# Recent advancements in Temporomandibular Disorders (TMDs)

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## SUMMARY POINTS

- TMDs are a group of conditions affecting the joint and or the muscles of mastication.
- TMDs consist of three main groups of conditions: myofascial pain; disc disorders; TMJ arthritides.
- The gold standard diagnostic criteria for research involving TMDs are the Research Diagnostic Criteria for TMDs (RDC/TMD). A pragmatic clinically applicable alternative is the Clinical examination protocol for TMDs (CEP-TMD).
- Signs and symptoms can include: pain in masticatory musculature and or the joint; noises associated with joint movements; locking; headache; otalgia.
- TMDs' aetiology is multifactorial and biopsychosocial in nature.
- Reversible conservative management as defined by the American Association of Dental Research is the initial management of choice for all subgroups of TMDs.

**Introduction**

Temporomandibular disorders (TMDs) have been known by many other previous names and debate over their classification is still ongoing[1]. It is appropriate at this point to highlight that TMDs is not a singular description[1] but a collective term describing a group of conditions affecting either the temporomandibular joint (TMJ), the masticatory musculature, or both.

TMDs can present with a multitude of signs and symptoms, which can sometimes be confusing to both the patient and clinician. The usual age group for presentation is in the second to fourth decades and despite the prevalence of TMDs being almost equal in the genders, females present clinically much more often[2]. The signs and symptoms of TMDs (Table 1) are familiar to dentists but not always to doctors.

**Table 1 Signs and symptoms of Temporomandibular Disorders**

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| Pain in masticatory musculature and or joint which can radiate and refer |
| "Locking" – can refer to closed lock, inability to open fully, or open lock, dislocation |
| Noises associated with movement of the joint: clicking or crepitus |
| Headache |
| Generalised "tightness" around face in the morning |
| Otalgia |

The most common of the conditions comprising TMDs are readily diagnosable using criteria such as the Research Diagnostic Criteria for TMDs (RDC/TMD)[3]:

- Myofascial pain
  - Myofascial pain with limited opening
  - Myofascial pain without limited opening
- TMJ Disc displacements
  - Disc displacement with reduction *(characterised by reproducible clicking)*

- Disc displacement without reduction with limited opening *(characterised by a "closed lock")*
- Disc displacement without reduction without limited opening

- TMJ Arthritides
  - Osteoarthritis
  - Osteoarthrosis
  - Arthralgia

Previous terminology for TMDs that is now superseded and largely falling into disuse includes: Facial Arthromyalgia, Pain-Dysfunction syndrome, TMJ, and temporomandibular joint dysfunction.

The aim of this paper is to discuss recent advances in the aetiology, diagnosis and management of TMDs

**Aetiology**

The aetiology of TMDs has been the subject of much debate over the years. Some of the debate has been scientific and some of it has been based on anecdote or experience. The aetiology of TMDs is regarded traditionally as multifactorial with predisposing, precipitating and prolonging factors, which conspire together variously in different patients. In reality, the aetiology of TMDs is still unclear with some suggesting that because of their link with other functional somatic syndromes TMDs may form part of the same phenomenon[4]. Clearly, patients with TMDs do present with psychological disorders but it is difficult to prove whether they are causative, or a result of the TMDs[5].

Much attention over the years has been paid to the way the teeth occlude (bite together). In most patients, however, occlusion has not been shown to have a strong enough causal relationship to be considered a general aetiological factor[6]. Reconstruction of the occlusion (occlusal rehabilitation, or occlusal equilibration) of the teeth is not therefore indicated in the majority of cases.

Potential breakthroughs have, however, recently occurred in understanding the possible physiological and genetic basis for some of the pain associated with TMDs. Recent data suggest that there may be adrenergic dysregulation in TMDs, which would help to account for their fluctuating nature especially during times of stress[7]. Further to this a US group based in North Carolina have been extensively investigating haplotypes of the gene encoding catecholamine-O-methyl-transferase (COMT).

Their findings suggest:

1) That COMT activity varies according to the three major haplotypes they have identified (low pain sensitivity, average pain sensitivity, high pain sensitivity)[8]

2) That haplotypes of the gene producing less COMT activity are associated with development of TMD and increased experimental pain sensitivity[8, 9]

3) Decreased COMT activity increases pain sensitivity through increased levels of circulating catecholamines activating ß2 and ß3 adrenergic receptors[9]

4) That COMT haplotype and psychological characteristics independently increase the risk of clinical pain[10]

5) That the relative risk of TMD associated with orthodontic treatment (which can act as an irritant through direct pressure on the teeth and changing the way the teeth occlude) was dependent on the pain sensitive haplotype of the gene encoding COMT[11].

