

This month we are introducing **Sophia Stone**, a new contributor to *TMJ News Bites*, whose passion is to separate temporomandibular (TMD) fact from TMD fiction. Sophia has a background in medicine and research and can draw on her personal experience as a TMD patient. She has recently moved to the Washington, DC, area and works as a content developer for a company preparing applicants for the admission tests required by professional health schools. She enjoys traveling, hopes to train for her next marathon, and occasionally eats crunchy foods she's not supposed to.



## Centralized Pain in TMD: Is it All in the Head?

I really love science. So much that I was part of an MD/PhD program so that I could be married to science for the rest of my life, but TMD (in part) thwarted those plans. Like many healthy 20-somethings, I developed TMD seemingly out of the blue during medical school. Admittedly this was a pretty stressful time of my life.

Fast forward a few years, I spent -- and spend -- a lot of my free time reading about TMD and trying to piece together all the different theories and ideas out there. The problem is that it's hard to get consistent advice from one healthcare provider to another, and even the scientific literature is littered with conflicting findings. Sigh.

Even with my background, it's been hard to sort through the fact and fiction. That's largely why I decided to start dissecting scientific articles, helping make this information more digestible and available to the rest of the TMD community, and geeking out about science. In these articles I will be discussing everything from review papers to new and interesting research findings, starting with the review paper [Pain Mechanisms and Centralized Pain in Temporomandibular Disorders](#) by Harper and colleagues (Harper DE, Schrepf A, Clauw DJ, 2016), published in the *Journal of Dental Research*.

### Background

Have you ever tried a treatment for TMD that you thought *should* work but didn't? Or a treatment that did work, but you have no idea why? I've been there, bought the t-shirt.

Normally, we expect the pain we experience from some stimulus to be directly proportional to the actual tissue damage present, whether in the jaw or anywhere else in the body, really. But in some chronic pain conditions, like TMD, the perception of pain doesn't match the actual amount of tissue damage present. Furthermore, there are vast disparities in how different people *with the same diagnosis* respond to different therapies. Why then is chronic pain so much worse than it "should" be, in many cases, and why are some treatments seemingly effective for some but not for others?

Well, first of all, TMD encompasses a broad range of symptoms and causes, as well as varied responses to treatment. My TMD is likely very different from your TMD. In fact, this review paper states that TMD can be defined as "persistent pain in the general orofacial region not clearly identifiable as headache." Well, that's helpful...

So, what's really going on here?

### **Pain Centralization**

The authors propose that we can categorize TMD patients on a spectrum based on how **centralized** their pain is. By centralized, they don't mean where the pain is localized in the body. In this context, the word "centralized" refers to the central nervous system (i.e., the brain and spinal cord), or in other words, how much does the central nervous system *amplify, maintain, or generate* pain, even with little or no pain signals from the peripheral location in the body where we feel our pain.

According to the authors, on one end of this spectrum, one's pain is more "peripherally-caused," meaning that the perceived pain in a peripheral location of the body, such as the jaw, is due almost entirely to the pain signals originating in the damaged joint or muscle tissue. On the other end of this spectrum, one's pain is more "centrally-caused," meaning that much of the perceived pain is *not* explained by the actual tissue damage, but rather explained by changes to the central nervous system.

The idea behind "centralized pain" is that the brain and spinal cord "remember" your pain and become hyperreactive to pain signals. This is thought to lower your threshold for pain and remind you that you're in pain. We can therefore define centralized pain as chronic pain where changes in the brain or spinal cord maintain or worsen your perception of pain.

### **The Evidence**

Do I buy it? Well, let's check out the evidence. What evidence is there that central sensitization plays a role in TMD? If TMD pain is really a brain-and-spinal-cord issue, then you'd expect the misfiring central nervous system to amplify pain not just in the TMJ region, but also elsewhere the body. (Note the irony of "centralized" pain really meaning that pain sensitivity is more *widespread* in the body.) The evidence for centralized pain playing a role in TMD can be grouped into 5 categories.

[Read more...](#)

## **TMJ Patient Featured in U.S. News & World Report Article**

The TMJA was recently contacted by a writer with U.S. News & World Report who was writing an article on temporomandibular disorders and asked us connect her with a TMJ patient to interview. We put her in touch with Lynn Tomfohrde of Spring, Texas who recently contacted us earlier this year about the difficulties she has faced in finding treatment and care for TMD. The TMJA is extremely grateful to Lynn for her willingness to be interviewed and educate readers about the realities of TMD by sharing her personal experience with a large audience. We invite you to read Lynn's interview at:

<https://health.usnews.com/health-care/patient-advice/articles/2018-04-05/what-is-tmd-and-why-cant-more-patients-find-effective-treatment>.

