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ISSUE HIGHLIGHTS

APSS 2012 Recap

Sleep Research Funding Advocacy Update

From the Desk at NIH: NCCAM and Sleep
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Dear Colleagues,

Welcome to the first of three President’s messages where I have an opportunity to update you on the various activities of our organization. First, I want you to know what a great honor it is to be able to serve you as the President of the SRS. I look forward to an active and successful year ahead for the society. Next, I would like to take this opportunity to thank Phyllis C. Zee, MD, PhD for the tremendous work she did as SRS President last year. She was able to successfully move several important initiatives forward, including expansion of our government and NIH Liaison activities, to promote sleep and circadian rhythms research. I look forward to her continuing service over the next year as the Chair of the Government Relations Committee and a member of the Board of Directors.

I also extend my gratitude to all members who attended SLEEP 2012, the premier meeting in our field. I am pleased to announce that SLEEP 2012 was the largest sleep meeting to date. The SLEEP meetings are joint meetings of the SRS and the American Academy of Sleep Medicine.

Another group that deserves a huge amount of gratitude are SRS Committee members and APSS Program Committee members who volunteer their time throughout the year in service of the society and take time out at the SLEEP meeting to attend meetings of their respective committees. In June, several members of the standing committees concluded their terms of service. The SRS thanks the following members, listed by committee, who rotated off of committees for their loyal service:

**Educational Programs Committee**
- Michael Christie, PhD
- Karen Heaton, PhD

**Membership and Communications Committee**
- James Tim McKenna, PhD
- Chris Ward, PhD

**Research Committee**
- Allison Harvey, PhD
- James Wyatt, PhD

**Trainee Education Advisory Committee (TEAC)**
- David M. Raizen, MD, PhD
- Jonathan Wisor, PhD
- Allison Brager, PhD, Trainee Member-at-Large

After reflecting on a tremendously successful meeting and the contributions of our superb volunteers, I would like to turn our attention to the tasks ahead for the SRS. Thanks to the hard work of past leaders and SRS volunteers, we have built a dynamic government relations program. In light of the current grant funding environment, it is my goal to continue the SRS efforts in this important area. This will include continuing our systematic approach to educating Congressional Leaders and NIH Officials about the value and relevance of sleep and circadian research. During our meetings with NIH Institute Directors, Center Directors, Program Officials and Members of Congress in the coming months we will be highlighting SRS priorities in the new NIH Sleep Research Plan and work for its implementation.

Like other associations, academic institutions and individuals, the SRS is not immune from the economic realities that exist today. I intend to continue to stress financial prudence while keeping the needs of our members as a priority. In order to address a need for additional revenue streams and to provide additional benefits to members, I will work with the Educational Programs Committee to continue developing new educational products and courses that will further the mission of the SRS and be a valuable resource for investigators in our field.

I am pleased to report that SRS Membership increased by approximately 100 individuals for the 2012 membership year. During the next year I will work with the Membership and Communications Committee to build on our success this past year. One strategy we plan to employ is reaching out to academic clinicians, clinical researchers and professionals in related fields who have not yet identified themselves as sleep researchers to bring them into the fold. Also, the membership renewal period began on October 1, please be sure to renew your membership today!

The SRS will continue to foster our young investigators by continuing to host the tremendously popular Trainee Symposia Series. The Trainee Symposia Series is a unique opportunity for young scientists to engage in collegial interaction with senior scientists with successful careers across the broad spectrum of sleep and circadian research. I view the Trainee Symposia Series as central to the SRS mission, and take it as a point of pride that the SRS has historically made significant investments in its trainees at all levels of development.

Over the next year, the SRS will continue to work with the AASM, on a number of initiatives including a Joint Task Force that will provide input to the Sleep Disorders Research Advisory Board, the National Center on Sleep Disorders Research and various NIH Institutes and Centers on promising developments in the field and help implement the new NIH Sleep Disorders Research Plan.

We will also continue to work with the AASM to better understand the current state of integrated academic sleep centers to provide consultation to help improve existing centers and assist in the establishment of new ones.

The SRS is currently working with the Society for Research on Biological Rhythms to develop a white paper on issues relating to animal care and use in sleep and circadian research. The goals of the white paper will be to provide investigators with a way to...
educate their local animal regulatory committees and lab animal veterinarians about the unique circumstances of animal care and use in sleep and circadian studies, and to provide them with strategies for meeting the new standards in the 8th edition of the Guide for Care and Use of Laboratory Animals, while preserving the ability to collect meaningful sleep and circadian data.

The coming year will be filled with opportunities and challenges for the SRS. I look forward to working with our members to address the challenges and capitalize on the opportunities presented to us. Your input and involvement in the SRS is appreciated and necessary for a healthy organization. Please contact the SRS national office if you wish to volunteer on a committee or have a good idea to improve the society. The national office can be contacted at ncekosh@srsnet.org or (630) 737-9763.

Sincerely,

Ronald Szymusiak, PhD
President
By Helen J. Burgess, PhD

Welcome to the fall issue of the Sleep Research Society’s Bulletin. As this issue follows the successful 2012 SLEEP meeting in Boston, we traditionally look back on some of the important events from that meeting. As part of our Meeting Recap we are fortunate to have a summary of the successful Trainee Symposia Series, details on SRS awardees, a summary of a keynote address, and a summary of a discussion group on sleep and health disparities. Following the change in leadership that occurs at the end of each annual SLEEP meeting, we have a description of our new SRS Leadership, and a message from our new President. We also have an update a year after the arrival of SRS on Facebook. As in each issue of the Bulletin, we also highlight exciting research, and the research and training opportunities available at a particular domestic and an international sleep research laboratory.

The Society has embarked on a number of important initiatives to advocate for continued sleep research funding, which is described in the Funding Advocacy Update and report on the recent Congressional briefing. How sleep and circadian grants are received at NIH is also critically important to our success. I am very grateful for the report provided by Dr Lee Alekel at NCCAM, and the report from SDRAB which maintain the ongoing communication between NIH and our membership.

I would like to thank Nicholas Cekosh the SRS Coordinator who assists with the production of each issue of the Bulletin three times a year. I want to also thank the Membership and Communications Committee for their continued assistance in both generating ideas for articles and in securing the appropriate contributors. Finally, I would like to thank all of the contributors of the articles included in this issue. It is always difficult to find time in our busy schedules to prepare such pieces for the Bulletin and so I am very grateful to those members who took the time to contribute to this issue.

As always, this Bulletin must serve the needs of all of the members of the Sleep Research Society. To that end I am very interested in receiving suggestions for new articles and/or suggested contributors. I would also like to hear from you if you would like your laboratory highlighted in one of the domestic or international laboratory spotlights. Please email me at Helen_J_Burgess@rush.edu with all your ideas and suggestions. Have a great autumnal season.
The question of the relationship between sleep and memory is at least 2,000 years old. In 95 CE, the rhetorician Quintillian noted the “curious fact, of which the reason is not obvious, that the interval of a single night will greatly increase the strength of the memory [perhaps because] the power of recollection ... undergoes a process of ripening and maturing during the [night]” [1]. But the first scientific report of such effects only appeared in 1885, when Ebbinghaus reported a reduction in forgetting across sleep compared to wake [2], and reports of sleep and specific sleep stages only appeared in the early 1970’s, when both Carlyle Smith and Elizabeth Hennevin published reports of sleep-dependent memory processing in REM [3, 4]. But although Smith has continued to publish reports of sleep’s role in memory consolidation since then, the current wave of interest in the field only dates from Karni et al’s 1994 Science paper, in which they reported that perceptual skills can improve overnight in a REM-dependent manner [5]. Publications in the field only began to rise in 2001, when a cover and special section on “Sleep, Dreams, and Memory” appeared in Science [6]. Indeed, since 2000, the rate of publication of articles of sleep and memory has increased 9-fold. 

In retrospect, the absence of more intense study is surprising. Even before the Karni et al. paper [5], there was a wealth of evidence suggesting that sleep must play a role in memory processing; (i) the multitude of EEG-based sleep stages made clear the importance of brain activity during sleep, as did (ii) the range of wave forms seen in the sleep EEG that were absent during wake. At the very least, the delta waves, sleep spindles, and K-complexes deserved more theoretical discussion. (iii) The variation in the neuromodulators acetylcholine [7], norepinephrine [8], and serotonin [9] across wake-sleep states similarly implied complex variations in brain function during sleep, and (iv) shifts in regional brain activation across wake and sleep argued for significant and varying cognitive processing across REM and NREM sleep [10]. (v) The specific reversal in direction of hippocampal-neocortical communication between REM and NREM [11] only made sense in terms of sleep-dependent memory processing. And if all of these neurophysiological findings were not enough, there was the persistent question of (vi) the nature and function of dreaming [12], which by any measure had to reflect at least the accessing and activation of memories. Still, few beyond Smith pursued these questions.

The Present
In contrast to the prior 2000 years, the last decade has shown dramatic growth in our understanding of the nature and function of sleep-dependent memory processing. One of the main conceptual outcomes of this research is that sleep does not merely “consolidate” memories, a term that refers to the stabilization of initially labile memories [13]; sleep plays a major role in “memory evolution” [14], a complex array of memory processes that alters the encoding and storage of memories, outside of awareness and without intent, after the initial formation of the memory.

Sleep enhances procedural learning: At the most basic level, sleep can enhance procedural learning. Following both perceptual and motor skill training, sleep can lead to improved performance. Thus, on the visual texture discrimination task originally studied by Karni et al. [5], subsequent sleep increases performance in proportion to the amount of SWS obtained early in the night and of REM obtained late in the night, with the product of these two sleep parameters explaining 79% of the intersubject variance in overnight improvement [15]. In contrast, overnight improvement on a motor sequence task correlates with Stage 2 NREM (N2) late in the night, which explains 52% of intersubject variance [16].

We have drawn two controversial conclusions from these findings. First, based on the strength of these correlations, and their dependence on different sleep stages, we have suggested the strong hypothesis that the multiple sleep stages evolved to provide discrete brain states optimized for the performance of distinct aspects of memory evolution. It is easy to imagine that the optimal brain state for extracting visual information from briefly presented images would be different from one optimized for enhancing performance of a complex motor sequence.

The second conclusion is that synaptic level and systems level memory processing are served by different brain states. For example enhancement of visual discrimination performance could result from a variant of synaptic level consolidation, in which all synapses involved in encoding the newly learned skill
are uniformly strengthened [17], or from synaptic homeostasis [18], whereby all synapses in the cortex are uniformly weakened, and the weakest ones are eliminated completely. But this could not account for the shift in the brain regions activated during performance of the motor sequence task following sleep [19], which would appear to require a systems level reorganization of the memories.

Sleep enhances the identification and extraction of salient features, gist representations, and rules from complex data structures: Systems level processing is also suggested by studies demonstrating that sleep can produce qualitative changes in memories, retaining specific elements of a memory while allowing other elements to be lost, or selectively retaining the gist of an experience while the details are forgotten, or extracting causal rules from hundreds of stimulus-response pairs. While many such findings have been reported (e.g., see [17]), we review two of our own here.

The first concerns the “emotional trade-off” described by Elizabeth Kensinger [20]. When subjects are shown photos of emotional scenes containing aversive objects in the foreground, their memory for these objects is better than for objects in neutral scenes that contain unemotional objects. But their memory for the neutral backgrounds of the emotional scenes is actually worse than for backgrounds in the neutral scenes – hence the “trade-off” between the foreground object and background scene. We looked at the impact of time spent awake or asleep on these memories, and found, first, that wake and sleep led to forgetting of neutral scenes at similar rates, with object- and background-memory both deteriorated by about 10% after 12 hrs with or without sleep. Time spent awake led to similar rates of forgetting of negative objects and their backgrounds. But following sleep, while the backgrounds of negative scenes showed 10% deterioration, memories of negative objects were preserved. Thus, sleep appears to selectively consolidate the emotional aspects of memory, the aspects that are arguably of greatest value to the organism.

The second example of qualitative changes in memory following sleep uses the Deese-Roediger-McDermott (DRM) false memory paradigm [21]. When subjects are asked to listen to and remember a list of word that are all related to some central “gist” word that they don’t hear, they often subsequently report having heard this gist word. For example, when subjects heard several lists, including the list “bed, rest, awake, tired, dream, wake, snooze, blanket, doze, slumber, snore, nap, peace, yawn, drowsy,” over 80% incorrectly report having heard the gist word “sleep” [22]. Subjects tested on their recall of these lists after a 12 hr delay showed general deterioration of recall for the words they actually heard, whether the delay occurs across a day or a night. False recall of the gist words (e.g., sleep) also decreased across 12 hr of daytime wake. But in a pattern reminiscent of the emotional trade-off study, subjects actually showed slightly increased rates of (false) recall for the gist words after a night of sleep, a rate significantly higher from that seen after wake [23]. Arguably, in this case a night of sleep results in memories that, while less accurate, are most useful. Interestingly, recall of the studied words correlated negatively with the amount of SWS subjects obtained prior to testing, suggesting that SWS-dependent processes were actually counterproductive, perhaps focusing too much on detail memory and not enough on gist extraction [23].

Other examples abound. Wagner et al. [24] have reported a two- and a half-fold increase in the number of subjects discovering a mathematical insight after a night of sleep; we have reported improved performance on a probabilistic learning task, where subjects must discover patterns within a complex set of stimulus-response pairs [25], improvement that correlates with REM sleep time [26]. Similarly, Cai et al. [27] have reported that REM sleep enhances the formation of associative networks and the integration of unassociated information. Thus, sleep, and REM sleep in particular, appear to support the extraction and selective retention and enhancement of salient information, gist, and patterns from complex memories.

The Future
Moving forward, our laboratory is exploring three promising areas. The first is attempting to link our dream studies to our work on sleep and memory processing. We have recently reported that sleep-dependent enhancement of performance on a virtual maze task is strongly correlated with reports of dreaming about the task, although the content of the dreams does not represent overt replay of the task [28]. This has led us to suggest that dreaming reflects a separate aspect of memory evolution, more related to determining the future uses of these memories than to their specific enhancement.

A second area of research is the exploration of deficits in sleep-dependent memory processing seen in neurologic and psychiatric disorders. Our studies of a deficit in sleep-dependent motor-skill consolidation in chronic, medicated schizophrenia patients has shown that this deficit correlates with a deficit in sleep spindles [29]. Pilot studies suggest that augmenting sleep spindles with eszopiclone, a non-benzodiazepine hypnotic leads to a recovery of normal overnight improvement on this task.

Finally, we have begun to extend our studies of sleep-dependent memory processing back to periods of pre-sleep quiet wake. Analyses of both EEG microstates [30] and fMRI functional connectivity during periods of post-training rest have identified brain activity that predicts subsequent sleep-dependent improvement on our virtual maze task. These findings suggest that post-training rest can serve to tag memories for subsequent sleep-dependent processing. In addition, the activity of a similar EEG microstate seen during NREM sleep predicts post-sleep improvement with a correlation of $r = 0.83$, suggesting that the sleep-dependent enhancement of this task is actually occurring in this microstate. And the possibility that this microstate also reflects the brain dreaming of the task is an exciting one that holds the potential of finally unifying dream and memory research [28].

References
2012 Distinguished Scientist Award

*Award Description:* The Distinguished Scientist Award is the highest award presented by the Sleep Research Society. Established in 1989, the award recognizes significant, original and sustained scientific contributions of a basic, clinical or theoretical nature to the sleep and circadian research field. This award honors a single individual for research contributions made over an entire career.

*Recipient:* Clifford Saper, MD, PhD, is the James Jackson Putnam Professor of Neurology and Neuroscience and Chairman of the Harvard Department of Neurology at Beth Israel Deaconess Medical Center at Harvard Medical School in Boston.

Dr. Saper received his MD and PhD and did his internship in internal medicine at Washington University School of Medicine in St. Louis before completing a neurology residency at Cornell University Medical Center - New York Hospital. He then joined the faculty of Washington University School of Medicine and served as Assistant and later Associate Professor of Neurology and Anatomy and Neurobiology from 1981 to 1985. He moved to the University of Chicago the following year and was an Associate Professor, the William D. Mabie Professor of Physiology and Neurology, and Chairman of the Committee on Neurobiology between 1985 and 1992. He has been at Harvard since 1992.

