Disclosures

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Advisory Board	None
Speaker	None
Consultant	3M Local anesthesia training
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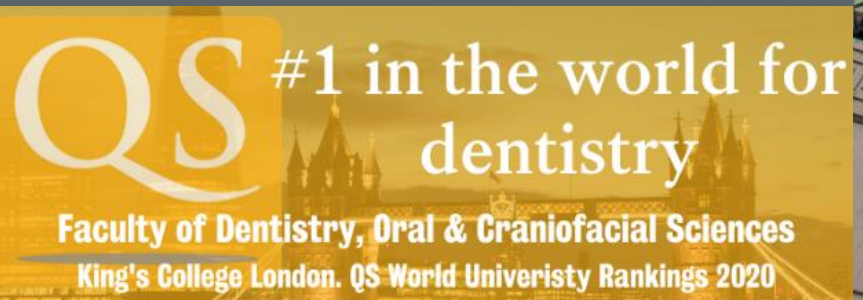
Support: Clinical trial site PI	None
Editorial Board	Associate Editor Journal Orofacial Pain and Headache Dental Update British Society Dental Hygienists and Therapists
Contributing author	National Guidelines (UK) for Third Molar Surgery, TMDs, Antimicrobial Therapy In Dentistry, National Local Surgical Safety Standards for Interventional procedures in dentistry

Refractory Orofacial Pain

Tara Renton
Professor Oral Surgery
Tara.renton@kcl.ac.uk



KING'S College LONDON

Overview

AAOP 2021

Tara.renton@kcl.ac.uk

- Definitions and Diagnostic criteria
- Why is pain persistent?
- When all else fails what treatment strategies are there?

45th SCIENTIFIC MEETING
May 6-9, 2021

Talking Stick Resort, Scottsdale, AZ

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Definitions Refractory Orofacial Pain

- ***Refractory***

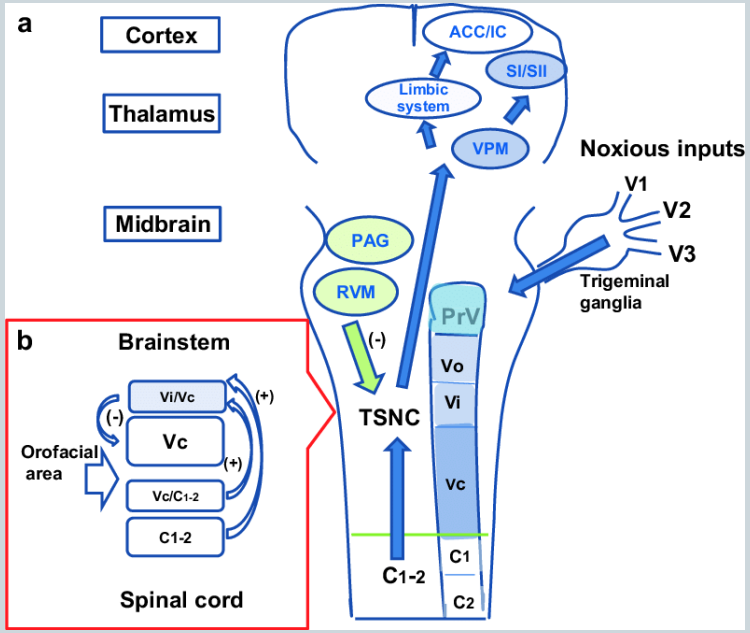
Intractable pain or refractory pain occurs when pain cannot be adequately controlled despite aggressive measures.

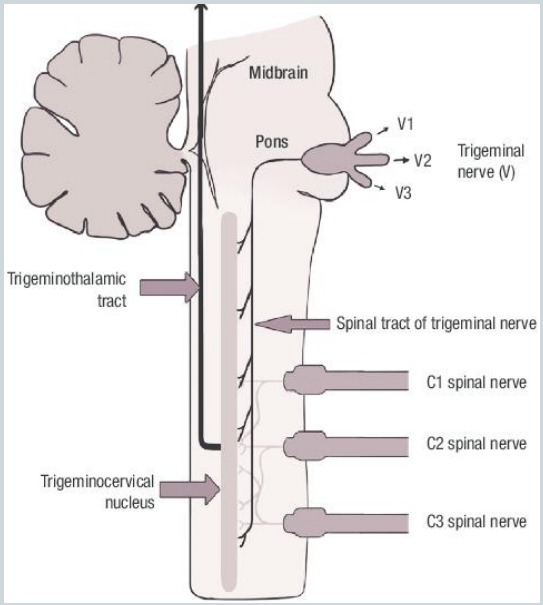
- ***Orofacial pain***

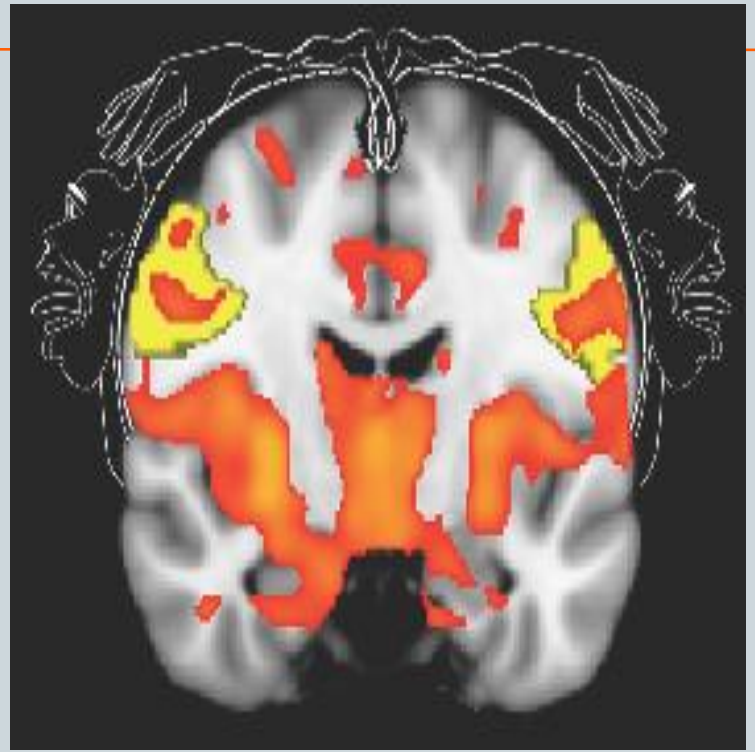
Pain in the head, neck and mouth region is a common affliction, affecting up to 26% of the population (MacFarlane et al 2002).

The problem complexity of the Trigeminal nerve

- Substantial Limbic component in V pain
- Trigemino-cervical complex
- Significant Autonomic input- Vagus
- Trigemino-vascular complex



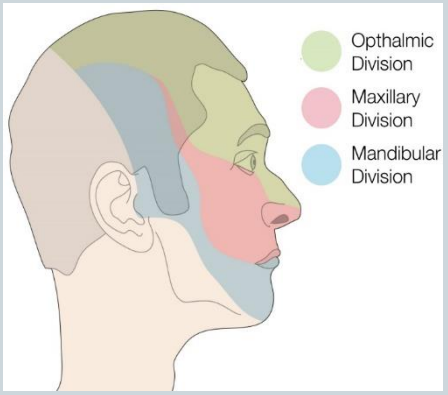




On a Pain Scale of 1 to 10, Trigeminal Neuralgia Can Feel Like 11

The problem the burden of Trigeminal Pain

- V is the great protector
- Sensory Feedback for all craniofacial functions
  - Eyes
  - Part Meninges
  - Nose
    - Airway
  - Face
    - Expression and communication
  - Mouth
    - Breathing
    - Speaking
    - Eating



Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology
ELSEVIER
Volume 123, Issue 1, January 2017, Pages 58-66

Oral medicine

The impact of chronic orofacial pain on daily life: the vulnerable patient and disruptive pain

Yaron Haviv DMD, PhD [a], Avraham Zini DMD, PhD, MPH [b], Yoni Etzioni DMD [c], Valeri Klitinich DMD [a], Alex Dobriyan DMD, MHA [d, e], Yair Sharav DMD, MS [a], Rafael Benoliel BDS, LDS, RCS [f], Galit Almoznino DMD, MSc, MHA [a, g]

JOURNAL OF ORAL REHABILITATION

REVIEW | Open Access

The impact of oro-facial pain conditions on oral health-related quality of life: A systematic review

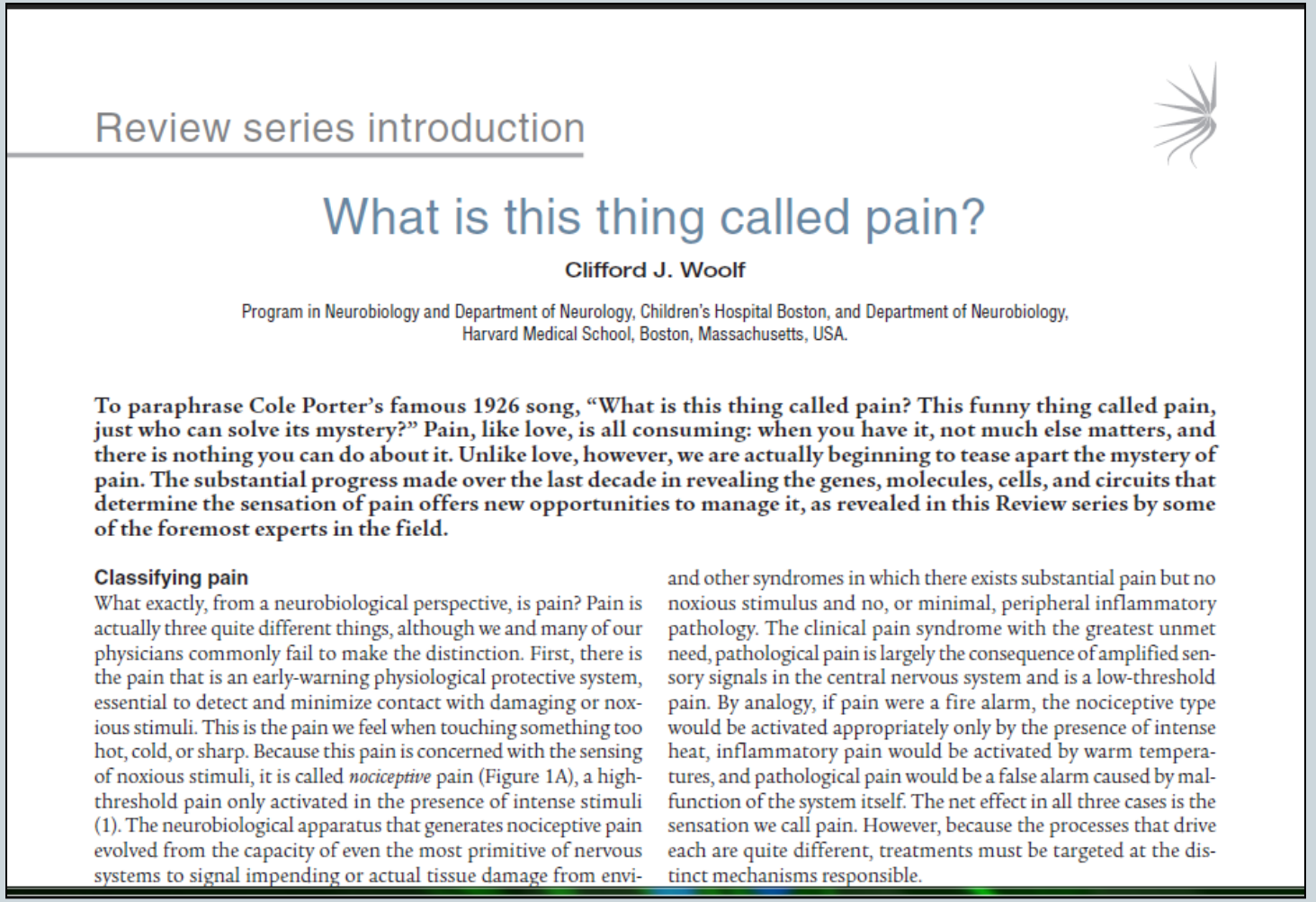
Ibrahim Oghli, Thomas List, Naichuan Su, Birgitta Häggman-Henrikson

First published: 16 May 2020 | https://doi.org/10.1111/joor.12994 | Citations: 1

Scandinavian Center for Orofacial Neurosciences: http://www.sconresearch.eu/
The peer review history for this article is available at https://publons.com/publon/10.1111/joor.12994

Head, heart or toothache?
Invited Steven Graff-Radford Award Lectureship 2020

Definitions Mechanistic and temporal types of pain……



Review series introduction

What is this thing called pain?

Clifford J. Woolf

Program in Neurobiology and Department of Neurology, Children's Hospital Boston, and Department of Neurobiology, Harvard Medical School, Boston, Massachusetts, USA.

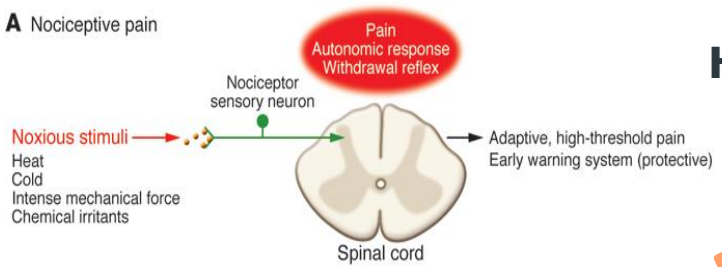
To paraphrase Cole Porter's famous 1926 song, "What is this thing called pain? This funny thing called pain, just who can solve its mystery?" Pain, like love, is all consuming: when you have it, not much else matters, and there is nothing you can do about it. Unlike love, however, we are actually beginning to tease apart the mystery of pain. The substantial progress made over the last decade in revealing the genes, molecules, cells, and circuits that determine the sensation of pain offers new opportunities to manage it, as revealed in this Review series by some of the foremost experts in the field.

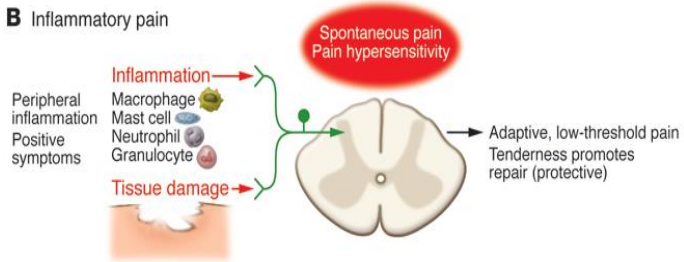
Classifying pain

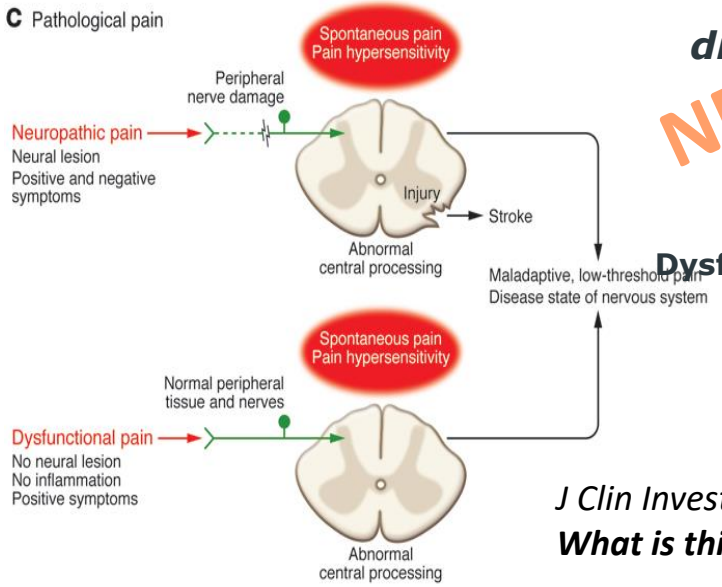
What exactly, from a neurobiological perspective, is pain? Pain is actually three quite different things, although we and many of our physicians commonly fail to make the distinction. First, there is the pain that is an early-warning physiological protective system, essential to detect and minimize contact with damaging or noxious stimuli. This is the pain we feel when touching something too hot, cold, or sharp. Because this pain is concerned with the sensing of noxious stimuli, it is called *nociceptive* pain (Figure 1A), a high-threshold pain only activated in the presence of intense stimuli (1). The neurobiological apparatus that generates nociceptive pain evolved from the capacity of even the most primitive of nervous systems to signal impending or actual tissue damage from envi-

and other syndromes in which there exists substantial pain but no noxious stimulus and no, or minimal, peripheral inflammatory pathology. The clinical pain syndrome with the greatest unmet need, pathological pain is largely the consequence of amplified sensory signals in the central nervous system and is a low-threshold pain. By analogy, if pain were a fire alarm, the nociceptive type would be activated appropriately only by the presence of intense heat, inflammatory pain would be activated by warm temperatures, and pathological pain would be a false alarm caused by malfunction of the system itself. The net effect in all three cases is the sensation we call pain. However, because the processes that drive each are quite different, treatments must be targeted at the distinct mechanisms responsible.

Types of pain –mechanistic and duration







Healthy acute pain

Nociceptive
healthy feeling pain 'pain'

NOCICEPTIVE

Inflammatory pain
healthy short lived after insult

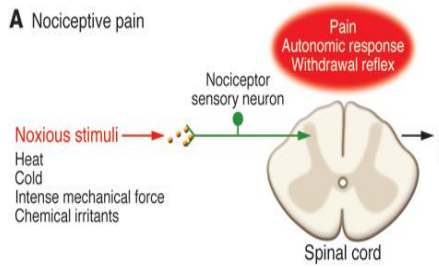
Chronic pain = disease of neuromatrix

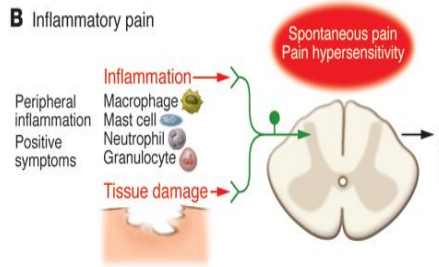
NEUROPATHIC

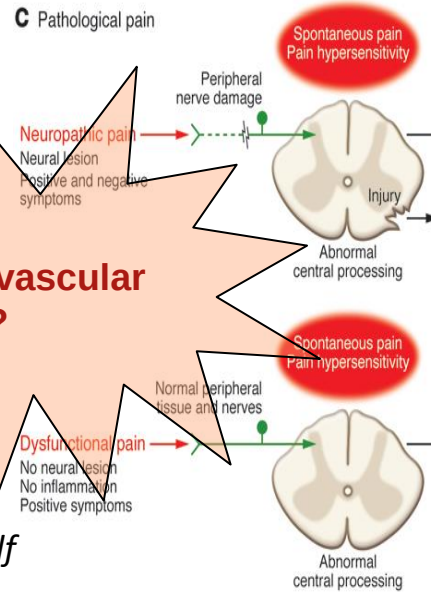
Neuropathic pain
Associated with nerve lesion

Dysfunctional or centralised pain
Unknown cause

NOCIPLASTIC







Dentine sensitivity

Pulpitis reversible +irreversible Periapical periodontitis

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

??
Neurovascular pain??

Fibromyalgia
PIFP
TMD
arthromyalgia
?

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

Regional orofacial pain ICOP 2020
Diagnostic criteria

Cephalalgia
An International Journal of Headache
International Headache Society

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

Cephalalgia
2020, Vol. 40(2) 129–221

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ICOP should include a brief description of the translation process, including the identities of the translators (of whom there should always be more than one). IHS will not endorse translations. Endorsements may be given by member national societies; wherever these exist, such endorsement should be sought.

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).

Regional orofacial pain ICOP 2020 Diagnostic criteria

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

Acute nociceptive pain

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

Acute chronic
Myogenous pain

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

Acute chronic joint pain

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

Neuropathic pain

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

Neurovascular pain

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

Nociplastic pain

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

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Tara.renton@kcl.ac.uk

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- **Why is the pain persistent?**
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Pathophysiology of chronic pain

Published in final edited form as:
Pain. 2018 December ; 159(12): 2421–2436. doi:10.1097/j.pain.0000000000001401.

When pain gets stuck: the evolution of pain chronification and treatment resistance

David Borsook[1,2], **Andrew M Youssef**[1], **Laura Simons**[3], **Igor Elman**[4], and **Christophe Eccleston**[5,6]

[1]Center for Pain and the Brain, Boston Children's (BCH), McLean and Massachusetts Hos
(M
[2]D MGH)
[3]D
[4]V
[5]C
[6]D

REVIEW FOCUS ON PAIN

nature neuroscience

Pain vulnerability: a neurobiological perspective

Franziska Denk[1], Stephen B McMahon[1] & Irene Tracey[2]

There are many known risk factors for chronic pain conditions, yet the biological underpinnings that link these factors to abnormal processing of painful signals are only just beginning to be explored. This Review will discuss the potential mechanisms that have been proposed to underlie vulnerability and resilience toward developing chronic pain. Particular focus will be given to genetic and epigenetic processes, priming effects on a cellular level, and alterations in brain networks concerned with reward, motivation/learning and descending modulatory control. Although research in this area is still in its infancy, a better understanding of how pain vulnerability emerges has the potential to help identify individuals at risk and may open up new therapeutic avenues.

Considerable advances have been made in understanding the neurobiology of chronic pain over the last two decades. The molecular mechanisms leading to amplification of pain-related signals in chronic pain states have been dissected. An unexpected contribution of non-neuronal cells in the CNS has been discovered, and functional, as well as structural, neuroimaging studies have revealed a brain organization likely to develop certain chronic pain conditions, as are older people, although age may function as a protective factor in some instances. The influence of genetics is supported by twin and population-based studies, which clearly indicate that painful conditions and acute pain sensitivity *per se* are heritable (see ref. 5 for a recent review). Other

COMMENTARY

Check for updates

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

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

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

ABSTRACT

Objective: Pain is one of the most common reasons for an individual to consult their primary care physician, with most chronic pain being treated in the primary care setting. However, many primary care physicians/non-pain medicine specialists lack enough awareness, education and skills to manage pain patients appropriately, and there is currently no clear, common consensus/formal definition of "pain chronification".

Methods: This article, based on an international Change Pain Chronic Advisory Board meeting which

ARTICLE HISTORY
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KEYWORDS
Chronic pain; chronification; pain; non-pain medicine specialist

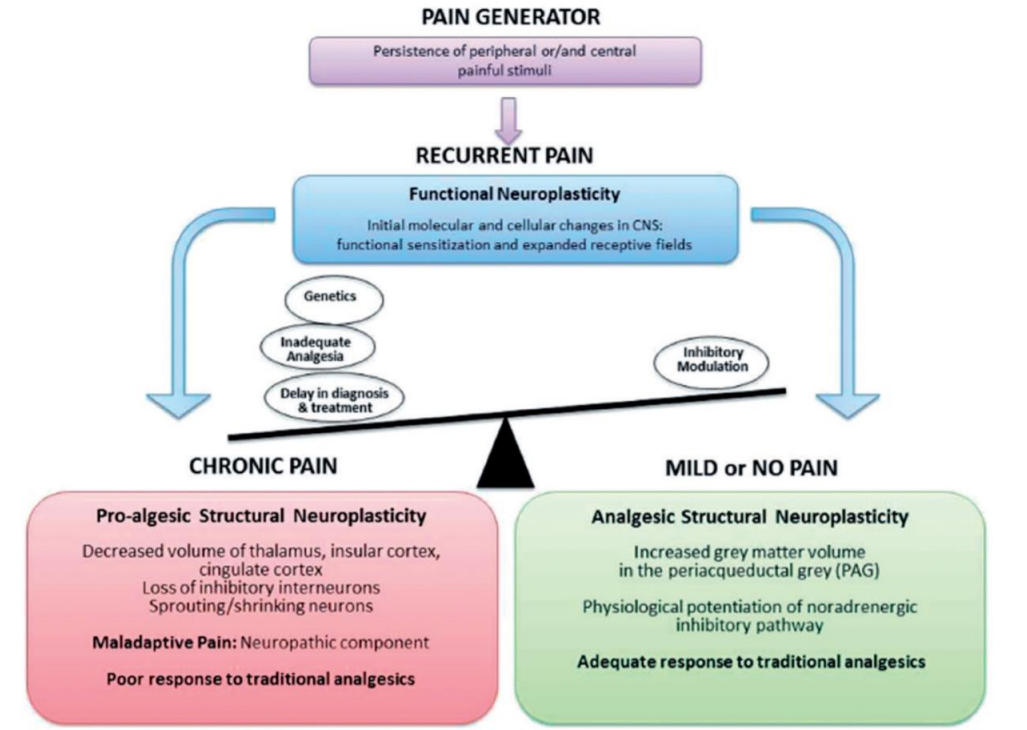
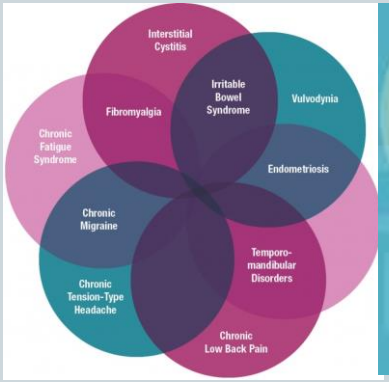


Figure 1. From the physiological perspective, an imbalance between enhanced ascending nociceptive inputs and inadequate inhibitory descending pathways is responsible for pain chronification[45]. Reproduced with permission from Coluzzi *et al.*[45]

Factors driving persistent pain
A holistic approach

Clinical phenotype
Age
Gender
Ethnicity
Religion
Beliefs
Misdiagnosis
Intolerance to medications
Multiple pain interventions



Medical Co-morbidities
CWP /FM
Sleep disorders
Smoking
Drug dependency
Vitamin C and D def
Malnutrition
DM, Hypothyroid, Autoimmune disorders
Medication overuse

Psychological factors
Anxiety
Depression
Neuroticism
Catastrophising
Introversion
Hypervigilance
Narcissism

Social factors
Support
Culture
Education level
Income
Prior significant life events

Physiological
Factors
Microbiome
Endogenous pain modulation
Neural plasticity
Gray / white matter degeneration
Connectivity
Neuropathy

Genetic Profile
Ethnicity
Gender
Genome
Epigenetics

Clinical phenotype

Age

Gender

Ethnicity

Religion

Beliefs

Misdiagnosis

Intolerance to medications

Multiple pain interventions

Age?

BJA

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doi: 10.1016/j.bja.2019.03.023
Advance Access Publication Date: 10 May 2019
Special Article

Chronic pain: a review of its epidemiology and associated factors in population-based studies

Sarah E. E. Mills*, Karen P. Nicolson and Blair H. Smith

Population Health and Genomics Division, University of Dundee School of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland, UK

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Summary

Chronic pain is a common, complex, and distressing problem that has a profound impact on individuals and society. It frequently presents as a result of a disease or an injury; however, it is not merely an accompanying symptom, but rather a separate condition in its own right, with its own medical definition and taxonomy. Studying the distribution and determinants of chronic pain allows us to understand and manage the problem at the individual and population levels. Targeted and appropriate prevention and management strategies need to take into account the biological, psychological, socio-demographic, and lifestyle determinants and outcomes of pain. We present a narrative review of the current understanding of these factors.

Keywords: chronic pain; epidemiology; genetics; incidence; prevalence; risk factors

Chronic pain is a common, complex, and distressing problem, which has a significant impact on society and individuals.[1] It commonly presents as a result of an injury or a disease; however, it is a separate condition in its own right, not merely an accompanying symptom of other ailments. Chronic pain, therefore, has both its own taxonomy and medical definition.[2–4]

The Global Burden of Disease Study 2016 reaffirmed that the high prominence of pain and pain-related diseases is the leading cause of disability and disease burden globally.[5] Worldwide, the burden caused by chronic pain is escalating: 1.9 billion people were found to be affected by recurrent tension-type headaches, which were the most common symptomatic chronic condition.[5] Measuring years lived with disability, low back and neck pain have consistently been the leading causes of disability internationally, with other chronic pain conditions featuring prominently in the top 10 causes of disability.[5]

In order to develop treatment plans and prevention strategies, chronic pain needs to be understood in the context of social, biological, psychological, and physical factors. This is a narrative synthesis of the epidemiology, particularly the risk factors and demographic associations, of chronic pain.

Importance of epidemiology in chronic pain

Epidemiology, the 'study of the distribution and determinants of health-related states or events in specified populations and the applications of this study to control health problems',[6] is vital to understanding chronic pain. According to the International Association for the Study of Pain, chronic pain is 'pain which has persisted beyond normal tissue healing time',[7] which, in the absence of other factors, is generally taken to be 3 months.[7] There are many risk factors for chronic pain, including socio-demographic, psychological, clinical, and

Editorial decision: 22 March 2019; **Accepted:** 22 March 2019

https://www.practicalpainmanagement.com/patient/resources/pain-self-management/continuum-chronic-pain-aging

Why is chronic pain more prevalent with age?

•Pain is a very common problem for older persons (ie, those **age 65 and over**), with persistent pain affecting more than **50% of such individuals persons living in the community setting and more than 80% of those living in nursing homes**.[1]
•Along with a greater prevalence rate of chronic medical comorbidities in later adulthood, the most **frequent pain complaints among elderly patients are osteoarthritic back pain, especially in the low back or neck (around 65%), musculoskeletal pain (around 40%), peripheral neuropathic pain (typically due to diabetes or postherpetic neuralgia, 35%), and chronic joint pain (15% to 25%).[2]**
•**75% of people age 65 or older have two or more chronic conditions**—such as heart disease, diabetes, chronic lung disease, or arthritis.[3]
•**Approximately 30% to 50% of people with dementia are likely to also experience chronic pain.**[2]
•Older persons with dementia or communication problems are even more at risk of under-treatment of pain, due to difficulties communicating their pain. They are known to receive fewer analgesics than others of similar age and pathology.[1]
•**Individuals with chronic pain had on average a 9.2% faster memory decline and a 7.7% faster increase in dementia probability**.[4]
•Among elderly veterans, 50% report suffering from chronic pain.[5] In a survey, approximately 65% percent of US Veterans reported having pain in the three months prior to being surveyed, with approximately 9% classified as having severe pain. Severe pain was 40% greater in veterans than non-veterans, especially among those who served in recent conflicts.[3]
•Interestingly, older military veterans who were not prescribed opioids were shown to have improved pain intensity over time than those who were prescribed opioids.[6]

- **More morbidity Trauma surgery infections**
- **Neuro-immunity decreases**
- **Brain structural changes**

Clinical phenotype

Age

Gender

Ethnicity

Religion

Beliefs

Misdiagnosis

Intolerance to medications

Multiple pain interventions

Gender?

BJA

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Population Health and Genomics Division, University of Dundee School of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland, UK

*Corresponding author. E-mail: s.e.e.mills@dundee.ac.uk

Summary

Chronic pain is a common, complex, and distressing problem that has a profound impact on individuals and society. It frequently presents as a result of a disease or an injury; however, it is not merely an accompanying symptom, but rather a separate condition in its own right, with its own medical definition and taxonomy. Studying the distribution and determinants of chronic pain allows us to understand and manage the problem at the individual and population levels. Targeted and appropriate prevention and management strategies need to take into account the biological, psychological, socio-demographic, and lifestyle determinants and outcomes of pain. We present a narrative review of the current understanding of these factors.

Keywords: chronic pain; epidemiology; genetics; incidence; prevalence; risk factors

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In order to develop treatment plans and prevention strategies, chronic pain needs to be understood in the context of social, biological, psychological, and physical factors. This is a narrative synthesis of the epidemiology, particularly the risk factors and demographic associations, of chronic pain.

Importance of epidemiology in chronic pain

Epidemiology, the 'study of the distribution and determinants of health-related states or events in specified populations and the applications of this study to control health problems',[6] is vital to understanding chronic pain. According to the International Association for the Study of Pain, chronic pain is 'pain which has persisted beyond normal tissue healing time',[7] which, in the absence of other factors, is generally taken to be 3 months.[7] There are many risk factors for chronic pain, including socio-demographic, psychological, clinical, and

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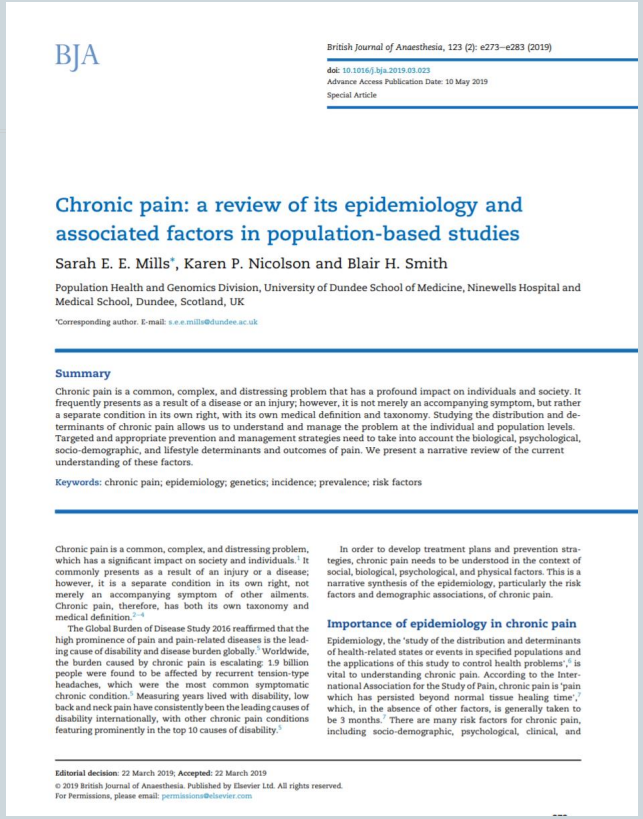
Why is chronic pain more prevalent in women?

