UNIVERSITY of MARYLAND
CENTER TO ADVANCE CHRONIC PAIN RESEARCH

CACPR NEWSLETTER
Relieving Pain in America

DECEMBER 2021

CACPR Member Spotlight:
Introducing Amber Kleckner, PhD, Research Assistant Professor at the University of Maryland School of Nursing.

Dr. Amber Kleckner, PhD is a nutrition scientist who is working to alleviate symptoms of cancer and the side effects of treatment. She has a BS and MS in Biochemistry and a Ph.D. in Human Nutrition (Ohio State). She completed a post-doctoral fellowship at Boston Medical School in medicine and, most recently, a fellowship in Supportive Care in Cancer at the University of Rochester. She joined the faculty in the School of Nursing in September 2021.

Dr. Kleckner designs and implements clinical trials that evaluate how quantity, quality, and timing of food affect symptoms during and after the cancer experience, including fatigue and pain. She recently completed a time-restricted eating intervention among cancer survivors and demonstrated the feasibility and acceptability of a 10-hour daytime eating window, as well as reductions in fatigue from pre- to post-intervention. She is currently building upon these preliminary results in a randomized controlled trial here at UMB. She is also currently conducting a study that tests the effects of a Mediterranean Diet vs. normal eating patterns on the development of cancer-related fatigue during chemotherapy treatment. These studies will help elucidate the components of the diet that are important in the short- and long-term symptom burden of the cancer experience.

As part of these clinical trials, Dr. Kleckner is exploring the metabolic and mitochondrial mechanisms underlying cancer-related fatigue and other symptoms to help understand

the mechanistic underpinnings and tailor nutritional programs accordingly. She is looking for collaborators, especially on the basic science side, to explore these mechanisms, so do not hesitate to reach out.

New Grant Spotlight

SBIR grant from NCI
Awarded amount: $300K direct
Leveraging Health Tech to Address Health Outcome of Cancer Survivors (POSTHOC-II)
Amber Kleckner, PhD: MPI
In a collaboration with Charles River Analytics (Boston, MA), we are developing a smartphone app to facilitate delivery of the cancer survivorship care plan. This app stores information regarding cancer diagnosis, treatment, and future plans. It also promotes and monitors healthy lifestyle behaviors (e.g., nutrition, physical activity) via a Fitbit/smartwatch and interfaces with the electronic medical record to promote conversations regarding healthy behaviors with the primary care physician and the clinical care team.

CACPR Member Laurels

Highlights of recent grant awards, publications, and presentations.

Man-Kyo Chung, DMD, PhD

Arora V, Li T, Kumari S, Wang S, Asgar J, **Chung MK.** Capsaicin-induced depolymerization of axonal microtubules mediates analgesia for trigeminal neuropathic pain. Pain. 2021 doi: 10.1097/j.pain.0000000000002529. Online ahead of print. PMID: 34724681

Capsaicin-induced activation of TRPV1 followed by the activation of calpain and the depolymerization of axonal microtubules determines capsaicin-induced ablation of nociceptive terminals and the extent of analgesia for trigeminal neuropathic pain in mice.

Luana Colloca, MD, PhD, MS

Wang Y, Chan E, Dorsey SG, Campbell CM, **Colloca L.** Who are the placebo responders? A cross-sectional cohort study for psychological determinants. Pain. 2021 doi: 10.1097/j.pain.0000000000002478. Online ahead of print. PMID: 34740998

We aimed to identify individual psychological factors that predicted the magnitude of placebo effects (PE) in chronic pain participants and controls using the Research Domain Criteria framework. Our findings indicate that a greater level of emotional distress was a significant predictor of smaller magnitude of PE and slower extinction rate of PE in both in chronic pain participants and controls. Greater reward-seeking was linked to greater reinforced expectations. These findings highlight that negative valence systems might play a role in impairing PE, with a larger impact in chronic pain participants than in healthy participants.

Geers AL, Clemens KS, Faasse K, Colagiuri B, Webster R, Vase L, Sieg M, Jason E, **Colloca L.** [Psychosocial Factors Predict COVID-19 Vaccine Side Effects.](#)
Psychother Psychosom. 2021 Nov 4:1-3. doi: 10.1159/000519853. Online ahead of print.
PMID: 34736267 No abstract available.