From 2006 to 2011, Dr. Saper served on the Board of Directors of the Sleep Research Society (SRS) and as SRS President in 2009–2010. He was the Editor-in-Chief of the Journal of Comparative Neurology between 1994 and 2011, serves on the editorial board of Neurology and has been on the editorial boards of Brain, the Journal of Neuroscience, SLEEP, and Physiological Genomics. He was elected to the Institute of Medicine in 2009; has been named a Fellow of the American Academy of Neurology, the American Association for the Advancement of Science, and the Royal College of Physicians in London; and is a member of the American Association of Physicians.

Dr. Saper has received a Javits Neuroscience Investigator Award from the National Institutes of Health (NIH) and was named one of the “100 Most Frequently Cited Neuroscientists” by the Institute for Scientific Information. He has served as Vice President and Councilor of the American Neurological Association and has chaired the Program Committee for the American Neurological Association and the Society for Neuroscience.

His research has explored circuitry of the brain that controls basic functions, such as wake-sleep cycles and circadian rhythms, as well as cardiovascular and respiratory function. His laboratory has contributed to the understanding of the ascending arousal systems in the brain, the sleep promoting systems in the brain and between different behavioral states, and the brainstem circuitry controlling autonomic and respiratory activity.

2012 Outstanding Scientific Achievement Award

*Award Description:* Established in 2006, the Outstanding Scientific Achievement Award is presented to individuals based on novel and seminal discoveries of a basic, clinical or theoretical nature that have made a significant impact on the sleep field.

*Recipient:* Joseph S. Takahashi, PhD, is Chair of the Department of Neuroscience and an Investigator for the Howard Hughes Medical Institute at the University of Texas Southwestern Medical Center in Dallas, where he currently holds the Loyd B. Sands Distinguished Chair in Neuroscience. Before moving to UT Southwestern, Dr. Takahashi was the Walter and Mary Elizabeth Glass Professor in the Life Sciences at Northwestern University in Evanston, Ill., for 26 years.

Dr. Takahashi pioneered the use of forward genetics and positional cloning in the mouse as a tool for the discovery of genes underlying neurobiology and behavior, and his discovery of the mouse and human clock genes led to a description of a conserved circadian clock mechanism in animals. He is the author of more than 225 scientific publications and the recipient of many awards, including the Honma Prize in Biological Rhythms Research, the National Sleep Foundation (NSF) Presidential Young Investigator Award, the Searle Scholars Award, the Bristol-Myers Squibb Unrestricted Grant in Neuroscience and the C. U. Ariens Kappers Medal.

Dr. Takahashi has served on a number of advisory committees for the National Institutes of Health (NIH) as well as scientific advisory boards for Eli Lilly and Company, the Genomics Research Institute for the Novartis Foundation, The Klingenstein Fund, the Searle Scholars Foundation, the McKnight Foundation, the Allen Institute for Brain Science, the Max Planck Institute for Biophysical Chemistry, the Bristol-Myers Squibb Neuroscience Award Selection Committee and the Restless Legs Syndrome Foundation. He is a member of the editorial boards for Proceedings of the National Academy of Sciences; PLoS Genetics; Current Opinion in Neurobiology; Journal of Biological Rhythms; Genes, Brain and Behavior; and the Faculty of 1000.

Dr. Takahashi was a co-founder of Hypnion Inc., a biotech discovery company now owned by Eli Lilly that investigates sleep/wake neurobiology and pharmaceuticals, and he is a co-founder of the biotech firm ReSet Therapeutics Inc., which works on the role of clocks in metabolism.

Dr. Takahashi received a bachelor’s degree in biology from...
Swarthmore College in Pennsylvania and a PhD in neuroscience from the University of Oregon in Eugene. For postdoctoral training, he was a pharmacology research associate at the National Institute of Mental Health (NIMH).

2012 Mary A. Carskadon Outstanding Educator Award

Award Description: Established in 2005, the Mary A. Carskadon Outstanding Educator Award is presented to honor excellence in the field of education related to sleep medicine and sleep research.

Recipient: Thomas Roth, PhD, is the director of the Sleep Disorders and Research Center at the Henry Ford Hospital in Detroit, which he founded in 1978. He is also a Professor in the Department of Psychiatry at Wayne State University - School of Medicine in Detroit and serves as a Clinical Professor in the Department of Psychiatry at the University of Michigan College of Medicine in Ann Arbor, Mich.

Dr. Roth was instrumental in the formation of the Association of Sleep Disorders Centers (ASDC), now the American Academy of Sleep Medicine (AASM), and served as the organization’s second president. He has been President of the Sleep Research Society (SRS) and a member of the Board of Directors for the Associated Professional Sleep Societies (APSS), serving as the first Chair of the Scientific Program Committee. Dr. Roth has received the Distinguished Scientist Award from the SRS and the AASM’s Nathanial Kleitman Distinguished Service Award. He is a past Editor-in-Chief of the journal SLEEP.

Dr. Roth has been Chairman of the Sleep Disorders Research Advisory Board (SDRAB) for the National Institutes of Health (NIH) and the World Health Organization’s (WHO) worldwide project on sleep and health. He also served on the governing board of the World Federation of Sleep Research Societies and served as its program chair. He is the founding President of the National Sleep Foundation (NSF) and has received the NSF Lifetime Achievement Award.

Dr. Roth’s research focuses on normal and pathological sleep processes. His work includes research on sleep loss, sleep fragmentation and deviation from normal sleep processes, including pharmacological effects and sleep pathologies. His studies of insomnia underscore the breadth of his research: He has published on the epidemiology, pathophysiology, diagnosis, comorbidity with other disorders, and treatment of insomnia. These contributions enabled him to serve as an expert speaker at the 1983 NIH Consensus Development Conference on Drugs and Insomnia: The Use of Medications to Promote Sleep, the 1995 NIH Technology Assessment Conference on Integration of Behavioral and Relaxation Approaches into the Treatment of Chronic Pain and Insomnia, and the 2005 NIH State-of-the-Science Conference on Manifestations and Management of Chronic Insomnia in Adults.

Dr. Roth received his doctorate in 1970 from the University of Cincinnati and has studied sleep and its disorders ever since.

SRS Young Investigator Awards

Award Description: The Young Investigator Award recognizes outstanding research efforts by new investigators in the field of sleep research.

Recipient: Jeffrey Donlea, PhD
University of Oxford & Washington University, Saint Louis

Title of Paper: “Inducing Sleep by Remote Control Facilitates Memory Consolidation in Drosophila”

Dr. Jeffrey Donlea is interested in using the fruit fly, Drosophila melanogaster, to examine the relationships between sleep, memory formation and synaptic plasticity. He received his BA from Swarthmore College and his PhD from Washington University in St. Louis in under the supervision of Dr. Paul Shaw. In the Shaw lab, Jeff identified a role for sleep in the consolidation of long-term memories in the fly and began to identify the genes and neural circuits that influence sleep-dependent plasticity. In 2010 he moved to the University of Oxford as an HFSP Postdoctoral Researcher in Dr. Gero Miesenbock’s lab at the Centre for Neural Bircuits and Behaviour.

Recipient: Maxime Bonjean, MBBCh, PhD
University of California, San Diego

Title of Paper: “Corticothalamic Feedback Controls Sleep Spindle Duration InVivo”

Recipient: David T. Plante, MD
University of Wisconsin – Madison

Title of Paper: “Reduced g-Aminobutyric Acid in Occipital and Anterior Cingulate Cortices in Primary Insomnia: A Link to Major Depressive Disorder”

I am a clinician-scientist whose work broadly focuses on the intersections of sleep medicine and psychiatry. I have examined sleep and psychiatric disorders through a broad array of methodological approaches, from which I have drawn a greater apprecia-

Continued on the following page →
tion of the genetic, naturalistic, physiologic, and neuroimaging tools available in the study of complex brain disorders. As a medical student at the University of North Carolina, I conducted molecular circadian research examining the role of per3 expression as a marker of circadian clock function in cry1/-/- cry2/-/- mice. As a resident in adult psychiatry at Massachusetts General Hospital and McLean Hospital, I expanded my expertise on the interface between sleep and psychiatric disorders by developing collaborative research projects in a number of areas, including sleep in borderline personality disorder and spectral analysis of sleep EEG in opioid-dependent subjects on methadone main-
tenance. I subsequently pursued clinical fellowship training in sleep medicine at Brigham and Women’s Hospital, which included a post-graduate year of research. I was sponsored by a Physician-Scientist Training Award from the American Sleep Medicine Foundation and studied gamma-aminobutyric acid (GABA) levels in primary insomnia using high field magnetic resonance spectroscopy (MRS). In July 2010, I joined the faculty at the University of Wisconsin School of Medicine and Public Health, where I conduct translational research at the interface of sleep medicine and psychiatry in a unique laboratory capable of high-density EEG polysomnography.
This discussion group served as a follow-up to a 2011 National, Heart, Lung and Blood Institute (NHLBI) workshop, “Reducing Health Disparities: The Role of Sleep Deficiency and Sleep Disorders” (http://www.nhlbi.nih.gov/meetings/workshops/disparities.htm). The goals of the 2011 NHLBI workshop were to assess the existing evidence on sleep and health disparities and to identify priority scientific opportunities for sleep research to advance our understanding of health disparities. The goal of the discussion group at SLEEP 2012 was to provide an interactive forum to address emerging scientific questions and opportunities for research focused on the role of sleep health in the etiology, prevention, and reduction of health disparities. Eliminating the disproportionate burden of disease among racial/ethnic and socioeconomic groups remains a pervasive challenge for the US health care system, and explanations for health disparities remain incomplete. The potential role of sleep health in accounting for some attributable risk in health disparities remains largely unexplored, and is therefore a timely and important area for scientific investigation and implementation.

The co-chairs of the discussion group were Michael Grandner, PhD, University of Pennsylvania; Aaron D. Laposky, PhD, NHLBI; and Kristen Knutson, PhD, University of Chicago. Panel discussants were: Nancy Kressin, PhD, Boston University; Lauren Hale, PhD, SUNY Stony Brook; Sanjay Patel, MD, MS, Harvard Medical School; Girardin Jean-Louis, PhD, SUNY Downstate Medical Center; and Orfeu Buxton, PhD, Brigham and Women’s Hospital and Harvard Medical School.

Learning objectives for this session included:

1. Discuss the significance of racial/ethnic and socioeconomic disparities in the diagnosis, treatment and adherence to treatment of sleep disorders.
2. Discuss the potential impact of applying and disseminating health disparities research to improve the delivery of care in clinical sleep medicine.
3. Identify research opportunities that will advance our understanding of disparities in sleep and the impact of sleep disturbance on health disparity disease risks and outcomes.
4. Discuss specific challenges investigators face in advancing research and clinical practice in sleep and health disparities.

The Discussion Group began with 5-minute presentations by each discussant. Dr. Laposky led with a brief review of the goals and discussion topics of the 2011 NHLBI Sleep and Health Disparities Workshop. He highlighted the timely opportunity for sleep research to advance our understanding of health disparities, and pointed to the 2011 NIH Sleep Disorders Research Plan as a scientific framework for moving this area of science forward. The second discussant was Nancy Kressin, PhD, who is a renowned health disparities researcher. Her presentation “Understanding Disparities in Sleep-Related Care and Outcomes in the Clinical Setting: Thoughts for Future Research”, focused on the contribution of health care system-level factors to sleep related disparities, including barriers to screening, diagnosis, and treatment of sleep disorders. Dr. Hale then presented a social epidemiological perspective on factors underlying disparities in sleep, with a particular emphasis on the role of individual autonomy. Dr. Grandner reviewed the current evidence for sleep disparities relative to race/ethnicity and socioeconomic position, which does indicate that minorities and individuals of lower socioeconomic position are more likely to experience sleep durations that are potentially too short (e.g. <6 hrs) or too long (e.g. >9 hrs), as well as other indices of sleep deficiency. Dr. Knutson then pointed out that these sleep disparities mirror the well-known disparities in cardiometabolic risk, suggesting the possibility that sleep may mediate disparities in cardiometabolic outcomes. Dr. Patel extended this theme with a clinical perspective on the importance of understanding how sleep disorders, including sleep apnea, contribute to disparities in cardiometabolic risk, and discussed the implications for clinical practice. Dr. Jean-Louis also provided a clinical perspective, presenting data on racial/ethnic disparities in the prevalence, treatment, and treatment adherence in sleep disorders, discussing implementation and dissemination strategies for treating sleep disorders in minority populations, and emphasizing the importance of community participation and engagement in these processes. Finally, Dr. Buxton presented data from the “Work, Family, and Health Network”, demonstrating that unique settings, such as the workplace, have a significant impact on sleep health, and may be mediating factors in sleep-related health disparities. In combination, the presentations demonstrated the need to advance our understanding of disparities in sleep health, the complex etiology underlying disparities in sleep, the contribution of sleep deficiency to disease burden, and improving sleep health and the treatment of sleep disorders in minority or lower socioeconomic populations.

The overview presentations were followed by active discussion and comments by audience members. For example, it was noted that sleep interventions, research methodology and treatment strategies need to be tailored culturally and linguistically. Perinatal and early life influences on sleep should be considered, as the role of healthy sleep across the life course needs to be better understood. The impact of the physical environment on sleep also warrants further examination to understand sleep disparities. Finally, it was also noted that the local political climate can prohibit access to health care and play a role in sleep and sleep-related disparities.

Taken together, a few overall common themes emerged from the discussion:

1. Research is needed to better characterize how contextual factors (e.g., race/ethnicity and socioeconomic) play a role in the relationship of sleep deficiency and sleep disorders to health outcomes such as cardiometabolic disease.
2. Research and clinical practice should be “community-specific”. First, this means that as researchers or clinicians, we

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need to be thoughtful and specific about the populations we are interested in either researching or treating. We should avoid aggregating overly heterogeneous groups, such as “Asians” or “Hispanics” as much as possible, and we should be more cognizant of subgroups and assess country of origin or, at least, subgroups (e.g., African vs. African-American). Second, we should involve the members of the community in the design and implementation of research and for improving treatment adherence (e.g. community leaders, such as church pastors, or locations of social importance). Exercising a community oriented approach could not only improve enrollment success, it could improve participation and adherence in research or health care and treatment, with the ultimate effect to yield new dimensions of discovery that would otherwise not be possible.

3. In terms of research, we need to move beyond simple observational and correlative data to develop a more granular and mechanistic understanding of sleep-related disparities and to delineate how sleep contributes to disparate health risks and outcomes. There was discussion about whether these research domains need to be better defined before intervention strategies to reduce sleep-related disparities can be optimized, or whether investigations of etiology, pathophysiology, and implementation can be done in parallel.

In summary, decrements in sleep health (e.g. those caused by insufficient sleep time, sleep apnea, insomnia, shift work, etc.) are associated with a range of health risks and outcomes for which pervasive socioeconomic and racial/ethnic disparities exist, including obesity, diabetes, and cardiovascular disease. Research is needed to elucidate the role and magnitude of impaired sleep in the etiology and pathophysiology of unexplained health disparity risks and outcomes. Insufficient data exist on disparities in the evaluation, diagnosis and/or treatment of sleep disorders in diverse population groups. Thus, carefully planned study designs, data collection and analysis strategies, and the use of community-based research will be needed to optimize our understanding of the mediating, moderating, and feedback mechanisms coupling sleep to disparities in disease risk and health care delivery.

**Michael Grandner, PhD**  
Center for Sleep and Circadian Neurobiology  
University of Pennsylvania

**Aaron D. Laposky, PhD**  
Program Director, Sleep & Neurobiology  
National Center on Sleep Disorders Research  
NHLBI/Division of Lung Diseases  
National Institutes of Health

**Kristen Knutson, PhD**  
Section of Pulmonary & Critical Care  
Department of Medicine  
University of Chicago

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**17TH ANNUAL TRAINEE SYMPOSIA SERIES**

To jump start SLEEP 2012, the 17th Annual Trainee Symposium Series (TSS) commenced on Saturday evening and it was a resounding success. The TSS has ceaselessly grown in popularity and attendance since its inception, and this year was no different. We had a record 338 trainees attend from diverse educational backgrounds, highlighting the interdisciplinary nature of the Sleep Research Society. Trainees ranged from undergraduates to postdoctoral and medical fellows representing fields including psychology, physiology, neuroscience, public health, medicine, pharmacology, psychoneuroimmunology, mathematics, and veterinarian sciences among others. All of these trainees came together to network among senior scientists and peers, learn the latest information on basic and clinical sleep and circadian rhythms research, and garner valuable career development skills.

