

Anti-inflammatory Drugs Associated with Increased Risk of Persistent Pain

A recent research article in *Science Translational Medicine* by an international team of researchers led by Luda Diatchenko of McGill University in Montreal, Canada has shed light on the role of an acute inflammatory response in preventing the transition to chronic pain and the surprisingly counterproductive role of non-steroidal anti-inflammatory drugs (NSAIDs) in enhancing the transition to a chronic condition. These researchers used results from multiple preclinical models and several human cohorts with low back pain (LBP) and temporomandibular disorder (TMD) to substantiate their conclusions.

In one study of 98 patients with acute LBP, those who had an early, robust inflammatory response as measured by increased gene expression and neutrophil (a type of circulating immune cell) activation, resolved their LBP rapidly. However, those patients who had no or a reduced early inflammatory response, with very few changes in gene expression and little neutrophil activation developed persistent LBP. The genes that showed the greatest changes in expression were related to an increased inflammatory response.

A second cohort of patients with TMD, a different but similar musculoskeletal pain condition, also showed comparable changes in acute inflammatory gene expression and neutrophil activation in those cases where TMD was rapidly resolved, but not in those patients who developed chronic TMD.

In preclinical pain models, early treatment with steroids or NSAIDs led to prolonged pain despite being analgesic at short times. Acute treatment with other analgesics like gabapentin, morphine or lidocaine did not prolong the pain.

A human population study utilizing data from the United Kingdom Biobank project found that patients with acute LBP were at higher risk of developing chronic LBP if they reported use of NSAIDs compared to LBP patients who reported no use of NSAIDs.

The results from this study show that an early, robust inflammatory response may be key to preventing the transition from acute to chronic pain conditions. The results substantiate the idea that chronic pain is a neuroinflammatory

condition involving the nervous and immune systems. The results suggest the perhaps counterintuitive concept that an active inflammatory biological process underlies pain resolution rather than pain progression to chronic status. The results further suggest impairment of such inflammatory responses in those with acute LBP or TMD increases the risk of developing chronic pain.

Source: <https://www.science.org/doi/10.1126/scitranslmed.abj9954>

From the National Academy of Medicine Report on Temporomandibular Disorders

The National Academies of Sciences, Engineering, and Medicine Consensus Study Report on Temporomandibular Disorders - Priorities for Research and Care was published in March 2020. The excerpt below is from the Introduction, pages 17-18. To view the full report, visit: <http://tmj.org/wp-content/uploads/2020/12/NAM-Report-on-TMD.pdf>.

TMD has affected every aspect of my life: physically, emotionally, financially, psychologically, professionally, and it has affected my relationships, my passions, my independence, and at times my dignity. It cut me off at the knees and changed the landscape of my life, and what I imagined my life would be. I have had to accept that, we've all had no choice but to accept that. — Adriana V.

Introduction

Consider the joints of the human body. What might first come to mind are the hips and knees—the large joints that support us in our mobility—followed by the wrists, ankles, elbows, fingers, and toes—the smaller joints that support nearly everything else. What can be overlooked, although clearly evident in the mirror, is one of the most used, most necessary, and perhaps most misunderstood set of joints—those of the jaw—which are critical to the vital work of human life, including eating, talking, kissing, and even breathing.

This report focuses on temporomandibular disorders (TMDs), a set of more than 30 health disorders associated with both the temporomandibular joint (TMJ) and the muscles and tissues of the jaw. TMDs have a range of causes and often co-occur with a number of overlapping medical conditions, including headaches, fibromyalgia, back pain, and irritable bowel syndrome. Both the range of causes and the overlapping conditions contribute to widespread misunderstandings regarding the importance and function of the jaw joints. TMDs can be transient or long lasting and may be associated with problems that range from an occasional click of the jaw to severe chronic pain involving the entire orofacial region. Often, one of the biggest challenges facing an individual with a TMD or TMD-related symptoms is finding the appropriate diagnosis and treatment, particularly given the divide between medicine and dentistry in the United States and much of the world—a divide that profoundly affects care systems, payment mechanisms, and professional education and training.

The national prevalence of TMDs is difficult to estimate due to challenges in conducting clinical examinations on a large scale, such that most prevalence data are based on self-reported symptoms associated with TMDs rather than

examiner-verified classification. For example, one analysis of 2018 data found that an estimated 4.8 percent of U.S. adults (an estimated 11.2 to 12.4 million U.S. adults in 2018) had pain in the region of the TMJ that could be related to TMDs. Orofacial pain symptoms may or may not be related to TMDs. As discussed throughout this report, TMDs are a set of diverse and multifactorial conditions that can occur at different stages in an individual's life with a range of manifestations and impacts on quality of life.