Vaccination for coronavirus disease 2019 (COVID-19) is essential to overcome the challenge of the pandemic. However, many have been concerned about being vaccinated due to the local and systemic side and adverse events that are frequently reported by individuals and media coverage. Community surveys found side effects to be key concerns of vaccine-hesitant individuals. One unexplored possibility is that reactogenicity of COVID-19 vaccines is in part worsened by psychosocial factors (e.g. Vaccine side effect expectations, worry about the COVID-19 pandemic, and depressive symptoms), particularly those responsible for nocebo effects. Nocebo effects refer to when negative expectations and related factors, such as worry and depression, trigger or exacerbate negative symptoms.

Mun CJ, Weaver KR, Hunt CA, Owens MA, Phillips J, Lerman SF, Buenaver LF, **Colloca L**, Tennen H, Haythornthwaite JA, Finan PH, Smith MT. [Pain expectancy and positive affect mediate the day-to-day association between objectively measured sleep and pain severity among women with temporomandibular disorder.](#)
J Pain. 2021 Nov 25:S1526-5900(21)00368-0. doi: 10.1016/j.jpain.2021.11.003. Online ahead of print.
PMID: 34839028

The majority of individuals with temporomandibular disorders (TMD) experience sleep disturbance, which can maintain and exacerbate chronic pain. However, the factors underlying the sleep-pain link have not been fully elucidated, especially beyond the laboratory. Sleep deprivation can induce threat interpretation bias, as well as impairment in positive affective

functioning. Using both actigraphy and daily diaries, we examined whether morning pain expectancy and positive affect mediate the association between the previous night's sleep disturbance and next-day overall pain severity. Reducing exaggerated daily pain expectancy and up-regulating positive affect may be important intervention targets for disengaging the sleep-pain link among individuals with co-occurring TMD and sleep disturbance.

Felix RB, Rao A, Khalid M, Wang Y, **Colloca L**, Murthi SB, Morris NA. [Adjunctive virtual reality pain relief following traumatic injury: protocol for a randomised within-subjects clinical trial.](#)
BMJ Open. 2021 Nov 30;11(11):e056030. doi: 10.1136/bmjopen-2021-056030. PMID: 34848527

Little is known about VR in the acute pain setting following traumatic injury. Furthermore, no studies have investigated VR in the setting of traumatic brain injury (TBI). This study aims to establish the safety and effect of VR therapy in the inpatient setting for acute traumatic injuries, including TBI at Shock Trauma Center.

MPower Named Professorship: https://www.umaryland.edu/news/archived-news/november-2021/university-of-maryland-strategic-partnership-announces-mpower-professorships.php

The [University of Maryland Strategic Partnership: MPowering the State](#) (MPower) announced the appointment of eight professors, four from the University of Maryland, Baltimore (UMB) and four from the University of Maryland, College Park (UMCP), as MPower Professors to recognize, incentivize, and foster collaborations between faculty who are working together on the most pressing issues of our time. Dr. Colloca was named MPower Professor for her work on pain management and mechanisms.

Barbara Resnick, PhD, RN, CRNP, FAAN, FAANP, Cynthia Renn, PhD, RN, FAAN & Susan Dorsey, PhD, RN, FAAN

Resnick, B., Galik, E., Kolanowski, A., Van Haitsma, K., Boltz, M., Ellis, J., Behrens L., Eshragi, K., **Renn, C., Dorsey, S**. (in press). [Invariance of the PAINAD Scale between Black and White Residents Living with Dementia Frontiers in Pain Management.](#)