We owe part of this year’s large attendance to continued financial support for merit-based and first-time travel awards through the Sleep Research Society. We also owe our high attendance to shifting the career reception and datablitz part of the TSS program to Saturday evening (from Saturday afternoon) to allow trans-national and international travelers to arrive on time. The main scientific portion of the TSS occurred throughout Sunday morning and included the welcoming and keynote addresses, and three workshops sessions.

Back by popular demand from last year’s series, the 2012 TSS program began on Saturday evening with an encore datablitz presentation, which featured superb performances by four speakers (two undergraduates and two graduate level) who submitted the top ranked abstracts. The trainees reported they found the experience to be a useful, lively, and interesting showcase of trainee research. Directly following the datablitz, a hors d’oeuvre reception and career fair was launched with 18 international research-oriented institutions and organizations involved including the National Heart Lung and Blood Institute and the Sleep Research Network. Trainees were able to mingle and exchange ideas with senior faculty, peers, and representatives of these organizations. The following Sunday morning, Dr. Phyllis Zee, the immediate past president of the Sleep Research Society, officially welcomed the trainees to the TSS program and thanked them for their enthusiasm and contributions to the growth of the field. Dr. Allison Brager, immediate past Trainee-Member-At-Large, then

Continued on the following page →
had the esteemed privilege of introducing Dr. David Dinges to the podium for what was a highly acclaimed keynote address entitled “Sculpting a Career in Sleep Science in the 21st Century: There Is Still a Great Deal to Discover.” Dr. Dinges beautifully intermixed scientific content with valuable career development advice that the trainees found to be ‘engaging,’ ‘inspiring,’ and ‘informative.’ Many trainees noted the keynote address as one of the major highlights of the TSS program. Subsequently, the trainees attended their choice of three back-to-back interactive workshops sporting multiple esteemed sleep researchers in the field. Some of the scientific content workshops were on topics such as managing shift work settings, disrupted sleep and circadian rhythms in relation to metabolic disease, sleep and immunity, and sleep loss-sensitive measures of cognitive performance. Career development workshops, such as building and enriching mentoring relationships, successful interviewing, and establishing connections for collaborative research, were also available and highly regarded by the trainees. At the completion of the TSS program, trainees were able to venture to the first sessions of the APSS scientific program.

The general impression of the TSS program the trainees expressed was one of appreciation for the opportunities to advance their careers, obtain exposure to a breadth of topics within and without their primary research interests, and network with leaders in the field in an intimate and comfortable setting. The entire organization and support of the TSS program took months in the making by a team of devoted sleep researchers, trainees, staff, and of course the Sleep Research Society. This year more outstanding trainees were provided with 21 first-time travel and 49 merit-based awards, all thanks to the Sleep Research Society, the TSS Trainee and Education Advocacy Committee (TEAC), and the TSS TEAC Trainee Subcommittee. The committees willingly spent many hours of their free time to developing an optimal experience for the trainees based on trainee feedback. The TEAC committee organized the structure and flow of both days in the series, approved of speakers and topics for the program, and meticulously read all nominated abstracts for the trainee awards. The Trainee Subcommittee, consisting of multiple representative trainees from basic and clinical science focuses and disciplines, were crucial in the organization and content of the TSS program. They nominated several speakers, topics, and career fair representatives for consideration. They also contacted and invited these speakers and representatives to take part in the TSS program. Without them, the TSS program would not have been possible and met with such enthusiasm. At this time we must humbly thank them for their contributions and insights. We also express our utmost appreciation to the Board of Directors of the Sleep Research Society for approving and supporting the numerous trainee awards, the administrative staff for ensuring the program run smoothly, and the speakers who gave their time and energy to another successful TSS program.

Trainee Education Advisory Committee (TEAC) Members: Drs. Philip Gehman, PhD – Chair; Lisa Meltzer, PhD – Vice Chair; Allan Pack, MD, PhD – Board Liaison; Jeanne Duffy, PhD; Rachel Manber, PhD; Sonia Ancoli-Israel, PhD; Jonathan Wisor, PhD; Monique LeBourgeois, PhD; Kelly Baron, PhD; David Raitzen, MD, PhD; Allison Brager, PhD – Trainee Member-at-Large, and Megan Ruiter, PhD – Trainee Member-at-Large Elect.

TEAC Trainee Subcommittee Members: Marishka Broan (University of Pennsylvania), Megan Crawford (University of Glasgow), Spencer Dawson (University of Arizona), Jacqueline Fairley (Emory University), Stuart Fogel (University of Montreal), Abigail Garrity (University of Michigan), Andrea Goldstein (University of Berkeley), Valentina Gumenyuk (Henry Ford Hospital), Roneil Malkani (Northwestern University), Jared Minkel (University of Pennsylvania), Christina Nash (Drexel University), Rachel Sharman (Northumbria University), Keith Summa (Northwestern University), and Christa Von Dort (Harvard/MIT).

Speakers: Ruth Benca, PhD; Orfeu M. Buxton, PhD; Daniel J. Buysse, MD; Colleen Carney, PhD; Mary Carskadon, PhD; Valerie Crabtree, PhD; Sean Drummond, PhD; Jeanne Duffy, PhD; Martica Hall, PhD; Allison Harvey, PhD; Elizabeth Klerman MD/PhD; Leon Lack, PhD; Gilles Lavigne, PhD; Steven Lockley, PhD; Mark Opp, PhD; Ketema Paul, PhD; Jerome Siegel, PhD; Michael Twery, PhD; Hans van Dongen, PhD; Aleksander Videnovic, PhD; Jonathan Wisor, PhD; Kenneth Wright, PhD

Administrative Staff: Nicholas Cekosh, Annie Walker-Bright, National Office Sleep Research Society.

Megan E. Ruiter, PhD
Trainee Member-At-Large
Ronald Szymusiak, PhD
President

Dr. Ronald Szymusiak received his PhD in Biological Psychology from the University of Illinois in 1982 and did postdoctoral training in Neurobiology at the University of California, Los Angeles from 1983-1985. He is currently Adj. Professor in the Departments of Medicine and Neurobiology at the David Geffen School of Medicine, UCLA and Research Career Scientist with the Veterans Administration, Greater Los Angeles Healthcare System. His research examines the functional neuroanatomy and neuropharmacology of sleep regulation, interactions between sleep and thermoregulation and the circadian control of sleep. He is the current Secretary-Treasurer of the SRS (2008-2011) and previously served the SRS as Program Chair for Trainees (2000-2002). He has also served as Scientific Program Committee Chair for the SLEEP Meeting (2003-2004).

Janet Mullington, PhD
President-Elect

Janet Mullington, PhD is an Associate Professor of Neurology at Harvard Medical School and Beth Israel Deaconess Medical Center. She received her PhD from the University of Ottawa in Canada and did postdoctoral work in Germany at the Max-Planck institute and at the University of Pennsylvania in Philadelphia. Her primary research interest is in the area of inflammatory systems and sleep loss. Dr. Mullington has been an Associate Program Director of the Harvard Clinical and Translational Science Center since 2008. In addition, she is the Research Fellow for the Oliver Wendell Holmes Society of Harvard Medical School, a role dedicated to serving the research training mission of the school, and she has served on the medical school’s Diversity and Multicultural Committee since 2008. She is an editorial board member of SLEEP and of Nature and Science of Sleep.

Over the last 15 years, Dr. Mullington has worked for the Sleep Research Society in many ways. She began service as a grant reviewer in 1997, volunteered as a member of the Educational Programs Committee from 2002-2005, and stemming from that experience, she was instrumental in putting together Career Development courses held at the APSS. Dr. Mullington was a contributing author for the second edition of the Basics of Sleep Guide (2009). She is an ex-officio member of the SRS Government Relations Committee, has participated in the NIH Liaison annual meetings with NIH Directors and staff and is also serving as an SRS liaison to the Academic Sleep Centers Task Force of the AASM. Dr. Mullington was elected to the SRS Board of Directors in 2008 and served as board liaison for the Trainee Education Advisory Committee (TEAC) from 2008-2011, and as SRS Secretary-Treasurer 2011-2012.

Sean P.A. Drummond, PhD
Secretary/Treasurer

I have been part of the sleep research community since I was an undergraduate at the University of Arizona and volunteered in the Sleep Research Laboratory there. I completed my PhD in Clinical Psychology in the SDSU-UCSD Joint Doctoral Program under the mentorship of Chris Gillin. Throughout my career, I have had the pleasure of working with and learning from several outstanding mentors, including Chris Gillin, Michael Perlis, Richard Bootzin, and Sonia Ancoli-Israel. I am currently on faculty in the Department of Psychiatry at UCSD and the Psychology Service in the VA San Diego Healthcare System. My program of research has two foci: a) effects of experimental and clinical sleep deprivation on cognition and brain function; b) treatment of sleep difficulties in comorbid psychopathology, especially PTSD. My research has been funded by NIH, the Defense Department, the National Science Foundation, and other organizations. Clinically, I co-run a Mood and Sleep Clinic at the VA. Within those clinics, I train graduate students, psychology interns, and fellows. I am also the Co-Director of the UCSD-VA Psychology Internship Training Program. Finally, I have been actively involved in serving the SRS since I was a graduate student. This service includes: a) the Trainee Committee (now the Trainee Subcommittee to the Trainee Education Advisory Committee (TEAC)), 1996-1998; b) organizing or participating in many Trainee Symposia Series; c) the Trainee Member at-Large to the SRS Board, 1997; d) the Committee for Animal Research Ethics, 1999-2003; e) TEAC, 2003-2007 (3 years as committee Chair); f) the Trainee Organizing Committee for Worldsleep07; g) the SRS 50th Anniversary Committee, 2008-2010; and h) SRS Board Member 2009-present.

Continued on the following page →
Dr. Duffy’s research interests are focused on human circadian rhythms; interactions between circadian rhythmicity and sleep-wake homeostasis; understanding individual differences in sleep-wake timing, duration, and need; and aging influences on sleep and waking performance.

She has been a member of the SRS since 1996, joining as a student member when she was in graduate school. She was the recipient of SRS research merit and excellence travel awards as a graduate student and post-doc, and in 1999 received the SRS Young Investigator Award. She was a High School Essay Contest Judge in 1996, 1999, and 2000; a member of the SRS Research Committee from 2006-2009; has been a member of the Trainee Education Advisory Committee since 2010; has reviewed Gillin and Weitzman grants; has chaired sessions and presented symposia talks at the annual meeting; drafted the SRS response to the NIA strategic plan in 2007; presented talks at SRS Trainee Day in 2006, 2007 and 2011; has reviewed for SLEEP since 2001; has been an abstract reviewer for the annual meeting since 2006; and has served as head of the SRS Circadian Rhythms Research Section since 2010.

In addition to membership in the SRS, Dr. Duffy is a member of the European Sleep Research Society, the Society for Neuroscience, and the Society for Research on Biological Rhythms; has been on grant review committees for the NIH, foundations, and several international grant agencies; and has reviewed manuscripts for more than a dozen journals.

Christopher Drake, PhD

Christopher Drake, PhD is Biomedical Scientific Staff at the Henry Ford Hospital Sleep Disorders and Research Center and an Associate Professor in the Department of Psychiatry and Behavioral Neuroscience, College of Medicine, Wayne State University. He received his PhD in Psychology from Bowling Green State University and joined the Sleep Center as Faculty in 2001.

Dr. Drake’s research interests are focused on human sleep research with an emphasis on the factors that predispose individuals to sleep disorders broadly and insomnia and circadian rhythm disorders specifically. He is a licensed clinical psychologist, board certified in behavioral sleep medicine and a fellow of the AASM. Dr. Drake has been a member of the SRS since 1997. For the past 2 years Dr. Drake has served on the Education Committee of the SRS and has been a past member of the membership committee (2004-2007) and chair of the Section on Sleep Disorders Research (2005-2006). He was the recipient of SRS research merit and travel awards as a graduate student (2000, 2001); he has attended, and been an active participant, in a variety of formats, at the annual sleep meeting since graduate school. He has presented several times at the annual trainee day. He is a reviewer for many journals and serves on the editorial board of SLEEP and the Journal of Behavioral Sleep Medicine since 2006; and has been an abstract reviewer since 2005. In addition to membership in the SRS, Dr. Drake is Vice Chairman of the National Sleep Foundation; has chaired the Education and Nominations committees of the NSF; was co-director of the “Hypersomnia and the MSLT” course for the AASM; was a member of the National Sleep Medicine Courses committee of the AASM; and has reviewed grants for NIH, NASA, and NIOSH. He is currently funded by the NIH to study the interaction between predisposing factors and exposure to severe life events in the development of insomnia.

Jeanne F. Duffy, PhD

Jeanne F. Duffy, MBA, PhD, is an Associate Professor of Medicine at Harvard Medical School, and an Associate Neuroscientist and Director of the Chronobiology Core in the Division of Sleep Medicine at Brigham and Women’s Hospital. She received her PhD in Biology from Northeastern University, and joined the Division of Sleep Medicine faculty after completing a postdoctoral fellowship there.

Dr. Duffy’s research interests are focused on human circadian rhythms; interactions between circadian rhythmicity and sleep-wake homeostasis; understanding individual differences in sleep-wake timing, duration, and need; and aging influences on sleep and waking performance.

She has been a member of the SRS since 1996, joining as a student member when she was in graduate school. She was the recipient of SRS research merit and excellence travel awards as a graduate student and post-doc, and in 1999 received the SRS Young Investigator Award. She was a High School Essay Contest Judge in 1996, 1999, and 2000; a member of the SRS Research Committee from 2006-2009; has been a member of the Trainee Education Advisory Committee since 2010; has reviewed Gillin and Weitzman grants; has chaired sessions and presented symposia talks at the annual meeting; drafted the SRS response to the NIA strategic plan in 2007; presented talks at SRS Trainee Day in 2006, 2007 and 2011; has reviewed for SLEEP since 2001; has been an abstract reviewer for the annual meeting since 2006; and has served as head of the SRS Circadian Rhythms Research Section since 2010.

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Paul Shaw, PhD

Paul Shaw, PhD

I received my PhD working with Allan Rechtschaffen at the University of Chicago investigating the effects of chronic total sleep deprivation in the rat. I subsequently joined The Neurosciences Institute as a postdoctoral fellow with Giulio Tononi where we began using the fruit fly as a model system to identify molecules that play critical roles in regulating sleep homeostasis. I was promoted to the rank of Associate Fellow in 2000 at the Neurosciences Institute. In 2003 I joined the Department of Anatomy and Neurobiology at Washington University School of Medicine where I am now an associate professor studying how sleep loss disrupts the ability of an organism to acquire and/or consolidate memories. I have served on the Research Committee, the Educational Program Committee and the Scientific Program Committee for the Annual Meeting of the of the Associated Professional Sleep Societies.
NEW SRS LEADERSHIP

Megan E. Ruiter, PhD  
Trainee Member-at-Large

I first discovered the Sleep Research Society (SRS) Trainee Day more than seven years ago at the APSS conference in Denver, CO. My experience was an exciting introduction to what the sleep research field has to offer in terms of intellectual stimulation and training opportunities. Since then I have attended each Trainee Day, and for the past year I have served as the SRS Trainee Member-at-Large Elect.

Along with the training experiences at the SRS Trainee Days, I have received extensive sleep research training throughout my academic career. My training in sleep research began as an undergraduate in Dr. Richard R. Bootzin’s sleep research laboratory at The University of Arizona, and at The University of Arizona Sleep Respiratory Laboratory under the supervision of Stuart Quan M.D. Next, my graduate career was spent at The University of Alabama under the mentorship of Dr. Kenneth L. Lichstein. During those years as a clinical psychology doctoral student I was afforded multiple research experiences. I completed many scientific publications as well as a year-long, accredited American Academy of Sleep Medicine Behavioral Sleep Medicine Training Program. My master’s thesis was a meta-analysis on ethnic differences in normal and disordered sleep, and my dissertation focused on the interaction between self-affirmation and working memory capacity on adherence to behavioral insomnia treatments. To finish my doctorate in clinical psychology I completed a clinical internship at the University of California San Diego/VA under the supervision of Dr. Sean P.A. Drummond with a focus on behavioral sleep medicine.

