

ABSTRACT

Persistent facial pain conditions

Persistent facial pains, especially temporomandibular disorders (TMD), are common conditions. As dentists are responsible for the treatment of most of these disorders, up-to date knowledge on the latest advances in the field is essential for successful diagnosis and management. The review covers TMD, and different neuropathic or putative neuropathic facial pains such as persistent idiopathic facial pain and atypical odontalgia, trigeminal neuralgia and painful posttraumatic trigeminal neuropathy. The article presents an overview of TMD pain as a biopsychosocial condition, its prevalence, clinical features, consequences, central and peripheral mechanisms, diagnostic criteria (DC/TMD), and principles of management. For each of the neuropathic facial pain entities, the definitions, prevalence, clinical features, and diagnostics are described. The current understanding of the pathophysiology of these entities is presented, and a description of the evidence based treatment methods is provided.

Persistent facial pain conditions

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Persistent facial pains, especially temporomandibular disorders (TMD), are common conditions; their prevalence is in the range of 8-15%. As patients often present complaints of facial pain to their dentist, it is important that dentists are familiar with these conditions. Many advances have been made during recent decades in the understanding of chronic facial pain, such as increased knowledge of the peripheral and central neural processes involved in different facial pain entities, recognition of the multidimensional nature of pain, and improvements in evidence-based treatments, both physical and behavioural, for different conditions. The present article aims to provide up-to-date information on different chronic facial pain entities to enhance their recognition and proper treatment or referral.

Temporomandibular disorders

Temporomandibular disorders (TMD) are recognized as a group of musculoskeletal and neuromuscular conditions that involve the temporomandibular joints (TMJs), the masticatory muscles, and associated tissues (1). The most common signs and symptoms of TMD are orofacial pain and impaired jaw function. TMD patients often suffer from other painful disorders, and other comorbidities, such as sleep disorders. The chronic forms of TMD pain may lead to absence from or impairment of work or social interactions, resulting in an overall reduction in the quality of life.

EMNEORD

Temporomandibular disorders; idiopathic facial pain; neuropathic facial pain; trigeminal neuralgia; pain pathophysiology

TMD is common in the adult population and seem to affect women more than men

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(2), and the prevalence is reported to be between 5-12 % (3). The prevalence is lowest in children, and symptoms and clinical findings increase through adolescence, peak in adulthood and seem to decrease in the elderly. Muscle disorders, disc displacements, and other joint disorders are frequent findings in the patients. As in other joints there may be pathological changes of the TMJs both because of localized degenerative joint diseases or systemic diseases. However, most disorders are primary and localized, and can be divided into non-infectious inflammatory disorders, and disc displacements and degenerative joint disorders. The conditions may be associated with a feeling of tenderness, stabbing or radiant pain from the joints during rest and shooting pain during jaw function. In addition the jaw movements may be restricted, irregular or asymmetric and associated with TMJ clicking or crepitation, and secondarily the chewing pattern may be changed and the bite force reduced (4). Disorders of the masticatory muscles often start gradually as episodes of fatigue, tension and stiffness, which may evolve into more persistent dull and pressing pain localized to the cheeks, jaws, temples or even headache.

Central and peripheral mechanisms

The pathophysiology and aetiology of TMD are not yet well understood. Peripheral and central sensitization seems to contribute synergistically to this condition, which may explain why many of these patients need multidisciplinary and multimodal approaches to diagnostics and therapy (5).

The relation between peripheral pathology and pain manifestations is often weak in chronic orofacial pain. For example, clinical signs and symptoms of TMD do not discriminate between treatment responders and non-responders (6). TMD patients seem to be more sensitive than TMD-free controls to experimental pain, both in the orofacial areas as well as in other parts of the body (7,8). While central mechanisms have been implicated in this increased sensitivity, there is also a role of peripheral sensitization that contributes to changes in nociceptive and sensory input. Experimental injections of algescic substances like bradykinin, serotonin and glutamate into jaw muscle tissue result in muscle pain similar to that observed in patients with chronic myalgia of the masticatory muscles (8,9). There is also convincing evidence that peripheral changes in the levels of certain mediators in the TMJ and masticatory muscle are related to pain. In particular, mediators like cytokines and serotonin have been investigated in both the TMJ and muscle tissues (10).

