Issue Highlights:

• APSS 2009 Recap
• Interview with the Editor: Barbara E. Jones, Ph.D.
• Sleep Research Highlight: Mathematical Model of Sleep Loss
• A Grander Scale for Sleep Medicine Research: Promoting Sleep Research Networks
The Sleep Research Society (SRS) is a member organization of more than 1,200 scientists committed to fostering scientific investigation on all aspects of sleep and its disorders, promoting training and education in sleep research, and providing forums for the exchange of knowledge pertaining to sleep.

Through its members and leadership, the SRS is organized exclusively for scientific, educational, and charitable purposes. The SRS invites you to continue your commitment by renewing your membership for 2010. By renewing your membership today you will continue to be among the many distinguished scientists in the field of sleep research who continue to commit to success.

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- The Elliott D. Weitzman, M.D. Research Grant which is intended for researchers to gather additional pilot data for NIH or other federal grants that are scored but not funded

For information or questions regarding membership, please contact the SRS membership department at (708) 492-1093 or SRSmembership@srsnet.org
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Dear Colleagues,

This is the first of several “President’s Messages” that I will have the opportunity to author over the coming year. I would like to begin by first thanking the members of the SRS for placing their trust in me and allowing me to serve as President for the coming year. I am humbled and grateful for this opportunity. I extend my thanks to Michael Vitiello, PhD, for his successful tenure as president of the Sleep Research Society. Dr. Vitiello’s dedication to the SRS is a great example to us all.

During the SRS Annual Membership Meeting at SLEEP 2009, I outlined my goals for the SRS over the next year. I would like to share my vision for those who were not able to attend SLEEP 2009.

Researchers, like many other professions have not been immune to the economic downturn this past year. Certainly the SRS will continue to adjust our budget, and our priorities, based on the current economic realities while keeping the needs of our members as a priority.

Research funding is a major concern for SRS members. Although the American Recovery and Reinvestment Act gave a one-time boost for NIH-funded scientists, long-term NIH funding is less clear. Additionally, private foundations and private sector funding has eroded due to the state of the economy leaving more competition for limited federal grants.

In light of increasing competition for federal grants, and as a result of the SRS trip to Washington, DC last spring, I am working to establish a permanent structure to advocate for funding sleep research. The Executive Committee recently voted to establish a new SRS Advocacy Committee. The members of the Advocacy Committee are Sonia Ancoli-Israel, Charles Czeisler, Mark Opp, Eric Nofzinger, Susan Redline, and Fred Turek, who will Chair the committee. Dr. Terri Weaver will act as the Board Liaison for the committee.

The mission of the committee is to guide SRS volunteers in their advocacy efforts. The targets of our advocacy efforts will be members of Congress that sit on the House and Senate Appropriations Committee, and NIH Directors and Program Officers. The goal is to build meaningful relationships over time in order to enhance the stature of our profession and to eventually increase funding through congressional action and through communicating the value of our research to NIH officials.

Another goal for the coming year is to increase the involvement of Sections as a conduit for volunteers and society leadership, I hope to increase the interest and activity of Sections.

Trainees are the future of sleep research. I will continue to foster the careers of our young investigators through the SRS sponsorship of Trainee Day. Trainee Day is a unique opportunity for young scientists to engage in collegial interaction with senior scientists with successful careers across the broad spectrum of sleep research. This year nearly 300 trainees registered for this event, making it our largest trainee day ever.

The SRS will continue to support the formation of a national network for sleep clinical studies by working with the Clinical-Translational Science Centers (CTSCs) funded by the NIH. Many of the CTSCs have large numbers of patient bed-nights devoted to sleep research which is crucial to establishing this network. Additionally, I would like the SRS to help the sleep teams at the CTSCs produce a national network that would facilitate collecting physiological data and genetic material in a standardized way that would foster collaboration across sleep centers and lead to the creation of a Gene Chip for sleep.

Before I conclude my first message, I would like to take a moment and thank the members of the Board of Directors who concluded their terms this year: Drs. Ron Chervin; Eric Nofzinger; Susan Redline; and Eliza Van Reen, the Trainee Member-at-Large. I would also like to thank the members of SRS committees who concluded their terms this year: Drs. Bob Strecker, Chair of the Membership Committee; Jason Ellis, Dalia Lorenzo; Jeanne F. Duffy; Shantha Rajaratnam; and William Wohlgemuth. Being a member of the Board of Directors or a SRS Committee is a significant time commitment and the efforts of these individuals should be commended.

The coming year for the SRS promises to be filled with new endeavors and much hard work. With the dedication of our members I believe we can make great strides toward accomplishing our mutual goals for the SRS and the field of sleep research. If you would like to become more involved in the society and volunteer your time and efforts in one of our ongoing project, I encourage you to do so by e-mailing Nick Cekosh in the SRS National Office at ncekosh@srsnet.org.