The purpose of this study was to test the reliability and validity of the PAINAD and particularly consider whether or not this measure was invariant when used among Black and White residents. Baseline data from an implementation study testing that included a sample of 553 residents, 30% of who were Black, from 55 nursing were included in this study. The Winsteps statistical program was

used to perform the Rasch Analysis and evaluate the reliability and validity of the measure based on internal consistency, INFIT and OUTFIT statistics, mapping and a DIF analysis. The AMOS statistical program was used for Confirmatory Factor Analysis. The findings supported the reliability and validity of the PAINAD when used with these individuals and demonstrated that there was no evidence of invariance between Black and White residents. All the items fit the model but there was not a good spread of the items across the pain level of the participants. The majority of the participants (75%) were so low in pain signs or symptoms that they could not be differentiated. Based on clinical practice and observations, it is recommended that additional items be added to the measure such as observing the individual for evidence of resisting care, retropulsion when trying to stand, hitting or kicking when turning in bed, hitting or kicking when transferring from bed to chair, hitting or kicking when ambulating, or hitting or kicking when raising arms, less engagement with others, and decreased participation in activities previously enjoyed.

A Review of the Movie: *This Might Hurt*
Written by CACPR member, Yang Wang, PhD

Pain is Inevitable. Suffering is Optional

"When the mind is ill at ease, the body is affected.

-Ovid"

This Might Hurt is a documentary that focuses on a psychological therapy called Emotional Awareness and Expression Therapy (EAET) for treating chronic pain. The documentary filmed three chronic pain patients who have searched for years for effective treatments for their pain entered EAET which aims to retrain their brain to alleviate and eventually cure pain. The EAET program was run by Dr. Howard Schubiner from Ascension Providence-Providence Hospital, and Michigan State University College of Human Medicine. This new medical program EAET, together with other behavioral health approaches including cognitive behavioral therapy, acceptance and commitment therapy, and mindfulness-based stress reduction therapy has been recommended by the United States Department of Health and Human Services (HHS) as important approaches to fight against the opioid epidemic.[1]

Principle of EAET

Pain is defined by the International Association for the Study of Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". [2] As a highly subjective experience, it has been well accepted since the last decades that psychological factors such as stress, anxiety, depression, and fear play magnificent roles in an individual's response to pain, maintaining chronicity of pain, and increasing the risk of pain-related disability. [3,4] Individuals with chronic pain, on the other hand, were also more vulnerable for psychological distress, catastrophizing coping style, and fear of injury that would lead to avoidance behavior. [5] In the documentary, this vicious circle was observed in one of the chronic pain patients who

had irritable bowel syndrome. The patient was in so much pain and fear that she was not able to work and had to rely on medications and the heating belt every time when pain attacks. The avoidance behavior, in turn, would contribute to the maintenance of pain chronicity.

The core of EAET principle was simple: pain that lacks tissue damage or pain that persists after damage healing could be generated from, or more likely to be influenced by, psychological factors rather than physical conditions. Dr. Schubiner suggests that when no clear peripheral etiology is found, the pain should be assumed to be central, meaning that pain was amplified, or generated directly in the brain. [6] For this type of pain, the treatment should focus on the brain and mind, rather than unspecific physical findings such as degenerative disc disease. In particular, the pain brain is shaped by prior experiences including trauma, psychological distress, and interpersonal conflict. Therefore, recognizing and resolving the trauma and conflict is the key technique of EAET.

In the EAET program, patients were taught to unveil the unresolved emotional trauma or conflict that could have influenced the neural pathways related to pain. Once patients become aware of suppressed/avoided emotional experiences, they were encouraged to *express* their negative emotions. The expression of trauma-related emotion would lead to an alleviation of pain symptoms. [6] Patients would learn from the positive reinforcement that emotional expression, rather than inhibition or avoidance of conflict, could result in better pain management and increasing life quality. [7]

Heterogeneity of response to treatment

Despite EAET appearing to be extremely effective in curing pain in the three chronic pain patients that were depicted in the documentary, it should also be noted that not everyone responded positively to the EAET. Out of the 8 participants who have completed EAET program, 6 of them experienced significant reductions in pain. The other two experienced little benefit. This renders the question of what factors cause the individual heterogeneity in responding to the treatment.