Central sensitization refers to neurofunctional changes of the somatosensory system in the spinal cord, brain stem and the brain pain matrix (11). There is substantial evidence that central pain mechanisms are disturbed in chronic orofacial pain. For example, reduced cognitive ability predicts treatment outcome (6). Furthermore, chronic orofacial pain patients show increased spatial distribution of TMD pain, increased temporal summation in remote body areas (12) and impaired

central modulation of pain (13,14). Aberrant activation patterns have been demonstrated in response to painful stimuli in chronic pain states such as fibromyalgia (15), a chronic pain condition often associated with TMD.

The multidimensionality of pain perception is supported by activation of brain areas not only associated with the perception of sensory features (e.g. somatosensory cortices) but even more so regions associated with emotional and cognitive aspects of pain (16). These regions are known to play critical roles in various aspects of pain experiences. In addition, brain areas involved in the regulation of the autonomic nervous system and endogenous pain modulation are affected. In an fMRI study, during periods of ongoing low back pain only brain regions of importance for emotional and cognitive aspects of pain were activated (17). These findings indicate that the perception of chronic, ongoing pain requires only limited involvement of the somatosensory areas. Central sensitization is still difficult to clinically assess and quantify but may impact all levels of the biopsychosocial model of chronic pain: biological changes, psychological aspects and social aspects.

Diagnosis of TMD in general and specialist practice

The recently published Diagnostic Criteria for Temporomandibular Disorders (DC/TMD; 18) provides a simple and highly accurate methodology to diagnose TMD. DC/TMD comprises two axes; Axis I that provides a diagnosis of the clinical condition (orofacial pain of myogenous or arthrogenous origin, headache attributed to TMD as well as disc displacement and degenerative joint disease) while Axis II provides a biopsychosocial estimate of the degree of psychosocial distress. The DC/TMD is currently available in English and Swedish but translations into at least 25 more languages are ongoing. For Finnish, Dutch and German the translation process is very near completion and these translations may very well be available at this time. Please see www.rdc-tmdinternational.org for details.

DC/TMD diagnostics is divided into three levels: screening, a short version for general dentistry and a comprehensive version to be used in specialist clinics. The aim of the screening is to identify patients with potential TMD symptoms. This is possible by asking each patient two questions with a "Yes" or "No" alternative: i) Do you have pain in the temples, face, temporomandibular joints or jaws once a week or more often? and ii) Do you have pain when you open your mouth or chew once a week or more often? If the patient answers "Yes" on one or two questions, it is highly likely that the patient has a DC/TMD diagnosis (sensitivity: 0.98, specificity 0.83 for the two first questions; 19). The majority of patients identified with this instrument request treatment for their problems, making this instrument clinically relevant and useful (20).

The clinical DC/TMD examination may lead to one or more Axis I diagnoses and will provide information about psychosocial factors of importance in Axis II. Axis I diagnostics uses information from a questionnaire as well as findings in the struc-

tured clinical examination. The clinical examination is strictly specified, including commands to the patient and palpation sites. Axis II evaluation of psychosocial factors uses validated questionnaires with established cut-offs. The questionnaires recommended in DC/TMD cover most aspects of pain and its consequences as well as risk factors for chronic pain (18). The purpose is to assess to what degree psychosocial factors contribute, and to use this information to guide treatment planning and to evaluate prognosis. In general practice, these instruments can also guide whether to refer the patient or to begin treatment.

The DC/TMD does not cover all chronic orofacial pain and jaw dysfunction conditions. The Expanded DC/TMD Taxonomy (21) attempts to broaden the list of conditions, including generalized pain conditions involving the orofacial region. Conditions not covered by the current DC/TMD, like neuropathic or cervicogenic types of pain, arthritis, fibromyalgia etc., so far need to be assessed and diagnosed according to other diagnostic methodologies and criteria.

