

## The Scoop on TMD Pharmaceuticals

Article by [Sophia Stone](#), TMJA contributing author

Let's say the National Institutes of Health (NIH) just handed us a multi-million dollar grant to get to the bottom of TMD and find a cure once and for all. I mean, we could start handing out heating pads left and right, but that kind of relief can only get us so far. Whenever I try a different form of therapy or medication, I like to think about the biology, right down to the cellular and molecular level. Why are the cells that make up my jaw region being such jerks?

I think it's important to have some kind of understanding of what's going on in my body and how medications will affect me, especially for a chronic illness that can require long-term medication use. It's also especially important in a field like TMD healthcare, with 14 different sub-specialists recommending 14 different treatments.

To guide our thought experiment, we'll be using the paper [Pharmacotherapy in Temporomandibular Disorders: A Review by Ouanounou and colleagues \(2017\)](#). This review paper explores seven major categories of the most commonly prescribed medications for TMD pain and examines the literature on how these drugs work, *if* they work, and the evidence to back it up.

### The Science

Before sinking our teeth in, probably the first place to start to identify a TMD cure is to consider the biology. TMD (also referred to as TMJ) stands for *temporomandibular joint disorder*, which isn't exactly a neat, simple diagnosis. Rather, it's an umbrella term that encompasses a number of different etiologies (causes) and symptoms. The temporomandibular joint itself is part of the underlying etiology in some-but not all-cases, but most chronic TMD patients experience some kind of pain in their facial or jaw *muscles*. We experience pain only because our nerves send a signal to the brain, instructing it to make us feel pain (thanks a lot). For that reason, a significant number of TMD medications affect our neurons and nervous tissue.

Now why do our neurons send these pain messages to the brain? So first, a philosophical or evolutionary perspective. Why the heck would we spend billions of years evolving only to cower in pain from a measly hot coal or the pinch of a bee sting? In reality, it's not the *pain* that kills us. The pain is the smoke alarm. It's the lighthouse off the rocky pier. It's just the *thought* of having to go to the DMV (...kidding). People born without pain receptors, whose alert systems are broken, tend to die in childhood because feeling physical pain that alerts us to dangerous situations-like being on fire-is critical to human life. Pain confers an evolutionary advantage...but sometimes it goes haywire.

[Click here to read full article on our website.](#)

# Opportunity to Voice Your Opinion: U.S. Government Officials Want To Hear from Patients with Pain

## FDA Public Meeting on Patient-Focused Drug Development for Chronic Pain

On July 9, 2018, FDA hosted a public meeting on Patient-Focused Drug Development for Chronic Pain. <https://www.federalregister.gov/documents/2018/05/15/2018-10284/patient-focused-drug-development-on-chronic-pain-public-meeting-request-for-comments>

**FDA is interested in hearing patients' perspectives on chronic pain**, views on treatment approaches, and challenges or barriers to accessing treatments for chronic pain. FDA is particularly interested in hearing from patients who experience chronic pain that is managed with analgesic medications such as opioids, acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants; other medications; and non-pharmacologic interventions or therapies.

## II. Topics for Discussion at the Public Meeting

### Topic 1: Symptoms and Daily Impacts of Chronic Pain That Matter Most to Patients

1. How would you describe your chronic pain? (Characteristics could include location, radiation, intensity, duration, constancy or intermittency, triggers etc.)
2. What are the most significant symptoms that you experience resulting from your condition? (Examples may include restricted range of motion, muscle spasms, changes in sensation, etc.)
3. Are there specific activities that are important to you but that you cannot do at all or as fully as you would like because of your chronic pain? (Examples of activities may include work or school activities, sleeping through the night, daily hygiene, participation in sports or social activities, intimacy with a spouse or partner, etc.)
4. How has your chronic pain changed over time? (Considerations include severity and frequency of your chronic pain and the effects of chronic pain on your daily activities.)

