



Sleep for Science

Brown University

Bradley Hospital

WILLIAM C. DEMENT
SLEEP AND CHRONOBIOLOGY
BEHAVIORAL SCIENCE
RESEARCH APPRENTICESHIP

Retreat Colloquium

17-19 August 2009

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

Summer Sleep Retreat, 2009

Monday	Event	Speaker	Topic
1200	Lunch		
1330		Erin Hanlon, Ph.D. , Young Investigator	Effects of Skilled Reaching on Sleep Homeostasis and Cortical Gene Expression in the Rat
1430	Break		
1500		Joe Plaksin, Supervising Tech	Sleeping Insomnias
1515		Garry Woodward, Dement Fellow	The Effects of Sleep Loss on Emotion
1530		Maggie Gordon- Fogelson, Dement Fellow	The Effects of Sleep Loss on Satiety Hormones and Appetite
1545		Becca Berger, Visiting Student	The Importance of Napping on Emotional Functioning and Attention in Early Childhood
1600	Break		

Summer Sleep Retreat, 2009

Monday	Event	Speaker	Topic
1630		Jonathan Richman, Dement Fellow	Sleep Loss and Decision Making
1645		Kledia Spiro, Dement Fellow	Sleep, Public Policy and Work Hour Safety in the Medical Profession
1700	Break		
1715	Hors d'oeuvres		
1800	Dinner		
1930		William C. Dement, M.D., Ph.D.	Potpourri: Selections from 59 Years of Sleep Research, Sleep Medicine, Sleep and Circadian Management, Sleep Education, and Sleep Politics
2100	Camp Fire		
2230	Lights Out		

Summer Sleep Retreat, 2009

Tuesday	Event	Speaker	Topic
0930		Jonathan Lipton, M.D., Ph.D., Young Investigator	Tuberous Sclerosis Complex: A Window into Sleep Dysfunction in Neurodevelopment
1030		Tracey Slonim, Dement Fellow	CBT as Treatment for Insomnia
1045	Break		
1115		Adam Leonard, Dement Fellow	Sympathetic Nervous System Activation and Nightmares
1130		Sarah Marzetta, Dement Fellow	Hormone Replacement Therapy as a Possible Treatment for Sleep Disturbance during Menopause
1145		Lauren Schmitt, Dement Fellow	Autism and Sleep Problems
1200	Lunch		

Summer Sleep Retreat, 2009

Tuesday	Event	Speaker	Topic
1330		Daniel J. Mollicone, Ph.D., Young Investigator	Novel Fatigue Mitigation Strategies for Space Operations and Beyond: Basic, Applied, and Translational Research Steps Toward Commercialization
1430	Break		
1445	Walk in the Woods		
1600	Assemble at Playground		
1605	Games!		
1730	Hors d'oeuvres		
1800	Dinner		
1930	Fun Night		
2130	Bonfire		
2300	Lights Out		

Summer Sleep Retreat, 2009

Wednesday	Event	Speaker	Topic
0915		Hawley Montgomery-Downs, Ph.D., Young Investigator	Developmental Psychobiology of Pediatric Sleep-Disordered Breathing and Postpartum Sleep Disturbance
1015	Break		
1045		Jonathan Lassonde, Dement Fellow	How Sleep Evolved: A Darwinian Look at Why We Sleep
1100		Emily Mephram, Dement Fellow	Restless Sleepers: ADHD and Sleep
1115		Paul Zhu, Dement Fellow	Pharmacogenetics of the Adenosine Pathway
1130		Meghan Hewlett, Dement Fellow	Men vs. Women: Sex Differences in Sleep
1145		Mary A. Carskadon, Ph.D., Program Director	Farewell
1200	Lunch		

Summer Sleep Retreat, 2009

Young Investigator Presentations

Erin C. Hanlon, PhD, Postdoctoral Research Associate, University of Wisconsin-Madison, Department of Psychiatry, Madison, WI

Effects of Skilled Reaching on Sleep Homeostasis and Cortical Gene Expression in the Rat