Principles of management

As TMD is considered to be a complex, multisystem disorder with multiple causes and comorbidities, and a strong genetic susceptibility (22), management rather than cure is the realistic approach to the treatment of this disorder. The general goal of management is to alleviate pain, minimize the consequences of the chronic pain on the patient and restore normal jaw functions. Unless there are specific and justifiable indications to the contrary, treatment of TMD patients should be based on the use of conservative, reversible therapeutic modalities as studies of the natural history of many TMDs suggest that they tend to improve or resolve over time (1). The fact that widely differing treatment modalities produce comparable treatment effects, suggesting that the positive outcomes of treatment are probably at least partially due to non-specific factors, also speaks for the use of simple methods. When planning treatment several factors, such as physical symptoms and findings, psychosocial status of the patient, the impact of pain, pain chronicity, the presence of comorbid pain conditions, and the presence of comorbid disorders need to be taken into account. A special focus should be on person-specific or Axis II factors, as these are very important in terms of affecting disease course and response to treatment (23). According to a recent study, most primary care TMD patients report mild symptoms and are psychosocially well functioning, while only about 10% of patients report severe symptoms and pain-related psychosocial distress (24).

As there is evidence showing that functional TMD patients can be helped by simple means such as counselling, self-care and jaw exercises (25), most TMD patients can be easily treated by primary care dentists. Thus TMD pain may be reduced and jaw mobility, chewing function and bite force restored with conservative therapy in terms of reassurance and counselling, therapeutic home exercises and relaxation of the jaw, occlusal

appliances, thermal physical therapy and temporary use of analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), and intra-articular injections with glucocorticoid (26). In severe and complicated TMD, a team approach, usually consisting of a dentist, psychologist, and a physiotherapist, is needed. The efficacy of different TMD treatment methods, as well as the multidisciplinary/multimodal management of patients with severe symptoms is described in other articles of the Nordic Theme 2016.

Regarding TMJ surgery, numerous articles over the past 35 years have dealt with interventions of the TMJ from injections to open surgery, but these interventions have not yet been sufficiently evaluated except for ankylosis cases or severe functional disturbances (27). Controlled trials have been sparse and comparison of different treatment strategies is therefore important. Schiffman et al (28) found no difference between treatment strategies relative to any treatment outcome of medical treatment; non-surgical rehabilitation, arthroscopic surgery and open TMJ surgery. Further studies are needed to evaluate the long-term effects of different treatment modalities. To compare the outcome of different treatments it is necessary to use standardized evaluation methods such as diagnostic criteria for TMD (28) or surgical classifications for TMD (29).

Persistent idiopathic facial pain and atypical odontalgia

Persistent idiopathic facial pain (PIFP), also known as atypical facial pain (AFP), is defined as a chronic facial pain in which signs of structural pathology or other specific causes of pain are not identified. The term atypical odontalgia (AO) is used when chronic pain is felt in a tooth region. AO is considered a subcategory of PIFP (30). Prevalence and incidence estimates of PIFP and AO are limited, but both are rare conditions. Clinical case series indicate a preponderance of middle-aged or older women among PIFP patients, and chronicity of the symptoms.

PIFP is usually felt as deep, poorly localized continuous pain. Up to one third may experience bilateral pain. The pain is aching, throbbing, or pressing, and the intensity varies from moderate to severe. AO patients report persistent, moderately intense, usually well localized intraoral pain. The pain can include any tooth or mucosa of an extraction site, and it may move from tooth to tooth following dental procedures. Many PIFP and AO patients report that the onset of pain is related to some type of trauma or surgical procedure, e.g. endodontic treatment, extraction of teeth, or sinus surgery (31).