Sincerely,

Clifford B. Saper, MD, PhD
President

SRS Bulletin – 4 –
As we move into another fall season and the start of a new academic year is upon us, this issue of the bulletin looks back to the recent past and ahead to the future. Thanks to the efforts of the APSS Program Committee and numerous SRS staff members among others, the APSS meeting in Seattle, WA was a resounding success. This issue remembers the illuminating keynote address of Dr. Howard Roffwarg, recaps a very relevant Discussion Group on Funding Sources beyond NIH, summarizes the events from Trainee Day, and pictures the winners of the major SRS awards. The Interview with the Editor features an in-depth discussion with Barbara Jones, Ph.D., 2009 winner of the Distinguished Scientist Award, the SRS’ highest honor. Dr. Jones shares her views on her most significant scientific achievements, major influences on her research career, and the differences between a research career in Canada and the United States.

This issue also looks ahead by welcoming the group of incoming SRS leaders, including president Dr. Clif Saper. Please read Dr. Saper’s inaugural President’s Message for a recap of recent and ongoing society activities as well as his vision for SRS priorities over the next year. The outgoing President, Dr. Michael Vitiello, deserves congratulations for his capable leadership of the society during particularly challenging economic times.

In addition to domestic and international laboratory spotlights, this issue of the bulletin features an update by Dr. Susan Redline of four complementary initiatives currently underway: (1) Sleep Research Society-sponsored Task Forces on Genetics and on Academic Sleep Centers; (2) Establishment of a national Clinical and Translational Science Award (CTSA) Sleep Research Network; (3) Establishment of the Academic Alliance for Sleep Research (AASR); and (4) National Center for Research Resources-supported sleep informatics development. The primary goal of these initiatives is to broaden the scope of sleep research to facilitate advances in basic and clinical sleep and circadian science.

The bulletin continues its focus on highlighting recent scientific achievements by our members. This issue features a contribution by Dr. Peter McCauley and colleagues from the Sleep and Performance Research Center at Washington State University, who describe their work on a new mathematical model that predicts the homeostatic effects of sleep loss on neurobehavioral performance. As is evident from the summary of their recently published manuscript, this model may ultimately have applications that extend beyond the laboratory into environments that rely on extended work hours for providing services.

We recently lost a pioneer in the development of digital polysomnography in Jack Smith, Ph.D. Two of his close friends and colleagues, Drs. Augustin de la Peña and Wilse Webb, provide a heartfelt tribute to his personal and professional achievements in this bulletin issue. In a similar vein, Dr. Vladimir M. Kovalzon, Chairman of the Russian Somnological Society, celebrates the life of a little-known pioneer of sleep research, Maria Mikhailovna Manasseina-Korkunova (1843-1903), on the 165th anniversary of her birth.

Comments about the bulletin and ideas for future issues can be submitted to me at tarnedt@med.umich.edu. Have a happy, healthy, and productive fall season.
PARTICIPATION OF REM SLEEP IN THE DEVELOPMENT OF THE BRAIN: STARTING HYPOTHESIS, UNFOLDING DATA, CURRENT PERSPECTIVE

The discovery of REM sleep (REMS) in the late 1950s was a surprise, but recognition of the stunning biological implication of this sleep stage for brain development had to wait upon disclosure of the relatively voluminous amounts of REMS observed in neonatal land mammals and (some) birds. The great preponderance of the state in the young, its decrease during maturation, and the exuberant brainstem activity discharged and widely distributed during REMS to central sensory and motor sites in the CNS, appealed for explanation. Why, we wondered, is the brain subjected to a second state of activation beyond what is provided in waking? A promising response to that question presented itself as we were considering the striking dilemma confronting young mammals in the formative period: Whereas plentiful sensory stimulation is crucial for normal growth and differentiation of immature neural tissue, this important CNS requirement conflicts with a unique developmental actuality; namely, the relative absence of exogenous stimulation owing to the cushioned intrauterine environment and prevalence of sleep following parturition.

Already informed in the early 1960s about the copiousness and activating nature of REMS, we advanced the proposal in 1966 that, in the Wake state-spare developmental period, REMS is uniquely configured to execute, within sleep, a critical function, that of augmenting stimulation-dependent CNS development so that the brain can self-organize sufficiently to handle waking input. We believed REMS may accomplish this function by virtue of its state-related generation of intense activation in the lower brain, activation that is transmitted to diverse brain areas. At the time, the concept that a stage of sleep may “revive” the (immature) mechanisms for induction of mental LTP by altering the balance between excitatory and inhibitory (GABA) mechanisms and release of BDNF --- are delayed. Development of the CP --- probably cortical maturation of GABA inhibitory mechanisms and release of BDNF --- are delayed. Development of the central visual CNS is retarded during a period of REMSDEP, paralleling the aftermath of sharply reduced bilateral afferentation with dark-rearing. In sum, absence of REMS during development increases synaptic plasticity, denoting a delay or distortion of expectable maturation. In contrast, REMS activation appears to support a template of normative growth.