The final development from this large programme of work is a proof-of-concept study using Propranolol versus placebo in patients suffering from TMDs with varying numbers of low-pain sensitivity alleles[12]. The sample tested included patients with TMDs, which were diagnosed by the RDC/TMD either as myofascial pain, or as myofascial pain with arthralgia. All participants had been experiencing pain for more than three months. A lower number of low-pain sensitivity alleles were significantly associated with greater net change in the pain index when low-dose propranolol was administered (20mg bd). Given that propranolol's mechanism of action is through non-selective antagonism of beta-receptors (Beta-1 and Beta-2) its positive effect on reducing the pain index would seemingly substantiate the potential role of circulating catecholamines on pain in TMDs.

Unsurprisingly the same group are helping lead the multi-million dollar OPPERA study in the U.S. (**O**rofacial **P**ain: **P**rospective **E**valuation and **R**isk **A**ssessment: https://www.oppera.org/). This prospective large cohort-type study seeks to examine and catalogue baseline physical and psychological data, including genotyping, on thousands of volunteers to attempt, for the first time, to prospectively identify risk factors and predictors for the myofascial and arthritides TMDs. One potential risk factor recently determined by genetics is that a polymorphism of the oestrogen alpha-receptor leads to a three-fold increase in risk of developing a painful TMD and a two-fold risk of developing a non-painful TMD as diagnosed by the RDC/TMD. It is possible that oestrogen influences the pain felt in TMDs through an effect on the Dopamine system[13] and degenerative disease through modulation of cellular responses in the TMJ[14].

Research on the aetiology of osteoarthritis and disc disorders in the TMJ has focussed largely on the role of protracted or excessive mechanical stress. This type of mechanical stress can be produced

in a number of ways but one of the more common mechanisms is parafunction (excessive clenching or grinding of teeth). It is suggested that protracted or excessive mechanical stress can result in the production of free radicals through a number of mechanisms[14-16]:

- homolytic fission through shear stress within articular tissues
- microbleeding into joint space leading to producing Ferryl radicals
- phospholipid catabolism caused by shear stress
- hypoxia-reperfusion injury – pressure created when mechanical stress exceeds end capillary pressure thereby causing a shift in cell metabolism
- stimulation of neuropeptide release giving rise to neurogenic inflammation causing further microbleeding.

A number of factors can then impair the normal scavenging system for free radicals in the TMJ system including: genotype, nutritional deficiency, or compromised synthesis of scavengers due to cells being mechanically stressed[14]. If the scavenging system is compromised there will be excess free radicals within the TMJ system[17,18]. Within the literature there are a number of hypotheses and some data to suggest that free radicals may exert a number of effects on the TMJ articular system[14-16, 19-27] (Table 2).

A particularly important effect of free radicals is the inhibition of hyaluronic acid synthesis. The lubrication system of the TMJ relies on free full fluid film provided through hyaluronic acid's highly viscous nature, and boundary lubrication to allow the joint and its disc to move smoothly and synchronously. Hyaluronic acid also helps protect the phospholipids present on the articular surfaces which form part of the boundary lubrication system. The decreased levels of hyaluronic acid make these phospholipids more prone to lysis by Phospholipase A2[21]. In health, the phospholipids' non-polar ends are exposed to the joint space creating a low friction surface through their hydrophobic nature (boundary lubrication). The degradation of the phospholipids by Phospholipase A2 results in a surface with higher friction and adhesive properties[21, 28, 29] and it has been suggested that this can result in an anchored disc phenomenon.