The diagnoses of PIFP and AO can only be made after careful exclusion of pathology in teeth or adjacent structures, neurological disorders, and related systemic diseases, which may demand collaboration with several medical specialties. A thorough clinical and radiological examination is essential. Examination of trigeminal sensory function with neurophysiologic recordings and quantitative sensory tests (QST) are recommended to improve diagnostic accuracy, as well as head MRI examination to exclude intracranial pathology. As always in



cases of chronic pain, attention should also be paid to possible psychological distress (31).

In recent years, clinical neurophysiology, QST, and functional brain imaging have provided sensitive tools for detailed investigation of pain mechanisms (32). Clinical neurophysiological studies have revealed nerve fibre dysfunction in PIFP and AO (33,34). Damage to the large tactile nerve fibres and the trigeminal brainstem complex may also occur in both conditions. PET scanning of the brain dopamine system has suggested that PIFP may be associated with striatal dopaminergic hypofunction (35). The current evidence supports the concept that in the majority of patients with PIFP and AO, the condition is a subclinical trigeminal neuropathic pain arising from minor peripheral nerve trauma or a more central trigeminal system lesion (31).

There are no curative treatments available for PIFP and AO, and patients frequently have difficulties in accepting these diagnoses and their management, seeking help from different specialists, and therefore potentially receiving unnecessary invasive dental and surgical treatments, which carry a high risk of pain aggravation. This stresses the need for patient education, and management should be multidisciplinary as the pain is often complicated by physical and psychiatric co-morbidity (31). Randomized controlled trials performed on PIFP and AO are scarce. However, the experience gained in treatment of other neuropathic pain conditions (36) can be transferred to PIFP and AO. The recommended pharmacologic treatment of PIFP and AO includes tricyclic antidepressants and gabapentinoids. Behavioural therapies are beneficial complements to biomedical approaches.

Trigeminal neuralgia

Trigeminal neuralgia (TN) is neuropathic pain with specific characteristics. The classical type of TN is a sudden, unilateral, superficial, shooting or electric-shock like pain occurring repeatedly within the distribution of one or more branches of the trigeminal nerve (30). TN is most common in the maxillary and mandibular branch, and the paroxysms usually last some seconds, but may persist up to 2 minutes. The attacks are often initiated by non-painful physical stimulation of specific areas, trigger points. The frequency of the paroxysms varies from a few to even hundreds per day, but there may also be remission periods with days or even months without attacks. In addition to the classical paroxysmal pain attacks, TN patients may also suffer from continuous background pain, especially those with more chronic condition (30).

TN is a rare; the presented incidence rates range from 12.6/100 000 person years to 28.9/100,000 person years (37). The incidence increases with age, and is highest in patients older than 60 years.

The diagnosis of TN can only be made on clinical grounds, and is based on the patient's pain description, and may therefore be mistaken for tooth pain, by patients, dentists and medi-

CLINICAL RELEVANCE

Persistent facial pains, especially temporomandibular disorders are common conditions in the adult population. Their symptoms may be quite similar to pain arising from the teeth and periodontium. It is therefore important for the

dental practitioner to have knowledge of the diagnosis and treatment of different persistent facial pain conditions in order to avoid misdiagnosis and to give the right treatment for the various pain conditions.

cal specialists. When the diagnosis of TN is suspected, the patient should be sent to neurologists for the confirmation of the diagnosis, and necessary further examinations. Brain MRI is considered a routine examination for TN patients. Very rarely, posterior fossa tumours may cause typical TN pain. In younger patients with TN symptoms, the possibility of multiple sclerosis should be considered, as TN may be the first manifestation of the disease.

Dentists should know the characteristic features of TN, especially because it is important to differentiate the brief, intense, shooting type of pain in TN from pain of dental origin, because of the similarities between TN and dental conditions such as pulpitis and cracked tooth syndrome. As a result patients with TN may be treated with ineffective dental treatments. The pain provoking factors aid in differential diagnostics: TN is provoked by tactile stimuli such as touching the skin or brushing the teeth, whereas tooth pain is provoked by thermal (cold or hot) and sweet stimuli or percussion or pressure on the teeth.

