nerve.

Differential diagnosis and treatment: Important differential diagnoses include trigeminal autonomic cephalalgias, posttraumatic or postherpetic pain and other facial pains. First line treatment is prophylactic medication with sodium channel blockers, and second line treatment is neurosurgical intervention.

Future perspectives: Future studies should focus on genetics, unexplored etiological factors, sensory function, the neurosurgical outcome and complications, combination and neuromodulation treatment as well as development of new drugs with better tolerability.

Keywords

Trigeminal neuralgia, diagnostic criteria, guidelines, treatment, etiology, pathophysiology

Date received: 11 October 2016; revised: 21 November 2016; accepted: 7 December 2016

Definition

According to the beta version of the 3rd edition of the International Classification of Headache Disorders (ICHD-3 Beta) (1) (Table 1), trigeminal neuralgia (TN) is defined by recurrent unilateral brief electric shock-like pain that is abrupt in onset and termination. The pain is restricted to one or more of the trigeminal divisions and is triggered by innocuous sensory stimuli. TN is divided into either classical TN (CTN) or secondary TN (STN) caused by multiple sclerosis or a space-occupying lesion such as a tumor, cerebral aneurism or a megadolicho basilar artery.

Recently the International Association for the Study of Pain (IASP) has produced an independent classification, definition and diagnostic process of trigeminal

Symptomatology

In early descriptions of TN, the disorder was called tic douloureux (3), addressing the characteristic wince that TN patients may exhibit at a pain paroxysm; TN pain is not only extremely painful, it is also characteristic that the pain is sudden and unexpected, and short-lasting, hence the term pain paroxysm. The pain quality is stabbing, electrical shock-like, or shooting. Although one single

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[2]Department of Neurology and Psychiatry, Sapienza University, Rome, Italy

Trigeminal Neuralgia Fact Sheet

What is trigeminal neuralgia?

Trigeminal neuralgia (TN), also called *tic douloureux*, is a chronic pain condition that affects the trigeminal or 5th cranial ne
most widely distributed nerves in the head. TN is a form of neuropathic pain (pain associated with nerve injury or nerve les

https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Trigeminal-Neuralgia-Fact-Sheet

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.

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. 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.

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.

Trigeminal neuralgia (TN) is a disorder characterized by repetitive lancinating pain along one or more branches of the trigeminal nerve and is commonly triggered by chewing and manipulation of the gums. The second and third divisions are most commonly affected. Due to these symptoms, patients are likely to consult their local dentist when symptoms first develop and may receive further dental evaluation and treatment before they are referred to a neurologist or neurosurgeon.

We sought to answer questions regarding evaluation and possible dental treatment as well as referral patterns in TN patients. Using a surgical database, we obtained data of patients undergoing an intervention for trigeminal neuralgia. Telephone interviews were conducted, focusing on initial evaluation and possible dental treatment, on referral patterns, and on present status. Secondly, a written questionnaire was mailed to local dentists.

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.

Neurosurgical pain management of drug-resistant trigeminal neuralgia (TN) is highly challenging. Microvascular decompression is a first-line neurosurgical approach for classical TN with neurovascular conflict, but can show clinical relapse despite proper decompression. Second-line destructive techniques like radiofrequency thermocoagulation have become reluctantly used due to their potential for irreversible side effects. Subcutaneous peripheral nerve field stimulation (sPNFS) is a minimally invasive neuromodulatory technique which has been shown to be effective for chronic localised pain conditions. Reports on sPNFS for the treatment of trigeminal pain (sTNFS) are still sparse and primarily focused on pain intensity as outcome measure. Detailed data on the impact of sTNFS on attack frequency are currently not available.

METHODS: Patients were classified according to the International Headache Society classification (ICHD-3-beta). Three patients had classical TN without (n = 3) and another three TN with concomitant persistent facial pain (n = 3). Two patients suffered from post-herpetic trigeminal neuropathy (n = 2). All eight patients underwent a trial stimulation of at least 7 days with subcutaneous leads in the affected trigeminal area connected to an external neurostimulator. Of those, six patients received permanent implantation of a neurostimulator. During the follow-up (6-29 months, mean 15.2), VAS-scores, attack frequencies, oral drug intake, complications and side effects were documented.

RESULTS: Seven out of eight patients responded to sTNFS (i.e. ≥50 % pain reduction) during the test trial. The pain intensity (according to VAS) was reduced by 83 ± 16 % (mean ± SD) and the number of attacks decreased by 73 ± 26 % (mean ± SD). Five out of six patients were able to reduce or stop pain medication. One patient developed device infection. Two patients developed stimulation-related side effects which could be resolved by reprogramming.

CONCLUSIONS: Treatment by sTNFS is a beneficial option for patients with refractory trigeminal pain. Prospective randomised trials are required to systematically evaluate efficacy rates and safety of this low-invasive neurosurgical technique.

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.

Peripheral nerve field stimulation (PNFS) is a promising modality for treatment of intractable facial pain. However, evidence is sparse. We are therefore presenting our experience with this technique in a small patient cohort.

METHODS: Records of 10 patients (five men, five women) with intractable facial pain who underwent implantation of one or several subcutaneous electrodes for trigeminal nerve field stimulation were retrospectively analyzed. Patients' data, including pain location, etiology, duration, previous treatments, long-term effects and complications, were evaluated.

RESULTS: Four patients suffered from recurrent classical trigeminal neuralgia, one had classical trigeminal neuralgia and was medically unfit for microvascular decompression. Two patients suffered from trigeminal neuropathy attributed to multiple sclerosis, one from post-herpetic neuropathy, one from trigeminal neuropathy following radiation therapy and one from persistent idiopathic facial pain. Average patient age was 74.2 years (range 57-87), and average symptom duration was 10.6 years (range 2-17). Eight patients proceeded to implantation after successful trial. Average follow-up after implantation was 11.3 months (range 5-28). Using the visual analog scale, average pain intensity was 9.3 (range 7-10) preoperatively and 0.75 (range 0-3) postoperatively. Six patients reported absence of pain with stimulation; two had only slight constant pain without attacks.

CONCLUSION: PNFS may be an effective treatment for refractory facial pain and yields high patient satisfaction.

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.

Unique among the different neuropathic pain conditions, trigeminal neuralgia frequently has an excellent response to some selected drugs, which, on the other hand, often entail disabling side effects. Physicians should be therefore acquainted with the management of these drugs and the few alternative options. Areas covered: This article, based on a systematic literature review, describes the pharmacological options, and indicates the future perspectives for treating trigeminal neuralgia.
The article therefore provides current, evidence-based knowledge about the pharmacological treatment of trigeminal neuralgia, and suggests a practical approach to the various drugs, including starting dose, titration and side effects.
Expert commentary: Carbamazepine and oxcarbazepine are the reference standard drugs for treating patients with trigeminal neuralgia. They are effective in most patients. The undesired effects however cause withdrawal from treatment or a dosage reduction to an insufficient level in many patients. Sodium channel blockers selective for the sodium channel 1.7 (Nav1.7) receptor, currently under development, might be an alternative, better-tolerated pharmacological option in the next future.

Di Stefano G[1], Truini A[1]. **Pharmacological treatment of trigeminal neuralgia.** Expert Rev Neurother. 2017 Oct;17(10):1003-1011. doi: 10.1080/14737175.2017.1370375. Epub 2017 Sep 4.

Current standard of care for trigeminal neuralgia is treatment with the sodium channel blockers carbamazepine and oxcarbazepine, which although effective are associated with poor tolerability and the need for titration. BIIB074, a Nav1.7-selective, state-dependent sodium-channel blocker, can be administered at therapeutic doses without titration, and has shown good tolerability in healthy individuals in phase 1 studies. We therefore assessed the safety and efficacy of BIIB074 in patients with trigeminal neuralgia in a phase 2a study.

METHODS: We did a double-blind, multicentre, placebo-controlled, randomised withdrawal phase 2a trial in 25 secondary care centres in Denmark, Estonia, France, Germany, Italy, Latvia, Lithuania, Romania, South Africa, Spain, Switzerland, and the UK. After a 7-day run-in phase, eligible patients aged 18-80 years with confirmed trigeminal neuralgia received open-label, BIIB074 150 mg three times per day, orally, for 21 days. Patients who met at least one response criteria were then randomly assigned (1:1) to BIIB074 or placebo for up to 28 days in a double-blind phase. We used an interactive web response system to assign patients with a computer-generated schedule, with stratification (presence or absence of existing pain medication). Patients, clinicians, and assessors were masked to treatment allocation. The primary endpoint was the difference between groups in the number of patients classified as treatment failure during the double blind phase assessed in the modified intention-to-treat population. We assessed safety in all patients who received one or more doses of BIIB074. This study is registered with ClinicalTrials.gov (NCT01540630) and EudraCT (2010-023963-16).

FINDINGS: The first patient was enrolled on April 23, 2012, and the last patient completed the study on February 26, 2014. We enrolled 67 patients into the open-label phase; 44 completed open-label treatment, and 29 were randomly assigned to double-blind treatment (15 to BIIB074 and 14 to placebo). During the double-blind phase, five (33%) patients assigned to BIIB074 versus nine (64%) assigned to placebo were classified as treatment failures (p=0·0974). BIIB074 was well tolerated, with similar adverse events in the double-blind phase to placebo. Headache was the most common adverse event with BIIB074 in the open-label phase (in 13 [19%] of 67 patients), followed by dizziness (in six [9%] patients). In the double-blind phase, headache, pyrexia, nasopharyngitis, sleep disorder, and tremor were the most frequent adverse events in patients assigned to BIIB074 (in one [7%] of 15 patients for each event), and headache, dizziness, diarrhoea, and vomiting were the most frequent adverse events in patients assigned to placebo (in one [7%] of 14 patients for each event). No severe or serious adverse events were reported in the BIIB074 group during the double-blind phase. One patient assigned to placebo reported intestinal adhesions with obstruction as a severe and serious adverse event, which was considered as unrelated to study medication.

INTERPRETATION: The primary endpoint of treatment failure was not significantly lower in the BIIB074 group than in the placebo group. However, our findings provide a basis for continued investigation of BIIB074 in patients with trigeminal neuralgia in future clinical trials.

FUNDING: Convergence Pharmaceuticals.

Zakrzewska JM[1], Palmer J[2], Morisset V[2], Giblin GM[2], Obermann M[3], Ettlin DA[4], Cruccu G[5], Bendtsen L[6], Estacion M[7], Derjean D[2], Waxman SG[7], Layton G[8], Gunn K[2], Tate S[2]; study investigators. **Safety and efficacy of a Nav1.7 selective sodium channel blocker in patients with trigeminal neuralgia: a double-blind, placebo-controlled, randomised withdrawal phase 2a trial.** Lancet Neurol. 2017 Apr;16(4):291-300. doi: 10.1016/S1474-4422(17)30005-4. Epub 2017 Feb 17

Drugs. 2018 Sep;78(14):1433-1442. doi: 10.1007/s40265-018-0964-9.

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

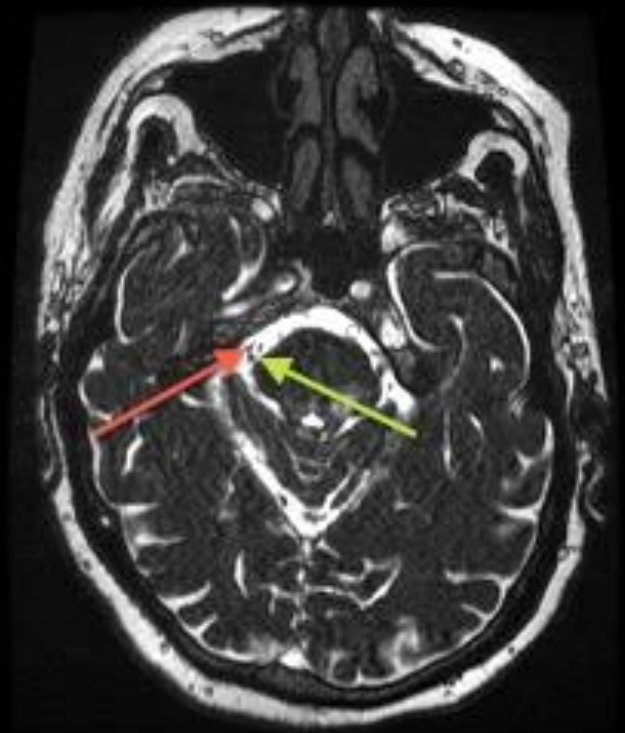
Di Stefano G[1], Truini A[1], Cruccu G[2].

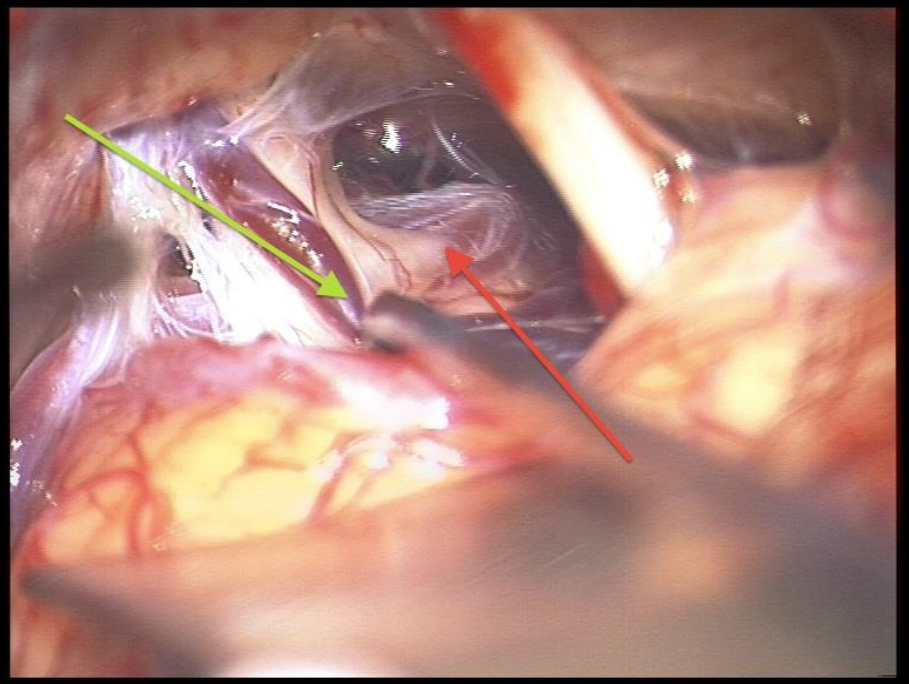
Author information

Abstract

Trigeminal neuralgia is a representative neuropathic facial pain condition, characterised by unilateral paroxysmal pain in the distribution territory of one or more divisions of the trigeminal nerve, triggered by innocuous stimuli. A subgroup of patients with trigeminal neuralgia [TN (previously defined as atypical TN)] also suffer from concomitant continuous pain, i.e. a background pain between the paroxysmal attacks. The aim of this review is to provide current, evidence-based, knowledge about the pharmacological treatment of typical and atypical TN, with a specific focus on drugs in development. We searched for relevant papers within PubMed, EMBASE, the Cochrane Database of Systematic Reviews and the Clinical Trials database (ClinicalTrials.gov), taking into account publications up to February 2018. Two authors independently selected studies for inclusions, data extraction, and bias assessment. Carbamazepine and oxcarbazepine are the first-choice drugs for paroxysmal pain. When sodium channel blockers cannot reach full dosage because of side effects, an add-on treatment with lamotrigine or baclofen should be considered. In patients with atypical TN, both gabapentin and antidepressants are expected to be efficacious and should be tried as an add-on to oxcarbazepine or carbamazepine. Although carbamazepine and oxcarbazepine are effective in virtually the totality of patients, they are responsible for side effects causing withdrawal from treatment in an important percentage of cases. 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.

MVD
Sup cerebellar artery vascular compromise

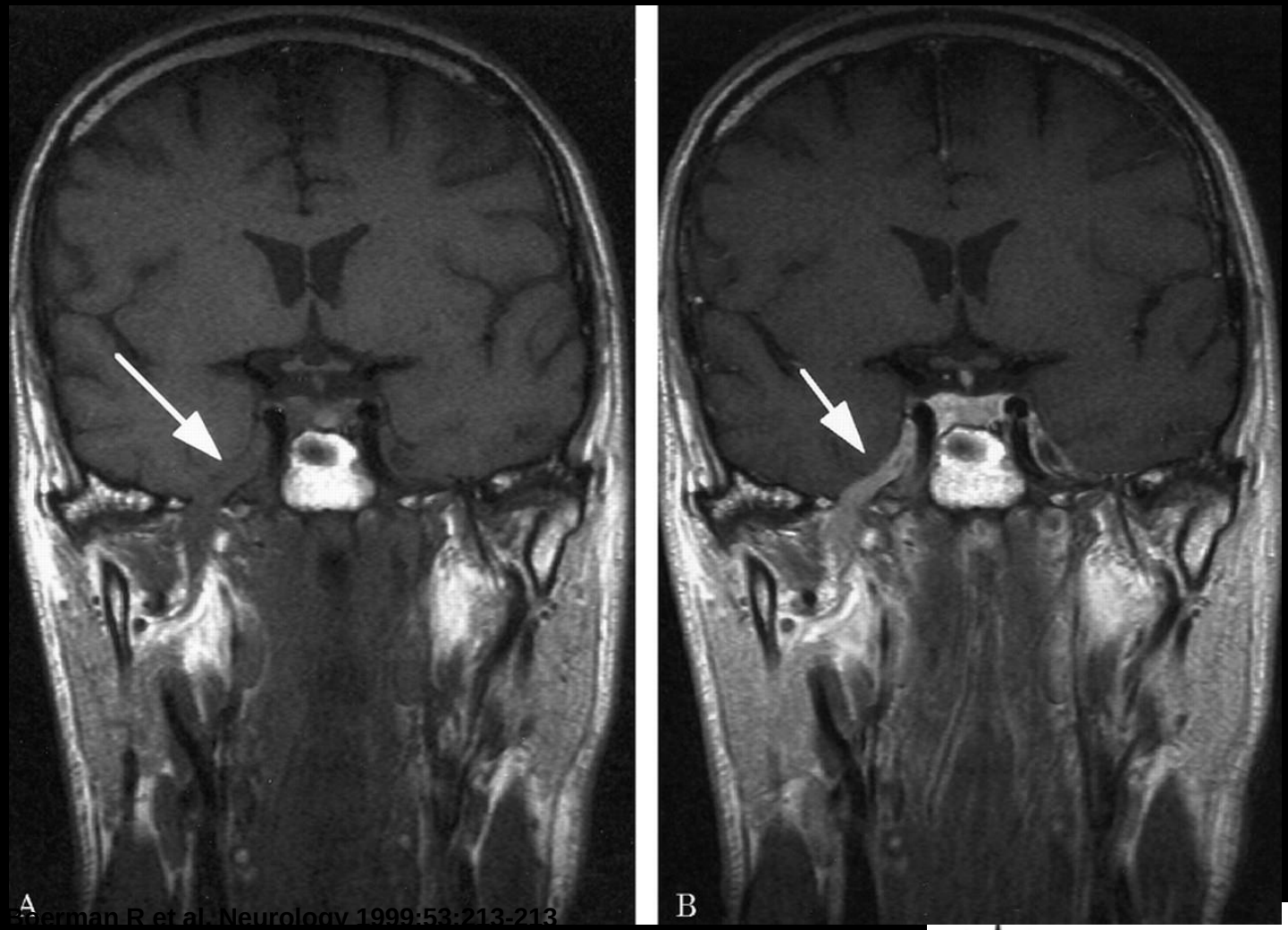




Green arrow shows retraction of trigeminal vein in contact with but not compressing V; red arrow shows a branch of the superior cerebellar artery passing medial to and severely compressing V at the root entry zone
Courtesy Mr Sinan Barazi Neurosurgeon KCH

Tumours

Coronal T1-weighted spin echo image of Patient 1 before (A) and after (B) gadolinium enhancement.



Eberman R et al. Neurology 1999;53:213-213

Issues with TN

- Wrong diagnosis
  - GMP toothache
  - SUNCT/SUNA
- Mainly managed by GMPs ‘toothache’
- 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.

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

Wait for resolution

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

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

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Psychological 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.