- Men are less likely to report or experience chronic pain than women,25 and girls are more likely to report pain in multiple sites than boys.23 Several reviews have studied how gender (role) and sex (biological) differences are related to the way men and women experience pain.26e29
- One recent systematic review found **that women who experience pain are more likely to use maladaptive coping strategies, which predispose them to chronic pain and poorer functional ability.**26
- Women have been shown **to have lower pain thresholds and tolerance, a**nd are more likely to experience greater intensity and unpleasantness with pain.30 The evidence also suggests that women have different sensitivities to analgesia.27
- When corrections are made for the prevalence of pain in the different genders, **women are more likely to seek treatment for their pain**.
- In a recent study from one specialist pain clinic, there were twice as many women as men.31
- **Women reported a higher level of pain intensity and higher pain-related disability** than men.32
- Although there is insufficient information on the mechanisms behind these sex-specific differences in pain perception and pain prevalence,26 there is some evidence for the role of oestrogens33 and genetics, including sex-specific differences in the contribution of pain-related genes.34



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Special Article

Chronic pain: a review of its epidemiology and associated factors in population-based studies

Sarah E. E. Mills*, Karen P. Nicolson and Blair H. Smith

Population Health and Genomics Division, University of Dundee School of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland, UK

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Clinical phenotype

Age

Gender

Ethnicity

Religion

Beliefs

Misdiagnosis

Intolerance to medications

Multiple pain interventions

Ethnicity?

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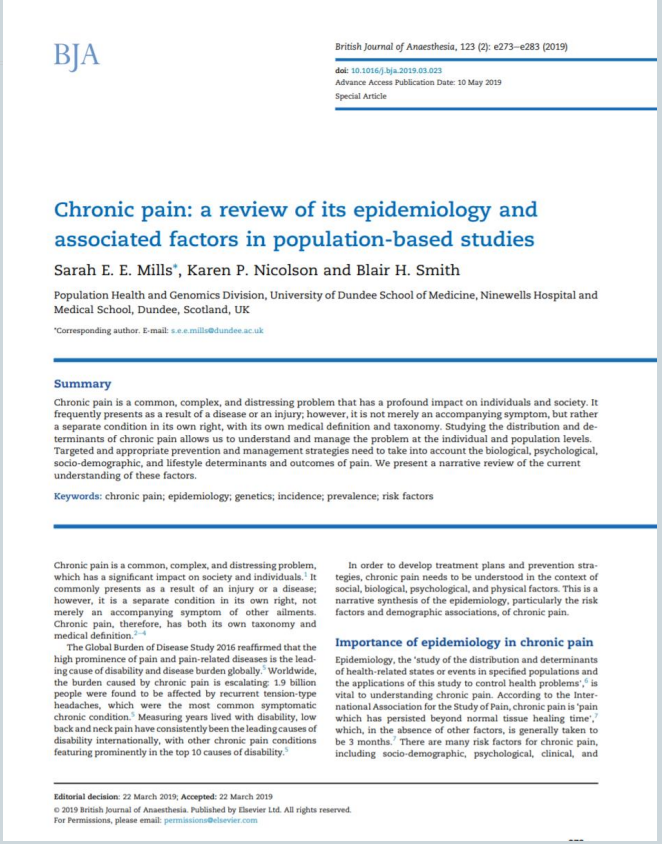
Why is chronic pain more prevalent with non white ethnicity?

There are substantial and complex ethnic variations in prevalence and outcomes of pain-related conditions, although the mechanisms behind these remain poorly understood.11,35

Caucasian patients have been found to experience less pain and less pain-related disability than black patients.35,36

A survey of 500 000 people in the UK showed that **those who self-identified as white were less likely to report chronic pain than those reporting black, Asian, or mixed ethnicity**.37 However, once adjusted for income employment and adverse life events, the association between self-reported ethnicity and chronic pain was significantly attenuated. The prevalence of chronic pain and its associated disability has been found to be greater in developing countries than in developed countries.5



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Religion

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Misdiagnosis

Intolerance to medications

Multiple pain interventions

Wrong diagnosis?

Headache
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Review Article

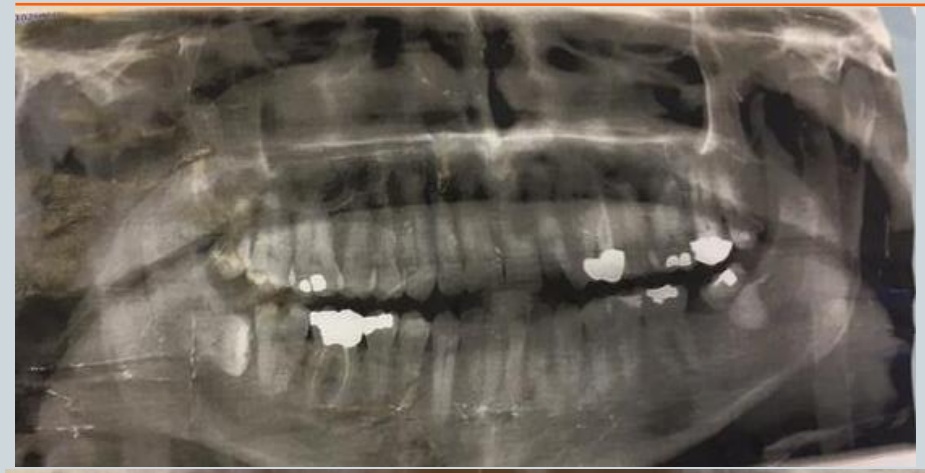
Tooth-Related Pain or Not?

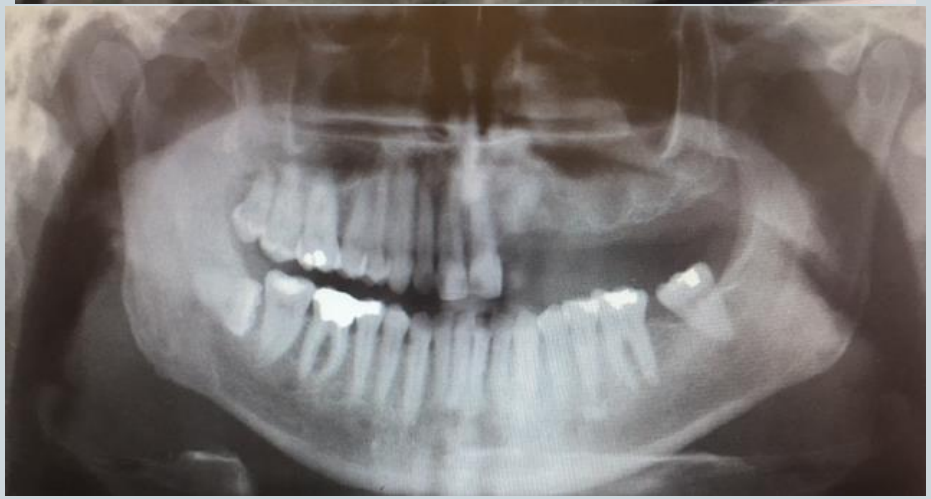
Tara Renton, BDS, MDSc, PhD

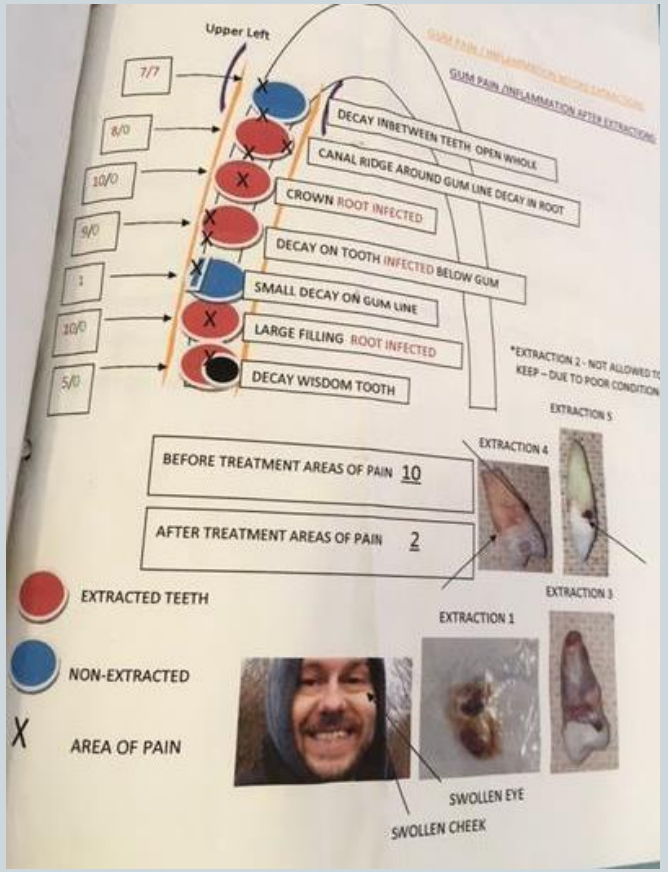
Dental pain is the most common acute pain presenting in the orofacial region; however, chronic pain conditions are also frequent and include; temporomandibular joint disorders (TMDs), primary headaches (neurovascular pain), painful post-traumatic trigeminal neuropathy (PPTTN) and less commonly referred pain and idiopathic or centralized pain conditions. All of these conditions can mimic toothache and vice versa. Many of these conditions are comorbid with high levels of tension headache and migraine reported in patients with TMD; however, dentists remain unfamiliar with headaches and medics unfamiliar with toothache's multiple presentations. The anatomical complexity of the region, the potential exhaustive differential diagnoses and the multiple siloed training of specialties, leads to incorrect and delayed diagnosis and often results in patients undergoing inappropriate surgical and medical treatments. The continued inappropriate interventions may also complicate the later presentation of the patient with pain, by changing its phenotype, preventing a timely and correct diagnosis. Due to the variable presentation of toothache, which can mimic many different chronic pains including; episodic throbbing pain of migraine, the dull continuous pain of myofascial and arthrogenous TMDs or centralized facial pain, diagnosis can be complex. Neuralgic pain occurs in the dentition in health and with disease, mimicking conditions like PPTTN, trigeminal neuralgia (TN), and trigeminal autonomic cephalalgias (TACs), many patients are inappropriately diagnosed and treated, either by general medical practitioners assuming that the neuralgia is due to TN rather than more commonly presenting toothache or by a dentists or other surgeons continuing to treat TN or TACs with routine surgical care. Many patients are prescribed countless courses of antibiotics and undergo multiple surgical interventions simply as a result of poor education due to siloed specialty training. This must be addressed to improve patient safety.

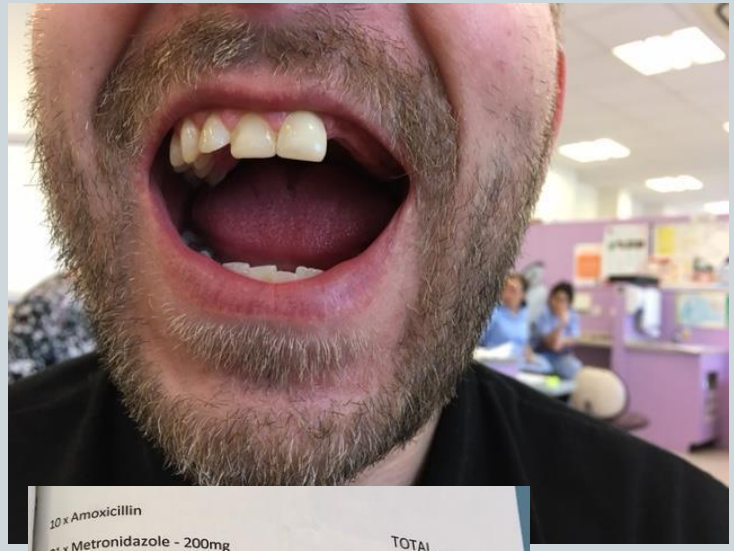
Key words: toothache, headache, temporomandibular disorders, sinusitis, trigeminal nerve injury, neuralgia

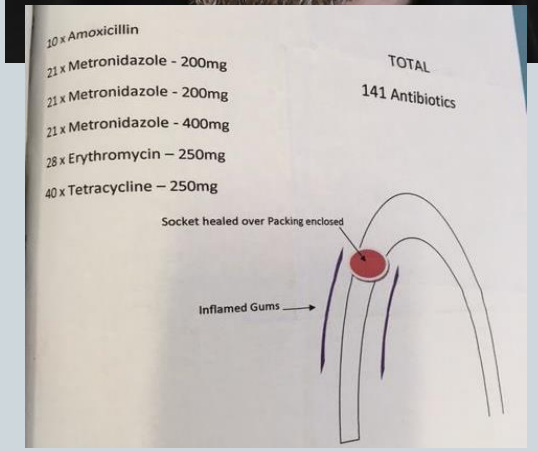
The consequence of misdiagnosis is Patient Harm











Head, heart or toothache?
Invited Steven Graff-Radford Award Lectureship 2020

Is the OFP V2/3 Migraine or TAC OR variant TN?

What's in a name?

- Facial Migraine
- Below orbito-meatal migraine
- Neurovascular orofacial pain
- Headache attributed to facial pain (ICHD3)

Key features

- Older pain cohort
- More autonomic signs
- Trauma onset (dental or ENT surgery)

3 types

- Patients who get migraine affecting V1 + V2 +/- V3
- Patients with previous classic migraine V1 for many years then absent then represents as Facial V2 +/- V3 migraine
- Patients presenting with de novo V2 +/- V3 migraine

Recommendation?

- Educate dentists in recognition of concomitant migrainoid and autonomic signs

Migraine presenting as isolated facial pain: A prospective clinical analysis of 58 cases

Giorgio Lambru, Leigh-Ann Elias, Pankaew Yakkaphan, more... Show all authors

First Published June 17, 2020 | Research Article | Find in PubMed | Check for updates

https://doi.org/10.1177/0333102420933277

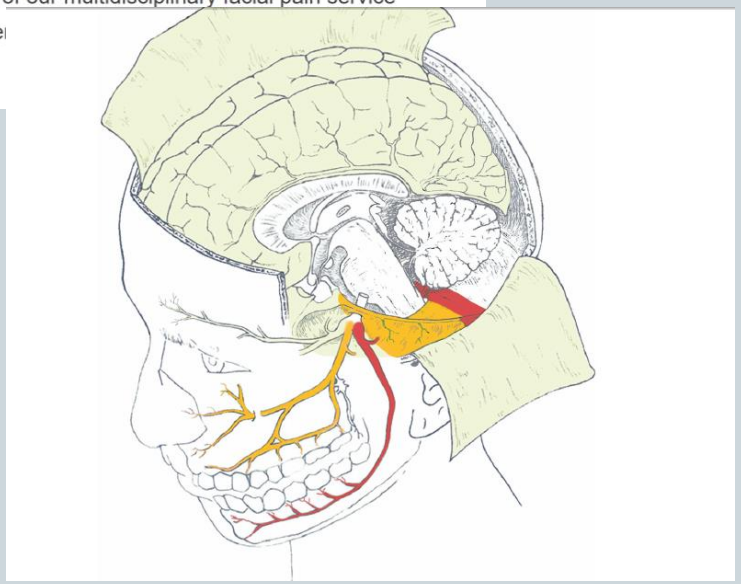
Article information | Altmetric 7

Abstract

Background

Sparse evidence has detailed the clinical phenotype of migraine presenting as isolated facial pain.

Objective and methods: This was a prospective audit, part of our multidisciplinary facial pain service evaluation, aiming to phenotype patients with migraine prese
service between 2013 and 2018.



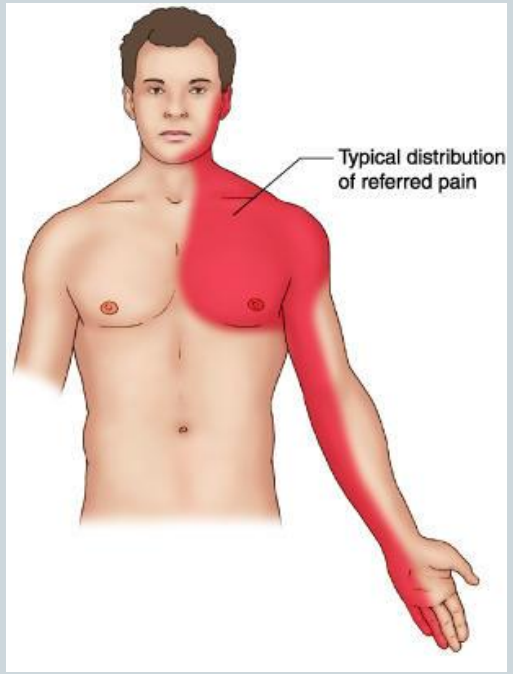
Migraine presenting as isolated facial pain: A prospective clinical analysis of 58 cases.**Lambru G**, Elias LA, Yakkaphan P, **Renton T.**Cephalalgia. 2020 Oct;40(11):1250-1254. doi: 10.1177/0333102420933277. Epub 2020 Jun 17.PMID: 32551980

Case Series of Four Different Headache Types Presenting as Tooth Pain
Aurelio A. Alonso, DDS and Donald R. Nixdorf, DDS, MS**

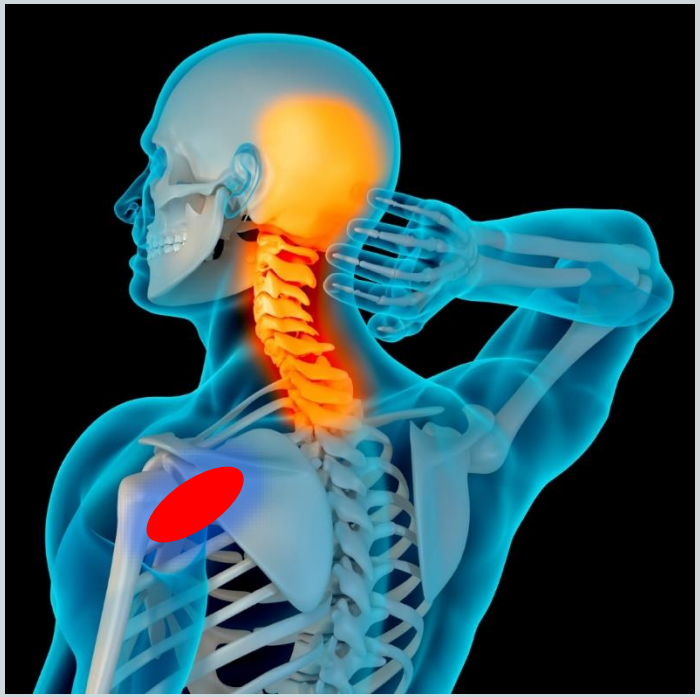
Is the OFP convergent pain / referred heterotopic pain

Referred pain
Heart
Cervical
Lung
CANCER

Angina pain



Cervical referred



Neoplasia

Or a rare Diagnosis?

- Auriculotemporal neuralgia occurs at a frequency of 0.4 % at a tertiary headache outpatient clinic [1]. However, this frequency may be even higher in outpatient orofacial pain due to the possible involvement of lateral pterygoid muscle in the etiology of auriculotemporal nerve entrapment.
- Diagnostic block
- The auriculotemporal nerve was then blocked with 0.5 ml 2 % lidocaine and 0.5 ml of a suspension containing dexamethasone disodium sulfate (2 mg/ml) and dexamethasone acetate (8 mg/ml) as follows: the needle is inserted below the TMJ, in the posterior margin of the head of the mandible immediately in front of the tragus, to a depth of 1–1.2 cm, at a horizontal 458 angle in the direction of the nose, with

J Headache Pain (2012) 13:415–417
DOI 10.1007/s10194-012-0439-4

BRIEF REPORT

Refractory facial pain attributed to auriculotemporal neuralgia

Juliana Stuginski-Barbosa · Rafael Akira Murayama · Paulo Cesar Rodrigues Conti · José Geraldo Speciali

Received: 28 November 2011 / Accepted: 12 March 2012 / Published online: 30 March 2012

Introduction

One of the biggest challenge for the clinician is when the patient still persists with complaints of orofacial pain, even with the adoption of well known and appropriate treatment. One of the reasons for this fact can be the misdiagnosis, very often in the field of orofacial pain, since the trigeminal system is frequently influenced by a diversity of different neural inputs. The presence of systemic diseases affecting the masticatory apparatus is also part of this scenario. One of this is a rare condition: auriculotemporal neuralgia (AN) [1].

The aim of the present study was to report a case of refractory facial pain after successful temporomandibular disorder (TMD) management, attributed to AN.

Case report

A 43-year-old Caucasian female patient presented for treatment of facial pain, with complaint of severe episodic pain in right face, ear and neck, first appeared 12 years ago, worsening in the last 3 months, with crisis of sharp and severe pain. The patient was previously diagnosed with sleep bruxism, depression and insomnia.

Physical examination revealed moderate pain upon palpation of right temporomandibular joint (TMJ), superficial masseter, occipital and sternocleidomastoid muscles. A trigger point was found in right medium masseter muscle referring pain to the ipsilateral ear and TMJ. The maximum mouth opening (MMO) with pain was 39 mm and no other significant signs were detected.

Masticatory myofascial pain and cervicalgia were the initial diagnosis and treatment consisted of advisement of the condition, counseling to avoid clenching her teeth during the day, hot packets and the nocturnal use of an occlusal stabilization splint in the upper jaw. The patient was also referred to a psychologist, physician and physical therapist for management of depression, insomnia and cervicalgia.

After 3 months, the patient reported a significant improvement, with no pain upon muscle palpation or function, and the MMO was 46 mm. However, she complained of a paroxysmal, short-duration pain below the right TMJ and in the temporal region, triggered by MMO and mastication. Intraoral and radiographic exams were unremarkable. Extra oral physical examination revealed that the palpation of the right auriculotemporal nerve region elicited a sharp pain familiar to the patient, which extended from below TMJ to the temporal region.

The hypotheses diagnosis was AN. The auriculotemporal nerve was then blocked with 0.5 ml 2 % lidocaine and 0.5 ml of a suspension containing dexamethasone disodium sulfate (2 mg/ml) and dexamethasone acetate (8 mg/ml) as follows: the needle is inserted below the TMJ, in the posterior margin of the head of the mandible immediately in front of the tragus, to a depth of 1–1.2 cm, at a horizontal 45° angle in the direction of the nose, with

J. Stuginski-Barbosa (✉) · P. C. R. Conti
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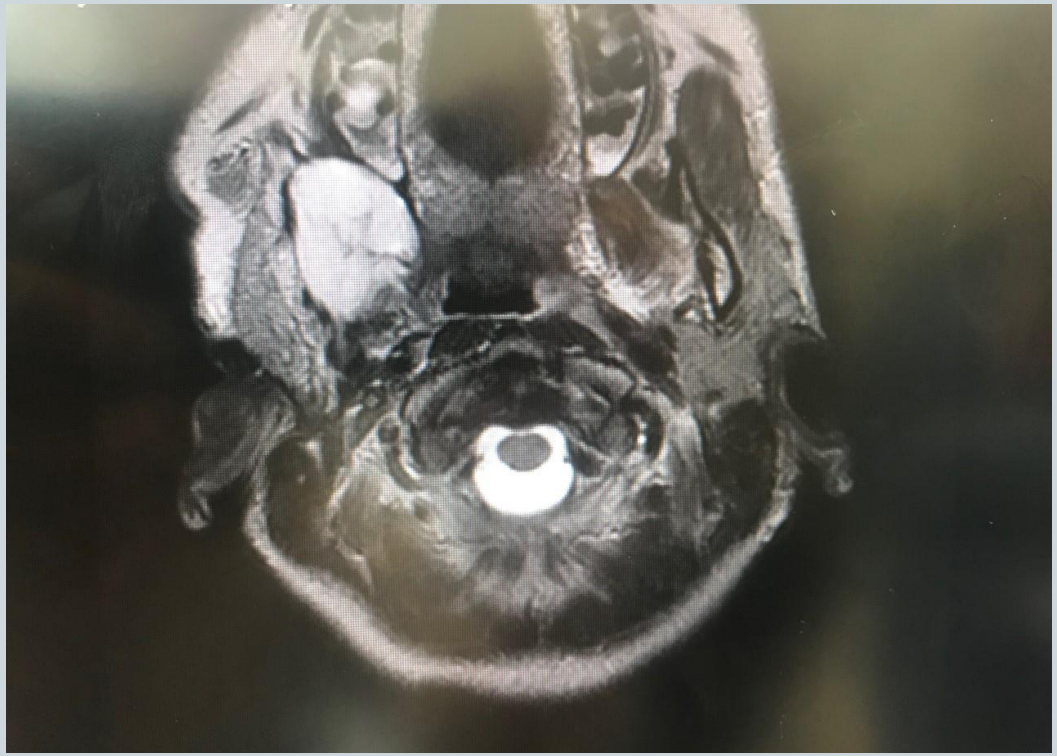
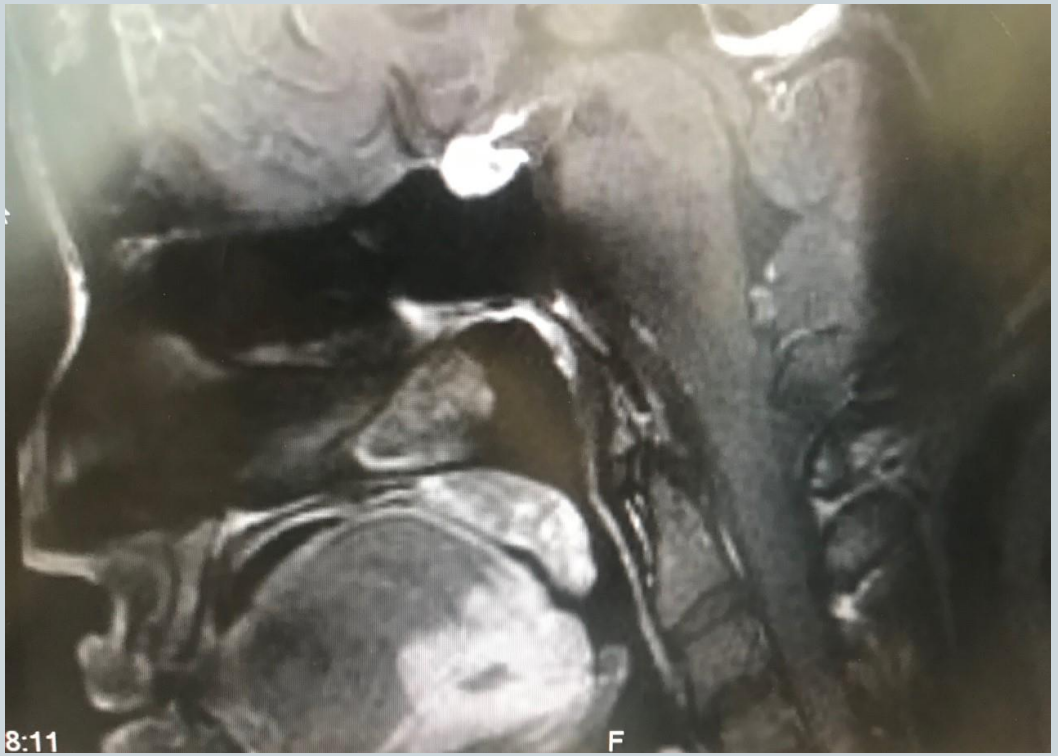
Faculty of Medicine of Ribeirao Preto, University of Sao Paulo, Ribeirao Preto, SP, Brazil

Or…..covert neoplasia?

- Neoplasia treated as toothache or headache





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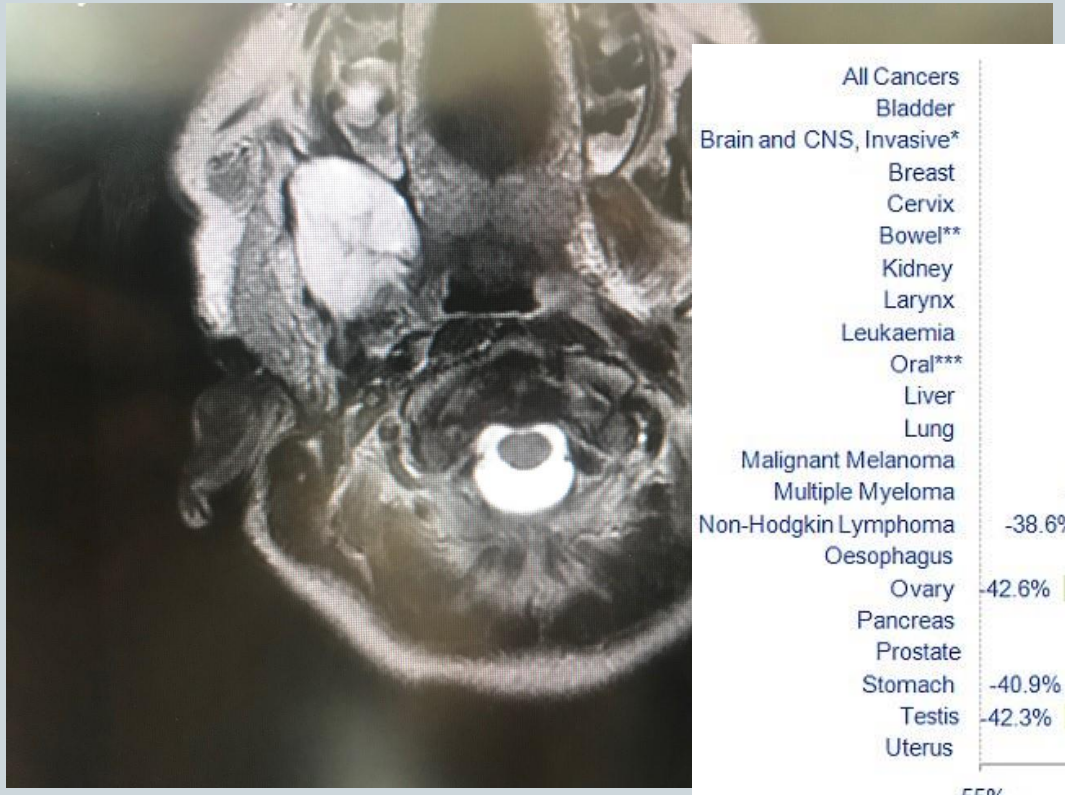

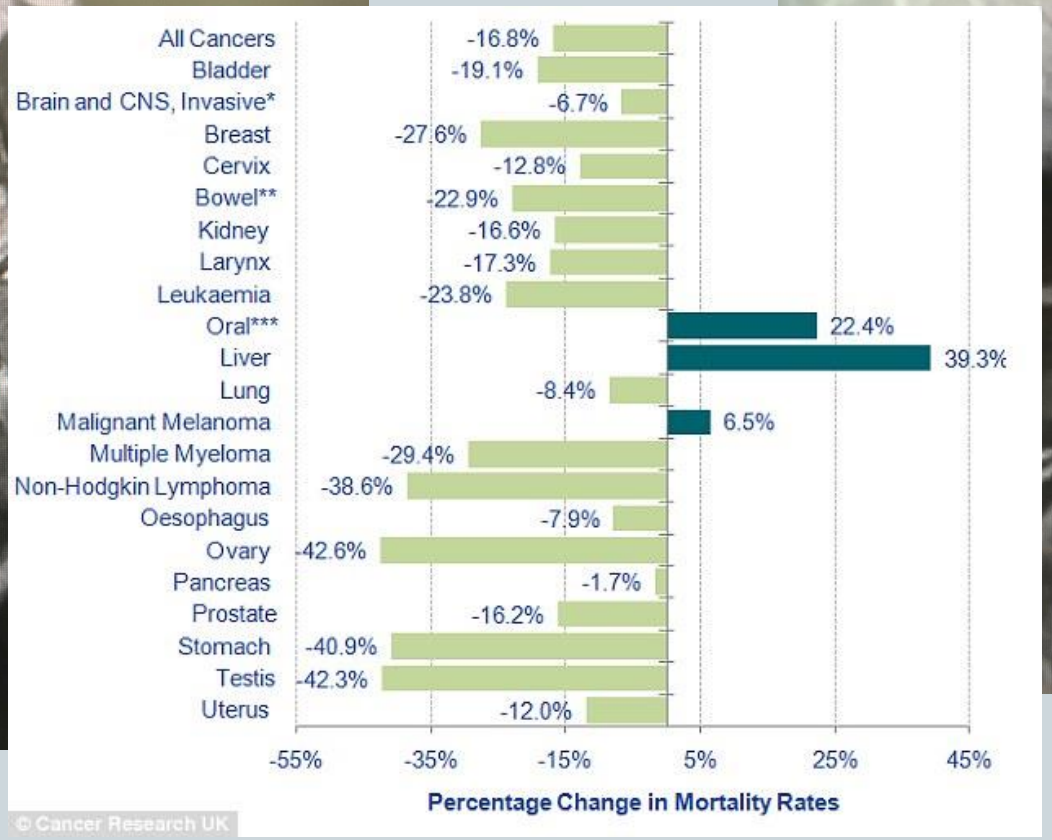

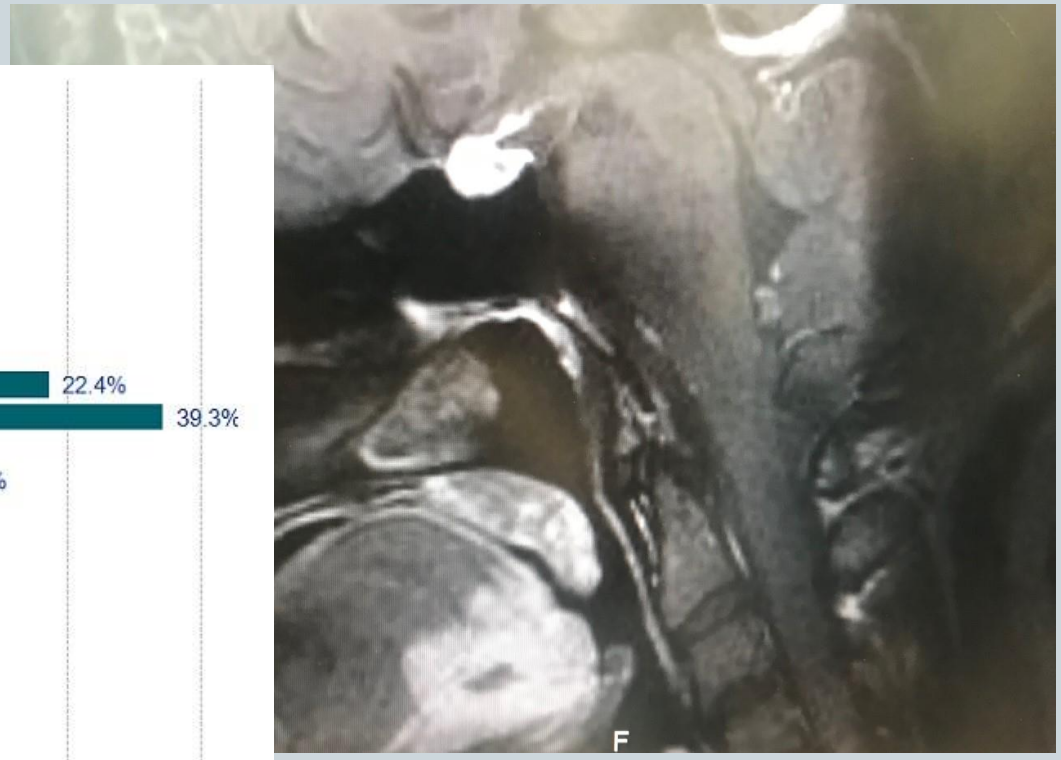

Any spontaneous pain or neuropathy think

Red flags of malignancy

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

NHS 2 (NICE 3) weeks Referral pathway

- 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

Review Article

Multiple Drug Intolerance Syndrome: An Underreported Distinct Clinical Entity

Author(s): Sapan K. Behera, Saibal Das, Kavadichanda G. Chengappa, Alphienes S. Xavier, Sandhiya Selvarajan*

Journal Name: Current Clinical Pharmacology

Volume 14 , Issue 2 , 2019 **DOI** : 10.2174/1574884713666181112125714

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Misdiagnosis

Intolerance to medications

Multiple pain interventions

Intolerance to medications

› Br J Health Psychol. 2013 Feb;18(1):18-30. doi: 10.1111/j.2044-8287.2012.02071.x. Epub 2012 Apr 23.