## Tissue-engineering Advance Grows Superior Cartilage for Joint Repairs

Articular cartilage is a substance that few people are aware of until they begin to experience pain, often debilitating, in their knees, shoulders and other joints. Then it is simple to understand that articular cartilage is the smooth surface that allows bones to interact efficiently at the joints during movement-performing flawlessly until nicked and scraped from injury or years of wear and tear. Bioengineers created a technique to repair articular cartilage with superior mechanical strength and durability.

[Click here to read more...](#)

## Prevalence of TMD in Sjögren Syndrome Patients

### Abstract

**Aims:** Sjögren Syndrome is a disorder involving oral tissues, with xerostomia, dysgeusia, dysphagia, tooth decay, gingivitis, angular cheilitis and glossitis. Temporomandibular disorders are a generic term referred to clinical conditions involving the jaw muscles and temporomandibular joint. The aim of this study was to investigate the prevalence of oral manifestations and temporomandibular disorders (TMD) in Sjögren Syndrome (SS) patients compared with healthy people.

**Methods:** The study group included 72 SS patients (2 men, 70 women) diagnosed according to the American-European Consensus Group (AECG) Criteria. A randomly selected group of 72 patients, matched by sex and age, served as control group. The examination for TMD signs and symptoms was based on the standardized Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) through a questionnaire and clinical examination.

**Results:** SS patients complained more frequently (95.8%) of oral symptoms (xerostomia, dysgeusia, dysphagia) than controls (22.2%) ( $\chi^2= 80.66$   $p< 0.001$ ). TMD symptoms (muscle pain on chewing, difficulty in mouth opening, arthralgia, headaches, tinnitus) were complained by 91.7% of SS patients and by 84.7% of controls ( $\chi^2= 1,667$   $p= 0,196$ ). At the clinical examination, 91.7% of SS had at least one oral sign respect to 75% of controls. The salivary flow measurements showed high statistical significance between the two groups (Unpaired test,  $p< 0,0001$ ). Myofascial pain (caused by muscular contracture) was significantly higher in the study group than in the control one ( $p\leq 0,05$ ). Furthermore 18.05% of SS patients showed deflection versus 5.5% of controls ( $\chi^2=5,402$   $p=0,020$ ).

**Conclusions:** Sjögren's Syndrome seems to play a role in temporomandibular joint disorders.

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**Source:** Crincoli V, Di Comite M, Guerrieri M, et al. [Orofacial Manifestations and Temporomandibular Disorders of Sjogren Syndrome: An Observational Study](#). *International Journal of Medical Sciences*. 2018;15(5):475-483. doi:10.7150/ijms.23044.

## Early Molecular Response and Microanatomical Changes in the Masseter Muscle and Mandibular Head After Botulinum

## Toxin Intervention in Adult Mice

We thank Dr. Susan Herring for providing our readers with this research summary.

In this small study, young adult mice received an injection of Botox in the right masseter muscle, while the left masseter received the same volume of saline as a control. The authors examined gene expression in the mandibular condyles 2 days after the injections and in the muscles 7 days after the injections. Two weeks after the injections, they looked for structural changes in the condyles and masseters.

The results showed dramatic early changes in gene expression. Only 2 days after treatment, the Botox side condyles showed four times as much activity in a gene that promotes bone resorption (RankL) than the saline side condyles. The Botox-injected masseters had greatly increased expression of genes involved in muscle atrophy at the 1 week time point compared to the control side muscles. At the end of the study, 2 weeks after injection, the Botox-injected masseters were about 20% smaller than the control side masseters, and the Botox-side condyles had lost about 40% of relative bone area compared to the control side condyles.

This study is preliminary in many ways. Sample size was very small and only included male mice of one inbred strain. Each outcome was measured at just one time point. The findings that Botox treatment of the masseter cause atrophy of the paralyzed muscle and severe loss of bone in the TMJ region are not new. Nevertheless, the study illustrates how rapidly the tissues react to treatment with this powerful toxin. It is striking that bone loss in the condyles was already triggered by the second day, because this bone loss is likely not a direct effect of the toxin, but rather a response to the absence of muscle loading.