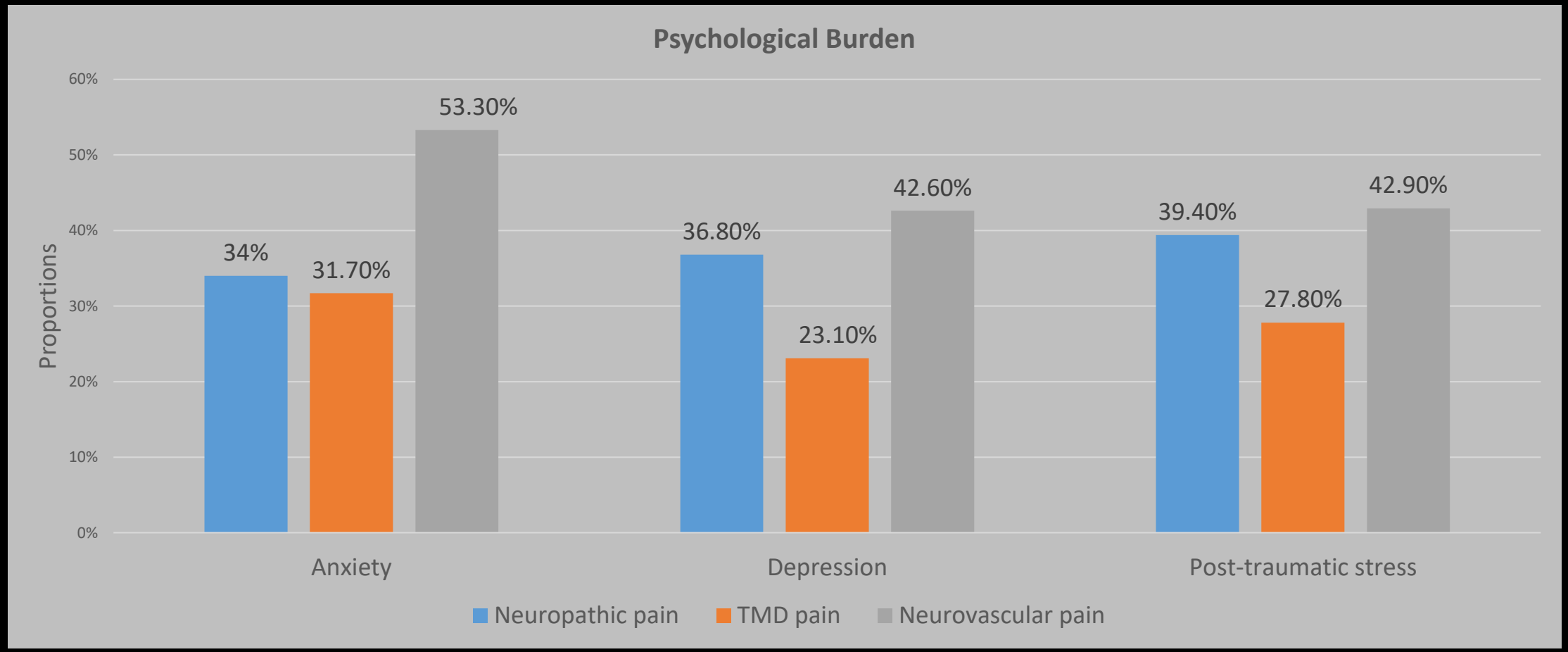
RESULTS: The majority of patients reported pain associated with their nerve injury (86%). Nerve injury had a significant impact on all investigated domains, and this was closely linked with reported pain levels. Patients with severe pain showed particularly elevated levels of depression and pain catastrophizing, 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]

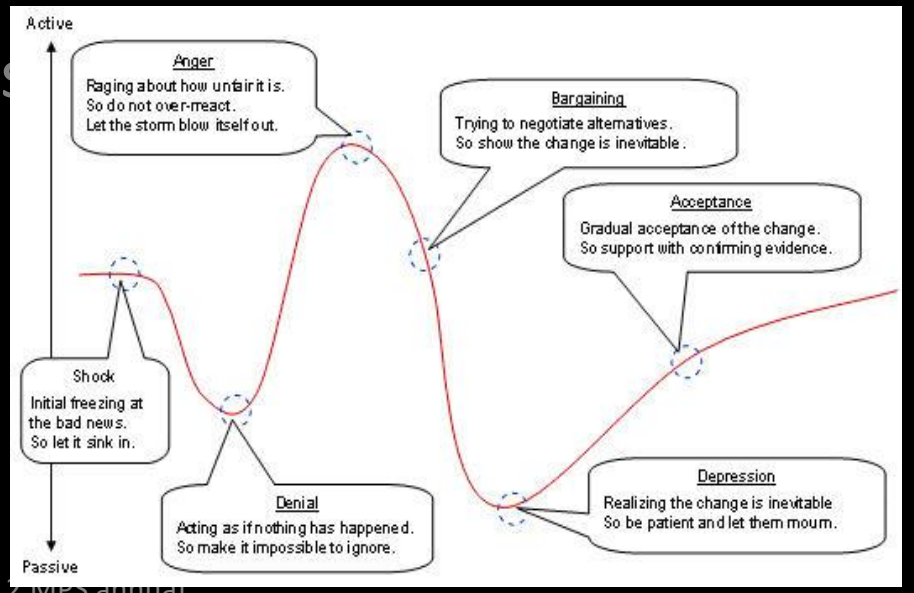
Psychological burden of orofacial pain (n=600)

Dr Aalia Karamat PhD unpublished



Psychological interventions

- Management of existing mental health problems
- Cognitive behavioural therapy
- acceptance commitment
- Mindfulness
- NLP



- Smith J et al Psychological morbidity of iatrogenic trigeminal nerve injuries Accepted J Orofacial pain August 2012 MPS annual report Dec 2011

8 The impact of error on the patient

Dr Lisa Page is a consultant psychiatrist to the Facial Pain Clinic at the King's Dental Institute in London where she has helped develop a unique multi-disciplinary approach to the management of trigeminal nerve injuries

What happens to a dental patient after a mistake?

Patients generally agree to dental treatment expecting a good outcome. Consequently they are often ill-prepared should an injury occur. When major mistakes happen, patients usually experience an initial period of disbelief and shock. For many there may be a protracted period before the extent of the injury is confirmed and it is not uncommon for the patient to be in denial during this stage. Initial difficulties can be worsened if a dentist seeks to avoid a patient's attempts to contact them, or if the patient is given inaccurate

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Management principles of patient with NI+/- pain

- **Early – Remedial**
  - Known or Suspected nerve injury –**immediate exploration** +/- repair
  - <36 hours to treat implant or Endo related nerve injuries
  - Non resolving injury 2-8 weeks early?
    - Medical
      - Systemic
      - topical
    - Surgical
- **Later >8 weeks**
  - Medical
    - Systemic
    - topical
  - Surgical
  - Pain management interventions for refractory patients
- **Sit and Wait therapeutic**

All patients need psychological assessment and support
As these may predict

- persistence and levels of pain,
- improvement in functional outcomes

and surgical outcomes!

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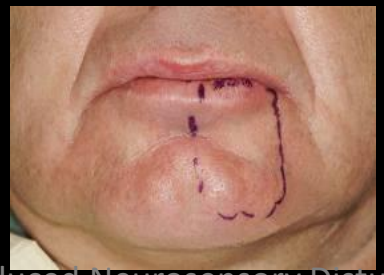
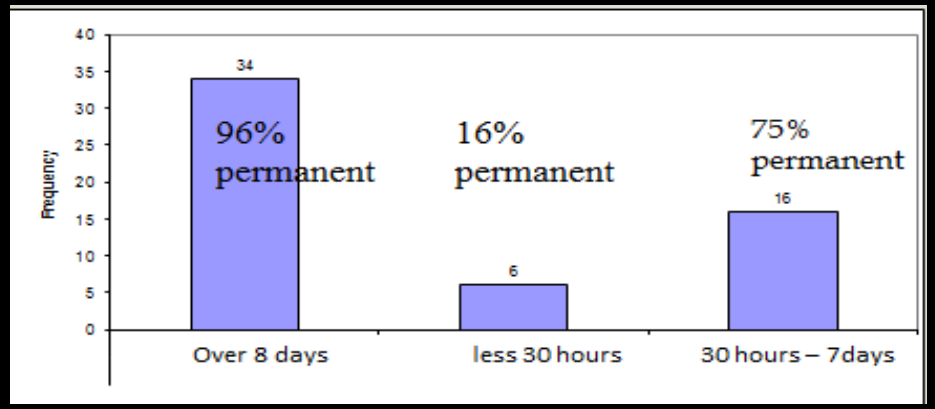
Acute surgical intervention

- **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

Why is the timing of nerve repair so paramount?

Peripheral consequences of nerve injury

Central consequences of nerve injury

Improved outcomes with early repair

- Susarla et al 2007
- Ziccardi 2007

Seddon's dictum (1943) 'if a purely expectant policy is pursued the most favourable time for operative intervention will always be missed'

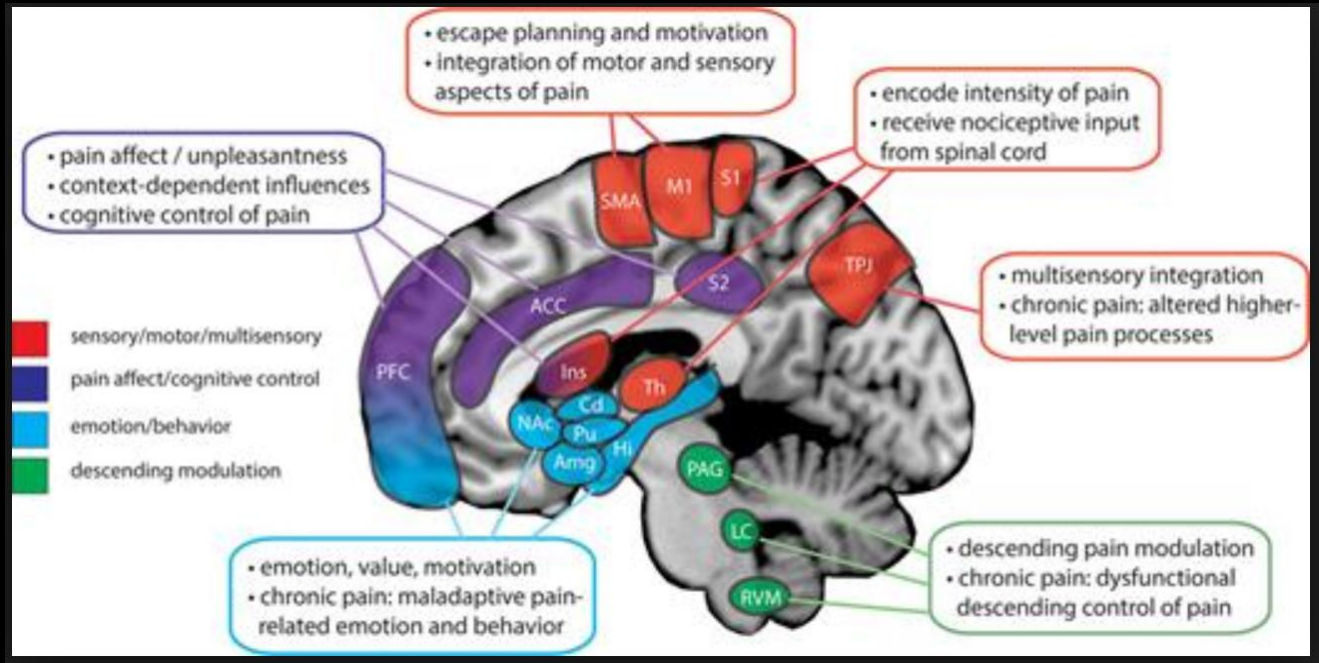
Mean delay before repair for 21 studies is **16 months = too late!**

Are we operating far too late?

Central changes after peripheral nerve injury

Central changes increased with catastrophising

- 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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Amplified parabrachial nucleus activity in a rat model of trigeminal neuropathic pain

Olivia Uddin[a,b,1], **Paige Studlack**[a,b,1], **Titilola Akintola**[a], **Charles Raver**[a], **Alberto Castro**[a,b], **Radi Masri**[b,c], and **Asaf Keller**[a,b,*]

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[c]Department of Advanced Oral Sciences and The
Dentistry, 650 W. Baltimore St, Baltimore, MD 21

Abstract

The parabrachial (PB) complex mediates both asc
pain modulatory information in the affective/emo
hyperactivity influences chronic pain behavior af
induction of neuropathic pain using the chronic c
ION) model, rats displayed spontaneous markers
beyond the receptive field of the injured nerve. Pl
displayed amplified activity, manifesting as signi
compared to shams. These findings suggest that c
hyperactivity.

Keywords

Chronic pain; Affective pain; Facial grimace; Chr

Experimental Brain Research (2018) 236:1357–1368
https://doi.org/10.1007/s00221-018-5226-2

RESEARCH ARTICLE

Face sensorimotor cortex undergoes neuroplastic changes in a rat model of trigeminal neuropathic pain

Dongyuan Yao[1,2] · **Barry J. Sessle**[2]

Received: 20 September 2017 / Accepted: 2 March 2018 / Published online: 8 March 2018

Abstract

Trigeminal nerve injury can result in neuropathic pain behavior and alterations in motor function, but it is unclear if such injury produces neuroplastic alterations in face sensorimotor cortex that could contribute to the alterations in motor function. Therefore, this study aimed to determine if trigeminal nerve injury in a rat neuropathic pain model induces neuroplastic changes in jaw and tongue motor representations in face sensorimotor cortex in association with facial nociceptive behavior. Right infraorbital nerve transection was performed in adult male Sprague–Dawley rats; sham-operated rats served as controls. Nociceptive behavior was assessed by testing facial mechanical sensitivity pre-operatively and post-operatively (1–28 days). Intracortical microstimulation was also applied post-operatively in a series of microelectrode penetrations to map jaw and tongue motor representations in the face sensorimotor cortex by analyzing anterior digastric and genioglossus electromyographic activities evoked by microstimulation at histologically verified sites in face primary somatosensory cortex (face-SI) as well as face primary motor cortex (face-MI). Compared to sham, infraorbital nerve injury induced a significant (2-way repeated-measures analysis of variance, $P<0.001$) bilateral decrease in facial mechanical threshold that lasted up to 28 days post-operatively. Nerve injury also induced a significant bilateral decrease compared to sham ($P<0.05$) in the number of anterior digastric and/or genioglossus sites in face-MI and in face-SI. These findings indicate that trigeminal nerve injury induces neuroplastic alterations in jaw and tongue motor representations in face sensorimotor cortex that are associated with facial nociceptive behavior and that may contribute to sensorimotor changes following trigeminal nerve injury.

Research Paper

PAIN

Reversal of insular and microstructural nerve abnormalities following effective surgical treatment for trigeminal neuralgia

Danielle D. DeSouza[a,b], Karen D. Davis[a,b,c,*], Mojgan Hodaie[a,b,c]

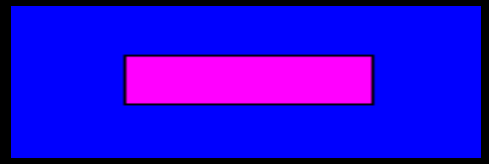
Abstract

Classical trigeminal neuralgia (TN) is a severe neuropathic facial pain disorder commonly associated with neurovascular compression at the trigeminal nerve root entry zone (REZ). Neurosurgical interventions can relieve TN pain, but the mechanisms underlying these effects are unknown. We determined whether the abnormalities we previously reported at the REZ of TN patients using diffusion tensor imaging (DTI) and brain gray matter (GM) analyses resolve after effective neurosurgical treatment. Twenty-five patients who underwent either microvascular decompression surgery or Gamma Knife radiosurgery for right-sided TN had magnetic
treatment and were compared with age-matched controls. Cortical thickness and voxel-
ain GM we previously reported as abnormal in TN. White matter metrics of fractional
fusivities (MD, RD, and AD, respectively) were extracted bilaterally from each trigeminal
spread GM abnormalities including thinner ventral anterior insula (vAI) cortex, and REZ
d higher MD, RD, and AD) compared with controls. We considered a 75% reduction in
as the only GM region that normalized toward the level of healthy controls after effective
reversed FA, MD, RD, and AD abnormalities and was correlated with pain relief after
t treatment can effectively resolve pain by normalizing REZ abnormalities, which may
es should consider DTI as an adjunct to assess the patient outcome and subtle

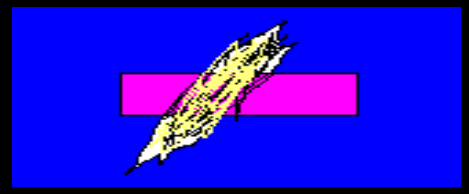
ent, Pain, MRI, DTI, Neurosurgery

Nerve exploration what do we find?

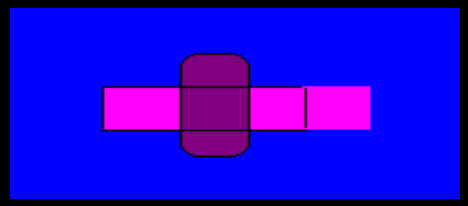
- Exploration



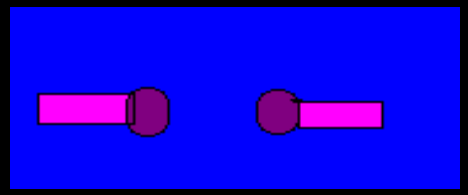
- Decompression



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

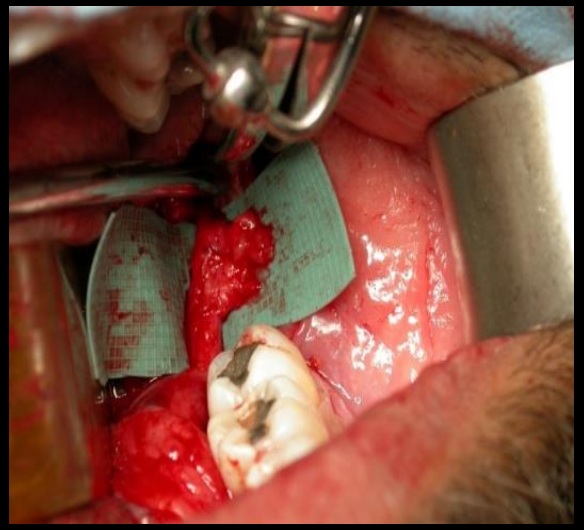


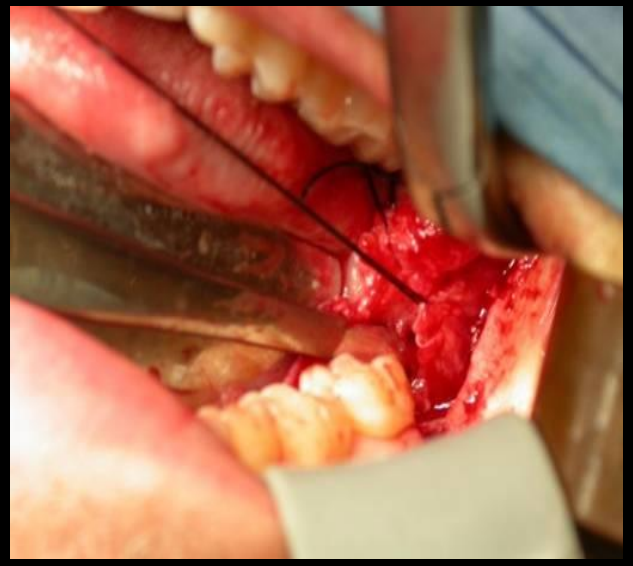
- End neuromata EN) excision and re-approximation with minimal tension

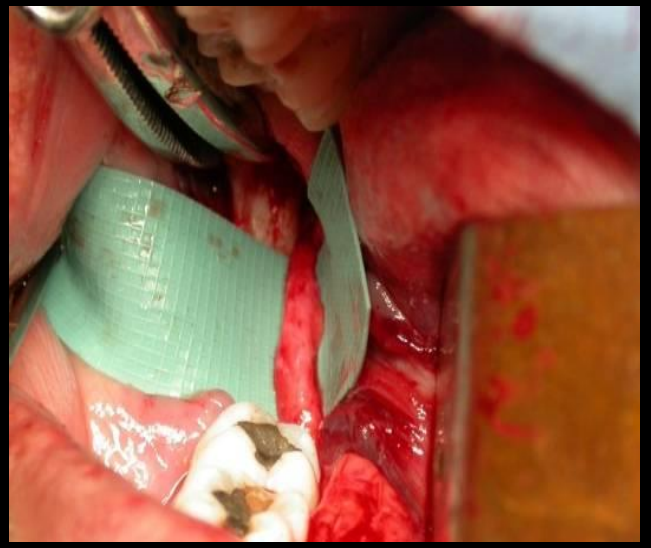


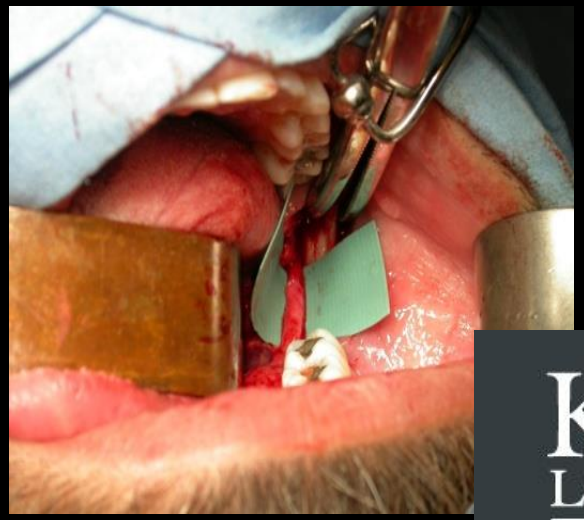
Key surgical procedures carried out for LNI patients

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









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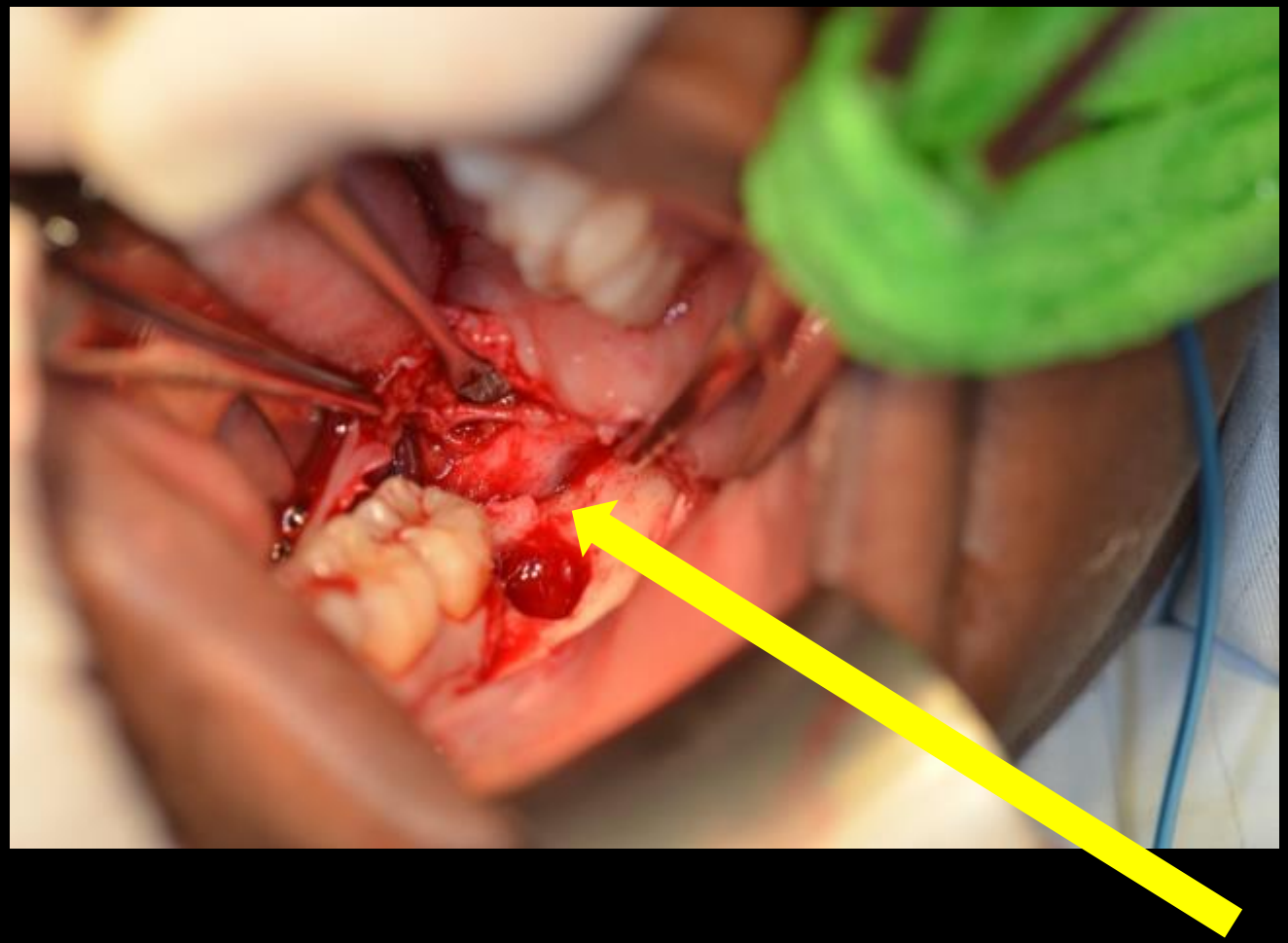
Findings during lingual nerve exploration .....we can see damaged lingual plates

