NATIONAL ACADEMIES Sciences Engineering Medicine

Forum on NEUROSCIENCE and NERVOUS SYSTEM DISORDERS

Exploring Sleep Disturbance in Central Nervous System Disorders

A Workshop

Keck Center (Room 100) | 500 Fifth Street, NW, Washington, DC 20001

Wednesday, November 2 - 9:30am–5:00pm (ET)

Thursday, November 3 – 9:30am–2:00p.m. (ET)

WORKSHOP OBJECTIVES

This public workshop will bring together experts and key stakeholders from academia, industry, government, philanthropic foundations, and disease-focused non-profit organizations to explore the role of sleep in central nervous system (CNS) disorders and opportunities to mitigate sleep disturbances commonly associated with these disorders.

Invited presentations and discussions may:

- Examine the prevalence and nature of sleep disturbances across CNS disorders;
- Review the current state of knowledge regarding the mechanisms, function, and characterization of sleep, including changes across the human lifespan;
- Discuss research gaps, including those around methodological considerations and harmonization, and opportunities for cross-disciplinary collaboration between sleep experts and those focused on CNS disorders along the basic to clinical spectrum;
    - Consider opportunities to better understand underlying mechanisms of sleep by leveraging advances from ongoing efforts (e.g., BRAIN Initiative) to integrate behavioral outputs with brain network and neural circuit activity;
    - Explore how a genes-first approach can illuminate the bi-directional relationship between disturbed sleep and CNS disorders;
- Consider potential relationships among disturbed sleep, CNS disorders, and environmental factors associated with both disturbed sleep and increased risk for CNS disorders, including discussing related disparities and approaches to disentangling causal versus contributing factors;
- Consider the impact of altered circadian timing (in shift work, and otherwise in modern society) on sleep quantity and quality and associated co-morbidities e.g. CNS disorders; and
- Explore the potential of sleep as a mitigatable target by drugs, devices, and behavioral modifications, as well as a measurable marker related to CNS function, including standardization and common data format requirements to facilitate deeper and cross-therapeutic understanding of sleep.

WEDNESDAY, NOVEMBER 2, 2022 (All times listed in ET)

9:30–9:35am **Welcome**
FRANCES JENSEN, University of Pennsylvania; *Co-chair, Forum on Neuroscience and Nervous System Disorders*

9:35–9:45am **Workshop Overview**
LOUIS PTÁČEK, University of California, San Francisco; *Workshop Co-Chair*
HEATHER SNYDER, Alzheimer's Association; *Workshop Co-Chair*

9:45–10:15am **Keynote Talk: Current State of Knowledge regarding the Mechanisms, Function, and Characterization of Sleep, including Changes across the Human Lifespan**
AMITA SEHGAL, University of Pennsylvania, *Planning Committee Member*

10:15–11:20 am **Session 1: Sleep Disorders and Sleep Disruption in CNS Disorders**

- Examine the prevalence and nature of sleep disturbances across CNS disorders to include insomnias, hypersomnias, disorders of the sleep-wake schedule, and parasomnias.
- Discuss methodological gaps in sleep research and the need for standardization and harmonization of approaches.

10:15–10:20am **Session Overview**
KATHLEEN MERIKANGAS, National Institute of Mental Health, *Planning Committee Member, Session Moderator*

10:20–10:50am **Overview**
PHYLLIS ZEE, Northwestern University Feinberg School of Medicine

Understanding and Addressing Underlying Determinants of Disparities in Sleep
DAYNA JOHNSON, Emory University

Measurements of Sleep and Rest Activity: Where are we and where would we like to go?
NATHANIEL WATSON, University of Washington School of Medicine

10:50–11:25am **Moderated Panel Discussion and Audience Q&A**
Discussants:
UMA RAO, University of California, Irvine; *Planning Committee Member*
KARLA DZIENKOWSKI, Restless Legs Syndrome Foundation

11:25–11:40am **BREAK**

11:40–1:00pm **Session 2: Underlying Mechanism of Sleep**

- Consider opportunities to better understand underlying mechanisms of sleep by leveraging advances from ongoing efforts (e.g., BRAIN Initiative) to integrate behavioral outputs with brain network and neural circuit activity.
- Explore how a genes-first approach can illuminate the bi-directional relationship between disturbed sleep and CNS disorders.
- Consider the impact of altered circadian timing on sleep quantity and quality and associated co-morbidities e.g. CNS disorders.