The perceived sensitivity to medicines (PSM) scale: an evaluation of validity and reliability

Rob Horne [1], Kate Faasse, Vanessa Cooper, Michael A Diefenbach, Howard Leventhal, Elaine Leventhal, Keith J Petrie

Affiliations + expand

PMID: 22524270 DOI: 10.1111/j.2044-8287.2012.02071.x

› Pharmacoepidemiol Drug Saf. 2015 Jun;24(6):592-9. doi: 10.1002/pds.3751. Epub 2015 Apr 7.

High perceived sensitivity to medicines is associated with higher medical care utilisation, increased symptom reporting and greater information-seeking about medication

Kate Faasse [1 2], Andrew Grey [1 2], Rob Horne [1 2], Keith J Petrie [1 2]

Affiliations + expand

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Drug intolerance

- Drug intolerance or drug sensitivity refers to an inability to tolerate the **adverse effects** of a medication, generally at therapeutic or subtherapeutic doses. Conversely, a patient is said to be "tolerating" a drug when they can tolerate its **adverse effects**.

- Multiple drug intolerance syndrome is defined as having greater than 3 or more unrelated drug intolerances or allergies. Based on medical record data, about 2 to 5% of the population in North America and Europe, with higher rates seen in hospitalized patients.

  Multiple drug intolerance syndrome is more likely to occur with increasing age, in females and in individuals being treated for higher numbers of different specific health conditions.

- In another study Over 20% of the general population reported being very sensitive to the effects of medication (20.2%) and that small amounts of medicines can upset their body (25.3%). Participants who reported high levels of perceived sensitivity to medicines reported significantly more symptoms (M = 9.54, SE = 0.47) than people with low (M = 5.04, SE = 0.49) or moderate (M = 5.91, SE = 0.24) levels, ps < .001. This relationship was strongest in participants who were currently taking prescription medication. Those with high perceived sensitivity also reported being more likely to seek information about medicines, and had significantly more general practitioner visits.

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Omer HMRB, Hodson J, Thomas SK, Coleman JJ. Multiple drug intolerance syndrome: A large-scale retrospective study. *Drug Saf*, 2014;37:1037-45
Faasse K, Grey A, Horne R, Petrie KJ. High perceived sensitivity to medicines is associated with higher medical care utilisation, increased symptom reporting and greater information-seeking about medication. Pharmacoepidemiol Drug Saf. 2015 Jun;24(6):592-9. doi: 10.1002/pds.3751. Epub 2015 Apr 7. PMID: 25851232.

Intolerance to medications……

- Abstract
- **Background** Poor adherence to antihypertensive drug regimens is common and may increase the risk for cardiovascular morbidity and mortality. Adverse effects of the drugs can contribute to poor adherence, but some patients who discontinue several different antihypertensive drugs may misinterpret nonspecific symptoms as adverse effects of the drug because of psychiatric morbidity. We examined the relationship between intolerance to antihypertensive drugs and the presence of panic disorder, panic attacks, anxiety, and depression.
- **Methods** We included all patients with hypertension who attended a hospital hypertension clinic during 1 year with at least 2 episodes of intolerance (resulting in reduction of the dosage or stopping an antihypertensive drug) recorded on standardized problem lists and a similar number of patients with no recorded episodes of intolerance. Psychiatric morbidity, assessed by self-administered questionnaires, was analyzed against the number of episodes of nonspecific and drug-specific intolerance, verified by means of individual case-note scrutiny, and scored independently by 2 assessors masked to patient identity.
- **Results** **Analyzable questionnaires** were returned by **233** (84%) of 276 patients who had experienced 576 (85%) of 679 episodes of intolerance assessed. **Five hundred thirty-two episodes (92%) were subjective (patient was symptomatic); of these, 284 were judged to be drug specific; 248, nonspecific**. Having more episodes of **nonspecific intolerance was associated with significantly higher diastolic blood pressure** (*P* = .003). **Episodes of nonspecific intolerance were associated with panic attacks (*P* = .008), anxiety (Hospital Anxiety and Depression Scale score, *P* = .04), and depression (Hospital Anxiety and Depression Scale score, *P* = .005).** Drug-specific intolerance was not associated with psychiatric morbidity.
- **Conclusions** **Intolerance to multiple antihypertensive drugs, particularly non–drug-specific intolerance, is strongly associated with psychiatric morbidity.** Physicians treating hypertensive patients need to recognize and manage the psychiatric aspects of intolerance to multiple antihypertensive drugs

Simon J. C. Davies; Peter R. Jackson; Lawrence E. Ramsay; et al Parviz Ghahramani **Drug Intolerance Due to Nonspecific Adverse Effects Related to Psychiatric Morbidity in Hypertensive Patients.** *Arch Intern Med.* 2003;163(5):592-600. doi:10.1001/archinte.163.5.592

Clinical phenotype

Cultural

Religion

Beliefs

Misdiagnosis

Intolerance to medications

Multiple pain interventions

Headache
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Review Article

Tooth-Related Pain or Not?

Tara Renton, BDS, MDSc, PhD

Dental pain is the most common acute pain presenting in the orofacial region; however, chronic pain conditions are also frequent and include; temporomandibular joint disorders (TMDs), primary headaches (neurovascular pain), painful post-traumatic trigeminal neuropathy (PPTTN) and less commonly referred pain and idiopathic or centralized pain conditions. All of these conditions can mimic toothache and vice versa. Many of these conditions are comorbid with high levels of tension headache and migraine reported in patients with TMD; however, dentists remain unfamiliar with headaches and medics unfamiliar with toothache's multiple presentations. The anatomical complexity of the region, the potential exhaustive differential diagnoses and the multiple siloed training of specialties, leads to incorrect and delayed diagnosis and often results in patients undergoing inappropriate surgical and medical treatments. The continued inappropriate interventions may also complicate the later presentation of the patient with pain, by changing its phenotype, preventing a timely and correct diagnosis. Due to the variable presentation of toothache, which can mimic many different chronic pains including; episodic throbbing pain of migraine, the dull continuous pain of myofascial and arthrogenous TMDs or centralized facial pain, diagnosis can be complex. Neuralgic pain occurs in the dentition in health and with disease, mimicking conditions like PPTTN, trigeminal neuralgia (TN), and trigeminal autonomic cephalalgias (TACs), many patients are inappropriately diagnosed and treated, either by general medical practitioners assuming that the neuralgia is due to TN rather than more commonly presenting toothache or by a dentists or other surgeons continuing to treat TN or TACs with routine surgical care. Many patients are prescribed countless courses of antibiotics and undergo multiple surgical interventions simply as a result of poor education due to siloed specialty training. This must be addressed to improve patient safety.

Key words: toothache, headache, temporomandibular disorders, sinusitis, trigeminal nerve injury, neuralgia

Obscured phenotype due to multiple interventions

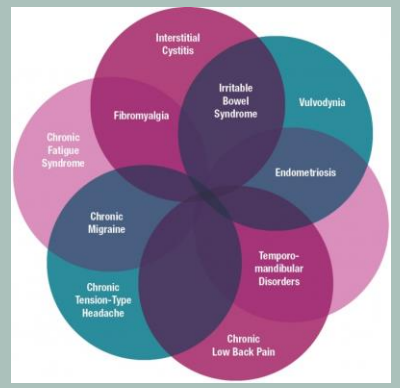
Audit of patients seen at Tertiary Multi-discplinary clinic at St Thomas Input Pain Management Centre

Reason for attendance and outcome

Team

Madeleine Murphy	Headache nurse
Dr Giorgio Lambru	Headache neurologist
Dr Stefano Palmisani	Pain management
Sinan Barazi	Neurosurgeon
Tara Renton	Oral Surgeon

Data Collated by PhD Student Pankaew Yakkaphan



Medical Co-morbidities
CWP /FM
Sleep disorders
Smoking
Drug dependency
Vitamin C and D def
Malnutrition
DM, Hypothyroid, Autoimmune disorders

Comorbid pain conditions?

BJA

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Special Article

Chronic pain: a review of its epidemiology and associated factors in population-based studies

Sarah E. E. Mills*, Karen P. Nicolson and Blair H. Smith

Population Health and Genomics Division, University of Dundee School of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland, UK

*Corresponding author. E-mail: s.e.e.mills@dundee.ac.uk

Summary

Chronic pain is a common, complex, and distressing problem that has a profound impact on individuals and society. It frequently presents as a result of a disease or an injury; however, it is not merely an accompanying symptom, but rather a separate condition in its own right, with its own medical definition and taxonomy. Studying the distribution and determinants of chronic pain allows us to understand and manage the problem at the individual and population levels. Targeted and appropriate prevention and management strategies need to take into account the biological, psychological, socio-demographic, and lifestyle determinants and outcomes of pain. We present a narrative review of the current understanding of these factors.

Keywords: chronic pain; epidemiology; genetics; incidence; prevalence; risk factors

Chronic pain is a common, complex, and distressing problem, which has a significant impact on society and individuals.[1] It commonly presents as a result of an injury or a disease; however, it is a separate condition in its own right, not merely an accompanying symptom of other ailments. Chronic pain, therefore, has both its own taxonomy and medical definition.[2–4]

The Global Burden of Disease Study 2016 reaffirmed that the high prominence of pain and pain-related diseases is the leading cause of disability and disease burden globally.[5] Worldwide, the burden caused by chronic pain is escalating: 1.9 billion people were found to be affected by recurrent tension-type headaches, which were the most common symptomatic chronic condition.[5] Measuring years lived with disability, low back and neck pain have consistently been the leading causes of disability internationally, with other chronic pain conditions featuring prominently in the top 10 causes of disability.[5]

In order to develop treatment plans and prevention strategies, chronic pain needs to be understood in the context of social, biological, psychological, and physical factors. This is a narrative synthesis of the epidemiology, particularly the risk factors and demographic associations, of chronic pain.

Importance of epidemiology in chronic pain

Epidemiology, the 'study of the distribution and determinants of health-related states or events in specified populations and the applications of this study to control health problems',[6] is vital to understanding chronic pain. According to the International Association for the Study of Pain, chronic pain is 'pain which has persisted beyond normal tissue healing time',[7] which, in the absence of other factors, is generally taken to be 3 months.[7] There are many risk factors for chronic pain, including socio-demographic, psychological, clinical, and

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Nociplastic (Centralised or dysfunctional) pain states
Usually with comorbid pain states- chronic widespread pain / Fibromyalgia

- Most common and costly illness in humans
- Used to be termed idiopathic or somatisation
- Characterised by
- Chronic overlapping conditions-multisystem illness typically begins in childhood or young adult hood
- Chronic pain or discomfort in several body regions
- TMD, IBS, Migraine, back pain, Tension headaches, interstitial cystitis, dry eye disease (NIH PA 14-244)
- Multiple other somatic disorders of CNS origin
  - Fatigue, sleep disorder, mood, memory
- By stressful trigger
- Post deployment Gulf war syndrome
- Post infection (Lyme disease chronic EBV)
- Post emotional trauma Death of spouse

Orofacial pain conditions by definition refractory

Is Persistent idiopathic facial or intraoral pain
Oro facial presentation of CWP or FM?

BMS?

Nociplastic (Centralised or dysfunctional) pain states

Usually with comorbid pain states- chronic widespread pain / Fibromyalgia

COMMENTARY

Check for updates

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

Bart Morlion[a], Flaminia Coluzzi[b], Dominic Aldington[c], Magdalena Kocot-Kepska[d], Joseph Pergolizzi[e],

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

ABSTRACT

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

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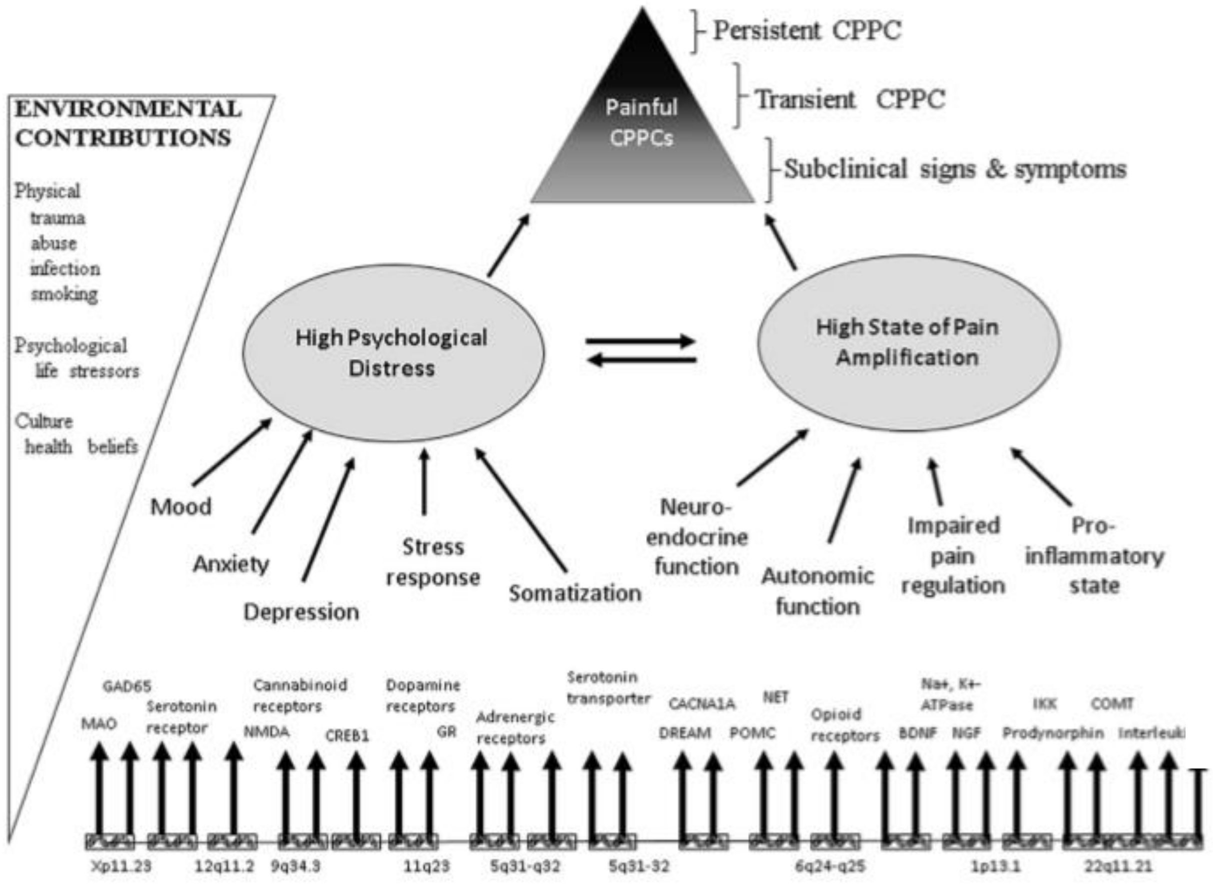
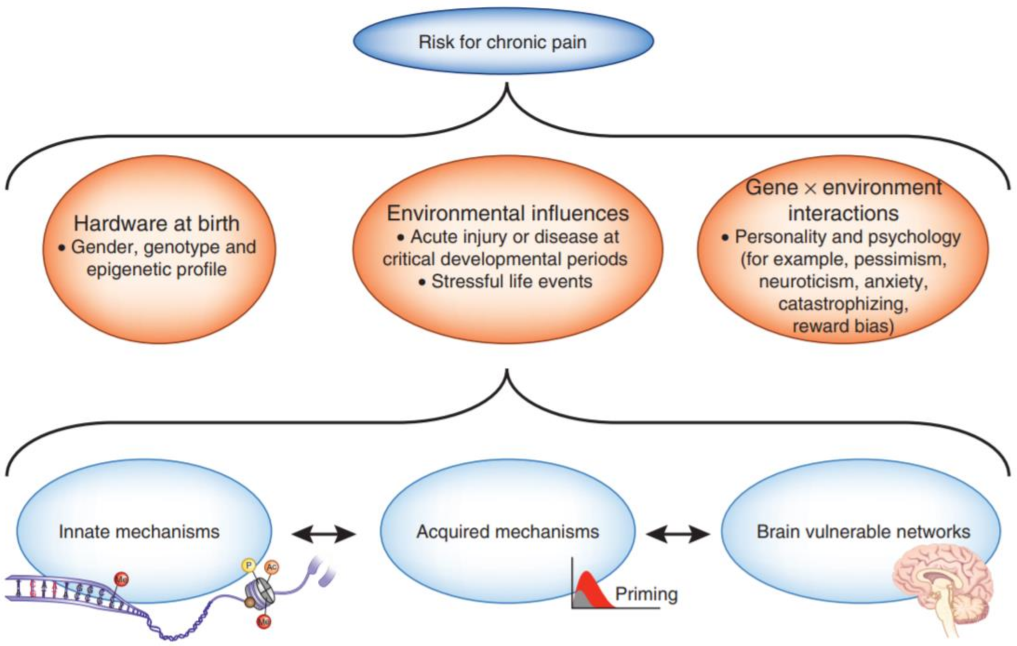
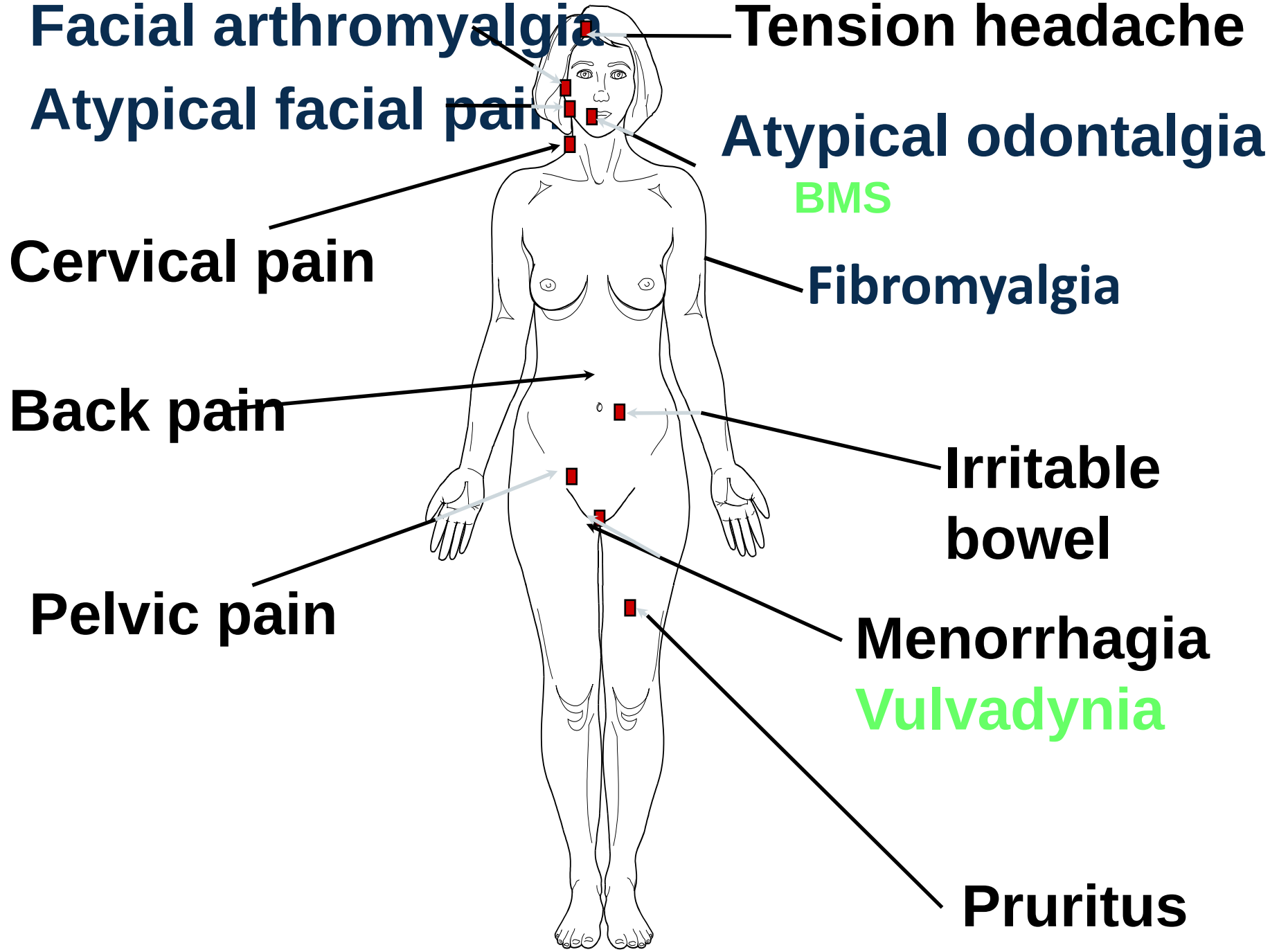


Figure 4. This model depicts likely determinants that contribute to the risk of onset and maintenance of common chronic overlapping pain conditions (COPCs). These factors are determined by genetic variability and environmental events that determine an individual's psychological profile and pain amplification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

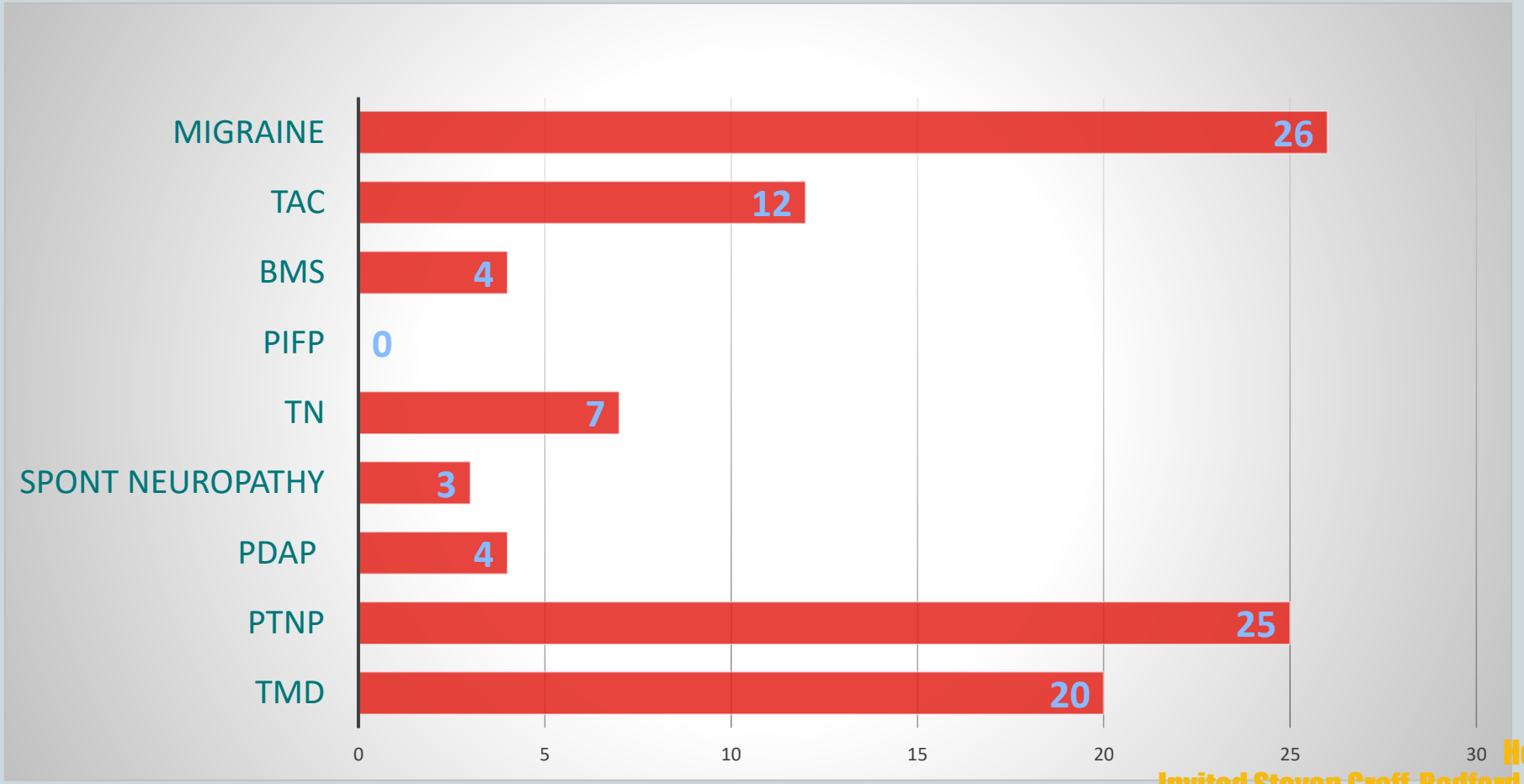


Denk F, McMahon SB **Neurobiological basis for pain vulnerability: why me?** Pain. 2017 Apr;158 Suppl 1:S108-S114.


Facial arthromyalgia
Tension headache
Atypical facial pain
Atypical odontalgia
BMS
Cervical pain
Fibromyalgia
Back pain
Irritable bowel
Pelvic pain
Menorrhagia
Vulvadynia
Pruritus

What we see
Prevalence of OFP conditions (%)

(Unpublished n=1241 consecutive patients)



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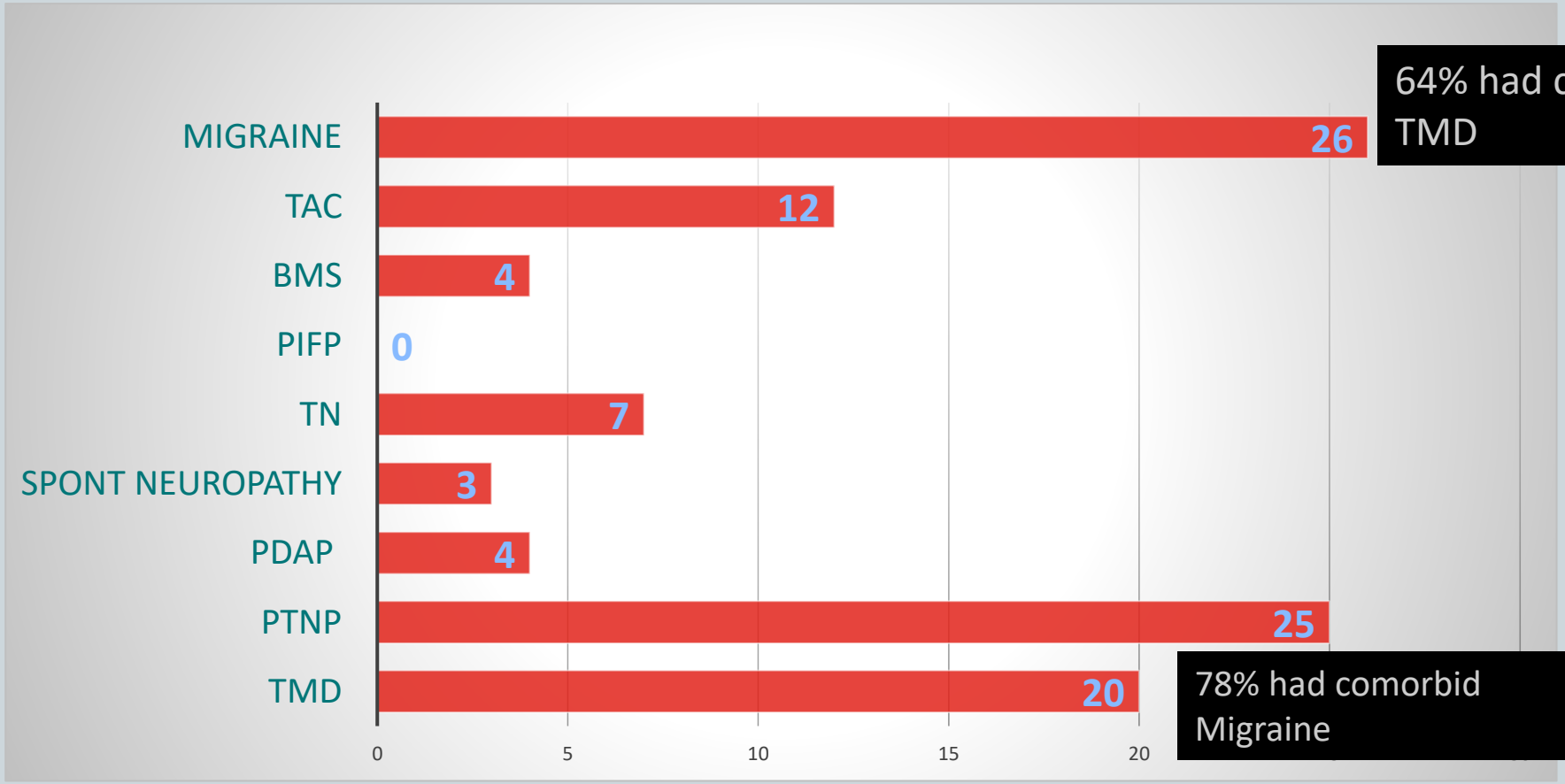

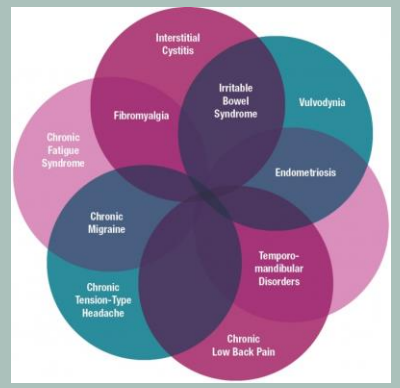

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Sleep disorders?