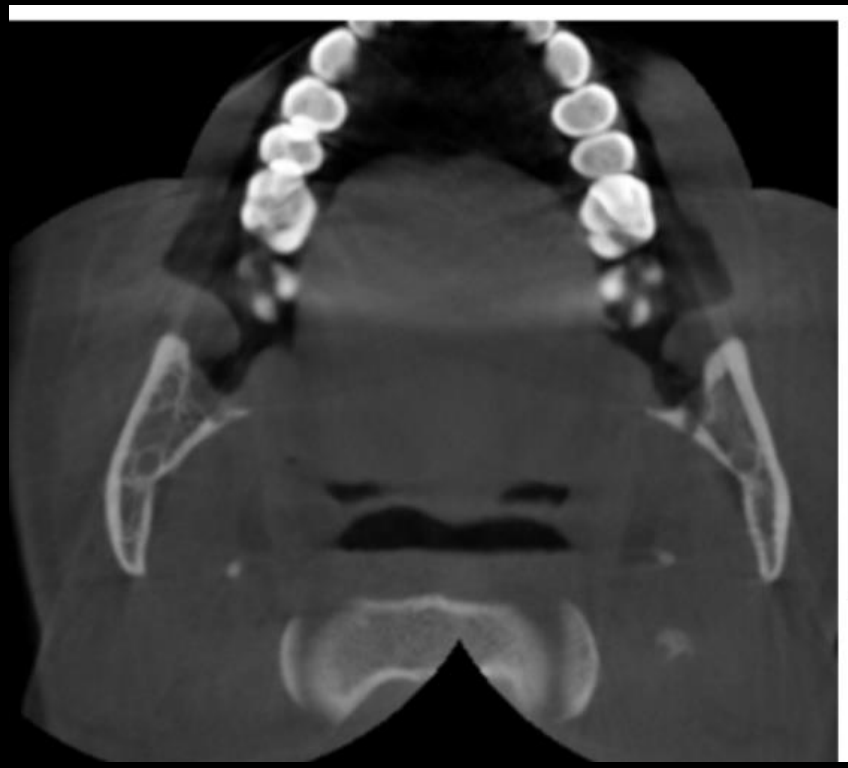


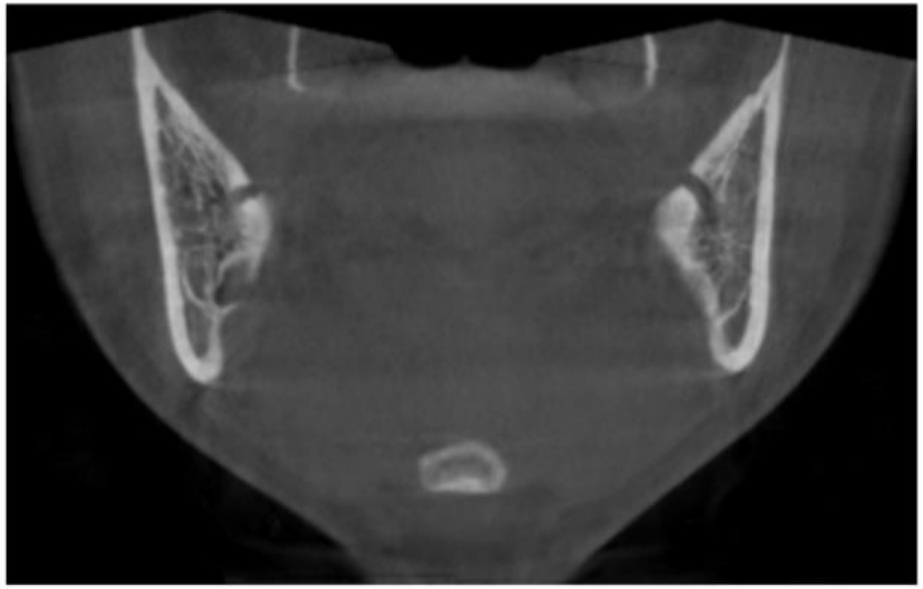
Damaged Lingual plate can be detected by CBCT scanning early post surgically

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

Lingual nerve injury
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)

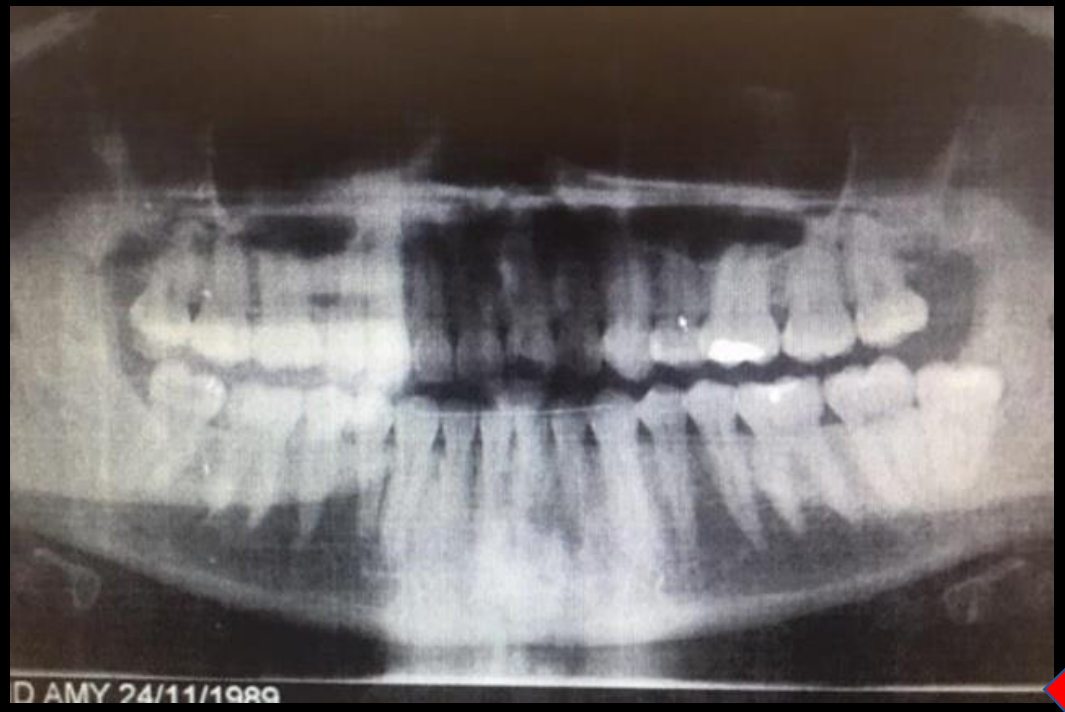
Recent Case Pre op findings

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

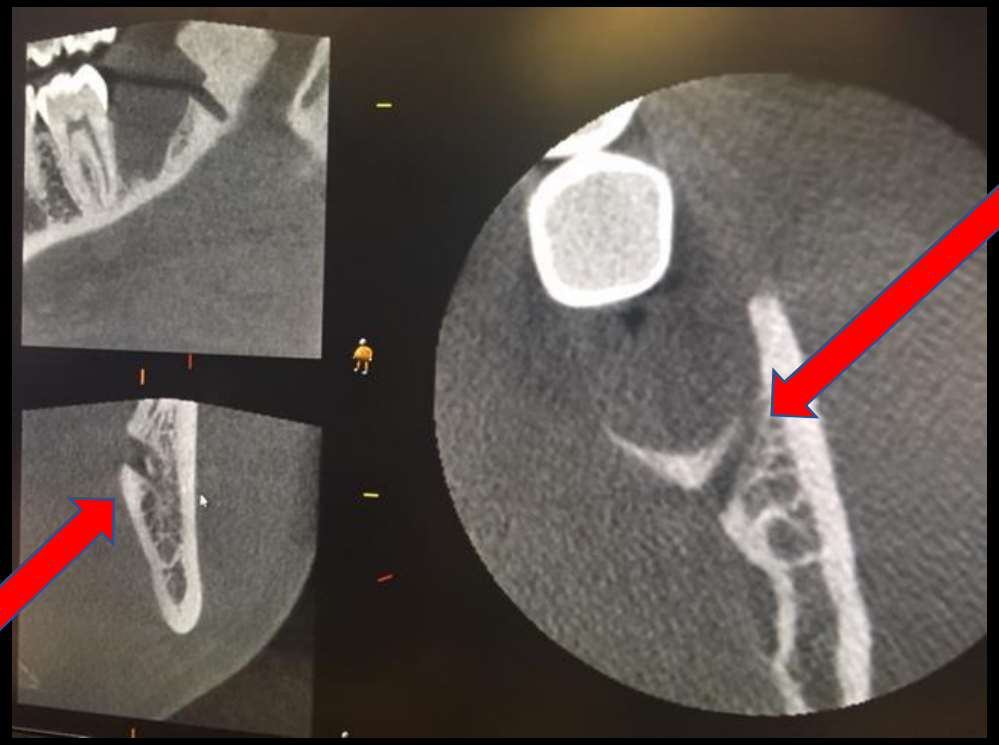
c/o numbness with occ spontaneous paraesthesia, functional difficulty speaking and eating.

mechanosensory sf 2/10, no SB detection or LT

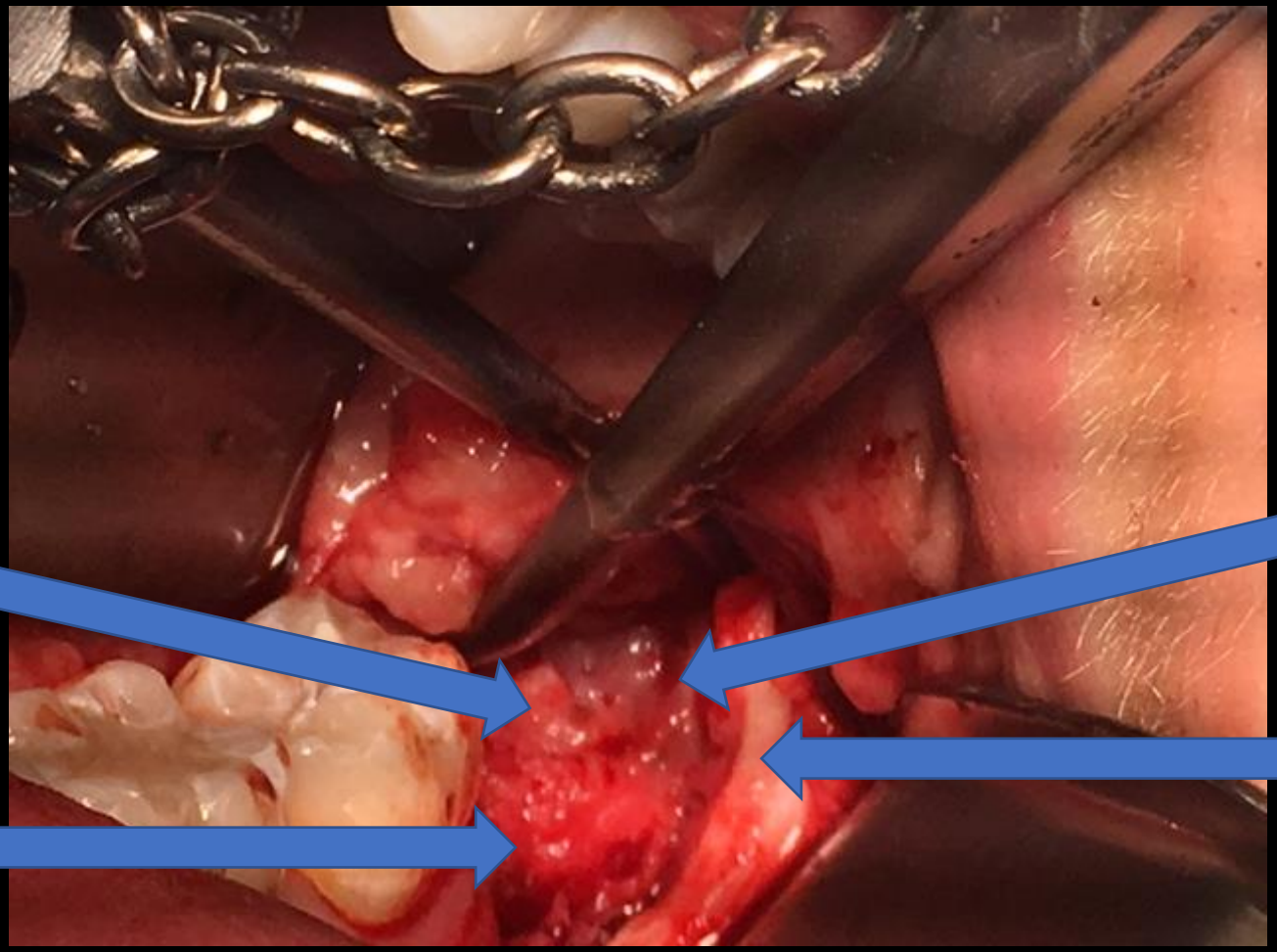
Preop DPT



CBCT taken 14/08/18



Operative findings lingual nerve injury 22/8/18



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

Granulation tissue in healing socket

Nerve tissue pulled into 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].

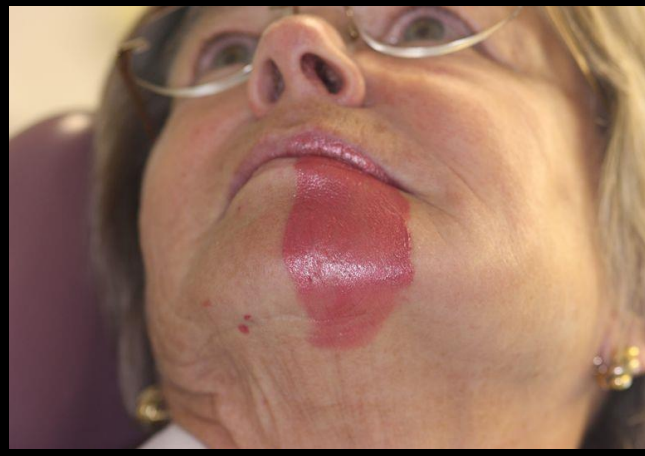
Anesthesia or paresthesia of the lower lip (consequent mental nerve sensory function disturbance) can significantly change patients' quality of life. Missing or reduced sensory innervation of the lower lip causes difficulties during eating and drinking, and uncontrolled bite trauma of the soft tissues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

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

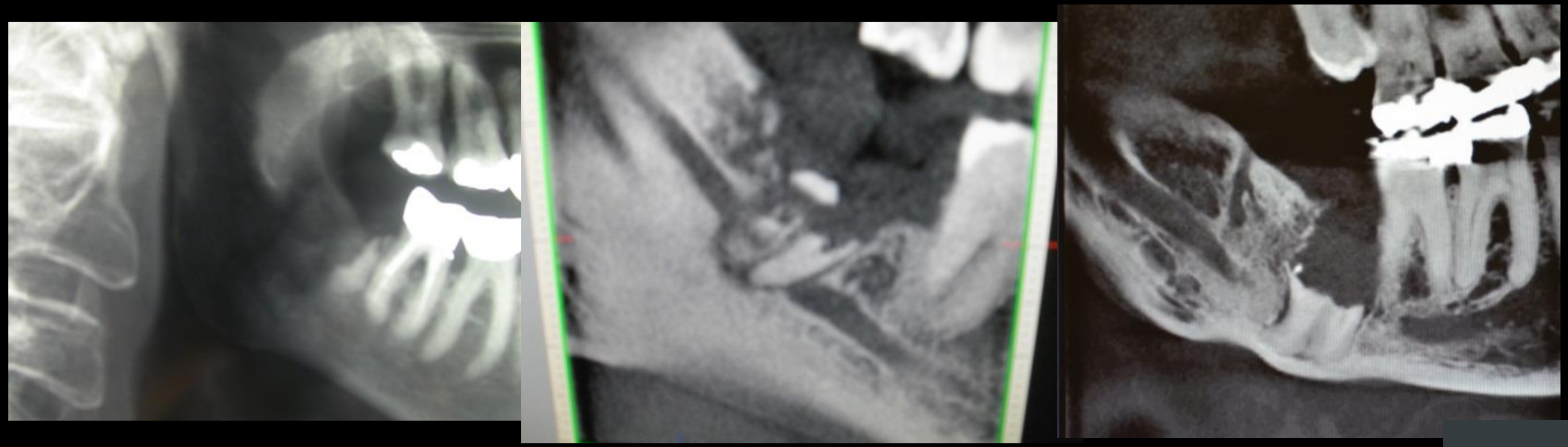
as the neurovascular bundle can "vibrate together" with piezoelectric-tips avoiding irreversible injury) when bone removal is necessary near to the IAN at the apical region of third molars.

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 additio

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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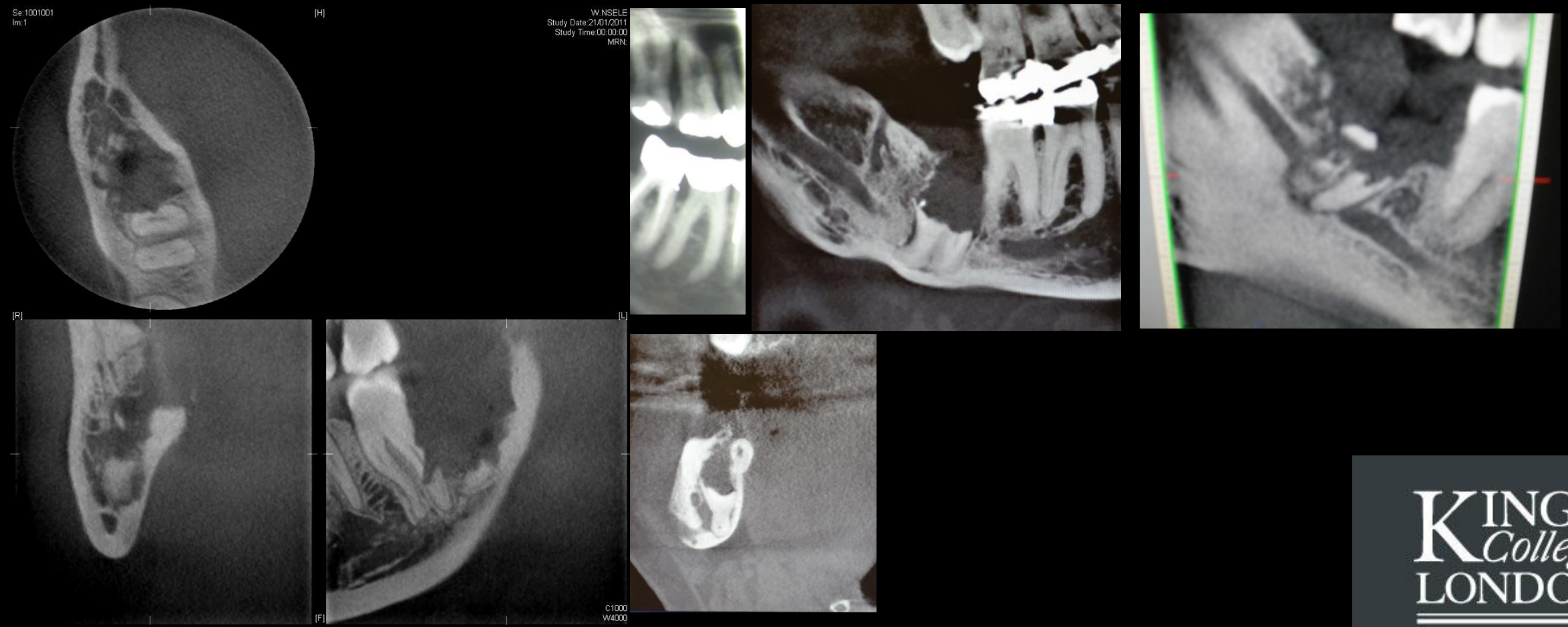
Inferior alveolar nerve injury with root retention

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



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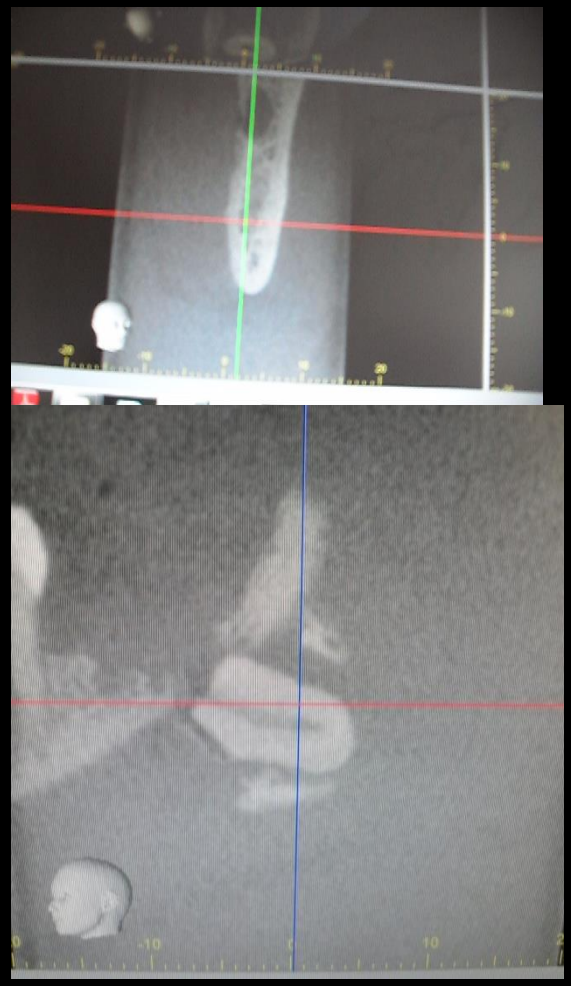
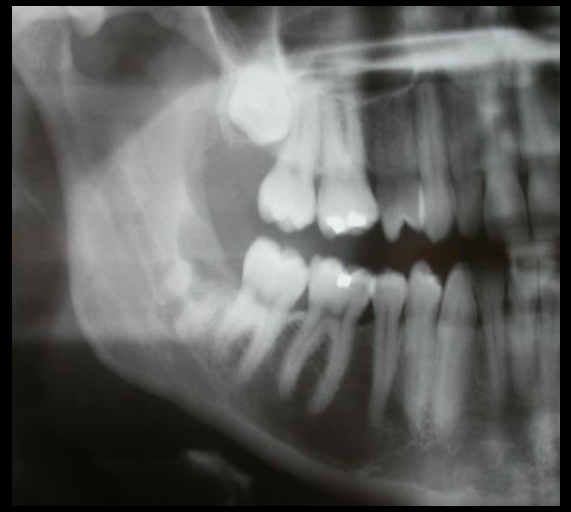
CBCT important to locate
Displaced retained roots in sublingual or submandibular spaces

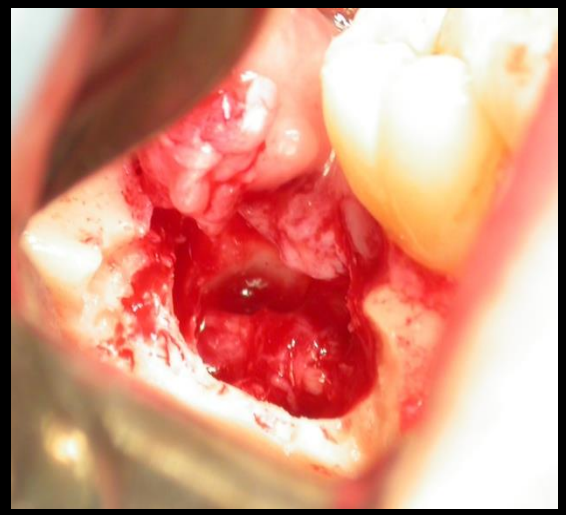
retained roots in mandibular region on DPT?
BUT……
Retained roots? In submandibular space?

