# Possible etiological factors in temporomandibular disorders of articular origin with implications for diagnosis and treatment

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#### Abstract

The authors reviewed the factors involved in the etiology, diagnosis and treatment of temporomandibular joint disorders (TMD). Although essential, specific criteria for inclusion and exclusion in TMD diagnosis have shown limited usefulness. Currently, the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) offer the best evidence-based classification for the most common TMD subgroups. The RDC/ TMD includes not only methods for physical diagnostic classification, comprised in Axis I, but also methods to assess the intensity and severity of chronic pain and the levels of non-specific depressive and physical symptoms, in Axis II. Although historically malocclusions have been identified as risk factors for the development of TMD--including those predominantly joint-related—in many cases the association established between these variables seems to have taken opposite directions. Regarding internal TMJ derangements, the results of studies on the induced shortening of the mandibular ramus, secondary to anterior articular disk displacement, indicate that repositioning the displaced disk in children or young adolescents may make more sense than previously imagined. The therapeutic use of dietary supplements, such as glucosamine sulfate, seems to be a safe alternative to the anti-inflammatory drugs commonly used to control pain associated with TMJ osteoarthritis, although evidence of its effectiveness for most TMD patients has yet to be fully established.

Keywords: Temporomandibular disorders. RDC/TMD. Disk displacement. Osteoarthritis. Malocclusion.

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#### INTRODUCTION

Temporomandibular disorders (TMD) refers to a set of conditions that affect the masticatory muscles and/or the temporomandibular joint (TMJ).<sup>30</sup> These conditions have failed to demonstrate a common etiology or biological basis in terms of clear signs and symptoms and, therefore, are considered a heterogeneous group of health problems related to chronic pain. Characteristic symptoms such as muscle and/or joint pain and/or pain on palpation, limited mandibular function and joint noises may be prevalent in isolation or in association, with a prevalence of up to 75% in the adult population.<sup>15</sup> Nevertheless, the emergence of some symptoms, such as joint noises, does not appear to be related—in the majority of the population—to pain or other important risk factors that require treatment.

Epidemiological studies suggest that the prevalence of symptoms such as pain and restricted movement range from 5-15%, with most cases occurring in young adults aged between 20 and 40 years, especially in females.<sup>15</sup> The low prevalence of TMD among older age groups, as seen in cross-sectional and longitudinal studies,<sup>18</sup> is consistent with the typically limiting nature of the symptoms.

The current classification is largely descriptive, based more on the presence of signs and symptoms than on etiology, mainly due to the fact that a full understanding of the relationship between etiological factors and pathophysiological mechanisms has not yet been achieved. From a clinical standpoint, however, it is probably irrelevant to extend the division of so-called diagnostic subgroups if all disorders within the same subgroup can be controlled using similar therapeutic procedures.

Therefore, specific inclusion and exclusion criteria for the diagnosis of these disorders would only prove crucial if tested to determine their validity. Currently, the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) provides the best evidence-based classification for the most frequent TMD subgroups,<sup>6</sup> i.e., those subgroups which experts now agree are different, based on criteria that can be replicated and scientifically evaluated. Thus, the RDC/TMD, a dual axis diagnosis and classification system designed for clinical research on TMD, comprises methods for the physical classification of TMD diagnoses (Axis I) as well as methods to assess the intensity and severity of chronic pain and levels of non-specific depressive and physical symptoms (Axis II). RDC/ TMD reliability has been tested and found to be satisfactory in adult populations,<sup>7,8</sup> whereas in children and adolescents<sup>29</sup> its validity and clinical utility has been demonstrated for Axis I but not completely for Axis II (although extensive studies by the National Institutes of Health/ NIH are currently well underway to examine the validity of all RDC/TMD components).

RDC/TMD Axis I addresses the physical conditions of TMD and aims to establish standardized diagnostic criteria for use in scientific research. The suggested system is hierarchical, allowing not only group diagnosis but also the possibility of multiple diagnoses for the same individual. It is thus divided into three major groups representing the vast majority of clinical TMD cases, i.e.: myofascial pain; articular disk displacement; and arthralgia, osteoarthritis and osteoarthrosis (Table 1).

The purpose of this study was to address possible etiologic factors involved in the development of temporomandibular disorders of articular origin (groups II and III according to the RDC/TMD) and suggest implications for diagnosis and treatment.

#### **INTERNAL TMJ DERANGEMENTS**

Internal TMJ derangement is an orthopedic term defined as a mechanical failure related to improper positioning of the TMJ articular disk combined with an interference in normal

TABLE 1 - Categories of clinical TMD conditions according to the RDC/TMD.