**Table 2 Potential actions of free radicals on TMJ articular system**

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| 1) Free radicals are proposed to damage the biomechanical properties of the articular tissues. The damaged articular tissues are then more susceptible to any further mechanical stresses placed upon them. This vicious circle is continued by the release of extracellular matrix degradation products from the damaged articular tissue. These degradation products attract inflammatory cells resulting in the release of cytokines that help further degrade the articular tissues[15]. |
| 2) Alongside mechanical stress, free radicals present in the joint space can stimulate the release of neuropeptides and Nitric Oxide from peripheral sensory nerve endings[23, 25, 26, 69]. The neuropeptides and Nitric oxide help increase the localised inflammatory response within the TMJ system and thereby contribute to further damaging the articular tissues through production of further free radicals and cytokines. |
| 3) Free radicals can help produce adhesions within the joint space[24,27]. |
| 4) Free radicals play a role in changing the lubrication system within the TMJ through inhibiting hyaluronic acid synthesis and facilitating the degradation of the articular surfaces' phospholipids[19]. |

Anchored disc phenomenon is suggested to be present when the articular disc is adhered to the glenoid fossa and renders the condyle unable to translate producing a considerable reduction in mouth opening suggested to be much more pronounced than disc displacement without reduction with limited opening and not necessarily preceded by clicking[19]. It is possible, however, that disc displacement without reduction and anchored disc phenomenon may be differing stages of the same clinical entity and distinguishing between them on clinical and radiological investigations may be somewhat subjective. The major difference asserted between the two is the very positive response of an anchored disc to arthrocentesis[19].

**Diagnosis**

In routine clinical practice diagnosis of TMDs has largely depended on a careful history and clinical exam with imaging, ionising or otherwise, playing a limited role. Electronic devices such as jaw tracking, vibratography, sonography have insufficient evidence to suggest their use as diagnostic devices[30]. Imaging of the temporomandibular complex is also not without its limitations in the main due to false positives: condylar shape and osseous changes on plain radiographs can occur in asymptomatic individuals and have little bearing on treatment[31, 32]; asymptomatic individuals have been shown to have disc displacements or joint effusions on MRI[33-37]. Cone-beam and computed tomography have been shown to have good sensitivity and specificity for osseous changes but evidence-based indications for their use have still to be determined[37]. Ultrasound is now being used to image the Temporomandibular complex and has varying sensitivity and specificity but maybe an area of future development[38], but at present imaging within the scope of TMDs is probably best employed as an adjunct to clinical diagnosis as opposed to a definitive diagnostic test.

In the research setting there was a need to reliably select homogenous samples to trial interventions. Clinical examination did not always fulfil the rigorous requirements for sample selection. The introduction of the RDC/TMD criteria in 1992 helped solve this problem and allowed researchers for the first time to be certain they were selecting samples with a reliable and valid diagnostic instrument[3].

The RDC/TMD has not, however, formed part of routine clinical practice within the UK perhaps largely due to an unfair reputation of being complex and somewhat time-consuming. Efforts have recently been made to simplify and shorten the RDC/TMD criteria for routine busy clinical practice[39]. This has produced a clinical examination protocol (CEP-TMD), which produces as reliable diagnoses in the same diagnostic categories as the RDC/TMD

but in significantly quicker examination times. The CEP-TMD is available for download and viewing at www.ncl.ac.uk/dental/AppliedOcclusion/. The RDC/TMD is currently undergoing revision for two purposes: (1) to provide a new updated RDC; (2) to provide a version, which is applicable in the everyday clinical setting[40].

Red flag signs and symptoms that might suggest a more sinister condition is mimicking TMDs include:

- Cranial nerve dysfunction especially in cranial nerves[1, 5, 7, 8]
- Late onset (>50) sudden profound limitation in mouth opening
- Recurrent epistaxis or discharge from nose
- Ipsilateral lymphadenopathy.

TMDs may occasionally present as part of a systemic condition affecting the joints, muscles or ligaments. Examples include rheumatoid arthritis, fibromyalgia and systemic joint laxity. As well as diagnosing the type of TMD it is also important to determine if such systemic conditions are present and properly addressed rather than manage TMD in isolation.

*Management*

Since the late 1970s it has been identified that patients with TMDs have a high placebo response rate and evidence has emerged over the generic biologically real effect of the placebo[41-47]. A recent paper has discussed the need to ethically and morally harness that biologically real effect within therapeutic interactions with TMDs patients without giving a placebo per se[48].

The paucity of high quality evidence on which to base management of TMDs is one of the main reasons that the American Association of Dental Research has issued a new scientific statement indicating reversible conservative therapy, for instance basic intra-oral appliances, biobehavioural therapy, physiotherapy, simple analgesia, as the initial management of TMDs[49].