Upon completion of my doctorate in 2011, I began my current position as a postdoctoral research fellow in Health Outcomes and Services Research supported by a T32 Agency of Healthcare Research and Quality grant, located at The University of Alabama at Birmingham. Since my fellowship began my research interests have developed into a focus on the factors underlying sleep health disparities across sociodemographic groups, and determining the relationships between sleep health and the development of chronic illnesses such as cardiovascular and rheumatologic diseases. Through the mentorship of Laurence A. Bradley, PhD, and multiple interdisciplinary collaborations, I have launched a research program on these interests through primary data collection, and secondary data analyses of ongoing cohort studies (e.g., REGARDS study; CARDIA study). Notably, my work during my fellowship on the association between short sleep duration and incident stroke symptoms among persons of normal weight gained international attention during the APSS 2013 Boston conference. My long-term professional goals are to continue my sleep research program and transition into an academic position as an independent scientist.
Setting Lofty Goals for Sleep and Circadian Science

We are at a unique juncture of time. While the -omics era, transgenic models, interference RNA, and other exciting new tools are affording greater insight into the biology of health and disease we are confronted by a turbulent economy and shrinking budget in an election year. In the face of such uncertainty, in order to advance sleep and circadian science, we need to dig deep and rally as a field to surmount the obstacles that confront us. The 2011 Sleep Disorders Research Plan 1 was timely in that it provided a scientific framework with the goals, objectives, and strategies for advancing the field over the next 3-5 years and was put forth by the National Center for Sleep Disorders Research (NCSDR) of the National Institutes of Health (NIH) with input from the Sleep Disorders Research Advisory Board (SDRAB), scientists, clinicians, and patients. But, as Mark Twain famously quipped, “It is wiser to find out than suppose.” We need to implement! More needs to be done.

Recently, the SDRAB met for a two-day public meeting on May 30-31, 2012 at the NIH. The meeting was packed with information that set the stage for inspiring discussions that this article hopes to communicate in a succinct manner and entertain feedback. Such bidirectional communication is vital for the SDRAB’s objective which is to provide advice to the Director of NIH, NHLBI, NCSDR, and the trans-NIH Sleep Research Coordinating Committee on matters pertaining to the planning, execution, conduct, support and evaluation of research in sleep and circadian disorders. The presence of the leadership and representatives from the Sleep Research Society (SRS), American Academy of Sleep Medicine (AASM), and patient advocacy groups was highly conducive for the cross-pollination of ideas and knowledge between the Trans-NIH Sleep Research Coordinating Committee and other SDRAB members. This article will serve to disseminate such information for those who were unable to attend the proceedings or call in to the public webcast.

The meeting started with an update of the NCSDRs activities in fiscal year 2012. Three workshops, four sessions at annual conferences, three published letters, and four invited presentations represented some of the activities. A notable aspect of this presentation involved matching the current roster of sleep and circadian rhythms grants that are funded by the NIH with the five goals of the sleep research plan to see where we stand in the implementation of the 2011 NIH Sleep Research Plan (Fig. 1). With the input of Board members, 692 active NIH grants were identified in fiscal year 2010 and categorized under goal 1 (basic research; n=282), goal 2 (pathophysiology; n=248), goal 3 (prevention, diagnosis and treatment; n=58), and goal 4 (dissemination and implementation; n=36). Goal 5 that focuses on research training in sleep and circadian rhythms constituted a total of 130 grants that included Ks, Fs, T32s, R13 and R25. While these constituted active grants, the active FOAs that solicit the submission of sleep-related research proposals amounted to 111 currently and some selected examples are provided in Table 1. Selected examples of grants funded through such initiatives are provided in Table 2. While these funded grants and FOAs constitute the engines and chassis for the advancement of sleep and circadian science, we should aspire for more than to just maintain our standing in relation to other fields. The question that can be raised at any time is whether appropriate amount of resources are allocated to the advancement of a scientific field and whether the human workforce in an area of study is being developed adequately. One should probably understand that such seeming “allocations” are essentially a direct function of the research grant applications received that competed successfully in the peer-review process. The historical information in Fig. 2 may shed some light on this topic. The number of sleep-related R01 grants funded over the past 4 years is shown (blue circles; Fig. 2) in comparison to expenditure towards all R01 grants funded by all NIH Institutes (black shaded area; $ Billions). Sleep-related R01 grants funded per $1 Billion spent by NIH on funding all R01 grants is shown as an adjusted number (black squares; Fig. 2). While we are in a better position in 2011 than in 2008, more needs to be done to reverse a small trend for a reduction in sleep research funding seen between 2010 and 2011.

How do we energize sleep and circadian research? We need to rally together as a field and put forth transformational ideas into effective research proposals that could potentially propel the field of sleep and circadian science forward on a firm footing while paving the way for other transformative ideas to follow. For example, a transformational idea could come from any of the astute investigators in sleep and circadian rhythms research, but can only be accomplished as team-based science. Such transformational ideas do not happen overnight and we need to bring to bear the combined vision and expertise of experienced researchers to convert the transformational idea into effective research. As...
Figure 1. 2011 NIH Sleep Research Plan. Click to get a PDF of the document.

**Goal 1.** Advance the understanding of sleep and circadian functions and of basic sleep and circadian mechanisms, in both the brain and the body, across the lifespan.

**Goal 2.** Identify genetic, pathophysiological, environmental, cultural, lifestyle factors and sex and gender differences contributing to the risk of sleep and circadian disorders and disturbances, and their role in the development and pathogenesis of co-morbid diseases, and disability.

**Goal 3.** Improve prevention, diagnosis, and treatment of sleep and circadian disorders, chronic sleep deficiency, and circadian disruption, and evaluate the resulting impact on human health.

**Goal 4.** Enhance the translation and dissemination of sleep and circadian research findings and concepts to improve health care, inform public policy, and increase community awareness to enhance human health.

**Goal 5.** Enable sleep and circadian research training to inform science in cross-cutting domains, accelerate the pace of discovery, and the translation of enhanced therapies from bench to bedside to community.

### Table 1. Current active Program Announcements that solicit Sleep and Circadian rhythms grant applications (Selected examples)*

<table>
<thead>
<tr>
<th>Announcement Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA-11-178</td>
<td>Circadian Rhythms and Alcohol-induced Tissue Injury</td>
</tr>
<tr>
<td>PA-11-122</td>
<td>Etiology and Pathophysiology of Sleep Disordered Breathing in Pregnancy</td>
</tr>
<tr>
<td>PAR-11-038</td>
<td>Preclinical Research Model Organisms Predicting Treatment Outcomes for Intellectual/Developmental Disabilities</td>
</tr>
<tr>
<td>PAR-11-130</td>
<td>Genetic Screens to Enhance Zebra fish Research</td>
</tr>
<tr>
<td>PAR-11-131</td>
<td>Enhancing Zebra fish Research with Research Tools and Techniques</td>
</tr>
<tr>
<td>PAS-11-029</td>
<td>Collaborative Studies on The Central Nervous System and Glycaemia</td>
</tr>
<tr>
<td>PAR-11-203</td>
<td>Predictive Multiscale Models for Biomedical, Biological, Behavioral, Environmental and Clinical Research</td>
</tr>
<tr>
<td>PAR-11-307</td>
<td>Discovery of Genetic Basis of Mendelian or Monogenic Heart, Lung, and Blood Disorders</td>
</tr>
<tr>
<td>PAR-12-155</td>
<td>Integrative Omics Data Analysis for Discovery in Lung Diseases</td>
</tr>
<tr>
<td>PAR-11-314</td>
<td>Systems Science and Health in the Behavioral and Social Sciences</td>
</tr>
<tr>
<td>PAR-12-138</td>
<td>NHLBI Systems Biology Collaborations</td>
</tr>
<tr>
<td>PAR-10-285</td>
<td>NHLBI Program Project Applications</td>
</tr>
<tr>
<td>PA-09-148</td>
<td>Studies of Energy Balance and Cancer in Humans</td>
</tr>
<tr>
<td>PA-09-130</td>
<td>Exploratory Grants for Behavioral Research in Cancer Control</td>
</tr>
<tr>
<td>PA-09-124</td>
<td>Exploratory/Developmental Clinical Research Grants in Obesity</td>
</tr>
<tr>
<td>PA-09-108</td>
<td>Women’s Mental Health and Sex/Gender Differences Research</td>
</tr>
<tr>
<td>PAR-09-203</td>
<td>Ancillary Studies in Clinical Trials of CNS/PNS Disorders NINDS</td>
</tr>
<tr>
<td>PA-09-193</td>
<td>Mechanisms…and Management of Pain in Aging: Molecular/Clinical</td>
</tr>
<tr>
<td>PA-09-243</td>
<td>Nutrition Physical Activity Res.: Cardiovascular/Pulmonary Health</td>
</tr>
<tr>
<td>PA-09-216</td>
<td>Mechanisms Linking Psychosocial Stress, Aging, Brain and the Body</td>
</tr>
<tr>
<td>RFA-HL-13-003</td>
<td>Ancillary Studies in Clinical Trials</td>
</tr>
<tr>
<td>PA-10-152</td>
<td>Diet Composition and Energy Balance</td>
</tr>
<tr>
<td>PAR-12-093</td>
<td>Biomedical/Behavioral Research for Equity in Maternal Child Health</td>
</tr>
<tr>
<td>PA-11-064</td>
<td>Neuroimmune Mechanisms Of Alcohol Related Disorders</td>
</tr>
<tr>
<td>PA-11-200</td>
<td>Research on Children in Military Families:</td>
</tr>
<tr>
<td>PA-11-180</td>
<td>Research on Ethical Issues in Biomedical, Social and Behavioral Res</td>
</tr>
</tbody>
</table>

*Table 1 continues*
**Table 1 continued**

- PA-11-235 Gene-Environment Interplay in Substance Use Disorders
- PA-12-061 Maternal Nutrition & Pre-pregnancy Obesity:
- PA-12-177 Alcohol Abuse, Sleep Disorders and Circadian Rhythms
- RFA-NR-12-006 Centers of Excellence in Symptom Science
- RFA-NR-12-009 Symptom Science: Building Research Teams for the Future
- RFA-NR-12-011 Assist Caregivers Assessing/Managing Alzheimers Symptoms
- PA-12-160 Integrative Approaches to Symptom Management in Military Populations
- RFA-HL-12-022 Phase II Clinical Trials of Novel Therapies for Lung Diseases
- PA-10-045 Clinical Trial Planning Grants for Critical Illness and Injury in Aging
- PA-10-011 Behavioral and Integrative Treatment Development Program
- PA-10-007 Mechanisms, Models, Measurement, & Management in Pain Research
- PA-10-127 Home/Family Based Approaches for Prevention/Management of Overweight or Obesity in Early Childhood
- PAS-10-246 Strategies for Treatment of Young Adults with Alcohol Use Disorders
- PAR-11-242 Interventions for SIDS and Other Sleep Related Infant Deaths
- PA-11-070 Chronic Illness Self-Management in Children and Adolescents

**Training**

- NOT-HL-12-143 RFA Career Development Program in Omics of Lung Diseases (K12)
- PAR-11-098 Education Research in Sleep Health and Sleep-Circadian Biology
- PAR-10-257, Chronic, Non-Communicable Diseases and Disorders
- Across the Lifespan: FIC Research Training Award (NCD-LIFESPAN)(D43)
- RFA-HL-13-011 Limited Competition: NHLBI Research Centers at Minority Serving Institutions - Phase II
- PAR-10-020 Drug Abuse Dissertation Research: Epidemiology, Prevention, Treatment, Services, and/or Women and Sex/Gender Differences
- RFA-HL-13-020 Short-Term Research Education Program to Increase Diversity in Health-Related Research

*Sourced from talk by Dr. Michael Twery [https://webmeeting.nih.gov/sdrab201205tab04/] and available at [http://grants.nih.gov/grants/guide/], Active FOA, keyword “sleep”

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Number of Sleep-related R01 grants funded per $1 Billion spent by NIH on all R01 grants. The chart shows an increasing trend in the number of Sleep-related R01s funded per $1 Billion spent on R01s over the past four years. The data is presented in a line graph with the x-axis representing the years 2008 to 2011 and the y-axis showing the number of Sleep-related R01s per $1 Billion. The graph indicates a significant increase in funding for Sleep-related research over the specified period.

**Figure 2.** Sleep Research Funding over the past decade.

Number of Sleep-related R01 grants funded over the past 4 years is shown (blue symbols) in comparison to expenditure towards total R01 grants funded by all NIH Institutes (black shaded area; $ Billions). Sleep-related R01 grants funded per $1 Billion spent by NIH on funding all R01 grants that is shown as an adjusted number (black squares). Source: [http://projectreporter.nih.gov/reporter.cfm?icde=](http://projectreporter.nih.gov/reporter.cfm?icde=) (Search term “sleep”; R01 Supplements and ARRA grants have been excluded)
Thomas Kuhn would say, “...effective research scarcely begins before a scientific community thinks it has acquired firm answers to questions like the following: What are the fundamental entities [of a field]? How do these interact with each other? What questions may legitimately be asked about such entities and what techniques employed in seeking solutions?”3. Such a systematic and consensus-derived process by the sleep and circadian science community could serve as a blueprint to improve health, effectively treat or prevent disease while infusing the required confidence into funding institutions and program officials who may need to be reassured of the potential for scientific impact. Discussions on this important issue ensued with the expectation that a consensus-derived white paper would be developed by the SRS-AASM Taskforce with input from sleep and circadian rhythms experts. As a field we need to develop consensus on a transformative idea that is high-impact and high-priority while guaranteeing feasibility while ensuring equipoise. Dr. Phyllis Zee (President of the SRS) made an eloquent presentation to SDRAB on behalf of the SRS-AASM Joint Taskforce on sleep and circadian research and called for transformational ideas from sleep and circadian researchers.

The NIH office of communications and accomplishment presented how the NIH communicates with researchers and lay public and the importance of such communications. Social media is front and center in such efforts, and the sleep researcher should probably friend NHLBI on Facebook and tune in to tweets from #SleepChat to stay in touch. With over 14,000 followers on Twitter and 150,000 on Facebook and 43 uploaded videos on YouTube, the sleep and circadian researcher would have their finger on the pulse of the latest and greatest, which may, in turn, spur one’s imagination on to their next innovation.

Presentations and comments from the members of the Trans-NIH Sleep Research Coordinating Committee were thoughtful and deliberate. Opportunities for translational research in the NHLBI were presented along with epidemiological cohorts that may be ideal for secondary analysis posed by sleep and circadian researchers by Dr. Catherine Stoney from the NHLBI, Clinical Applications and Prevention Branch. An array of potential opportunities for secondary analyses were highlighted with special emphasis on dissemination and implementation research (Fig. 3). There are many aspects of the translation continuum that are well suited for sleep and circadian rhythms research, but the field needs to develop and amass more intervention-based clinical evidence in order to progress further right in this translational continuum towards dissemination and implementation. Such progression will require the development and successful comple-

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**Table 2. Selected examples of currently funded grants**

**Basic Science Research**
- Development Of ROR Ligands For Treatment Of Circadian Rhythm Disorders (NIMH)
- Genetics Of Sleep In Zebra fish (NHLBI)
- Integration of Feeding and Glucose Metabolism by the Circadian Gene Network (NIDDK)
- Cross-talk between the circadian clock and the cAMP signaling pathway (NIDDK)
- Circadian Photoentrainment in Mammals (NEI)

**Clinical research**
- Mild Cognitive Impairment and Obstructive Sleep Apnea (NIA)
- Pathogenesis and Outcomes of Sleep Disordered Breathing in COPD (NHLBI)
- Is Insomnia a Risk Factor for Decreased Influenza (e.g., H1N1) Vaccine Response? (NIAID)
- The Role of Circadian Periodicity in Human Cardiovascular Disease and Diabetes (NHLBI)
- Sleep, Reproductive Transitions, and Health in Women (NHLBI)
- Investigating Genetics of Human Natural Short Sleepers (NINDS)
- Pharmacologic Interventions for Cardiovascular Disease in Obstructive Sleep Apnea (NHLBI)
- Validation of Urinary Biomarkers in Diagnosis of Pediatric OSA (NHLBI)
- Metabolic and Cognitive Consequences of Sleep Loss (NHLBI)
- Frontal Cerebral Hypothermia as a Treatment for Insomnia (NHLBI)
- Sleep Patterns as a risk factor for disease in the Hispanic Community Health Study (NHLBI)
- Aging: Sleep and Inflammatory Mechanisms in Depression Prevention (NIA)
- Inflammation, Stress, and Social Behavior: Using Ecological Assessments and Model (NCCAM)
- Improving Dementia Caregiver Sleep and The Effect on Heart Disease Biomarkers (NIA)
- Evaluating cardio metabolic and sleep health benefits of workplace intervention (NHLBI)
- Chronic Moderate Sleep Restriction in Older Long and Older Average Sleepers (NHLBI)

**Source:** [http://grants.nih.gov/grants/guide/](http://grants.nih.gov/grants/guide/), Active FOA, keyword “sleep”
tion of competitive grant applications. The sleep and circadian researcher, however, needs to be aware that a majority of such funded research is investigator-initiated in response to a parent program announcement (PA) and that only a minority of NIH-funded research stems from a request for applications (RFA). Moreover, the illuminating presentations on the leadership of the NHLBI Lung Division -- Drs. James Kiley and Gail Weinmann -- revealed an arduous and methodical process by which such funding announcements are conceived, generated, announced, and evaluated by the NHLBI.

