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**NIH HEAL Workshop - Interface between sleep and pain: symptomatology, pathobiology and treatment response**

 **(NHLBI, NCCIH, NINDS)**

**Dates and Times (EST)**

**December 16, 2024 10am – 4:45 pm**

**December 17, 2024 10am – 4:00 pm**

**Virtual Workshop**

**Workshop Rationale:** Sleep deficiency (e.g., short sleep duration, irregular timing, poor sleep quality) and sleep disorders (e.g., insomnia, sleep apnea, shift work sleep disorder) are frequently co-morbid in individuals with acute and chronic pain conditions (e.g., osteoarthritis, neuropathy, cancer, sickle cell disease, temporomandibular disorders, fibromyalgia). Evidence points to a bi-directional relationship where sleep deficiency exacerbates pain sensitivity, and pain triggers sleep disruption. Sleep and circadian disturbances are modifiable and potential therapeutic targets to mitigate pain pathobiology and improve pain management and treatment response. This workshop is designed to identify medically imperative research questions, gaps and opportunities to better understand the mechanisms, clinical targets and interventions needed to mitigate the self-reinforcing cycle of sleep deficiency and chronic pain. Discussions will focus on advancing strategies to improve sleep in the context of chronic pain and to optimize chronic pain outcomes by addressing co-morbid sleep complications and disorders.

**3-5 overarching objectives**

* Delineate neural and peripheral mechanisms/therapeutic targets linking sleep disturbance and chronic pain pathophysiology
* Discuss the significance of circadian rhythms in pain symptomatology and hyperalgesia
* Identify strategies to improve sleep and circadian rhythm disturbances in the context of chronic pain conditions
* Examine whether sleep and circadian interventions should be integrated into pain management strategies, i.e., improve clinically relevant pain outcomes and underlying biological processes

**Goal**

Identify knowledge gaps, critical unmet needs, and opportunities for translating sleep and circadian discoveries to the prevention, diagnosis and management of chronic pain conditions.

