



WILLIAM C. DEMENT
SLEEP AND CHRONOBIOLOGY
BEHAVIORAL SCIENCE
RESEARCH APPRENTICESHIP

Retreat Colloquium

17-19 August 2015

Whispering Pines Conference Center
URI Alton Jones Campus, West Greenwich, RI

Summer Sleep Retreat, 2015

Summer Sleep Retreat, 2015

Monday	Event	Speaker	Topic
1200	Lunch		
1315		Amy “AJ” Schwichtenberg, PhD, Young Investigator	Developmental Correlates of Circadian Patterns in Toddlers Born Preterm
1415	Break		
1445		Abby Hulverson, Dement Fellow	A look at the past, present, and future of narcolepsy and hypocretin
1500		Westley Youngren, Dement Fellow	Emotional Processing, Such Stuff as Dreams are Made On
1515		Tom Wooten, Dement Fellow	Multiple Sclerosis and Sleep Disturbances: Exploring Therapeutics
1530	Break		

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Monday	Event	Speaker	Topic
1600		Jade Gingras, Dement Fellow	Cognitive Consequences of Shift Work
1615		Lisa Gniewkowski, Dement Fellow	The Development of Infant Sleep: How Complex Neurobiological Processes Develop Simultaneously
1630		Ashley Ernst, Supervising Tech	Slow-wave Sleep in Alzheimer's Disease: Could adenosine help save memory?
1700	Hors d'oeuvres		
1800	Dinner		
1930		William C. Dement, MD, PhD	An Evening with Dr. Dement-- Reminiscences from 60+ Years of Sleep: Science, Medicine, Politics—just ask...
2030	Camp Fire		
2230	Lights Out		

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Tuesday	Event	Speaker	Topic
0915		Huiyan "Winnie" Huang, PhD, Young Investigator	What can we learn about sleep from <i>C. elegans</i> ?
1015	Break		
1045		Julie Erwin, Dement Fellow	The Efficacy of Cognitive Behavioral Therapy for Insomnia in Adults
1100		Cindy Okamoto, Dement Fellow	Effects of Circadian Dysrhythmia on Athletic Performance
1115		Nishath Rahman, Dement Fellow	Gender Influences in Obstructive Sleep Apnea: Diagnosis & Pathophysiology
1130		Brett Messman, Dement Fellow	Landau-Kleffner Syndrome: An acquired auditory aphasia in children with a disruptive pathology during slow wave sleep

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Tuesday	Event	Speaker	Topic
1200	Lunch		
1330		Bryce Mander, PhD, Young Investigator	β -Amyloid is associated with NREM slow wave disruption and impaired hippocampus-dependent memory consolidation
1430	Break		Change into 'Play Clothes'
1445	Walk in the Woods	Assemble in Groups as Instructed	Small Group Conversations about Graduate/Medical School, Careers, etc.
1600	Assemble at Playground	Games!	[Please return from the Walk in the Woods promptly]
1715	Hors d'oeuvres		
1800	Dinner		
1930	Fun Night	Dement Fellows and Others Arrive at 1930	Faculty, Young Investigators, Staff: Assemble in Conference Center at ~1915 to Set Up
2130	Camp Fire		
2300	Lights Out		

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Wednesday	Event	Speaker	Topic
0930		Jared Minkel, PhD, Young Investigator	Why should treating sleep disturbance improve outcomes for mood disorders?
1030	Break		
1100		Ryan Bahar, Dement Fellow	The Role of Orexin in Alzheimer's Disease as Observed through the Lens of Sleep
1115		Corinna Cluckey, Dement Fellow	Surgical Interventions for Sleep Apnea
1130		Karen Konkoly, Dement Fellow	Falling Awake: Special Cases of Sleeping Consciousness
1145		Mary A. Carskadon, PhD, Program Director	Thanks and Farewell
1200	Lunch		

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Young Investigator Presentations

AJ Schwichtenberg, PhD, Assistant Professor, Department of Human Development & Family Studies/Psychological Sciences/Speech, Language and Hearing Sciences, Purdue University