The selection of special initiatives for release and competition generally reflects a broad consensus recognition across both the Institute leadership and its Advisory Committees on the “need” and scientific opportunity posed by the proposal. Funding for special initiatives is limited and the selected programs must stand out above the competition. Typically, the starting point for nearly all Institute initiated programs stems from scientific community input and recent breakthroughs in a certain area of study, workshops and symposiums held at National Meetings or the NIH. At the NHLBI, new concepts are initially discussed in an “idea forum” that is attended by program staff. Concepts selected for further development are then discussed and prioritized by a Board of External Experts (BEE). The recommendations of the BEE are presented to the National Heart, Lung, and Blood Advisory Council and there it is further discussed. All of this input is then taken into consideration when the Institute selects specific initiatives for final development, publication, competition, and award. Following which the Director of NHLBI may give approval for the development of an initiative after NHLBI council deliberates on such initiatives. The program official writes the funding announcement which is then circulated internally for critiques before it is approved and published. The entire process of initiative development and consideration often takes 12 – 24 months. An additional 6 – 12 months may elapse during which applications are received, undergo primary review, secondary review by the Advisory Council, and finally a funding decision is made under that initiative. While the sleep and circadian researcher needs to be savvy about this process, the expediency and greater success rate of a high-quality (competitive) grant application going in for regular peer review in the next NIH cycle cannot be overstated.

Thought provoking presentations on sleep and health disparities (Dr. Jean-Louis Girardin from SUNY Downstate Medical Center), healthcare delivery research (Dr. Kate Bent, NIH/CSR), Center for Disease Control (CDC) health surveillance (Dr. Anne Wheaton), and NIH Science Education Module (Drs. Cynthia Allen and Lisa Strauss) gave way to input from the public before further discussions on how sleep and circadian research can be advanced resumed. The elaborate agenda and invited speakers were organized by NCSDR Director (Dr. Michael Twery), NCSDR staff (Dr. Danny Lewin and Aaron Laposky) and the SDRAB Chairperson (Dr. Michael Vitiello). Input and comments from the patient advocacy representatives (Ms. Julie Flygare, JD [Community relations, Narcolepsy advocate]; Ms. Kathy Page [Restless Leg Syndrome Foundation]; Gagandeep Walia [Business leader, sleep apnea]; and Hon. Ila Sensenich, JD) were

Continued →
welcomed and helped put in perspective the reason for sleep and circadian rhythms research.

Acknowledgements
A special thanks to all of the members of the NIH Sleep Disorders Research Advisory Board (SDRAB) and the Trans-NIH Sleep Research Coordinating Committee. All members of the SDRAB board are listed at the following website: http://www.csr.nih.gov/Roster_proto/members_print.asp?srg=SDRAB&cid=100735&title=Sleep+Disorders+Research+Advisory+Board.

References

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SRS FACEBOOK: ONE YEAR LATER

It’s been a year since the Sleep Research Society began its first foray into social media, with the launch of a Facebook page. In that time, the page has accumulated 343 Likes. Currently, the page is overseen by Patrick Murray, who works at the SRS/AASM home office (and also oversees the other social media ventures for the APSS), as well as the SRS Membership and Communications Committee, chaired by Dr. Kathy Reid. Over the past year, the Committee, Mr. Murray, and the SRS board have been looking to see if the SRS can implement a successful social media presence.

The Facebook page is updated at least once per week (usually more) with new content, and the average post gets 3-4 Likes from the community. Examples of recent posts linked to articles include: “Nominate Speakers for SLEEP 2013,” “Oddly timed study finds that sleep apnea may cause more breathing pauses per hour during the winter,” “Circadian research may unlock new methods to regulate body clock in blind people,” “U.S. Labor Department American Time Use Survey suggests the average American sleeps 8.71 hours per night. Do you think people are over-reporting how much they sleep per night?” and “Coffee really isn’t so bad when consumed in moderation and in the morning or early afternoon.” Visitors to the page can also access basic information about the SRS, including links to the website.

As more SRS members (and others interested in sleep research) join the Facebook page, there is a hope that this can be a great way to stay informed about the field, a way to stay in touch with the SRS, and even a platform for sharing interesting news and findings with some of your other Facebook friends. With time, as more people participate in discussion, the Facebook page can become a place where we can exchange ideas in an informal way with one another.

The SRS as an organization encourages this sort of open exchange of ideas. That said, the goal is to maintain an atmosphere of professionalism and courtesy. So links and comments will not be allowed if they are in any way advertisements or endorsements for commercial products or entities. Several vendors have tried to post links to the page, but we have had to reject those. Although the products may be scientifically sound, we want to avoid these sort of posts. Also, negative remarks that are derogatory or that otherwise do not contribute to the conversation in a scientifically acceptable manner may be removed. That said, there have not been any instances where this has been an issue.

As a community, the SRS is very diverse, but we also enjoy a good discussion and debate. This avenue, and others to come, will hopefully help us as a community strengthen and make the most of our greatest resource: us.

Michael A. Grander, PhD
Membership and Communications Committee
NCCAM’s Interest in the Sleep—Pain Connection

A central focus of NCCAM is to provide investigators with funds to conduct research in managing symptoms of underlying diseases/conditions and alleviating chronic pain and insomnia (Strategic Plan, Goal 1 http://nccam.nih.gov/sites/nccam.nih.gov/files/about/plans/2011/NCCAM_SP_508.pdf). NCCAM maintains that it is important to not only determine whether complementary health approaches exert beneficial effects, but also how such interventions might be working at the cellular or molecular level to advance the science and practice of symptom management. The second goal in NCCAM’s Strategic Plan is to develop effective, practical, personalized strategies for promoting health and well-being; it is clear that supporting research in the areas of sleep and pain is central to this goal. The third goal is to enable better evidence-based decision-making regarding complementary health approaches and their integration into health care and health promotion; it is also clear that supporting sleep and pain research should serve to improve health care and the quality of life of Americans. This past decade has demonstrated that investment in this research has provided us with an emerging evidence base, including systematic reviews by independent organizations, to inform complementary health practices and guide health professionals’ recommendations.

What is the Evidence for Complementary Health Approaches to Alleviate Sleep Disorders?

Sleep disorders affect an estimated 25-30% of the adult American population, as well as a similar percentage of children and adolescents. Likewise, at least 20% of Americans suffer from chronic pain that is not well managed with conventional medicine alone. Sleep disturbances contribute to disability, morbidity, and mortality, with evidence suggesting that they also contribute to chronic pain (Roehrs 2009). Whereas chronic pain may result in sleep disturbances, they may also substantially increase the chance that someone will transition from acute pain to a chronic pain syndrome. Although scientists do not understand definitively how sleep disturbances contribute to chronic pain, we do know that experimental sleep restriction or deprivation may impair how we process pain, thereby enhancing pain sensitivity. We also know that pain perception and sleep-wake pathways share common neurobiological systems. Further, patients with chronic illnesses characterized by pain are more likely to experience sleep disturbances than similar patients without chronic pain.

Considering the bidirectional relationship between sleep and pain, this begs the question: How might complementary health approaches to lessen sleep disturbances in turn aid in alleviating chronic pain that has been refractory to conventional approaches? We first turn to natural products and mind-body therapies to facilitate sleep. These approaches have become popular largely because pharmacotherapy (such as benzodiazepines and other sedative hypnotics) produces significant side effects and only offers short-term relief. Natural products that top the list to alleviate sleep disturbances include melatonin, L-tryptophan, and valerian. Melatonin is the hormone produced by the pineal gland in the brain (and in the retina) mainly at night, L-tryptophan is an amino acid that is a precursor to both serotonin and melatonin, and valerian is the most commonly used medicinal herb for inducing sleep. Melatonin regulates the circadian day–night rhythm and seasonal biorhythm, but also has been shown to influence the immune system and the gastrointestinal tract (Carpentieri et al. 2012). Melatonin also provides neuroprotection against oxidative damage and interacts with numerous medications to minimize side effects (Carpentieri et al. 2012). There is good evidence that melatonin may assist with falling asleep faster and may help those who have an internal “clock” disruption (circadian rhythm abnormality), but only has a marginal effect on sleep maintenance. The evidence for L-tryptophan or valerian is not as compelling, in part because of few well-designed clinical studies. However, a three-week randomized controlled trial with 57 participants (13 males, 44 females) diagnosed with primary insomnia were assigned to one of three treatments: 1) pharmaceutical grade tryptophan, 2) protein source tryptophan, or 3) placebo (Hudson et al. 2005). Each treatment was combined with carbohydrate to induce a sufficient insulin response to reduce the competition for transport sites across the blood brain barrier. Both the pharmaceutical grade tryptophan and protein source tryptophan groups (but not placebo) displayed significant improvement on subjective and objective measures of insomnia, whereas the protein source tryptophan was the only group that experienced a significant reduction in wake time during the night. Another exception was a randomized placebo-controlled four week clinical trial (N=100) demonstrating that valerian (530 mg) extract improved sleep quality (p<0.001) in 30% (versus 4% in placebo group) of 50 to 60 year old postmenopausal women with insomnia (Taavoni et al. 2011), supporting the effectiveness of valerian in clinically managing insomnia. To provide evidence that valerian exerts pharmacological activity related to its hypnotic effects, valeric acid can be used as a quantitative marker to assess the pharmacokinetic properties of valerian. Investigators demonstrated that there was substantial inter- and intra-individual variability in the pharmacokinetics of valerian in 55 to 80 year old women (N=16) with self-reported insomnia, suggesting that this variability may contribute to the reported inconsistencies in the effect of valerian as a sleep aid (Anderson et al. 2010). There is relatively little evidence for the efficacy of other herbs (such as hops, lavender, or lemon balm) in relieving sleep-related disorders. However, the use of mind-body interventions, such as mindfulness, yoga, massage therapy or other relaxation techniques, acupuncture, guided imagery (hypnosis), and biofeedback may indeed aid some individuals with sleep disturbances. A recent systematic review (Sarris and Byrne, 2011) indicated that there was substantive support for acupressure, tai chi, and yoga, but mixed evidence for acupuncture and a lack of evaluable data on massage, aromatherapy, or homeopathy in chronic insomnia treatment.

All of the above studies suggest that there is much room for additional research in the area of treating sleep disorders with complementary health therapies. Further, there is much less known about how sleep disturbances affect pain, although there are a few examples from the literature that support the dependence of some forms of chronic pain on poor sleep quantity or quality. For example, a dose-dependent association was reported between sleep disturbances and fibromyalgia risk (p for trend <0.001), with an adjusted risk ratio=3.43 among women who reported frequent sleep problems compared to women without sleep problems (Mork and Nilsen 2011). A prominent complaint of fibromyalgia...
patients is nonrestorative sleep, but scientists do not yet understand its physiological basis, or how disturbed sleep impacts pain. Interestingly, among 292 chronic pain (116 facial pain, 55 back pain, 121 fibromyalgia) patients between 18 and 65 years of age, structural equation modeling analyses revealed a significant direct relationship between poor sleep and pain, with evidence that negative mood almost fully mediated the relationship between sleep and pain (O’Brien et al. 2010). This study highlighted the need to assess and treat both sleep and negative mood in chronic pain patients, suggesting that treating sleep problems would likely benefit both mood and pain. To examine the relationship between experimental sleep disruption and pain, one group of researchers (Haack et al. 2009) randomly assigned participants to either three days of 88 hours of total sleep deprivation (n=15) or 8 hours of sleep per night (n=9), followed by one night of sleep recovery. Compared to the sleep condition, spontaneous pain significantly increased by 5 to 14 units (100 unit scale) and urinary prostaglandin E2 increased by ~30% during total sleep deprivation. In particular, the increase in headache and muscle pain correlated significantly with the increase in urinary prostaglandin E2 excretion, suggesting that the prostaglandin E2 system may be a potential mediator of this sleep loss-induced pain response.

Clearly, experimental manipulations, behavioral therapies, and other interventional studies need to be conducted to determine the nature of the relationship between sleep and pain, the biomarkers that might be useful in monitoring pain responses, and the underlying mechanism(s) by which this connection occurs. NCCAM is interested in promoting and sponsoring research in this multidimensional and interrelated area of sleep and pain.

References

D. Lee Alekel, PhD
Program Director, Women’s Health
National Center for Complementary and Alternative Medicine (NCCAM)
SRS Organizes and Hosts Congressional Briefing on Capitol Hill

During the past several months SRS officers and staff, working in conjunction with the Health and Medicine Counsel of Washington, have undertaken a comprehensive outreach effort to raise Congressional awareness of the National Institutes of Health’s Sleep Disorders Research Plan which was issued in November, 2011. The outreach effort has included dissemination of the research plan to all 535 individual Congressional offices; key Congressional committee staff, as well as personal outreach to staff members in key Congressional offices. As a result of these efforts Congressman Mike Honda (D-CA-15) and Congressman Hank Johnson (D-GA-4) sent a joint letter inviting NIH Director Dr. Francis Collins to brief congressional staff on the findings and recommendations of the plan. The letter also highlighted their interest in the plan’s goal to enhance the translation and dissemination of sleep and circadian research findings and concepts to improve healthcare, inform public policy, and create community awareness to enhance human health.

Dr. Collins and the leadership at the National Heart, Lung, and Blood Institute (NHLBI) responded to Congressmen Honda and Johnson and agreed to coordinate a Congressional briefing with SRS and Congressman Honda’s office. The focus of the briefing would be to educate Members of Congress and their staff about the health risks associated with sleep disorders and the benefits of investing in sleep and circadian research as outlined in the NIH plan.

The SRS hosted the Congressional briefing on Thursday, May 31, 2012, in room S-115 of the U.S. Capitol building. Presentations were given by Susan Shurin, MD, Acting Director of NHLBI; David Dinges, PhD; and Phyllis Zee, MD, PhD, and each speaker addressed questions and comments from a standing-room only audience. The event was attended by approximately 80 individuals and numerous others were unable to be accommodated in the meeting room. Congressional offices represented included:

- Representatives Rosa DeLauro (D-CT-3), C.A. Ruppersberger (D-MD-2), Nita Lowey (D-NY-18), Jeff Fortenberry (R-NE-1), Howard McKeon, (R-CA-25), William Clay (D-MO-1), Renee Ellmers (R-NC-2), Austin Scott (R-GA-8), Kevin Brilbray (R-CA-50), Jesse Jackson Jr. (R-IL-2), Ileana Ros-Lehtinen (R-FL-18), Hal Rogers (R-KY-5), Kevin McCarthy (R-CA-22), Tim Holden (R-PA-17), and Senators Dick Durbin (D-IL), Mike Lee (R-UT), Charles Schumer (D-NY), Sheldon Whitehouse (D-RI), Mark Kirk (R-IL), John Kerry (D-MA)

In addition, the following NIH institutes, centers, and offices sent at least one representative:

- National Institute on Aging (NIA), National Institute of Alcohol Abuse and Alcoholism (NIAAA), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Mental Health (NIMH), National Institute of Neurological Disorders and Stroke (NINDS), National Heart, Lung, and Blood Institute (NHLBI), National Institute on Drug Abuse (NIDA), National Institute of Child Health and Human Development (NICHD), National Center for Complementary and Alternative Medicine (NCCAM), and the Office of Research on Women’s Health (ORWH)

The National Transportation Safety Board (NTSB), Federal Aviation Administration (FAA), and National Institute of Occupational Safety and Health (NIOSH) also were represented. Finally, representatives from the American Academy of Sleep Medicine and the American Academy of Neurology attended, as did a number of patient advocates.

Follow up activities are underway with those legislator’s offices who attended the briefing to ensure they remain engaged and support sleep research.