### Topic 2: Patients' Perspectives on Current Approaches to Treatment of Chronic Pain

1. What are you currently doing to help treat your chronic pain? (Examples may include prescription medicines, over-the-counter products, and non-drug therapies.)
  - a. How has your treatment regimen changed over time, and why? (Examples may include change in your condition, change in dose, or treatment side effects.)
  - b. What factors do you take into account when making decisions about selecting a course of treatment?
2. How well does your current treatment regimen manage your chronic pain? (Considerations include severity and frequency of your chronic pain and the effects of chronic pain on your daily activities.)
3. What are the most significant downsides to your current treatments, and how do they affect your daily life?
4. What challenges or barriers to accessing or using medical treatments for chronic pain have you or do you encounter?
5. What specific things would you look for in an ideal treatment for your chronic pain?

Electronic comments must be submitted on or before September 10, 2018. The <https://www.regulations.gov> electronic filing system will accept comments until midnight Eastern Time at the **end of September 10, 2018**.

## Future NIH Research Initiative for TMD

Concepts represent early planning stages for initiatives in which the National Institute of Dental and Craniofacial Research (NIDCR) seeks to support research in an understudied and significant area of science. Council approval does not guarantee that a concept will become a program announcement, request for applications, or request for proposals. NIDCR bases this determination on scientific and programmatic priorities balanced with the amount of funds available.

The following new concept clearance was presented by Dr. Yolanda Vallejo and approved by Council at the [218th NIDCR Council Meeting: May 2018](#):

### **TMD: Identifying Pathways Involved in Chronic Pain and Endogenous Resolution**

#### **Goals:**

- Catalyze multi-disciplinary research addressing central and peripheral plasticity mechanisms that promote chronic TMD and its endogenous resolution.
- Delineate brain changes in human and animal models that can be correlated with molecular changes in animal and human craniofacial tissue.
- Evaluate TMD animal models to identify those that best recapitulate human pathophysiology to preclinical studies.

#### **Gaps and Opportunities:**

- Precision Medicine approaches to pain management necessitate:
  - Determination of the mechanisms that sustain or promote resolution of chronic TMD pain.
  - Elucidation of strategies to intrinsically and extrinsically modulate these mechanisms
- Recent technological advances and resources developed through the NIH BRAIN, Blueprint, and SPARC Initiatives are poised to enable significant advances.

#### **Specific Areas of Interest:**

- Determine underlying mechanisms that mediate maladaptive and/or adaptive plasticity changes in modulatory circuits that either promote chronic TMD pain or facilitate endogenous resolution.
- Adaptation/utilization of new technologies to assess brain-wide connectivity changes in TMD animal models that can parallel human imaging studies.
- Development of new lines of research that leverage the availability of human tissue banks with advancing technology.
- Elucidation of interactions of the skeletal, muscular, cartilage, nervous, immune and circulatory systems in TMD.
- Strategies to address sex-based differences/influences.

*The Council meeting video is available for viewing at <https://videocast.nih.gov/summary.asp?live=27372&bhcp=1>. The TMD concept presentation starts at 1:53:10.*

*The TMJA will stay abreast of this new development and will report updates in future issues of TMJ News Bites.*

## Consider Including the TMJA in Your Financial Planning

We were recently contacted by Tom P. who informed us that he was including The TMJ Association (TMJA), in his financial planning. Tom wrote the following for us to share with our readers:

Dear Terrie,

It was great to talk to you yesterday. I have used the resources of The TMJ Association for at least 20 years and it has been my main source for unbiased information and networking since I came down with TMD in 1984. You have helped me avoid more mistakes in my treatment and management of this widespread malady and I take much comfort in knowing you are vigorously seeking research that might lead to much better treatments! I am amazed that you have done so much with a very low budget. I found out recently that I can donate at this time some or all of my IRA retirement assets to your organization upon my passing and you are currently a named T.O.D. beneficiary. I think this is the best way I can help society and save estate taxes. I hope many others will consider this option to possibly maximize the good from one's estate. Keep up the great work!

Sincerely,  
Tom P., Euless, Texas

## Gifts to The TMJ Association

This communication prompted us to ask you to consider including the TMJ Association in your financial planning. Below are a number of ways you can help:

### Planned Gift

Consider a planned gift to The TMJ Association. Planned giving takes into careful consideration both your family's financial needs and your personal charitable goals, allowing you to leave a portion of your assets to The TMJ Association in your will, trust, beneficiary designation in your retirement accounts, insurance contract or planned gift arrangement.