This report explores a broad range of issues relevant to improving the health and well-being of individuals with a TMD. To address the study's Statement of Task, the National Academies of Sciences, Engineering, and Medicine appointed an 18-member committee with expertise in public health; pain medicine; basic, translational, and clinical research; patient advocacy; physical therapy; dentistry; self-management; TMDs and orofacial pain; oral and maxillofacial surgery; health care services; internal medicine; endocrinology; rheumatology; law; nursing; psychiatry; and communications. The study was sponsored by the Office of the Director at the National Institutes of Health and the National Institute of Dental and Craniofacial Research.

Meet Maddy



Hi I am Maddy. Writing about TMJ vulnerability is very traumatic for me, yet it is very important. No one understands or takes TMJ pain seriously. Most health care providers in India were not sensitive towards my TMJ pain. Many thought I was doing it to get doctor's attention and reduced to anxious female's syndrome.

As a 20-year old, I didn't understand why mental well-being was not as important as physical well-being - in my case both were seemingly compromised. I was given high doses of strong pain killers. I didn't take steroid shots as I was scared of its effects.

I tried three different dental treatments and my TMJ pain calmed down. I was excited as if high in life - I could chew again, laugh and socialize again a bit with ease. I didn't feel out of control, and no longer had to pop in pain pills to be able to write exams.

During my TMJ bad days, I had migraines, dizziness and had to take huge doses of Flexeril -- I used to take around 8-10 per day so that I could sit in classes escaping pain. It wrecked my mental health, the ability to socialize, my performance in academics and ability to believe in myself. Due to not being able to talk I had to cut back meeting others which created a social anxiety - something I still haven't overcome easily. I always thought I was probably imagining popping, clicking, immense pain, migraines, fatigue and ear pain as it wasn't visible.

When I read stories of TMJ coping I realized I wasn't alone in my suffering. I

am very scared of invasive procedures so I have refused them. My dental procedures were so painful I don't think I can live through anything more invasive. I have tried laser and physiotherapy to breathe easy.

I stopped taking pain killers as I got bronchial asthma due to taking them out of measure. At that point, I had felt useless and purposeless. I now know there is someone else giving a voice to my pain. I feel uneasy today as my symptoms are back again due to a cold and cough. TMJ may destabilize our lives, make us vulnerable professionally and personally, yet I am sending out solidarity of love and hope. Xoxo ☐ Maddy

Changing the Face of TMJ

We cannot change the face of TMJ without YOU!

When you donate, you are making the following happen:

- Advancing TMJ Scientific Research
- Advocating for TMJ Patients
- Supporting and Guiding Patients
- Educating Health Care Professionals
- Providing Trusted Information

Your contribution is more than a donation. It is how we will ensure that TMJ patients have a voice — through education, patient support and advocacy.

We cannot do this important work without you! Help us to continue our progress towards advancing research, public awareness and safe and effective treatments for this debilitating condition. [Donate today!](#)



**“Sometimes a TMJ patient needs
inspiration just to
get through each day.”**

- The TMJ Association, Ltd.

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CPRA Director & Scientific Advisory Board Member Present on TMD and Chronic Overlapping Pain Conditions

[The Chronic Pain Research Alliance](#) – an initiative of The TMJ Association – was created in 2009 to advance high-caliber research on Chronic Overlapping Pain Conditions (COPCs), of which TMD is one.

