



## TMJ News Bites

Issue 4 2019

### It's Time For You To Be Part of the Solution!

The National Academy of Medicine (NAM) [Study on Temporomandibular Disorders \(TMD\)](#) is well underway. The NAM's next meeting is August 21-22 (committee members only). **We strongly encourage everyone affected by TMD to write to the NAM committee letting them know what it is like to live with TMD and your experiences with getting care. Please don't let this opportunity pass by! Simply send an email to: [TMDstudy@nas.edu](mailto:TMDstudy@nas.edu).**

Take time and watch the public meeting proceedings if you haven't done so already.

- **January 29-30, 2019 Public Workshop.** ([View agenda](#)). No recording is available, however presentations by the following can be viewed:
  - [Dr. Malvina B. Eydelman](#)
  - [Dr. Danica Marinac-Dabic](#)
  - [Drs. Richard Ohrbach and Roger Fillingim](#)
  - [Terrie Cowley](#)
- **March 28-29 2019 Public Workshop.** ([View agenda](#)). [To watch the public workshop from March 28-29, click here.](#) Please note you need to click the link "By Session" or "All Videos" to watch each presentation as they are saved as individual files on the NAM website.
- **June 19, 2019 Webinar on Patient Care.** Dental providers were asked to share their experiences and perspectives on caring for people with TMD ([View agenda](#)). [Click here to watch the June 19th recording.](#)
- **July 31, 2019 Webinar on Professional Education, Research and Specialization.** The webinar provided perspectives from dental educators about professional education, research, and specialization related to TMD ([View agenda](#)). [To watch the July 31st webinar, click here.](#)

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### Predicting Pain that Persists

*Clinical clues may foretell chronic temporomandibular disorder*

In Brief:

- Researchers found that pain-related clinical

measures—but not psychosocial factors such as stress and negative

- These predictive measures might help clinicians identify the most at-risk patients and take steps to prevent or provide earlier treatment for chronic painful TMD.

TMD is the most common facial pain condition, affecting 5% to 12% of US adults. Because up to two-thirds of patients with TMD have jaw-related pain that lasts at least six months, it's important to identify and treat those at high risk for persistent, or chronic, painful TMD. However, researchers had lacked clear evidence of clinical indicators that might identify patients most likely to have enduring pain associated with a TMD diagnosis.

Now a team of NIDCR-supported scientists report that they've identified several clinical symptoms and signs that can help predict whether TMD pain will linger and turn into chronic painful TMD. Among their findings: During a clinical exam, pain elicited by an examiner, and/or pain coupled with clicking or crunching sounds when opening the mouth or moving the jaw, may indicate a person is at increased risk of developing chronic TMD. The research, published in the July issue of the *Journal of the American Dental Association*, could help providers treat high-risk patients early to prevent the condition from progressing.

"A patient's first visit to a provider for jaw-related pain is an important timepoint to assess whether pain is likely to be self-limiting or to persist," says Richard Ohrbach, DDS, PhD, senior author and professor of oral diagnostic sciences at the University at Buffalo. "Our results identify simple clinical measures that can be easily obtained during that first consultation to determine whose pain may progress and to intervene early."

The authors analyzed clinical data from 260 research participants at first diagnosis of a painful TMD and then eight months later. The research was part of the larger NIDCR-funded Orofacial Pain Prospective Evaluation and Risk Assessment (OPPERA) study, which followed nearly 3,000 initially TMD-free participants over several years to find out what causes the condition.

In the study published here, patients who developed chronic TMD were more likely to have a recent history of pain from jaw movement during activities such as eating or talking. They were also more likely to have muscle and joint pain elicited during an exam, as well as pain coupled with clicking or crunching sounds when instructed by an examiner to open the mouth or move the jaw back and forth. Using a mathematical model, the researchers found that these pain-related clinical measures strongly predicted chronic painful TMD.