The best characterized marker of sleep homeostasis is the amount of slow wave activity (SWA, 0.5–4 Hz) during NREM sleep. SWA increases as a function of previous waking time and declines during sleep, but the underlying mechanisms remain unclear. We have suggested that SWA homeostasis is linked to synaptic potentiation associated with learning during wakefulness. Indeed, studies in rodents and humans found that SWA increases after manipulations that presumably enhance synaptic strength, but the evidence remains indirect. In the current study, Long Evans rats were trained on skilled reaching, a task known to elicit long-term potentiation in the trained motor cortex, and immediately after learning measured SWA, with intracortical local field potential recordings, and cortical protein levels of c-fos and Arc, two activity-dependent genes involved in motor learning. We found that SWA increased post-training in the trained cortex with smaller or no increase in other cortical areas. This increase was reversible within 1 hour, specific to NREM sleep, and positively correlated with changes in performance during the prior training session, suggesting that it reflects plasticity and not just motor activity. Fos and Arc levels were higher in the trained relative to untrained motor cortex immediately after training, but this asymmetry was no longer present after 1 hour of sleep. Thus, learning to reach specifically affects gene expression in the trained motor cortex and, in the same area, increases sleep need as measured by a local change in SWA.

Jonathan O. Lipton, MD, PhD, Instructor in Neurology, Division of Sleep Medicine, Harvard Medical School, Boston, MA

Tuberous Sclerosis Complex: A Window into Sleep Dysfunction in Neurodevelopment

Sleep disorders are common in patients with epilepsy or autistic spectrum disorders (ASD); however, little is known about their etiology or pathophysiological impact. Tuberous Sclerosis Complex (TSC) is an autosomal dominant disease caused by mutation in either the Tsc1 or Tsc2 genes and affects approximately 1 in 6000 newborns and is characterized by eponymic tumor formation, epilepsy, and ASD. TSC1 and TSC2 proteins (hamartin and tuberin, respectively) form a complex that serves to inhibit the function of the mTOR kinase, a critical regulator of growth control, responses to nutrients, and development. Thus, mutation of either Tsc1 or Tsc2 results in the disinhibition of the mammalian target of rapamycin (mTOR) pathway and resultant over-activation of protein synthesis, gene expression, and cellular stress pathways. We have hypothesized that unbridled activity of the mTOR pathway results in sleep disorders by a combination of dysregulation of the circadian timing mechanism as well as inappropriate activation of cellular stress machinery in the response to a sleep-deprived state. Our group is using mouse models of TSC to initiate work in cell culture, molecular genetics, and behavioral assays, as well as questionnaire-

Summer Sleep Retreat, 2009

based studies in TSC patients to fully characterize the phenotype of sleep disorders in TSC and their underlying mechanisms. Our hope is that TSC will prove a useful springboard by which the pathological effects of sleep dysfunction can be better understood in neurodevelopment.

**Daniel J. Mollicone, PhD, President, CEO Pulsar Informatics, Inc.,
Philadelphia, PA**

Novel Fatigue Mitigation Strategies for Space Operations and Beyond: Basic, Applied, and Translational Research Steps Toward Commercialization

Fatigue-causing factors such as inadequate sleep and circadian misalignment, common in many workplace settings, contribute to increased risk of accidents caused by human error due to sleep related performance impairments. The mitigation of fatigue related risk requires real-time, objective, measurement of performance capability and the application of fatigue countermeasures. My research seeks to address these issues by combining basic research examining the biological mechanisms that govern cognitive performance, applied research developing operationally valid performance tests, and translational research constructing bio-mathematical models of alertness to apply fatigue countermeasures.

**Hawley Montgomery-Downs, PhD, Assistant Professor of
Psychology-Behavioral Neuroscience Program, West Virginia
University, Morgantown, WV.**

Developmental Psychobiology of Pediatric Sleep-Disordered Breathing and Postpartum Sleep Disturbance