The aetiology of TN is considered to be due to compression of the trigeminal nerve root by a vascular loop in the posterior fossa. This is thought to lead to local changes, such as disruption of myelin sheet, ephaptic conduction, and secondary hyperexcitability, which can explain most of the characteristics of TN (38).

The treatment of TN is usually pharmacological. Standard treatment is with anticonvulsants, and the first choice is usually carbamazepine, but the efficacy may be compromised by poor tolerability and pharmacokinetic interactions. A better-tolerated alternative is oxcarbazepine with similar efficacy. Other anticonvulsants may be used as add-on medications (39). Neurosurgical procedures, preferably microvascular decompression surgery should be considered in case of poor response to pharmacotherapy or because of intolerable side effects caused by medication (40).

Painful posttraumatic trigeminal neuropathy

Trigeminal neuropathic pain may arise from intra- or extracranial lesions within the trigeminal system or general diseases

causing peripheral neuropathy such as diabetes, connective tissue diseases, or herpes zoster infection. The most important form of trigeminal neuropathic pain which dentists, and especially oral- and maxillofacial surgeons, should be aware of is, however, neuropathic pain caused by iatrogenic nerve damage. This entity belongs to peripheral painful posttraumatic trigeminal neuropathies (PPTTN). These are defined by a history of an identifiable traumatic event to the trigeminal nerve with clinically or neurophysiologically evident signs of sensory alteration, and pain which is located within the affected trigeminal distribution and has developed within 3-6 months of the traumatic event (30).

Many dental and surgical procedures, such as orthognathic surgery, third molar extraction, implant surgery, root canal therapy, and even local anaesthesia carry a risk of trigeminal nerve damage. Fortunately, neuropathic pain evolves in only a minority of these. The incidence of PPTTN has been reported to vary from 3 % to 6 % after endodontic treatment, and to be 5 % after surgical endodontics, 5 % after mandibular sagittal osteotomy, and 3 % after facial fractures. The prognosis of nerve damage greatly depends on the type of the damage; injuries in which only the myelin sheath is involved usually recover completely within four months, whereas the recovery of axonal injuries is much slower, and mostly incomplete. Posttraumatic neuropathic pain has been particularly related to axonal nerve damage of the small fibre system (41). Other risk factors for development of neuropathic pain include genetic factors, comorbid pain or psychosocial distress (42,43).

PPTTN is described as moderate to severe pain, which usually occurs consistently or daily. The pain is often characterized as burning, lancinating, stabbing, pressing or tingling (44), and is accompanied by sensory alterations, in most cases in the form of reduced function. Diagnosis of PPTTN can in some cases be straightforward when a patient after a procedure reports sensory symptoms and pain that persists beyond the normal healing time of tissue injury. However, after minor nerve injuries, sensory signs may not be obvious in clinical examination. Therefore thorough history taken with respect to previous surgery and trauma is important. Clinical sensory tests should be done carefully, testing different sensory modalities, but they are too crude to detect minor or old nerve injuries (41). Clinical neurophysiology offers many sensitive methods such as neurography, blink reflex test, QST and contact heat or laser evoked potential recordings to confirm the diagnosis, to localize the lesion, and to assess the type and profile of nerve fibre damage, which form the prerequisite for reliable appraisal of the prognosis (41). The tests are available in major hospitals of Nordic countries and they offer objective means to diagnose nerve damage, which is especially valuable in litigation cases.