While an earlier study showed that psychosocial factors such as pre-existing stress and negative mood predicted first onset of TMD, the researchers were surprised to find that these measures did not predict chronic painful TMD. Psychosocial distress may continue at the same level before and after TMD onset, so it may not offer any additional predictive value for chronic TMD, the authors suggest. Still, assessing patients' psychosocial status at the time of clinical consultation remains important, because it could shed light on contributing factors and treatment options. The authors conclude that the predictive clinical signs and symptoms are easy for clinicians to measure and could help them provide care that is better tailored to a patient's level of risk for chronic TMD.

### Reference

Meloto, Slade, Lichtenwalter, Bair, Rathnayaka, Diatchenko, Greenspan, Maixner, Fillingim, Ohrbach. [Clinical predictors of persistent temporomandibular disorder in people with first-onset temporomandibular disorder](#). *JADA*, July 2019, 150 (7): 572-581. PMID: 31248483

<https://www.nidcr.nih.gov/news-events/predicting-pain-persists>



# Condition Long Thought To Be Imaginary

*New research suggests serotonin could be involved in a condition where patients experience physical discomforts for which there is no physiological explanation*

An international team spearheaded by researchers at McGill University has discovered a biological mechanism that could explain heightened somatic awareness, a condition where patients experience physical discomforts for which there is no physiological explanation.

Patients with heightened somatic awareness often experience unexplained symptoms - headaches, sore joints, nausea, constipation or itchy skin - that cause emotional distress, and are twice as likely to develop chronic pain. The condition is associated with illnesses such as fibromyalgia, rheumatoid arthritis and **temporomandibular disorders**, and is thought to be of psychological origin.

"Think of the fairy tale of the princess and the pea," says Samar Khoury, a postdoctoral fellow at McGill's Alan Edwards Centre for Research on Pain. "The princess in the story had extreme sensitivity where she could feel a small pea through a pile of 20 mattresses. This is a good analogy of how someone with heightened somatic awareness might feel; they have discomforts caused by a tiny pea that doctors can't seem to find or see, but it's very real."

Thanks to an existing study on genetic association, Samar Khoury and her colleagues might have found the elusive pea capable of explaining somatic awareness.

Their work, recently published in the *Annals of Neurology*, used data available through the Orofacial Pain: Prospective Evaluation and Risk Assessment cohort and demonstrates that patients who suffer from somatic symptoms share a common genetic variant. The mutation leads to the malfunctioning of an enzyme critical for the production of serotonin, a neurotransmitter with numerous biological functions.

"I am very happy and proud that our work provides a molecular basis for heightened somatic symptoms," says Luda Diatchenko, lead author of the new study and a professor in McGill's Faculty of Dentistry. "We believe that this work is very important to patients because we can now provide a biological explanation of their symptoms. It was often believed that there were psychological or psychiatric problems, that the problem was in that patient's head, but our work shows that these patients have lower levels of serotonin in their blood."

The results of their study have laid the groundwork for the development of animal models that could be used to better characterize the molecular pathways in heightened somatic awareness. Above all, Diatchenko and Khoury hope their work will pave the way for treatment options.

"The next step for us would be to see if we are able to target serotonin levels in order to alleviate these symptoms," says Diatchenko, who holds the Canada Excellence Research Chair in Human Pain Genetics.

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This work was supported by the Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, the National Institutes of Health and the National Institute of Dental and Craniofacial Research.

"A functional substitution in the L-aromatic amino acid decarboxylase enzyme worsens somatic symptoms via a serotonergic pathway," by Samar Khoury et al. was published in the *Annals of Neurology*.

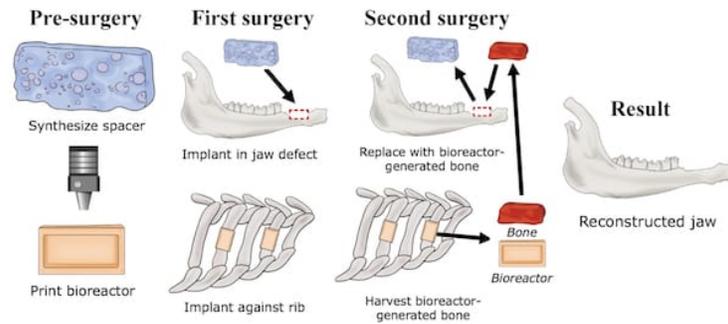
[https://www.eurekalert.org/pub\\_releases/2019-06/mu-slt061919.php](https://www.eurekalert.org/pub_releases/2019-06/mu-slt061919.php)