James K. Walsh, PhD
Government Relations Committee, SRS Past President
A Survey of the Consumption of Energy and Sleep Promoting Functional Foods

In the past decade, the beverage industry has become crowded with companies selling “functional foods”. Though not clearly defined, this typically refers to foods and beverages with particular functions conferred by supplements. In 2009, this industry represented 6% of the total food and beverage market with the energy drink sector of functional foods projected at $14 billion in US sales for 2015 (NBJ 2010). Though these include foods that claim to improve health such as relieving joint pain or an “angry stomach,” it also includes products that use stimulants or sedatives and claim to restore vitality or help maintain restorative sleep. Interestingly, a product can be sold on the market without prior approval from the FDA (FDA 1994). The responsibility of ensuring the safety of the “supplement” is left to the manufacturer. These products are sold everywhere, easily obtained and have attractive marketing. People who use these functional foods and drinks may not realize the possible negative outcomes. Clear and informative labeling of contents and consumer advisories allows consumers to make better informed decisions about purchasing and consuming some of these products, but these are not widespread practices in the industry. This article highlights some of the current trends, regulations and attitudes relevant to the wake and sleep promoting segment of these functional foods. Additionally, we have included the initial results from a pilot survey addressing the prevalence, motivation and effects of consumption of these functional foods in a young adult population.

The prevalence or increased use of these products may reflect changes in attitudes or beliefs of today’s society. Consumption of wake-promoting foods and (frequently subsequent) sleep-promoting products, might lead to adverse effects on physical and mental health. Sleep loss can lead to metabolic disorders including obesity, as well as an increased risk of stroke (Van Cauter et al. 2008; Ruiter et al. 2012). Energy drinks can’t completely hide the cognitive deficits that accrue with sleep dept and may exacerbate aggression or other behavioral problems (William et al. 2012).

Energy drinks are not just used to prolong wakefulness or as a substitute for sleep; they are often used for maintaining optimal wake and increasing performance (Malinauskas et al. 2007). This leads to increased susceptibility to heart problems and in some rare cases heart failure has been reportedly attributed to energy drink usage (Temple News 2009; Herald Mail 2012). Some of the ingredients in these products interact with certain medicines and are often not labeled as such. For example, some energy drinks contain supplements that are blood thinners and should not be used by people already taking prescription anticoagulants. Another example is the supplement of 5-HTP in some energy drinks which may interact with people taking MAOIs.

If there are so many adverse effects, why is there such demand for these products? One explanation would be that sleep is considered less important than work or fun. Society can be very fast-paced and competitive, and people are expected to work all hours to get and stay ahead. Whether working as a stock broker, a medical resident, a truck driver, a student, or working multiple jobs, time is scarce and importance is placed on staying focused. A common belief is that borrowing from sleep time puts more food on the table, earns better grades, and/or facilitates advancement ahead of the competition. Even within our own sleep community, we do not all practice what we preach (unpublished observations).

Getting less sleep is often glamorized or venerated in the media. For example, in an interview with Kelly Ripa in Good Housekeeping magazine, they discuss how she manages to get everything done:

‘One sacrifice Ripa learned to make early on: nights of long, luxurious shut-eye. “Sleeping is not something I do a lot of,” says Ripa, who usually nods off between midnight and 1 A.M. after watching Nightline…Her day usually starts at 6:15 A.M., when she gets up and makes breakfast for the kids.’

Additionally, people are inundated with around-the-clock options for fun, making it difficult to resist the temptation of allowing entertainment to cut into their sleep time. The choice to skimp on sleep is portrayed as widely acceptable in the media. It is also common practice to combine energy drinks with alcohol.

Economic instability, overwhelming workloads or unemployment are increasingly familiar factors that can lead to insomnia and/or lack of sleep. This disruption of sleep often results in the use of stimulants for the working hours and sleep aids for inducing or maintaining sleep. The use of sleep promoting foods and relaxation drinks has also increased visibility in the media, sometimes in a positive light, such as the NeuroSleep drink showcased on the CBS Early Show. The Lazy Larry (melatonin) brownies however, have had some negative press on ABC news due to FDA concerns about the serving size.

Currently, energy drinks are loosely regulated and may contain a mix of other caffeine or stimulant supplements such as guarana or ginseng. There are also energy drinks which do not have caffeine and claim to be healthy energy drinks. The FDA regulates caffeine to 71 mg in soft drinks, and anything over this amount is considered an energy drink due to the supplemented caffeine (amongst carbonated beverages). Most energy drinks are considered supplements with or without caffeine and are thus not subject to the same rules as food and beverages. Although there is likely a difference between “healthy” vitamin energy drinks and caffeinated energy drinks, neither are substitutes for sleep.

Given the rise in energy food and drink consumption, as well as the reinvention of sleep promoting products, we surveyed the prevalence, motivation and effects of consumption of this sector of functional foods.

Methods

We conducted a simple online survey of college students as a pilot study of practices and attitudes about energy foods/drinks. The survey could be completed in less than ten minutes. The survey protocol was approved by the institutional review board of the University of Pennsylvania.

The survey was anonymous, and included basic demographics, including age, sex, and race/ethnicity. Sleep characteristics that were assessed included bedtime and wake time on days in the past 2 weeks when the respondent got the least sleep, the most sleep, or typical sleep. Overall sleep quality (Sleep Quality item from the Pittsburgh Sleep Quality Index), daytime sleepiness (Karolinska Sleepiness Scale), self-reported sleep need, self-
SURVEY RESULTS OF STIMULANT USE BY COLLEGE STUDENTS

Of 54 total respondents, most (89%) were female, the mean age was 22 yrs (SD=4.5yrs), and 65% were Non-Hispanic White. There were 21 who had used energy products in the past month, and 33 who had not. This represents a prevalence of 39%. Only 9 (17%) individuals reported use of any relaxation products. Respondents predominantly reported an ‘evening person’ chronotype, with 55.5% reporting this (n=30), and 22.2% (n=12) self-described as ‘morning type’. Another 22.2% (n=12) did not characterize themselves as either type.

Among those who reported having consumed energy drinks or snacks in the past month, over the past month, they were more likely to have used coffee (90.4% vs. 60.6%), p<0.05, and were the only ones to have used caffeine pills (9.5% vs. 0.0%). These individuals were also more likely to have begun using energy drinks at an earlier age (17.10 ± 2.28 vs. 19.00 ± 2.20), p<0.05 (Fig. 1).

Of those who had used energy products in the past month, 33.3% (n=7) had used them in the morning, 66.7% (n=14) used them in the evening, and 57.1% (n=12) used them at night. These individuals were also more likely to have begun using energy drinks at an earlier age (19.00 ± 2.20) than those who had not (17.10 ± 2.28), p<0.05.

Continuous variables were assessed as mean ± standard deviation, and categorical data was assessed as N and percent. Differences between those who have used energy drinks in the past month, compared to those that have not, were examined using t-tests (for continuous data) and chi-square (for categorical data). An alpha of 0.05 was used as a cutoff for statistical significance.

Results

Fig. 1. The ages (mean ± SEM) at which past month user and past month non-users had first used energy drinks in their lifetime. For non past-month users, 17.10 ± 0.50; past-month users, 19.00 ± 0.61.

Fig. 2. Among past-month users, the percentage who reported having used energy drinks during each of several times of day.

Fig. 3. Among past-month users, the percentage who reported having used energy drinks for various purposes or in various contexts.
(n=13) had used them in a group context (Fig. 3). The most popular brands reported by recent users (among brands polled) were ‘Red Bull’ 66.7% (n=14), ‘5 hour Energy’ 19% (n=4), ‘Monster’ 19.0% (n=4), and ‘Neurogasm’ [now called NeuroPassion] 9.5% (n=2). 14.2% (n=3) had used other energy products not listed.

Between those who had and had not used energy products in the past month, there was no significant relationship to self reported chronotype, happiness, or whether their use of energy drinks had affected their happiness. There was also no significant relationship between use of energy drinks over the past month and either sleep quality or quantity, use of relaxation products, self-reported daytime sleepiness or sleep need. The likelihood of pulling an ‘All-Nighter’ was not significantly related to the use of energy drinks in the last month, nor was the tendency to drink tea or soft drinks. Furthermore, there was no significant difference in use of relaxation or sleep-promoting beverages associated with use of energy drinks in the past month.

Conclusion

In this pilot study, we assessed energy and relaxation drink consumption and the motivations for consuming these products within the extended college community. The most popular reason for energy drink consumption was to maintain wake. Recreation (particularly in the context of alcohol consumption) and sports performance were also common factors.

It was not evident from this survey that users of energy or sleep promoting drinks (within the last month) had significantly unfavorable effects of consumption. In a young population that tends to be more resilient to sleep loss, adverse effects may be more difficult to detect (especially in such a small sample). Although this population was predominantly female, young and socioeconomically homogeneous, these pilot findings are consistent with the current trends suggesting the sacrifice of sleep time for other pursuits. This also demonstrates that this audience targeted by advertisements is indeed consuming these products. It would be interesting to assess consumption, motivation, and effects in populations outside of the target audience. Further research will help to inform the public if regulations are necessary.

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Kristan Singletary, PhD
Jason Gilliland, BA
Michael Grandner, PhD

University of Pennsylvania
**Notable Publications in Sleep 2011**

At the annual meeting of the Basic Sleep Research section of the Sleep Research Society, held at Sleep 2012, we decided as a group to start an annual tradition of selecting, by poll, the most notable publications in sleep from the previous year.

Here is how the publications were selected. All members of the section were asked to independently choose the three most-notable primary literature (i.e., non-review) publications in sleep from the year 2011, and email their choices to me. I tallied the total number of votes for all nominated publications. We report the results here. Commentaries on the two most frequently selected publications (Vyazovskiy et al. and Rolls et al.) were provided by section members. Eight honorable mention publications, which received 2-3 votes each, are listed here as well.

Thank you to the section members who voted, and a special thank you to those who wrote the thoughtful commentaries printed here.

**Jonathan P. Wisor, PhD**  
*Section Head Basic Sleep Research*

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**Most Notable Publications in Sleep 2011**


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**Honorable Mention**

Brooks PL, Peever JH IMPAIRED GABA AND GLYCINE TRANSMISSION TRIGGERS CARDINAL FEATURES OF RAPID EYE MOVEMENT SLEEP BEHAVIOR DISORDER IN MICE. J Neurosci 31:7111-7121.


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**Panossian L., Fenik P., Zhu Y., Zhan G., McBurney MW., Veasey S.**  
*SIRT1 regulation of wakefulness and senescence-like phenotype in wake neurons.* J Neurosci 31:4025-4036.

**Wu MF, Nienhuis R, Maidment N, Lam HA, Siegel JM Role of the hypocretin (orexin) receptor 2 (Hcrt-r2) in the regulation of hypocretin level and cataplexy.** J Neurosci 31:6305-6310.

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**Commentary on Rolls et al., “Optogenetic disruption of sleep continuity impairs memory consolidation”**  
James T. McKenna, PhD  
*Research Services, VA Boston Healthcare System  
Department of Psychiatry, Harvard Medical School*

Is there a direct link between sleep and memory consolidation? Minimal amounts of sleep (around 7-8 hours per night) are necessary for successful cognitive performance, and insufficient sleep leads to hypersomnia and cognitive dysfunction, among other physiological and psychological costs. It remains to be determined, though, what particular aspects of sleep dysfunction may lead to cognitive impairment. In Rolls et al. (2011), Dr. Luis de Lecea and colleagues employed a groundbreaking method of hypocretin-specific optogenetic photostimulation, in which sleep was fragmented without any physical manipulations (such as handling or external stimuli) or induction of stress. This protocol specifically disrupted sleep continuity, but not overall vigilance state amounts or sleep quality, and produced impairment in a memory task.

Hypocretin (also known as orexin) neurons of the lateral hypothalamus play a major role in arousal and vigilance state stability, and loss of these neurons is the major cause of narcolepsy (for review, Brown et al., 2012). De Lecea et al. previously established a causal link between hypocretin activity and sleep-wake transitions using optogenetics (Adamantidis et al., 2007; Carter et al., 2009), and employed similar techniques here (Rolls et al., 2011). A lentivirus carrying the mouse prepro-orexin gene promoter (Hcrt:ChR2-mCherry) was injected into male C57BL/6 mice. Cell-specific unilateral 20 Hz in vivo optogenetic photostimulation of the lateral hypothalamus (20 Hz, 20 mW, 477nm; 15 millisecond light pulses for 10 seconds) was later delivered in intervals of every 30 or 60 seconds (separate animals) over a four hour period. Both stimulation protocols produced an increase of sleep-wake transitions and decreased NREM bout lengths. Interestingly, the 60 second photostimulation protocol did not alter the overall amount of time awake, and EEG power (0.5-20 Hz) was largely unperturbed in either NREM or REM sleep, indicating that sleep quality was preserved. Following four hours of the 60 second photostimulation protocol, neither corticosterone levels nor open field test performance indicated stress or anxiety. De Lecea and colleagues therefore established a sleep fragmentation protocol (60 second interval photostimulation, four hours) in which the particular sleep characteristic of continuity is disrupted, without disturbing overall vigilance state amounts, quality of sleep, or inducing stress.

Would sleep disruption, particular to continuity, impair perfor-

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mance in a memory task? For the novel object recognition task, animals were first exposed to two different objects preceding photostimulation. Half an hour later, virally transfected ChR2 mice, as well as non-Chr2 mice, were subjected to photostimulation for four hours, at intervals of 30, 60, 120, or 240 seconds. Mice were then exposed to one new novel object, and one object from the previous (pre-photostimulation) exposure. ChR2 transfected mice subjected to 30 or 60 second, but not 120 or 240 second, photostimulation intervals spent significantly less time attending to the novel object compared to non-Chr2 controls. Therefore, sleep bouts of greater than one minute allowed retention of the previous memory of objects, but mice exposed to 30 or 60 second hypocretin-specific photostimulation intervals did not remember the two pre-stimulation objects. The authors conclude that the protocol of sleep fragmentation, when sleep bouts were under 60 seconds in length, may impair consolidation of memory, suggesting disruption of the transfer of short- to long-term memory, which involves interplay between the hippocampus and cortex. Of utmost interest, the 60 second interval protocol, when sleep continuity is specifically disrupted, was effective in producing memory impairment.

This study illustrates that a particular aspect of sleep, continuity, in itself may play a role in cognition. Of clinical importance, the sleep continuity decrement investigated here is similar to that seen in select pathologies, such as apnea, Alzheimer’s disease, and depression, and may be responsible for cognitive dysfunction. Future directions employing this mouse model may include a direct measure of increased sleep pressure following photostimulation protocols, such as rodent multiple sleep latencies tests (Veasey et al., 2004; McKenna et al., 2008). This study evaluated the retention of memory, but it remains to be determined if disruption of sleep continuity may also affect acquisition/learning. Therefore, photostimulation could be employed before the learning phase of the cognitive task. Although not discussed here, the De Lecea group previously investigated cFos protein activation (indicating neuronal activation) following these photostimulation protocols (Carter et al., 2009). cFos activation, combined with anatomical tracer techniques and immunohistochemical determination of neuronal neurotransmitter phenotype, could allow further delineation of the neuronal circuitry involving the hypocretin arousal-promoting neurons. Also, local field potential and single unit recordings may be performed in brain regions upstream from photostimulated hypocretin lateral hypothalamic neurons. Overall, this is an elegant study employing novel groundbreaking techniques to further understanding of what aspects of sleep may be important in mnemonic processing.

References


Commentary on Vyazovskiy et al., “Local sleep in awake rats”
Jaime E. Heiss, PhD
Lars Dittrich, PhD
Thomas S. Kilduff, PhD
Center for Neuroscience, Biosciences Division, SRI International

The concept that sleep is a use-dependent function of local neuronal assemblies rather than a global organisal process seemed odd when initially proposed nearly 20 years ago (Krueger and Obal, 1993). Within a relatively short period of time, however, studies of sleep after a period of unilateral somatosensory stimulation during wakefulness in human subjects provided evidence in support of this idea (Kattler et al., 1994). So much evidence has now amassed to support the “local sleep” hypothesis that an entire issue of Current Topics of Medicinal Chemistry was recently devoted to this topic (Krueger and Wisor, 2011). Perhaps the ultimate example of local sleep is the unihemispheric sleep of cetaceans (Lyamin et al., 2008). “Local sleep in awake rats” (Vyazovskiy et al., 2011) is the latest contribution to this burgeoning literature and addresses some of the mechanisms that may underlie use-dependent local sleep.