Pharmacological management targeted to the pathophysiology of TMDs has been examined recently by two systematic reviews. The conclusions of the reviews were that pharmacological management of TMDs is largely empirical and there is a need to perform research to further establish key pathophysiological mechanisms in TMDs that would be suitable targets for pharmacological agents[50, 51]. There has been a recent promising trial of gabapentin in myofascial pain that shows a significant effect on pain although the effect may only be over a short time span[52].

A recent systematic review[53] of all relevant systematic reviews of management of TMDs drew the following conclusions:

- Occlusal appliances, acupuncture, behavioural therapy, and jaw exercises have some evidence showing they are effective in alleviating pain for patients with TMDs
- Occlusal adjustment appears to have no evidence supporting a therapeutic effect and has the disadvantage of being irreversible
- There is insufficient evidence to support surgical or electrophysical interventions in TMDs.

Similarly to occlusal adjustment orthodontic treatment has previously been used in the management of TMDs. A recent Cochrane review has, however, highlighted the lack of evidence to support or refute orthodontics as a preventative or therapeutic modality for TMDs and has suggested that orthodontics cannot, therefore be recommended as a treatment either to prevent, or relieve, TMDs[54].

The results of meta analyses such as those cited in the previous paragraph need to be interpreted with care so that a treatment which shows no therapeutic effect when used in a general population of TMDs is not withheld from TMDs patients who have a specific need and who have not responded to conservative management. For example, occlusal adjustment is certainly no better than placebo when used as a general primary treatment for a TMD, but if the TMD began at the placement of a recent restoration and this restoration is shown to create an occlusal interference it would be warranted to adjust this restoration. In this sort of a situation the occlusion may be a precipitating or a prolonging factor, which may exacerbate a TMD in patients predisposed to TMDs. The most important matter in these cases is that there needs to be a very good clinical indication to embark on irreversible treatment, this indication should be documented and its disadvantages fully discussed with the patient.

Whilst conservative management strategies should always be considered the first line of management of TMDs it is important to highlight the development of interest in TMJ surgical corrections. In this way the specialist pain team members can keep abreast of developments in this area. Surgical procedures for the TMJ include arthrocentesis, arthroscopy, open joint procedures, and total joint replacement. Arthrocentesis is the most minimally invasive of the four options but has the disadvantage of being a "blind" procedure only allowing lysis and lavage. Arthroscopy has the added benefit of being able to visualise the interior of the joint capsule, usually the upper joint space. This visualisation has led some to suggest it aids diagnosis as well as providing a therapeutic benefit. One meta-analysis has found it impossible to demonstrate a therapeutic advantage of arthroscopy over arthrocentesis[55], but another meta-analysis has highlighted the lack of evidence to support or refute the use of arthrocentesis in TMDs involving some form of internal derangement[56]. The best summary of both of these meta-analyses is that the current evidence base is of a poor quality and further work is required to help determine the indications for arthrocentesis and arthroscopy.

Both arthroscopy and arthrocentesis can be used to introduce medications into the joint capsule. Other than analgesics or anaesthetics, one of the more extensively examined medications is sodium hyaluronate. A group of European researchers have produced promising results with Sodium hyaluronate in combination with arthrocentesis for osteoarthritis of the TMJ[57-63]. Unfortunately though the level of evidence is still insufficient for recent systematic reviews to draw firm conclusions about Sodium hyaluronate's efficacy in the arthritides and disc disorders sub-classification of TMDs[64,65].

In recent years since the advent of arthroscopy open joint procedures have received less attention in the literature, but there has been a recent and limited resurgent interest in Temporomandibular joint replacement[66, 67]. This resurgent interest has led NICE to issue guidelines based on expert and patient opinion, and the current evidence base[68]. The British Association of TMJ Surgeons clearly state that this is a procedure to be carried out in end stage **disease** and has **few actual indications** within the spectrum of conditions comprising TMDs. There is also a danger that in patients with a degree of central sensitisation as a result of chronic pain related to TMDs such an acute insult to the peripheral nociceptive system might produce a further decline in their quality of life and pain management.

## Conclusion

There are some exciting new advances in understanding the pathophysiology of TMDs and the ongoing OPPERA study will further advance our understanding. At the current time patients suffering from TMDs still need a biopsychosocial approach to management, which may need to be carefully tailored in patients not responding to conservative management. In the future it may be possible to determine indications for treatment and target treatments on a genetic basis.

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