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Sleep disorders and pain

Sleep disorders have been shown to affect nearly half of people reporting chronic pain, with a quarter of chronic pain patients suffering from clinical insomnia.132

The association is bidirectional, with chronic pain causing poor sleep, and poor sleep increasing the intensity and duration of chronic pain.132

Sleep deprivation was found to be a risk factor for chronic pain in a prospective survey of women over a 17 yr period.133

Another study showed that having chronic pain made people more likely to suffer from sleep problems and depression, and suggested that treating sleep disorders should be considered as part of chronic pain management.134

Severe chronic pain after concussion was significantly related to insomnia.135 There is a high prevalence of sleep apnoea in patients who take opioid medications long term, but patients with chronic pain are at higher risk of developing sleep apnoea irrespective of opioid medication.136

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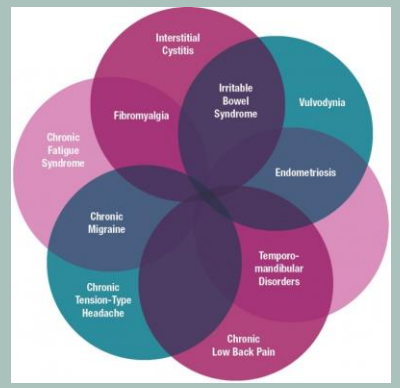

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Smoking and chronic pain

People with chronic pain are more likely to smoke than those with no pain.49e51

Patients who are heavy smokers report higher pain intensity scores than non-smokers, and report a higher number of painful sites.52e54

Smoking is involved in the aetiology of several conditions that cause chronic pain,55 and the relationship between smoking and chronic pain appears to be dose related.53

Smokers affected by chronic pain are more likely to be dependent on tobacco, smoke more cigarettes a day, and have more difficulty in quitting smoking than those who do not have the condition.52,56

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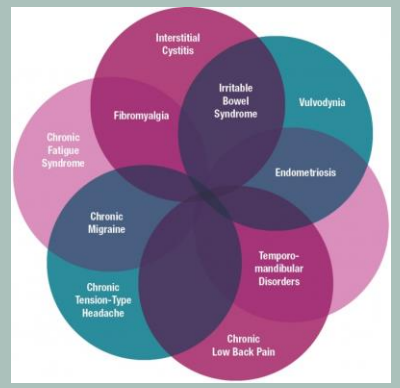

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Nutrition Vi D and C def….? Microbiome?

The role of nutrition in the development and prevention of chronic pain is unclear.

Nutrition management plans may be of benefit to patients with chronic pain by improving pain management and reducing cardiovascular risk factors that are related to chronic pain.

Omega-3 as a diet supplement in preclinical trials did show an improvement in inflammatory pain,71 whilst garlic has been suggested to reduce pain severity in overweight women with knee arthritis.72

A recent systematic review and metaanalysis of 23 papers found that **interventions based on nutrition, particularly those testing an altered overall diet or a single nutrient, had a significant effect on reducing participants' reported pain severity and intensity**.73 However, the studies in the field of nutrition and chronic pain, including those included in the meta-analysis, were of low quality,73e76 and there is insufficient evidence to make specific dietary recommendations.

More rigorous studies examining nutrition with chronic pain as a primary outcome are needed in order to determine the role of nutrition in chronic pain.73

Sunshine and vitamin D Colder climates and lack of sunshine correlate with chronic pain; a study showed less pain was experienced on longer, sunnier days. A relationship between **high levels of reported pain and low levels of vitamin D has been demonstrated**, with the suggestion that **low vitamin D levels cause anatomic, endocrine, neurological, and immunological changes**, which predispose to onset and perpetuation of chronic pain.77,78 However, the effect is not replicated across all studies with only 25% of studies concluding that there is a correlation between low levels of vitamin D and chronic pain.79,80

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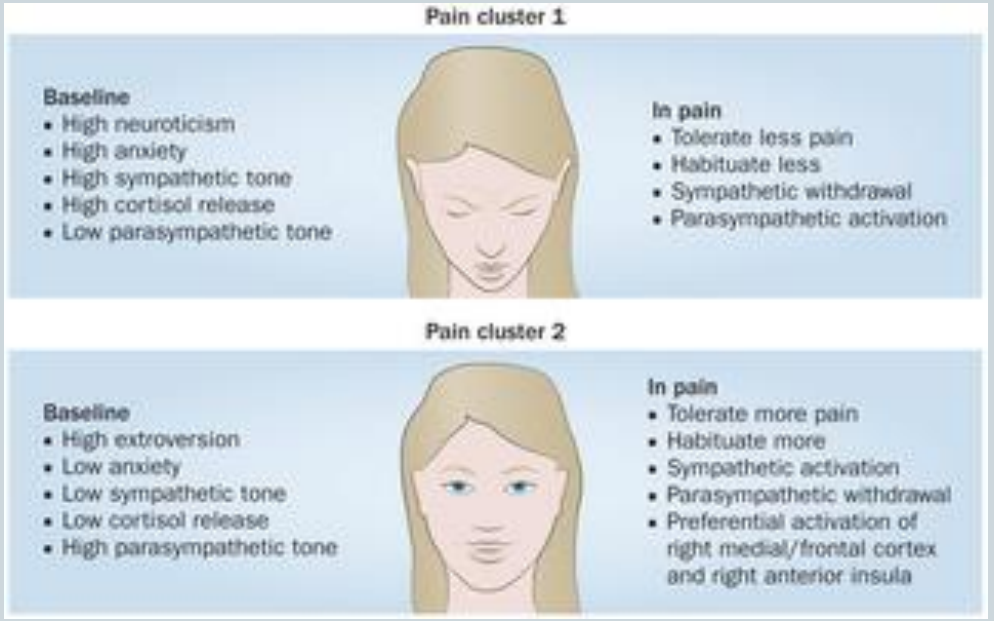
Psychological factors
Anxiety Depression
Neuroticism
Catastrophising
Introversion
Hypervigilance

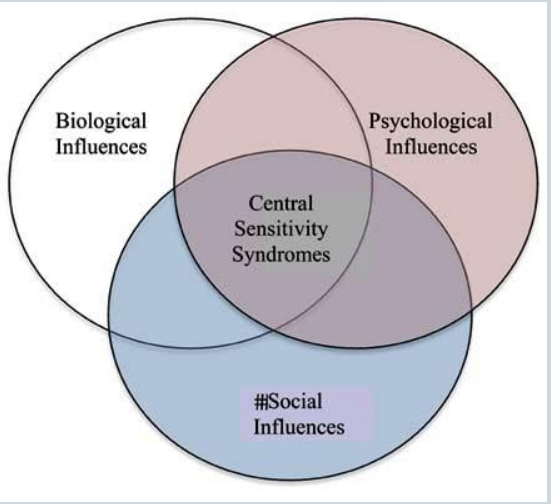
Psychological factors?

Section subtitle

Psychosocial risk factors predictive of chronic post surgical pain

- 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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- Type of patient
  - Stoic
  - Resilient
  - Non complainer
  - Great pain modulation

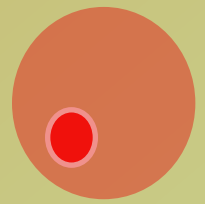
Nociception

Sensation

Behaviour

Suffering

- Type of patient
  - Non-Resilient
  - Complainer
  - Poor pain modulation



Nociception

Sensation

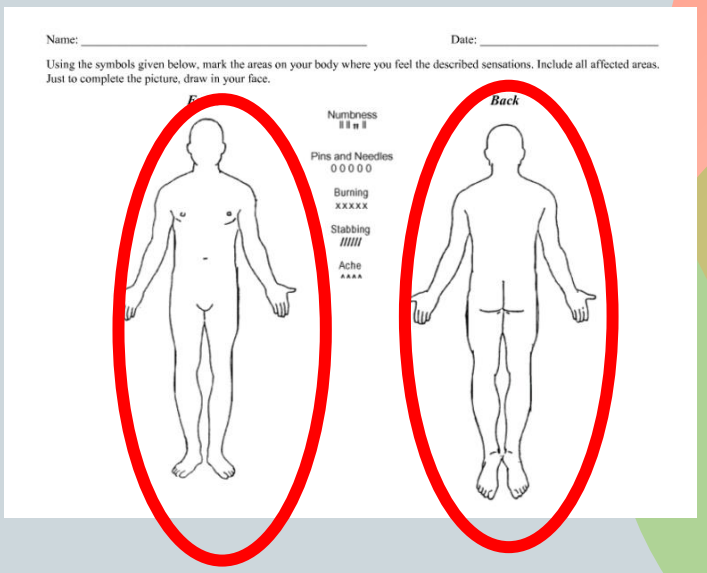
Behaviour

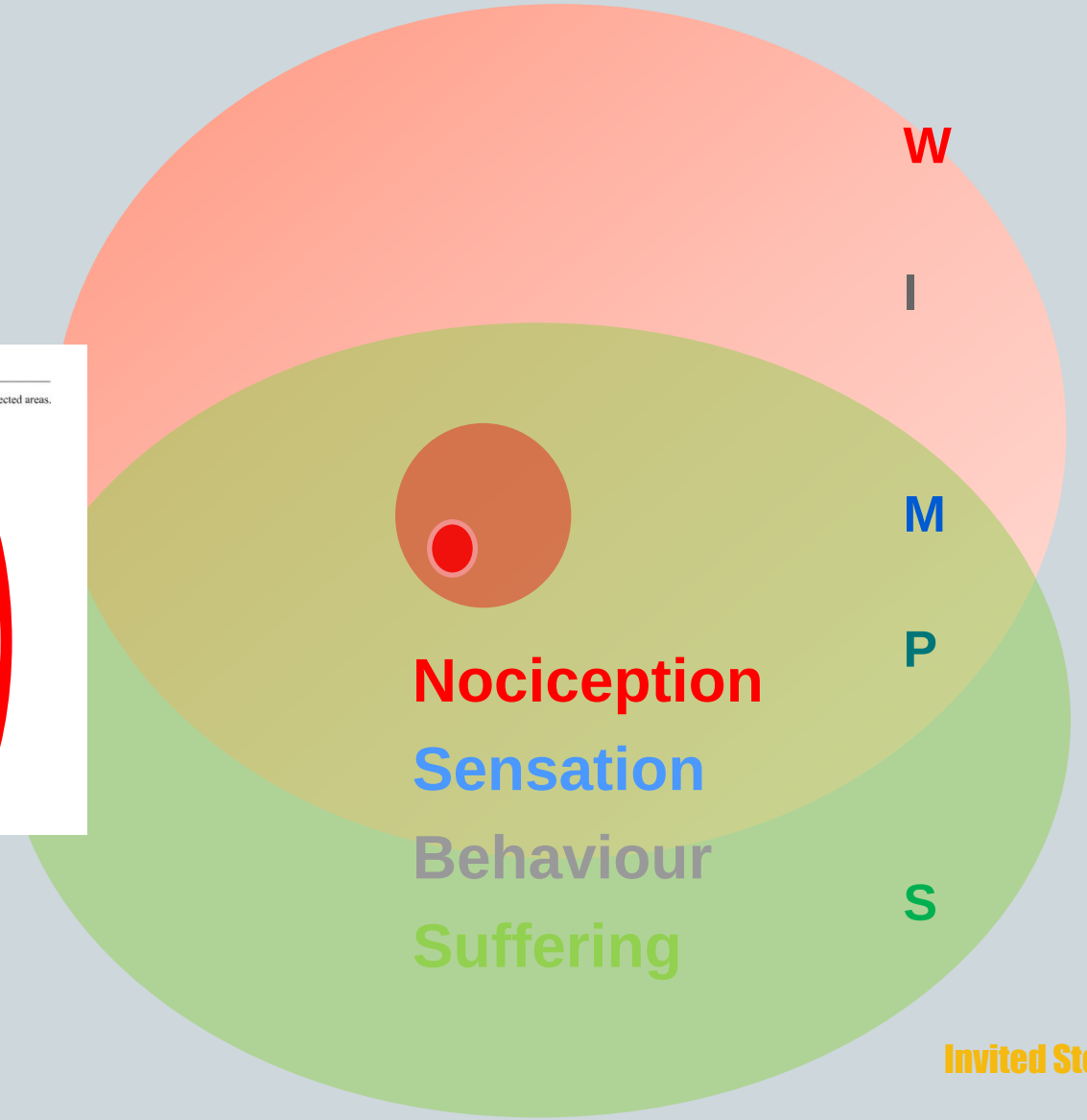
Suffering

Head, heart or toothache?
Invited Steven Graff-Radford Award Lectureship 2020

Reasons for non resilience

- WIMPS





W **Women**

GWAS

I **Injury- PTSD**

Inhibition is poor &

Facilitation is high

M **Mood disorders**

Anxiety & Stress

P **Personality disorders**

introspective, catastrophiser and hypervigilance

Prior abuse and neglect

S **Sleep deprivation / Stress**

Head, heart or toothache?
Invited Steven Graff-Radford Award Lectureship 2020

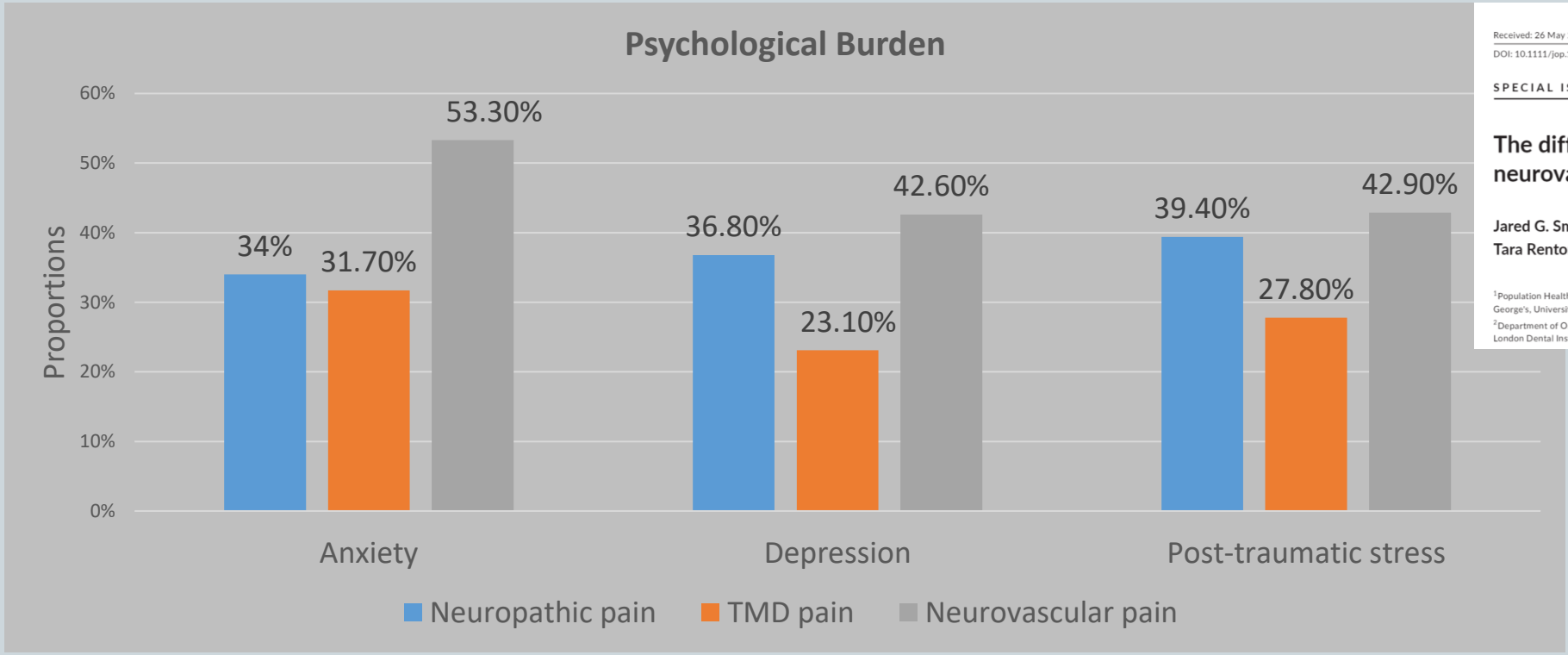
AXIS II pre consultation extensive psychosocial assessment

- All patients:
  - **EQ-5D**
  - **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

Severe Anxiety
Probable Major depression
Somatic disorder
PTSD
Likely NP

Prevalence of comorbid psychosocial morbidity



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DOI: 10.1111/jop.13071

SPECIAL ISSUE ARTICLE

Journal of Oral Pathology & Medicine WILEY

The differential impact of neuropathic, musculoskeletal and neurovascular orofacial pain on psychosocial function

Jared G. Smith[1] | Aalia Karamat[2] | Lydia N. Melek[3] | Simone Jayakumar[4] | Tara Renton[2]

[1]Population Health Research Institute, St George's, University of London, London, UK
[2]Department of Oral Surgery, King's College London Dental Institute, London, UK

Abstract

Background: While the psychosocial morbidity of orofacial pain (OFP) is widely rec-
ognized, the differential impact of musculoskeletal, neuropathic and neurovascular

Smith JG, Karamat A, Melek LN, Jayakumar S, Renton T. The differential impact of neuropathic, musculoskeletal and neurovascular orofacial pain on psychosocial function. J Oral Pathol Med. 2020 Jul;49(6):538-546. doi: 10.1111/jop.13071. Epub 2020 Jul 2. PMID: 32531812.

Prevalence of comorbid psychosocial morbidity in pain

International Journal of Oral and Maxillofacial Surgery
Volume 47, Issue 7, July 2018, Pages 869-878

Systematic Review
Oral Medicine

The psychosocial impact of orofacial pain in trigeminal neuralgia patients: a systematic review

L.N. Melek [1], M. Devine [2], T. Renton [2]

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.

Psychological impact of orofacial neuropathic and non-neuropathic pain: a systematic review

Karamat A, Smith JG, Melek L, Renton T. J Orofacial Pain 2019 In Press

Abstract

Aims: This systematic review aims to explore the psychological function in patients with neuropathic and non-neuropathic orofacial pain conditions. **Methods:** A systematic online search of Medline (PubMed) and Ovid databases was performed from 2006-2016. Observational studies, including cross sectional, case control and case series and longitudinal prospective studies were included. Search strategy was restricted to studies in English with patients aged 18 years and older. Seventy-five articles were selected. The standardised

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SPECIAL ISSUE ARTICLE

Journal of Oral Pathology & Medicine WILEY

The differential impact of neuropathic, musculoskeletal and neurovascular orofacial pain on psychosocial function

Jared G. Smith[1] | Aalia Karamat[2] | Lydia N. Melek[3] | Simone Jayakumar[4] | Tara Renton[2]

[1]Population Health Research Institute, St George's, University of London, London, UK
[2]Department of Oral Surgery, King's College London Dental Institute, London, UK

Abstract

Background: While the psychosocial morbidity of orofacial pain (OFP) is widely recognized, the differential impact of musculoskeletal, neuropathic and neurovascular

Head, heart or toothache?
Invited Steven Graff-Radford Award Lectureship 2020

Social factors
Support
Education level
Income
Prior significant life events
Vulnerability

Social factors driving persistent pain?

Section subtitle

Prior significant life events

- The severity and development of chronic pain experience are affected by early life factors: people who experience **adversity or emotional trauma (e.g. death of parent and being raised in the care system) or physical trauma (e.g. substantial hospitalisation and preterm birth) in childhood have a higher risk of chronic pain in their adult lives**.153
- **Early stress in life can alter the function of the hypothalamic pituitary adrenal axis, affecting the stress response**.153
- Young people **who have experienced traumatic adverse childhood experiences (ACEs) have a greater chance of developing chronic pain** than those who have not. A study of children and 9-19 years with chronic pain found that the most common ACE in children with chronic pain was having family members with mental health illnesses; 55% of children with multiple ACEs experience chronic pain.154
- The **more ACEs, the greater the level of chronic widespread pain** and psychological distress, such as anxiety and depression (which have been noted previously to be related to the development and severity of chronic pain).154
- People who **have experienced personal violence or abusive relationships are more likely to experience subsequent chronic pain.**43,155
- This has been found to be true regardless of the age at which the violence or abuse was experienced, or whether it was domestic or public violence or abuse.155,156

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- Published: 20 June 2020
- The Relationship Between Psychological Resilience and Pain Threshold and Tolerance: Optimism and Grit as Moderators
- Ashley Buckingham &
- Elizabeth J. Richardson
- *Journal of Clinical Psychology in Medical Settings* (2020)Cite this article
- **259** Accesses
- **1** Citations
- **1** Altmetric
- Metricsdetails
- Abstract
- This study examined factors that may enhance the relationship between resilience and time to pain threshold and tolerance during experimentally induced pain among 62 healthy adults recruited from a student population. Specifically, dispositional optimism and psychological grit were examined as moderators of the relationship between resilience and pain outcomes. Zero-order correlations revealed that resilience was positively related to grit and optimism, though grit and optimism were not significantly related to each other. Resilience, grit and optimism were all positively related to time to pain threshold and tolerance, but not pain severity. Moderation models showed that dispositional optimism enhanced the effect of resilience on both time to pain threshold and tolerance. Grit, on the other hand, was found to enhance the effect of resilience on time to pain threshold, but not time to pain tolerance. These results suggest that positive psychological factors and their interactions may be important with persevering during adverse experiences such as pain

Future Medicine

JOURNALS BOOKS ABOUT US CONTACT US

PAIN MANAGEMENT, VOL. 6, NO. 1 | REVIEW

Social pain and physical pain: shared paths to resilience

John A Sturgeon & Alex J Zautra

Published Online: 17 Dec 2015 | https://doi.org/10.2217/pmt.15.56

Although clinical models have traditionally defined pain by its consequences for the behavior and internal states of the sufferer, recent evidence has highlighted the importance of examining pain in the context of the broader social environment. Neuroscience research has highlighted commonalities of neural pathways connecting the experience of physical and social pain, suggesting a substantial overlap between these phenomena. Further, interpersonal ties, support and aspects of the social environment can impair or

Physiological Factors
Microbiome
Endogenous pain modulation
Neural plasticity
Gray / white matter degeneration
Connectivity
Neuropathy

Physiological resilience to pain?

Endogenous pain modulation

Microbiome and pain

The balancing act: endogenous modulation of pain in functional gastrointestinal disorders

PDF

Abstract

Functional gastrointestinal disorders (FGIDs) are characterised by visceral pain or discomfort with an unknown cause. There is increasing evidence for abnormal processing of sensory input in FGIDs. Modulation of sensory input occurs at all levels of the nervous system, with a dynamic balance between facilitation and inhibition and close integration with the body's wider homoeostatic control. Cognitive, emotional, autonomic and spinal reflex pathways effectively orchestrate supraspinal and spinal pain modulation, as demonstrated in neurophysiological and brain imaging studies. Endogenous pain modulation has been studied in visceral pain conditions and abnormal regulation has been shown in irritable bowel syndrome (IBS) and functional dyspepsia, as well as other chronic pain syndromes. A majority of patients with IBS have diminished pain inhibition or even pain facilitation compared with healthy controls. Brain imaging during specific activation of endogenous pain modulation demonstrates a fairly consistent functional hub of mainly frontal, limbic and brainstem modulatory regions in healthy humans. Patients with IBS have a different pattern of activation and a correlation between the imaging and sensory changes. Because the modulatory balance of inhibition and facilitation appears to be distributed within the same functional network, future imaging studies of modulation mechanisms should include conditions allowing quantification of inhibitory and facilitatory components. An altered modulatory balance may well be a unifying pathophysiological mechanism in FGID as it can be driven by both top-down (ie, CNS pathology) and bottom-up (ie, peripheral immune activation) influences, but further validation in diverse FGID groups over time is required. Therapeutic manipulation of the modulatory system is possible by both pharmacological and non-pharmacological means.

Recent advances in clinical practice

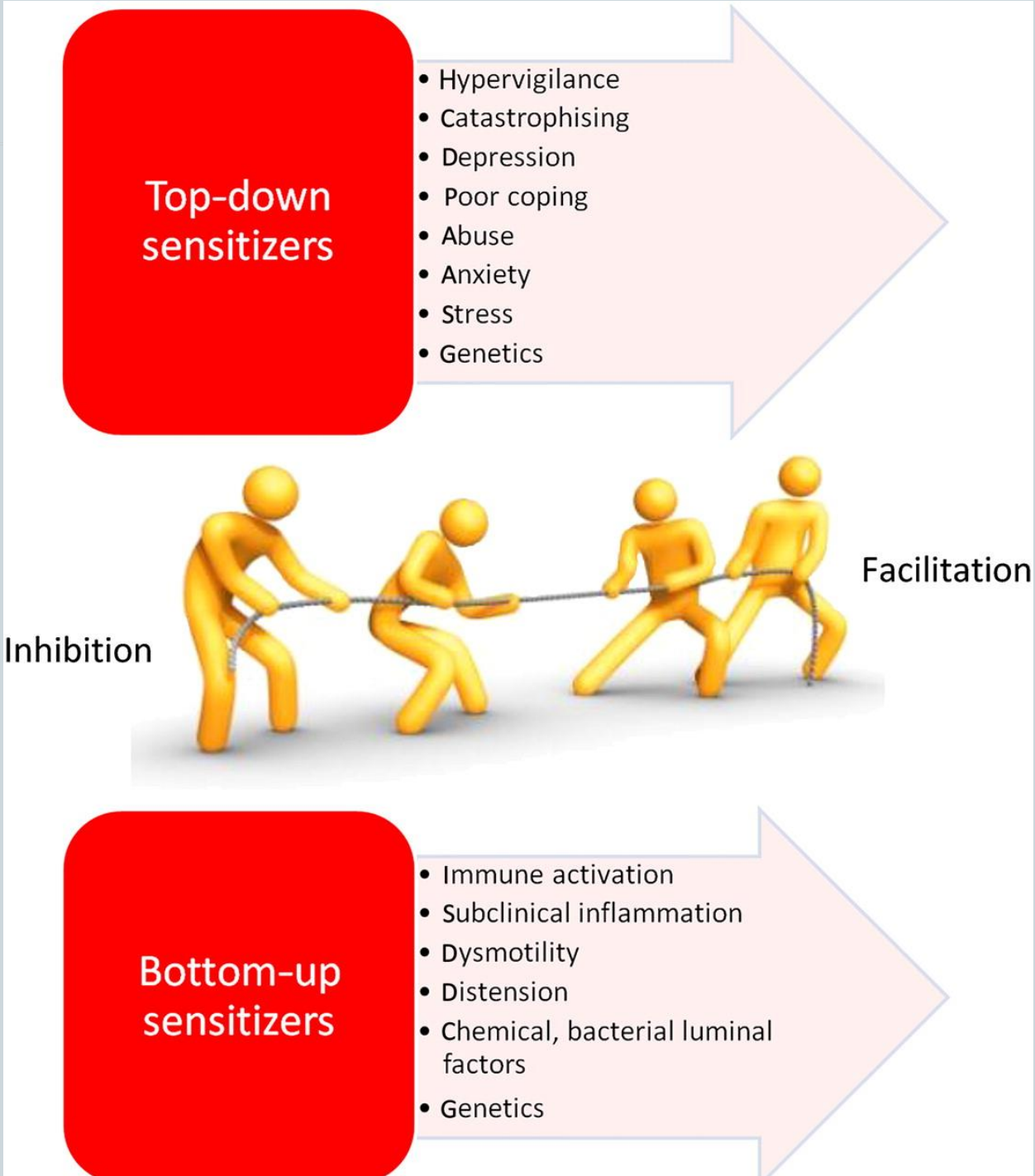
The balancing act: endogenous modulation of pain in functional gastrointestinal disorders Clive H Wilder-Smith BMJ GUT Volume 60, Issue 11

Autonomic drive

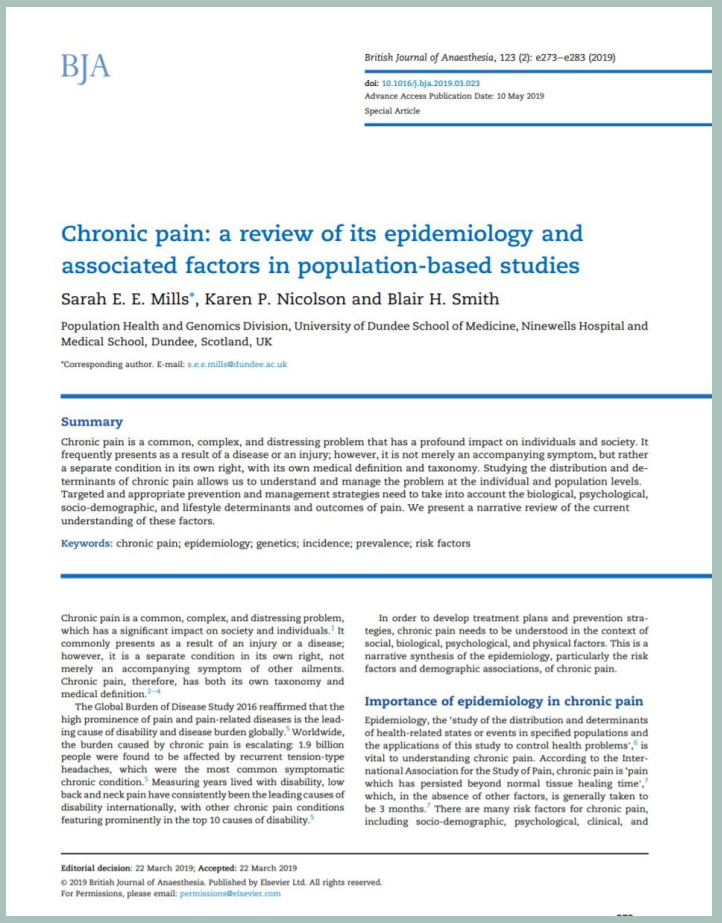
- Variable heart rate

Endogenous pain mechanisms

- Medication overuse



Genetic Profile
Ethnicity
Gender
Genome
Epigenetics



BJA

British Journal of Anaesthesia, 123 (2): e273–e283 (2019)

doi: 10.1016/j.bja.2019.03.023
Advance Access Publication Date: 10 May 2019
Special Article

Chronic pain: a review of its epidemiology and associated factors in population-based studies

Sarah E. E. Mills*, Karen P. Nicolson and Blair H. Smith

Population Health and Genomics Division, University of Dundee School of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland, UK

*Corresponding author. E-mail: s.e.e.mills@dundee.ac.uk

Summary

Chronic pain is a common, complex, and distressing problem that has a profound impact on individuals and society. It frequently presents as a result of a disease or an injury; however, it is not merely an accompanying symptom, but rather a separate condition in its own right, with its own medical definition and taxonomy. Studying the distribution and determinants of chronic pain allows us to understand and manage the problem at the individual and population levels. Targeted and appropriate prevention and management strategies need to take into account the biological, psychological, socio-demographic, and lifestyle determinants and outcomes of pain. We present a narrative review of the current understanding of these factors.

Keywords: chronic pain; epidemiology; genetics; incidence; prevalence; risk factors

Chronic pain is a common, complex, and distressing problem, which has a significant impact on society and individuals.[1] It commonly presents as a result of an injury or a disease; however, it is a separate condition in its own right, not merely an accompanying symptom of other ailments. Chronic pain, therefore, has both its own taxonomy and medical definition.[2–4]

The Global Burden of Disease Study 2016 reaffirmed that the high prominence of pain and pain-related diseases is the leading cause of disability and disease burden globally.[5] Worldwide, the burden caused by chronic pain is escalating: 1.9 billion people were found to be affected by recurrent tension-type headaches, which were the most common symptomatic chronic condition.[5] Measuring years lived with disability, low back and neck pain have consistently been the leading causes of disability internationally, with other chronic pain conditions featuring prominently in the top 10 causes of disability.[5]

In order to develop treatment plans and prevention strategies, chronic pain needs to be understood in the context of social, biological, psychological, and physical factors. This is a narrative synthesis of the epidemiology, particularly the risk factors and demographic associations, of chronic pain.

Importance of epidemiology in chronic pain

Epidemiology, the 'study of the distribution and determinants of health-related states or events in specified populations and the applications of this study to control health problems',[6] is vital to understanding chronic pain. According to the International Association for the Study of Pain, chronic pain is 'pain which has persisted beyond normal tissue healing time',[7] which, in the absence of other factors, is generally taken to be 3 months.[7] There are many risk factors for chronic pain, including socio-demographic, psychological, clinical, and

Editorial decision: 22 March 2019; **Accepted**: 22 March 2019

Genetic drivers for persistent pain?