Based on intracellular studies conducted in vivo and in vitro, cortical neurons have been proposed to exist in two stable states: the UP state, in which neurons are depolarized and generate spontaneous action potentials, and the DOWN state, in which most cortical neurons are hyperpolarized and exhibit a reduced firing rate. Oscillations of cortical neurons between these states are thought to underlie the slow oscillation of the EEG characteristic of NREM sleep. In this and prior (Vyazovskiy et al., 2009) studies, the authors use extracellular multiunit (MUA) rather than intracellular recordings and thus refer to oscillations of cortical neurons between ‘on-periods’, when neurons tend to fire as in the awake brain, and ‘off-periods’, when neurons cease firing. The authors first show that off-periods can also occur during wakefulness and that the probability of occurrence is correlated with the amount of sleep pressure during both sustained wakefulness and recovery sleep (Fig. 1). Simultaneous MUA recordings from the parietal and frontal cortices revealed that off-periods can occur both locally at one recording site and globally, i.e., at both sites (Fig. 2). The proportion of global off-periods increased during sleep deprivation and decreased during recovery sleep.
The authors confirmed previous observations that local neuronal silencing coincides with a brief slow wave in the local field potential (LFP); off-periods were associated with 0.5-4 Hz waves during NREM sleep and with 2-6 Hz waves during wakefulness. Finally, the authors showed that the number of off-periods during wakefulness is correlated with impairment in the behavioral performance of sleep deprived rats in a sugar pellet grasping task (Fig. 3). If an off-period occurred 300-800 ms before a reaching attempt, the probability of successful task execution decreased by 37.5%. Interestingly, this correlation was only detected for the off-periods measured in the frontal cortex and not for those measured in the parietal cortex.

This study provides substantial support for the concept of local sleep. The procedures utilized by Vyazovskiy et al. allow the direct visualization of off-periods and quantification of changes in their occurrence, resulting in a clear illustration of how the firing patterns of cortical neurons change with sleep pressure in freely behaving, drug-free animals. The authors confirm prior evidence that a characteristic feature of sleep is the simultaneous occurrence of neuronal off-periods. By demonstrating that off-periods can occur locally while an animal is either behaviorally asleep or awake, the authors provide evidence that off-periods may be the electrophysiological correlate of local sleep. In agreement with the predictions for such a correlate, the probability of the occurrence of off-periods parallels the build-up and decay of sleep pressure. By simultaneously measuring cortical activity in two different areas, the authors could demonstrate and study both the local and global occurrence of off-periods. Lastly, the authors provide a possible explanation of how sleepiness could impair performance at the single neuron level, as the local increase in the incidence of off-periods during prolonged wake might be causal for the decrement in performance observed in sleep deprived subjects.

On the other hand, the paper provides few clues regarding the possible mechanisms involved in the generation of the off-periods and how they relate to the sleep homeostat. The authors observed a correlation between performance impairment and the number of off-periods in the frontal cortex but did not show clear causality, although they claimed that “Local off-periods in an awake state lead to behavioral deficits”. The case for causality would have been strengthened had the authors reported firing rates of frontal vs. parietal cortex neurons and found that changes in firing rates of frontal cortex neurons were more tightly correlated with successful task performance than parietal cortex neurons. The authors do not provide any information about the properties of neurons being recorded (e.g., the duration of action potentials to distinguish putative inhibitory neurons from excitatory cells). Intracellular recordings in head-fixed mice (Poulet and Petersen, 2008) and rats (Okun et al., 2010) show that, during waking, some cortical neurons exhibit a persistent up state but others show a bimodal distribution in their membrane potential, implying possible cell-type differences in the phenomena studied by Vyazovskiy et al. The possibility of laminar differences in firing patterns or cell-type differences was not addressed. The authors show that local silencing was generally, but not always, associated with the generation of a slow wave in the LFP. Post hoc histological reconstruction of recording sites and spike width analysis could have revealed a possible link between the occurrence of the wave and the laminar location and type of neurons being recorded. Combined anatomical/neurochemical/physiological studies are likely among the next steps to be conducted.

Although much progress has been made in understanding the subcortical mechanisms that regulate sleep, the mechanism responsible for the strong correlation between homeostatic sleep drive and EEG slow wave activity (SWA) remains unclear. The work presented in this study may provide a partial explanation for this correlation, since the single LFP slow waves associated with off-periods during NREM sleep should contribute to SWA as homeostatic sleep drive increases. Thus, uncovering the mechanism responsible for the abrupt silencing of neuronal ensembles is crucial to the understanding of the neurobiology of sleep. Based on the properties of off-periods described by Vyazovskiy et al., such a mechanism must have three attributes: (1) it should change accordingly to global sleep pressure; (2) it should influence the entire cortex; and (3) it should reflect differences in local activity. Factors that might contribute to this mechanism include synaptic depression in the ascending arousal system, partial silencing of thalamic relay neurons, intrinsic activity-dependent changes in cortical neurons, local accumulation of activity-dependent inhibitory factors, and direct hyperpolarization by “sleep-active” inhibitory neurons. In this regard, we have described a population of GABAergic neurons that are selectively activated during sleep, are responsive to sleep pressure, and appear to correspond to cortical projection neurons (Gerashchenko et al., 2008; Kilduff et al., 2011; Wisor et al., 2011). Although the firing rate profile of these sleep-active nNOS-expressing neurons remains to be determined, the relationship between these cells and off-periods will be of interest.

To understand the nature of the off-periods, efforts should be directed to determine whether they are produced by reduction in excitation, by increased inhibition, or some combination. Electrophysiological and pharmacological approaches can be used to address this in combination with newer tools such as chemical genetics and optogenetics that allow the activation or inhibition of specific brain regions and/or specific neuronal populations. Whether off-periods during wake have a physiological function or rather are to be viewed as malfunction of an overstressed network that causes performance errors remains to be determined. Once the mechanism of local off-periods is identified, this question may be answered by artificially evoking this phenomenon, e.g., by optogenetic methods. Such a manipulation would also allow testing whether local off-periods are indeed causal to decrements in performance.

Lastly, the hypothesis of local, activity-dependent sleep should be reconciled with the conventional view of centrally-controlled, globally regulated sleep. Along with the expanding literature mentioned above, the Vyazovskiy et al. study underscores that, to achieve a full understanding of sleep regulation and sleep function, it will be necessary to construct hypotheses that incorporate both local and global sleep to establish a single unified vision of sleep regulation.

Acknowledgements

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References


SRS Member Ralph Lydic, PhD Receives Prestigious Award
On October 15, 2012 the American Society of Anesthesiologists (ASA) presented Ralph Lydic, PhD with its 2012 ASA Excellence in Research Award at the ANESTHESIOLOGY™ 2012 annual meeting in Washington, D.C.

Dr. Lydic has focused his research efforts on three primary areas, including arousal state-dependent respiratory depression, sleep and pain, and the neurochemical control of sleep and anesthesia. Since 1988, Dr. Lydic’s research has been continuously funded by grants from the National Heart, Lung, and Blood Institute. Dr. Lydic is a past President and long-time member of the SRS.

The SRS congratulations Dr. Lydic on receiving this prestigious award!

SRS Member Clif Saper, MD, PhD, Named Editor of The Annals of Neurology
SRS past President Clif Saper, MD, PhD was recently named editor of the journal The Annals of Neurology during the annual meeting of the American Neurological Association in Boston, MA. Dr. Saper will begin his new role as Editor-in-Chief on January 1, 2014. The Annals of Neurology is co-owned by the American Neurological Association and the Child Neurology Society.

The SRS congratulates Dr. Saper on his tremendous accomplishment.

Renew Your SRS Membership for 2013
You can now renew your Sleep Research Society (SRS) 2013 membership online! Renew today to continue receiving a complimentary subscription to SLEEP, opportunities for education and training, members only discounts on professional resources, national representation, and much more!

To renew your membership, log in or register an account on the SRS website and submit an online payment. Renewal invoices were mailed to members in late October and are currently available for download online, giving you the option of renewing via mail or fax.

Please contact the SRS membership department with questions regarding your membership at 630-737-9756 or SRSMembership@srsnet.org.

SRSF Announces 2013 Grant Opportunities
The Sleep Research Society Foundation is pleased to announce two funding opportunities for 2013.

J. Christian Gillin, MD, Research Grant
The Sleep Research Society Foundation J. Christian Gillin, MD, Research Grant supports beginning investigators in sleep research with the purpose of collecting pilot data to be used for future grant applications. The grant includes one-year of support in the amount of up to $20,000 for one year. PDF application

Elliot D. Weitzman, M.D. Research Grant
The SRSF Elliot D. Weitzman, M.D. Research Grant is intended to facilitate established researchers in developing novel and innovative lines of research that differ from their previous areas of research by assisting them in developing pilot data that will support applications for NIH or other federal grants. The criteria for the Weitzman grant makes it similar to a NIH R21 grant. The Weitzman Grant is funded up to a maximum of $20,000 over one year.

PDF application

The submission deadline for applications is November 30, 2012.

Medical Officer Position Open at NCSDR
The NHLBI invites eligible candidates to apply for the position of program director to join the National Center on Sleep Disorders Research (NCSDR) focusing on sleep disorders medicine and the development of a portfolio in sleep research training.

The NHLBI mission area is primarily concerned with the fundamental regulation of sleep; sleep disordered breathing (SDB) etiology, pathophysiology, epidemiology, diagnosis, and treatment; SDB as an etiological risk factor for heart, lung and blood disorders; circadian rhythm disorders, and the relationship of sleep deficiency to risk and outcomes of heart, lung, and blood disorders.

For more information or to apply for this position, click on the following link:
https://www.usajobs.gov/GetJob/ViewDetails/32989980

Tips from NIH for Reviewing Your Summary Statement & Resubmitting an Application
Sally Rockey, PhD, NIH Deputy Director for Extramural Research recently posted valuable information on her blog for investigators, especially junior investigators, on how to interpret your NIH Summary Statements and steps you should take if your grant application was not funded and you are thinking about resubmitting it to NIH. Click here to view the blog post.

Keep Up to Date on Extramural Funding Issues
The NIH Nexus is a valuable resource for investigators to receive news and announcements about NIH Extramural Research. You can access the NIH Nexus by clicking here.

Editorial on Obtaining a NHLBI K08 and K99/R00 Award
The journal Circulation Research recently published an article by Steven Hauser, “How to obtain a National Heart, Lung, and Blood Institute-sponsored K08 and K99/R00 grant in the current funding climate.” This is a great resource for SRS members looking to apply for a K Award. You can access the article through the National Library of Medicine by clicking here.

New NICHD “Spotlight” Features the Link Between Sleep and Health
The National Institute of Child Health & Human Development (NICHD) recently posted a new “Spotlight” on the front page of the Institute’s website highlighting the link between and health. The article also provides insights into sleep and circadian research that is sponsored by NICHD. Click here to read the full “Spotlight” article.

Continued on the following page →
NIH Funding Announcements

Ancillary Studies in Clinical Trials (R01) (RFA-HL-14-004)

NHLBI invites research grant applications to conduct time-sensitive ancillary studies related to heart, lung, and blood diseases and sleep disorders in conjunction with ongoing clinical trials and other large clinical studies supported by NIH or non-NIH entities.

NOTE: This RFA requires a compelling and transparent rationale to justify the expedited review under this program.

Secondary Dataset Analyses in Heart, Lung, and Blood Diseases and Sleep Disorders (R21)

The National Heart, Lung, and Blood Institute (NHLBI) invites R21 applications for well-focused secondary analyses of existing human datasets to test innovative hypotheses concerning the epidemiology, pathophysiology, prevention or treatment of diseases/conditions highly relevant to the NHLBI mission. Applicants may use data from a variety of sources, including, but not limited to, investigator-initiated research activities, contracts from public or private sources, administrative data bases, the NHLBI BioLINCC resource (https://biolincc.nhlbi.nih.gov/home/).

NOTE #1: This FOA includes special programmatic requirements! It is essential to read the full text of the announcement and consult with a listed NHLBI staff contact to assess whether your plans would be responsive.

NOTE #2: The NHLBI only accepts “R21” applications in response to specific FOAs where NHLBI is participating. The NHLBI does not participate in the parent R21 FOA.

Alcohol Abuse, Sleep Disorders and Circadian Rhythms (R21/R01)

The National Institute on Alcohol Abuse and Alcoholism (NIAAA), invites R21 and R01 applications proposing to conduct studies on the functional relationships between alcohol abuse, circadian rhythms and sleep disorders. Collaborative efforts between experts in circadian and/or sleep research and established alcohol investigators to facilitate the development of proposals incorporating both areas of research are encouraged.

These announcements include special programmatic considerations. It is critical that applicants considering the possibility of developing an application carefully read the full text of the announcement and consult with the listed NIAAA staff contact.

Functional Assays to Screen Genomic Hits (R21/R33)(RFA-HL-13-027)

National Heart, Lung, and Blood Institute (NHLBI) invites applications to conduct functional analyses of identified genetic variations related to heart, lung, blood and sleep phenotypes, using amenable in vitro or animal model systems. Exploratory/Developmental Phased Innovation (R21/R33) grant applications should identify and justify the genetic variants that they propose to test for functionality, the phenotype(s) the variants are associated with, and the functional measures that will be used to validate them. This FOA provides support for two years (R21 phase) for research planning activities and feasibility studies, followed by possible transition of up to three years of expanded research support (R33 phase).

NHLBI Clinical Trial Pilot Studies (R34) (PAR-13-002)

NHLBI invites applications proposing pilot studies to obtain data critical for the design of robust clinical trials. This Funding Opportunity Announcement (FOA) should be used to fill gaps in scientific knowledge necessary to develop a competitive full-scale clinical trial. Proposals that primarily aim to organize studies would not be responsive.

Exploratory/Developmental Bioengineering Research Grants (EBRG) [R21] (PA-12-284)

Exploratory/Developmental Bioengineering Research Grants (EBRG) establish the feasibility of technologies, techniques or methods that: 1) explore a unique multidisciplinary approach to a biomedical challenge; 2) are high-risk but have a considerable pay-off; and 3) develop data which can lead to significant future research.

An EBRG application may propose hypothesis-driven, discovery-driven, developmental, or design-directed research and is appropriate for evaluating unproven approaches for which there is minimal or no preliminary data.

Education Research in Sleep Health and Sleep-Circadian Biology (R25)

This initiative invites educational research (R25) grant applications focused on scientific advances in sleep health and circadian and sleep biology. The goal is to stimulate development of innovative, well-validated education tools, platforms and programs that will transfer health information and scientific advances in sleep and circadian biology to research scientists, health care providers, and educators, to specific populations including youth, older adults, women, racial and ethnic minorities, and veterans. Proposals are to address plans for future partnerships with appropriate stakeholder communities that could potentially facilitate dissemination and implementation. Applications from interested educational and outreach researchers partnering with appropriate expertise are encouraged.

NIOSH Exploratory/Developmental Grant Program (R21)

The purpose of this grant program is to develop an understanding of the risks and conditions associated with occupational diseases and injuries, to explore methods for reducing risks and for preventing or minimizing exposure to hazardous conditions in the workplace, and to translate significant scientific findings into prevention practices and products that will effectively reduce work-related illnesses and injuries.

This FOA was issued by CDC/NIOSH (not NIH). For questions, see the staff contact listed in the full text of the announcement at http://grants.nih.gov/grants/guide/par-files/PAR-12-252.html.

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Materials Available from NTSB SLEEP 2012 Keynote
“From Bench to Planes Trains and Automobiles”

At the SLEEP 2012 Plenary Session, Mark Rosekind, PhD, an SRS member and National Transportation Safety Board Member, delivered a memorable keynote speech on the dangers of fatigue across all modes of transportation. Materials from Dr. Rosekind’s speech are now available through the NTSB. This includes a PDF of the full PowerPoint presentation and a call to action on the NTSB Director’s blog. “This nation needs much more from the world of sleep science,” wrote Rosekind. “We need more operationally relevant research that provides the scientific basis to change further the laws, policies, and practices affecting transportation safety.”

Unfunded NIH Grant?
The National Health Council (NHC) announced a site that will help unfunded NIH applicants find potential funders. Called “Health Research Funding,” the database will allow unfunded NIH applicants to enter some basic information about their unfunded NIH grant applications in order to make that application information available to other potential funding organizations.