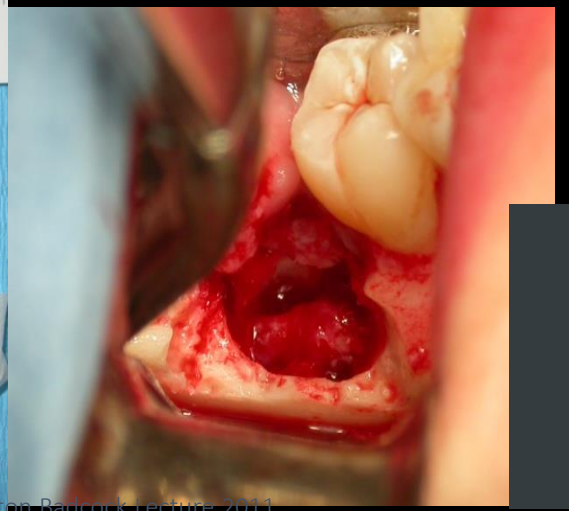


Early surgical intervention for patients IANI (< 2 weeks)

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

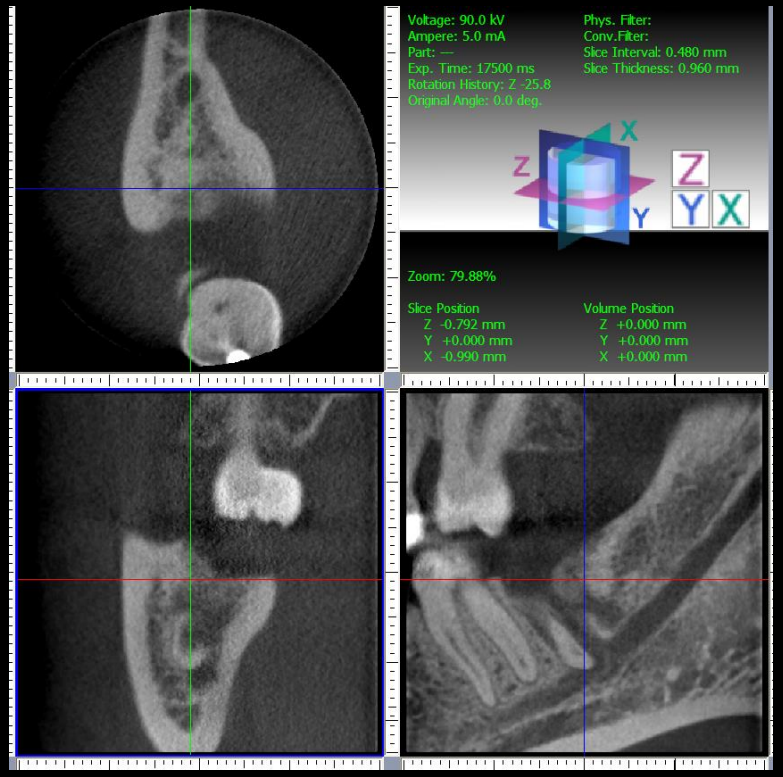


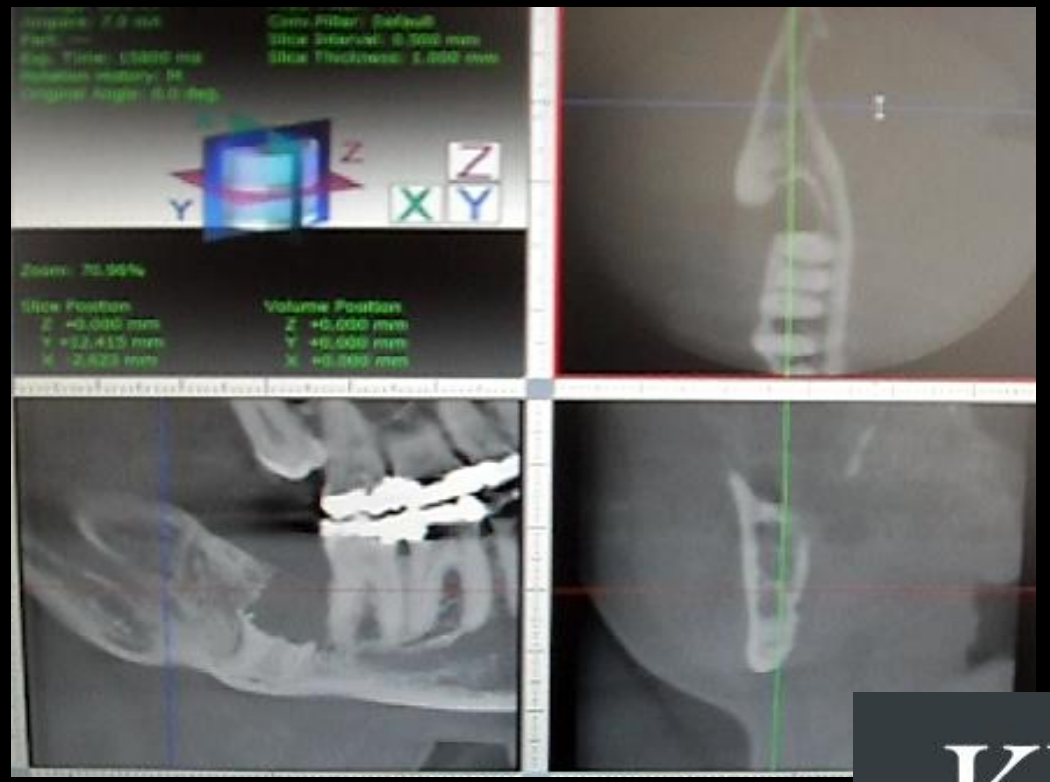




Late management of inferior alveolar nerve injury

Root retention with persistent
Chronic infection-external draining sinus (20 years post surgical) Plan surgical approach





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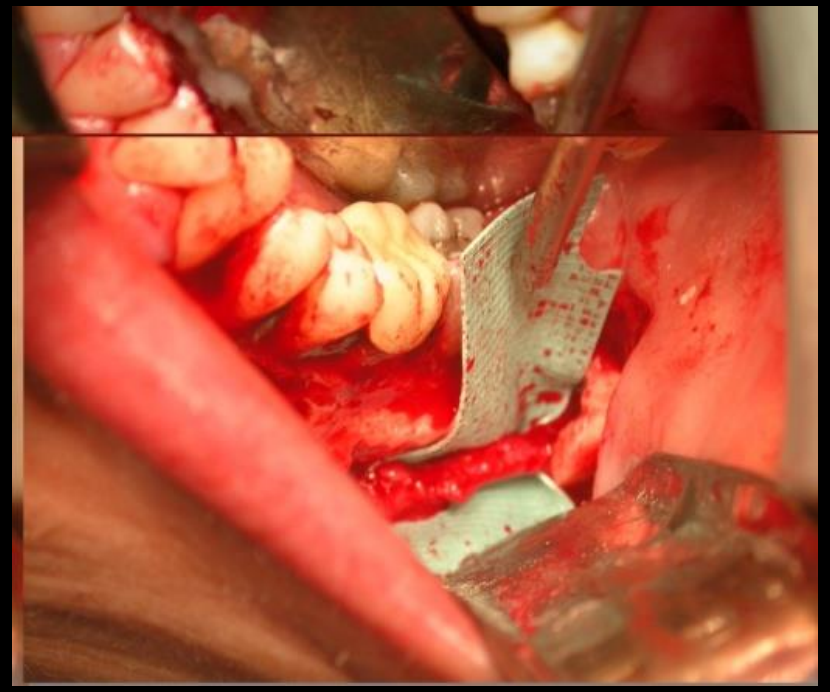
Late management of inferior alveolar nerve injury

If injury is > 36 hours days old or more

Manage therapeutically

- Surgery - removal of implant **doesn't work**
- Reassure patient
    - Psychological support
- Pain management **Medical management**
    - Topical Lidocaine patches, Capsaicin, Amitriptyline
    - Systemic Pregabalin / Tricyclic antidepressants



Rodriquez-Lozano F, Sanchez-Perez A, Moya-Villaescusa MJ, Rodriguez-Lozano A, Saez-Yuguero MR. Neuropathic orofacial pain after dental implant placement: review of the literature and case report. OOOE 2010; **109:** e8-e12. Renton T, Yilmaz Z. Profiling of patients presenting with posttraumatic neuropathy of the trigeminal nerve. J Orofac Pain. 2011 Fall;25(4):333-44. 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

However Neuropathic pain does not respond to surgery

Surgical impact on NP

Lingual nerve repair and recurrence of neuropathic pain

27 patientsmm Various procedures

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

*Chairman, Division of Oral and Maxillofacial Surgery; Professor, Departments of Surgery and Neurology and Neurotherapuetics, The University of Texas Southwestern Medical Center at Dallas, Dallas, TX.

†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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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-

Medical management- Pain medication

- **Acute phase**
  - Step down steroids prednisolone 50/40/30/20/10 mg over 5 day
  - 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.

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HHS Public Access
Author manuscript
Lancet Neurol. Author manuscript; available in PMC 2016 February 01.

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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]

[1]Corresponding author: Nadine ATTAL, INSERM U 987 and Centre d'Evaluation et de Traitement de La Douleur, Hospital Ambroise Pare, Boulogne-Billancourt, France Tel.: 0033149094433 ; nadine.attal@apr.aphp.fr.
[*]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 The
Biogen IDEC outside the submitted work. PS has a patent System
resonance spectroscopy, US Patent 08755862 issued. BHS has cc
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 ar
members contributed to the guidelines in formulating the recomm
external reviewers contributed to the final text version.

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American Society Neurology recommendations

- Medical management of neuropathic pain

TABLE 5. Level A and level B recommendations from the American Academy of Neurology for the treatment of painful diabetic neuropathy[15]

	Recommended drugs and doses and other treatments	Drugs and other treatments not recommended
Level A	Pregabalin, 300–600 mg/d	Oxcarbazepine
Level B	• Gabapentin, 900–3600 mg/d • Sodium valproate, 500–1200 mg/d • Venlafaxine, 75–225 mg/d • Duloxetine, 60–120 mg/d • Amitriptyline, 25–100 mg/d • Dextromethorphan, 400 mg/d • Morphine sulfate, titrated to 120 mg/d • Tramadol, 210 mg/d • Oxycodone, mean of 37 mg/d, maximum of 120 mg/d • Capsaicin cream, 0.075% 4 times daily • Isosorbide dinitrate spray • Electrical stimulation, percutaneous nerve stimulation, 3–4 wk	• Lamotrigine • Lacosamide • Clonidine • Pentoxifylline • Mexiletine • Magnetic field treatment • Low-intensity laser therapy • Reiki therapy

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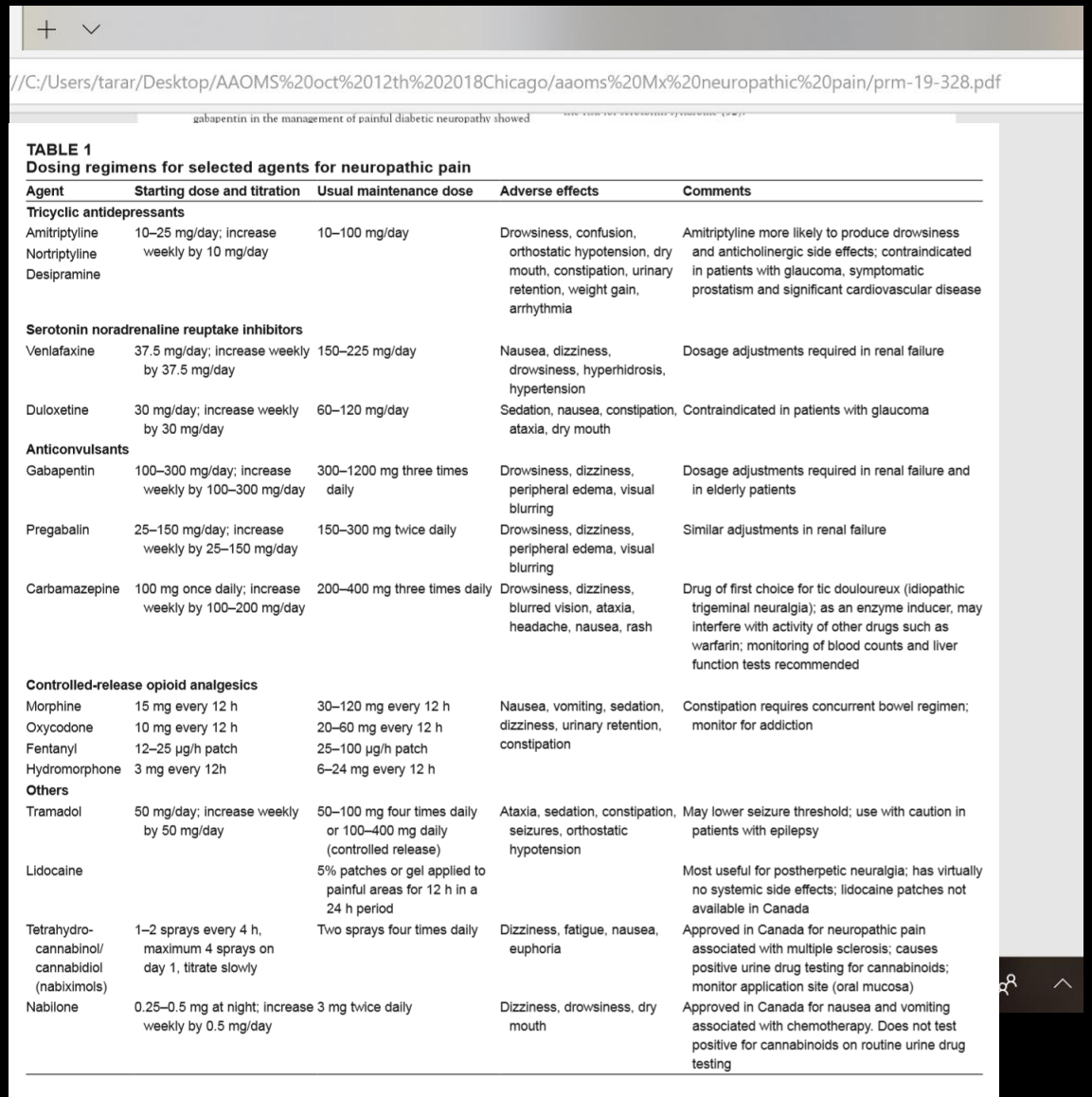
Canadian Pain society recommendations
Medical management of neuropathic pain



//C:/Users/tarar/Desktop/AAOMS%20oct%2012th%202018Chicago/aaoms%20Mx%20neuropathic%20pain/prm-19-328.pdf

gabapentin in the management of painful diabetic neuropathy showed

TABLE 1
Dosing regimens for selected agents for neuropathic pain

Agent	Starting dose and titration	Usual maintenance dose	Adverse effects	Comments
Tricyclic antidepressants				
Amitriptyline Nortriptyline Desipramine	10–25 mg/day; increase weekly by 10 mg/day	10–100 mg/day	Drowsiness, confusion, orthostatic hypotension, dry mouth, constipation, urinary retention, weight gain, arrhythmia	Amitriptyline more likely to produce drowsiness and anticholinergic side effects; contraindicated in patients with glaucoma, symptomatic prostatism and significant cardiovascular disease
Serotonin noradrenaline reuptake inhibitors				
Venlafaxine	37.5 mg/day; increase weekly by 37.5 mg/day	150–225 mg/day	Nausea, dizziness, drowsiness, hyperhidrosis, hypertension	Dosage adjustments required in renal failure
Duloxetine	30 mg/day; increase weekly by 30 mg/day	60–120 mg/day	Sedation, nausea, constipation, ataxia, dry mouth	Contraindicated in patients with glaucoma
Anticonvulsants				
Gabapentin	100–300 mg/day; increase weekly by 100–300 mg/day	300–1200 mg three times daily	Drowsiness, dizziness, peripheral edema, visual blurring	Dosage adjustments required in renal failure and in elderly patients
Pregabalin	25–150 mg/day; increase weekly by 25–150 mg/day	150–300 mg twice daily	Drowsiness, dizziness, peripheral edema, visual blurring	Similar adjustments in renal failure
Carbamazepine	100 mg once daily; increase weekly by 100–200 mg/day	200–400 mg three times daily	Drowsiness, dizziness, blurred vision, ataxia, headache, nausea, rash	Drug of first choice for tic douloureux (idiopathic trigeminal neuralgia); as an enzyme inducer, may interfere with activity of other drugs such as warfarin; monitoring of blood counts and liver function tests recommended
Controlled-release opioid analgesics				
Morphine	15 mg every 12 h	30–120 mg every 12 h	Nausea, vomiting, sedation, dizziness, urinary retention, constipation	Constipation requires concurrent bowel regimen; monitor for addiction
Oxycodone	10 mg every 12 h	20–60 mg every 12 h		
Fentanyl	12–25 µg/h patch	25–100 µg/h patch		
Hydromorphone	3 mg every 12h	6–24 mg every 12 h		
Others				
Tramadol	50 mg/day; increase weekly by 50 mg/day	50–100 mg four times daily or 100–400 mg daily (controlled release)	Ataxia, sedation, constipation, seizures, orthostatic hypotension	May lower seizure threshold; use with caution in patients with epilepsy
Lidocaine		5% patches or gel applied to painful areas for 12 h in a 24 h period		Most useful for postherpetic neuralgia; has virtually no systemic side effects; lidocaine patches not available in Canada
Tetrahydro-cannabinol/ cannabidiol (nabiximols)	1–2 sprays every 4 h, maximum 4 sprays on day 1, titrate slowly	Two sprays four times daily	Dizziness, fatigue, nausea, euphoria	Approved in Canada for neuropathic pain associated with multiple sclerosis; causes positive urine drug testing for cannabinoids; monitor application site (oral mucosa)
Nabilone	0.25–0.5 mg at night; increase weekly by 0.5 mg/day	3 mg twice daily	Dizziness, drowsiness, dry mouth	Approved in Canada for nausea and vomiting associated with chemotherapy. Does not test positive for cannabinoids on routine urine drug testing

CONSENSUS STATEMENT

Pharmacological management of chronic neuropathic pain: Revised consensus statement from the Canadian Pain Society

DE Moulin MD, A Boulanger MD, AJ Clark MD, H Clarke MD PhD, T Dao DMD PhD, GA Finley MD, A Furlan MD PhD, I Gilron MD MSc, A Gordon MD, PK Morley-Forster MD, BJ Sessle MDS PhD, P Squire MD, J Stinson RN PhD, P Taenzer PhD, A Velly DDS PhD, MA Ware MD, EL Weinberg MD, OD Williamson MBBS

DE Moulin, A Boulanger, AJ Clark, et al. Pharmacological management of chronic neuropathic pain: Revised consensus statement from the Canadian Pain Society. Pain Res Manag 2014;19(6):328-335.

BACKGROUND: Neuropathic pain (NeP), redefined as pain caused by a lesion or a disease of the somatosensory system, is a disabling condition that affects approximately two million Canadians.
OBJECTIVE: To review the randomized controlled trials (RCTs) and systematic reviews related to the pharmacological management of NeP to develop a revised evidence-based consensus statement on its management.
METHODS: RCTs, systematic reviews and existing guidelines on the pharmacological management of NeP were evaluated at a consensus meeting in May 2012 and updated until September 2013. Medications were recommended in the consensus statement if their analgesic efficacy was supported by at least one methodologically sound RCT (class I or class II) showing significant benefit relative to placebo or another relevant control group. Recommendations for treatment were based on the degree of evidence of analgesic efficacy, safety and ease of use.
RESULTS: Analgesic agents recommended for first-line treatments are gabapentinoids (gabapentin and pregabalin), tricyclic antidepressants and serotonin noradrenaline reuptake inhibitors. Tramadol and controlled-release opioid analgesics are recommended as second-line treatments for moderate to severe pain. Cannabinoids are now recommended as third-line treatments. Recommended fourth-line treatments include methadone, anticonvulsants with lesser evidence of efficacy (eg, lamotrigine, lacosamide), tapentadol and botulinum toxin. There is support for some analgesic combinations in selected NeP conditions.
CONCLUSIONS: These guidelines provide an updated, stepwise approach to the pharmacological management of NeP. Treatment should be individualized for each patient based on efficacy, side-effect profile and drug accessibility, including cost. Additional studies are required to examine head-to-head comparisons among analgesics, combinations of analgesics, long-term outcomes and treatment of pediatric, geriatric and central NeP.

