



The TMJ Association, Ltd.

Issue 1, 2019

## Genetic Differences Contributing to TMD Susceptibility in Males

*Dr. Shad Smith in the Department of Anesthesiology, Center for Translational Pain Medicine, Duke University, Durham, North Carolina wrote the following summary of this new publication for our readers. We thank you.*

Temporomandibular disorders (TMD) are the leading cause of chronic orofacial pain. They represent a type of "idiopathic" pain disorder, meaning that the cause or causes are unknown, but research over the decade suggests a genetic component contributing to susceptibility. There is also a well-known gender difference in frequency of TMD, with more women affected than men, especially in more severe and chronic cases. Further, evidence is accumulating that there are sex differences in the way men and women perceive and respond to pain.

To shed light on the role of genes in susceptibility to TMD, investigators are analyzing data from the Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA) study, a multi-university project led by investigators at the University of North Carolina at Chapel Hill. Initiated in 2006, the investigators recruited a diverse group of over 3,000 American adults, collected data and tissue samples reflecting behavioral, environmental, and genetic factors that might be associated with TMD. Over time, some of these subjects developed TMD; others did not. DNA from the volunteers was analyzed using a "gene chip" that assessed the presence of over two million genetic markers, single places in the genetic code called single nucleotide polymorphisms ("SNPs"). The aim was to detect any SNPs that distinguished TMD cases from controls for over 20,000 genes. The investigators found groups of SNPs on three different chromosomes that were associated with TMD status in the OPPERA subjects, including a set of variants on chromosome 3 near a gene called *MRAS*. Interestingly, the correlation between the SNPs and TMD only existed in male TMD subjects; there was no effect in females. They then checked seven other oral/facial pain studies, representing over 160,000 participants in total, to see if the chromosome 3 SNPs affected pain in those cohorts as well. It did. They saw that the same sex-specific effect was replicated in the other cohorts, confirming the OPPERA finding.

To understand the relationship of the SNP markers to nearby genes, the researchers examined how they affected the expression of these genes. It turned out that the SNP variants that were associated with greater TMD risk were associated with **lower** production of the RNA signal transcript of *MRAS*, indicating **lower** expression of the protein coded for by the gene. They then tested the pain sensitivity of mice engineered to have either two, one, or zero functional copies of the analogous *MRAS* gene. Female mice that had an injection of a substance into their paw producing inflammation showed a typical period of hypersensitivity to pain followed by recovery within 7-14 days, regardless of how many copies of *MRAS* they had. Male mice with functional versions of *MRAS* also showed a typical pain recovery pattern, but male mice with no functioning

MRAS remained hypersensitive to pain beyond two weeks. Evidence from both humans and mice therefore suggests that MRAS is part of an injury recovery pathway, and is needed for this pathway to function properly in males, but not females. This finding may lead to treatments that leverage MRAS function to recruit a person's innate resiliency against pain, although this approach may only be effective in males.

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## Self-care Treatments for Temporomandibular Disorders Most Beneficial, Study Finds

The following article appeared on [Dental Tribune](#).

**Dentists and patients use a variety of treatments to manage temporomandibular disorders (TMD). In a new study, researchers have found that patients rate treatments such as splints and bite guards as less helpful than self-care treatments, such as jaw exercises or warm compresses.**

"Oral appliances are a common first-line treatment for TMD, despite mixed research results regarding their benefit. Even when oral splints have been found to have some benefit, they have not been found to be as effective for patients who also have widespread pain in the treatment of myofascial TMD (mTMD)," said Vivian Santiago, assistant research scientist at the Department of Oral and Maxillofacial Pathology, Radiology and Medicine at New York University (NYU) College of Dentistry and the study's lead author.

In the study, researchers explored what non-medication treatments women with mTMD use to manage their pain and how effective patients perceive the treatments to be. Of the 125 women examined, oral appliances were used by 59 percent of participants, physical therapy by 54 per cent and at-home jaw exercises by 34 percent. Less common treatments included acupuncture, chiropractic treatments, trigger point injections, exercise or yoga and meditation or breathing, with 2.4 participants using more than one kind of treatment. Additionally, 26 patients of the 126 had both mTMD and fibromyalgia, allowing researchers to determine whether treatment differed for patients with widespread pain.