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## Researchers Grow Bone at Rib to Restore Facial

# Bone

A team led by Rice University bioengineers with support from the National Institute of Biomedical Imaging and Bioengineering (NIBIB) used bone engineered in a shape defined by a 3D-printed mold and grown alongside the ribs



of sheep to successfully replace a portion of the animals' jaw bones. The researchers hope to develop the tissue regenerative procedure for human application so that craniofacial injuries could be treated with bony tissue grown alongside natural bone rather than removing bone from elsewhere in the body for grafting and implantation. "Restoring bone structure lost to injury or disease is an important target for tissue engineering research," said Šeila Selimović, director of the NIBIB program in Technologies for Tissue Chips, Engineered Tissues, and Biosensors and Physiological Detectors. "The research applies a complex process that makes innovative use of biomaterials and tools such as 3D printing to generate bony tissue for jaw reconstruction."

The human jaw sustains repetitive force while biting and chewing a varied solid-food diet. Sheep use similar biomechanics to macerate feed pellets and hay. A set of muscles connected to bone work in combination, pivoting the lower jaw—or mandible—up and down and from side to side. When injury or disease causes jaw damage and tissue loss, bone implants are sometimes required to reconstruct the jaw, which must be able to replicate this hard-working anatomical structure.

Researchers developed a technique to grow custom-fit bone implants to repair jawbone injuries from a patient's own rib. Illustration: Mikos lab.

A multi-institution team, led by bioengineer Antonios Mikos, Ph.D., the Louis Calder Professor of Bioengineering and Chemical and Biomolecular Engineering at Rice University and a director of the NIBIB-funded Center for Engineering Complex Tissues, performed the sheep study based on the team's vision of a process, called biomaterials-aided mandibular reconstruction. Among the team are members from the University of Texas Health Science Center at Houston.

"We have been gratified to contribute a regenerative solution for the potential treatment of craniofacial defects," Mikos said. "This work is testament to the value of team science." In their study, published in the March 18, 2019, Proceedings of the National Academy of Sciences, the researchers created rectangular defects in the lower jaw of six sheep. They used a spacer, which temporarily preserved the shape of the jaw at the defect site, and produced 3D printed molds, called bioreactors, used to grow replacement bone tissue. They filled the bioreactors with either a biocompatible ceramic or with crushed bone, anticipating that each material would be a good medium for growth of replacement tissue.

The researchers implanted four bioreactors in each sheep, next to rib bones with

exposed periosteum, a layer of vascularized connective tissue that surrounds bones. Bone tissue was then allowed to grow from the periosteum into the bioreactor during a period of nine weeks. After that time, the researchers removed the spacers from the lower jaws and implanted the bioreactor-grown tissue in their place. Researchers found that the two materials grown in the bioreactors that were initially filled with either the ceramic or crushed bone were sufficient for implantation, however, the tissue grown from crushed bone had mechanical properties more similar to natural bone so they used these in the ultimate implantation procedure.

Twelve weeks after implantation of the bioreactor-grown tissues in the jaw, the researchers observed that the new bone knitted to the natural bone and that soft tissue grew to cover the wound site. The results demonstrated that viable bone tissue that could substitute for grafts taken from one's leg, the current clinical procedure, could be made from bony materials grown with 3D printed bioreactors.

The research was supported in part by NIBIB (EB023833), the National Institute of Dental and Craniofacial Research (DE027586), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (AR071258 and AR067606), all parts of the National Institutes of Health, as well as by an NIH-cosponsored Armed Forces Institute of Regenerative Medicine grant (W81XWH-14-2-0004). Additional support for the research came from the Osteo Science Foundation, the Barrow Scholars Program, and the Robert and Janice McNair Foundation.

