



## Chronic Pain and COVID-19

As everyone's life is upended by the COVID-19 pandemic, we thought it would be worthwhile to note the ramifications of this situation for chronic pain sufferers and chronic pain research. The following websites have valuable information about COVID-19 and its impact in this area.

### Recommendations on Chronic Pain Practice during the COVID-19 Pandemic

A [Joint Statement](#) by American Society of Regional Anesthesia and Pain Medicine (ASRA) and European Society of Regional Anesthesia and Pain Therapy (ESRA) provides guidance in treating chronic pain patients during this period of high health care demand. Summarizing infographics at the start of the article is a good reference.

### Ibuprofen and COVID-19

There have been several stories in the news regarding the potential for ibuprofen having deleterious effects upon COVID-19 symptoms. A scholarly and detailed elaboration of this issue can be found [here](#).

While **NIH** has not specifically addressed any ties between coronavirus and chronic pain, they do maintain a [regularly updated website](#) containing coronavirus information, including research-related content.

**And finally...**

Dr. Anthony Fauci's contributions to our understanding of the COVID-19 virus and pandemic has been of great benefit to all of us. What is less recognized is [his contribution to pain measurement!](#)

## UMSON Campaign Sews Masks, Sows Hope

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When student Maria Segovia received an email from the [University of Maryland School of Nursing \(UMSON\)](#), inviting students, alumni, faculty, and staff to sew cloth masks to be donated to University of Maryland Medical Center (UMMC) to assist employees on the front lines of the COVID-19 pandemic, she knew she wanted to get

involved.

Additional coverage of face masks delivery from WBAL [here](#) and WJZ [here](#). Truly fantastic job from the UMSON faculty, staff, alumni, students, and community!

[Learn more](#)

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## CACPR Member Accolades

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*Highlights of recent grant awards, authorships, and other CACPR member news.*

*Vinita Agarwal*

### **Recent Publication**

Agarwal, V. (February 21, 2020, Invited talk). *Patient-centered care: Communication that counts*. Primary care office care coordinator staff training: Patient engagement and education. Peninsula Regional Medical Center, PRINC, INC. Salisbury, Maryland USA.

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*Luana Colloca*

### **Recent Publications**

Wai-Lan Yeung V, Geers AL, Colloca L. Merely Possessing a Placebo Analgesic Improves Analgesia Similar to Using the Placebo Analgesic. *Ann Behav Med*. 2020 Mar 30. pii: kaaa007. doi: 10.1093/abm/kaaa007. [Epub ahead of print] PubMed PMID: 32227161.

Collaborative work showing that merely possessing a placebo reduces evoked-experimental acute pain.

Okusogu C, Wang Y, Akintola T, Haycock NR, Raghuraman N, Greenspan JD, Phillips J, Dorsey SG, Campbell CM, Colloca L. Placebo hypoalgesia: racial differences. *Pain*. 2020 Mar 20. doi: 10.1097/j.pain.0000000000001876. [Epub ahead of print] PubMed PMID: 32205528.

Race does influence pain sensitivity but race influences placebo effects only minimally in TMD participants but not in healthy participants. This reinforces the concept that placebo effects are pervasive. No matter what...

Wang Y, Tricou C, Raghuraman N, Akintola T, Haycock NR, Blasini M, Phillips J, Zhu S, Colloca L. Modeling Learning Patterns to Predict Placebo Analgesic Effects in Healthy and Chronic Orofacial Pain Participants. *Front Psychiatry*. 2020 Feb 12;11:39. doi: 10.3389/fpsyt.2020.00039. eCollection 2020. PubMed PMID: 32116854; PubMed Central PMCID: PMC7029355.

This is the first study on LCA approach and computational modeling applied to placebo effects to predict responsiveness. We were able to identify patterns predictive of responsiveness to placebos in TMD patients.