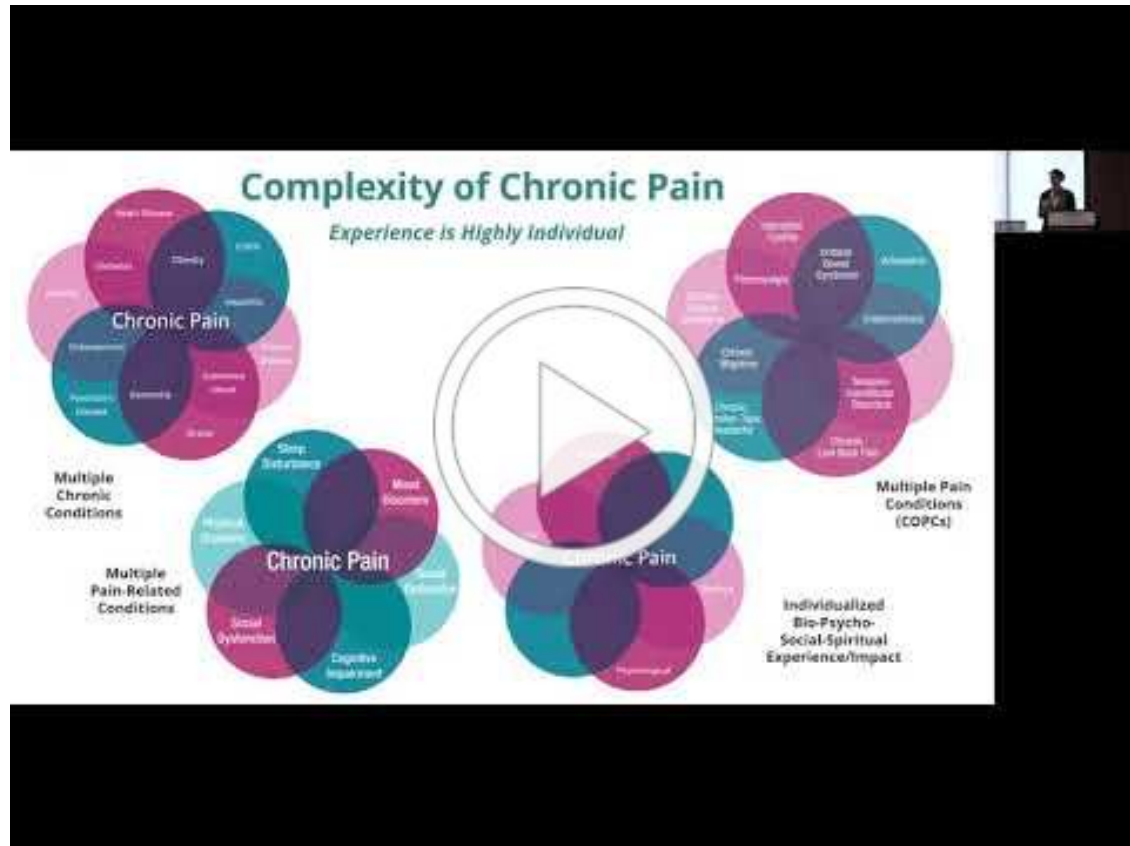
This spring, the CPRA’s director, Christin Veasley, and Scientific Advisory Board Member, Sean Mackey, MD, PhD, Chief of the Division of Pain Medicine and Redlich Professor of Anesthesiology, Perioperative and Pain Medicine at Stanford University, gave a presentation on COPCs at the 38th annual meeting of the [American Academy of Pain Medicine](#) (AAPM).

Meeting attendees gave their presentation, The Latest in Chronic Overlapping Pain Conditions (COPCs), the second highest ranking out of the 35 total presentations given at the meeting. Ms. Veasley and Dr. Mackey summarized recent findings from large-scale COPCs studies, highlighted current evidence on common underlying mechanisms of disease and discussed recent efforts to develop patient-centered measurement tools for COPCs. They concluded the presentation by summarizing how recent developments can help to transform the current state of poor care and treatment of COPCs to a patient-centered,

personalized model of care that incorporates principles of shared decision-making and goal-setting.

Ms. Veasley also discussed COPCs in a second presentation on whole-person care for chronic back pain and was the recipient of the AAPM's 2022 Patient Advocacy Award.

To view their presentation, click the image below.



TMJ Patient Clinical Study Opportunities

Erenumab as a therapeutic approach for the management of painful chronic temporomandibular disorders

The Brotman Facial Pain Clinic at the University of Maryland School of Dentistry is conducting a study comparing a new medication to a placebo in reducing temporomandibular disorders (TMD/TMJ) pain.

You may be eligible if you are:

- Between the ages of 18 and 65
- Have had jaw or muscle pain for at least the past 3 months

Participation involves:

- An evaluation to confirm temporomandibular disorders (TMJ/TMD)
- Completing at-home daily diaries for 1 month to determine eligibility

If eligible:

- Attend 6 clinic visits over a period of 21 weeks
- Receive study medication or a placebo designed to treat TMD pain.
- Earn \$200 over the duration of the study and free parking vouchers

For more information, please call Jane Phillips at (410) 706-4678 or email

Additional clinical study information is available at:
<https://www.clinicaltrials.gov/ct2/show/NCT05162027?term=erenumab&draw=2&rank=4>

TMD Online Study

The [Herman Darrow Lab](#) at the University of Minnesota invites those diagnosed with TMD to participate in an online study to understand how TMD affects brain circuitry.