Key Words: *Analgesic agents; Neuropathic pain; Randomized controlled trials*

La prise en charge pharmacologique de la douleur neuropathique chronique : une déclaration de consensus révisée de la Société canadienne de la douleur

HISTORIQUE : La douleur neuropathique (DNe), redéfinie comme une douleur causée par une lésion ou une maladie du système somatosensoriel, est un trouble invalidant dont sont affligés environ deux millions de Canadiens.
OBJECTIF : Examiner les essais aléatoires et contrôlés (EAC) et les analyses systématiques liées à la prise en charge pharmacologique de la DNe pour préparer une déclaration de consensus révisée, fondée sur des faits probants, à l'égard de sa prise en charge.
MÉTHODOLOGIE : Les EAC, les analyses systématiques et les lignes directrices sur la prise en charge pharmacologique de la DNe ont été évaluées lors d'une réunion de consensus en mai 2012, puis mises à jour en septembre 2013. Les médicaments étaient recommandés dans le document de consensus si leur efficacité analgésique était soutenue par au moins une EAC solide sur le plan méthodologique (classe I ou II), qui démontrait des avantages marqués par rapport à un placebo ou à un autre groupe témoin pertinent. Les recommandations thérapeutiques reposaient sur la qualité des preuves d'efficacité analgésique, d'innocuité et de facilité d'utilisation.
RÉSULTATS : Les analgésiques recommandés pour le traitement de première intention sont les gabapentinoïdes (gabapentine et prégabaline), les antidépresseurs tricycliques et les inhibiteurs spécifiques du recaptage de la sérotonine et de la noradrénaline. Le tramadol et les opioïdes à libération contrô
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Neuropathic pain (NeP) has been redefined as pain caused by a lesion or a disease of the somatosensory system, and may be generated by either the peripheral or central nervous system, or both

newe
higher rate of 4% to 8% (6,7), which suggest that approximately two million Canadians experience this disabling condition. Even

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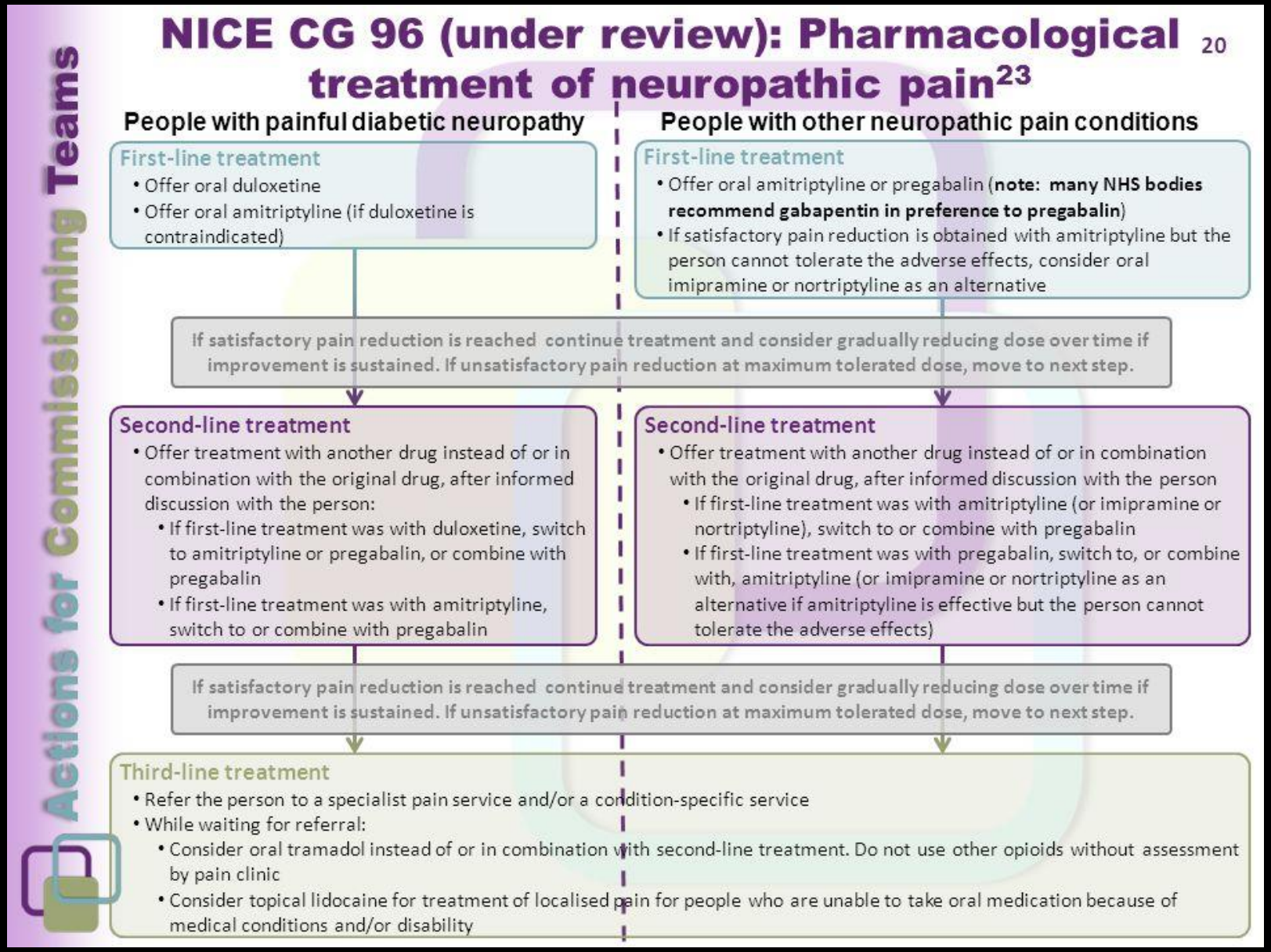
National Institute Clinical excellence (NICE) NHS recommendations Guidance for prescribing for adult neuropathic pain



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Go to drugs

Nortriptyline (TCA) (10-40mgs nocte)

Lyrica Pregabalin (25mgs nocte / BD)

Indication	Dosing regimen	Maximum dose
DPN pain	3 divided doses per day	300 mg/day within 1 week
PHN	2 or 3 divided doses per day	300 mg/day within 1 week. Maximum dose of 600 mg/day
Adjunctive therapy for adult patients with partial onset seizures	2 or 3 divided doses per day	Maximum dose of 600 mg/day
Fibromyalgia	2 divided doses per day	300 mg/day within 1 week Maximum dose of 450 mg/day
Neuropathic pain associated with spinal cord injury	2 divided doses per day	300 mg/day within 1 week. Maximum dose of 600 mg/day

	Gabapentin	Pregabalin
Chemistry	Analog of GABA	Substituted analog of gabapentin
Absorption	Saturable	Non-saturable
Oral bioavailability	60% – 300 mg 33% – 3600 mg 27% – 4800 mg	90%
Onset of action	≥ 9 days	1–3 days
Renal elimination (half-life)	70–80% (5–7 hours)	90–99% (5–7 hours)
Dose (normal renal function)	300 mg po TID; ↑ q week as tolerated to maximum 3600 mg/day	75 mg po BID; ↑ every 3–7 days as tolerated to maximum 600 mg/day
T_{max}	0.7–1.5 hours	
Half-life	4.6–6.8 hours	5–7 hours
Percent excreted uncharged in urine	98%	

Actions for Commissioning Teams

21

Pregabalin or gabapentin?

- Pregabalin and gabapentin are structurally related and have a similar pharmacological action and adverse events.
- Limited data - no published head-to-head RCTs comparing gabapentin and pregabalin in post-herpetic neuralgia or diabetic neuropathy. One small trial in neuropathic cancer pain.
- Pregabalin is much more expensive than gabapentin (see next slide)
  - In 2012, the NHS in West Midlands spent nearly £19 million on pregabalin . Although it has other indications, the majority of pregabalin prescriptions are for neuropathic pain. If half of the pregabalin prescriptions had been prescribed as gabapentin, this could have saved more than £8 million.
- Current NICE guidance for neuropathic pain recommends pregabalin as a first line option but does not recommend gabapentin.[23]
  - NICE concluded that pregabalin is more effective than gabapentin based on indirect comparisons of the two treatments. Pregabalin *vs.* gabapentin, has lower number needed to treat (NNT) values for at least 30% pain reduction and 50% pain reduction.
- Decision by NICE to recommend pregabalin over gabapentin has been heavily criticised because c
  have agreed to review their

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Side effects and compliance

only 11% of PTNP patients continue with medication

TABLE 4

MOST COMMON ADVERSE SNRI DRUG REACTIONS[1-4]

Venlafaxine[1]	*Duloxetine*[2]	*Milnacipran*[3]	*Desvenlafaxine*[4]
Nausea	Nausea	Anxiety	Nausea
Sweating	Increased sweating	Excessive sweating	Hyperhidrosis
Somnolence	Somnolence	Vertigo	Somnolence
Anorexia	Decreased appetite	Hot flush	Decreased appetite
Tremor	Constipation	Dysuria	Constipation
Nervousness	Fatigue		Anxiety
Dry mouth	Dry mouth		
Dizziness			
Abnormal dreams			
Abnormal ejaculation			

Adverse reactions as defined as oc
twice the rate for placebo for venlafa
European Medicines Agency for miln

SNRI=serotonin norepinephrine reup

Shelton RC. *Primary Psychiatry.* Vol

Common side effects associated with tricyclic antidepressants

	Sedation	Anti-cholinergic effects	Hypo-tension	Cardiac effects	Seizures	Weight gain
Amitriptyline	+++	+++	+++	+++	++	++
Clomipramine	++	+++	++	+++	+++	+
Desipramine	0/+	+	+	++	+	+
Nortriptyline	+	+	+	++	+	+

0/+=minimal; +=mild; ++=moderate; +++=moderately severe.
From Goodman and Gilman's, *The Pharmacological Basis of Therapeutics*, 9th edition.

Table 2. Common Adverse Effects from Treatment for Diabetic Peripheral Neuropathic Pain

Drug	*Adverse effect*	*Patients who experienced effect (%)*
Amitriptyline*[8,30]	Constipation	14
	Dizziness	28
	Dry mouth	90
	Somnolence	66
Capsaicin cream (Zostrix)[19]	Cough	8
	Skin irritation	54
Duloxetine (Cymbalta)[5,19]	Constipation	9
	Diarrhea	6
	Fatigue	9
	Headache	10
	Nasopharyngitis	6
	Nausea	22
	Somnolence	8
	Sweating	6
abapentin (Neurontin)[11]	Confusion	7
	Diarrhea	10
	Dizziness	24
	Headache	10
	Nausea	8
	Somnolence	20
docaine 5% patch (Lidoderm)[20]	No adverse effects significantly different from placebo	—

Drug	*Adverse effect*	*Patients who experienced effect (%)*
Opiates[14]	Constipation	33
	Dizziness	21
	Nausea	33
	Somnolence	29
	Vomiting	15
Pregabalin (Lyrica)†[9,10]	Dizziness	7 to 28
	Edema	6 to 16
	Somnolence	5 to 13
	Weight gain	4 to 9
Tramadol (Ultram)[18]	Constipation	22
	Headache	17
	Nausea	23
	Somnolence	12
Venlafaxine (Effexor)[8]	Anorexia	5
	Dyspepsia	10
	Flatulence	6
	Impotence	5
	Insomnia	10
	Myalgia	5
	Nausea	10
	Sinusitis	7
	Somnolence	15
	Swe	
	Vom	

—Amitriptyline chosen to represent tricyclic antidepressants.
—Range of percentages is based on range of doses in study; adverse effects were dose-related.
formation from references 5, 8 through 11, 14, 18 through 20, and 30.

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Medical Trigeminal Ne pain management

Grade A for TN (Tegretol)
Grade B for BMS (Nortriptyline & clonazepam)
limited for other conditions

Alonso-Ezpeleta O, Martín PJ, López-López J, Castellanos-Cosano L, Martín-González J, Segura-Eg JJ. Pregabalin in the treatment of inferior alveolar n paraesthesia following overfilling of endodontic sea Clin Exp Dent. 2014 Apr 1;6(2):e197-202.

CASE REPORT

Inferior alveolar nerve injury resulting from overextension of an endodontic sealer: non-surgical management using the GABA analogue pregabalin

1. J. López-López[1],
2. A. Estrugo-Devesa[1],
3. E. Jané-Salas[1] and
4. J. J. Segura-Egea[2]

Article first publish

DOI: 10.1111/j.136

© 2011 Internationa

López-López J, Estrugo-Devesa A, Jané-Salas E, Segura-Egea JJ Infe alveolar nerve injury resulting from overextension of an endodontic management using the GABA analogue pregabalin. Int Endod J. 201 doi: 10.1111/j.1365-2591.2011.01939.x. Epub 2011 Aug 23.

Issue

International End

AIM:To describe a case of endodontic sealer (AH Plus) penetration within the after root canal treatment with resolution of pain and paraesthesia after a nc including treatment with prednisone and pregabalin.
SUMMARY:A 37-year-old woman underwent root canal treatment of the left molar tooth. Postoperative periapical radiographs revealed the presence of r sealer in the mandibular canal. The day after, the patient reported severe pa paraesthesia/anaesthesia in the region innervated by the left inferior alveola Diagnosis of injury to the inferior alveolar nerve because of extrusion of AH The non-surgical management included 1 mg kg(-1) per day prednisone, tw regimen on a daily basis, and 150 mg per day pregabalin, two doses per day progress with periodic follow-up visits. One month after the incident, the sig were gone.
KEY LEARNING POINTS: This case illustrates the care required when performing root canal treatment, especially when the root apices are in close proximity to the inferior alveolar nerve canal. The complete resolution of paraesthesia and the control of pain achieved in

Haviv Y, Zadik Y, Sharav Y, Benoliel R. Painful traumatic trigeminal neuropathy: an open study on the pharmacotherapeutic response to stepped treatment. J Oral Facial Pain Headache. 2014 Winter;28(1):52-60. doi: 10.11607/jop.1154.

AIMS: To evaluate pharmacotherapeutic success in patients with painful traumatic trigeminal neuropathy (PTTN) and to identify patient or pain characteristics that may predict treatment outcome.

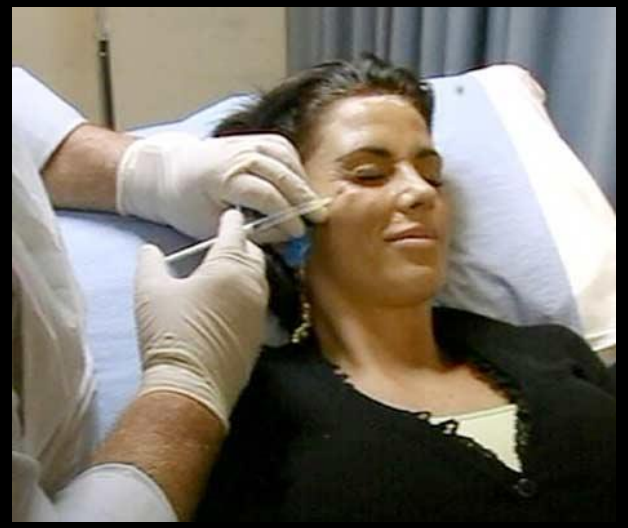
METHODS: Pharmacotherapy was instituted for PTTN patients and was based on widely accepted protocols fo neuropathic pain and conducted in an open fashion. Outcome was assessed by employing prospective diaries recording pain intensity measured with an 11-point (0 to 10) verbal pain score (VPS). Individual characteristics in the patients and their influence on outcome were analyzed. Treatment results in the PTTN patients were compared with those in classical trigeminal neuralgia (CTN) patients, who were used as a comparative cohort. Data were analyzed with a Pearson chi-square test for nominal variables and with an independent samples t test or analysis of variance for continuous variables.

RESULTS: A total of 145 patients were included: 91 with PTTN and 54 with CTN. In PTTN patients, 11% had ≥ 50% reduction in pain intensity. Higher VPS scores in the PTTN patients were associated with a significantly reduced response to therapy (P = .03). No other pain-related or demographic parameters were associated with treatment outcome in the PTTN patients. Also the response rate of PTTN patients was significantly inferio to that of CTN patients, 74.1% of whom attained a significant reduction in pain intensity (P < .001).

CONCLUSION: This study underpins the poor pharmacotherapeutic prognosis of PTTN. The results support findings on neuropathic pain in other sites and point to the need for further research and reexamination of current PTTN treatment protocols.

Local medications

- Botoxin A injections
- Peripheral local anaesthetic block
- Capsaicin patches
- Topical LA patches



Ngeow WC, Nair R Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010 Mar;109(3):e47-50.
Injection of botulinum toxin type A (BOTOX) into trigger zone of trigeminal neuralgia as a means to control pain
.

Nadine Khawaja, Zehra Yilmaz, Tara Renton Case studies illustrating the management of trigeminal neuropathic pain using topical 5% lidocaine plasters British Journal Pain 2013 https://doi.org/10.1177/2049463713483459 Nadine

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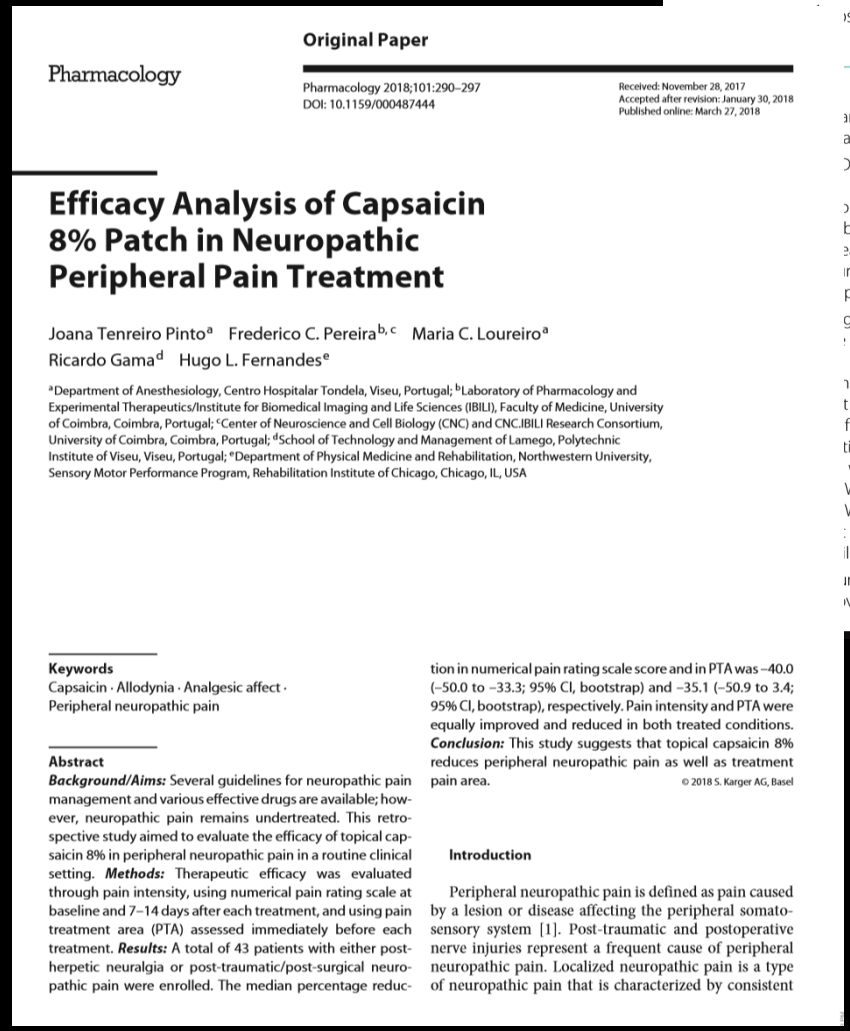
Capsaicin patches

- 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]

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

…D 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 …ild or moderate reversible application site reactions.