Lesions of the bilateral, brainstem PGO pathways to LGN in the immature brain yield results similar to those seen in LGN laminae after instrumental REMSDEP. The data validated Davene and Adrien’s demonstrations that REMS phasic activity is the essential element in REMS-related maturational effects. The LGN findings after PGO pathway-interruption --- a very different approach (from REMSDEP) to preventing REMS-related activation from reaching LGN --- support other evidence that REMSDEP has a CNS “protective” effect against, asymmetries or excesses of induced plasticity.

The outcomes in summaries 1-4 above reveal CNS synaptic plasticity, as displayed in structural adaptations to aberrant stimulation (e.g., MD) during development. Heightened synaptic plasticity due to REMSDEP during development is also experimentally demonstrated by extension of the critical period (CP) for inducing developmental long-term potentiation (LTP) in visual cortex. The mechanisms for closing this developmental CP --- probably cortical maturation of GABA inhibitory mechanisms and release of BDNF --- are delayed. Development of the central visual CNS is retarded during a period of REMSDEP, paralleling the aftermath of sharply reduced bilateral afferentation with dark-rearing. In sum, absence of REMS during development increases synaptic plasticity, denoting a delay or distortion of expectable maturation. In contrast, REMS activation appears to support a template of normative growth.

1. As indicated by the consequences of REMSDEP, we concluded that REMS ascending activation stimulates and promotes maturation of central visual sensory sites. REMS activation blunts the severity of the physical asymmetries caused by MD.

2. REMS internal “autostimulation” and waking sensory stimulation of the binocular laminae of the lateral geniculate nuclei (LGN) have complementary and additive structural effects. This was particularly evident in our study in one of the two LGN monocular segments not at all influenced by MD. In that segment, it was clearly observed that REMS-related “afferentation” has an amplifying effect on LGN cell size over and above the effect of waking visual input.

3. REMS PGO waves were demonstrated to symmetrically and simultaneously invest the binocular LGN laminae, indicating that REMS activation is hemispherically bilateral.

4. The bilateral wash of REMS activation continually buffers, i.e., has a CNS “protective” effect against, asymmetries or excesses of induced plasticity.

5. Lesions of the bilateral, brainstem PGO pathways to LGN in the immature brain yield results similar to those seen in LGN laminae after instrumental REMSDEP. The data validated Davene and Adrien’s demonstrations that REMS phasic activity is the essential element in REMS-related maturational effects. The LGN findings after PGO pathway-interruption --- a very different approach (from REMSDEP) to preventing REMS-related activation from reaching LGN --- support other evidence that stress does not critically affect our data obtained with use of instrumental REMSDEP.

6. The outcomes in summaries 1-4 above reveal CNS synaptic plasticity, as displayed in structural adaptations to aberrant stimulation (e.g., MD) during development. Heightened synaptic plasticity due to REMSDEP during development is also experimentally demonstrated by extension of the critical period (CP) for inducing developmental long-term potentiation (LTP) in visual cortex. The mechanisms for closing this developmental CP --- probably cortical maturation of GABA inhibitory mechanisms and release of BDNF --- are delayed. Development of the central visual CNS is retarded during a period of REMSDEP, paralleling the aftermath of sharply reduced bilateral afferentation with dark-rearing. In sum, absence of REMS during development increases synaptic plasticity, denoting a delay or distortion of expectable maturation. In contrast, REMS activation appears to support a template of normative growth.

7. REMSDEP probably prevents closing of the CP for developmental LTP by altering the balance between excitatory and inhibitory (GABA) mechanisms in visual cortex. REMSDEP may “revive” the (immature) mechanisms for induction of developmental LTP in a young rat (though not in a naive REMSDEP adult), extending the CP into adolescence. Low frequency stimulation in developing visual cortex, which usu-
ally evokes LT depression (LTD), tends to elicit LTP in young REMSDEP rats.

8. REMS strengthens, whereas very early REMSDEP impairs, LTP stability in hippocampus. REMSDEP animals have low levels of the glutamatergic receptor subunits and downstream signaling molecules required to stabilize hippocampal neuronal circuits.