You may be eligible for an online TMJ/TMD study that should take up to 1.5 hours on a computer. You will be paid a \$35.00 Amazon gift card upon completion of the whole study.

If you are interested in participating, please send an email to the Herman-Darrow lab at: hdlab@umn.edu.

Here's a teaser to see what you might expect if you participate in the study.
<https://vimeo.com/689289420>

TMD Research Informing Clinical Practice: A Call for Manuscripts

The National Academy of Sciences, Engineering and Medicine report on Temporomandibular Disorders (TMDs) "[Temporomandibular Disorders: Priorities for Research and Care \(2020\)](#)" set forth several recommendations to improve quality care for individuals suffering from TMD and a call to action from diverse groups of health care researchers and providers to address these recommendations. One set of recommendations included the need for more evidence-based research to inform clinical practice. Toward this latter need, we would like to bring your attention to a recent Research Topic set forth in *Frontiers in Dental Medicine*.

Frontiers in Dental Medicine is a scientific journal that focuses on ensuring that dental, oral and craniofacial health and diseases are understood in the context of the whole body. It advocates for a transdisciplinary research approach with the ultimate goal of accelerating oral and overall health outcomes for all communities. The Journal publishes scientific articles comprising a broad range of topics related to oral health research.

The Journal is currently accepting manuscripts for review in a special Research Topic focus area, [Temporomandibular Disorder: New Directions in Research and Patient Care](#). The goal of this Research Topic is to reimagine the disparate and siloed approaches to basic, translational, and clinical research that have plagued the field of TMDs and to accelerate the inclusion of medical and dental research expertise in the quest for improved, patient-centered, interprofessional care for TMD patients. Two broad research themes define the Scope of this Research Topic. The first theme is the application of a systems biology approach to basic TMD research. The second theme is the integration and assimilation of medical and dental sciences expertise in basic and clinical research in a patient-centered, whole-body approach to scientific

discovery and care for TMD patients. Multifaceted teams with expertise in neurology, immunology, endocrinology, rheumatology, physical therapy, musculoskeletal diseases, and biobehavioral science are encouraged to submit manuscripts. A broad range of biologic, pharmacologic, behavioral, and physical treatment approaches that have substantial backing from recent discoveries by the international TMD research community also are encouraged.

The deadline for submitting manuscripts for review is July 31, 2022 We encourage the submission of manuscripts from the broad scientific research community that address the many topics pertinent to basic discovery and patient treatment for TMDs.

Additional information may be found at the *Frontiers in Dental Medicine* Website: <https://www.frontiersin.org/journals/dental-medicine> or you may contact John W. Kusiak, Ph.D. Topic Editor, for further information at johnwaku12@gmail.com if you would like to discuss your research topic to determine its appropriateness for this special Research Topic.

Research Grant Opportunities: A Call for Applications

Notice of Special Interest (NOSI): Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations (Admin Supp Clinical Trial Optional)

The TMJA welcomes the announcement by the NIH Office of Research on Women's Health of the availability of Administrative Supplements to support research on the health of women in understudied, underrepresented, and underreported populations in biomedical research. The prevalence of TMJ is higher in women and yet support for biomedical research specifically targeted to sex and gender topics in TMJ is lacking. Clearly, more research is needed to address molecular, genetic, musculoskeletal, endocrine, neurological, and bio-behavioral aspects of TMJ in women. We hope this announcement will result in many new avenues of research that will clarify the causes of TMJ, elucidate the arc of disease progression, and ultimately, hasten the development of precision treatments for TMJ patients.

<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-031.html>

FY22 Chronic Pain Management Research Program

The US Department of Defense Chronic Pain Management Research Program invites scientists to submit pain research applications under three targeted areas: Clinical Exploration Award, Investigator-Initiated Research Award and Translational Research Award. Pre-applications are due July 12, 2022.

For additional information, please visit: <https://cdmrp.army.mil/funding/cpmrp>

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 (TMJ). For over 30 years, we have shared reliable information on TMJ with people like you. We invite you to visit our website, www.tmj.org.



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