The treatment of neuropathic pain relies mainly on pharmacotherapy, but thorough patient information, and helping patients to cope with the pain are essential parts of the treatment process, too. Surgical procedures are usually of no use, and can exacerbate the pain. First line drugs to treat neuropathic pain include tricyclic antidepressants, serotonin-noradrenaline reuptake inhibitors, gabapentin and pregabalin (36). Thera-

Facial pain conditions

	Pain character	Other symptoms, findings	Location	Duration	Provoking/aggravating factors
TMD	Aching, pressing, stabbing	Muscle/joint tenderness, functional disturbances, joint sounds	Cheek, temple, TMJ region	Varying, often continuous	Jaw opening, chewing
PIFP/AO	Aching, pressing	Usually none, subtle sensory symptoms possible	Varying/ tooth region	Continuous	Psychological factors
TN	Sharp, brief, electric shock like	Usually none	Trigeminal nerve distribution	Seconds – a few minutes	Tactile stimuli
Neuropathic pain	Burning, tingling, aching	Sensory alterations	Trigeminal nerve distributions	Continuous, may fluctuate in intensity	Often: Tactile/ thermal stimuli

TMD; temporomandibular disorder, TMJ; temporomandibular joint, PIFP; persistent idiopathic facial pain, AO; atypical odontalgia, TN; Trigeminal neuralgia

Table 1. Frequent features of different facial pain conditions.

Tabel 1. Karakteristiske træk ved faciale smertetilstande.

peutic brain stimulation (transcranial magnetic stimulation and motor cortex stimulation) offers a novel treatment line for treatment-resistant neuropathic pain within the orofacial region (45).

Differential diagnostics

Correct diagnosis is the *sine qua non* of successful treatment. Table 1, which features the most common or typical signs of different facial pain conditions, aims to provide a basis for the diagnostic work-up of chronic facial pain conditions.

Concluding remarks and future scenarios

Considerable progress has been made during the last decades in the understanding of the processes involved in facial pain. The complexity and multidimensionality of pain is increasingly comprehended, and more insights have been gained into the risk factors predisposing to chronic pain. In addition, improved and more reliable diagnostic systems and approaches have been introduced, and some advances have been made in the treatment of certain facial pain entities, such as neuropathic fa-

cial pains. However, many aspects of facial pain are still poorly understood, and much needs to be done to validate many of the methods used to treat facial pain, and to develop new improved, more effective treatment approaches with fewer side effects.

Science is advancing rapidly in the field of pain, including facial pain. The special areas of interest in facial pain research include molecular biology, biomarkers, imaging, genetics, and pain and psychological comorbidities, among others. It is to be expected that increased understanding of the pain mechanisms and other aspects of facial pain will in the future bring some novel therapeutic possibilities. For our patients a correct treatment is of uttermost importance. Treatment of chronic pain disorders have to be based on correct diagnosis and evidence based treatment modalities. The future will most probably also witness the rise of personalized pain medicine, where treatments are customized to fit each patient's pain and psychosocial, as well as genetic characteristics. In the light of rapid advances in the field of pain, much more emphasis should be put on pain education in the dental curriculums.

ABSTRACT (DANSK)

Persisterende faciale smertetilstande

Kroniske ansigtssmerter er en almindeligt forekommende lidelse, i særdeleshed i forbindelse med temporomandibulær dysfunktion (TMD). Da tandlæger er ansvarlige for behandlingen af de fleste af disse tilstande, er opdateret viden om de nyeste fremskridt inden for området helt afgørende for at kunne foretage vellykket diagnostik og behandling. Denne oversigt omfatter TMD og forskellige typer af neuropatiske eller formodede neuropatiske ansigtssmerter i form af vedvarende idiopatiske ansigtssmerter og atypisk odontalgi,

trigeminusneuralgi og smertefuld posttraumatisk trigeminus neuropati. Artiklen giver et overblik over TMD-smerter som en biopsykosocial tilstand, dens prævalens, karakteristika, centrale og perifere mekanismer, diagnostik (DC/TMD) og principper for behandling. Ligeledes beskrives definitioner, prævalens, karakteristika og diagnostik for hver af de forskellige typer af neuropatiske ansigtssmerter. Den aktuelle forståelse af patofysiologien af disse neuropatiske tilstande præsenteres, og der gives en beskrivelse af de evidensbaserede behandlingsmetoder.

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