Data collected by other investigators, using techniques different from ours, have resulted in notable progress on several fronts. These contributions have afforded an opportunity for more comprehensive syntheses of concepts relating to participation of sleep in development. For example, Marcos Frank and his coworkers have documented and confirmed that activity-dependent synaptic remodeling initiated by MD in visual cortex is promoted, compared to other post-MD conditions, by an immediately succeeding period of sleep. This increase in plasticity is significantly correlated with the amount of NREMS in the sleep period. It also depends upon cortical activity. Further, these workers have identified many mechanisms bearing on plasticity processing in sleep and reviewed the operative steps of numerous other candidates. Mark Blumberg and his group have demonstrated that REMS, as a state, is cohesive virtually from birth in the rat. The brainstem centers and mechanisms that are critical to REMS-related phasic discharge and muscle atonia in the adult, as well as the networks carrying stimulatory feedback from motor twitches in REMS to hippocampus, are already enabled and in phase in the first postnatal days. These investigators had earlier, in effect, corrected a false distinction between so-called “Active Sleep” (AS), primarily identified by a neonate’s prominent myoclonic activity, and the developed REMS state by documenting that (probable) REMS descending neural-control mechanisms are in action and exert an influence upon, though are not totally responsible for, the spinal segmental twitching observed in AS.

The timing of appearance of well differentiated (e.g., REMS) sleep stages must hinge on the extent of an animal’s general brain development. The latter’s relationship to point of birth is not easy to comprehend and varies broadly among species. Nevertheless, it may be predicted that sleep stages will mature sooner (sometimes before birth) in precocial and avian animals and later (well after birth) in altricial animals. Because of the early, more apparent than real, overlap of states observed in certain altricial species, it was proposed that the mature, finally defined stages evolve from a premature and undifferentiated sleep anlage. But it is to be expected that, in their earliest stages of expression, neuropysiological processes that mediate even a highly delineated, single state will display initial immaturity and lack of coherence. (The fully developed sleep stages of a precocial animal must first be immature at the starting point in their development.) Accordingly, the highly distinctive neuropysiological features of REMS and NREMS as well as the recent data bias us to the conclusion that the two sleep states, from their beginnings, are products of exclusive mechanisms.

Our concept of a developmental function of REMS long ago incorporated Jouvet’s thinking that REMS phasic activity is under genetic control but also epigenetically modulated. We believe that REMS is pre-programmed to actively “urge” the CNS towards the maturational pattern prescribed for each species.

Finally, because it is now understood that REMS is not the sole stage of sleep participating in brain development, the “ontogenetic hypothesis” (1966) requires revision to include the role of NREMS. Increased consolidation of previously instigated thrusts of synaptic remodeling apparently takes place in the NREMS stage. Repeatedly succeeding each other in sustained sleep (an oscillation itself suggestive of mutuality), the NREMS and REMS phases appear to perform reciprocal but also necessary and functionally incremental pieces of the physiological task of brain maturation. In our view, REMS stimulates growth but seems also to modulate CNS plasticity, whereas NREMS functions to reify the remodeling pressures it encounters from preceding Wake- and, possibly, REMS activations. We would view the two states as even more closely meshed were it ultimately demonstrated that NREMS also consolidates the processes of “normal growth plasticity,” which we believe are encouraged during REMS episodes We look to future investigations to supply the data we need to understand the full range of interlacing functions and mechanisms of the two sleep states.

Howard P. Roffwarg, M.D.
University of Mississippi Medical Center
The **Distinguished Scientist Award** is the Sleep Research Society's highest award and recognizes significant, original and sustained scientific contributions of a basic, clinical or theoretical nature to the sleep research field.

**Barbara E. Jones, Ph.D.**

Dr. Barbara E. Jones was born in Philadelphia and has also lived in New York, New Jersey, Connecticut and Delaware and attended the University of Delaware. For her graduate studies, she remained affiliated with the University of Delaware while traveling to France to perform her thesis research with Michel Jouvet in Lyon. There she was able to bring together her love of the French language and culture with her fascination for the physiology of sleep. Realizing her anticipated entry into the new frontiers of research championed by Jouvet in the 60s, she completed her thesis work on the organization and role of catecholamine containing neurons in vigilance states. She also further kindled through Jouvet’s inspiring and creative approach a lifelong passion for the search of what generated the states of sleep and wake. After completing her PhD (1970), she engaged in postdoctoral research in neurochemistry with Jacques Glowinski in Paris, studying the release of noradrenaline and acetylcholine. She took a position at the University of Chicago (1972), where she established a laboratory for continuing the study of noradrenergic systems. She benefitted at Chicago from association with Allan Rechtschaffen in his sleep lab and collaboration with Robert Moore in neuroanatomy. Accompanying her anthropologist husband, John Galaty, to Kenya, she also taught one year at the University of Nairobi (1974) and initiated a program on the sleep-wake and correlated neural changes in monkeys associated with the encephalitis of African trypanosomiasis.