I - Muscular Diagnoses			
a - m	nyofascial pain		
b - myofascial pain with limited opening			
II - Disk Displacement			
a - di	isk displacement with reduction		
b - disk displacement without reduction and with limited opening			
c - disk displacement without reduction and without limited opening			
III - Arthralgia, osteoarthritis and osteoarthrosis			
a - a	rthralgia		
b - te	emporomandibular joint (TMJ) osteoarthritis		

c - temporomandibular	: - : - + /TN/I	
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mandibular movements. Articular disk displacement is only a subset of these disorders. When it is called articular disk displacement with reduction, it can be recognized by a 'pop' or 'click' sound in opening and closing the mouth, which only subsides when the mouth is open and maintained at maximum protrusion (RDC/ TMD Axis I, Group IIa).

Patients presenting with articular disk displacement have been characterized in terms of occlusion by the presence of unilateral posterior crossbite and long shifts from centric relation (CR) to maximal habitual intercuspation (MHI).<sup>26</sup> This correlation, however, was established without sufficient and unequivocal evidence to support the fact that this malocclusion is a risk factor for disk displacement.

Whereas the anterior articular disk displacement asymptomatic and unaccompanied by any other TMD indication (RDC/TMD Axis I, Group IIa) is quite common, with a prevalence of 20-35% of the population, on the other hand, disk displacement without reduction—which need not necessarily to be associated with pain, but may be associated with limitations in mouth opening (RDC/TMD Axis I groups IIb and IIc)—is relatively rare, with occurrence frequency ranging from 1-5% according to studies conducted in TMD clinics around the world.<sup>30</sup>

In some animal studies, where anterior displacements of the articular disk were surgically created in rabbits-keeping the ligament intact in the posterior condyle-their mandibles became significantly smaller in the side where the disk had been displaced, resulting in a midline shift in the affected side. Mandibular asymmetry was not observed in the group that had their articular disk displaced.<sup>16</sup> These results suggest that displacement of the articular disk may precede the development of mandibular asymmetry and can therefore be considered as a risk factor for the development of transverse malocclusion. Whether or not this sequence of events is relevant to the growth and development of the human mandible has not yet been established.

For appropriate treatment protocols to be implemented, however, it is first necessary to determine under what conditions and for which individuals it might prove wise to control and prevent these diseases. Future investigations are required, preferably focusing on the study of the biomechanical and biochemical events that can trigger disk displacement, such as changes in joint lubricating,<sup>22,23</sup> to determine whether there are specific conditions for the emergence of specific malocclusions.

Biomechanical analyses of TMJ hard and soft tissues have revealed that these tissues are normally capable of withstanding and adapting to the functional loads and pressures that occur during physiological mandibular movement. These tissues, however, cannot withstand compression for a long period of time, such as that associated with clenching in some individuals and at certain levels.<sup>22</sup>

In assessing the levels of intra-articular pressure in the TMJ of awake patients undergoing arthrocentesis procedures, Nitzan<sup>22</sup> found that voluntary clenching produced high levels of intra-articular pressure (as high as 200 mm Hg). Intra-articular pressure above 40 mmHg exceeds peripheral capillary pressure and can cause temporary intra-articular hypoxia followed by re-oxygenation as soon as the compression subsides, resulting in the release of free radicals.

A variety of effects caused by free radicals in articular tissue has been described<sup>22</sup>, including the degradation of hyaluronic acid, which, once degraded, loses the ability to inhibit enzyme phospholipase A2 and break the active surface of phospholipids, which are primarily responsible for the process of TMJ lubrication. Potentially, any increase in friction accompanied by a lack of proper lubrication is aimed at preventing the smooth functioning of the articular disk in conjunction with the mandibular condyle during normal functional movements. This condition may hypothetically trigger the anterior displacement of the articular disk, as described in detail by Nitzan<sup>23</sup>. However, these hypotheses have not hitherto been scientifically confirmed.

Theories and clinical observation have ascribed to articular disk displacement the occurrence of joint pain, limited mandibular movement, joint noises and degenerative TMJ changes. These reports are not at present supported by longitudinal data of any kind and suggest the possibility that the articular disk effectively protects the underlying tissues and that its displacement might expose these tissues to an additional, excessive pressure, thereby causing degenerative changes. This assumed sequence of events has led to the use of surgical procedures seeking to restore normal mandibular anatomy and movements, often resulting in serious complications<sup>20</sup> and eventually forcing professionals to question their belief in a necessary relationship between articular disk displacement and TMD related pain.<sup>5</sup>

Clinical observation has shown that articular disk displacement may be present in asymptomatic as well as symptomatic patients.<sup>14</sup> Likewise, the drainage of the upper TMJ compartment during arthrocentesis—in the presence of articular disk displacement without reduction—proved, in the short term, to be able to relieve pain and restore function without modifying the mandibular relationship between condyle and articular disk.<sup>24</sup>

Thus, as the symptoms associated with disk displacement are not always the outcome of this internal TMJ derangement, the concept of second stage therapy—whereby irreversible changes such as occlusion adjustment, prosthetics, orthodontics or orthognathic surgery are indicated—does not appear justified at this time<sup>2</sup>.