…uropean 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

Disease-a-Month 62 (2016) 353–357

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

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). [illegible] research exploring the use of BoNT for other chronic pain disorders, i[illegible] pain, intra-articular pain, myofascial pain, and complex regional pain sy[illegible]

BoNT mechanism of action and rationale for use in chronic pain co[illegible]

The primary mechanism of action of BoNT is blockage of ac[illegible] transmitter release from the presynaptic nerve at the neuromuscular j[illegible] 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

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Botulinum toxin A
Grade B for TN but low evidence for PTN

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.clinicaltrialsregister.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,[a] Jon Ryder, DDS, MS,[a] 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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[d]Associate Professor of Clinical Dentistry, Herman Ostrow School of

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 botuli-

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

The Journal of Headach
and Pai

REVIEW ARTICLE Open Acces

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 c

Keywords: Botulinum, BTX-A, Trigem

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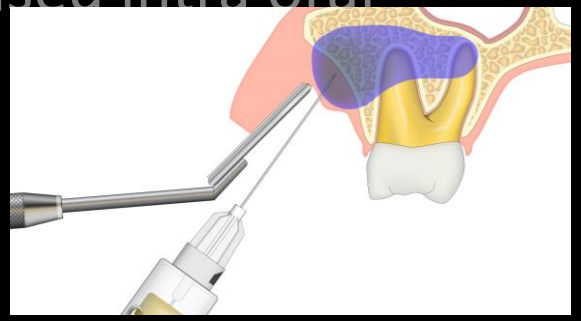
Pre Botox LA injections for focal neuropathic pain

Lidocaine 2% (1:80K epinephrine) 1-2mls infiltrations
positive response prerequisite for BTX treatment but not predictive

PDAP 1 or primary localised intra oral Ne Pain

- 7 patients
- Mean age 55yrs
- 60% Female
- Site
  - 40% mandibular posterior molar region
  - 40% posterior maxillary molar region
  - 20% anterior maxilla
- Response rate
  - Complete 3 (1 hour-30days)
  - Partial 2
  - None 2



PPTTN localised intra oral Ne Pain

- 18 patients
- Mean age 42 yrs
- 75% female
- Site
  - 15% mandibular posterior molar region
  - 5% posterior maxillary molar region
  - 80% anterior maxilla
- Response rate
  - Complete 14 (duration 1 hour -42 days)
  - Partial 2
  - None 2

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Interventional pain management includes;

- **Peripheral stimulation**
  - Superficial sessional neurostimulation
- **Central Neurostimulation/ neuromodulation**
  - SPG - Ganglia implanted neurostimulation
  - TG Pulsed Radiofrequency
  - Spinal cord stimulation (not for OFP)
  - Deep brain stimulation
  - Transmagnetic stimulation

ABLATIVE TECHNIQUES

Gasserian Ganglion interventions

- Radiofrequency ablation
- Thermocoagulation
- Balloon compression
- Glycerolysis
- Cryosurgery

Sphenopalatine ganglion injections

Stereotactic radiosurgery

Gamma knife may be indicated If there is medical contraindications to MVD

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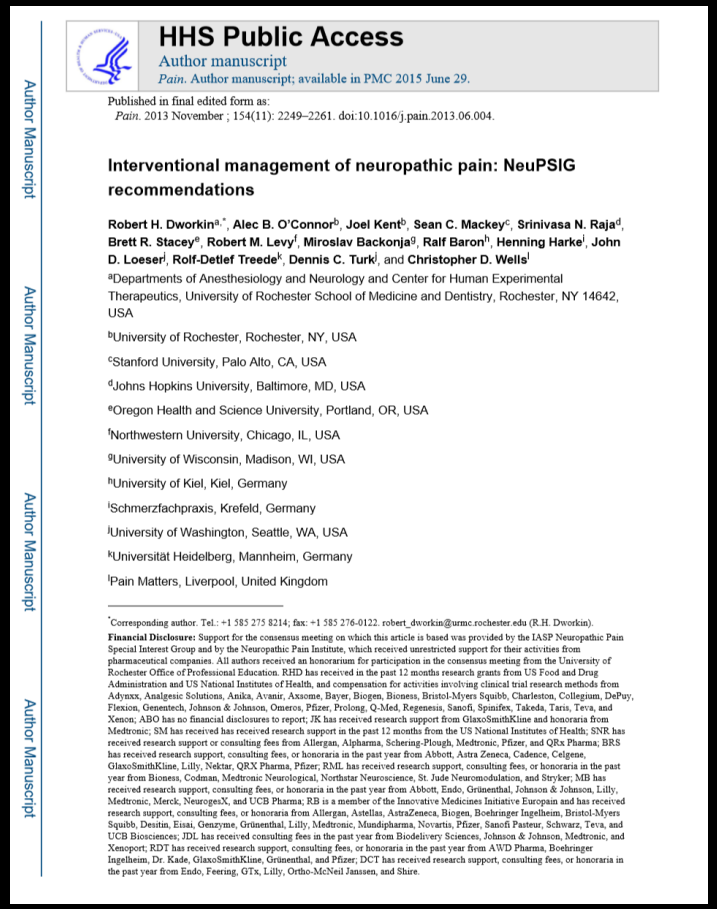
IASP Neuropathic SIG Recommendations interventional procedures for Ne Pain



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Interventional management of neuropathic pain: NeuPSIG recommendations

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Neuropathic pain (NP) is often refractory to pharmacologic and non-interventional treatment. On behalf of the International Association for the Study of Pain Neuropathic Pain Special Interest Group (NeuPSIG),

Ne pain due to

- peripheral and central NP conditions
- herpes zoster and postherpetic neuralgia (PHN)
- painful diabetic and other peripheral neuropathies
- spinal cord injury NP
- central post-stroke pain
- radiculopathy
- failed back surgery syndrome (FBSS)
- complex regional pain syndrome (CRPS)
- **trigeminal neuralgia and neuropathy**

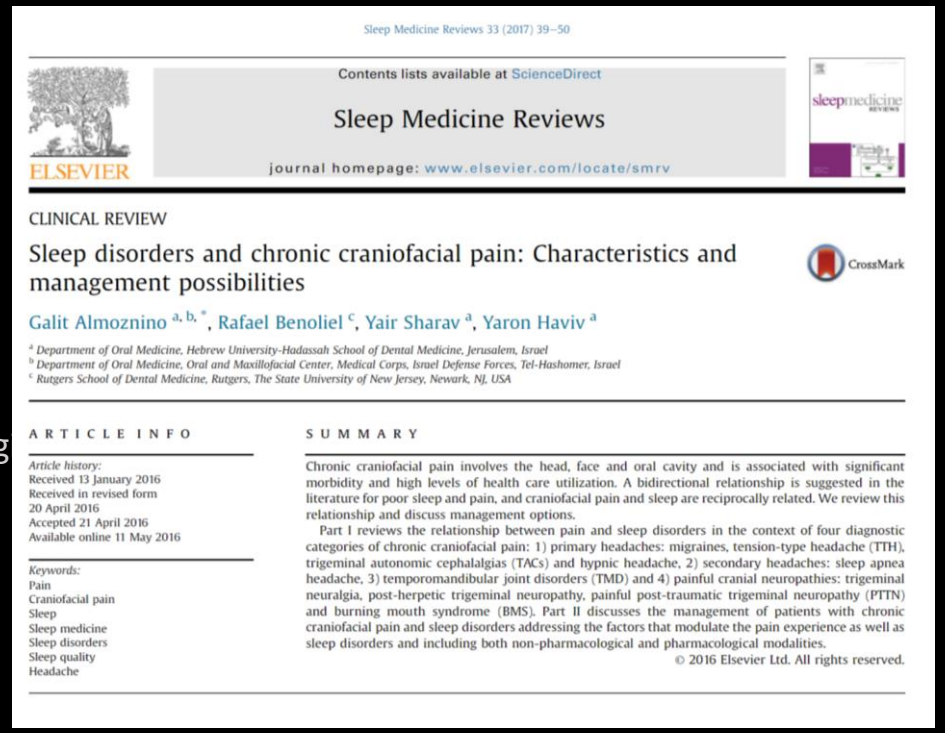
Evidence is summarized and presented for

- neural blockade,
- spinal cord stimulation (SCS),
- intrathecal medication,
- and neurosurgical interventions

evidence, including degree of efficacy and safety, are: (1) epidural injections for herpes zoster; (2) steroid injections for radiculopathy; (3) SCS for FBSS; and (4) SCS for CRPS type 1. Based on the available data, we recommend not to use sympathetic blocks for PHN nor RF lesions for radiculopathy

Alternative analgesic therapies

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



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

CLINICAL REVIEW

Sleep disorders and chronic craniofacial pain: Characteristics and management possibilities

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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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Summary what do we need to do? Recommendations

- Ensure that you are familiar with the ICOP orofacial pain classification even if there are weaknesses
- TN is a well recognised condition but often misdiagnosed
- There are clear medical and surgical pathways for treatment of TN
- Prevention of PTNP is possible
- Identify when urgent treatment is needed (early referral)
- Focus on a patient centred holistic approach is required
- A multi multi disciplinary approach is required

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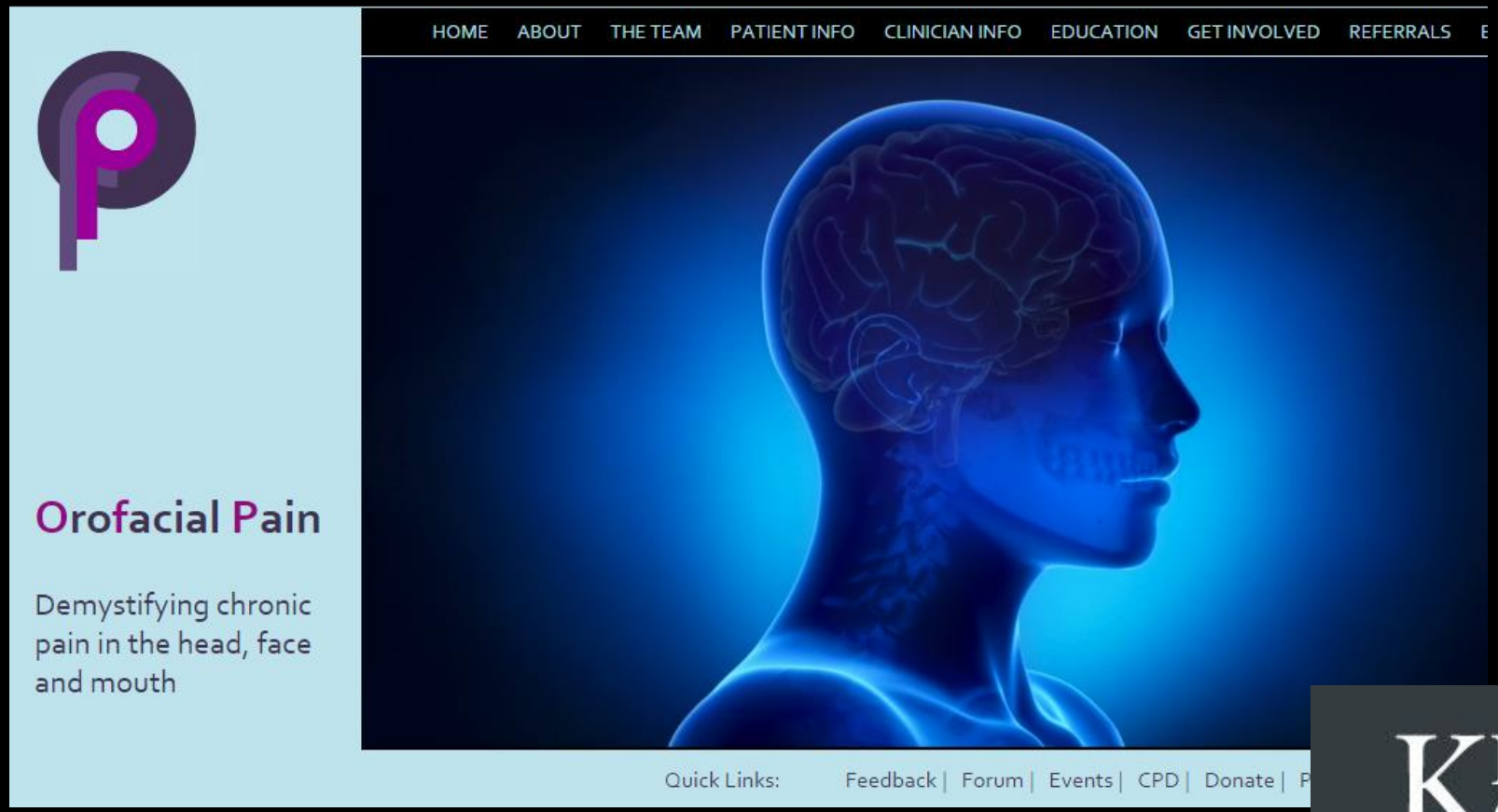
THANK YOU

http://www.orofacialpain.org.uk



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University of London

TIMING

Mechanism	Duration	Treatment
Known/suspected nerve section		**Immediate exploration**
TMS IANI –retained roots	**<30 hours**	**Immediate exploration**
Implant	**<30 hours**	**Remove implant**
Endodontic	**<30 hours**	After development of neuropathy **Remove tooth / overfill**
Implant / Endodontic	>30 hours	Treat therapeutically
TMS IANI large neuropathic area, pain and disability	<3 months	Consider exploration
TMS LNI – large neuropathic area, pain and disability	<3 months	Consider exploration
TMS IANI –	>6 month	Treat therapeutically
TMS LNI–	>6 month	Treat therapeutically
LA, fracture, orthognathic, other surgery		Treat t therapeutically

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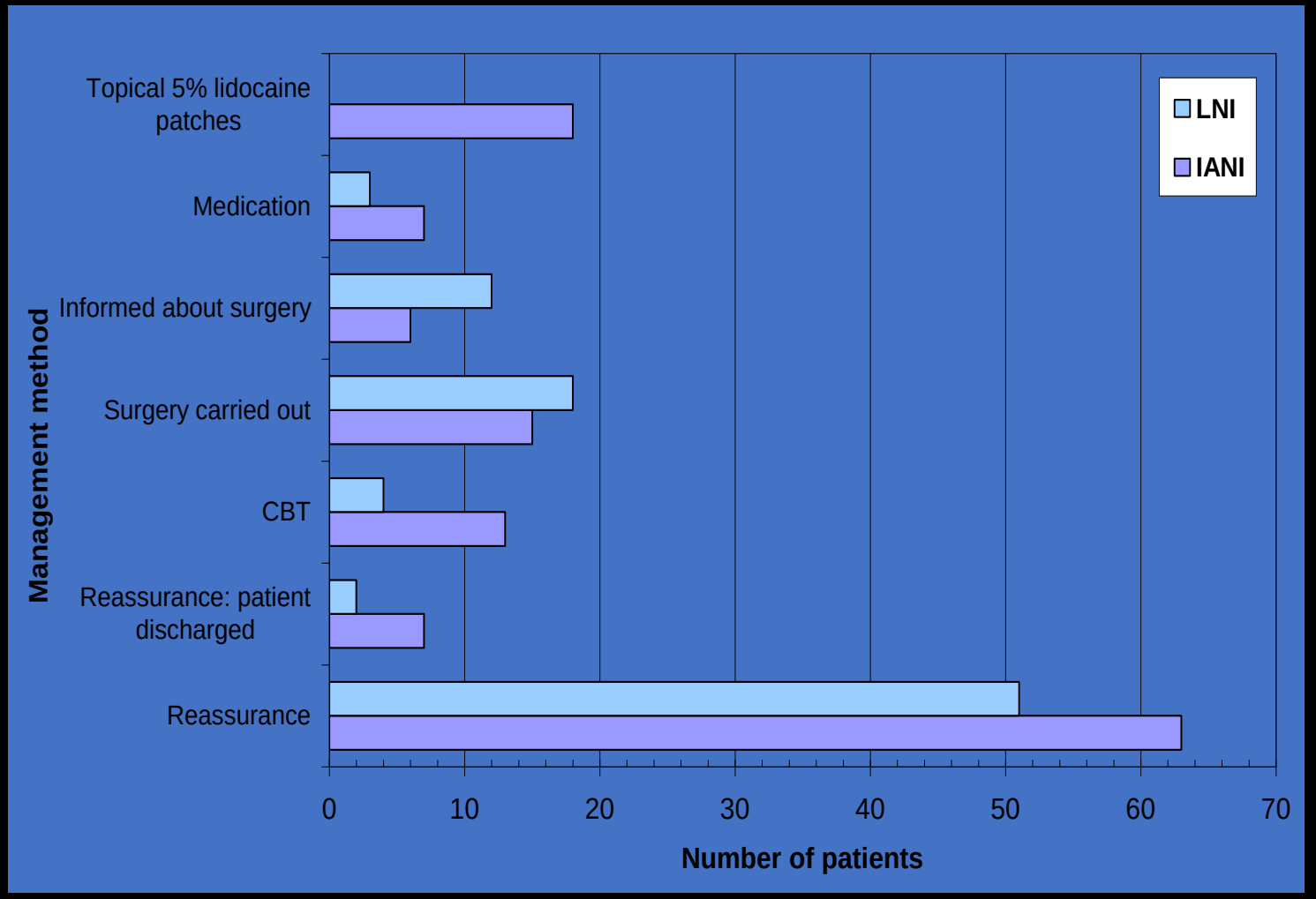
MULTIMODAL PATIENT CENTRED TREATMENT



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

recommendations

Post traumatic trigeminal neuropathy can be avoided, an international consensus is needed

Pre existing Neuropathic pain MUST be assessed prior to ‘REPARATIVE’ surgery for pain.

in order to identify and trial predictors for risk of, resolution or persistence of TRIGEMINAL Nerve injury and neuropathic pain. There is a need for holistic future studies on nerve injuries with neuropathic pain to be rigorous in applying an agreed criteria for;

- diagnostic classification using ICHD beta 3 classification
- international consensus for pre and post injury Axis I, Axis II and Axis III assessment protocols
- Phenotyping
  - Health-category of personal factors especially age
  - psychological factors
  - sensory signs and symptoms QST and CPM
  - genetics
  - International Classification of Functioning/ Disability and Health model is used as a framework to categorize these predictors
  - Neural profiling
- Outcomes?
- Systematic reviews identify that predictors in the category of

environmental factors, activities and participation were less frequently described in studies

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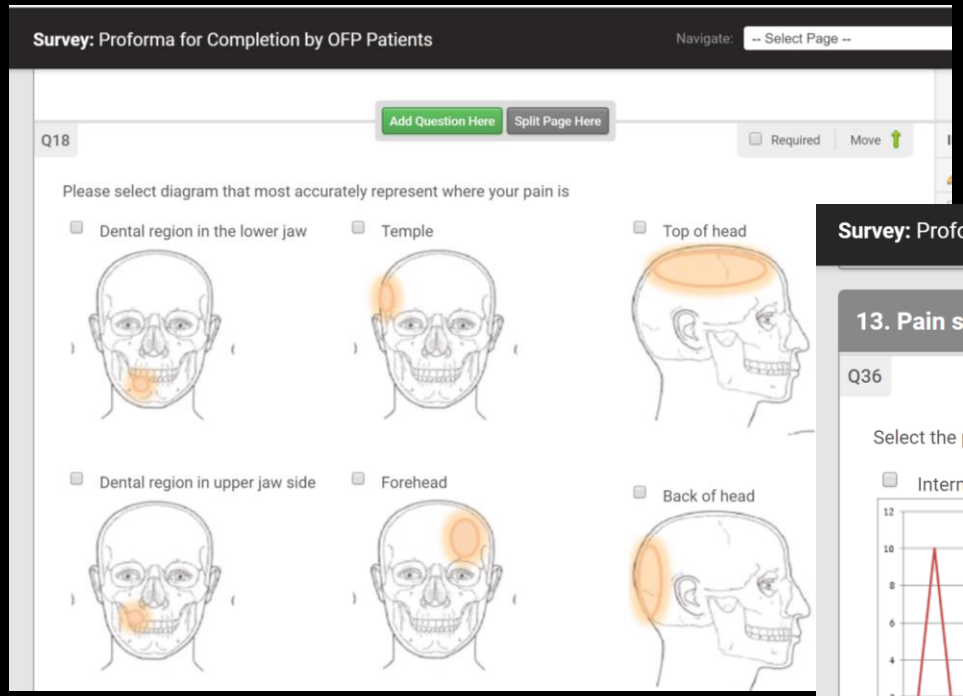
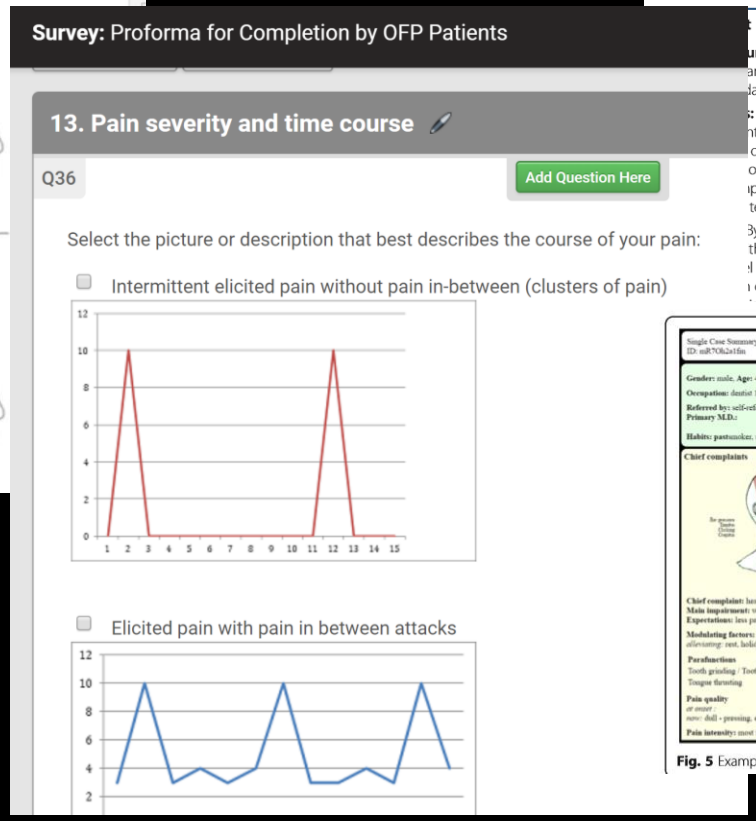
Online questionnaires-dashboard collaboration (inform)

Big Data/ Machine learning





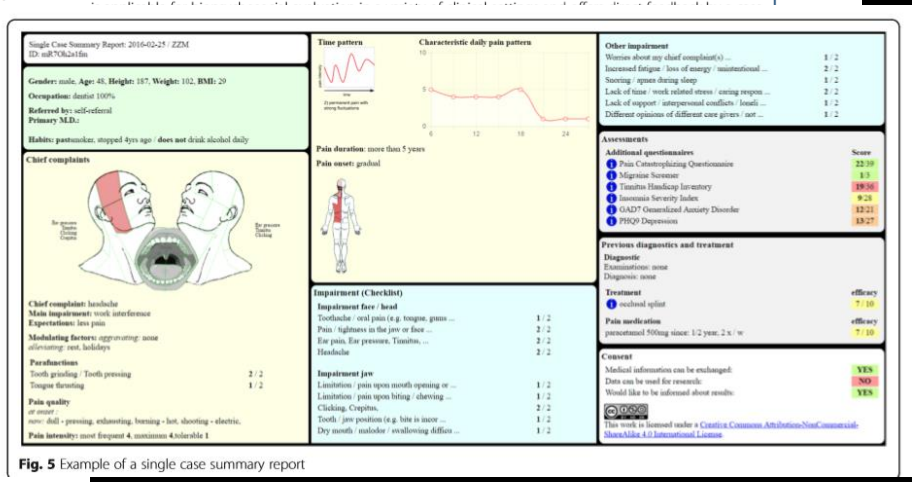


Fig. 5 Example of a single case summary report

Orofacialpain.org.uk

MRI for V Nerve injuries

ANESTHESIA/FACIAL PAIN

Magnetic Resonance Neurography of Traumatic and Nontraumatic Peripheral Trigeminal Neuropathies

John R. Zuniga, DMD, MS, PhD, Cyrus Mistry, DDS, MD,† Igor Tikhonov, DDS, MD,† Riham Dessouky, MD,‡ and Avneesh Chhabra, MD§*

Purpose: The clinical neurosensory testing (NST) is currently the reference standard for the diagnosis of traumatic and nontraumatic peripheral trigeminal neuropathies (PTNs), but exhibits both false-positive and false-negative results compared with surgical findings and frequently results in treatment decision delays. We tested the hypothesis that magnetic resonance neurography (MRN) of PTNs can serve as a diagnostic modality by correlating the NST, MRN, and surgical findings.

Materials and Methods: Sixty patients with traumatic and nontraumatic PTN of varying etiologies and Sunderland classifications underwent NST, followed by MRN using 1.5T and 3.0T scanners. The protocol included 2-dimensional and 3-dimensional (3D) imaging, including diffusion imaging and isotropic 3D PSIF. The MRN findings were read by 2 readers in consensus with the clinical findings but without knowing the side of abnormality. The MRN results were summarized using the Sunderland classification. In 26 patients, surgery was performed, and the Sunderland classification was assigned using the surgical photographs. Agreement between the MRN findings and NST/surgical classification was evaluated using kappa statistics. Pearson's correlation coefficient was used to assess the correlation between continuous measurements of MRN/NST and surgical classification.

Results: Of the 60 patients, 19 males and 41 females, mean age 41 years (range 12 to 75), with 54 complaints of altered sensation of the lip, chin, or tongue, including 16 with neuropathic pain and 4 with no neurosensory complaint, were included. Third molar surgery (n = 29) represented the most common cause of traumatic PTN. Assuming 1 nerve abnormality per patient, the lower class was accepted, a kappa of 0.57 was observed between the MRN and NST classification. A kappa of 0.5 was found between MRN and surgical findings with a Pearson correlation coefficient of 0.67.