The objective of our most recent study of postpartum sleep has been to describe the normative course of maternal sleep and performance during the first four months postpartum. To achieve this goal, we performed longitudinal assessment of two overlapping cohorts' 24-hour sleep during postpartum weeks one through 16 using a field study with continuous wrist actigraphy and personal-digital assistant-based electronic sleep diary, daily psychomotor vigilance testing, and multidaily subjective sleepiness reports. Fifty mothers participated during postpartum weeks two through 13; 24 participated during postpartum weeks nine through 16. Twenty-seven nulliparous controls participated for one week. Maternal sleep time (7.1 [SD±1.0]) hours did not change across postpartum weeks two through 16 and was higher than controls at weeks three and four. Maternal sleep efficiency improved across weeks two (80.0% [SD±6.1]) through 16 (90.0% [SD±3.5]), and was lower than controls through week 13. The increased sleep efficiency was explained by a decrease in sleep fragmentation across week two (21.1 [SD±6.0]) through 16 (12.9 [SD±3.4]), which was higher than controls through week 13. Though postpartum mothers' total sleep time was higher than expected during the initial postpartum months, this sleep was highly fragmented (similar to fragmenting sleep disorders) through the first three postpartum months. Postpartum psychomotor vigilance and subjectively reported sleep and sleepiness were significantly worse than controls. This profile should be considered in intervention designs and family leave policies.

Summer Sleep Retreat, 2009

2009 William C. Dement Fellows

Maggie Gordon-Fogelson

2009 Graduate, Vassar College

Meghan Hewlett

2009 Graduate, University of Michigan-Ann Arbor

Jonathan Lassonde

Rising Senior, Yale University

Adam Leonard

Rising Senior, Brown University

Sarah Marzetta

Rising Junior, Brown University

Emily Mephram

Rising Sophomore, Brown University

Jonathan Richman

Rising Junior, University of Wisconsin-Madison

Lauren Schmitt

Rising Senior, University of Notre Dame

Tracey Slonim

Rising Senior, San Diego State University

Kledia Spiro

Rising Senior, College of the Holy Cross

Garry Woodward

2009 Graduate, Loughborough University

Paul Zhu

Rising Junior, Brown University

Visiting Student

Becca Berger

2009 Graduate, University of Michigan-Ann Arbor

Summer Sleep Retreat, 2009

Research Apprenticeship Faculty, Staff, & Trainees

APPRENTICESHIP FACULTY

Brown Medical School, Department of Psychiatry and Human Behavior

Mary A. Carskadon, PhD, Director
Tamara Bond, PhD
John McGeary, PhD
Katie Sharkey, MD, PhD
Ron Seifer, PhD

Valencia Community College, Department of Communications

Kathleen Perri, MA

PRE & POSTDOCTORAL TRAINEES

Brown University

Sara Nowakowski
Tifenn Raffray, MD
Megan Sands
Leisha Smith
Leila Tarokh, PhD

RETREAT VISITING FACULTY

Brown University

Rachel Herz, PhD
Monique LeBourgeois, PhD

Alpert Medical School of Brown University

Willoughby Britton, PhD
Chantelle Hart, PhD
Erin O'Brien, PhD
Amy Salisbury, PhD
Kristen Stone, PhD

College of the Holy Cross

Amy Wolfson, PhD

CONSULTING PHYSICIANS

Keith Callahan, MD & Judith Owens, MD

E.P. BRADLEY HOSPITAL SLEEP LAB RESEARCH STAFF

James Bass, Data Entry Specialist
Jena Burgner, Research Assistant
David Bushnell, Sr. Research Assistant
Will Coon, Sr. Research PSG Technologist
Danni Dunlap, Data Entry Specialist
Marc D'Uva, Research PSG Technologist
Ellyn Ferriter, Research PSG Technologist
Max Elliott, Administrative Secretary
Clayton Kim, Research PSG Technologist
Jen Norton King, Research Assistant
Laura Kulm, Summer Intern
Denise Maceroni, Assay Technologist
Joe Plaksin, Research PSG Technologist
Grace To, Summer Intern

VISITING FORMER TRAINEES

Brown University, Psychology PhDs

Tracy Rupp, PhD (2005)
Eliza Van Reen, PhD (2007)

Dement Fellows

Allison Brager (2006)
Jared Saletin (2006)

ACKNOWLEDGEMENTS

This summer apprenticeship program was funded in part by a generous grant from Brown University alumnus, Bob Daly.

The summer research project was funded by NIMH grant MH076969.