According to the study's results, 84 percent of participants reported that self-care activities, including jaw exercises, yoga or exercise, meditation, massage and warm compresses, helped them at least a little. In contrast, only 64 percent of those who used oral appliances reported that they helped a little. Of the women who used oral appliances, 11 per cent said that they had made their pain worse. The researchers did not find significant differences between the number of treatments reported by women with or without fibromyalgia.

**"Oral appliances did not outperform self-management care techniques in**

**improving facial pain.** Our results support the use of self-management as the first line of treatment for mTMD before considering more expensive interventions," said Karen Raphael, professor at NYU College of Dentistry and the study's co-author.

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Santiago, V. & Raphael, K.G. *Perceived helpfulness of treatments for myofascial TMD as a function of comorbid widespread pain.* *Clin Oral Invest* (2019).

<https://doi.org/10.1007/s00784-018-02797-6>

## National Academy of Medicine Study on Temporomandibular Disorders: From Research Discoveries to Clinical Treatment

An ad hoc committee, under the auspices of the National Academies of Sciences, Engineering, and Medicine's Health and Medicine Division, has been convened to study temporomandibular disorders (TMD) in a project entitled ***From Research Discoveries to Clinical Treatment***. The members will address the current state of knowledge regarding TMD research, education and training, safety and efficacy of clinical treatments of TMD, and burden and costs associated with TMD.

The members will identify approaches to advance basic, translational, and clinical research in the field. Their findings, conclusions, and recommendations will also inform development of policies related to evidence-based treatment and clinical management of TMD patients.

Specifically, the committee's task calls for members to:

**Review** and estimate the public health significance of TMDs, including prevalence, incidence, burden and costs; and review challenges to data collection and reliability.

**Evaluate** the evidence base for assessment, diagnosis, treatment, and management of acute and chronic TMD. Recognizing that TMDs are diverse and multifactorial conditions influenced by genetics, sex and gender, environmental, physiological, and psychological factors, this effort will:

- Address patient heterogeneity and challenges to patient stratification to better target therapies toward patients.
- Identify similarities and differences between chronic TMD, other chronic pain states (as well as chronic overlapping pain conditions), and other joint disorders such as phenotypic features that might predict responsiveness to treatments.
- Identify and characterize other non-pain comorbidities that diminish quality of life, including those that affect etiology and influence resilience, such as nutritional challenges and other neurological, metabolic, and mental health conditions (e.g. anxiety, depression).
- Examine the evidence-base for defining chronic TMD as a multi-system disorder that necessitates multidisciplinary research and interventions.

**Identify** barriers to appropriate patient-centered TMD care, in the presence and absence of an evidence base, and strategies to reduce these barriers along the continuum of TMD pain. This effort will:

- Evaluate elements and outcomes of patient-centered TMD care.
- Identify challenges to dissemination and implementation of evidence-based treatments and prevention strategies that are safe and effective.
- Determine and characterize health inequities in clinical TMD management.

**Review** the state of science for TMD and provide an overview of basic, translational, and clinical research for TMD. This effort will:

**Examine** existing or emerging TMD animal models and their preclinical utility.

**Identify** gaps and opportunities in TMD research relating to central and peripheral mechanisms, genetic/epigenetic contributions, heterogeneity of molecular mechanisms, joint mechanics, neuroimmune processes, endocrine influences, role of the microbiome, and endogenous mechanisms of resilience.

- Assess the intersection of sex differences in immune/neuroimmune and inflammatory responses in chronic TMD with other autoimmune diseases that are more prevalent in females or males.
- Assess progress on identification and validation of targets and biomarkers (genetic, neuroinflammation, neuroimaging, proteomic, behavioral, etc.) for use in establishing risk, diagnoses, treatment, outcomes, and reoccurrence.
- Identify potential approaches to using artificial intelligence for pattern recognition in patient datasets (e.g., genetic, biological, psychological, social traits, electronic health records, and patient-reported outcomes) to distinguish disease subtypes, develop individualized clinical decision support, and predict patient responses.
- Identify new and rapidly evolving tools and technologies with potential to significantly advance research, diagnosis, and treatment of TMD.

**Identify** opportunities and challenges for development, dissemination, and clinical implementation of safe and effective clinical treatments for TMD, including pharmacological agents, regenerative medicine, behavioral interventions, and complementary and integrative approaches.

**Identify** scientific and clinical disciplines needed to advance TMD science and the development, dissemination, and implementation of safe and effective treatments; as well as strategies to enhance education and training in these disciplines.