11:40–11:45am **Session Overview**
LOUIS PTÁČEK, University of California, San Francisco; *Workshop Co-Chair; Session Moderator*

11:45–12:25pm **Circadian Timing**
ERIK HERZOG, Washington University in St. Louis

Model Systems
DAVID RAIZEN, University of Pennsylvania

A Genes-First Approach
YING-HUI FU, University of California, San Francisco

Neural Circuitry and Cortical Activity
LUIS DE LECEA, Stanford University

12:25–1:00pm **Moderated Panel Discussion and Audience Q&A**
Discussant:
JOHN HOGENESCH, University of Cincinnati; Cincinnati Children's Hospital Medical Center

1:00–2:00pm **LUNCH**

2:00–3:10pm **Session 3 (Part A): Risk and Mitigatable Targets for Brain Disorders (Psychiatry)**

- Consider potential relationships among disturbed sleep, CNS disorders, and environmental factors associated with both disturbed sleep and increased risk for CNS disorders, including discussing related disparities and approaches to disentangling causal versus contributing factors.
- Explore the potential of sleep as a mitigatable target by drugs, devices, and behavioral modifications, as well as a measurable marker related to CNS function, including standardization and common data format requirements to facilitate deeper and cross-therapeutic understanding of sleep.

2:00–2:05pm **Session Overview**
JOHN SPIRO, Simons Foundation; *Planning Committee Member; Session Moderator*

2:05–2:45pm **Neurodevelopmental Disorders**
ASHURA BUCKLEY, National Institute of Mental Health

Schizophrenia
DARA MANOACH, Harvard Medical School

Mood Disorders
ANDREW KRYSTAL (*via Zoom*), University of California, San Francisco

INDUSTRY PERSPECTIVE
MARGARET MOLINE, Eisai Pharmaceuticals

2:45–3:20pm	**Moderated Panel Discussion and Audience Q&A**
3:20–3:35pm	**BREAK**
3:35–4:05pm	**Biomarkers of Sleep and Sleep Disturbance** AARTI SATHYANARAYANA, Northeastern University VADIM ZIPUNNIKOV, Johns Hopkins University JOHN HOGENESCH, University of Cincinnati; Cincinnati Children's Hospital Medical Center
4:05–4:40pm	**Moderated Discussion and Audience Q&A**
4:40–5:00pm	**Day 1 Synthesis and Preview to Day 2 of the Workshop** LOUIS PTÁČEK, University of California, San Francisco; *Workshop Co-Chair* HEATHER SNYDER, Alzheimer's Association; *Workshop Co-Chair*

THURSDAY, NOVEMBER 3, 2022 (All times listed in ET)

9:30–9:35am — **Welcome and Recap of Day 1 Themes**
LOUIS PTÁČEK, University of California, San Francisco; *Workshop Co-Chair*
HEATHER SNYDER, Alzheimer's Association; *Workshop Co-Chair*

9:35–11:15am — **Session 3 (Part B): Risk and Mitigatable Targets for Brain Disorders (Neurology)**

- Consider potential relationships among disturbed sleep, CNS disorders, and environmental factors associated with both disturbed sleep and increased risk for CNS disorders, including discussing related disparities and approaches to disentangling causal versus contributing factors.
- Explore the potential of sleep as a mitigatable target by drugs, devices, and behavioral modifications, as well as a measurable marker related to CNS function, including standardization and common data format requirements to facilitate deeper and cross-therapeutic understanding of sleep.

9:35–9:40am — **Session Overview**
PERCY GRIFFIN, Alzheimer's Association; *Planning Committee Member; Part 2 Session Moderator*

9:40–10:20am — **Neurodegenerative Disorders**
ERIK MUSIEK, Washington University School of Medicine in St. Louis

Influence of Light on Sleep and Health
TIFFANY SCHMIDT, Northwestern University

Central Nervous System Hypersomnias and Progress in Understanding Narcolepsy
THOMAS SCAMMELL, Beth Israel Deaconess Medical Center

Industry Perspective
HAO WANG, Takeda, *Planning Committee Member*

10:20–11:15am — **Moderated Panel Discussion and Audience Q&A**
Discussants:
YING-HUI FU, University of California, San Francisco

11:15-12:15pm — **LUNCH**

12:15–2:00pm — **Session 4: Synthesis and Potential Next Steps**

- Synthesize key themes from the workshop.
- Discuss research gaps and opportunities for cross-disciplinary collaboration between sleep experts and those focused on CNS disorders along the basic to clinical spectrum.

12:15–12:20pm	**Session Overview** CLIFFORD SAPER, Harvard University; Beth Israel Deaconess Medical Center; *Session Moderator*
12:20–1:20pm	**Panel Discussion** MARISHKA BROWN, National Heart, Lung, and Blood Institute BRIAN FISKE, Michael J. Fox Foundation for Parkinson's Research; *Planning Committee Member* MORTEN GRUNNET, H. Lundbeck A/S MATTHEW PAVA, Defense Advanced Research Projects Agency AMITA SEHGAL, University of Pennsylvania; *Planning Committee Member* ANDREW VARGA, Icahn School of Medicine at Mount Sinai; American Academy of Sleep Medicine
1:20–1:55p.m.	**Audience Q&A**
1:55–2:00p.m.	**Concluding Remarks** LOUIS PTÁČEK, University of California, San Francisco; *Workshop Co-Chair*
2:00pm	**ADJOURN**