Initially, members of the NHC will have access to the database to be able to peruse ideas for potential funding. These members include more than 40 patient advocacy organization representing a diverse group of potential funders who are looking to take advantage of the tremendous rigor of the NIH peer review process to efficiently identify fundable proposals. Ultimately, the NHC plans to expand access to their database to include other types of funders as well.
The UF Sleep Research Lab investigates the mechanisms underlying normal and pathological sleep, the link between sleep and cognition, the daily variability inherent in sleep and sleep-related behaviors, and the efficacy and effectiveness of cognitive-behavioral interventions to treat insomnia in diverse populations (e.g., older individuals, dementia caregivers, and medical populations, including pain, cardiac disease, cancer, and end stage renal disease). As a result of these research emphases, we collaborate with a broad range of investigators within clinical psychology that specialize in aging, cognition, cardiac psychology, neuroimaging, pain, and psycho-oncology, as well as colleagues from cardiology, immunology, nursing, rheumatology, and sleep medicine.

Current Research

Sleep and Pain Interventions in Fibromyalgia: Hyperalgesia and Central Sensitization (SPIN; AR055160 & AR055160-S1; McCrae, PI).

Approximately 50-70% of patients with chronic pain, particularly fibromyalgia sufferers, report sleep difficulties. Because it is not possible to randomly induce chronic pain or chronic insomnia in otherwise healthy participants, the exact nature of the sleep/pain relationship is not well understood. SPIN examines the relationship between chronic pain and sleep disturbance in fibromyalgia patients and involves a randomized clinical trial (RCT) to evaluate the effects on sleep and pain of two established behavioral treatments [Cognitive-Behavioral Treatment of Insomnia (CBTi) and Cognitive-Behavioral Treatment of Pain (CBTp)]. SPIN tests specific hypotheses inherent to the Cognitive Activation Theory of Stress (CATS), which posits that sustained arousal and lack of arousal resolution (i.e., through restful sleep) results in the development of Central Sensitization (increased responsiveness of dorsal horn neurons, and perhaps other central nervous system structures to stimuli). Thus, insomnia may play an etiological role in the development and maintenance (i.e., chronicity) of chronic pain conditions. SPIN uses psychophysical and behavioral measures to evaluate changes in Central Sensitization as a result of treatment. An ARRA Supplemental award extends the aims of SPIN to include the investigation of the neural underpinnings of those changes.

Collaborators: Richard Berry, MD, (pulmonology, sleep medicine); Jason Craggs, PhD (neuroimaging, biostatistics); William Perlsstein, PhD (neuroimaging); Donald Price, PhD (physiology; neuroscience); Michael Robinson, PhD (pain psychology, biostatistics; Roland Staud, MD (rheumatology); Lori Waxenberg, PhD (pain psychology)

Sleep in Patients with Implantable Cardioverter Defibrillators (SAVE; HL087831 & HL087831-S1, McCrae, PI).

Cardiac disease is the leading cause of death in the U.S. The Implantable Cardioverter Defibrillator (ICD) significantly reduces cardiac mortality, and rates of ICD implantation are ~200,000 in the U.S. each year. Although sleep disturbance represents a significant comorbidity for ~57% of ICD patients, very little is known about sleep in these patients. SAVE examines the rates of specific sleep disorders in ICD patients, and as anticipated, our preliminary data indicates obstructive sleep apnea (OSA) and insomnia are the two most common. While effective treatments exist for OSA, the best treatment approach for insomnia in these patients is unclear. Cognitive behavioral therapy for insomnia (CBTI) represents an attractive to alternative sleep medication. Unfortunately, no definitive conclusions can be drawn about its effectiveness in ICD patients, because they are typically excluded from behavioral intervention protocols. Thus, SAVE also tests the effectiveness of a brief behavioral intervention specifically designed to improve sleep in ICD patients with insomnia (BBT). An ARRA Supplemental award extends the aims of SAVE

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to include investigation of the cognitive profiles of ICD patients and how cognitive functioning may be related to type of sleep disturbance. It also examines the effects of BBTi.icd on cognitive functioning.

Collaborators: Richard Berry, MD, (pulmonology, sleep medicine); Jamie B. Conti, MD (cardiology); Wei Hou, PhD (biostatistics); Samuel Sears, PhD (cardiac psychology)

Dementia Caregiver Sleep and The Effect on Heart Disease Biomarkers (AG039495; Rowe, PI).

Caregivers of dementia patients are particularly vulnerable to sleep disruption. Concern about the person with dementia’s (PWD) nighttime activities contributes to sleep interfering arousal in these caregivers. Previous research found that a nighttime monitoring device that alerts the caregiver to the PWD’s nighttime activities did not improve caregivers’ sleep, but did decrease unwanted home exits by the PWD. This study examines whether a nighttime monitoring device combined with cognitive-behavioral treatment for insomnia (CBTi) will produce better sleep and other biopsychosocial outcomes in caregivers of PWDs than a nighttime monitoring device alone. This study will use videoconferencing to remotely deliver a brief CBTi protocol specifically designed for caregivers (CBTi.icd). Our lab is responsible for the design and administration of the remote CBTi.icd.

Collaborators: Meredith Rowe, PhD (PI; nursing), Maureen Groer, PhD (nursing, psychoneuroimmunology) John Kairalla, PhD (biostatistics)

Intraindividual Variability in Sleep and Cognitive Performance in Older Adults with Insomnia – Research Evaluating Sleep and Thinking (REST; AG024459; McCrae, PI).

Insomnia affects up to 35% of individuals aged 65 and older. Although older adults with insomnia (OAWI) frequently complain of impaired cognitive functioning, objective evidence of such impairment has been sparse. Correlational studies have found evidence of deficits in cognitive performance in OAWI. Unfortunately, because the typical correlational design utilizes ‘one shot’ assessments, such studies provide only a ‘snapshot’ of the sleep/cognition relationship. This approach could be improved as both sleep and cognitive performance may exhibit considerable day-to-day variability, particularly in older adults. Using repeated daily assessments, these fluctuations in sleep and cognition (intraindividual variability or IVV) can be captured and modeled. SPIN participants completed daily sleep diaries and brief daily cognitive diaries throughout the course of a brief (4 session) behavioral treatment program for insomnia. We believe studying OAWI intensively over the course of treatment will provide insights into the day-to-day fluctuations in sleep and cognition within individuals (i.e., IVV) and will permit a detailed examination of the extent to which IVV in cognitive performance is related to fluctuations in sleep.

Collaborators: Richard Berry, MD, (pulmonology, sleep medicine); Michael Marsiske, PhD (geropsychologist; biostatistician)

Other Ongoing Projects
• Cognitive Behavioral Effects on Sleep, Pain, and Cytokines in Gynecologic Cancer (CA138808, Pereira, PI)

• Improving Sleep for Caregivers of Persons with Dementia (AG039495; Rowe, PI)
• Impact of Exercise on Sleep and Cognition in Older Adults – The Active Adult Mentoring Program (AAMP)
• Healthcare Utilization Pre- and Post-Cognitive Behavioral Therapy for Insomnia
• Impact of Age on Fatigue, Fatigability, and Sleep in Adult End State Renal Disease

Training Opportunities
Dr. McCrae is a core faculty member for the University of Florida’s APA accredited training program in Clinical Psychology. Graduate students in the lab are typically pursuing their doctoral degree in Clinical Psychology with special emphases on Health Psychology and Behavioral Sleep Medicine or Clinical Geropsychology. The behavioral sleep training program is currently in the process of applying for accreditation from the Society of Behavioral Sleep Medicine. Additional clinical and research training opportunities in behavioral sleep medicine and medical disorders comorbid with insomnia are available at the graduate and intern levels. A graduate course in Behavioral Sleep Medicine is also offered.

Behavioral Sleep Medicine Clinic
Dr. McCrae is also the Director of the Insomnia & Behavioral Sleep Medicine Clinic at the UF&Shands Sleep Disorders Center. Clinical practicums are available to graduate students and interns who are interested in working with pediatric and adult patients with various sleep-related disorders in a medical setting.

Methodology and Techniques
Psychological questionnaires, self-report sleep measures (i.e., daily sleep diaries), actigraphy, and ambulatory polysomnography (PSG) are used to collect data on sleep and sleep-related behaviors. Our research protocols typically involve microlongitudinal designs to better understand the variability inherent in sleep and related health behaviors (i.e., affect, cognition, pain). We use a variety of statistical techniques to examine that variability. Our research protocols also often include brief behavioral (BBTi) or cognitive behavioral treatment of insomnia (CBTi). Sometimes these protocols examine the efficacy or effectiveness of BBTi or CBTi, while other protocols are hybrid designs that include both clinical trial and experimental components to increase our understanding of sleep and sleep-related behaviors in older adults with insomnia and individuals with comorbid insomnia. We also use neuroimaging to study the impact of CBT protocols for insomnia and pain on brain structure and function.

Recent Publications

Continued on the following page →
Domestic Laboratory Spotlight


*denotes current or former mentee
Background
Our sleep physiology laboratory, which was established in 2009, lies within the Department of Drug Design and Pharmacology in the Faculty of Health Sciences at the University of Copenhagen, which is situated in the Scandinavian country of Denmark. The laboratory is headed by Dr. Kristi A. Kohlmeier, who is a graduate of the Multi-Site Training Program for Basic Sleep Research. Under the auspices of this National Institutes of Health sponsored training program, Dr. Kohlmeier performed her graduate work on the REM sleep-specific motor inhibitory system in the laboratory of Dr. Michael H. Chase, a pioneer in the field of sleep neurophysiology. To further her training in sleep research, with postdoctoral funding from the National Sleep Foundation and the National Institutes of Health, Dr. Kohlmeier studied mechanisms controlling the activity of brainstem neurons importantly involved in generating states of sleep and wakefulness at the University of British Columbia and New York Medical College with Drs. Peter B. Reiner and Christopher S. Leonard, respectively. Now at the University of Copenhagen, Dr. Kohlmeier continues studies of sleep physiology with a focus on examination of the cellular and synaptic effects of pharmaceutical agents on arousal-related neurons, with the goal of determination of the neuronal correlates of behavior and the hope of gaining information towards development of the next generation of agents indicated for the management of behavioral state disorders.

Current Research
Many disorders present with dysfunctions in arousal including disturbances in cycling between sleep and wakefulness. However, incomplete understanding of how the human brain cycles between varying states of consciousness hinders development of the most efficacious treatment strategies for these dysfunctions. Our research centers on studies of mechanisms controlling activity of neuronal groups important in state control with the expectation that findings will expand upon our knowledge of how behavioral state is generated and further efforts towards therapeutic drug design. As neurons that control REM sleep have been recognized to also play a role in assignment of relevance and saliency to environmental stimuli with a positive valence, our studies have widened from an initial focus of elucidating the processes underlying the neural control of sleep and wakefulness states to include study of the processes contributing to the high-degree of arousal associated with drug-seeking behavior.

Most recent examinations have been on the role cholinergic, glutamatergic and GABAergic mechanisms play in control of activity of arousal-related pontine neurons. Accordingly, we have investigated the modification of activity of these neurons by drugs acting at receptors for these neurotransmitter systems. To monitor activity of neurons involved in generation of arousal and REM sleep engendered by exposure to neuroactive compounds, we utilize high-tech methodologies, specifically patch clamp electrophysiology and calcium imaging.

Technical Specialization
We utilize in vitro patch clamp techniques to study electrophysiological activity induced by pharmaceutical agents in single, immunohistochemically-identified neurons from mouse brain slices. We also perform concurrent high speed calcium imaging with calcium binding dyes and CCD cameras in order to correlate changes in calcium with alterations in electrical activity. Use of caged compounds and subsequent delivery via photorelease allows us to apply agonists quickly and locally so we can uncover differences in receptor activity on neuronal somas and dendrites to assist design of precisely-targeted therapies. In our studies, we utilize naïve mice as well as manipulated mice serving as mouse models of disease, such as the nicotine pre-natally exposed mouse. Collaborators within our Institute assist us with conducting in vivo, systems-level studies, enabling testing of predictions of actions on behavior of neuroactive compounds based on in vitro cellular findings of effects of pharmaceutical agents. In addition, our Institute includes a very active medicinal chemistry faculty who design novel and highly-targeted compounds that can be screened for functional activity in native neurons in collaboration with our laboratory.

Taken together, we have hope that findings from our studies will further our understanding of the neurobiology underlying generation of arousal state and thereby contribute to development of future generation pharmaceutical agents that can more successfully manage disorders of aberrant control of arousal such as drug-seeking and the sleeping disorders of insomnia, narcolepsy.

Continued on the following page →
Training Opportunities
We are always happy to be contacted by highly-motivated individuals who are interested in joining our laboratory. Local and international students with a bachelor's degree who are interested in sleep or drug addiction related graduate work are welcome to apply to our MSc program in Pharmaceutical Sciences (English language) or Pharmacy (Danish fluent students only). The PhD program in Pharmaceutical Sciences admits candidates who already have obtained a MSc degree and welcomes students from all over the world as this doctoral training program is conducted entirely in English. Those interested in conducting postdoctoral training within the laboratory are supported by Danish Government grants, foundation grants such as from the Lundbeck Foundation or grants from Pharmaceutical companies with whom the University has a close collaboration such as Lundbeck or Novo Novartis. The standard of living within Denmark is considered quite high and the country offers a plethora of outdoor activities in a mild, temperate climate and serves as an easy springboard to the other Scandinavian countries and the rest of Europe.

Representative Publications

Book Chapters
At the beginning of August, Congress adjourned for the extended summer recess. Many high-profile legislative issues await consideration pending the outcome of the November elections, but appropriators managed to advance work on a number of fiscal year 2013 (FY13) spending measures before leaving Capitol Hill.

The Senate Appropriations Committee has approved its FY13 Labor-Health and Human-Services-Education (L-HHS) Appropriations bill, which funds the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC). The bill included $30.7 billion for the National Institutes of Health (NIH)—an increase of $100 million—and $7 billion for the Centers for Disease Control and Prevention (CDC)—an increase of $61 million. The Senate committee bill made very strong recommendations on sleep research and public health surveillance.

Following the Senate’s action, the House L-HHS Appropriations Subcommittee marked up its FY13 appropriations measure. The bill was met with harsh criticism for slashing funding to public health and education programs, and was not considered by the full House Appropriations Committee.

With limited legislative days on the calendar before the beginning of the fiscal year on October 1st, leaders in the House and Senate announced they had reached agreement on a stopgap spending measure or continuing resolution (CR). The six-month CR is based on the $1.047 trillion discretionary funding level agreed to in last year’s bipartisan Budget Control Act and, if enacted, would fund federal programs through March 31st, 2013.

Part of the reasoning behind passing a CR is to free up time for Congress to focus on critical issues before adjourning at the end of the year. Following the November elections, lawmakers will need to negotiate legislative packages to raise the debt ceiling and deal with the potential expirations of a litany of tax cuts. Congress will also need to, once again, patch the sustainable growth rate system to prevent a cut to the rate at which Medicare reimburses physicians for the services they provide to beneficiaries. In addition, pressure is mounting on lawmakers to avert or mitigate sequestration, an automatic, across-the-board funding cut to nearly all federal programs that is presently scheduled to take effect in January of 2013.

As Congress prepares for the end of the year, the SRS government relations team has been preparing to expand its advocacy efforts. Over the past year SRS officers and staff, working in conjunction with the Health and Medicine Counsel of Washington, have undertaken a comprehensive outreach effort to raise Congressional awareness of the health risks associated with sleep disorders and the benefits of investing in sleep and circadian research. The outreach effort has included dissemination of the National Institutes of Health’s Sleep Disorders Research Plan that was issued in November 2011, to all 535 individual Congressional offices; key Congressional committee staff, as well as personal outreach to staff members in key Congressional offices. Following this effort, Congressman Mike Honda (D-CA-15) and Congressman Hank Johnson (D-GA-4) sent a joint letter inviting NIH Director Dr. Francis Collins to brief congressional staff on the findings and recommendations of the plan. On Thursday, May 31, 2012 SRS had the opportunity to host a congressional briefing in the U.S. Capitol building. Presentations were given by Susan Shurin, MD, Acting Director of NHLBI; David Dinges, PhD; and Phyllis Zee, MD, PhD, and each speaker addressed questions and comments from a standing-room only audience. Recognizing the potential for collaboration and interest shown by congressional offices, SRS looks forward to continuing to expand on congressional outreach activities over the next few months and into a new congress following the election.

Dale P. Dirks
Meaghan Pilarcik
Health and Medicine Counsel of Washington
The Sleep Research Society welcomes members who recently joined the organization. Our membership continues to grow — help us strengthen the impact of the profession by encouraging your colleagues to join. Information regarding membership can be found on the Society website (www.sleepresearchsociety.org).

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<th><strong>FULL MEMBERS</strong></th>
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