Dr. Jones moved to Montreal to take a position at McGill University (1977) and the Montreal Neurological Institute (MNI) where she has remained until the present, associate, associate (1982) and full professor (1989) in neurology and neurosurgery. From there, she also took a sabbatical leave at Oxford University (1984) and multiple leaves at the Université de Genève (1991, 1998, 2006). Over the years, she established in her laboratory a program concerning the chemical neuroanatomical and in vivo neurophysiological study of the neural systems regulating sleep-wake states. She has also benefitted greatly from her long term collaboration and visits with Michel Muhlethaler in Geneva concerning the in vitro electrophysiological study of these same systems.

Over these years of research, Dr. Jones has examined the way in which noradrenergic and dopaminergic neurons influence waking, how cholinergic brainstem and forebrain neurons stimulate cortical activation and promote both waking and REM sleep, how GABAergic neurons play diverse roles in gating activity of other state generating cell groups, and how orexin and MCH neurons can reciprocally regulate waking and sleeping. She is currently examining the way in which discharge during different states by different cell populations can regulate their receptors and excitability such as to determine their activity and homeostatic regulation across the sleep-waking cycle.

The **Mary A. Carskadon Outstanding Educator Award**, established in 2005, is presented on an annual basis by the Sleep Research Society to honor excellence in the field of education related to sleep medicine and research. This award is given to an investigator to honor his/her outstanding effort in disseminating basic and/or clinical sleep research as a mentor, teacher, or through public education.

**David F. Dinges, Ph.D.**

David F. Dinges is a Professor of Psychology in Psychiatry, Chief of the Division of Sleep and Chronobiology, and Director of the Unit for Experimental Psychiatry in the Department of Psychiatry at the University of Pennsylvania School of Medicine. Dr. Dinges is also Associate Director of Penn’s Center for Sleep and Respiratory Neurobiology, and a member of the Psychology Department Graduate Group, Penn’s Institute for the Translational Medicine and Therapeutics, the Center for Functional Neuroimaging, and a popular undergraduate teacher in Penn’s Biological Basis of Behavior Program. In addition to his lectures, and training of graduate and post doctoral students, in the past 20 years, more than 500 undergraduate students have worked and trained in his laboratory. He has received teaching awards from both Penn’s School of Medicine and College of Arts and Sciences.

Dr. Dinges has devoted most of his career to the study of human sleep need. His research focuses on biological and behavioral effects of sleep loss and disturbances of circadian biology. He has conducted extensive scientific work on development and validation of behavioral, technological, and biological interventions for these effects to promote human health and safety. His research has been supported by major grants from the National Institutes of Health, NASA, Department of Defense, Department of Transportation, Department of Homeland Security, foundations and industry. Dr. Dinges currently leads the Neurobehavioral and Psychosocial Factors Team for the NASA funded National Space Biomedical Research Institute. He has served on NIH Council and as President of the Sleep Research Society and of the World Sleep Federation, as well as on the Board.
of the American Academy of Sleep Medicine and the National Sleep Foundation. He is currently Editor-in-Chief of SLEEP. He has been awarded the 2001 Senator Mark O. Hatfield Public Policy Award from AASM; the 2004 Decade of Behavior Research Award from the American Psychological Association; and the 2007 NASA Distinguished Public Service Medal.

OUTSTANDING SCIENTIFIC ACHIEVEMENT AWARD

The Outstanding Scientific Achievement Award is presented to individuals based upon novel and seminal discoveries of a basic, clinical or theoretical nature that have made a significant impact on the field of sleep.

David Rye, M.D., Ph.D.

Dr. David Rye is Professor of Neurology within the Emory University School of Medicine and Director of Emory Healthcare’s Program in Sleep. Dr. Rye received his doctorates in neurobiology and medicine from the University of Chicago’s Pritzker School of Medicine. Here he trained in Neurology and was Chief Resident 1991-1992. Since moving to Emory University in 1992 he has helped establish and build a clinical and research program in Sleep Medicine with an emphasis on movement disorders in sleep including Restless Legs Syndrome, Parkinson’s disease, and the role of dopamine in normal and pathological wake/sleep states. His work in rodents, non-human primates, and humans spans the spectrum from systems neurobiology to animal models of disease and human genetics. He is board certified in both Sleep Medicine and Neurology, is past chair of the Restless Legs Syndrome Foundation’s Medical Advisory Board, and has served on the editorial boards of Sleep Medicine, Sleep Medicine Reviews, Experimental Neurology, Neurology, and is a Deputy Editor for Sleep. He has been a member of the SRS for 3 years.