**Identify** multidisciplinary/interdisciplinary research approaches necessary in the short- and long-term to advance basic, translational, and clinical TMD research and to improve the assessment, diagnosis, treatment, and management of TMDs.

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The first meeting of the Committee was held on Tuesday, January 29, 2019 at the National Academy of Sciences building in Washington, D.C.

Terrie Cowley, President and Co-Founder of The TMJ Association, was asked to address the meeting. [Click here to view her presentation before the committee.](#)

The next National Academy of Medicine meeting will be held on March 28 and 29 in Washington D.C. and will include an open session to the public both days. More details are available

at: <http://www.nas.edu/hmd/Activities/PublicHealth/TemporomandibularDisorders/2019-MAR-28.aspx>

## National Institute of Biomaterials, Tribocorrosion and Nanomedicine Meeting Announcement

*The TMJ Association was asked to post the following meeting announcement.*

On April 15, 2019 in Chicago, IL the National Institute of Biomaterials, Tribocorrosion and Nanomedicine (IBTN) will hold its annual research meeting organized by UIC, Rush,

Midwestern and NU researchers. The conference offers the latest developments in healthcare materials and includes invited lectures, research and poster presentations.

The IBTN Annual Meeting provides numerous opportunities to hear the latest research discoveries from the experts, learn about technology advances in the field, participate in panel discussions and poster presentations, and build new network.

The theme this year is **"Advances in diagnostic and sensor technologies in health care."** Dr. Asimina Kiourti, Ohio State University will deliver the plenary talk on "Wireless biosensor: New development." There will be around eight lectures from the experts in the area of sensors and biomaterial/implant in healthcare research. The conference will end with a panel discussion on the presented subjects and a general discussion on upcoming research areas in health care sector.

The participants will get chance to meet and discuss with expert speakers and researchers at their poster presentations covering latest advancement in the following topics:

- Regenerative Medicine,
- Biomaterials, Implants,
- Tissue Engineering,
- Nano-medicine,
- Surface modifications,
- Cell-material interactions,
- Tissue imaging, Total Joint Replacements,
- Bio-Tribocorrosion,
- Bio-sensors, Bio-mineralization,
- In-Situ liquid-TEM Bio-imaging, 3D printing,
- Computational modeling,
- Tribology and Corrosion

More details at: <https://dentistry.uic.edu/calendar/8th-annual-ibtn-symposium>

## Meet Caryn...

I'm 36 and had issues with TMD as a child but was told my TMD was mild and wouldn't cause me any problems. Truthfully, I thought everyone experienced flashes of nerve pain and popping sometimes. When I got out on my own I realized none of the insurance I was paying for covered TMD. Literally, there'd be sections in the booklets devoted to telling me that TMD diagnosis and treatment was not covered. I didn't understand how my jaw was so controversial that no one would touch it. At least now insurance coverage is the teeniest bit better.

Three years ago, my jaw became stuck partially open twice, once while cleaning my teeth at home and the second time while receiving bitewing X-rays. Both times I "fixed" it myself by putting my thumbs in my mouth and forcing the joint. That same year, I found out I have Ehlers Danlos Hypermobility Syndrome on top of everything else.

After these accidents, my jaw started seizing up. I went to my GP who gave me a muscle relaxer and told me that a dentist would have to treat this issue. I chose a new dentist, who was very gentle and kind but told me I would need to see a specialist. He found an oral surgeon.



The oral surgeon sent me to a neurologist to screen me for trigeminal neuralgia because I had some numbness in my face when the pain was at its worst. The neurologist was very impatient with me and said I wasn't in anywhere near enough pain. I agreed that I didn't have TN but I don't know why he had to be so rude. He sent me back to the oral surgeon.

The oral surgeon did not allow note taking in his office as he said that it would cause me to not listen. When I told him I was in the process of getting an EDS diagnosis, he scoffed at me. He did tell me I had arthritis and a displaced disc. I spent \$1200 on a temporary splint that I was to wear 24/7 unless I was eating or brushing my teeth. It made me gag and lisp and after a month it hadn't gotten better. I couldn't tell if it was working or not. I was supposed to spend even more money getting a permanent version made to wear in perpetuity. I bailed on the treatment. If I could do it all over I would have asked more questions and maybe asked if there was a physical therapist I could see first.