Colloca L, Barsky AJ. Placebo and Nocebo Effects. *N Engl J Med*. 2020 Feb 6;382(6):554-561. doi: 10.1056/NEJMra1907805. Review. PubMed PMID: 32023375.

A compelling solicited review for the NEJM readers providing recommendations for patients, clinicians and scientists dealing with placebo and nocebo effects.

Schenk LA, Colloca L. The neural processes of acquiring placebo effects through observation. *Neuroimage*. 2020 Apr 1;209:116510. doi: 10.1016/j.neuroimage.2019.116510. Epub 2019 Dec 30. PubMed PMID: 31899287; PubMed Central PMCID: PMC7107761.

First elegant demonstration of the neural mechanisms underlying placebo effects related to the observation of a benefit experienced by another person - our dear demonstrator - thank you, SK!

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*Susan G. Dorsey*

### **Recent Publications**

Ji Y, Hu B, Klontz C, Li J, Dessem D, Dorsey SG, Traub RJ. Peripheral mechanisms contribute to comorbid visceral hypersensitivity induced by preexisting orofacial pain and stress in female rats. *Neurogastroenterol Motil*. 2020 Mar 10:e13833. doi: 10.1111/nmo.13833. [Epub ahead of print] PMID: 32155308

Okusogu C, Wang Y, Akintola T, Haycock NR, Raghuraman N, Greenspan JD, Phillips J, Dorsey SG, Campbell CM, Colloca L. Placebo hypoalgesia: racial differences. *Pain*. 2020 Mar 20. doi: 10.1097/j.pain.0000000000001876. [Epub ahead

of print] PubMed PMID: 32205528.

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*Joel D. Greenspan*

**Recent Publications**

Sharma S, Ohrbach R, Fillingim RB, Greenspan JD, Slade G. Pain Sensitivity Modifies Risk of Injury-Related Temporomandibular Disorder. *J Dent Res*. 2020 Mar 20. [Epub ahead of print] PubMed PMID: 32197057.

This study evaluated contributions of jaw injury and experimental pain sensitivity to the risk of developing painful temporomandibular disorders (TMD). Analysis identified a pronounced influence of jaw injury on painful TMD incidence, as expected. Additionally, seemingly minor events such as yawning and sustained mouth opening likewise contributed risk for painful TMD incidence. Moreover, the effects of injury on painful TMD were amplified in individuals with heightened pain sensitivity, thus illustrating the interaction of constitutive and experiential factors in painful TMD susceptibility.

Okusogu C, Wang Y, Akintola T, Haycock NR, Raghuraman N, Greenspan JD, Phillips J, Dorsey SG, Campbell CM, Colloca L. Placebo hypoalgesia: racial differences. *Pain*. 2020 Mar 20. doi: 10.1097/j.pain.0000000000001876. [Epub ahead of print] PubMed PMID: 32205528.

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*Asaf Keller*

**Recent Publications**

Charles Raver, Olivia Uddin, Yadong Ji, Ying Li, Nathan Cramer, Carleigh Jenne, Marisela Morales, Radi Masri and Asaf Keller. An amygdalo-parabrachial pathway regulates pain perception and chronic pain. *Journal of Neuroscience* 26 March 2020, JN-RM-0075-20; DOI: <https://doi.org/10.1523/JNEUROSCI.0075-20.2020>

We describe a novel pathway, consisting of inhibition by dynorphin, somatostatin and corticotropin-releasing hormone expressing neurons in the central nucleus of the amygdala that project to the parabrachial nucleus (PB). We show that this pathway regulates the activity of pain-related neurons in PB, and that, in chronic pain, this inhibitory pathway is suppressed, and that this suppression is causally related to pain perception. We propose that this amygdalo-parabrachial pathway is a key regulator of both chronic and acute pain, and a novel target for pain relief.