Abstract

A Genetic Risk Factor for Periodic Limb Movements in Sleep*

Hreinn Stefansson, Ph.D., David B. Rye, M.D., Ph.D., Andrew Hicks, Ph.D., Hjorvar Petursson, B.Sc., Andres Ingason, B.Sc., Thorgerir Thorgeirsson, Ph.D., Stefan Palsson, M.S., Thordur Sigmundsson, M.D., Albert P. Sigurdsson, M.D., Ingibjorg Eiriksdottir, B.Sc., Emilia Saebach, B.Sc., Donald Blwise, Ph.D., Joseph M. Beck, B.S., Ami Rosen, M.S., Salina Waddy, M.D., Lynn M. Trotti, M.D., Alex Iranzo, M.D., Madhav Thambisetty, M.B., B.S., D.Phil., Gudmundur A. Hardarson, M.S., Kristjulfur Kristjansson, M.D., Larus J. Gudmundsson, B.Sc., Unnur Thorsteinsdottir, Ph.D., Augustine Kong, Ph.D., Jeffrey R. Gulcher, M.D., Ph.D., Daniel Guddbjartsson, Ph.D., and Kari Stefansson, M.D., Ph.D.

Background The restless legs syndrome (RLS) is a common neurologic disorder characterized by an irresistible urge to move the legs. It is a major cause of sleep disruption. Periodic limb movements in sleep are detectable in most patients with RLS and represent an objective physiological metric.

Methods To search for sequence variants contributing to RLS, we performed a genomewide association study and two replication studies. To minimize phenotypic heterogeneity, we focused on patients with RLS who had objectively documented periodic limb movements in sleep. We measured serum ferritin levels, since iron depletion has been associated with the pathogenesis of RLS.

Results In an Icelandic discovery sample of patients with RLS and periodic limb movements in sleep, we observed a genomewide significant association with a common variant in an intron of BTBD9 on chromosome 6p21.2 (odds ratio, 1.8; P = 2x10^{-8}). This association was replicated in a second Icelandic sample (odds ratio, 1.8; P = 4x10^{-8}) and a U.S. sample (odds ratio, 1.5; P = 4x10^{-8}). With this variant, the population attributable risk of RLS with periodic limb movements was approximately 50%. An association between the variant and periodic limb movements in sleep without RLS (and the absence of such an association for RLS without periodic limb movements) suggests that we have identified a genetic determinant of periodic limb movements in sleep (odds ratio, 1.9; P = 1x10^{-4}). Serum ferritin levels were decreased by 13% per allele of the at-risk variant (95% confidence interval, 5 to 20; P = 0.002).

Conclusions We have discovered a variant associated with susceptibility to periodic limb movements in sleep. The inverse correlation of the variant with iron stores is consistent with the suspected involvement of iron depletion in the pathogenesis of the disease.

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Juliane Winkelmann, M.D.

Dr. Juliane Winkelmann is a Professor of Neurology and Neurogenetics at the Technical University Munich. Her main areas of research are movement and sleep disorders. For many years her research focused on the restless legs syndrome (RLS) with a special interest in the genetics of the disease. She is Assistant Medical Director at the Department of Neurology and Institute of Human Genetics. She also heads the Research Group Neurogenetics at the Institute of Human Genetics at the Helmholtz Zentrum Munich. Dr. Winkelmann is a member of many national and international medical societies and boards and published numerous papers on sleep and movement disorders. She founded and heads the European Consortium on the genetics of RLS “EURLSGENE”. Recently, her group in collaboration with a large international consortium identified for the first time genetic variants associated with RLS in the genes MEIS1, BTBD9, LBX2OR1 and PTPRD. This provided the first prerequisite to study the molecular mechanisms of the disease.

Abstract

Genome-Wide Association Study of Restless Legs Syndrome Identifies Common Variants in Three Genomic Regions.**

Restless legs syndrome (RLS) is a frequent neurological disorder characterized by an imperative urge to move the legs during night, unpleasant sensation in the lower limbs, disturbed sleep and increased cardiovascular morbidity. In a genome-wide association study we found highly significant associations between RLS and intronic variants in the homeobox gene MEIS1, the BTBD9 gene encoding a BTB(POZ) domain as well as variants in a third locus containing the genes encoding mitogen-activated protein kinase MAP2K5 and the transcription factor LBXCOR1 on chromosomes 2p, 6p and 15q, respectively. Two independent replications confirmed these association signals. Each genetic variant was associated with a more than 50% increase in risk for RLS, with the combined allelic variants conferring more than half of the risk. MEIS1 has been implicated in limb development, raising the possibility that RLS has components of a developmental disorder.