Evidence for genetic basis for neuropathic and nociplastic pain

Genetics and pain

- The relationship between chronic pain and genes is complex.
- Genes act at many levels to shape the experience of chronic Epidemiology of chronic pain - e277 pain, influencing emotional, behavioural, and biological processes.137
- Sensitivity to painful stimuli and pain tolerance are partly genetically determined.138,139 Chronic pain is a heritable phenotype, and the presence of chronic pain clusters in family groups140,141 through genetic and 'maternal' effects. It also may be as a result of important genetic contributions to underlying diseases, which will include chronic pain.63,140,141
- One of the current challenges in chronic pain epidemiology is to determine which genes contribute to chronic pain and what their individual roles are.
- **Currently, there are known to be at least 150 genes associated with chronic pain in humans**, and this number is ever expanding.137,142 Amongst others, they include genes from immune, inflammatory, and stressrelated pathways, including COMT and OPRM. 143 Specific genetic variants have been identified with rare chronic pain conditions, such as SNC9A with erythromelalgia.144
- **A recent systematic review of genetic factors associated with chronic neuropathic pain** found that variants in HLA genes, COMT, OPRM1, TNFA, IL6, and GCH1, were identified in more than one study.145
- At a human population level, research has failed to identify any single genetic variant that contributes substantially to the population risk of developing chronic pain; there is no 'chronic pain gene'. It is more likely that a combination of genetic variants increases the risk of developing chronic pain. However, identifying relevant genes may help to understand underlying biological mechanisms and the search for therapeutic targets.
- Gene identification from genome-wide association studies (GWAS) may offer hope, particularly as genetic data from large numbers of samples, such as the UK Biobank,146 are accessible. In one GWAS, a genetic variant on Chromosome 5 was found to be associated with chronic widespread pain in both human genome- and animal-wide association study meta-analyses.147 A more recent GWAS and meta-analysis of 158 000 individuals identified three novel genetic variants associated with chronic back pain.148

Genetics pain refs

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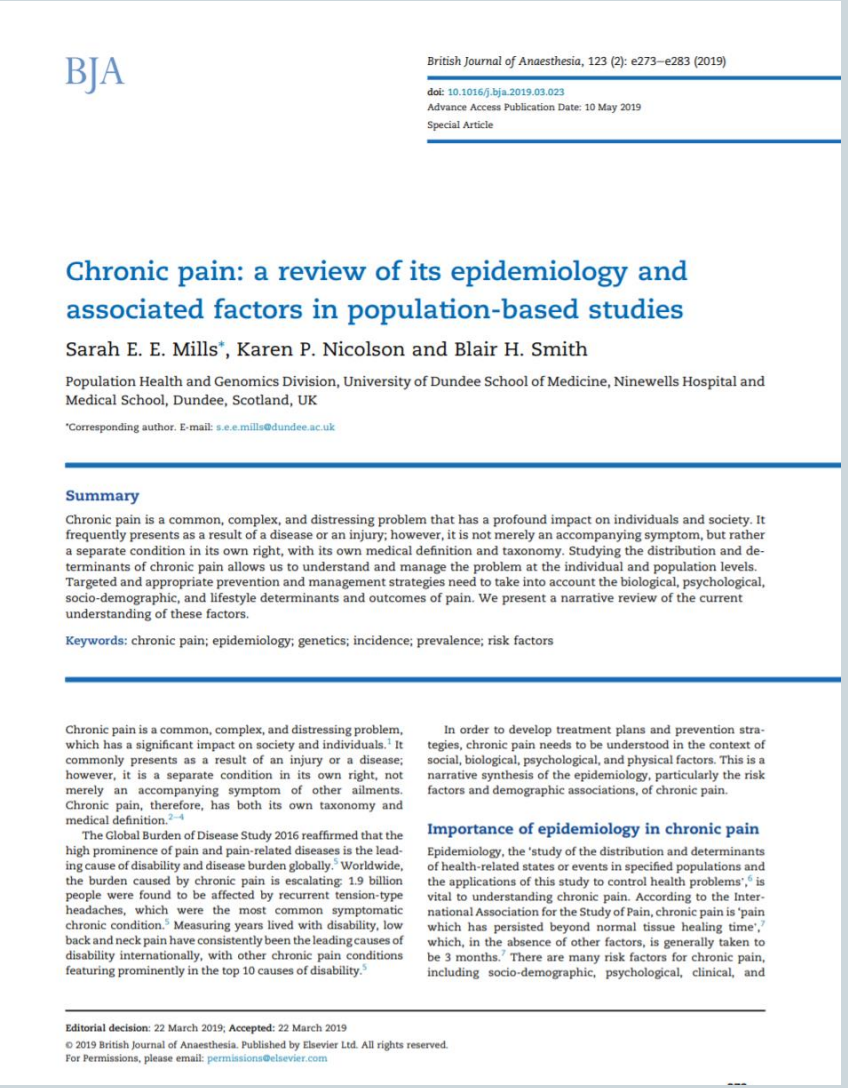

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Sarah E. E. Mills*, Karen P. Nicolson and Blair H. Smith

Population Health and Genomics Division, University of Dundee School of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland, UK

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Editorial decision: 22 March 2019; **Accepted:** 22 March 2019

Genetic basis for NePain

Neuron
Review

CellPress

The Genetics of Neuropathic Pain from Model Organisms to Clinical Application

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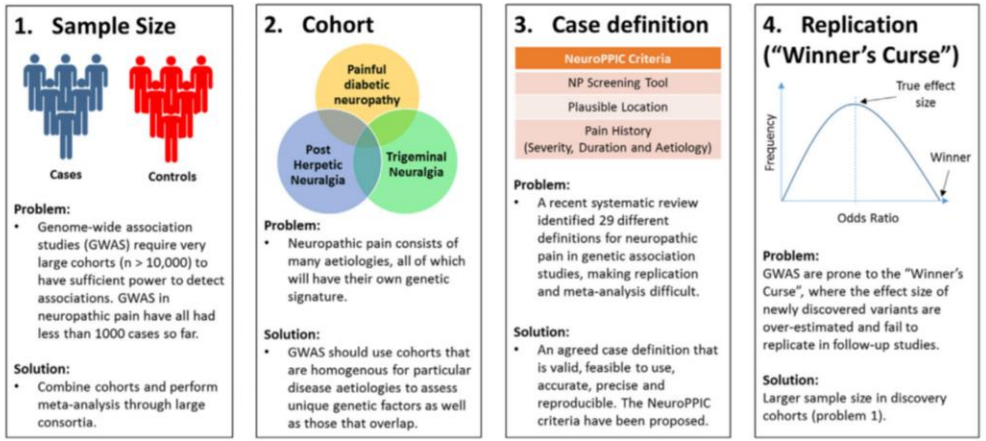
https://doi.org/10.1016/j

Neuropathic pain (N
disabling, renderin
conservation of pai



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

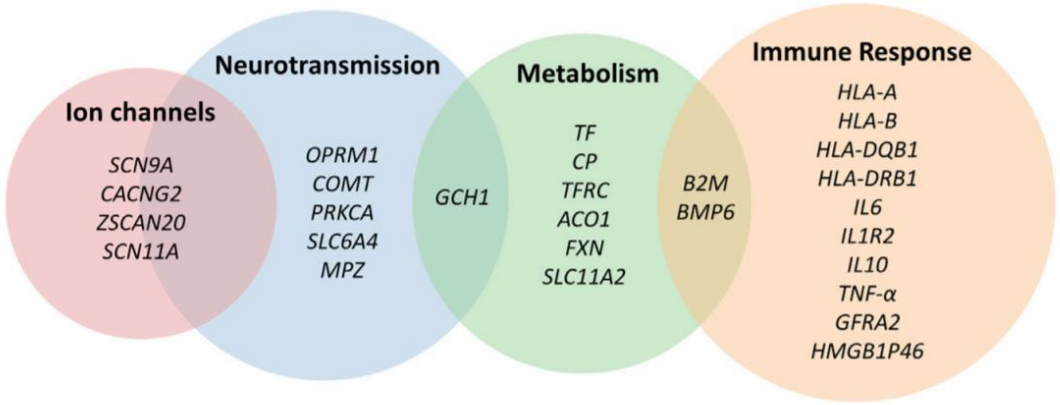


Figure 3. A Venn Diagram of Genes Reaching Study Specific or Suggestive Significance in Human Candidate Gene and Genome-wide Studies So Far in NeuP and the Overlap of Biological Pathways

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

Trends in Molecular Medicine

Log in

VIRTUAL SPECIAL ISSUE: CLINICAL NEUROSCIENCE | VOLUME 26, ISSUE 10, P924-935,
OCTOBER 01, 2020

Purchase

Resilience to Stress and Resilience to Pain: Lessons from Molecular Neurobiology and Genetics

Eric J. Nestler • Stephen G. Waxman

Published: April 18, 2020 • DOI: https://doi.org/10.1016/j.molmed.2020.03.007 •

Check for updates

Overview

AAOP 2021

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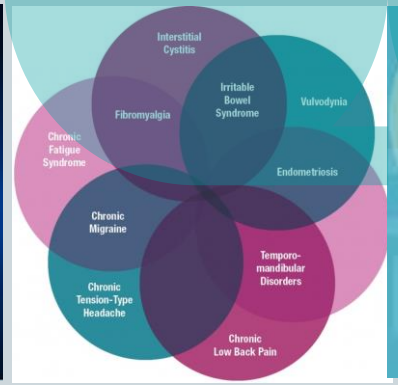
- Definitions and Diagnostic criteria
- Why is pain persistent?
- **When all else fails what treatment strategies are there?**

Before considering new treatments these factors must be revisited

Re phenotype the patient

Clinical phenotype
Age
Gender
Ethnicity
Religion
Beliefs
Misdiagnosis
Intolerance to medications
Multiple pain interventions

Address comorbid conditions



Medical Co-morbidities
CWP /FM
Sleep disorders
Smoking
Drug dependency
Vitamin C and D def
Malnutrition
DM, Hypothyroid, Autoimmune disorders
Medication overuse

AXIS II assessment and treatment

Psychological factors
Anxiety
Depression
Neuroticism
Catastrophising
Introversion
Hypervigilance
Narcissism

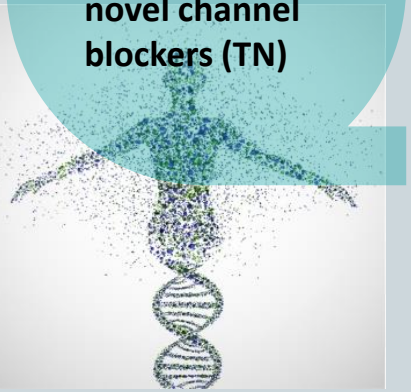
Get social support where necessary modify lifestyle factors

Social factors
Support
Culture
Education level
Income
Exercise
Obesity
Prior significant life events

Investigate other pain driving factors

Physiological
Factors
Microbiome
Endogenous pain modulation
Neural plasticity
Gray / white matter degeneration
Connectivity
Neuropathy

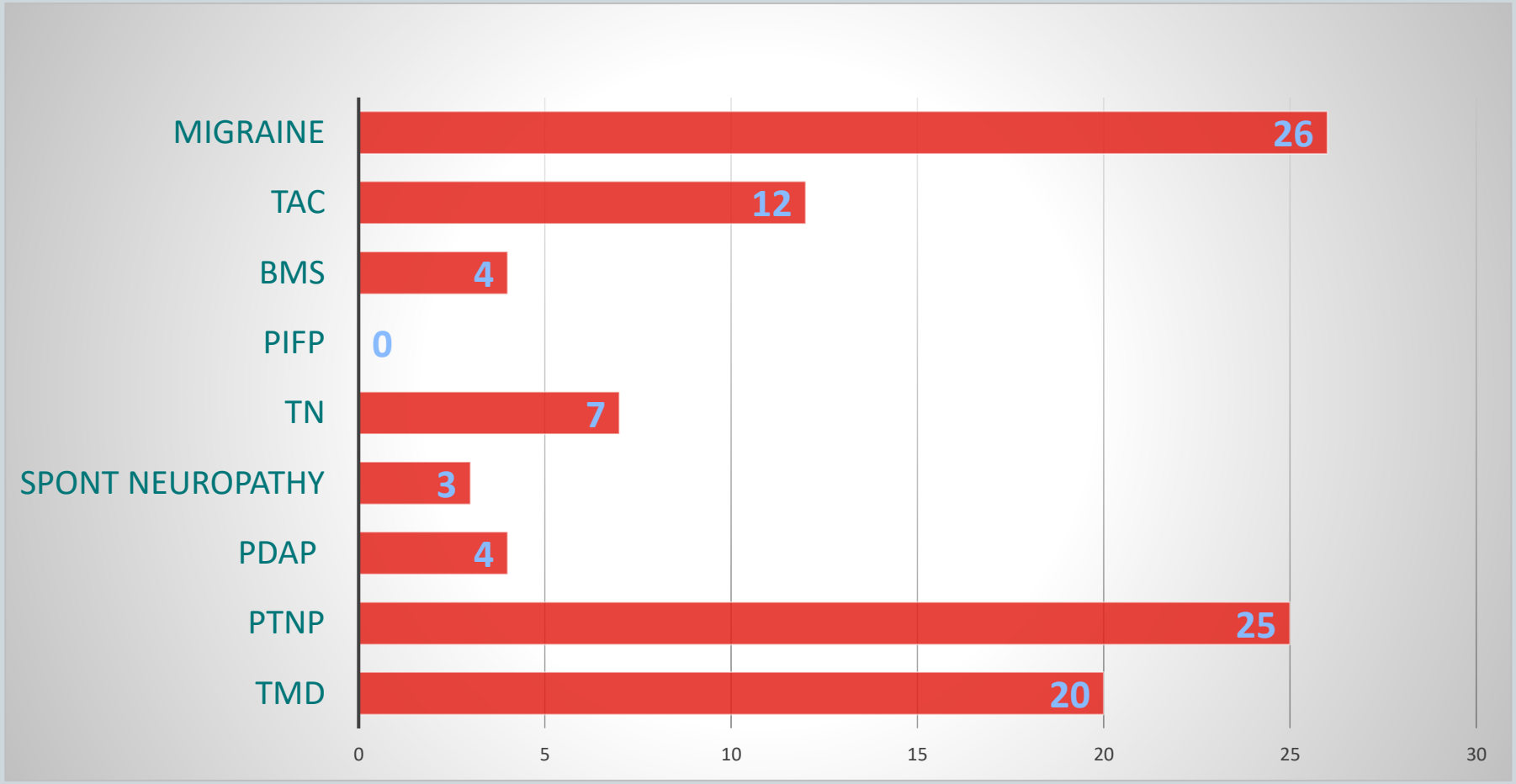
Family history? May be candidate for novel channel blockers (TN)



Genetic Profile
Ethnicity
Gender
Genome
Epigenetics

Diagnosis?
We rarely make a diagnosis of PIFP

- After re phenotyping most patients are TACS, Facial migraine OR PTNP



What treatments are there for refractory patients?

Non ablative interventions

- **Psychological interventions**
- **Alternative techniques**
- Systemic medication – IV Lidocaine, steroids, indomethacin challenge
- Therapeutic Injections /Blocks
  - Botulinum toxin dermal injections
  - LA +/- steroids
    - nerve ON, V1/2/3, Auricular temporal N
    - Ganglion SPG Gasserian
- Neurostimulation
  - Peripheral stim /Superficial sessional neurostimulation, V IX C2/3
  - Ganglia implanted neurostimulation (SPG)
  - Spinal cord stimulation
  - Pulsed radiofrequency PRF
  - Deep brain stimulation (DBS)
- Trans-magnetic stimulation motor cortex

Ablative techniques

Gasserian Ganglion interventions

- Radiofrequency ablation = Thermocoagulation
- Balloon compression
- Glycerolysis
- Alcohol
- cryotherapy

Microvascular decompression
Rhizotomy
Internal neurolysis
Stereotactic radiosurgery
Gamma knife may be indicated If there is medical contraindications to MVD

What treatments are there for refractory patients?

For all refractory patients

Non ablative interventions

- **Psychological interventions**
- **Alternative techniques**
- **Systemic medication** – IV Lidocaine, steroids, indomethacin challenge
- Therapeutic Injections /Blocks
  - Botulinum toxin dermal injections
  - LA +/- steroids
    - nerve ON, V1/2/3, Auricular temporal N
    - Ganglion SPG Gasserian
- Neurostimulation
  - Peripheral stim /Superficial sessional neurostimulation, V IX C2/3
  - Ganglia implanted neurostimulation (SPG)
  - Spinal cord stimulation
  - Pulsed radiofrequency PRF
  - Deep brain stimulation (DBS)
- Trans-magnetic stimulation motor cortex

Ablative techniques

Gasserian Ganglion interventions

- Radiofrequency ablation = Thermocoagulation
- Balloon compression
- Glycerolysis
- Alcohol
- cryotherapy

Microvascular decompression

Rhizotomy

Internal neurolysis

Stereotactic radiosurgery

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

What treatments are there for refractory patients?

Non ablative interventions

- **Psychological interventions**
- **Alternative techniques**
- Systemic medication – **IV Lidocaine**, steroids, indomethacin challenge
- **Therapeutic Injections** /Blocks

  Botulinum OR LA +/- steroids

  nerve ON, VAGUS V1/2/3, Auricular temporal N

  Ganglion SPG Gasserian
- Neurostimulation

  Peripheral stim /Superficial sessional neurostimulation, V IX C2/3

  Ganglia implanted neurostimulation (SPG)

  Spinal cord stimulation

  Pulsed radiofrequency PRF SPG

  SPG stim implant

  Deep brain stimulation (DBS)
- **Trans-magnetic stimulation motor cortex**

For patients with refractory neurovascular pain Migraines TACs

Ablative techniques

Gasserian Ganglion interventions

Radiofrequency ablation = Thermocoagulation

Balloon compression

Glycerolysis

Alcohol

Cryotherapy

Microvascular decompression

Rhizotomy

Internal neurolysis

Stereotactic radiosurgery

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

What treatments are there for refractory patients?

Non ablative interventions

- **Psychological interventions**
- **Alternative techniques**
- Systemic medication – **IV Lidocaine**, steroids, indomethacin challenge
- **Therapeutic Injections /Blocks**

  Botulinum toxin dermal injections

  LA +/- steroids

  nerve ON, V1/2/3, Auricular temporal N

  Ganglion SPG Gasserian
- **Neurostimulation**

  Peripheral stim /Superficial sessional neurostimulation, V IX C2/3

  Ganglia implanted neurostimulation (SPG)

  Spinal cord stimulation

  Pulsed radiofrequency PRF

  Deep brain stimulation (DBS)
- Trans-magnetic stimulation motor cortex

For patients with refractory neuropathic pain TN or PTNP

Ablative techniques

Gasserian Ganglion interventions

Radiofrequency ablation = Thermocoagulation

Balloon compression

Glycerolysis

Alcohol

cryotherapy

Microvascular decompression (TN ? SUNCT SUNA?)

Rhizotomy

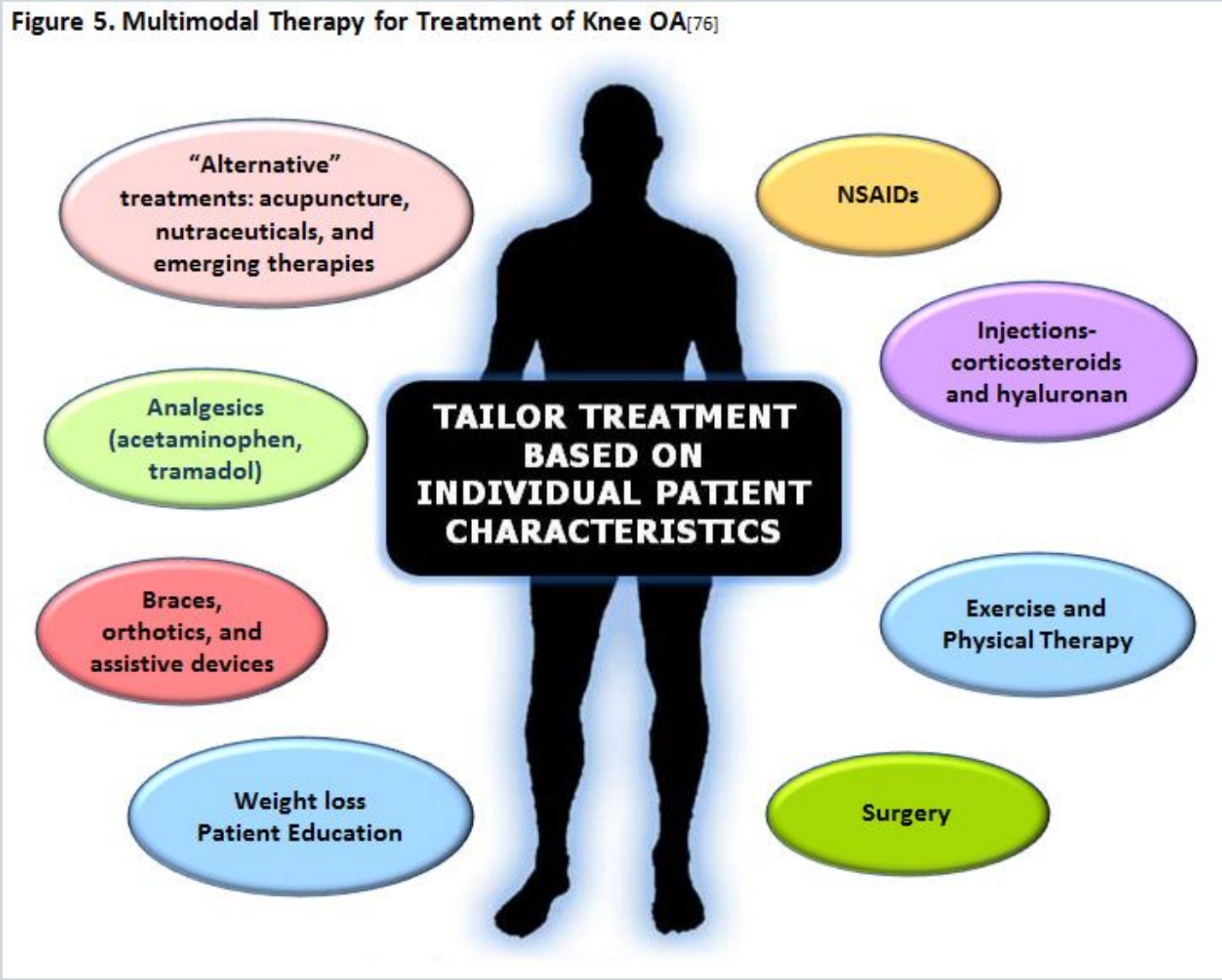
Internal neurolysis

Stereotactic radiosurgery

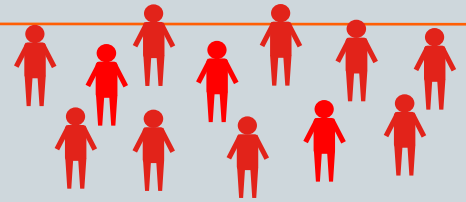
Gamma knife may be indicated If there is medical contraindications to MVD (TN)

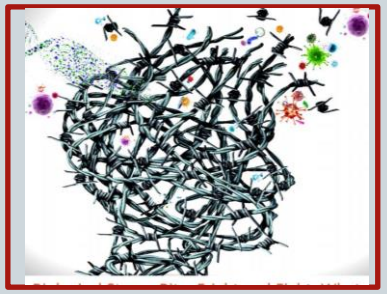
Remember we must tailor the treatment to the patient
Using a Stratified / personal approach

Figure 5. Multimodal Therapy for Treatment of Knee OA[76]



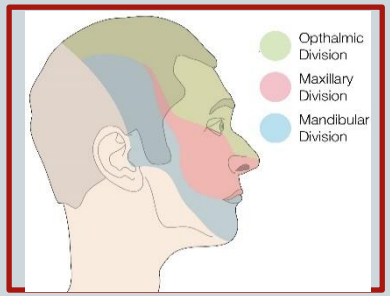
Orofacial Pain research at Kings College London
Stratification approach hoping to lead to personalised treatments



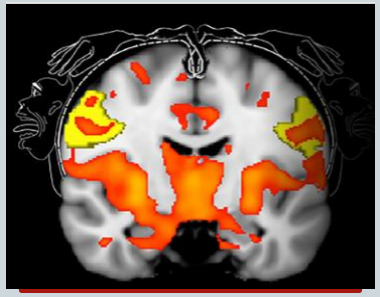


Clinical
disease or lesion, neurological deficits, family history

Psychological medical / Co-morbidities
IMPARTS system



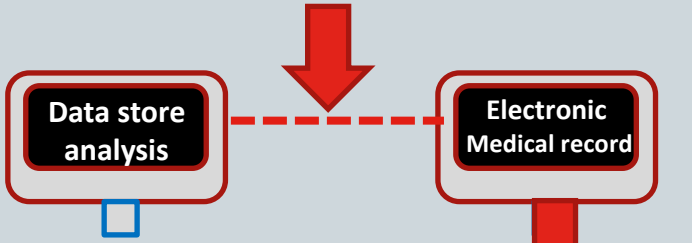
Sensory Profile
Pain quality, Qual and Quant sensory testing



Physiological
Electrophysiology
Functional imaging

Molecular Profile OMICs
Genome, proteome, metabolome

Big Data
Machine learning and Ai to improve diagnosis and clustering for treatment



678 patients sampled to date

2 datasets of over 1200 pts

Thank you

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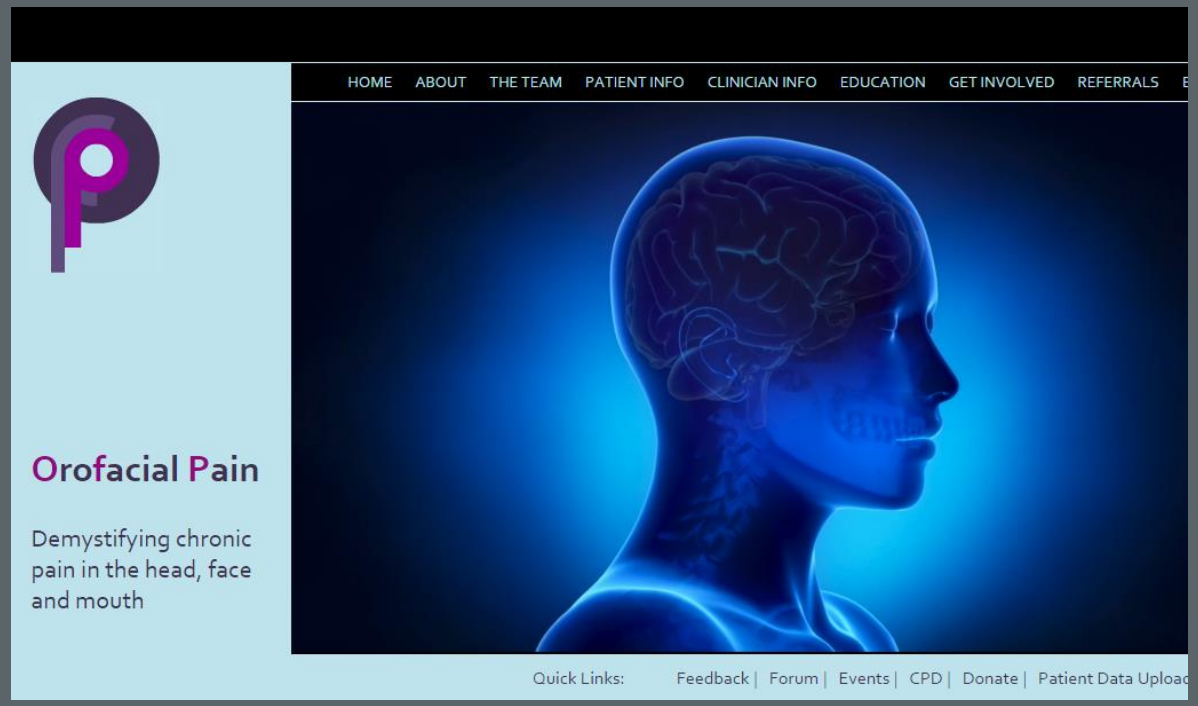
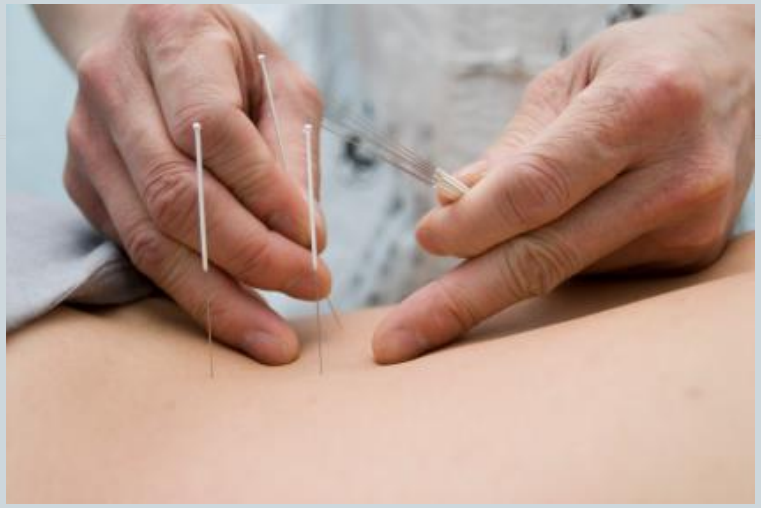


http://www.orofacialpain.org.uk

Non pharmacological methods

- Psychological
- Alternative
- Education
- Sleep

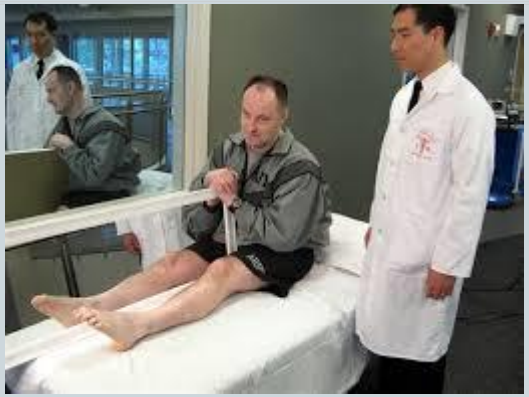


Interpersonal strategies

- Communication
  - reassurance
  - Empathy
  - understanding
- Caring
- Comfort
- Consideration
- Clinical Competence

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

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
- Tens shown to reduce the discomfort of ID blocks
- Pet therapy
- Mirror therapy

Systemic medications

Intravenous Lidocaine

Lidocaine acts by

Peripheral effects

- suppression of abnormal ectopic discharges which are generated by damaged primary afferents or dorsal root ganglion neurons.16
- suppression of mechanical allodynia17, 18 and hyperalgaesia.16

Central effects.