As far as it was noticed, the clinical trials [8-10] testing the effectiveness and efficacy of EAET included imbalanced more women than men as participants, limiting the comparison for sex differences in the effects of EAET on pain reductions. Moreover, social-economic status including income, occupation, and education disparities may also create distinct trauma characteristics such as the onset of the pain-related trauma and unique early childhood adverse events, which could also contribute to the individual differences in responding to the EAET as a nonpharmacological therapy for pain. Thus, studies on deep-phenotyping patients for the purpose of precise individualized treatment would be needed to maximize the effects of mind-body pain therapies.

References

1. Health, U. D. o. & Services, H. Pain management best practices inter-agency task force report: Updates, gaps, inconsistencies, and recommendations. *Washington, DC: US Department of Health and Human Services* (2019).
2. Merskey, H. E. Classification of chronic pain: Descriptions of chronic pain syndromes and definitions of pain terms. *Pain* (1986).

3. Kerns, R. D., Sellinger, J. & Goodin, B. R. Psychological treatment of chronic pain. *Annu Rev Clin Psychol* **7**, 411-434, doi:10.1146/annurev-clinpsy-090310-120430 (2011).
4. Manchikanti, L., Fellows, B. & Singh, V. Understanding psychological aspects of chronic pain in interventional pain management. *Pain Physician* **5**, 57-82 (2002).
5. Crombez, G., Vlaeyen, J. W. S., Heuts, P. H. T. G. & Lysens, R. Pain-related fear is more disabling than pain itself: evidence on the role of pain-related fear in chronic back pain disability. *Pain* **80**, 329-339 %@ 0304-3959 (1999).
6. Lumley, M. A. & Schubiner, H. Emotional Awareness and Expression Therapy for Chronic Pain: Rationale, Principles and Techniques, Evidence, and Critical Review. *Curr Rheumatol Rep* **21**, 30, doi:10.1007/s11926-019-0829-6 (2019).
7. Burger, A. J. *et al.* The effects of a novel psychological attribution and emotional awareness and expression therapy for chronic musculoskeletal pain: A preliminary, uncontrolled trial. *J Psychosom Res* **81**, 1-8, doi:10.1016/j.jpsychores.2015.12.003 (2016).
8. Ziadni, M. S. *et al.* A life-stress, emotional awareness, and expression interview for primary care patients with medically unexplained symptoms: A randomized controlled trial. *Health Psychol* **37**, 282-290, doi:10.1037/hea0000566 (2018).
9. Carty, J. N. *et al.* The Effects of a Life Stress Emotional Awareness and Expression Interview for Women with Chronic Urogenital Pain: A Randomized Controlled Trial. *Pain Med* **20**, 1321-1329, doi:10.1093/pm/pny182 (2019).
10. Lumley, M. A. *et al.* Emotional awareness and expression therapy, cognitive behavioral therapy, and education for fibromyalgia: a cluster-randomized controlled trial. *Pain* **158**, 2354-2363, doi:10.1097/j.pain.0000000000001036 (2017).

Accolade
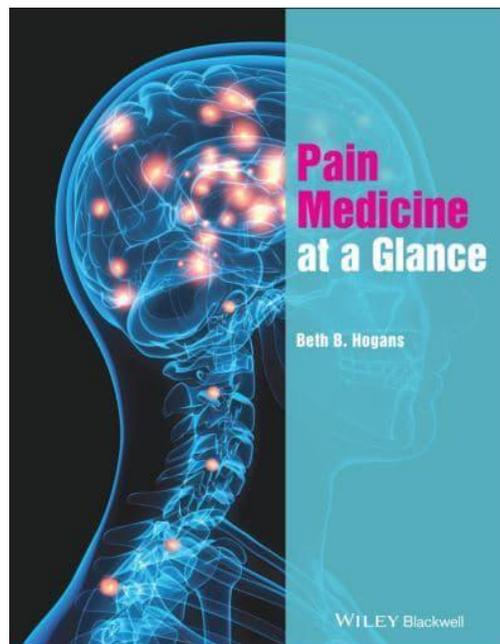
Pain Medicine at a Glance

[Beth Hogans - Associate Professor - Johns Hopkins School of Medicine | LinkedIn](#)

ISBN: 9781118837665
Publisher: Wiley
Imprint: Wiley Blackwell
Pub date: 25 Nov 2021

The market-leading at a Glance series is popular among healthcare students and newly qualified practitioners for its concise, simple approach and excellent illustrations. Each bite-sized chapter is covered in a double-page spread with clear, easy-to-follow diagrams, supported by succinct explanatory text. Covering a wide range of topics, books in the at a Glance series are ideal as introductory texts for teaching, learning, and revision, and are useful throughout university and beyond.