Developmental Correlates of Circadian Patterns in Toddlers Born Preterm

Children born preterm are at elevated risk for developmental and behavioral concerns (Bhutta et al., 2002). Preterm infant survival rates are increasing, as is our need to understand the developmental cascade associated with preterm birth. Early sleep patterns may play a crucial role in later health and developmental concerns. The current study assesses the roles of toddler circadian sleep/activity patterns on later outcomes. We used time series modeling to examine circadian sleep/activity patterns at two years of age in 91 children born preterm. Prematurity and family sociodemographic assets were recorded at hospital discharge. Child school-age concerns were assessed using parent and teacher reports on the Child Behavior Checklist, Conners 3, and a health questionnaire. Sleep/activity data (actigraphy) were assessed via cosinor models with two sinusoidal waves. The first wave modeled nighttime sleep and the second wave modeled a mid-day nap. We compared each child to this prototypical circadian pattern (PCP) and assessed their daytime activity patterns. Child sleep/activity parameters were regressed onto school-age concerns with gender, prematurity, and family sociodemographic assets as covariates.

Sleep variations from the PCP at age two are associated with cognitive skills at three. Toddlers with patterns that closely aligned with the PCP had higher abbreviated IQ scores at 3 years of age ($p < .01$). Additionally, at 6 years of age these children had fewer parent-reported behavioral concerns and fewer health concerns/medical visits (all $p < .05$). Higher toddler mean activity level adjusted for rhythm was associated with fewer health concerns/medical care visits at both 3 and 6 years of age (all $p < .05$). The novel approach used in this study to index child circadian patterns provides a holistic analysis of sleep/activity, which may prove to be developmentally consequential. These findings may help practitioners identify preterm infants/toddlers at increased risk for later cognitive and health difficulties.

Winnie Huang, PhD, Postdoctoral Fellow in Translational Neuroscience, Department of Neuroscience, Brown University

What can we learn about sleep from *C. elegans*?

C. elegans sleep has all the behavioral hallmarks of sleep in other species, making *C. elegans* an ideal genetic model for sleep research. Characterization of sleep in this system has already shed light on the molecular mechanisms of sleep regulation—revealing conserved neurotransmitter systems and genes critical

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for sleep across species. My research focuses on identifying previously unknown genes required for sleep. By undertaking an unbiased genetic screen, I have uncovered a pivotal role for conserved channels regulating sleep.

During sleep, animals exhibit a heightened arousal threshold and decreased behavioral response to external stimuli. The molecular mechanisms underlying these changes are not fully understood. We found that the activity of the *C. elegans*' NALCN sodium leak channel, NCA, is critical for normal sleep and arousal. The EGL-4 protein kinase is downstream of NCA channels in regulating sleep. Moreover, the UNC-7 and UNC-9 gap junction proteins act further downstream during sleep. Combined, these results emphasize the conservation and importance of neuronal activity during sleep, demonstrate a role for gap junctions in sleep, and identify possible targets for the modulation of sleep entry and maintenance.

Bryce Mander, PhD, Associate Specialist, Sleep and Neuroimaging Laboratory, University of California, Berkeley

β -Amyloid is associated with NREM slow wave disruption and impaired hippocampus-dependent memory consolidation

Independent evidence associates β -amyloid pathology with both NREM sleep disruption and memory impairment in older adults. However, whether the influence of β -amyloid pathology on hippocampus-dependent memory is, in part, driven by impairments of NREM slow wave activity (SWA) and associated overnight memory consolidation is unknown. Here, we show that β -amyloid burden within medial prefrontal cortex (mPFC) is significantly correlated with the severity of impairment in prefrontal NREM SWA generation within the slow oscillation range (0.6-1Hz) but not the delta range (1-4 Hz). Moreover, reduced prefrontal NREM SWA generation in the low frequency range (0.6-1Hz) was further associated with impaired overnight memory retention and impoverished hippocampal-neocortical memory transformation. Furthermore, structural equation models revealed that the association between mPFC β -amyloid pathology and impaired hippocampus-dependent memory consolidation is not direct, but instead, statistically depends on the intermediary factor of diminished prefrontal NREM SWA in the slow oscillation range. These relationships were specific to low frequency activity during NREM sleep and were not present during REM sleep. In conclusion, by linking β -amyloid pathology with impaired prefrontal NREM SWA, these data implicate sleep disruption as a novel mechanistic pathway through which β -amyloid pathology may contribute to hippocampus-dependent cognitive decline in the elderly.