- suppression of polysynaptic C-fibre evoked flexor responses without evidence of conduction block at the periphery;19
- suppression of the activity of dorsal horn neurons evoked by ionophoretically administered glutamate;20
- and selective inhibition of a nociceptive response in the isolated rat spinal cord.21 Clinical studies23, 24 and human experimental models25, 26 have reached similar conclusions as to the action of intravenous lidocaine on mechanical allodynia and hyperalgaesia.
- In one study on healthy volunteers using the heat/capsaicin sensitisation model, intravenous lidocaine (5 mg/kg) was shown to have a selective effect on secondary hyperalgaesia.25

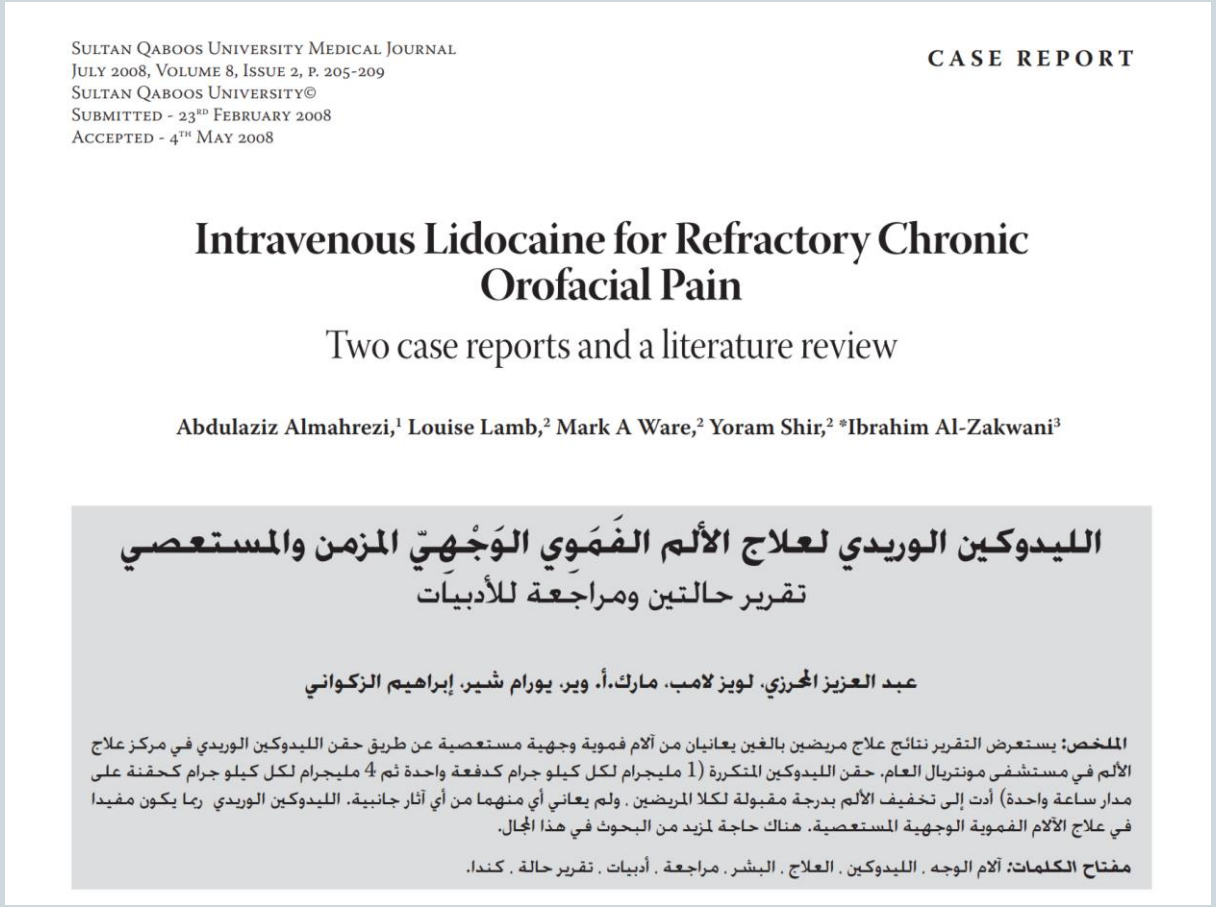
16. Abram SE, Yaksh TL. Systemic lidocaine blocks nerve injury-induced hyperalgesia and nociceptor-driven spinal sensitization in the rat. Anesthesiology 1994; 80:383-391. 17. Abdi S, Lee DH, Chung JM. The anti-allodynic effects of amitriptyline, gabapentin, and lidocaine in a rat model of neuropathic pain. Anesth Analg 1998; 87:1360-1366. 18. Chaplan SR, Bach FW, Shafer SL, Yaksh TL. Prolonged alleviation of tactile allodynia by intravenous lidocaine in neuropathic rats. Anesthesiology 1995; 83:775-785. 19. Woolf CJ, Wiesenfeld-Hallin Z. The systemic administration of local anaesthetics produces a selective depression of C-afferent fibre evoked activity in the spinal cord. Pain 1985; 23:361-374. 20. Biella G, Sotgiu ML. Central effects of systemic lidocaine mediated by glycine spinal receptors: an iontophoretic study in the rat spinal cord. Brain Res 1993; 603:201-206. 21. Jaffe RA, Rowe MA. Subanesthetic concentrations of lidocaine selectively inhibit a nociceptive response in the isolated rat spinal cord. Pain 1995; 60:167-174. 22. Wallace MS, Dyck JB, Rossi SS, Yaksh TL. Computercontrolled lidocaine infusion for the evaluation of neuropathic pain after peripheral nerve injury. Pain 1996; 66:69-77. 23. Attal N, Rouaud J, Brasseur L, Chauvin M, Bouhassira D. Systemic lidocaine in pain due to peripheral nerve injury and predictors of response. Neurology 2004; 62:218-225. 24. Wallace MS, Laitin S, Licht D, Yaksh TL. Concentration-effect relations for intravenous lidocaine infusions in human volunteers: effects on acute sensory thresholds and capsaicin-evoked hyperpathia. Anesthesiology 1997; 86:1262-1272. 25. Dirks J, Fabricius P, Petersen KL, Rowbotham MC, Dahl JB. The effect of systemic lidocaine on pain and secondary hyperalgesia associated with the heat/capsaicin sensitization model in healthy volunteers. Anesth Analg 2000; 91:967-972.

Systemic Lidocaine

2 case presentations

Orofacial pain one Myalgic TMD and one PTNP

Both had significant drop in pai during trial and continued effect for 4 months



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Submitted - 23rd February 2008
Accepted - 4th May 2008

CASE REPORT

Intravenous Lidocaine for Refractory Chronic Orofacial Pain

Two case reports and a literature review

Abdulaziz Almahrezi,[1] Louise Lamb,[2] Mark A Ware,[2] Yoram Shir,[2] *Ibrahim Al-Zakwani[3]

الليدوكين الوريدي لعلاج الألم الفَمَوي الوَجْهيّ المزمن والمستعصي

تقرير حالتين ومراجعة للأدبيات

عبد العزيز المحرزي، لويز لامب، مارك.أ. وير، يورام شير، إبراهيم الزكواني

الملخص: يستعرض التقرير نتائج علاج مريضين بالغين يعانيان من آلام فموية وجهية مستعصية عن طريق حقن الليدوكين الوريدي في مركز علاج الألم في مستشفى مونتريال العام. حقن الليدوكين المتكررة (1 مليجرام لكل كيلو جرام كدفعة واحدة ثم 4 مليجرام لكل كيلو جرام كحقنة على مدار ساعة واحدة) أدت إلى تخفيف الألم بدرجة مقبولة لكلا المريضين . ولم يعاني أي منهما من أي آثار جانبية. الليدوكين الوريدي ربما يكون مفيدا في علاج الآلام الفموية الوجهية المستعصية. هناك حاجة لمزيد من البحوث في هذا المجال.

مفتاح الكلمات: آلام الوجه . الليدوكين . العلاج . البشر . مراجعة . أدبيات . تقرير حالة . كندا.

IV Lidocaine for Cluster Headaches

- Intravenous lidocaine given for 7–10 days led to improvement in 90% of patients

OPEN ACCESS

Original research

Medical treatment of SUNCT and SUNA: a prospective open-label study including single-arm meta-analysis

Giorgio Lambru,[1] Anker Stubberud,[2,3] Khadija Rantell,[4] Susie Lagrata,[1,5] Erling Tronvik,[2,3] Manjit Singh Matharu [1,5]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/jnnp-2020-323999).

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ABSTRACT

Introduction The management of short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) remains challenging in view of the paucity of data and evidence-based treatment recommendations are missing.

Methods In this single-centre, non-randomised, prospective open-label study, we evaluated and compared the efficacy of oral and parenteral treatments for SUNCT and SUNA in a real-world setting. Additionally, single-arm meta-analyses of the available reports of SUNCT and SUNA treatments were conducted.

Results The study cohort comprised 161 patients. Most patients responded to lamotrigine (56%), followed by oxcarbazepine (46%), duloxetine (30%), carbamazepine (26%), topiramate (25%), pregabalin and gabapentin (10%). Mexiletine and lacosamide were effective in a meaningful proportion of patients but poorly tolerated. Intravenous lidocaine given for 7–10 days led to improvement in 90% of patients, whereas only 27% of patients responded to a greater occipital nerve block. No statistically significant differences in responders were observed between SUNCT and SUNA. In the meta-analysis of the pooled data, topiramate was found to be significantly more effective in SUNCT than SUNA patients. However, a higher proportion of SUNA than SUNCT was considered refractory to medications at the time of the topiramate trial, possibly explaining this isolated difference.

Conclusions We propose a treatment algorithm for SUNCT and SUNA for clinical practice. The response to sodium channel blockers indicates a therapeutic overlap with trigeminal neuralgia, suggesting that sodium channels dysfunction may be a key pathophysiological hallmark in these disorders. Furthermore, the therapeutic similarities between SUNCT and SUNA further support the hypothesis that these conditions are variants of the same disorder.

INTRODUCTION

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) are considered separate clinical entities encompassed within the trigeminal autonomic cephalalgias (TACs) group under the umbrella term 'Short-lasting unilateral neuralgiform headache attacks' (SUNHA).[1] Given the rarity of SUNCT and SUNA, there is sparse literature on their clinical presentation, underlying pathophysiological mechanisms and response to treatments. A recent prospective comparative study refined the SUNCT and SUNA clinical phenotype in a large series of patients, confirming key overlapping characteristics with other TACs but also highlighting clinical similarities with trigeminal neuralgia (TN).[2] It has been postulated that these shared clinical similarities may be driven by cross-talk between impaired functioning regions considered pivotal in the pathophysiology of TACs, such as the posterior hypothalamic area and structurally abnormal preganglionic trigeminal sensory root due to a vascular contact.[3–5] In view of the clinical and pathophysiological similarities, several treatments known to be effective in other TACs and TN have been tried in SUNCT and SUNA.[6] However, the current evidence is limited to small case series and one small randomised placebo-controlled trial, preventing robust treatment recommendations in clinical practice.[7–11]

The aim of this study was to describe the efficacy outcomes of oral and parenteral treatments used in our practice to treat a large series of SUNCT and SUNA patients. In addition, we pooled our results together with the available published data in single-arm meta-analyses to synthesise the available published data and derive a treatment algorithm.

METHODS

Study design and study population

This was a single-centre, non-randomised, prospective open-label study conducted in consecutive patients diagnosed by the headache team with SUNCT and SUNA between 2007 and 2014. Diagnosis was based on the criteria of the International Classification of Headache Disorders (ICHD-2 and ICHD-3 beta).[12 13] With publication of the ICHD-3 criteria, we subsequently ensured that all patients included in the study fulfilled these criteria.[1] When a treatment was prescribed in clinic, clinical details were collected by two of the authors (MM and GL) directly from patients at the start of the treatment, using a semistructured standardised questionnaire. The questionnaire was designed to capture: headache characteristics including attack frequency, severity and duration at baseline and at follow-up when treatment outcome was evaluated, name of

Non-ablative interventions Neuromodulation /Stimulation?

Section subtitle

Botulinum Toxin Type A (BTxA) Botulinum toxin type A for TN

- has a beneficial role in the treatment of neuropathic pain [41–46]. It has both antinociceptive and anti-inflammatory activity, the two mechanisms being dissociated. Botulinum toxin A acts at both peripheral and central sites. Peripherally, it blocks the docking of intraneuronal vesicles to the inner membrane of the nerve terminal inhibiting the release of neuropeptides and neurotransmitters. Consequently, the extracellular concentrations of acetylcholine, substance P, serotonin, calcitonin gene-related peptide (CGRP), glutamate, and proinflammatory mediators are decreased. Plasma CGRP levels decrease in TN patients who respond well to BTxA treatment, whereas non-responders show no decrease in plasma CGRP levels [41]. Centrally, botulinum toxin A acts at the spinal dorsal horn as a result of retrograde toxin transport. Microglial activation, an important component of nociception, is also attenuated [43,47]. Furthermore, BTxA inhibits sodium ion channel activity. A single case report of TN treatment by BTxA was published in 2002 [48]; since then have been a small number of studies and generally they included a relatively small number of subjects. One randomized controlled trial of 40 subjects in whom structural lesions were excluded showed significant benefit [49]. BTxA was administered in the area of pain by means of both subcutaneous and submucosal injections. The major adverse effect was transient facial weakness. Two systematic reviews and meta-analyses of the efficacy and safety of BTxA treatment of TN were published in 2016 [50,51], citing the same four randomized controlled trials with a total of 178 patients. Ninety-nine patients received BTxA and 79 received placebo treatment. There was no standardized dosage or method of injection, the doses of onabotulinumtoxin A ranging from 25 to 100 units. Injections were generally administered either subcutaneously or intradermally in the region of clinically evident pain. The intensity of pain and the frequency of attacks were both significantly lower with BTxA compared to placebo, the benefit lasting 3 months. Transient facial asymmetry and edema were the two main adverse effects and were said to be well tolerated. A non-randomized, uncontrolled, unblinded study of 27 subjects evaluated the effect of BTxA over 6 months. BTxA was injected about the mandibular branch of the trigeminal nerve, around the pterygopalatine ganglion and the maxillary branch of the trigeminal nerve near the trigeminal ganglion. A total of 63% of subjects had a greater than 50% reduction in pain after the first week, 74.1% achieved that after the second month, and 88.9% at the end of 6 months. 15/27 subjects required a second injection approximately 2 months after the initial injection, and 7/15 required a third injection at a mean of 87 days. 44% were pain-free at 6 months. There was a similar decrease in frequency of attacks per day from a baseline of 217.7 +/− 331.5 to 55.15 +/− 196.3 at the sixth month. Adverse effects were infrequent, with one patient experiencing facial weakness that cleared by the second month, and two patients experiencing ipsilateral masseter muscle weakness that was permanent but mild [52]. An open-label study of the effect of BTxA injection of the sphenopalatine ganglion in 10 subjects with maxillary (second division) TN showed a decrease in pain at 4 weeks from a VAS score of 8.1 +/− 1.0 to 1.9 +/− 1.4 and a decrease in the daily attack frequency from 19.4 +/− 8.8 to 4.9 +/− 5.4 [53]. Another pilot study of BTxA injected in the sphenopalatine ganglion region in 10 subjects showed similar results [54]. There were four responders with at least a 50% reduction in attack frequency among the nine subjects completing the trial. Pain intensity in the responders decreased from a mean of 5.8 +/− 2.1 to 3.65 +/− 3. Adverse effects were mild and transient, although one patient had diplopia that lasted 1 month. The authors reported that all subjects had involvement of the maxillary division of the trigeminal nerve, that 9 of the original 10 subjects also had involvement of the mandibular division, and 7/10 also had involvement of the ophthalmic division. Int. J. Environ. Res. Public Health 2020, 17, 7012 8 of 20 This is unusual, as TN most commonly affects primarily just one division, raising the issue that the patients may have been misdiagnosed. It is possible that the difference in presentation from classic TN accounted for the relatively few subjects who were responders [54]. We can conclude that BTxA offers an effective form of treatment for those individuals for whom oral medication such as oxcarbazepine has failed or for whom interventional therapies such as peripheral nerve ablations or microvascular decompression are not suitable.

SPG

- sphenopalatine ganglion is a promising target for treating cluster headache using blocks, radiofrequency ablation and neurostimulation. Sphenopalatine ganglion block also has some evidence supporting its use in a few other conditions. However, most of the controlled studies were small and without replications. Further controlled studies are warranted to replicate and expand on these previous findings

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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 and neurostimulation for cluster headache. Sphenopalatine ganglion block also has evidence in treating trigeminal neuralgia, migraines, reducing the needs of analgesics after endoscopic sinus surgery and reducing pain associated with nasal packing removal after nasal operations.

Conclusions: Overall, sphenopalatine ganglion is a promising target for treating cluster headache using blocks, radiofrequency ablation and neurostimulation. Sphenopalatine ganglion block also has some evidence supporting its use in a few other conditions. However, most of the controlled studies were small and without replications. Further controlled studies are warranted to replicate and expand on these previous findings.

Keywords: Sphenopalatine ganglion, Block, Radiofrequency ablation, Neurostimulation, Nerve stimulation, Neuromodulation

Sphenopalatine block

Table 4. Treatments for PIFP. The following treatments are used or have been proposed for use in treating PIFP. Unfortunately, none have sufficient evidence available to make an evidenced-based recommendation for treatment.

Tricyclic Antidepressants
(amitriptlyline)
Serotonin norepinephrine reuptake inhibitors
(duloxetine)
(venlefaxine)
Antiepileptics (i.e., lamotrigine)
Cannabinoids
Low-level laser
Cognitive behavioral therapy
Temporomandibular joint dysfunction and gnathic dysfunction
Sphenopalatine ganglion block

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MDPI

Review

Chronic Facial Pain: Trigeminal Neuralgia, Persistent Idiopathic Facial Pain, and Myofascial Pain Syndrome—An Evidence-Based Narrative Review and Etiological Hypothesis

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check for updates

Abstract: Trigeminal neuralgia (TN), the most common form of severe facial pain, may be confused with an ill-defined persistent idiopathic facial pain (PIFP). Facial pain is reviewed and a detailed discussion of TN and PIFP is presented. A possible cause for PIFP is proposed. (1) Methods: Databases were searched for articles related to facial pain, TN, and PIFP. Relevant articles were selected, and all systematic reviews and meta-analyses were included. (2) Discussion: The lifetime prevalence for TN is approximately 0.3% and for PIFP approximately 0.03%. TN is 15–20 times more common in persons with multiple sclerosis. Most cases of TN are caused by neurovascular compression, but a significant number are secondary to inflammation, tumor or trauma. The cause of PIFP remains unknown. Well-established TN treatment protocols include pharmacotherapy, neurotoxin denervation, peripheral nerve ablation, focused radiation, and microvascular decompression, with high rates of relief and varying degrees of adverse outcomes. No such protocols exist for PIFP. (3) Conclusion: PIFP may be confused with TN, but treatment possibilities differ greatly. Head and neck muscle myofascial pain syndrome is suggested as a possible cause of PIFP, a consideration that could open new approaches to treatment.

Keywords: chronic facial pain; trigeminal neuralgia; persistent idiopathic facial pain; myofascial pain syndrome

Peripheral stimulation

- Though there are no randomized trials, peripheral neuromodulation has been shown to be an effective means of treating TNP refractory to medical management in a growing number of case series.
- 3 cases of PTNP There was an overall 87% reduction of pain at 2 years

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Peripheral Nerve Stimulation for Trigeminal Neuropathic Pain

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Abstract

Facial pain is a complex disease with a number of possible etiologies. Trigeminal neuropathic pain (TNP) is defined as pain caused by a lesion or disease of the trigeminal branch of the peripheral nervous system resulting in chronic facial pain over the distribution of the injured nerve. First line treatment of TNP includes management with anticonvulsant medication (carbamazepine, phenytoin, gabapentin, etc.), baclofen, and analgesics. TNP, however, can be a condition difficult to adequately treat with medical management alone.

Patients with TNP can suffer from significant morbidity as a result of inadequate treatment or the side effects of pharmacologic therapy. TNP refractory to medical management can be considered for treatment with a growing number of invasive procedures. Peripheral nerve stimulation (PNS) is a minimally invasive option that has been shown to effectively treat medically intractable TNP.

We present a case series of common causes of TNP successfully treated with PNS with up to a 2 year follow-up. Only one patient required implantation of new electrode leads secondary to electrode migration. The patients in this case series continue to have significant symptomatic relief, demonstrating PNS as an effective treatment option for intractable TNP.

Though there are no randomized trials, peripheral neuromodulation has been shown to be an effective means of treating TNP refractory to medical management in a growing number of case series. PNS is a safe procedure that can be performed even on patients that are not optimal surgical candidates and should be considered for patients suffering from TNP that have failed medical management.

Keywords

Trigeminal neuropathic pain; peripheral nerve stimulation; neuromodulation; intractable pain; facial trauma; postherpetic neuralgia

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Disclaimer: Emil Annabi, MD is a Consultant for Medtronic.

Conflict of interest: None.

Peripheral Stimulation TN

TABLE 1
Chronological assessment of patient's analgesic progress ba

Evaluation	Pain at evaluation*
Before implantation	7
One week after trial implantation	3
One week after generator implantation	3
One month after generator implantation	3–4
Six months after generator implantation	3–4

**All pain scores based on a visual analogue scale (scored from 0 to 10)*

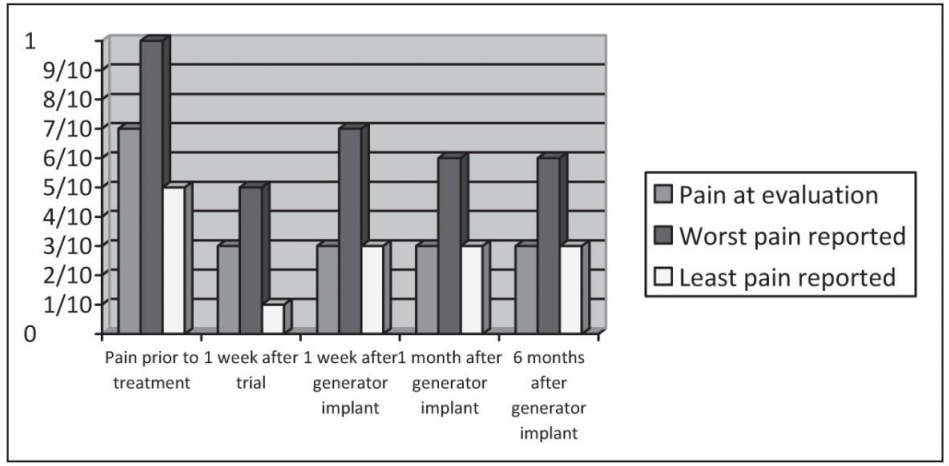

Figure 1) *Chronological assessment of the patient's analgesic progress based on visual analogue scale scores*

CASE REPORT

Peripheral neuromodulation for the treatment of refractory trigeminal neuralgia

Naum Shaparin MD, Karina Gritsenko MD, Diego Fernandez Garcia-Roves MD, Ushma Shah MD, Todd Schultz MD, Oscar DeLeon-Casasola MD

N Shaparin, K Gritsenko, DF Garcia-Roves, U Shah, T Schultz, O DeLeon-Casasola. Peripheral neuromodulation for the treatment of refractory trigeminal neuralgia. Pain Res Manag 2015;20(2):63-66.

Trigeminal neuralgia is a type of orofacial pain that is diagnosed in 150,000 individuals each year, with an incidence of 12.6 per 100,000 person-years and a prevalence of 155 cases per 1,000,000 in the United States. Trigeminal neuralgia pain is characterized by sudden, severe, brief, stabbing or lancinating, recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve, which can cause significant suffering for the affected patient population.

In many patients, a combination of medication and interventional treatments can be therapeutic, but is not always successful. Peripheral nerve stimulation has gained popularity as a simple and effective neuromodulation technique for the treatment of many pain conditions, including chronic headache disorders. Specifically in trigeminal neuralgia, neurostimulation of the supraorbital and infraorbital nerves may serve to provide relief of neuropathic pain by targeting the distal nerves that supply sensation to the areas of the face where the pain attacks occur, producing a field of paresthesia within the peripheral distribution of pain through the creation of an electric field in the vicinity of the leads.

The purpose of the present case report is to introduce a new, less-invasive interventional technique, and to describe the authors' first experience with supraorbital and infraorbital neurostimulation therapy for the treatment of trigeminal neuralgia in a patient who had failed previous conservative management.

Key Words: *Peripheral neuromodulation; Trigeminal neuralgia*

La neuromodulation périphérique pour traiter la névralgie réfractaire du trijumeau

La névralgie du trijumeau est un type de douleur buccofaciale diagnostiquée chez 150 000 personnes chaque année, pour une incidence de 12,6 cas sur 100 000 personnes-année et une prévalence de 155 cas sur 1 000 000 habitants des États-Unis. La névralgie du trijumeau se caractérise par des douleurs aiguës violentes, brèves et soudaines ou par des épisodes récurrents de douleurs lancinantes le long d'au moins une ramification du nerf trijumeau, ce qui provoque des souffrances importantes pour la population de patients touchée.

Chez de nombreux patients, une association de médicaments et de traitements d'intervention peut se révéler thérapeutique, mais pas toujours. La stimulation des nerfs périphériques a gagné en popularité, car c'est une technique de neurostimulation simple et efficace pour traiter de nombreuses douleurs, y compris les céphalées chroniques. Dans le cas de la névralgie du trijumeau, la neurostimulation des nerfs sus-orbitaire et infra-orbitaire pourrait soulager la douleur neuropathique en ciblant les nerfs distaux qui transmettent la sensation dans les régions du visage où les crises de douleur se manifestent et qui produisent un champ de paresthésie dans la distribution périphérique de la douleur grâce à la création d'un champ électrique à proximité des dérivations.

Le présent rapport de cas vise à présenter une nouvelle technique d'intervention moins effractive et à décrire la première expérience des auteurs avec la thérapie par neurostimulation sus-orbitaire et infra-orbitaire pour traiter la névralgie du trijumeau chez un patient réfractaire à un traitement prudent.

Trigeminal neuralgia (TN) is characterized by sudden, severe, brief, stabbing or lancinating, recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve (1). According to the American Association of Neurological Surgeons, TN is diagnosed in 150,000 individuals each year; the incidence is 12.6 per 100,000 person-years and the prevalence is 155 cases per 1,000,000 in United States, with female sex and age >50 years being two common risk factors (2). The clinical course of TN is variable, with recurrence being common and some patients experiencing continuous pain.

There are several classifications systems for TN relating to specific causes. As per the International Headache Society (*International Classification of Headache Disorders – Beta*, 2013) and the American Academy of Orofacial Pain (2013), orofacial pain can be classified as classical TN or painful trigeminal neuropathy. Classical TN can be purely paroxysmal or with concomitant persistent facial pain. Painful trigeminal neuropathy can be caused by acute herpes zoster, postherpetic, post-traumatic, multiple sclerosis-related or attributed to space-occupying lesions (3). The present discussion will focus specifically on classical TN, which can develop without apparent cause other than neurovascular compression. According to the *International Classification of Headache Disorders, 3rd edition* (3), the following criteria must be met for diagnosis:

1. At least three attacks of unilateral facial pain fulfilling criteria 2 and 3;
2. Occurring in one or more divisions of the trigeminal nerve, with no radiation beyond the trigeminal distribution;
3. Pain has at least three of the following four characteristics:
   a) recurring in paroxysmal attacks lasting from a fraction of a second to 2 min;
   b) severe intensity;
   c) electric shock-like, shooting, stabbing or sharp in quality;
   d) precipitated by innocuous stimuli to the affected side of the face.
4. No clinically evident neurological deficit;
5. Not better accounted for by another *International Classification of Headache Disorders, 3rd edition*, diagnosis (2).

As mentioned, classical TN can be further characterized as purely paroxysmal, which is usually initially responsive to pharmacotherapy, or classical TN with concomitant persistent facial pain, which fulfills the diagnostic criteria of classical TN along with persistent facial pain of moderate intensity in the affected region. The latter has shown poor response to medical treatment.

From etiological and pathophysiological viewpoints, TN is either idiopathic or symptomatic; ie, patients with typical 'tic douloureux' but

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Peripheral stim

Indications

- The four most common indications for peripheral nerve stimulation applicable to the craniofacial region that have been described in the literature are

    postherpetic neuralgia involving the territory of the trigeminal nerve (20,21),

    post-traumatic or postsurgical neuropathic pain that is related to an underlying dysfunction of the infraorbital, supraorbital (22) or occipital nerve,

    ‘transformed migraine’ presenting with occipital pain and discomfort

    occipital neuralgia or cervicogenic occipital pain (23).

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- Good evidence for intractable chronic headaches.

    posterior hypothalamic deep brain stimulation with implantation of brain electrodes with the aim of inhibiting hyperactive neurons has been used to treat the central modality of chronic headaches, such as cluster headaches and short-lasting unilateral neuralgiform headache with conjunctival injection and tearing, with effective relief (10,11).

    Current therapies to target peripheral nerves include occipital nerve stimulation with the use of implanted pulse generators for the treatment of occipital neuralgia and other facial painful syndromes (12,13), as well as vagal nerve stimulation for the treatment of migraine attacks (14).

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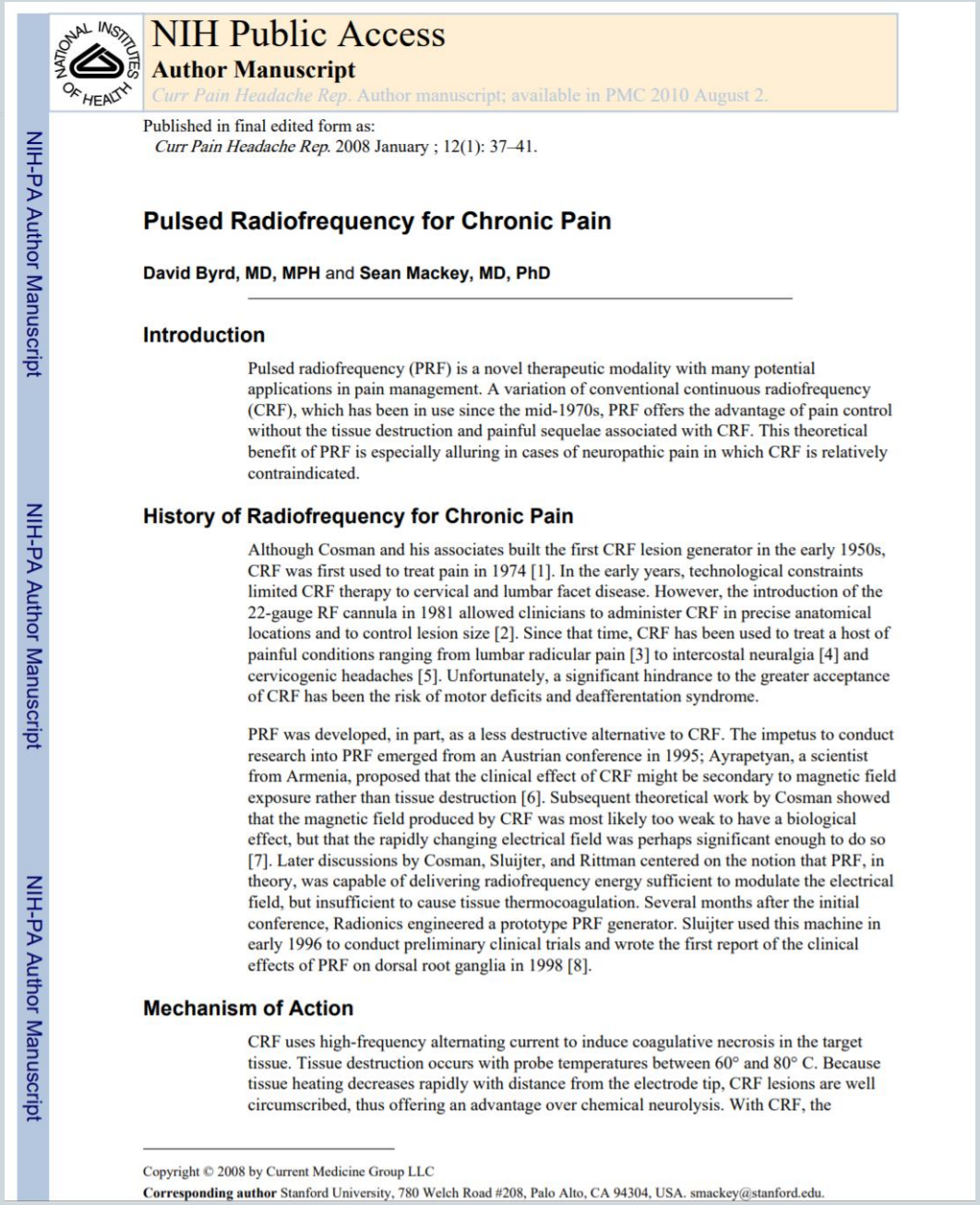
Pulsed radiofrequency of V

- InPRF uses radiofrequency current in short (20 ms), high-voltage bursts; the “silent” phase (480 ms) of PRF allows time for heat elimination, generally keeping the target tissue below 42° C.
- Although conventional theory espouses the notion that PRF does not cause thermal lesions, Cosman and Cosman demonstrated that even PRF can produce bursts of heat within the range requisite for tissue destruction.
- The possibility of tissue destruction with PRF is substantiated by in vitro egg white studies using PRF electrodes at 60° C or higher [10]. However, histopathologic work in rat dorsal root ganglia and sciatic nerves using PRF electrodes at 42° C has shown that PRF causes only transient endoneurial edema; this in contrast with the wallerian degeneration effected by CRF at 80° C [11]. Similar studies in rabbit dorsal root ganglia corroborate the notion that PRF is orders of magnitude less disruptive of cellular morphology than CRF [12]. Therefore, it appears that any thermal damage from PRF is minimal and not the manner by which PRF exerts its clinical effect. Pulsed radiofrequency (PRF), a technology related to continuous radiofrequency, is unique in that it provides pain relief without causing significant damage to nervous tissue. The mechanism by which PRF controls pain is unclear, but it may involve a temperature-independent pathway mediated by a rapidly changing electrical field. Although much anecdotal evidence exists in favor of PRF, there are few quality studies substantiating its utility

PRF of V for refractory OFP

- Van Zundert et al. [22] reported results from their study of five patients with idiopathic trigeminal neuralgia treated with PRF at 42° C for 120 seconds. Three of five patients demonstrated complete pain relief at long-term follow-up, ranging from 10 to 20 months. One patient had 90% pain relief at 22 months. The final patient indicated 75% pain relief at 1 month but eventually elected to undergo microvascular decompression.