My jaw did eventually feel better, with some spikes after eating something I shouldn't have or having dental work done. Recently, however, I had dental work done and then, while my jaw was still fragile, moved my face too hard (I was enunciating during play practice) and felt my jaw kick out to the side and heard a buzz in my ear. Now, I struggle with intermittent pain in my ear canal, tooth pain, spasms in my face, and nerve and muscle pain from my eye down to the back of my neck. Every day I experience spikes of severe pain. I am treating it with OTC medication, massage, stretches, and hot and cold packs. I'm trying to avoid hard food and things like salads and subs. I just can't afford to pay out of pocket for treatment in the dental world and the medical world has told me that they can't do anything but send me to the ER.

## Your Voice is Needed

The Pain Management Best Practices Inter-Agency Task Force released a draft report with recommendations to improve the management of acute and chronic pain. The recommendations cover a range of topics, from the importance of multidisciplinary care to considerations with opioid dosing. After a 90-day public comment, the report will be finalized and submitted to Congress.

We encourage you to read the report and provide comments prior to the April 1st deadline. For more information go to:

<https://www.hhs.gov/.../advisory-comm.../pain/reports/index.html>

## Attention Canadian TMJ Implant Patients

The TMJ Association has been asked by the lawyers for this class action lawsuit to publicize the following message:

*The Trial of the Class Action brought by Canadian patients who were implanted with Vitek Proplast TMJ implants, against Health Canada, alleging negligent regulation starts on April 1, 2019 in Toronto.*

*Class counsel are very interested in hearing from any TMJ implant patient (Proplast, Silastic, or other) who have spoken to or have communicated with Health Canada at any time from the 1980's to the present about problems they have been experiencing with their TMJ implants.*

*They are asked to contact either David Steeves ([dsteeves@leggeandlegge.com](mailto:dsteeves@leggeandlegge.com)) or*

## 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:

#### New Funding Opportunities:

- Achieving Tissue Robustness Through Harnessing Immune System Plasticity (R21)(R01)
- HEAL Initiative: Translational Development of Devices to Treat Pain (U18)
- HEAL Initiative: Translational Devices to Treat Pain (UG3/UH3)
- HEAL Initiative Translational Devices to Treat Pain (U44I)
- HEAL Initiative: Clinical Devices to Treat Pain (UH3)
- HEAL Initiative: Stimulating Peripheral Activity to Relieve Conditions (SPARC): Anatomical and Functional Mapping of Pain-Related Visceral Organ Neural Circuitry (U01)
- Promoting Research on Music and Health: Fundamentals and Applications (R01) (R21)
- Mechanisms, Models, Measurement, and Management in Pain Research (R01) (R21)
- Global Brain and Nervous System Disorders Research Across the Lifespan (R21)
- NIDCR Small Research Grants for Data Analysis and Statistical Methodology Applied to Genome-wide Data (R03)

#### Additional Funding Opportunities:

- Research on Chronic Overlapping Pain Conditions (R01)(R21)
- Analytical and/or Clinical Validation of a Candidate Biomarker for Pain (R61/R33)
- Clinical Validation of Candidate Biomarkers for Neurological Diseases (U01)
- Discover and Validation of Novel Targets for Safe and Effective Pain Treatment (R01)(R21)
- Factors Underlying Differences in Female and Male Presentation for Dental, Oral, and Craniofacial Diseases and Conditions (R01) (R21)
- NIDCR Small Research Grants for Secondary Analysis of FaceBase Data (R03)
- Tailoring Dental Treatment for Individuals with Systemic Diseases that Compromise Oral Health (R01) (R21)
- Blueprint Neurotherapeutics Network (BPN): Small Molecule Drug Discovery and Development for Disorders of the Nervous System (UH2/UH3) (U44)
- 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
- Blueprint Neurotherapeutic Network Applications Directed at Small Molecule Drug Discovery and Development of Disorders of the Nervous System

**Connect anonymously with others  
who understand what you are going  
through!**

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TMJ Cafe Support Community**

**TMJ.Inspire.com**

## 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.



**CUTTING EDGE** a publication of CHRONIC PAIN  
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[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 [postal 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).

- If you're not currently receiving *TMJ News Bites* and would like to [be on our mailing list, sign up here.](#)
- [Read Past issues of TMJ News Bites](#) available on our website.

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