Conclusions: MRN anatomically maps PTNs and stratifies the nerve injury and neuropathies with moderate to good agreement with NST and surgical findings for clinical use.

J Oral Maxillofac Surg 76:725-736, 2018

ORIGINAL RESEARCH
HEAD & NECK

Role of MR Neurography for the Diagnosis of Peripheral Trigeminal Nerve Injuries in Patients with Prior Molar Tooth Extraction

R. Dessouky, Y. Xi, J. Zuniga, and A. Chhabra

ABSTRACT

BACKGROUND AND PURPOSE: Clinical neurosensory testing is an imperfect reference standard to evaluate molar tooth extraction related peripheral trigeminal neuropathy. The purpose was to evaluate the diagnostic accuracy of MR neurography in this domain and correlation with neurosensory testing and surgery.

MATERIALS AND METHODS: In this retrospective study, nerve caliber, T2 signal intensity ratio, and contrast-to-noise ratios were recorded by 2 observers using MR neurography for bilateral branches of the peripheral trigeminal nerve, the inferior alveolar and lingual nerves. Patient demographics and correlation of the MR neurography findings with the Sunderland classification of nerve injury and intraoperative findings of surgical patients were obtained.

RESULTS: Among 42 patients, the mean ± SD age for case and control patients were 35.8 ± 10.2 years and 43.2 ± 11.5 years, respectively, with male-to-female ratios of 1:1.4 and 1:5, respectively. Case subjects (peripheral trigeminal neuropathy or injury) had significantly larger differences in nerve thickness, T2 signal intensity ratio, and contrast-to-noise ratios than control patients for the inferior alveolar nerve and lingual nerve (P = .01 and .0001, .012 and .005, and .01 and .01, respectively). Receiver operating characteristic analysis showed a significant association among differences in nerve thickness, T2 signal intensity ratio, and contrast-to-nois
curve, 0.83–0.84 for the inferior alveolar nerve and 0.77–0.78 for the lingual nerve). Interobserv
alveolar nerve (intraclass correlation coefficient, 0.70–0.79) and good to excellent for the lingual
0.75–0.85). MR neurography correlations with respect to clinical neurosensory testing and surgica
Pearson correlation coefficients of 0.68 and 0.81 and κ of 0.60 and 0.77 were observed for diffe

CONCLUSIONS: MR neurography can be reliably used for the diagnosis of injuries to the peri
tooth extractions, with good to excellent correlation of imaging with clinical findings and surgic

ABBREVIATIONS: IAN = inferior alveolar nerve; LN = lingual nerve; MRN = MR neurography; NST = neurosensor
state precession; PTN = peripheral trigeminal neuropathy; T2SIR = T2 signal intensity ratio; SI = signal intensity

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Peripheral Stimulation

EMERGING EVIDENCE BASE FOR TN

Neurol Sci (2014) 35 (Suppl 1):S77–S81
DOI 10.1007/s10072-014-1748-y

SESSION III LOCAL TREATMENTS

Peripheral neurostimulation in primary headaches

iorgio Lambru · Manjit Singh Matharu

bstract Peripheral neurostimulation techniques have merged as promising treatments for patients with medically intractable, highly disabling chronic daily headaches including chronic migraine (CM) and chronic cluster eadache (CCH) besides other less common headache yndromes. Encouraging controlled and open label data in edically intractable CM and trigeminal autonomic cephalalgias (TACs) have suggested a meaningful therapeutic le for occipital nerve stimulation (ONS). In view of the equent occurrence of pain in the first branch of trigeminal erve, percutaneous supraorbital nerve stimulation alone or combination with ONS has been used successfully in pen label series of CM and CCH patients. In view of its onnections with the trigeminovascular system, the stimlation of the sphenopalatine ganglion has been used as a erapeutic target for the treatment of acute cluster headche attacks, with promising results. Preliminary data in atients with epilepsy and migraine have suggested a otential efficacy of vagus nerve stimulation in the treatent of primary headaches. Non-invasive devices targeting eripheral nerves have been developed and initial experince is emerging for the acute and preventive treatments of rimary headache disorders. This review analyses the available evidence on the efficacy and safety of the different peripheral neurostimulation techniques.

Keywords Occipital nerve stimulation · Sphenopalatine ganglion stimulation · Vagus nerve stimulation · Chronic migraine · Trigeminal autonomic cephalalgias

Introduction

Chronic daily headache is a major worldwide health problem that affects 3–5 % of the population [1] and results in substantial disability. Advances in the management of headache disorders have meant that a high proportion of patients can be effectively treated with medical treatments.
patients are
There is, th
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Headache Currents

HEADACHE CURRENTS

Cluster Headache and Other TACs: Pathophysiology and Neurostimulation Options

Miguel JA Láinez, MD, PhD; Edelmira Guillamón, MD

Background.—The trigeminal autonomic cephalalgias (TACs) are highly disabling primary headache disorders. There are several issues that remain unresolved in the understanding of the pathophysiology of the TACs, although activation of the trigeminal–autonomic reflex and ipsilateral hypothalamic activation both play a central role. The discovery of the central role of the hypothalamus led to its use as a therapeutic target. After the good results obtained with hypothalamic stimulation, other peripheral neuromodulation targets were tried in the management of refractory cluster headache (CH) and other TACs.

Methods.—This review is a summary both of CH pathophysiology and of efficacy of the different neuromodulation techniques.

Results.—In chronic cluster headache (CCH) patients, hypothalamic deep brain stimulation (DBS) produced a decrease in attack frequency of more than 50% in 60% of patients. Occipital nerve stimulation (ONS) also elicited favorable outcomes with a reduction of more than 50% of attacks in around 70% of patients with medically intractable CCH. Stimulation of the sphenopalatine ganglion (SPG) with a miniaturized implanted stimulator produced a clinically significant improvement in 68% of patients (acute, preventive, or both). Vagus nerve stimulation (VNS) with a portable device used in conjunction with standard of care in CH patients resulted in a reduction in the number of attacks. DBS and ONS have been used successfully in some cases of other TACs, including hemicrania continua (HC) and short-lasting unilateral headache attacks (SUNHA).

Conclusions.—DBS has good results, but it is a more invasive technique and can generate serious adverse events. ONS has good results, but frequent and not serious adverse events. SPG stimulation (SPGS) is also efficacious in the acute and prophylactic treatment of refractory cluster headache. At this moment, ONS and SPG stimulation techniques are recommended as first line therapy in refractory cluster patients. New recent non-invasive approaches such as the non-invasive vagal nerve stimulator (nVNS) have shown efficacy in a few trials and could be an interesting alternative in the management of CH, but require more testing and positive randomized controlled trials.

Key words: trigeminal autonomic cephalalgia, migraine pathophysiology, hypothalamus, neuromodulation

Abbreviations: **TAC trigeminal autonomic cephalalgia, SUNCT short-lasting unilateral neuralgiform headaches with conjunctival injection and tearing, SUNA short-lasting unilateral neuralgiform headache attacks with autonomic features, CH cluster headache, CCH chronic cluster headache, drCCH drug refractory chronic cluster headache, PH paroxysmal hemicrania, DBS deep brain stimulation, ONS occipital nerve stimulation, SGS sphenopalatine ganglion, SCS spinal cord stimulation, VNS vagus nerve stimulation**

Trigeminal autonomic cephalalgias (TACs) are a group of primary headaches characterized by attacks of unilateral short-lasting severe head pain associated with ipsilateral autonomic manifestations in the facial distribution of the trigeminal nerve.[1] To date, the following syndromes belong to the TACs:[2] episodic and chronic cluster headache (CH), episodic and chronic paroxysmal hemicrania (PH), short-lasting unilateral neuralgiform headache attacks, and hemicrania continua. Attack duration is the main feature that distinguishes the first three TACs.[3] Despite the diagnostic challenges, the shortlasting primary headaches are important to recognize because of their different response to treatments.

CLUSTER HEADACHE

CH is the most common type of the TACs and is considered one of the most severe and debilitating pain syndrome in humans. CH prevalence is approximately 0.1% of the population and mostly affects men. Typically it presents with strictly unilateral severe head pain accompanied by autonomic symptoms ipsilateral to the pain, and a sense of restlessness or agitation.[3] The stereotypical attacks may strike up to 8 times a day and last between 15 minutes to 180 minutes.[4] Another clinical landmark of the syndrome is circadian rhythmicity and timing of attacks seems to be related to the sleep-wake

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Neuromodulation TG

Low level evidence base for refractory TN and PIFP

- Neural stimulation
- Pulsed radiofrequency
- Non pulsed radiofrequency = Thermocoagulation= radiofrequency ablation

Curr Pain Headache Rep (2017) 21: 14
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TRIGEMINAL AUTONOMIC CEPHALALGIAS (M MATHARU, SECTION EDITOR)

Non-invasive Neuromodulation in Primary Headaches

Sarah Miller[1] · Manjit Matharu[1]

Published online: 7 March 2017

Abstract
Purpose of Review There is growing interest in neuromodulation for primary headache conditions. Invasive modalities such as occipital nerve stimulation, deep brain stimulation and sphenopalatine ganglion stimulation are reserved for the most severe and intractable patients. Non-invasive options such as vagal nerve stimulation (nVNS), supraorbital nerve stimulation (nSONS) and transcranial magnetic nerve stimulation (TMS) have all emerged as potentially useful headache treatments. This review examines the evidence base for non-invasive neuromodulation in trigeminal autonomic cephalalgias and migraine.
Recent Findings Although a number of open-label series of non-invasive neuromodulation devices have been published, there is very little controlled evidence for their use in any headache condition. Open-label evidence suggests that nVNS may have a role in the prophylactic treatment of cluster headache and there is limited evidence to suggest it may be useful in the acute treatment of cluster and potentially migraine attacks. There is limited controlled evidence to suggest a role for nSONS in the prophylactic treatment of episodic migraine but there is no evidence to support its use in cluster headache. TMS may be efficacious in the acute treatment of episodic migraine has no controlled evidence to support its use as a preventative in any headache condition.
Summary Non-invasive neuromodulation techniques are an attractive treatment option with excellent safety profiles but their use is not yet supported by high-quality randomised controlled trials.

Keywords Trigeminal autonomic cephalalgia · Migraine · Neurostimulation · Vagal nerve stimulation · Supraorbital nerve stimulation · Transcranial magnetic stimulation

This article is part of the Topical Collection on *Trigeminal Autonomic Cephalalgias*

✉ Sarah Miller
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Introduction

Primary headache conditions, especially migraine, are a cause of significant disability and economic burden worldwide. Although the treatment options for primary headaches have progressed with time, there is still a major issue with the efficacy, availability, adverse event and tolerability profiles of current pharmaceutical agents. It is estimated that under 25% of chronic migraine patients continue taking oral preventative agents for more than 12 months due to lack of efficacy or tolerability issues [1]. In cluster headache (CH), besides the above issues with preventative agents, there are major limitations to acute treatments also. For example, subcutaneous sumatriptan is expensive and can only be used twice daily even

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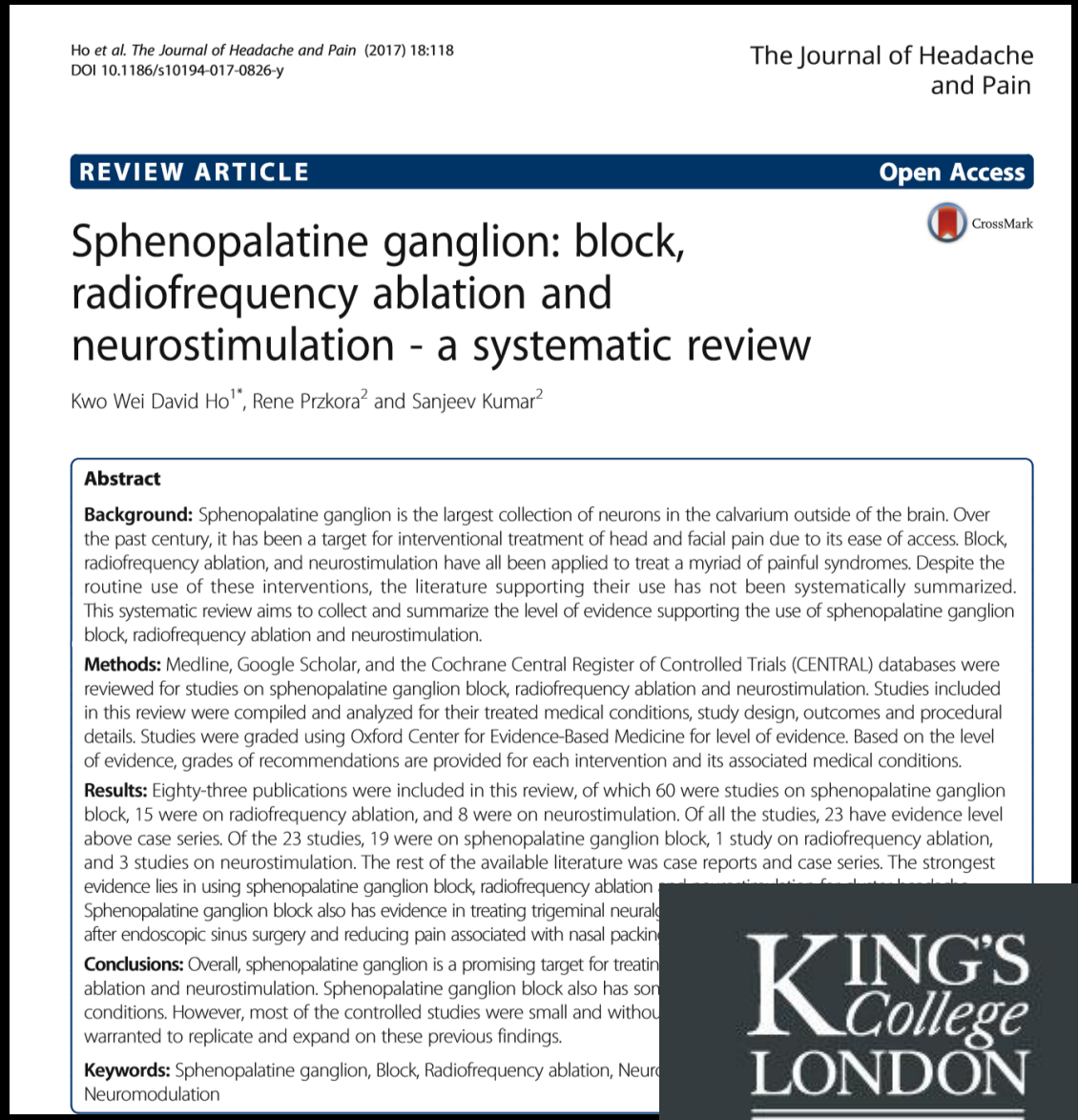
Sphenopalatine Ganglion neuromodulation

Only evidence base for Trigeminal autonomic cephalalgias



Ho *et al. The Journal of Headache and Pain* (2017) 18:118
DOI 10.1186/s10194-017-0826-y

The Journal of Headache and Pain

REVIEW ARTICLE Open Access

Sphenopalatine ganglion: block, radiofrequency ablation and neurostimulation - a systematic review

Kwo Wei David Ho[1*], Rene Przkora[2] and Sanjeev Kumar[2]

Abstract

Background: Sphenopalatine ganglion is the largest collection of neurons in the calvarium outside of the brain. Over the past century, it has been a target for interventional treatment of head and facial pain due to its ease of access. Block, radiofrequency ablation, and neurostimulation have all been applied to treat a myriad of painful syndromes. Despite the routine use of these interventions, the literature supporting their use has not been systematically summarized. This systematic review aims to collect and summarize the level of evidence supporting the use of sphenopalatine ganglion block, radiofrequency ablation and neurostimulation.

Methods: Medline, Google Scholar, and the Cochrane Central Register of Controlled Trials (CENTRAL) databases were reviewed for studies on sphenopalatine ganglion block, radiofrequency ablation and neurostimulation. Studies included in this review were compiled and analyzed for their treated medical conditions, study design, outcomes and procedural details. Studies were graded using Oxford Center for Evidence-Based Medicine for level of evidence. Based on the level of evidence, grades of recommendations are provided for each intervention and its associated medical conditions.

Results: Eighty-three publications were included in this review, of which 60 were studies on sphenopalatine ganglion block, 15 were on radiofrequency ablation, and 8 were on neurostimulation. Of all the studies, 23 have evidence level above case series. Of the 23 studies, 19 were on sphenopalatine ganglion block, 1 study on radiofrequency ablation, and 3 studies on neurostimulation. The rest of the available literature was case reports and case series. The strongest evidence lies in using sphenopalatine ganglion block, radiofrequency ablation
Sphenopalatine ganglion block also has evidence in treating trigeminal neuralg
after endoscopic sinus surgery and reducing pain associated with nasal packin

Conclusions: Overall, sphenopalatine ganglion is a promising target for treatin
ablation and neurostimulation. Sphenopalatine ganglion block also has son
conditions. However, most of the controlled studies were small and withou
warranted to replicate and expand on these previous findings.

Keywords: Sphenopalatine ganglion, Block, Radiofrequency ablation, Neuro
Neuromodulation

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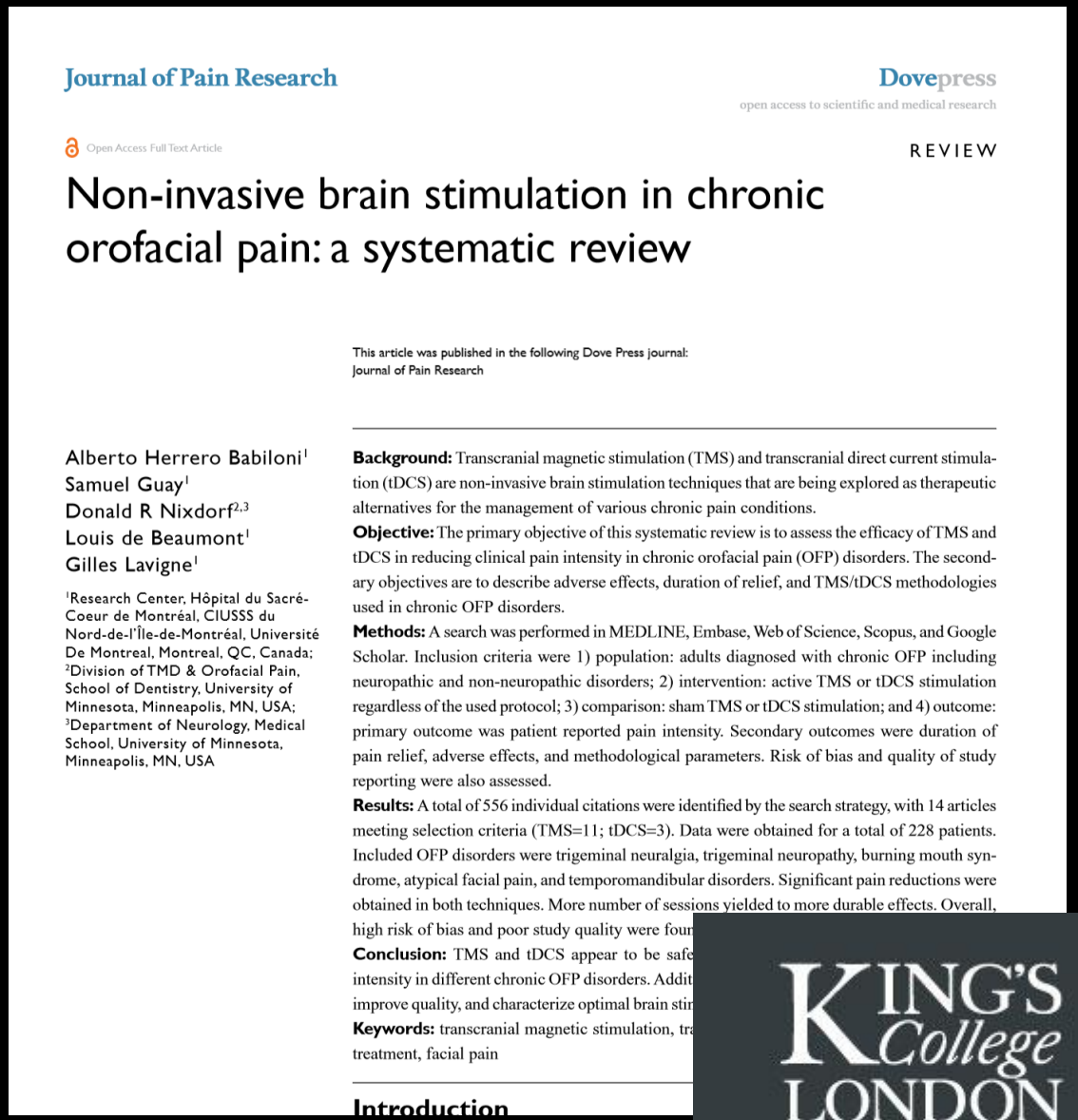
Brain Stimulation

Low evidence base for refractory TN and PIFP

Transmagnetic cranial stimulation

Transcranial direct current stimulation



Journal of Pain Research

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REVIEW

Non-invasive brain stimulation in chronic orofacial pain: a systematic review

This article was published in the following Dove Press journal:
Journal of Pain Research

Alberto Herrero Babiloni[1]
Samuel Guay[1]
Donald R Nixdorf[2,3]
Louis de Beaumont[1]
Gilles Lavigne[1]

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Background: Transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are non-invasive brain stimulation techniques that are being explored as therapeutic alternatives for the management of various chronic pain conditions.

Objective: The primary objective of this systematic review is to assess the efficacy of TMS and tDCS in reducing clinical pain intensity in chronic orofacial pain (OFP) disorders. The secondary objectives are to describe adverse effects, duration of relief, and TMS/tDCS methodologies used in chronic OFP disorders.

Methods: A search was performed in MEDLINE, Embase, Web of Science, Scopus, and Google Scholar. Inclusion criteria were 1) population: adults diagnosed with chronic OFP including neuropathic and non-neuropathic disorders; 2) intervention: active TMS or tDCS stimulation regardless of the used protocol; 3) comparison: sham TMS or tDCS stimulation; and 4) outcome: primary outcome was patient reported pain intensity. Secondary outcomes were duration of pain relief, adverse effects, and methodological parameters. Risk of bias and quality of study reporting were also assessed.