### **TMJ DEGENERATIVE CHANGES**

TMJ degenerative changes are characterized by the presence of clinical signs of continuous crackling noises (crepitus) in the joint. According to the RDC/TMD, crackling may be accompanied by arthralgia. It is named osteoarthritis or, in the absence of pain, osteoarthrosis.<sup>6</sup> Temporomandibular arthralgia is characterized by spontaneous pre-auricular pain or palpation and/or function induced pain, which is occasionally referred to the temporal region.

Patients with osteoarthritis are more consistently characterized by long shifts from CR to MHI, increased overjet and a tendency towards anterior open bite. An increased risk for these disorders is predominantly associated with extremes of these conditions.<sup>26</sup> Practitioners, however, are confronted with a dilemma to determine whether these malocclusions are etiological factors or consequences of dysfunctional joint remodeling.

It should be underscored that while osteoarthritis is a prevalent joint disease affecting multiple joints in the body with increasing prevalence in old age, TMJ osteoarthritis is a rare disorder according to epidemiological studies. Spontaneous pain in the TMJ decreases in prevalence with advancing age, especially in men over 55-60 years of age, where the prevalence of TMJ pain is extremely low. The possible relationship between osteoarthritis and anterior open bite does not seem to be frequent but may be a clinical finding that does not necessarily correlate to TMJ pain.

Morphological changes in the TMJ that are not associated with any significant change in joint dynamics or occlusion are features of functional remodeling. This remodeling becomes dysfunctional when it adversely affects mechanical joint function or occlusion and is therefore characterized by reduced condyle head volume, ramus size decrease, progressive mandibular retrusion in adult patients or perhaps a reduction in growth rate between children. This condition can be generated by excessive mechanical stress applied to or sustained by joint structures to the extent that the pressure exceeds the joint's ability to adapt to such changes.<sup>1</sup>

Again, although there is radiological evidence of extensive TMJ remodeling, this remodeling may be within a normal biological variation because the occurrence of pain or TMJ pathology requiring treatment is a relatively rare phenomenon in older people.

In some cases, extensive remodeling of the mandible can lead to occlusal instability reflected in open bite, increased overjet and sometimes, in cases where the mandibular muscles manage to secure an MHI position, an increase in the distance between this position and the so-call centric relation position. These relations were demonstrated by Pullinger and Seligman,<sup>26</sup> although the hypothesis that the degenerative process is an etiological factor for malocclusion still remains inconclusive.

Multiple variables, including genetic and environmental factors, such as behaviors or harmful breathing habits, have been shown to influence facial growth rate.<sup>12</sup> The data mentioned above suggest that dysfunctional remodeling can also produce defects in mandibular growth, which together with the other variables mentioned, could be contributing factors to the final mandibular position and may cause specific malocclusions, such as, for example, anterior open bite.

The balance between anabolic and catabolic events appears to be highly individual and subject to a wide range of functional and genetic factors.<sup>17</sup> There is a need, however, to enhance the understanding of normal, biological and biomechanical TMJ function, including the identification of variables associated with changes and increases in joint pressure levels. These variables can lead to microtraumatic stimuli to the tissue and, consequently, can trigger a series of events that could lead to degeneration and joint pain.

Proinflammatory cytokines have been isolated in samples of synovial fluid drawn from the TMJ of symptomatic patients, since recent evidence shows that free radicals can stimulate the synthesis of cellular proteins by increased expression of specific genes.<sup>27</sup>

The cytokines predominantly involved in intraarticular degenerative processes are interleukin-1 beta (IL-1beta), interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-alpha).<sup>21</sup> Together, these cytokines stimulate the breakdown of arachidonic acid thus causing a major proinflammatory effect and triggering the synthesis and activation of metalloproteinases, which are responsible for the breakdown of extracellular structure, accelerating the joint degeneration process.

## THERAPEUTIC IMPLICATIONS

As regards therapies, clinical trials are especially useful and, therefore, required by the U.S. NIH as the gold standard to evaluate treatment effectiveness. Clinical trials play an even more important part in conditions such as TMD, where pain intensity can vary over time and placebo and nonspecific effects can be just as important as in other chronic pain conditions.<sup>13</sup>

Dworkin et al<sup>8,9</sup> conducted randomized clinical trials which compared standard, conservative TMD treatment with self-control interventions and cognitive-behavioral techniques.

After monitoring the groups for one year, both showed improvements in all clinical categories as well as those observed by the patients themselves. Patients undergoing alternative treatment programs, however, exhibited a more satisfactory response, defined as greater reduction in (a) pain intensity, (b) level of interference in daily activities and (c) number of masticatory muscles painful to palpation.