**Workshop Co-Chairs**

**Monika Haack, PhD**

*Associate Professor*

Department of Neurology

Beth Israel Deaconess Medical Center

<https://connects.catalyst.harvard.edu/Profiles/display/Person/29715>

**Michael T. Smith, PhD**

*Professor of Psychiatry and Behavioral Sciences*

Director, Division of Behavioral Medicine

Department of Psychiatry

Johns Hopkins University

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**Workshop Agenda**

**Day 1: 10:00 am – 4:45 pm EST**

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| **Time** | **Speakers** |
| 10:00 –10:20 am | Welcome and opening remarks (NIH)**Walter J. Koroshetz, MD (NINDS, Director)****Helene Langevin MD, (NCCIH, Director)** |
| 10:20 – 10:30 am | Workshop overview (Co-Chairs)**Michael T. Smith, PhD (Johns Hopkins U)****Monika Haack, PhD (Harvard Medical School)** |
| **Session 1** | **HEAL Program Overview**  |
|  | **Purpose**: Discuss goals and major scientific components of the NIH HEAL OUD and Pain programs. Identify opportunities for sleep and circadian science to contribute to HEAL priorities and scientific deliverables.  |
| 10:30 – 10:40 am | **Wilson Compton, MD, MPE (NIH/NIDA)** – “HEAL Opioid Use Disorder (OUD) program overview” |
| 10:40 –10:50 am | **Michael L. Oshinsky, PhD (NIH/NINDS)** – “HEAL Pain program overview” |
| 10:50 – 11:00 am | **Moderator: Sunila Nair, PhD (NIH/NIDA)** Questions/Discussion |
| **Keynotes** | **Sleep and Chronic Pain** |
|  | **Purpose**: Discuss conceptual models of sleep and chronic pain interface, and opportunities for scientific synergy. |
| 11:00 –11:20 am  | **Michael V. Vitiello, PhD (U Washington) –** “The complex relationship between sleep and chronic pain” |
| 11:20 am – 11:40 am | **Roger B. Fillingim, PhD (U Florida)** – “Emerging Themes in Chronic Pain Research and Their Relevance to Sleep” |
| 11:40 am– 12:00 pm | **Moderator: Larry Baizer, PhD (NIH/NHLBI/NCSDR)**Questions/Discussion |
| 12:00 –1:00 pm | Lunch break |
| **Session 2** | **Mechanisms Linking Circadian Rhythms, Hyperalgesia and Chronic Pain** |
|  | **Purpose:** Discuss importance of circadian rhythms in chronic pain symptomatology, pathobiology and management. What is the significance of circadian rhythms in mechanisms of pain? How to improve measurement of rhythms in pain cohort and trial studies? Identify circadian-based interventions to improve pain management and treatment outcomes.  |
| 1:00 – 1:15 pm | **Randy J. Nelson, PhD (West Virginia U)** – “Disrupted Circadian Rhythms and Altered Responses to Pain Stimuli and Opiates” |
| 1:15 –1:30 pm | **Helen J. Burgess, PhD (U Michigan)** – “Morning Light Treatment for Chronic Pain” |
| 1:30 – 1:45 pm | **Chung Jung Mun, PhD (Arizona State U)** – “The 24-Hour Cycle of Pain: Circadian Rhythmicity of Pain Sensitivity in Humans and Its Implications” |
| 1:45 –2:00 pm | **Moderator: Janet He, PhD (NIH/NINDS)** Questions/Discussion |
| **Session 3** | **Panel: Mechanisms linking sleep/circadian rhythms, hyperalgesia and chronic pain risk** |
|  | **Purpose:** Advance understanding of mechanisms linking sleep and acute/chronic pain at multiple levels of pain processing. Identify mechanisms by which sleep disturbance exacerbates hyperalgesia and/or makes the management of chronic pain more difficult. Apply basic discovery to identify potential mechanistic targets to intervene on the self-perpetuating cycle of sleep disturbance and chronic pain. Discuss novel strategies to investigate mechanisms linking sleep and chronic pain.  |
| 2:00 –2:10 pm | **Chloe Alexandre, PhD (Johns Hopkins U)** – “Unraveling the neurobiological mechanisms at the interface of sleep and pain” |
| 2:10 –2:20 pm | **Giancarlo Vanini, MD (U Michigan) -** “Preoptic-PAG Pathway Linking Sleep Loss and Pain” |
| 2:30 – 2:40 pm | **Rachel K. Rowe, PhD (U Colorado) –** “Inflammatory pathways that mediate the bidirectional relationship between sleep and pain” |
| 2:40 – 2:50 pm | **Tiffany J. Braley, MD, MS (U Michigan) -** “Intersections between sleep, pain, and cannabinoid use: Knowledge gaps and future directions” |
| 2:50 – 3:00 pm | **Lauren M. Hablitz, PhD (U Rochester) –** “The glymphatic system times sleep and pain” |
| 3:00 –3.15 pm | Short Break |
| 3:15 – 3:25 pm | **Fiona C. Baker, PhD (SRI International) –** “Sleep disturbance, alcohol use and chronic pain” |
| 3:25 –3:35 pm | **Jamie L. Rhudy, PhD (U Oklahoma)** – “How Sleep May Contribute to Native American Pain Inequities”  |
| 3:35 –3:45 pm | **Tony Cunningham, PhD (Harvard Medical School)** – “Sleep loss and emotional regulation in chronic pain pathobiology”  |
| 3:45 pm – 4:30 pm | **Moderator: Shailesh Kumar, PhD (NIH/NIAAA)**Questions/Discussion |
| **4:30 –** **4:45 pm** | Take-home points (Co-Chairs)Adjourn Day 1 |