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**Young Investigator Award**

This award recognizes an outstanding research effort by a new investigator in the field of sleep research.

**Sara Aton, Ph.D.**

Sara Aton, PhD, received her Ph.D. in Neuroscience from Washington University in St. Louis. Her thesis research, carried out in the laboratory of Dr. Erik Herzog, focused on how intercellular and intracellular signaling pathways coordinate daily activity rhythms among neurons within the suprachiasmatic nucleus - the master circadian clock in the mammalian brain. During her graduate studies she became extremely interested in the roles of sleep and circadian rhythms regulating basic nervous system functions like synaptic plasticity. In 2006, Dr. Aton began her postdoctoral research in the laboratory of Dr. Marcos Frank at the University of Pennsylvania. During her time in Dr. Frank’s lab, Dr. Aton and her colleagues studied a canonical model system of in vivo synaptic remodeling within the primary visual cortex known as ocular dominance plasticity, originally studied by Hubel and Wiesel over 40 years ago. This form of synaptic plasticity is initiated by briefly depriving input from one eye to the visual cortex (i.e., monocular deprivation) during a critical developmental window, and is consolidated by subsequent sleep. Her current studies address the roles of specific protein phosphatase and kinase signaling pathways – intracellular mediators of long term synaptic depression and potentiation, respectively - in the sleep-dependent consolidation of this plasticity. In parallel with studies of intracellular mechanisms, she is beginning to pursue the intercellular and network-level mechanisms in the sleeping cortex that underlie this process. Using multielectrode array technology to record large groups of individual neurons in freely moving, freely sleeping animals, she is assessing the roles of specific network interactions - including sleep-dependent changes in firing rate, spike timing, and cooperativity between neurons - in consolidating ocular dominance plasticity. It is likely that the cellular mechanisms underlying sleep dependent consolidation of ocular dominance plasticity also underlie sleep effects on other types of learning and memory. Therefore, understanding these mechanisms in a simple model system will broaden our understanding of the role of sleep in cognition, and how sleep deprivation adversely affects neural function.

**Georgina Cano, Ph.D.**

Georgina Cano, Ph.D., is currently a visiting assistant professor at the Department of Neuroscience and instructor at the Department of Psychiatry at the University of Pittsburgh. She received a doctoral degree in Neuroscience from the University of Pittsburgh in 2002 in the laboratories of Dr. Alan Sved and Dr. Pat Card, working on stress and central autonomic control. She did her postdoctoral studies at Harvard Medical School in the laboratory of Dr. Clif Saper, where she was a trainee in the Sleep Medicine Division and later an instructor in the Department of Neurology. Her research interest focuses on the characterization of brain circuitry activated in sleep disorders associated with stress (insomnia, PTSD) and dysregulation of the stress system (depression) using rodent models.

**Thien Thanh Dang-Vu, M.D., Ph.D.**

Born in Saigon, Thien Thanh Dang-Vu received his MD degree from the University of Liege in 2004. He then worked as an FNRS (Belgian national funds for scientific research) researcher at the Cyclotron Research Centre (University of Liege) under the supervision of Dr Pierre Maquet, as part of his doctorate in biomedical and pharmaceutical sciences (PhD), which he received in 2008. Simultaneously, he specialized in neurology in the Department of Neurology in Liege University Hospital.

His research has focused on studying the mechanisms of sleep using neuroimaging methods, including functional Magnetic Resonance Imaging (fMRI). In particular, he explores how the oscillations of sleep influence cerebral activity, the perception of the external environment and memorisation of information. He is also interested in sleep medicine and the use of neuroimaging in this context. As part of his clinical and scientific work, he has carried out several internships abroad, including at the University of Montreal and the Pitié-Salpêtrière Hospital in Paris. He has been awarded several scientific prizes, notably by the European Sleep Research Society (ESRS) and the Belgian Association for Sleep Research and Sleep Medicine (BASS).
SPECIAL RECOGNITION AWARD

The Sleep Research Society presented the Special Recognition Award for outstanding and continued commitment and support of sleep research.

Andrew A. Monjan, Ph.D. M.P.H.

Dr. Andrew A. Monjan is the former Chief of the Neurobiology of Aging Branch of the Division of Neuroscience within the National Institute on Aging. Prior to his retirement, Dr. Monjan’s duties included the development and monitoring of research on brain-behavior interactions in the aging process and their underlying cellular and molecular processes. Sleep research is an important priority within this program. Dr. Monjan served as the Executive Secretary of the National Commission on Sleep Disorders Research from 1990 to 1992. He also has worked with NASA on several joint conferences and initiatives, including STS-90 (Neurolab) and STS-95.