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Jared Minkel, PhD, Licensed Clinical Psychologist, Rhode Island
Cognitive Behavioral Therapy Clinic

Why should treating sleep disturbance improve outcomes for mood disorders?

Treating sleep disturbance in patients with major depression improves outcomes, but mechanisms underlying these effects are unknown. I will present two studies that suggest insufficient sleep influences depressive symptoms through effects on stress and reward. Study 1 exposed healthy adults to an experimental stressor in the context of a sleep deprivation experiment. Salivary cortisol assays revealed that sleep deprivation was associated with increased stress responses. In Study 2, patients with major depression completed the Psychomotor Vigilance Task (PVT) before completing an fMRI reward task. Those with greater sleepiness as estimated by the PVT also showed less brain reactivity to reward in the Nucleus Accumbens. Together, these studies suggest that insufficient sleep may be associated with greater biological responses to stress coupled with lower reward reactivity. This profile suggests a unique relationship with anhedonia, a core symptom of major depression with relatively well-described behavioral and biological features.

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2015 William C. Dement Fellows

Ryan Bahar

Rising sophomore, Brown University

Corinna Cluckey

Rising senior, University of Colorado, Boulder

Julie Erwin

Rising senior, Butler University

Jade Gingras

2015 Graduate, University of Arizona

Lisa Gniewkowski

2015 Graduate and Candidate for M.S. Neuroscience, The College of Staten Island of the City
University of New York

Abby Hulverson

Rising senior, Stonehill College

Karen Konkoly

Rising junior, Lehigh University

Cindy Okamoto

Rising junior, Harvard University

Brett Messman

Rising senior, University of North Texas

Nishath Rahman

Rising senior, Mount Holyoke College

Thomas Wooten

Rising senior, University of Massachusetts, Amherst

Westley Youngren

Rising senior, University of Tulsa

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Research Apprenticeship Faculty, Staff, & Trainees

APPRENTICESHIP FACULTY

**Alpert Medical School of Brown University,
Department of Psychiatry and Human
Behavior**

Mary A. Carskadon, PhD, Director

David Barker, PhD

Rachel Herz, PhD

Jeanne McCaffery, PhD

John McGeary, PhD

Ron Seifer, PhD

Eliza Van Reen, PhD

**Alpert Medical School of Brown University,
Department of Medicine**

Katherine M. Sharkey, MD, PhD

**Rush University, Department of Behavioral
Sciences**

Stephanie Crowley-McWilliam, PhD

**Temple University, Department of Public
Health**

Chantelle Hart, PhD

**University of Pennsylvania, Department of
Psychiatry**

Namni Goel, PhD

**University of Tennessee, Knoxville,
Department of Nutrition**

Hollie Raynor, PhD

**Valencia College, Department of
Communications**

Kathleen Perri, MA

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RETREAT VISITING FACULTY

Alpert Medical School of Brown University
Christine Acebo, PhD

PREDOCTORAL AND POSTDOCTORAL FELLOWS

Jared Saletin, PhD

Mary Beth Miller, PhD

Allison Brager, PhD

Sayako Earle

SLEEP LAB RESEARCH STAFF, E.P. BRADLEY HOSPITAL

Ashten Bartz, PSG Tech & Research
Assistant

David Bushnell, Sr. Research Assistant

Max Elliott, Administrative Secretary

Ashley Ernst, Supervising Tech

Ellyn Ferriter, Sr. Research PSG Tech

Logan Fickling, Supervising Tech

Caroline Gredvig-Ardito, Data Manager &
IRB Coordinator

Scot Kelly, Supervising Tech

Sarah Mickel, Student Research Assistant

Alexis Rodriguez, Research Assistant

PERINATAL SLEEP RESEARCH STAFF, RI HOSPITAL

Stephanie Blatch, MA, Brown Medical
Student

Geraldine Boni, Research Assistant

Sarah Carr, RN, Research Assistant

Julie Quattrucci, Research Assistant

Jason Sarte, Brown Medical Student