- Navani et al. [23] reported a single case of PRF of the greater occipital nerve for treatment of occipital neuralgia. The patient, a 62-year-old woman, had a 42-year history of left suboccipital pain. After a positive response to two diagnostic blocks, three rounds of PRF at 42° C for 120 seconds were performed on the medial branches of the C1 and C2 dorsal rami. At a 4-month follow-up, the patient had 60% to 70% pain relief and elected to undergo further PRF, which provided an additional 5 months of relief.



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Pulsed Radiofrequency for Chronic Pain

David Byrd, MD, MPH and **Sean Mackey, MD, PhD**

Introduction

Pulsed radiofrequency (PRF) is a novel therapeutic modality with many potential applications in pain management. A variation of conventional continuous radiofrequency (CRF), which has been in use since the mid-1970s, PRF offers the advantage of pain control without the tissue destruction and painful sequelae associated with CRF. This theoretical benefit of PRF is especially alluring in cases of neuropathic pain in which CRF is relatively contraindicated.

History of Radiofrequency for Chronic Pain

Although Cosman and his associates built the first CRF lesion generator in the early 1950s, CRF was first used to treat pain in 1974 [1]. In the early years, technological constraints limited CRF therapy to cervical and lumbar facet disease. However, the introduction of the 22-gauge RF cannula in 1981 allowed clinicians to administer CRF in precise anatomical locations and to control lesion size [2]. Since that time, CRF has been used to treat a host of painful conditions ranging from lumbar radicular pain [3] to intercostal neuralgia [4] and cervicogenic headaches [5]. Unfortunately, a significant hindrance to the greater acceptance of CRF has been the risk of motor deficits and deafferentation syndrome.

PRF was developed, in part, as a less destructive alternative to CRF. The impetus to conduct research into PRF emerged from an Austrian conference in 1995; Ayrapetyan, a scientist from Armenia, proposed that the clinical effect of CRF might be secondary to magnetic field exposure rather than tissue destruction [6]. Subsequent theoretical work by Cosman showed that the magnetic field produced by CRF was most likely too weak to have a biological effect, but that the rapidly changing electrical field was perhaps significant enough to do so [7]. Later discussions by Cosman, Sluijter, and Rittman centered on the notion that PRF, in theory, was capable of delivering radiofrequency energy sufficient to modulate the electrical field, but insufficient to cause tissue thermocoagulation. Several months after the initial conference, Radionics engineered a prototype PRF generator. Sluijter used this machine in early 1996 to conduct preliminary clinical trials and wrote the first report of the clinical effects of PRF on dorsal root ganglia in 1998 [8].

Mechanism of Action

CRF uses high-frequency alternating current to induce coagulative necrosis in the target tissue. Tissue destruction occurs with probe temperatures between 60° and 80° C. Because tissue heating decreases rapidly with distance from the electrode tip, CRF lesions are well circumscribed, thus offering an advantage over chemical neurolysis. With CRF, the

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PRF of sphenopalatine ganglion

- some have suggested pulsed radiofrequency treatment of the sphenopalatine ganglion (127), but this is based on an open trial in a small number of patients and there is no high level evidence for this or any other neurosurgical type of intervention (128,129). We do not recommend invasive procedures, as these always carry the risk for inducing a traumatic neuropathy and therefore may end up increasing pain.

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Spinal stimulation

- The high frequency cerico medullary junction stimulation (C3-4 and later C1-2) completely eliminated the electric shocks like pain component, but it also unmasked a background dull pain during the 3 months of follow up. This type of pain was treated with the addition of pregabalin (250mg/day) to HFSCS and CMM. This combination led to a complete pain relief (Table 2).

left and right side (in distinct sessions, approximately 2 cm apart

Table 2

Outcomes measured at baseline, 1 and 3 months after HFSCS.

Outcomes measured	Baseline	1 month follow up	3 months follow up
NRS	10	0	0
Drug intake			
Anticonvulsant drugs	Yes	Yes	Yes
Antidepressants	Yes	Yes	Yes
Opioids	No	No	No

Table 3

Neuropsychological test results (MIDI) at baseline, 1 and 3 months after HFSCS.

Pain interferes (0 = no; 1 = sometimes; 2 = often/always) with	Baseline	1 month follow up	3 months follow up
Working activities	2	1	1
Social and interpersonal relationships	2	1	1
Affective relationships	2	1	1
Pain prevents you from sleeping	Yes	No	No
Notes of anxiety	Yes	Yes	Yes
Notes of depression	Yes	Yes	No

Clinical Case Report

Medicine

OPEN

Effectiveness of high-frequency cervical spinal cord stimulation in the treatment of refractory trigeminal neuropathy

A case report

Daniela Floridia, MD, Francesco Cerra, MD, Francesco Corallo, PSY*, Marcella Di Cara, PSY, Salvatore Spartà, MD, Giovanni Nania, MD, Alessia Bramanti, PhD, Placido Bramanti, MD, Antonino Naro, MD

Abstract

Rationale: Treatment of chronic neuropathic pain in the head and face regions presents a challenge for pain specialists due to the lack of reliable medical and surgical approaches.

Patient concerns: A 62-year-old patient came to our attention for an intense facial pain secondary to a lesion of the right trigeminal nerve (all branches) due to a petroclival meningioma.

Diagnoses: The patient also presented with gait impairment as well as a deficit of the right facial, auditory, trochlear and abducens cranial nerves.

Interventions: Conventional medical management (CMM) as well as tonic SCS were already adopted but they all dramatically failed. We intervened with the use of high-frequency (10 kHz) spinal cord stimulation (HFSCS) at the cervicomedullary junction (CMJ). The patient was thus provided with HFSCS at the CMJ. Pain and quality of life (QoL) were assessed 1 and 3 months after implantation. We also tested the trigeminal-facial reflex responses.

Outcomes: HFSCS led to a full relief from the debilitating electric shocks like pain in the right hemiface, even though a background dull pain appeared. The gradual addition of pregabalin helped in fully relieving the painful symptomatology, with a significant improvement in QoL. Moreover, sensitivity amelioration on the inner portion of the mouth allowed the patient to start feeding again also using that side of the mouth. These findings were paralleled by a significant reshape of trigeminal-facial reflex responses suggesting an inhibition of nociceptive sensory inputs at brainstem level following HFSCS.

Lessons: This is the first report suggesting the usefulness of HFSCS at the CMJ in neuropathic pain due to trigeminal nerve neuropathy non-responsive to tonic SCS and CMM.

Abbreviations: BR = blink reflex, CMJ = cervicomedullary junction, HFSCS = high-frequency spinal cord stimulation, IPG = implantable pulse generator, LTMR = low-threshold mechanoreceptor, MRI = Magnetic Resonance Imaging, ms = milliseconds, nBR = nociceptive BR, PHN = post-herpetic neuralgia, SCS = spinal cord stimulation, sec = seconds, SpC = caudal spinal nucleus, SSEP = somatosensory evoked potential, TC = Computerized Tomography, TG = trigeminal ganglion, TMJ = temporo-mandibular joint.

Keywords: cervicomedullary junction, debilitating pain, quality of life, spinal cord stimulation, trigeminal nerve neuropathy

Introduction

Chronic pain is a debilitating condition for millions of people worldwide. Such form of pain can be due to different medical conditions, including peripheral nerve disorders (such as complex regional pain syndrome) and primary pain disorders (e.g., neuropathic pain and fibromyalgia).

Editor: Maya Saranathan.

Ethical approval of the Ethics Committee was not necessary.

Informed written consent was obtained from the patient for publication of this case report and accompanying images.

The authors declare that they have no conflicts of interest, including financial, consultant, institutional, and other and other relationships.

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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Brain Stimulation

Cochrane Library

Cochrane Database of Systematic Reviews

Non-invasive brain stimulation techniques for chronic

O'Connell NE, Marston L, Spencer S, DeSouza LH, Wand BM

Cochrane Trusted evidence.

Patient or population: adults with chronic pain

Settings: laboratory/ clinic

Intervention: active rTMS

Comparison: sham rTMS

Outcomes	Effect size	Relative and absolute effect (average % improvement (reduction) in pain (95% CIs) in relation to post-treatment score from sham group)* *Where 95%CIs do not cross the line of no effect.	No of participants (studies)	Quality of the evidence (GRADE)
Pain intensity (0 to < 1 week postintervention) measured using visual analogue scales or numerical rating scales	SMD -0.22 (-0.29 to -0.16)	This equates to a 7% (95% CI 5% to 9%) reduction in pain intensity, or a 0.40 (95% CI 0.53 to 0.32) point reduction on a 0 to 10 pain intensity scale.	655 (27)	⊕⊕⊖⊖ **low**[1]
Disability (0 to < 1 week postintervention) measured using self-reported disability/pain interference scales	SMD -0.29, 95% CI -0.87 to 0.29	-	119 (5)	⊕⊖⊖⊖ **very low**[2]
Quality of life (0 to < 1 week postintervention) measured using Fibromyalgia Impact Questionnaire	MD -10.80, 95% CI -15.04 to -6.55	-	105 (4)	⊕⊕⊖⊖ **low**[3]

CI: confidence interval; **MD**: mean difference; **rTMS**: repetitive transcranial magnetic stimulation; **SMD**: standardised mean difference

GRADE Working Group grades of evidence

High quality: we are very confident that the true effect lies close to that of the estimate of the effect;

Moderate quality: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different;

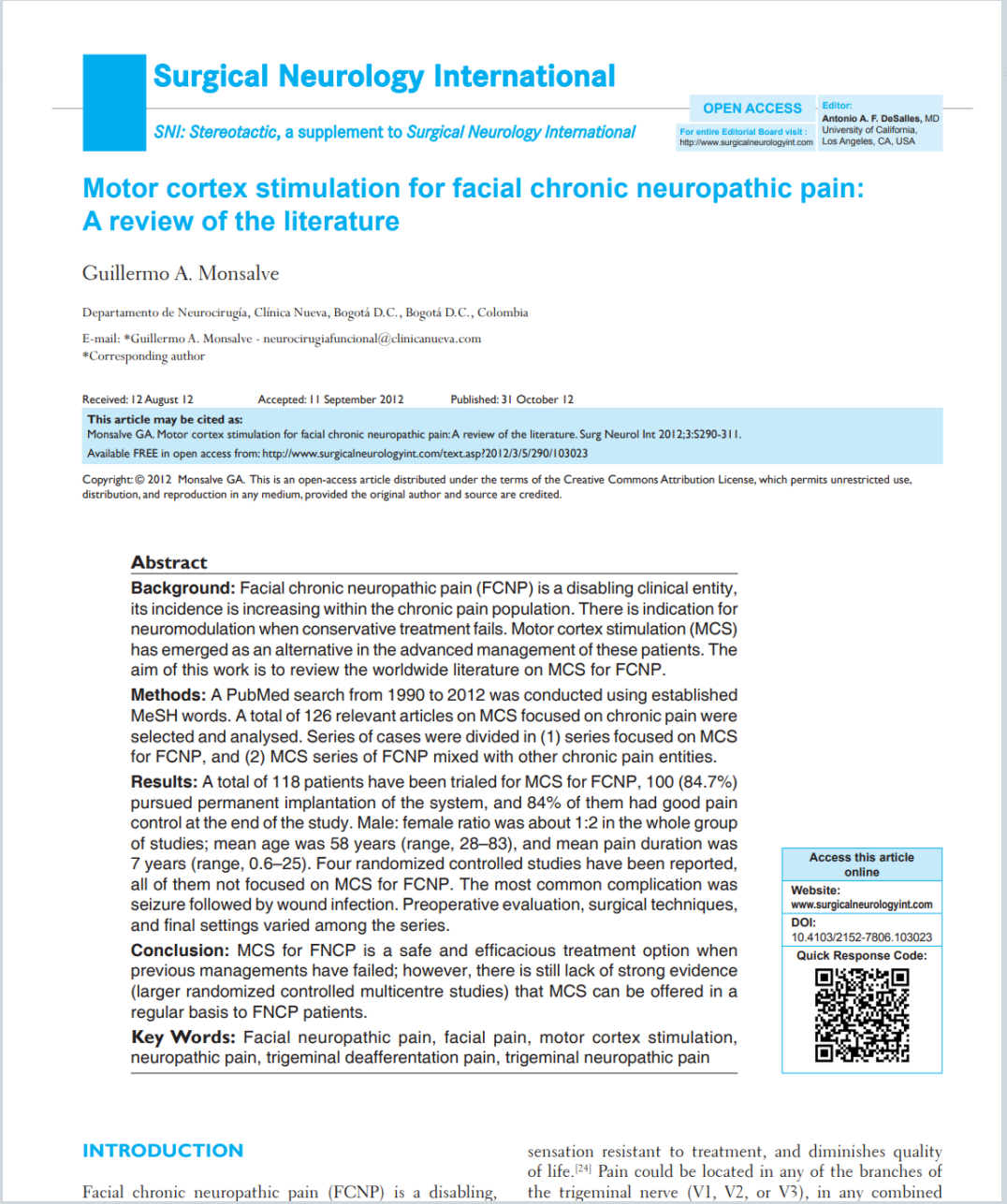
Low quality: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect;

Very low quality: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

MCS for OF neuropathic pain

: A total of 118 patients have been trialed for MCS for FCNP, 100 (84.7%) pursued permanent implantation of the system, and 84% of them had good pain control at the end of the study. Male: female ratio was about 1:2 in the whole group of studies; mean age was 58 years (range, 28–83), and mean pain duration was 7 years (range, 0.6–25). Four randomized controlled studies have been reported, all of them not focused on MCS for FCNP. The most common complication was seizure followed by wound infection. Preoperative evaluation, surgical techniques, and final settings varied among the series. Conclusion: MCS for FNCP is a safe and efficacious treatment option when previous managements have failed; however, there is still lack of strong evidence (larger randomized controlled multicentre studies) that MCS can be offered in a regular basis to FNCP patients.

Considering that in chronic pain management a good result means a decrease of at least 50% of the pain in the VAS, the pain relief for FCNP treated with MCS reported in the literature ranges from 45% to 84% including the present review.[12,22,72,78,79,118] Brown et al. hypothesized that a possible explanation for these particularly excellent results of MCS in FCNP is that the facial somatotopic representation on



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Editor: Antonio A. F. DeSalles, MD University of California, Los Angeles, CA, USA

Motor cortex stimulation for facial chronic neuropathic pain: A review of the literature

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Abstract

Background: Facial chronic neuropathic pain (FCNP) is a disabling clinical entity, its incidence is increasing within the chronic pain population. There is indication for neuromodulation when conservative treatment fails. Motor cortex stimulation (MCS) has emerged as an alternative in the advanced management of these patients. The aim of this work is to review the worldwide literature on MCS for FCNP.

Methods: A PubMed search from 1990 to 2012 was conducted using established MeSH words. A total of 126 relevant articles on MCS focused on chronic pain were selected and analysed. Series of cases were divided in (1) series focused on MCS for FCNP, and (2) MCS series of FCNP mixed with other chronic pain entities.

Results: A total of 118 patients have been trialed for MCS for FCNP, 100 (84.7%) pursued permanent implantation of the system, and 84% of them had good pain control at the end of the study. Male: female ratio was about 1:2 in the whole group of studies; mean age was 58 years (range, 28–83), and mean pain duration was 7 years (range, 0.6–25). Four randomized controlled studies have been reported, all of them not focused on MCS for FCNP. The most common complication was seizure followed by wound infection. Preoperative evaluation, surgical techniques, and final settings varied among the series.

Conclusion: MCS for FNCP is a safe and efficacious treatment option when previous managements have failed; however, there is still lack of strong evidence (larger randomized controlled multicentre studies) that MCS can be offered in a regular basis to FNCP patients.

Key Words: Facial neuropathic pain, facial pain, motor cortex stimulation, neuropathic pain, trigeminal deafferentation pain, trigeminal neuropathic pain

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INTRODUCTION

Facial chronic neuropathic pain (FCNP) is a disabling, sensation resistant to treatment, and diminishes quality of life.[24] Pain could be located in any of the branches of the trigeminal nerve (V1, V2, or V3), in any combined

Motor Cortex Stimulation

- Fontaine et al. in a critical review of the literature of MCS for chronic neuropathic pain reported that a good response to MCS (pain relief ≥40–50%) was observed in ~55% of patients who underwent surgery and in 45% in patients with follow-up ≥1 year. VAS scores revealed a 57% of pain improvement. A good response was achieved in 68% of the patients with TNP, higher than 54% of the patients with central pain. At follow-up >1 year this percentage was 50% of the patients improved with TNP treated with MCS. Complications were seizures in 12% in the early postoperative period, infection rate was found in 5.7%, hardware related problems in 5.1%.[29] DaSilva et al. in a structural and functional MRI study of patients with TNP, found changes in cortical thickness of TNP patients were frequently colocalized and correlated with functional allodynic activations, and include both cortical thickening and thinning in sensorimotor regions, and predominantly thinning in emotional regions of the brain. Overall, such patterns of cortical thickness suggest a dynamic functionally driven plasticity of the brain. These structural changes, which correlated with the pain duration, age-at-onset, pain intensity and cortical activity, may be specific targets for evaluating therapeutic interventions.[17]

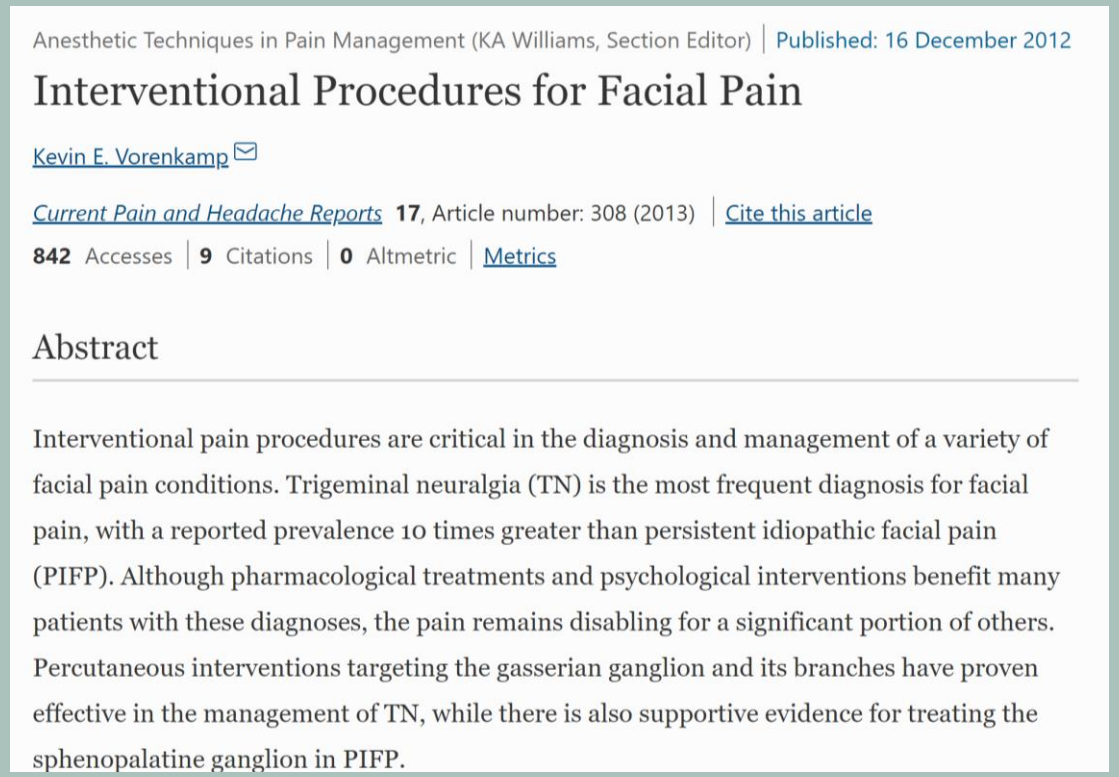
Motor Cortex Stimulation

- While MCS provides a significant treatment effect to many patients with FCNP, the mechanism underlying its efficacy remains largely unknown. A central analgesic mechanism has been proposed on the basis of comparative positron emission tomography (PET) studies performed before and after MCS. Neuronal activation (hypermetabolism) of cortical and thalamic areas related with sensory input (sensory thalamus), orbitofrontal cortex, mesencephalon/periaqueductal gray (PAG) and pons, posterior insula, areas of emotional interpretation of pain (cingulated cortex, Brodmann area 24, 32, and 10) was induced by MCS and remained after the stimulator was turned off,[33-36,53,82,83] interestingly, a similar posttherapy effect was also seen with the use of rTMS of the motor cortex.[52] It is hypothesized that the extent of pain alleviation from MCS also correlates with the increase of blood flow in the cingulate gyrus. This suggests that stimulation reduces the suffering experienced by a patient with chronic pain.[3,37] Ito et al. showed that successful MCS in poststroke pain patients significantly improves glucose use in the thalamus ipsilateral to MCS.[46]

Complications of MCS

Table 3: Reported side effects and complications with MCS therapy

Procedure-related complication
Bleeding
• Epidural hematoma[77,79]
• Subdural hematoma[104]
• Large cerebral hematomas[72,97,99]
Infection[5,12,18,25,45,79,81,86,93,99,104]
Postinfection arachnoiditis[18]
Wound dehiscence[25,79]
Transient neurological deficits[45,81,93]
Breakage and/or malfunction of the hardware [12,104]
Epidural fibrosis[122]
Stimulation-related complication
Seizures[22,41,48,72,81,86,90,93,97,100,102,104]
Painful stimulation of the dura mater[49,72,79]
Dysesthesias[32,48,77]
Dysarthria[12,77,104]
Dysphasia[104]
Fatigue[12,104]
Unusual events
Impairment in a motor imagery task[117]
Development of a painful supernumerary phantom arm[10]
Cognitive function alteration[74]
Unpleasant pain in the same area of the original pain[9]
Analgesia via ipsilateral MCS[9]
Bilateral analgesia (or sensory effects) from unilateral MCS[9]



Anesthetic Techniques in Pain Management (KA Williams, Section Editor) | Published: 16 December 2012

Interventional Procedures for Facial Pain

Kevin E. Vorenkamp

Current Pain and Headache Reports **17**, Article number: 308 (2013) | Cite this article

Abstract

Interventional pain procedures are critical in the diagnosis and management of a variety of facial pain conditions. Trigeminal neuralgia (TN) is the most frequent diagnosis for facial pain, with a reported prevalence 10 times greater than persistent idiopathic facial pain (PIFP). Although pharmacological treatments and psychological interventions benefit many patients with these diagnoses, the pain remains disabling for a significant portion of others. Percutaneous interventions targeting the gasserian ganglion and its branches have proven effective in the management of TN, while there is also supportive evidence for treating the sphenopalatine ganglion in PIFP.

Ablative interventions?

Section subtitle

Ablative techniques for refractory TN

Techniques include (first highest evidence base)

- microvascular decompression (MVD)
- gamma knife radiosurgery
- radiofrequency ablation (RFA)
- Pulsed radiofrequency PRF
- percutaneous balloon compression (PBC)
- Intragasserian phenol glycerite [13]
- Peripheral alcohol injection
- Cryotherapy
- stereotactic radiosurgery (SRS)
- partial sensory rhizotomy (PSR).

Table 2. Summary of commonly used therapies for trigeminal neuralgia.

Modality	Assessment	Comments
Pharmacologic Therapy	Carbamazepine: moderate level of evidence for long-term benefit, but loss of benefit (failure rate of 50% long term) Other anticonvulsant drugs: oxcarbazepine, lamotrigine, gabapentin—commonly used but low quality or insufficient evidence re: benefit	High degree of adverse effects with carbamazepine
Peripheral Nerve Intervention	Percutaneous rhizotomy (glycerol): high level of evidence for long-term benefit Radiofrequency thermocoagulation: high level of evidence for long-term benefit Balloon compression: high level of evidence for long-term benefit	Loss of benefit over time for all three techniques Low incidence of serious adverse effects, but anesthesia dolorosa can be a serious adverse effect No agreement on the optimal temperature for radiofrequency thermocoagulation
Botulinum Toxin	High quality of evidence for benefit	Low incidence of transient side effects, but treatment must be repeated to maintain benefit
Gamma Knife Radiosurgery	High quality of evidence in favor of long-term benefit. Benefit falls by almost half in 5–10 years, but treatment can be repeated	Onset of improvement is delayed from 2 to 6 months after treatment Low incidence of adverse effects is increased with repeated treatment
Microvascular Decompression	High level of evidence for long-term improvement that is maintained over 5 years	Low incidence of adverse effects Endoscopic microvascular decompression has a higher rate of benefit and a lower rate of recurrence with fewer adverse effects than traditional open microvascular decompression

MVD is the most effective surgical method for treating TN, with a recurrence rate between 6% and 47%.10–15 As a destructive operation, PSR has rarely been reported in recent years due to its high complications. In the existing literature, the recurrence rate of TN after the first simple PSR is reported to be between 30% and 50%.3,6–8,18

Radiofrequency for chronic pain

- CRF uses high-frequency alternating current to induce coagulative necrosis in the target tissue. Tissue destruction occurs with probe temperatures between 60° and 80° C. Because tissue heating decreases rapidly with distance from the electrode tip, CRF lesions are well circumscribed, thus offering an advantage over chemical neurolysis

Journal of Pain Research

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REVIEW

Orofacial pain management: current perspectives

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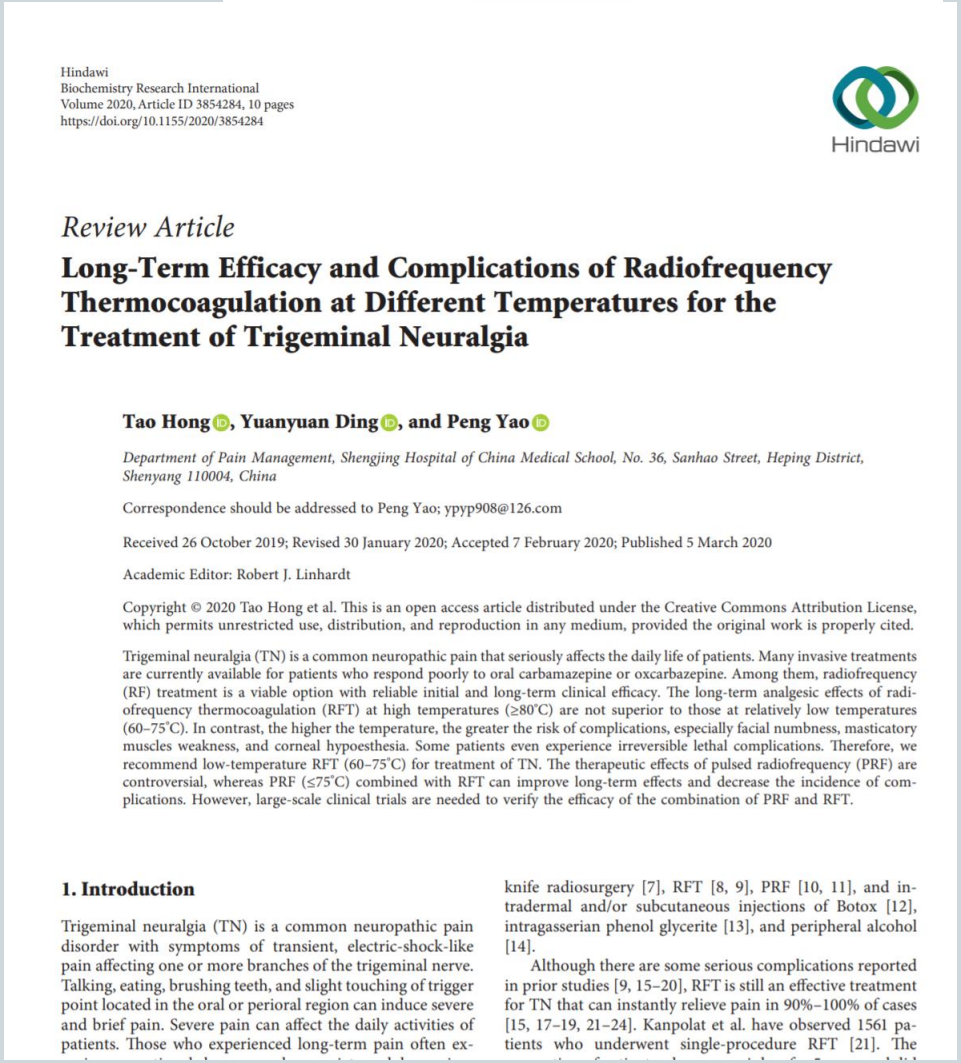

Hindawi
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Review Article

Long-Term Efficacy and Complications of Radiofrequency Thermocoagulation at Different Temperatures for the Treatment of Trigeminal Neuralgia

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Academic Editor: Robert J. Linhardt

Trigeminal neuralgia (TN) is a common neuropathic pain that seriously affects the daily life of patients. Many invasive treatments are currently available for patients who respond poorly to oral carbamazepine or oxcarbazepine. Among them, radiofrequency (RF) treatment is a viable option with reliable initial and long-term clinical efficacy. The long-term analgesic effects of radiofrequency thermocoagulation (RFT) at high temperatures (≥80°C) are not superior to those at relatively low temperatures (60–75°C). In contrast, the higher the temperature, the greater the risk of complications, especially facial numbness, masticatory muscles weakness, and corneal hypoesthesia. Some patients even experience irreversible lethal complications. Therefore, we recommend low-temperature RFT (60–75°C) for treatment of TN. The therapeutic effects of pulsed radiofrequency (PRF) are controversial, whereas PRF (≤75°C) combined with RFT can improve long-term effects and decrease the incidence of complications. However, large-scale clinical trials are needed to verify the efficacy of the combination of PRF and RFT.

1. Introduction

Trigeminal neuralgia (TN) is a common neuropathic pain disorder with symptoms of transient, electric-shock-like pain affecting one or more branches of the trigeminal nerve. Talking, eating, brushing teeth, and slight touching of trigger point located in the oral or perioral region can induce severe and brief pain. Severe pain can affect the daily activities of patients. Those who experienced long-term pain often ex-

knife radiosurgery [7], RFT [8, 9], PRF [10, 11], and intradermal and/or subcutaneous injections of Botox [12], intragasserian phenol glycerite [13], and peripheral alcohol [14].

Although there are some serious complications reported in prior studies [9, 15–20], RFT is still an effective treatment for TN that can instantly relieve pain in 90%–100% of cases [15, 17–19, 21–24]. Kanpolat et al. have observed 1561 patients who underwent single-procedure RFT [21]. The

PRS +/- MVD of V for Refractory TN

- We retrospectively analyzed 181 TN patients who received MVD or MVD+PSR treatment from the same surgeon in the neurosurgery department of China-Japan Friendship Hospital from March 2009 to December 2017

Table 3 Comparison of Outcomes Between MVD Group and MVD+PSR Group

Variables	MVD	MVD +PSR	P value
Immediate effect, n (%)			0.196
Cure	30 (75.0%)	54 (83.1%)	
Improvement	4 (10.0%)	8 (12.3%)	
No effect	6 (15.0%)	3 (4.6%)	
The BNI score at the last follow-up, n (%)			0.970
I	19 (47.5%)	33 (50.8%)	
II	5 (12.5%)	10 (15.4%)	
III	6 (15.0%)	9 (13.8%)	
IV	9 (22.5%)	11 (16.9%)	
V	1 (2.5%)	2 (3.1%)	
Recurrence, n (%)			0.819
Yes	11 (31.4%)	18 (28.6%)	
No	24 (68.6%)	45 (71.4%)	
Effect at the last follow-up, n (%)			0.333
No effect or recurrence	16 (40.0%)	20 (30.8%)	
Effective	24 (60.0%)	45 (69.2%)	
Pain-free survival time(month), mean ±SD	37.9±29.4	56.3±34.6	0.009

Journal of Pain Research

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ORIGINAL RESEARCH

Value of Partial Sensory Rhizotomy in the Microsurgical Treatment of Trigeminal Neuralgia Through Retrosigmoid Approach

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

Yin Liu[1,2]
Yanbing Yu[2]
Zheng Wang[1,2]
Zhu Deng[2,3]
Ruiquan Liu[2,3]
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Medica
Medica
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Purpose: Microvascular decompression (MVD) is the most effective surgical procedure for the treatment of refractory primary trigeminal neuralgia (TN), but due to the presence of non-neurovascular compression (NVC), the application of MVD is limited. In some cases, partial sensory rhizotomy (PSR) is required. The purpose of this study was to compare the outcome of MVD and MVD+PSR in the treatment of primary TN and to evaluate the application value of PSR in the treatment of TN.