### Bequests

Simply name the TMJ Association as a beneficiary of a sum of money, or a percentage of your estate in your will or living trust. This revocable gift allows you the flexibility to revise your wishes over time as life circumstances change.

Sample Bequest Language

- Specific: I give \$ \_\_\_\_\_ (number spelled out) to The TMJ Association, present address at P.O. Box 26770, Milwaukee, WI 53226-0770.
- Fraction: I give The TMJ Association \_\_\_\_\_ % (fraction spelled out) of the rest, residue, and remainder of my estate, after payment of all specified bequests, expenses, taxes, and debts, to The TMJ Association, present address at P.O. Box 26770, Milwaukee, WI 53226-0770.
- Residual: I give the rest, residue, and remainder of my estate, after the payment of all specified bequests, expenses, taxes, and debts to The TMJ Association, present address at P.O. Box 26770, Milwaukee, WI 53226-0770.

### Life Insurance

Life insurance is a low-cost, simple way to make a significant planned gift. Do you have a life insurance policy that you no longer need now that your children out of college and on their own? Name The TMJ Association as a partial, contingent, full beneficiary or even the owner of your policy.

### Retirement Assets

Designate The TMJ Association as a full or partial beneficiary of your qualified retirement plan (IRA, 401(k), 403(b)) using a beneficiary form.

*The above information is not intended as legal or tax advice. For such advice please consult an attorney or tax advisor. Examples are for hypothetical purposes only and are subject to change.*

## Well for Chronic Pain

Researchers have shown that pain-induced changes in the rat brain's opioid receptor system may explain the limited effectiveness of opioid therapy in chronic pain and may play a role in the depression that often accompanies it. These findings clearly show the impact of chronic pain on the brain and its relation to depression. The study, conducted by scientists at the National Institutes of Health (NIH) and colleagues from McGill University, Montreal, Quebec, Canada, was published in the journal *Pain*.

"We know that people with chronic pain have reduced availability of opioid receptors - the molecules opioid drugs bind to - in the brain," said Mark Pitcher, Ph.D., visiting fellow in the Division of Intramural Research at the National Center for Complementary and Integrative Health (NCCIH) and one of the authors of the study. "What we haven't known - until now - is why. Are there preexisting brain differences that might predispose some people to develop chronic pain? Or might chronic pain cause these differences? Our findings suggest that chronic pain itself is responsible."

In the study, cross-sectional positron emission tomography (PET) imaging was performed on the brains of 17 rats that had undergone surgery to produce a nerve injury that causes chronic pain and on 17 rats that had undergone sham surgery (a similar procedure that does not cause chronic pain). Three months later, the availability of opioid receptors had decreased in multiple regions of the brain in the nerve-injured rats, but no changes had occurred in the sham-surgery rats.

Other tests performed on the rats provided insight into the relationship between chronic pain and depression. Normal, healthy rats will drink water with sucrose (sugar) in it rather than plain water if given a choice. But animals with a decreased ability to experience pleasure, a recognized symptom of depression known as anhedonia, may not. In this study, the rats with chronic pain showed a decreased preference for sucrose water over plain water after injury; furthermore, animals in this group also displayed a positive correlation between opioid receptor availability and the preference for sucrose water.

"It's well known that there's a link between chronic pain and depression," explained M. Catherine Bushnell, Ph.D., scientific director of NCCIH's Division of Intramural Research and one of the authors of the study. "The results of this study indicate that pain-induced changes in the brain's opioid system may play a role in this association. Animals with the greatest decrease in opioid receptor availability showed the greatest increase in depression-like symptoms after experiencing chronic pain."

"These results provide insights into why we see limited effectiveness of opioid therapy in chronic pain and the mechanism of the depression that may accompany it," said NCCIH Acting Director Dr. David Shurtleff. "These basic research findings support NIH's efforts to better understand chronic pain and comorbid symptoms and to develop better ways to help chronic pain patients effectively manage their pain."