Everything you need to know about Pain Medicine... at a Glance!
Pain Medicine at a Glance is a user-friendly, visual introduction to the impact of pain in various clinical care settings, focusing on primary care needs. Aligned with learning objectives developed by the Johns Hopkins School of Medicine, this authoritative guide covers the basic forms and pathophysiology of pain, the clinical skills necessary for delivering excellent care, pharmacological and non-pharmacological treatments, and a variety of special cases such as healthcare ethics, integrative care, and treatment planning for chronic pain self-management therapy and the management of pain in children and older adults.

A new addition to the market-leading at a Glance series, the text offers concise and accessible chapters, full-color illustrations, self-assessment questions, and easy-to-follow diagrams. Topics include pain assessment, cognitive factors that influence pain, applying behavioral perspectives on pain, managing opioids, and other pharmacological therapies, treating acute pain in patients with substance abuse issues, and more. Perfect for learning, revision, and teaching, this book:

Provides a foundation of clinical and basic science knowledge about pain and its mechanisms. Describes major forms of pain, including surgical, orofacial, musculoskeletal, and obstetric pain. Offers advice on fostering empathy and compassionate practices in pain medicine. Covers non-pharmacological treatments such as physical therapy, hydrotherapy, meditation, acupuncture, massage, and various focal treatments
Includes discussion of recent advances and new discoveries in pain science
Pain Medicine at a Glance is the ideal companion for medical and healthcare students, junior doctors, advanced practice providers, nurse practitioners, and others involved in diagnosing and treating pain-associated illness.
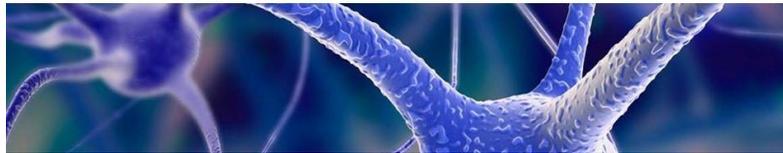
Announcements

To view the flyer above, please click here.

The Pain Journal Club

The Pain Journal Club consists of students, postdocs, and faculty from the UMB Schools of Dentistry, Medicine, and Nursing, whose research interests include mechanisms of pain in animal models and humans. A pain-related scientific article is presented by a volunteer and everyone discusses the findings of the article. The Pain Journal Club will be held virtually every **Wednesday at 8:30 am through May 2022.**

Below is the reoccurring Zoom link for the Pain Journal Club meeting.
Please click here to access the Pain Journal Club zoom meetings.

To view the full schedule for Pain Journal Club meetings, please click here.

PIG (Pain Interest Group)

The CACPR is delighted to announce the 2021-2022 Pain interest group (PIG) meeting series. PIG meetings are informal meetings for labs with an interest in Pain research to present what they are working on. The meetings are meant as a sounding board for new ideas or a place to present preliminary data to get feedback. It can also be used to give graduate students and postdocs practice at organizing and presenting their projects. It is a low-key meeting that is not meant to be intimidating, allowing people to talk through innovative ideas that might turn into something. Having attendance from people across campus can be a springboard to new collaborations. The meetings will be given remotely to favor attendance. Consider joining us to listen to the new research advances of our teams and faculty. We look forward to meeting you.

If you want to be included on the mailing list or for more information about the PIG meetings, contact Dr. Wei Guo at wguo@umaryland.edu or Dr. Luana Colloca at colloca@umaryland.edu.

To view the full schedule for Pain Interest Group (PIG) meetings, please click here.

From everyone at the UM Center to Advance Chronic Pain Research (CACPR), we wish you a joyous holiday season, a happy and healthy new year, and continued success in 2022!

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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