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*Ke Ren*

**Recent Publication**

Ren K. [Commentary on Ma et al. Resveratrol brings back happy bug's harmony](#). *Brain Behav Immun*. 2020 Mar 7. pii: S0889-1591(20)30298-1. doi: 10.1016/j.bbi.2020.03.005. [Epub ahead of print]

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*David A. Seminowicz*

### **Recent Publications**

Seminowicz DA, Burrowes SA, Kearson A, Zhang J, Krimmel SR, Samawi L, Furman AJ, Keaser ML, Gould NF, Magyari T, White L, Goloubeva O, Goyal M, Peterlin BL, Haythornthwaite JA. Enhanced mindfulness based stress reduction (MBSR+) in episodic migraine: a randomized clinical trial with MRI outcomes. *Pain*. 2020 Mar 13. doi: 10.1097/j.pain.0000000000001860. [Epub ahead of print] PubMed PMID: 32187119.

The study was the first randomized trial of an enhanced mindfulness (MBSR+) intervention for migraine and showed that MBSR+ was superior to an active control intervention in reducing the number of headache days experienced. Functional MRI was also collected at multiple timepoints and revealed that mindfulness was associated with an improvement in cognitive network function over time. MBSR+ is safe and effective for reducing headaches. It has virtually no side effects and it can be used on its own or in combination with pharmacological interventions.

Da Silva JT, Tricou C, Zhang Y, Seminowicz DA, Ro JY. Brain networks and endogenous pain inhibition are modulated by age and sex in healthy rats. *Pain*. 2020 Jan 17. doi: 10.1097/j.pain.0000000000001810. [Epub ahead of print] PubMed PMID: 31977940.

This study was published in PAIN and we used a capsaicin-induced DNIC test and resting-state functional MRI to investigate the impact of aging and sex on endogenous pain inhibition in healthy rats. We found that young males have the most efficient analgesia with the strongest connectivity between anterior cingulate cortex and periaqueductal gray. Pain inhibition is impaired in young females and old males and females, which was associated with widespread brain connectivity and strong involvement of the limbic system. Thus, distinct brain circuitries including the limbic system may contribute to higher susceptibility to pain modulatory deficits in the elderly population, and sex may be a risk factor for developing age-related chronic pain.

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*Joyce Teixeira da Silva*

### **Recent Publication**

Da Silva JT, Tricou C, Zhang Y, Seminowicz DA, Ro JY. Brain networks and endogenous pain inhibition are modulated by age and sex in healthy rats. *Pain*. 2020 Jan 17. doi: 10.1097/j.pain.0000000000001810. [Epub ahead of print] PubMed PMID: 31977940.

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*Richard J. Traub*

### **Recent Publication**

Ji Y, Hu B, Klontz C, Li J, Dessem D, Dorsey SG, Traub RJ. Peripheral mechanisms contribute to comorbid visceral hypersensitivity induced by preexisting orofacial pain and stress in female rats. *Neurogastroenterol Motil*. 2020 Mar 10:e13833. doi: 10.1111/nmo.13833. [Epub ahead of print] PMID: 32155308.

There were 2 main findings in this paper. First, using our models of transient stress-induced visceral hypersensitivity and chronic comorbid (orofacial pain + stress) pain hypersensitivity to model pain of irritable bowel syndrome (IBS) and temporomandibular disorder (TMD) we found that not all female rats developed visceral hypersensitivity, some were susceptible, and others were resilient. Since not all patients with IBS or TMD develop secondary pain syndromes, our animal model provides a tool to examine mechanisms that might contribute to development of multiple pain conditions characteristic of Chronic Overlapping Pain Conditions. The second finding in this paper was that similar peripheral mechanisms involving peripheral corticotrophin releasing factor (CRF) and mast cells contribute to the development of transient and chronic visceral hypersensitivity in the different stress/pain models.

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The UM Center to Advance Chronic Pain Research (CACPR) is a multidisciplinary center composed of nationally and internationally renowned clinical and preclinical translational scientists whose principle research focus is on the physiological, genetic, and psychosocial underpinnings of the development and persistence of debilitating chronic pain conditions.



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