There are neurological changes associated with chronic pain that have been known and described as neuroplasticity. Although this study suggests that neuropathic pain-evoked changes in cerebral opioid receptor expression may impact depression, human studies are needed to confirm these findings.

Original source: <https://www.nih.gov/news-events/news-releases/nih-study-explains-why-opioid-therapy-may-not-always-work-well-chronic-pain>

## Young Investigator Initiative Grant Mentoring and Career Development Program

*The TMJ Association is a member of the U.S. Bone and Joint Initiative and was asked to share the following announcement with our readers.*



## Fall Workshop - November 9-11, 2018 Toronto, ON

The United States Bone and Joint Initiative (USBJI) and Bone and Joint Canada are dedicated to increasing research of musculoskeletal diseases. To keep pace with the high and increasing burden of these diseases, a higher level of research performed by young investigators in the musculoskeletal diseases is required, and future levels of research assured. This is particularly important given the current environment for research funding, and academic careers. In response, the Young Investigator Initiative is a grant mentoring program providing early-career investigators an opportunity to work with experienced researchers in our field to assist them in securing funding and other survival skills required for pursuing an academic career.

To date 222 participants (57%) have successfully obtained \$354 million in grants for 1,359 new musculoskeletal research studies. Participants consider this program instrumental to their success. They rate highly the one-on-one mentoring with experienced researchers, the opportunity for inter-disciplinary and peer-to-peer exchange, and collaborations established during workshops.

This grant mentoring program and career development program is open to promising junior faculty, senior fellows or post-doctoral researchers nominated by their department or division chairs seeking to pursue a career in clinical or basic research. It is also open to senior fellows or residents that are doing research and have a faculty appointment in place or confirmed. Basic and clinical investigators, without or with training awards, are invited to apply. Investigators selected to take part in the program attend two workshops, 12-18 months apart, and work with faculty between workshops to develop their grant applications. The Fall 2018 workshop is scheduled to take place on November 9-11, 2018, in Toronto, Ontario. The unique aspect of this program is the opportunity for attendees to maintain a relationship with a mentor until their application is funded.

For more about the program and detailed application instructions, please refer to <https://www.usbji.org/programs/yii>

**DEADLINE FOR APPLICATION SUBMISSIONS: JULY 15, 2018**

## 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



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

- The TMJ Association, Ltd.

**Connect with others who understand in the  
new TMJ Cafe Support Community**

**Visit [TMJ.Inspire.com](http://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.

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](#).

## Digital Signals in Chronic Pain Study Seeks Participants

The CPRA took notice when Evidation Health announced a new study called the DiSCover Project (Digital Signals in Chronic Pain). We sat down with Evidation's co-founder and president, Christine Lemke, who has chronic pain herself, to learn about this exciting new initiative and [how those with pain can participate](#).

**CPRA:** Could you share with our readers a bit about your personal experience with pain?

**LEMKE:** About 10 years ago, I was diagnosed with a genetic disorder - it's a form of arthritis, which results in chronic pain that can be pretty severe. I am lucky. Most of the time, I'm able to go about my day without significant impact, but when I have a flare, the pain can be debilitating. My experience with the health care system has been frustrating. It took physicians years to diagnose me, and there weren't effective ways to measure my pain or to identify its triggers. The most that was offered was for me to keep a pain diary. It felt pointless and frustrating to diarize my pain episodes when my physicians didn't know what was wrong with me. Even today, most of my conversations aren't grounded in any objective measures. I know millions of others experience the same frustration, and I thought that there must be a better way.

**CPRA:** How did your experiences lead to launching the DiSCover Project?

**LEMKE:** I wanted to develop a study that would provide a solution to the frustration that I and millions of others with pain experience-the lack of objective pain measures. My company, Evidation Health, is a technology and services company helping individuals and the world's most innovative healthcare companies understand and influence the everyday behaviors that create better health outcomes. I wanted to bring this innovation into the pain space.

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

## 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.](#)

## Update on our Privacy Policy

We want you to know how we protect your privacy. We do not sell, rent, or exchange your information with anyone! You can read more about our privacy policy [here](#).

## 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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