From the point of view of The TMJ Association, important questions that remain include (1) does the bone of the condyle eventually recover, and if so, how long does it take? and (2) does the loss of condylar bone threaten the integrity of the TMJ and make it more vulnerable to injury? To date, there are no studies that address these questions in either animals or humans.

Source: Balanta-Melo J, Toro-Ibacache V, Torres-Quintana MA, Kupczik K, Vega C, Morales C, Hernández-Moya N, Arias-Calderón M, Beato C, Buvinic S. [Early molecular response and microanatomical changes in the masseter muscle and mandibular head after botulinum toxin intervention in adult mice](#) *Ann Anat.* 2018 Mar;216:112-119. doi: 10.1016/j.aanat.2017.11.009. Epub 2017 Dec 28.

## Beware of Ticks and Lyme Disease

Each year at this time we like to highlight the topic of Lyme disease because we have heard from a number of patients over the years who were misdiagnosed and underwent unnecessary Temporomandibular (TMD) treatments when they actually had Lyme disease.

The TMJ Association encourages patients who think they may have TMD to be sure to talk to their medical doctor in order to rule out other conditions which could be the cause their symptoms. Especially with Lyme disease, early diagnosis and treatment are important.

Chronic Lyme disease is called the "great imitator" because it is often misdiagnosed as another condition such as TMD, Multiple Sclerosis, Fibromyalgia, chronic fatigue, or anxiety. Misdiagnosis is a common experience for patients with chronic Lyme disease. [Click here to learn more about this topic and meet several patients who were misdiagnosed with TMD.](#)

## Sustained and Repeated Mouth Opening Leads to Development of Painful Temporomandibular Disorders Involving Macrophage/Microglia Activation in Mice

The following was published in the [March 2018 issue of Pain](#). This research was conducted by Guan Yun Frances Wang; Xiang Qun Shi; Wenjia Wu; Maria Gueorguieva; Mu Yang; Ji Zhang, Faculty of Dentistry, McGill University, Montreal, QC, Canada.

**Abstract:** Temporomandibular disorder (TMD) is a set of heterogeneous musculoskeletal conditions involving the temporomandibular joint (TMJ) and/or the masticatory muscles. Up to 33% of the population has had at least one symptom of TMD with 5-10% of them requiring treatment. Common symptoms include limited jaw movement, joint sound, and pain in the orofacial area. Once TMD becomes chronic, it can be debilitating with comorbidities that greatly reduce one's overall quality of life. However, the underlying mechanism of TMD is unclear due to the multicausative nature of the disease.

Here, we report a novel mouse model of TMD where a bite block was placed in between the upper and lower incisors such that the mouth was kept maximally open for 1.5h per day for 5 days. Following sustained mouth opening, mice developed persistent orofacial mechanical allodynia and TMJ dysfunction. At the cellular level, we found masseter muscle dystrophy, and increased proteoglycan deposition and hypertrophic chondrocytes in the mandibular condyle. Increased F4/80 macrophages were also observed in the masseter muscles and the TMJ posterior synovium. We also found ATF3 neuronal injury and increased F4/80 macrophages in the trigeminal ganglia. Microglia activation was observed in the trigeminal subnucleus caudalis. Inhibiting macrophage/microglia activation with a colony stimulating factor-1 receptor inhibitor prevented the development of orofacial mechanical allodynia, but not TMJ dysfunction.

This study suggests that mouth opening for an extended period of time during dental treatments or oral intubations may risk the development of chronic TMD and inflammation associated with macrophage/microglia in the tissue and trigeminal system contributes to the development of TMD pain.

## NIH Funding Opportunities

### Basic and Clinical Research

In an effort to promote greater understanding of TMD, and to develop safe and effective evidence-based diagnostics and treatments, The TMJ Association promotes and encourages basic and clinical research on Temporomandibular Disorders. [Click here to view the latest National Institutes of Health \(NIH\) funding opportunities for scientists interested in advancing TMJ research.](#) The following NIH research opportunities are currently available:

- Clinical Validation of Candidate Biomarkers for Neurological Diseases (U01 Clinical Trial Optional)
- Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY18 Administrative Supplement
- Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)
- Factors Underlying Differences in Female and Male Presentation for Dental, Oral, and Craniofacial Diseases and Conditions (RO1) (R21)
- NIDCR Small Research Grants for Secondary Analysis of FaceBase Data (RO3)
- Tailoring Dental Treatment for Individuals with Systemic Diseases that Compromise Oral Health (R01) (R21)
- Personalized Strategies to Manage Symptoms of Chronic Illness (R15) (R01) (R21)