[Biomaterials-aided mandibular reconstruction using in vivo bioreactors.](#) Tatara AM, Koons GL, Watson E, Piepergerdes TC, Shah SR, Smith BT, Shum J, Melville JC, Hanna IA, Demian N, Ho T, Ratcliffe A, van den Beucken JJJP, Jansen JA, Wong ME, Mikos AG. Proc Natl Acad Sci U S A. 2019 Mar 18.

## Patient and Caregiver Connection Town Hall

On Tuesday, June 18, Dr. Jeffrey Shuren, The Center Director of the Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) welcomed everyone to the FDA's Town Hall to introduce the new Patient & Caregiver Connection Pilot Program.



This program was established in 2018 to provide FDA with rapid access to individual patients and caregivers to better understand their direct, personal experience, with specific disease states and/or medical devices used for the diagnosis, treatment or assessment of various conditions, to further the mutual goals of considering the perspective of patients in FDA's decision making process. Dr. Shuren said the goals of the program are to understand the patient's perspectives and proactively incorporate them into FDA decisions and regulatory activities where appropriate. He said the benefits of hearing the patient voice will help inform device design and clinical trials, bring to light

new considerations to inform FDA's thinking on current issues, and raise or confirm problems that may exist with specific devices, as well as communicate treatment preferences, and identify population's views on benefit-risk for a given treatment.

Fourteen patient advocacy organizations participated, each presenting a brief overview of their organization's work and mission followed by a Q&A session and time for FDA staff to meet and talk with each of the patient groups. Deanne Clare, The TMJ Association's Administrator, participated in this event. Other nonprofit patient organizations in attendance included the National Alliance of Caregivers, International Children's Advisory Network, National Organization for Rare Diseases, Faces & Voices of Recovery, Global Health Living Foundation, COPD Foundation, Juvenile Diabetes Research Foundation, The Michael J. Fox Foundation for Parkinson's Research, Mended Hearts, North American SCI Consortium, American Association of Kidney Patients, and Facing our Risk of Cancer Empowered.

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## New CME on Chronic Overlapping Pain Conditions

The Chronic Pain Research Alliance, an initiative of The TMJ Association, in partnership with the International Pelvic Pain Society, is pleased to announce the release of our newly developed Continuing Medical Education (CME) program on Chronic Overlapping Pain Conditions (COPCs) titled, ["A Biopsychosocial Approach to the Clinical Management of Chronic Overlapping Pain Conditions."](#)

This activity - hosted by the International Association for the Study of Pain (IASP) - is designated for 1 AMA PRA Category 1 Credit. If you are not a current IASP member (or do not have IASP login credentials), please follow the instructions below to access the course free of charge by registering as a non-member. To access the program, visit: <https://www.pathlms.com/iasp/courses/11652>.

If you are interested in obtaining a copy of the course's PowerPoint slide set and corresponding slide notes for teaching purposes, please contact CPRA's Director, Christin Veasley by email ([cveasley@cpralliance.org](mailto:cveasley@cpralliance.org)).

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others who understand what  
you're going through!**

- The TMJ Association, Ltd.

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## **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**

- Limited Competition: Dental, Oral and Craniofacial Tissue Regeneration Consortium (U24 Clinical Trial Not Allowed)
- Request for Information (RFI): Identification of Potentially High Value Biomarkers for Predicting Acute to Chronic Pain Transition and Resilience
- 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)
- 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)
- Mechanisms Underlying the Contribution of Sleep Disturbances to Pain (R01) (R21)
- Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations an ORWH FY19 Administrative Supplement

## 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

## 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!](#)



## Educational Publications

### E-Newsletters

*TMJ News Bites*

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

### Chronic Overlapping Pain Conditions Brochure

This brochure addresses Chronic

If you're not currently receiving TMJ News Bites and would like to [be on our mailing list, sign up here.](#)

## **Cutting Edge - COPCs Research Advances**

*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.](#)



**CUTTING EDGE** a publication of CHRONIC PAIN Research Alliance  
COPCs Research Advances

## **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](#)

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.](#)

## **Your Guide to 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.

## **NIH Brochure on 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.](#)

[publication which is available in the publication section of our website as a pdf file.](#)

## 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 30 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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