Patients and Methods: We retrospectively analyzed the postoperative outcomes of patients who received MVD or MVD+PSR for the first time from the same surgeon in the neurosurgery department of China-Japan Friendship Hospital from March 2009 to December 2017. A total of 105 patients were included in the data analysis, including 40 in

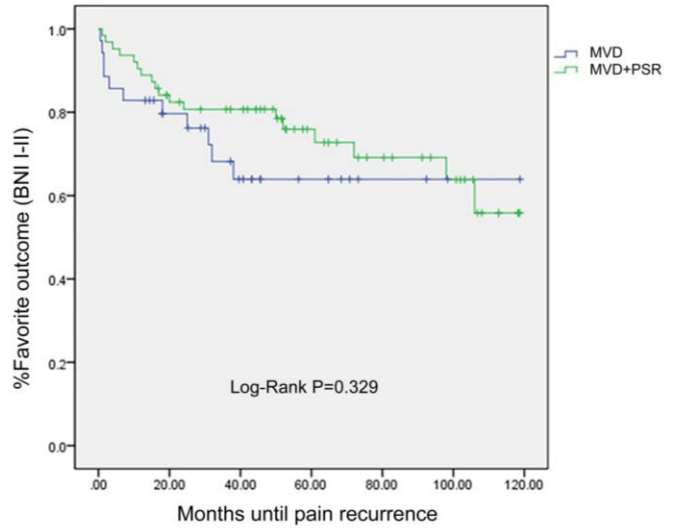

Figure 3 The Kaplan-Meier survival curves for the MVD and MVD+PSR groups are shown.
Abbreviations: MVD, microvascular decompression; PSR, partial sensory rhizotomy.

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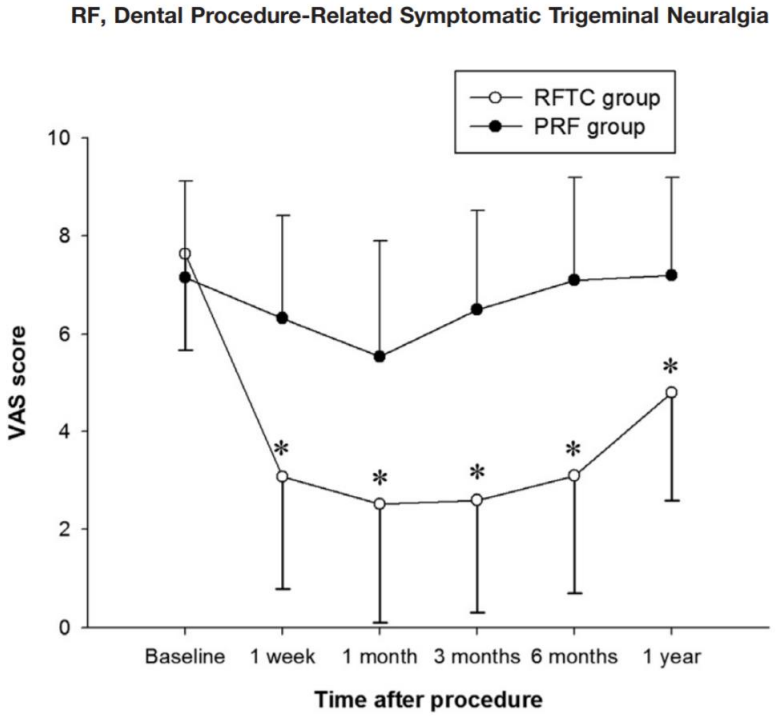
such as multiple sclerosis or cerebellopontine angle tumors).[2,3] Common surgical

Comparison of RF and PRF of V for PTNP

Table 1 Demographic data and pain characteristics in PRF and RFTC group

Parameters	PRF Group (N = 26)	RFTC Group (N = 28)
Sex (M/F)	8 (30.1%)/ 18 (69.9%)	10 (35.7%)/ 18 (64.3%)
Age (year)	50.0 ± 15.9	56.2 ± 15.8
Height (cm)	158.1 ± 5.3	159.0 ± 7.5
Weight (kg)	60.7 ± 14.0	69.1 ± 16.4
Pain side*		
Right	6 (23.1%)	17 (60.7%)
Left	17 (65.4%)	11 (39.3%)
Both	3 (11.5%)	0 (0%)
Associated nerve (V2/V3)	6 (23.1%)/ 20 (76.9%)	11 (39.3%)/ 17 (60.7%)
Persistent pain	7 (26.9%)	4 (14.3%)
Intermittent pain	19 (73.1%)	24 (85.7%)
Trigger factor (yes/no)	14 (73.7%)/ 5 (26.3%)	19 (79.2%)/ 5 (20.8%)
Satisfaction*†	2.19 ± 0.85	3.86 ± 1.38
Complication*	1 (3.8%)	13 (46.4%)



Pain Medicine

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Wiley Periodicals, Inc.

Pulsed and Conventional Radiofrequency Treatment: Which Is Effective for Dental Procedure-Related Symptomatic Trigeminal Neuralgia?

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Abstract

Objectives. Many patients develop dental treatment-related symptomatic trigeminal neuralgia. However, the effectiveness of pulsed radiofrequency (PRF) treatment and conventional radiofrequency thermocoagulation (RFTC) for treatment of this disorder has not been determined. This retrospective study was conducted to compare the effectiveness and complications of PRF and RFTC in these patients.

Methods. Fifty-four patients who experienced the onset of symptomatic trigeminal neuralgia after a dental treatment were managed by PRF or RFTC. Data were collected by reviewing their medical records and conducting a questionnaire. Patients' characteristics, the dental procedures that caused the trigeminal neuralgia, the baseline and post-treatment pain intensities, duration of pain relief, complications, and satisfactions to the treatment were evaluated.

Results. Pain intensities were lower at 1 week (3.0/10 vs 6.4/10), at 1 month (2.5/10 vs 5.9/10), 3 months (2.6/10 vs 5.5/10), 6 months (3.1/10 vs 7.1/10) and 1 year (4.8/10 vs 7.2/10) in the RFTC group (28 patients) than in the PRF group (26 patients) ($P < 0.05$). The duration of pain relief without medication in the RFTC group (10.8 months) was longer than that in the PRF group (0 months). The incidence of complications in the RFTC group (46.4%) was higher than that in the PRF group (3.8%) ($P < 0.05$). The RFTC group reported higher satisfaction ratings (3.86/5) than the PRF group (2.19/5) ($P < 0.05$).

Conclusions. Although the RFTC group had more complications than the PRF group, most were minor and transient, and the patient satisfaction rate with RFTC was very high. Therefore, RFTC is an effective tool for the treatment of dental procedure-induced trigeminal neuralgia.

Key Words. Dental Treatment; Pulsed Radiofrequency; Radiofrequency Thermocoagulation; Trigeminal Neuralgia

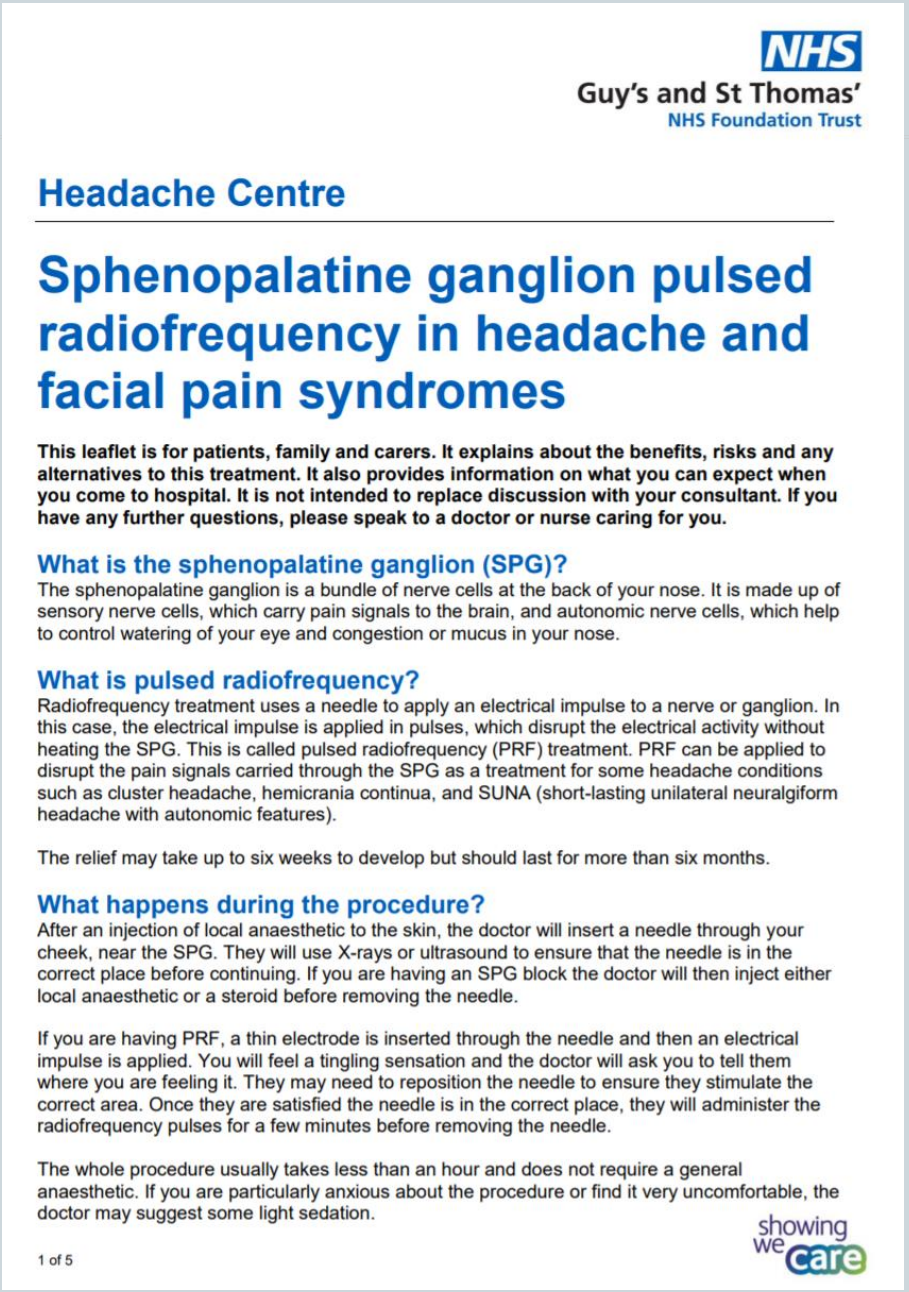
Trigeminal neuralgia and other facial pains are generally diagnosed on the basis of the medical history and neurological examination [1–3]. We have treated many patients with chronic pain in the facial areas innervated by the trigeminal nerve that began immediately after a dental procedure. The International Headache Society has categorized these pains as symptomatic trigeminal neuralgias [4].

Zuniga [5] reported that wisdom tooth extraction can cause damage to the inferior alveolar and/or lingual nerves. Nerve damage may occur during tooth extraction because of unintentional incision of the nerve or because of the bone pressing against the mental canal, leading to paresthesia and persistent neuropathic pain [6]. The alveolar nerve, mental nerve, or lingual nerve can be damaged during root canal treatment, implantation, or apicoectomy [7–9].

Although drug therapy is the preferred treatment for classical trigeminal neuralgia, interventional treatments are the other options for patients whose conditions are unresponsive to drugs or for those who develop side effects. For treatment of symptomatic trigeminal neuralgia, minimally

Ablative RF SPG

- Cluster headache
- Migraine
- PIFP



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Headache Centre

Sphenopalatine ganglion pulsed radiofrequency in headache and facial pain syndromes

This leaflet is for patients, family and carers. It explains about the benefits, risks and any alternatives to this treatment. It also provides information on what you can expect when you come to hospital. It is not intended to replace discussion with your consultant. If you have any further questions, please speak to a doctor or nurse caring for you.

What is the sphenopalatine ganglion (SPG)?

The sphenopalatine ganglion is a bundle of nerve cells at the back of your nose. It is made up of sensory nerve cells, which carry pain signals to the brain, and autonomic nerve cells, which help to control watering of your eye and congestion or mucus in your nose.

What is pulsed radiofrequency?

Radiofrequency treatment uses a needle to apply an electrical impulse to a nerve or ganglion. In this case, the electrical impulse is applied in pulses, which disrupt the electrical activity without heating the SPG. This is called pulsed radiofrequency (PRF) treatment. PRF can be applied to disrupt the pain signals carried through the SPG as a treatment for some headache conditions such as cluster headache, hemicrania continua, and SUNA (short-lasting unilateral neuralgiform headache with autonomic features).

The relief may take up to six weeks to develop but should last for more than six months.

What happens during the procedure?

After an injection of local anaesthetic to the skin, the doctor will insert a needle through your cheek, near the SPG. They will use X-rays or ultrasound to ensure that the needle is in the correct place before continuing. If you are having an SPG block the doctor will then inject either local anaesthetic or a steroid before removing the needle.

If you are having PRF, a thin electrode is inserted through the needle and then an electrical impulse is applied. You will feel a tingling sensation and the doctor will ask you to tell them where you are feeling it. They may need to reposition the needle to ensure they stimulate the correct area. Once they are satisfied the needle is in the correct place, they will administer the radiofrequency pulses for a few minutes before removing the needle.

The whole procedure usually takes less than an hour and does not require a general anaesthetic. If you are particularly anxious about the procedure or find it very uncomfortable, the doctor may suggest some light sedation.

showing we care

Percutaneous therapeutic approaches for TN

- Are directed to the trigeminal (gassarian or semilunar) ganglion located in Meckel's cave [55,56].
- he three common ablative techniques are
  - chemical (glycerol rhizotomy),
  - mechanical (balloon compression)
  - thermal (radiofrequency thermocoagulation).
- The goal in treatment is to selectively destroy the A delta and unmyelinated C fibers that mediate pain, while preserving the A alpha and beta fibers that mediate touch [57
- There is one systematic review and meta-analysis of the comparative safety and efficacy of per-cutaneous approaches for the treatment of trigeminal neuralgia, comparing each of the three types of treatment with each other [58].
- Radiofrequency thermocoagulation had significantly greater odds (OR, 2.65; 95% CI: 1.29–5.44; I2: 85.5%) for immediate pain relief than glycerol rhizotomy. The rates of pain recurrence over 5 to 30 months were similar between the two groups.
- There was a significantly higher risk of anesthesia with radiofrequency rhizotomy. The rates of complications such as anesthesia dolorosa, keratitis, and weakness of chewing were the same in the two groups.
- The rates of immediate pain relief and of pain recurrence over the long term (6–28.5 months) were similar for balloon compression and glycerol rhizotomy.
- The risk of mastication weakness was significantly (9-fold) higher for balloon compression compared to glycerol rhizotomy and diplopia was likewise more likely with balloon compression (4.8% compared to 0.45% for glycerol rhizotomy).
- Rates of immediate pain relief, of pain recurrence, and of adverse effects were similar for balloon compression and radiofrequency thermocoagulation.
- Post-operative herpes eruption was more likely with radiofrequency thermocoagulation than with glycerol rhizotomy. A
- s of 2019, there were no randomized trials comparing all three techniques together. Moreover, the studies were not blinded or randomized. Additionally, procedure techniques change over time, and vary from study to study, limiting the reliability of meta-analyses of studies conducted over many years. For example, there is no agreement about the optimal temperature to be used for radiofrequency thermocoagulation. Radiofrequency can be pulsed or continuous, and at different temperatures [59].
- Computerized tomography guidance has been proposed to decrease procedure time, anesthesia time, exposure to radiation and to improve the accuracy of needle placement [60]. Perhaps the most feared complication of the percutaneous procedures is anesthesia dolorosa, a severe and difficult to treat persistent pain that occurs rarely, up to 1% of cases [61], though it is usually much less frequent. The complication rate associated with radiofrequency thermocoagulation is directly related to the temperature used. Effective treatment associated with the lowest rate of adverse effects was achieved at temperatures of 65–70 degrees centigrade [62]. Variations of the peripheral approach to nerve ablation include endoscopic peripheral nerve ablation [63], cryotherapy nerve ablation [64], and acupuncture [65]

MVD

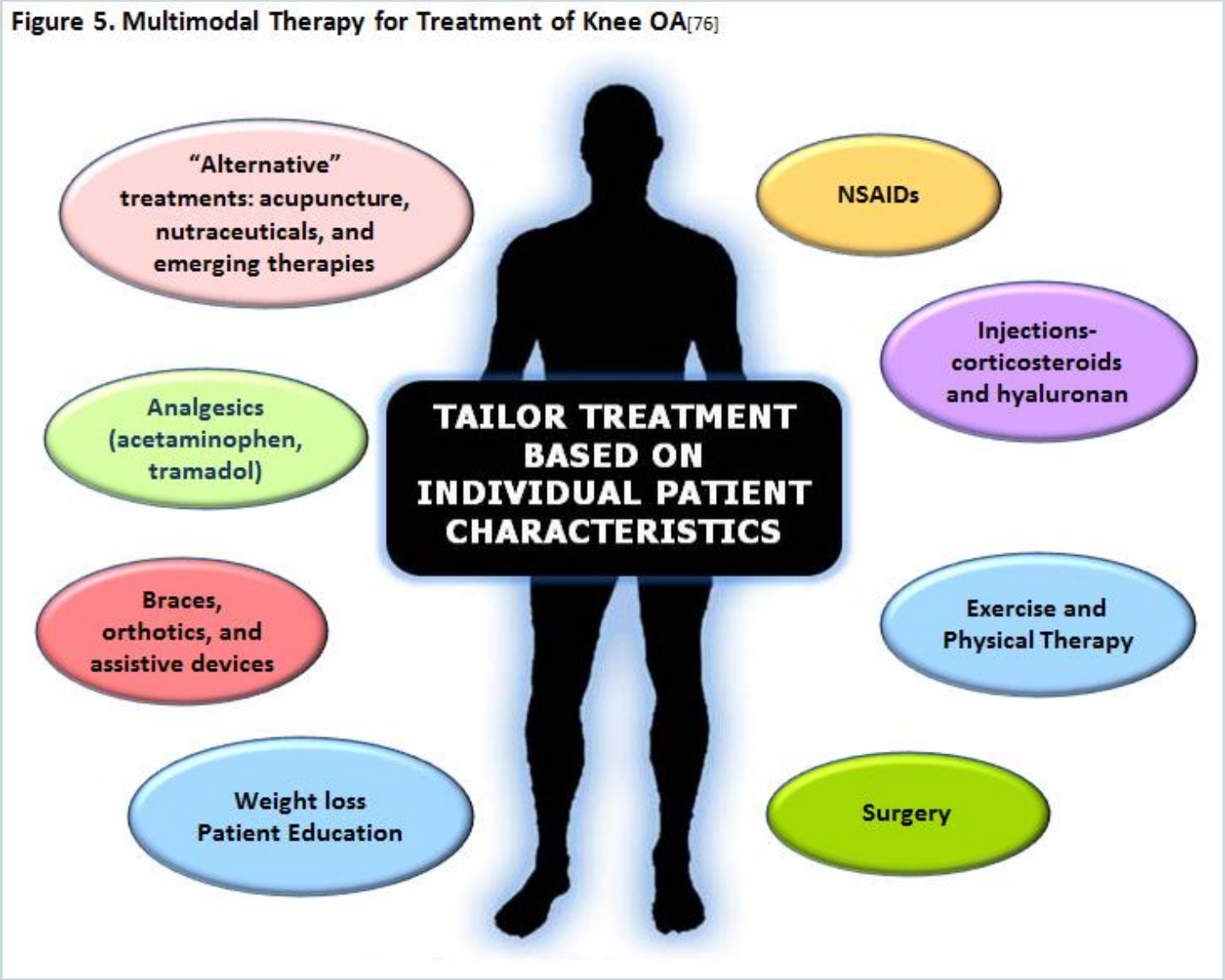
- Microvascular Decompression Microvascular decompression (MVD) is the gold standard of treatment for TN caused by vascular compression of the trigeminal nerve [71,77]. A meta-analysis of 46 studies totaling 3897 patients showed long-term freedom from pain in 76% of patients [70]. A greater likelihood of a successful outcome was associated with a duration of 5 years or less, compression by the superior cerebellar artery (SCA), compression by an artery, including the anterior inferior cerebellar artery (AICA), rather than a vein, and classical (rather than atypical) TN. Patients with classical TN were more likely to have arterial compression and patients with more persistent or atypical pain were more likely to have venous compression. Adverse effects were relatively few compared to percutaneous ablation techniques or GKRS. Adverse effects included facial numbness (5.5 to 13.9%), facial dysesthesia (5.3–5.7%) minor hearing impairment (2.7%), and dizziness (1.8%). More serious complications such as cerebrospinal fluid leaks and infection are rather rare, and mortality is quite uncommon (0.0–0.4%). A small subgroup of patients have TN caused by vertebro-basilar artery ectasia. The patients in this subgroup tend to be older than in TN with SCA or AICA involvement. The outcome after open MVD in this subgroup was comparable to the outcomes in open MVD of the more common smaller artery compression of the trigeminal nerve, but the complication and recurrence rates were lower [78]. The two main approaches to MVD are open microscopic microvascular decompression (OMVD) and minimally invasive endoscopic microvascular decompression (EMVD). OMVD was pioneered by Janetta [79], but has a number of problems associated with it that are minimized with the EMVD. Specifically, visualization is improved and instrument breakage with consequent neural and vascular injury is less with the EMVD. Post-operative complications such as hearing loss, spinal fluid leakage, and facial paresis or paralysis are significantly less with EMVD [80]. The first comparative meta-analysis of the two approaches was published in 2017 [81]. Thirteen studies of OMVD and 10 studies of EMVD, with a total of 6749 patients, were included in the meta-analysis. Of these, 993 had undergone EMVD. Good pain relief was achieved in 81% of OMVD procedures, and in 88% of the EMVD patients. The mean recurrence rate was 14% in the former and 9% in the latter. The rate of complications (facial weakness, hearing loss, cerebellar injury, infection, and death) was 19% for OMVD and 8% for EMVD. Improvements in surgical techniques in more recent years may bias these figures, as could the asymmetry in the numbers of patients in each treatment group, and the great heterogeneity among the studies

Gamma Knife

- Gamma Knife Gamma knife stereotactic radiosurgery (GKRS) is a minimally invasive approach for the management of trigeminal neuralgia refractory to medication [66,67]. Gamma knife radiosurgery (GKRS) produces axonal degeneration, ion channel destruction, and an electrophysiologic block that reduces nociceptive input [56]. Highly precise targeting of the trigeminal nerve or the trigeminal ganglion is possible, limiting adverse effects. The preferred target for GKRS has evolved from the trigeminal ganglion itself to the retrogasserian region and to the root entry zone. A meta-analysis of GKRS outcomes reported that pain relief ranged from 69 to 85% at one year, falling to 38 to 52% at 5 years and 30 to 45.3% at 10 years [56,68]. Onset of pain relief is delayed, ranging from 15 to 78 days on average, up to 6 months. As is the case with percutaneous treatments, retreatment is possible, but, though effective, there is a greater risk of complications [69]. The benefit of repeated GKRS has been greater in those subjects who also had facial sensory loss. A number of systematic reviews and meta-analyses compared GKRS with microvascular de-compression (MVD), which will be discussed below in connection with MVD, the only treatment that directly corrects the cause of TN in at least 50% of cases [70–76].

Tailor the treatment to the patient

Figure 5. Multimodal Therapy for Treatment of Knee OA[76]



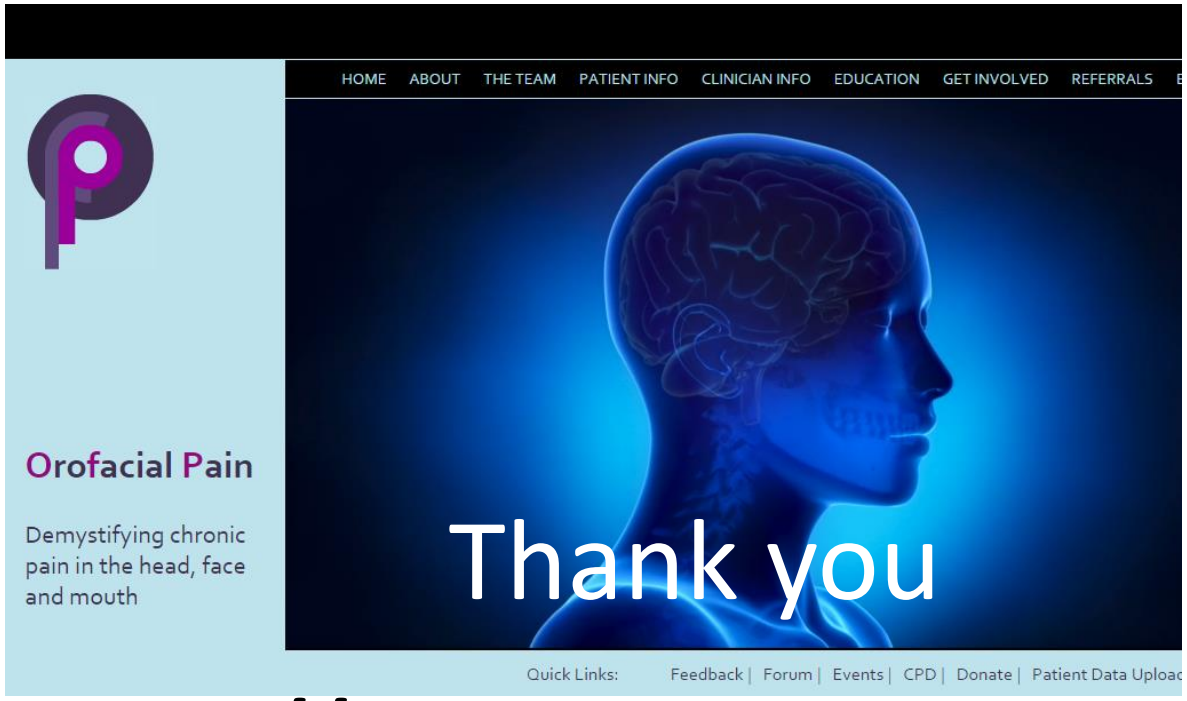
WHAT NEXT?

New classification

Phenotyping base upon clinical and psychological

Development artificial diagnostics

Mobile apps for patients and clinicians



http://www.orofacialpain.org.uk

Thank you

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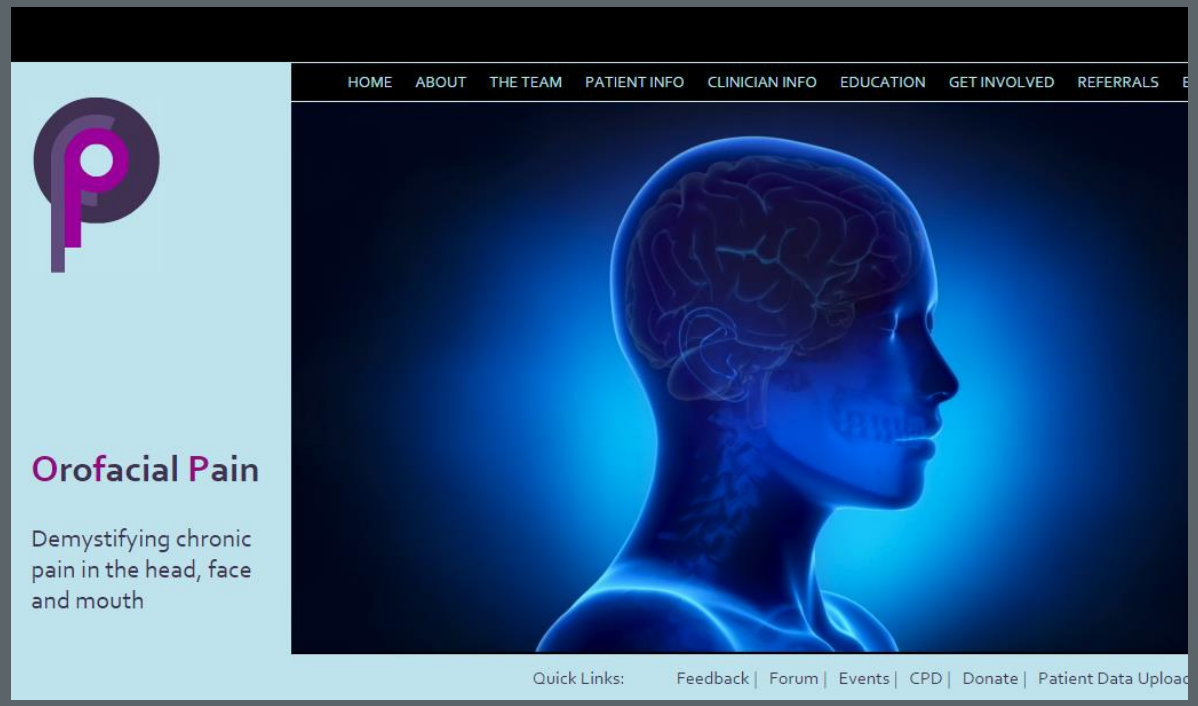

http://www.orofacialpain.org.uk

Mechanistic characterisation of pain
Any combination may be present simultaneously

• Peripheral • nociceptive	**Peripheral Inflammatory**	• Peripheral neuropathic	**Neurovascular**	**Centralised or dysfunctional pain**
• Thermal, chemical, mechanical damage in tissues • NSAID opioid responsive **Examples** • Needle stick • Injection	• Inflammation related to damage of tissues • NSAID opioid responsive • Responds to procedures / antibiotics if infection related **Examples** Acute pain due to injury / Surgery Osteo/Rheumatoid arthritis Cancer pain	• Damage or lesions of peripheral nerves • Responds to NA channel blockers, central (TCAs neuroactive compound Ca channel blockers) pharmacological therapy **Examples** Diabetic neuropathy	• **Neuropathic pain** with **autonomic input** • TAC- Facial flushing, ptosis, conjunctival irritation, nasal congestion • Migrainous-Vertigo, dizziness, phono/photo phobia **Examples-** Headaches, TACs	• Characterised by central disturbance in pain processing • Responds to neuroactive compounds altering levels of neurotransmitters involved in pain transmission **Examples** Fibromyalgia Irritable bowel syndrome Myalgic TMD Migraine, Tension headache

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REFRACTORY CRANIOFACIAL PAIN

Is there a role of periodontal disease as a comorbidity?

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Abstract – **Objetive:** To evaluate the influence of the periodontal disease (PD), a chronic infection, in patients with chronic craniofacial pain complaints. **Method:** Twenty patients with chronic craniofacial pain and PD (*CFP group*) and 20 patients with PD (*PD group*) were assessed before and after periodontal treatment (baseline, 30 and 180 days after treatment). The paramenters evaluated were: plaque index, bleeding index, clinical probe insertion, Visual Analogic Scale (VAS) for pain intensity and Numerical Rating Scale (NRS) and Verbal Rating Scale (VRS) for the "chief complaint". **Results:** After 180 days PD was controlled in both groups ($p<0.001$); the VAS decreased in *CFP group* ($p<0.001$); "chief complaint" improved ($p=0.005$ and $p=0.027$, respectively in *CFP and PD group*). VRS showed improvement between the groups in 30 ($p=0.004$) and 180 days ($p=0.001$). **Conclusion:** These results suggest a possible influence of periodontal disease, as a comorbidity, in refractory craniofacial pain patients and in their pain levels.

KEY WORDS: periodontal disease, orofacial pain, chronic headache, atypical facial pain.

Dor refratária crânio-facial: há algum papel para a doença periodontal como morbidade associada?

Resumo – **Objetivo:** Avaliar a influência da doença periodontal (DP) em pacientes com queixas de dores crônicas crânio-faciais. **Método:** Vinte pacientes com dor crônica crânio-facial e DP (*CFP group*) e 20 pacientes com DP

Why does pain become refractory?

- Causes
  - Incorrect diagnosis?
  - Multiple pain diagnoses?
  - Multiple previous medications and intervention changing phenotype?
  - Intolerance to medications ?
  - Presentation as part of Nociplastic pain?
    With chronic widespread pain and or Fibromyalgia
    Persistent idiopathic pain by definition is intractable
  - Vulnerabilty
    Axis II issues
    Prior significant life events
    Microbiome
    Sleep disorders
    Obesity smoking lack of exercise
    Family history
- Types
  - Refractory TMD
  - Refractory neuropathic pain
    - TN
    - PTNP
  - Refractory Headaches
    - Migraine
    - TACs
  - Idiopathic pain
    - BMS
    - PIFP

Management

- Non ablative interventions
  - Injections /Blocks
    Botulinum toxin dermal injections
    LA +/- steroids
    nerve ON, V1/2/3, Auricular temporal
    ganglion SPG Gasserian
  - Peripheral stim Superficial sessional neurostimulation, V IX C2/3
  - Ganglia implanted neurostimulation
  - Spinal cord stimulation (not for OFP)
  - Deep brain stimulation (DBS)
  - Transmagnetic stimulation motor cortex
  - Pulsed radiofrequency PRF
- Ablative interventions
- **Ablative techniques**
  - Gasserian Ganglion interventions
  - Radiofrequency ablation = Thermocoagulation
  - Rhizotomy
  - **MVD**
  - **Internal neurolysis**
  - Balloon compression
  - Glycerolysis
  - cryotherapy
  - Stereotactic radiosurgery
  - Gamma knife may be indicated If there is medical contraindications to MVD


KING'S
College
LONDON

Picture x1

Caption would go here if required

Picture x4

Captions would go here if required

Picture x6






Captions would go here if required