- Research on the Mechanisms and/or Behavioral Outcomes of Multisensory Processing (R01)
- MAPP Network Basic/Translational Science
- Blueprint Neurotherapeutics Network (BPN): Small Molecule Drug Discovery and Development for Disorders of the Nervous System (UH2/UH3) (U44)
- Building Genetics and Genomic Knowledge about Dental, Oral, and Craniofacial Diseases/Disorders (R01)
- Population Health Interventions: Integrating Individual and Group Level Evidence (R01)
- Family-Centered Self-Management of Chronic Conditions (R21) (R01)
- mHealth Tools for Individuals with Chronic Conditions to Promote Effective Patient-Provider Communication, Adherence to Treatment and Self-Management (R01) (R21)
- The Biomarkers Consortium
- Notice of National Institute of Neurological Disorders and Stroke (NINDS) and National Institute on Drug Abuse (NIDA) Interest in Blueprint Neurotherapeutic Network Applications Directed at Small Molecule Non-Addictive Pain Therapies

## Research E-Newsletter

*Cutting Edge - COPCs Research Advances*, is an electronic newsletter published by the Chronic Pain Research Alliance, an initiative of The TMJ Association. Developed to keep the medical-scientific community abreast of



recent research advances, this publication contains abstracts of recently published studies on the epidemiology, pathophysiology and clinical management of Chronic Overlapping Pain Conditions. These conditions include **temporomandibular disorders**, chronic low back pain, chronic migraine and tension-type headache, endometriosis, myalgic encephalomyelitis/chronic fatigue syndrome, fibromyalgia, vulvodynia, irritable bowel syndrome and interstitial cystitis/painful bladder syndrome.

The most current issues are now available for your review at:

[http://www.cpralliance.org/New\\_Findings](http://www.cpralliance.org/New_Findings). If you would like to receive future issues of *COPCs Research Advances*, [click here to register](#).

## Educational Brochures on Chronic Overlapping Pain Conditions

This brochure addresses Chronic Overlapping Pain Conditions (COPCs), how COPCs are diagnosed, the complexity of the chronic pain experience, and how to work with your health care provider to develop a treatment plan. It is available by [postal mail](#) or as a [PDF on our website](#).

## Educational Brochures on TMD

*Your Guides for Temporomandibular Disorders* - This brochure written by the TMJA is a straightforward, easy-to-read booklet that guides patients in how to make health care decisions. It is available [by mail](#) or as a [PDF on our website](#) and we encourage you to share it with your friends, health care professionals and family members.

*TMJ Disorders* - This brochure is produced and distributed by the National Institute of

Dental and Craniofacial Research in partnership with the Office of Research on Women's Health, components of the National Institutes of Health (NIH) in Bethesda, Maryland. Part of the U.S. Department of Health and Human Services, NIH is one of the world's foremost medical research centers and the federal focal point for medical research in the United States. This booklet is available in English and Spanish at: <https://www.nidcr.nih.gov/OralHealth/Topics/TMJ/TMJDisorders.htm>.

## Dental Care Guide

### *Temporomandibular Disorders, Dental Care and You*

The TMJ Association developed this guide to provide you with oral hygiene self-care tips that you can do at home, as well as suggestions for future dental appointments. Routine maintenance of your teeth and gums should reduce the risk of dental disease and the need for invasive dental treatments. [Click here to view on our website.](#)

## TMJ Science Journal

Our latest issue of *TMJ Science*, which includes the summary and recommendations from our 8th scientific meeting--*How Can Precision Medicine Be Applied to Temporomandibular Disorders and Its Comorbidities*--is now available. We hope you're impressed with how far the science of Temporomandibular Disorders has come. [We invite you to read this new publication which is available in the publication section of our website as a pdf file.](#)

## Support Our Work

The TMJ Association (TMJA) is the only patient advocacy organization fighting for the best science that will lead to a greater understanding of Temporomandibular and related disorders, as well as safe and effective treatments. We cannot *change the face of TMJ* without YOU.

[Click HERE to make a tax-deductible online contribution today!](#)



## About The TMJ Association

### *Changing the Face of TMJ*

The TMJ Association, Ltd. is a nonprofit, patient advocacy organization whose mission is to improve the quality of health care and lives of everyone affected by Temporomandibular Disorders (TMD). For over 25 years, we have shared reliable information on TMD with people like you. We invite you to visit our website, [www.tmj.org](http://www.tmj.org).

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- [Read Past issues of TMJ News Bites](#) available on our website.

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