Results: A total of 556 individual citations were identified by the search strategy, with 14 articles meeting selection criteria (TMS=11; tDCS=3). Data were obtained for a total of 228 patients. Included OFP disorders were trigeminal neuralgia, trigeminal neuropathy, burning mouth syndrome, atypical facial pain, and temporomandibular disorders. Significant pain reductions were obtained in both techniques. More number of sessions yielded to more durable effects. Overall, high risk of bias and poor study quality were four

Conclusion: TMS and tDCS appear to be safe intensity in different chronic OFP disorders. Addit improve quality, and characterize optimal brain stir

Keywords: transcranial magnetic stimulation, tr treatment, facial pain

Introduction

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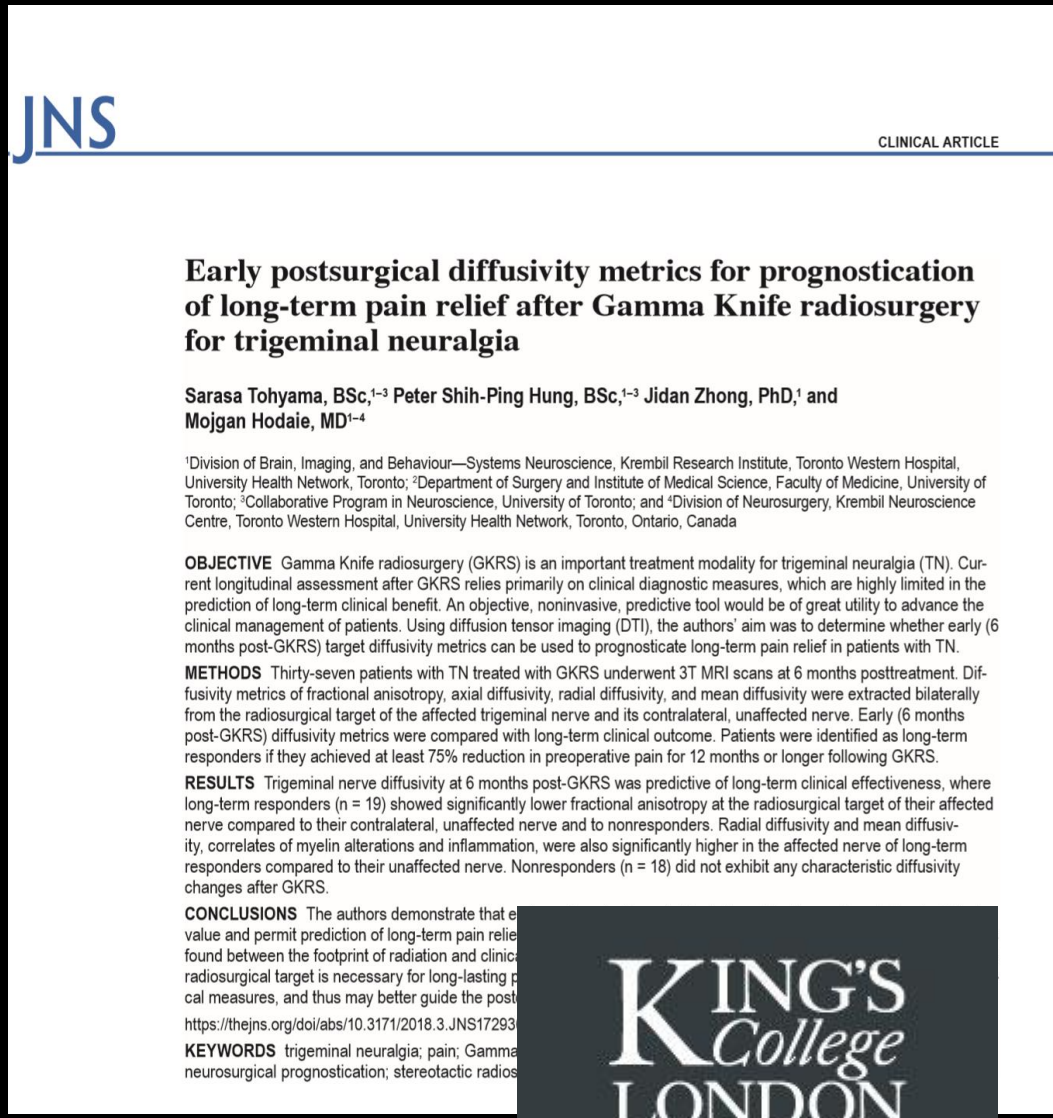
Gamma Knife

LOW EVIDENCE BASE FOR REFRACTORY TN in patients who cannot undergo Microvascular decompression



JNS

CLINICAL ARTICLE

Early postsurgical diffusivity metrics for prognostication of long-term pain relief after Gamma Knife radiosurgery for trigeminal neuralgia

Sarasa Tohyama, BSc,[1–3] Peter Shih-Ping Hung, BSc,[1–3] Jidan Zhong, PhD,[1] and Mojgan Hodaie, MD[1–4]

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OBJECTIVE Gamma Knife radiosurgery (GKRS) is an important treatment modality for trigeminal neuralgia (TN). Current longitudinal assessment after GKRS relies primarily on clinical diagnostic measures, which are highly limited in the prediction of long-term clinical benefit. An objective, noninvasive, predictive tool would be of great utility to advance the clinical management of patients. Using diffusion tensor imaging (DTI), the authors' aim was to determine whether early (6 months post-GKRS) target diffusivity metrics can be used to prognosticate long-term pain relief in patients with TN.

METHODS Thirty-seven patients with TN treated with GKRS underwent 3T MRI scans at 6 months posttreatment. Diffusivity metrics of fractional anisotropy, axial diffusivity, radial diffusivity, and mean diffusivity were extracted bilaterally from the radiosurgical target of the affected trigeminal nerve and its contralateral, unaffected nerve. Early (6 months post-GKRS) diffusivity metrics were compared with long-term clinical outcome. Patients were identified as long-term responders if they achieved at least 75% reduction in preoperative pain for 12 months or longer following GKRS.

RESULTS Trigeminal nerve diffusivity at 6 months post-GKRS was predictive of long-term clinical effectiveness, where long-term responders (n = 19) showed significantly lower fractional anisotropy at the radiosurgical target of their affected nerve compared to their contralateral, unaffected nerve and to nonresponders. Radial diffusivity and mean diffusivity, correlates of myelin alterations and inflammation, were also significantly higher in the affected nerve of long-term responders compared to their unaffected nerve. Nonresponders (n = 18) did not exhibit any characteristic diffusivity changes after GKRS.

CONCLUSIONS The authors demonstrate that e
value and permit prediction of long-term pain relie
found between the footprint of radiation and clinic
radiosurgical target is necessary for long-lasting p
cal measures, and thus may better guide the post

https://thejns.org/doi/abs/10.3171/2018.3.JNS17293

KEYWORDS trigeminal neuralgia; pain; Gamma
neurosurgical prognostication; stereotactic radios

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TN References

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The Presence of Neuropathic Pain Predicts Postoperative Neuropathic Pain Following Trigeminal Nerve Repair

John R. Zuniga, DMD, MS, PhD, David M. Yates, DMD, MD,† and Ceib L. Phillips, MPH, PhD‡*

Purpose: The risk for the continuation or recurrence of neuropathic pain following trigeminal nerve repair has never been examined. The objective of this study was to determine which risk factors might be associated with the continuation or recurrence of neuropathic pain following trigeminal nerve microneurosurgery.

Patients and Methods: An ambispective study design was used to assess subjects who underwent trigeminal nerve repair of the inferior alveolar nerve and lingual nerve between 2000 and 2010. The primary outcome was the presence or absence of neuropathic pain at 3, 6, and 12 months after surgery. Explanatory variables, including age at surgery, gender, presence of neuropathic pain before surgery, site of nerve injury, etiology of nerve injury, classification of nerve injury, duration of nerve injury, and type of repair performed, were abstracted from patient charts. Fisher exact tests were used to compare the demographic and injury characteristics of patients who presented with pain before surgery and those who did not. The McNemar test was used to assess whether there was a significant change in neuropathic pain report from before to after surgery. The level of significance was set at .50.

Results: Of the 65 patients analyzed, two-thirds were women; the average age was 36 ± 16.1 years, and the median time between the injury and surgery was 6.4 months (interquartile range, 6.7 months). Lingual nerve injury type was the most frequent (62%). There was no statistically significant change in pain status from before to after surgery ($P = .104$). Only 1 patient had pain after surgery who had not had pain before surgery, while 67% of those with pain before surgery continued to have pain after surgery. Pain prior to surgery as a predictor of pain after had sensitivity of 91%, specificity of 88%, positive predictive value of 67%, and negative predictive value 97%.

Conclusions: The presence of neuropathic pain prior to trigeminal microneurosurgery is the major risk factor for the continuation or recurrence of postoperative neuropathic pain. These findings suggest that trigeminal nerve surgery is not a risk factor for developing neuropathic pain in the absence of neuropathic pain before surgery.

J Oral Maxillofac Surg 72:2422-2427, 2014

Neuropathic pain is the painful condition that is characterized by a variety of positive and negative signs and symptoms (eg, allodynia, hyperpathia, hyperalgesia, painful numbness, painful paresthesia) within the distribution of an injured sensory nerve.[1] The definition of neuropathic pain has recently been redefined as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system."[2] Lesions or

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‡Professor, Department of Orthodontics, School of Dentistry, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Conflict of Interest Disclosures: Dr Zuniga is a consultant for AxoGen (Alachua, FL).

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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:
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 mecha
then, non-surgical treatment fo
remains a safer option. Risk facto
chronic post -surgical pain due
psychological, medical, and age
lie in preoperative screening ar
patients as the prevention of pos
absence of effective medical or s

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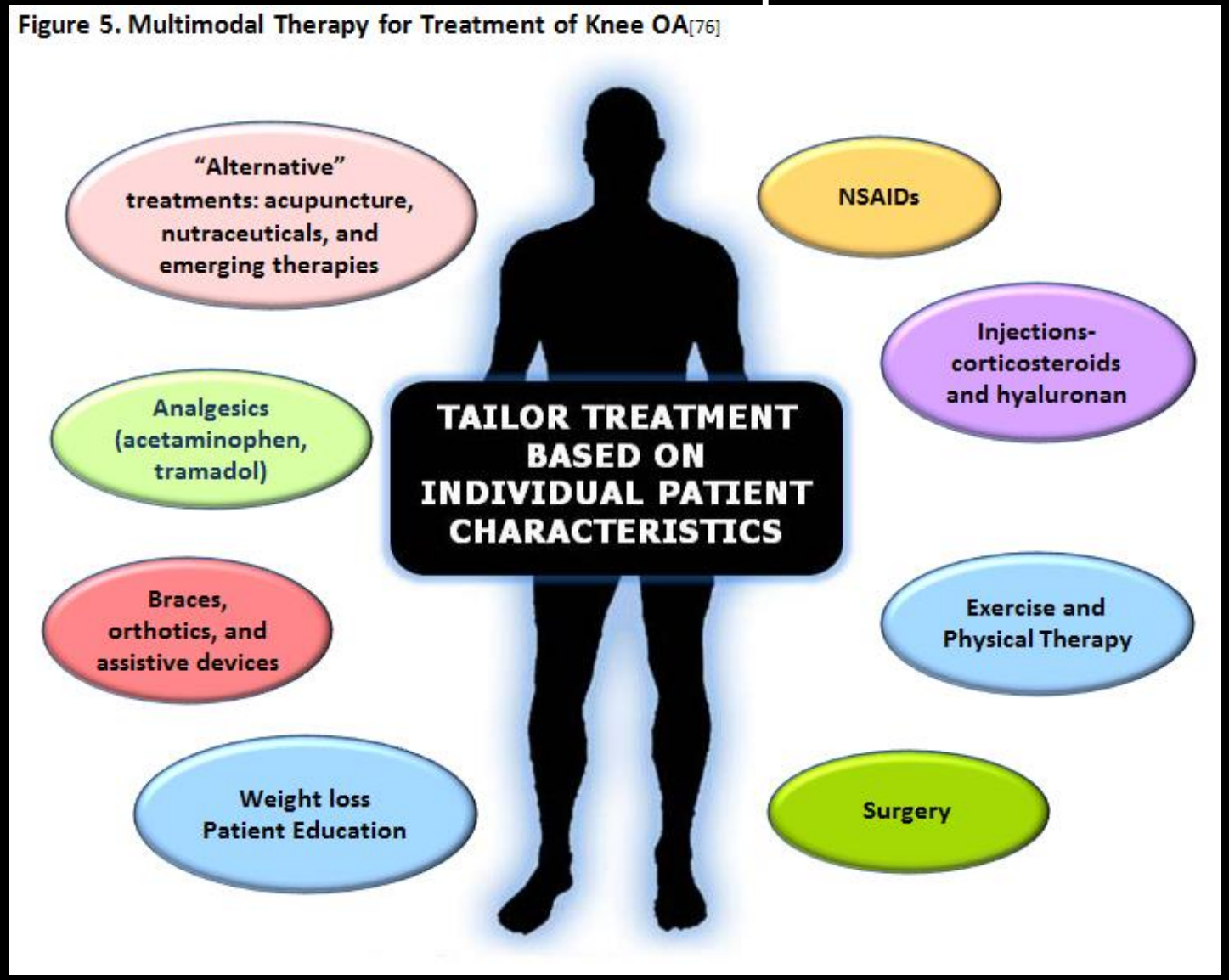
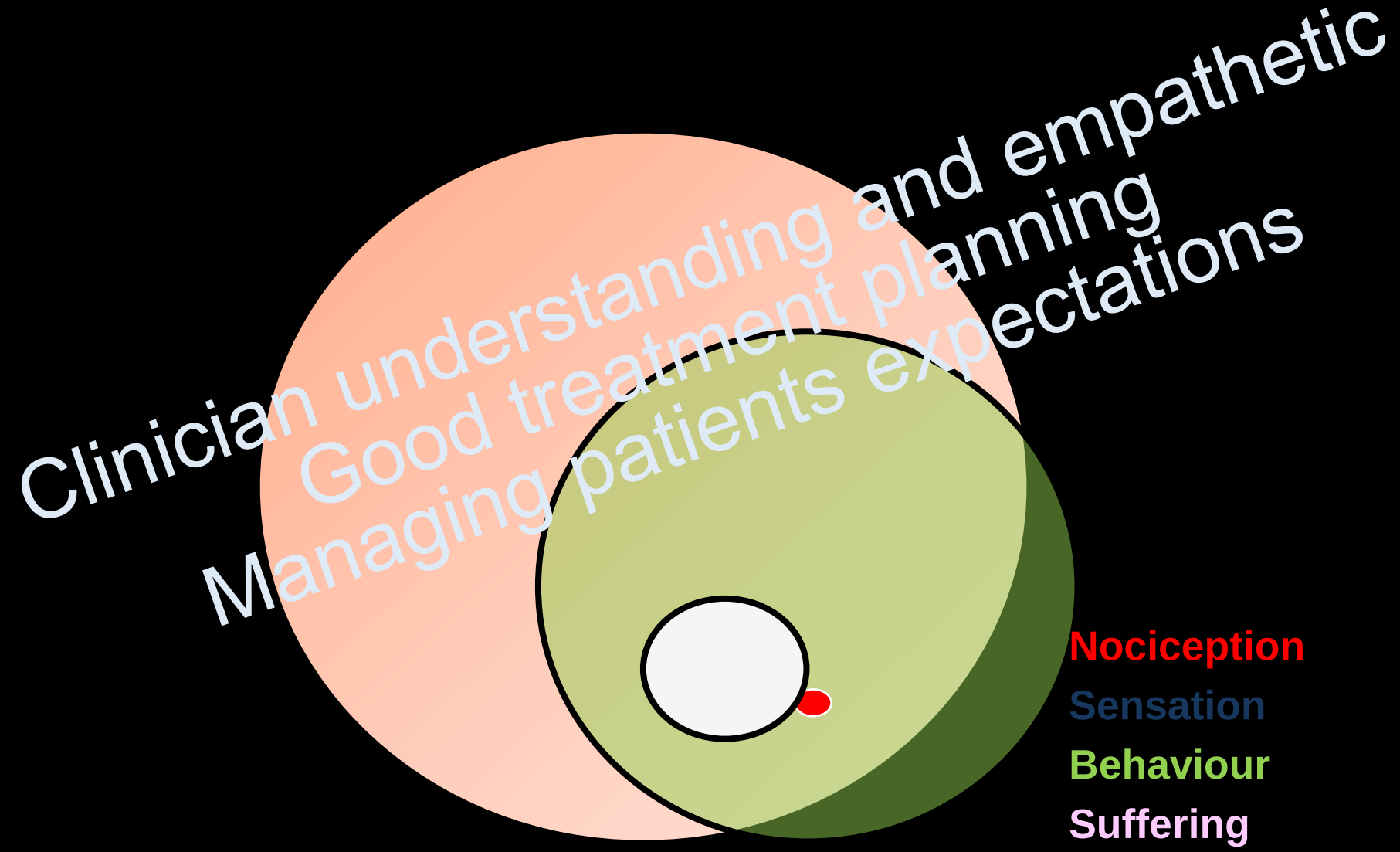
Tailor the treatment to the patient



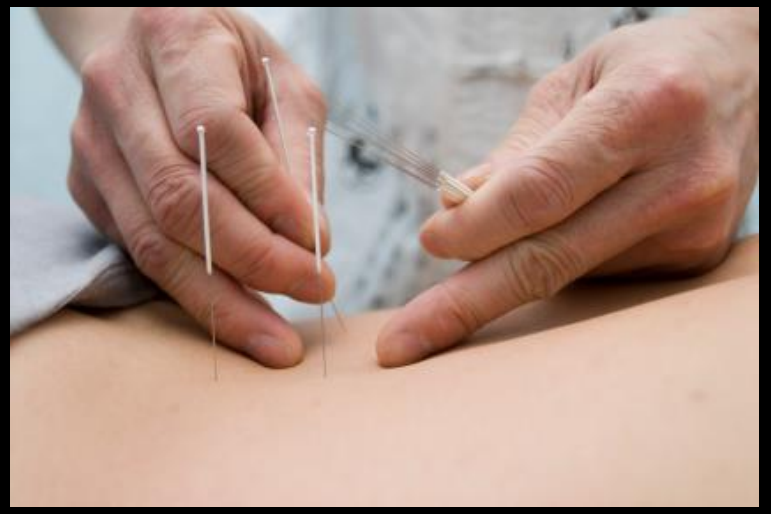


Alternative analgesic therapies

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

- Non pharmacological methods
  - Psychological
  - Alternative
  - Education
  - Sleep

- Interpersonal strategies
  - Communication
    - reassurance
    - sympathy
    - understanding
  - Caring
  - Comfort
  - Consideration
  - Clinical Competence



Riboflavin 400ug BD
Q10 co enzyme A 100ug TDS
Or
Magnesium 550ug/day
Or Melatonin 4ug90mins before bed

Rarely indicated Surgical pain management

- **Botoxin injections** these have to be placed at nerve endings with obvious risk of causing temporary 3 month motor palsy to local nerves
- **Neurostimulation**
  - Spinal cord stimulation (not for OFP)
  - Deep brain stimulation
  - Superficial sessional neurostimulation
  - Ganglia implanted neurostimulation
  - Transmagnetic stimulation
- **Ablative techniques**
  - Gasserian Ganglion interventions
    - Pulsed Radiofrequency ablation
    - Thermocoagulation
    - Balloon compression
    - Glycerolysis
  - Sphenopalatine ganglion injections
  - Stereotactic radiosurgery
  - Gamma knife may be indicated If there is medical contraindications to MVD

Not possible for BMS

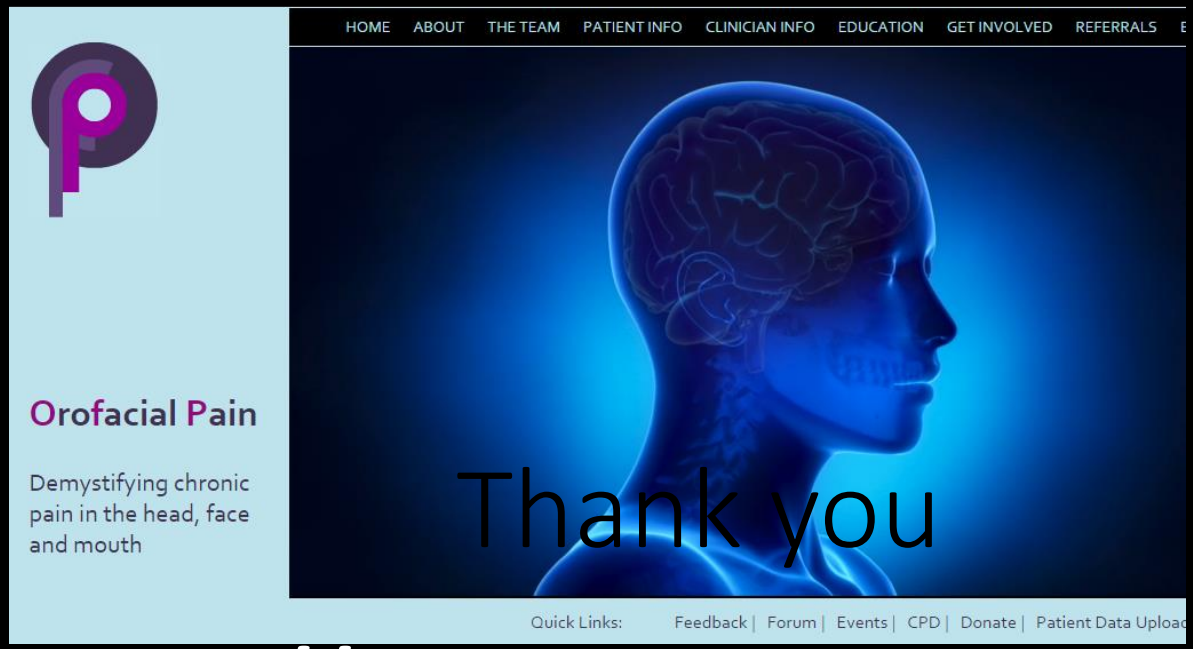
What next?

New classification

Phenotyping base upon clinical and psychological

Development artificial diagnostics

Mobile apps for patients and clinicians



http://www.orofacialpain.org.uk

TN

Notes:
1. In a few patients, pain may radiate to another division, but remains within the trigeminal dermatomes. 2. Duration can change over time, with paroxysms becoming more prolonged. A minority of patients will report attacks predominantly lasting for >2 minutes. 3. Pain may become more severe over time. 4. Some attacks may be, or appear to be, spontaneous, but there must be a history or Ending of pain provoked by innocuous stimuli to meet this criterion. Ideally, the examining clinician should attempt to conErm the history by replicating the triggering phenomenon. However, this may not always be possible because of the patient’s refusal, the awkward anatomical location of the trigger and/or other factors.