**Day 2: 10:00 pm – 4:00 pm EST**

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| 10:00 –10:10 am | Welcome and opening remarks (*NIH)* **Inna Belfer, MD, PhD (NCCIH)****Janet He, PhD (NINDS)** |
| **Keynotes** | **Sleep and Pain Pharmacology** |
|  | **Purpose**: Discuss current developments in sleep and pain pharmacotherapies and interactions between targets and efficacy across sleep and pain conditions. Do sleep medications interfere with and/or improve pain symptoms and management? Do pain medications interfere with and/or improve sleep? What are critical gaps and opportunities for research with respect to treating co-morbid sleep and pain conditions?  |
| 10:10 –10:30 am | **Andrew D. Krystal, MD, MS (UCSF)** – “Pharmacology to improve sleep in the context of chronic pain”  |
| 10:30 –10:50 am | **Clifford J. Woolf, MB, BCh, PhD (Harvard Medical School)** – “Advances and limitations of pharmacology of pain management”  |
| 10:50 – 11:10 am | **Moderator: Aaron D. Laposky, PhD (NIH/NHLBI/NCSDR)** Questions/Discussion  |
| **Session 4** | **Cross-cutting priorities: sex differences and disparities** |
| 11:10 am –12:25 pm | **Purpose:** Discuss cross-cutting factors to consider across all basic and clinical research in sleep and pain. Research has identified sex and health disparities as centrally important in the etiology, pathobiology and management of sleep and pain conditions. Examine the importance of sex and disparities to the intersection of sleep and chronic pain.  |
| 11:10 –11:25 am | **Jeffrey S. Mogil, PhD, FCAHS, FRSC (McGill U)** – “Pain, Sex, and Death” |
| 11:25 –11:40 am | **Sara Nowakowski, PhD, CBSM, DBSM (Baylor Coll Med)** – “Sleep in women across the lifespan in relation to pain disorders” |
| 11:40 –11:55 am | **Chandra L. Jackson, PhD, MS (NIH/NIEHS)** – “Disparities in Sleep Health: Implications for Sleep-Pain Research” |
| 11:55 –12:10am | **Carmen Renée Green, MD (City U of New York)** – “Disparities and Social Determinants in Chronic Pain” |
| 12:10 – 12:25 pm | **Moderator: Arielle Gillman, PhD, MPH (NIH/NIMHD)****Questions/Discussion** |
| 12:25 –1:15 pm | Lunch break |
| **Session 5** | **Panel: Sleep and Circadian Interventions in Chronic Pain** |
|  | **Purpose**: Discuss novel strategies to improve sleep in the context of chronic pain. Determine if improvements in sleep facilitate chronic pain management (i.e., person-centered and clinical outcomes). Does improving sleep result in better pain prevention, management and treatment? Do pain medications facilitate or impair sleep? Do sleep medications affect pain processing and symptoms? Do sleep problems vary by the type of pain condition? Is sleep adequately addressed in the assessment/treatment of chronic pain? If not, what is the barrier (e.g., education, lack of multi-disciplinary teams, lack of evidence that sleep will make a difference)? |
| 1:15 –1:25 pm | **Kristin L. Schreiber, MD, PhD (Harvard Medical School)** – “The Perioperative Period as a Workshop for Understanding the Sleep-Pain Relationship and Testing Preventive Interventions” |
| 1:25 –1:35 pm | **Fadel Zeidan, PhD (UCSD)** – “Neural mechanisms supporting the modulation of chronic pain by mindfulness meditation as compared to placebo” |
| 1:35 –1:45 pm | **Patrick H. Finan, PhD (U Virginia) –** “The Intersection of Sleep, Reward, and Pain: Pathways to Addiction Vulnerability” |
| 1:45 – 1:55 pm | **Tonja M. Palermo, PhD (Seattle Children’s) –** “Sleep, Chronotype, and Pain in Adolescents: Implications for Targeted Interventions” |
| 1:55 -2:05 pm | **Cornelius B. Groenewald, MD (Stanford U) –** “Sleep and acute postoperative pain in adolescents” |
| 2:05 – 2:15 pm | **Gilles Lavigne, DMD, PhD, FRCD (McGill U) –** “Sleep apnea and orofacial pain” |
| 2:15 –2:25 pm | **Daniel Whibley, PhD (U Michigan)** – “Combining sleep improvement and physical activity for pain management” |
| 2:25 –2:35 pm | **Michael R. Irwin, MD (UCLA) –** “Insomnia and inflammation: pathways to depression” |
| 2:35 – 2:50 pm | Short Break |
| 2:50 –3:45 pm | **Moderator: Inna Belfer, MD, PhD (NIH/NCCIH)**Questions/Discussion |
| 3:45 –4:00 pm | Closing Remarks. Take-home points (Co-Chairs)Adjourn Workshop |