These results indicate that the use of psychosocial assessment criteria such as, for example, those included in Axis II of the RDC/ TMD, can contribute to the success of clinical decision making regarding the control of TMD, especially muscle generated TMD. Conversely, predominantly articular disorders appear to suffer greater influence of localized phenomena.

In light of the wide array of studies that evaluate the efficacy of stabilizing plates in TMD pain control, Ekberg et al<sup>11</sup> argues that the differences raised in these studies may be due to the inclusion of different painful TMD subgroups, such as myofascial pain<sup>3</sup> and temporomandibular arthralgia.<sup>11</sup> The latter group has been shown to achieve significant therapeutic results in short<sup>11</sup> and long-term<sup>10</sup> follow-up.

In the study by Dao et al<sup>3</sup>, a randomized group used stabilizing plates only in the dental office during consultations. No significant effect was found on any clinical parameter that could distinguish it from other groups in the randomized study, i.e.: one group that used a stabilizing plate 24 hours a day and another that used a plate with no flat occlusion surface. In a randomized clinical trial scheduled for publication in the near future, a comparison was made between a group using a flat acrylic plate, another using a prefabricated soft device and a control group with no plates. No difference was found between the groups in course of pain, mandibular function or emergence of side effects after a one year follow-up.

Flat surface stabilizing acrylic plates may,

however, continue to be recommended for the treatment of TMJ arthralgia, although they still require further clarification as to the physiological mechanisms involved in their therapeutic effect, such as the reduction of parafunctionrelated mechanical stress.

Another study<sup>22</sup> that evaluated intra-articular pressure during functional and parafunctional movements also investigated 22 patients for intra-articular pressure against an interocclusal device, which uniformly increased the occlusion plane, reducing the force applied to the TMJ. A decrease in intra-articular pressure was observed at around 80% within a range of 0-40 mmHg.

The functional integrity of articular cartilage is determined by the balance between the synthesis of extracellular structure by chondrocytes and the breakdown of said structure. Glucosamine is normally found in human tissues and is directly involved in the synthesis of substances that are essential to maintaining joint function integrity, such as glycosaminoglycans, proteoglycans and hyaluronic acid, <sup>19</sup> although the precise mechanism behind this function has not yet been determined.

In osteoarthritis, this balance is disrupted by the increased presence of enzymes such as metalloproteinases, which are capable of breaking down the extracellular structure. Preliminary results of laboratory experiments<sup>4</sup> indicate that the dietary supplement glucosamine sulfate can stimulate the protein levels of the extracellular structure while simultaneously inhibiting the enzymatic production and activity of metalloproteinases in the chondrocytes of osteoarthritic joints.

Glucosamines were evaluated for their effectiveness in reducing pain associated with osteoarthritis in joints other than the temporomandibular joint and for its potential to change the course of the disease. In short-term clinical trials, symptom improvement was achieved in patients with osteoarthritis as well as promising results in altering disease progression after three years of follow-up,<sup>19</sup> although these findings have not yet been carefully evaluated.

Thie et al<sup>28</sup> compared the therapeutic potential of glucosamine sulfate with ibuprofen in patients with TMJ osteoarthritis. Both groups showed a significant improvement in the variables studied when these data were compared with those at the beginning of treatment. A comparison between these two groups showed that during the time period that patients used glucosamine sulfate they had a significant pain reduction in the affected joint and a decreased influence of pain on the patients' daily activities, thus reducing their related disability.

The specific effects of pain relief associated with the use of glucosamine sulfate are probably due to their anabolic properties in the cartilage. These effects, which change the degenerative condition of the disease, are not observed with the use of routine analgesics and can yield substantial benefits.

#### CONCLUSIONS

Although historically malocclusions have been identified as risk factors for the development of TMD—including those predominantly joint-related—in many cases the association established between these variables seems to wide of the mark. Thus, prospective clinical and laboratory investigations addressing issues related to the etiology of these conditions, especially in the early stages of development, can shed light on the future of therapy.

According to Legrell and Isberg,<sup>16</sup> the findings on induced mandibular ramus reduction secondary to articular disk displacement—indicate that the repositioning of the disk in children and young adolescents may make more sense than previously believed.

In view of the above, the use of orthopedic devices for mandibular advancement, such as the Herbst appliance, which has demonstrated effectiveness in improving the prior positioning of disks displaced in the early stages of this process,<sup>25</sup> should be tested by means of appropriate randomized clinical trials.

Whereas the therapeutic use of dietary supplements such as glucosamine sulfate seems to be a safe alternative to the use of anti-inflammatory drugs commonly used to control pain associated with TMJ osteoarthritis—in the same fashion as stabilizing plates—the evidence of their effectiveness for most TMD patients has not yet been fully established.

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