Dr. Monjan received his B.S. in Psychology from the Rensselaer Polytechnic Institute in 1960 and a Ph.D. in Psychology from the University of Rochester in 1965. He spent a further two years at the University of Rochester on a postdoctoral appointment within the Center for Brain Research studying visual neurophysiology. He has held academic appointments in the departments of Psychology and of Physiology at the University of Western Ontario (1966-69) and in the department of Epidemiology at the Johns Hopkins University School of Hygiene and Public Health (1971-83) following his receipt of an M.P.H. from that institution in 1970. His research interests varied from sensory neurophysiology to neuroimmunopathology to psychoneuroimmunology. In 1983, he joined the National Cancer Institute at the National Institutes of Health to help develop an extramural research program on the epidemiology of AIDS. Drawn by the challenges of health science administration, he joined the National Institute on Aging in 1985 to work on developing programs to help understand the aging process.

THE SLEEP RESEARCH SOCIETY FOUNDATION IS PLEASED TO PRESENT TWO GRANT OPPORTUNITIES FOR 2010.

The J. Christian Gillin, M.D. Research Grant is intended to support beginning investigators in sleep research for the purpose of gathering pilot data to be used for future grant applications. The grant is intended for young investigators who do not already have substantial independent research funding. These one-year grants will be funded up to $20,000.

The Elliot D. Weitzman, M.D. Research Grant is intended for researchers to gather additional pilot data for NIH or other federal grants that are scored but not funded. Applications are encouraged from investigators whose federal grant applications were not funded due to insufficient preliminary data. This one-year grant will be funded up to $20,000.

For additional information regarding these grants, including application information, please visit the Sleep Research Society Foundation Web site at www.sleepresearchsociety.org/foundation.
Editor: Congratulations on winning the Sleep Research Society Distinguished Scientist Award this year. What does winning this award mean to you?

Barbara E. Jones, Ph.D.: I am greatly honored by this award which communicates the regard of my peers for my life’s work. I also very much appreciate recognition of the work performed by many individuals in my laboratory and outside, to whom I am so indebted.

Editor: You have made so many seminal contributions to our basic understanding of sleep and wake. In your mind, what scientific achievements in your career stand out for you?

BEJ: I appreciate your appraisal of my contributions to the field. I consider my work as proceeding in an incremental fashion over many years now as I have asked basic questions and obtained, sometimes positive sometimes negative, answers in the investigation of the role and importance of particular systems in generating or regulating sleep-wake states. I began my research in documenting the structure and importance of catecholaminergic and particularly noradrenergic neurons in maintaining wakefulness, preceded with illuminating the role of cholinergic brainstem and then basal forebrain neurons in waking and paradoxical sleep and continued with defining the contributions of GABAergic and glutamatergic neurons through the reticular formation and basal forebrain. Most recently, I also revealed the activities of orexin and MCH neurons in relation to sleep-wake states. I, in each case, should be, since I began my research with my professors and continued through my life with my students, associates and colleagues.

Editor: Who were some of the researchers you admired during your early career? Who in particular influenced your career along the way?

BEJ: I had the great fortune to be able to work with Michel Jouvet in Lyon as a young graduate student and performed my thesis research in his laboratory. Through him, I learned an approach of integrative systems physiology as it applies to sleep-wake mechanisms. Highly rational and imbued with the scientific method, yet also highly inventive and creative, Jouvet served as a guide and inspiration to me as a young student and subsequently young researcher. Through his imaginative approach, he communicated the mystery of sleep and dreaming and represented the scientist’s search for its secrets as a life’s quest, full of passion. I also learned a rigorous and superlative approach to neuroscience research center based upon the interaction of basic and clinical scientists. The intimate atmosphere of mutual support and collaboration at the MNI was a very positive environment for me to develop my laboratory and research. Across Canada, research is conducted upon a smaller scale than in the United States and I have found quite suitable to my own style. On the other hand, most scientists are concerned that the current level of funding for basic research in Canada is low and needs to be increased for Canadian scientists to remain competitive.

Editor: In addition to your scientific accomplishments, how much opportunity do you get to mentor the next generation of sleep scientists? How have those experiences been for you?

Editor: What do you think should be some of the research priorities for basic sleep and circadian scientists over the next 5-10 years?

BEJ: We are in both a highly exciting and highly complex period of research in neuroscience as molecular biology has opened so many possibilities. Indeed, one aspect of this phase is a wide open investigation of new, unimagined factors involved in sleep-wake regulation. Discovery of orexin/hypocretin revealed the potential for these investigative scanning approaches looking for new peptides and genes that might be critically involved in controlling sleep-wake cycles. In this regard, a focus upon mechanisms of ultradian, not circadian, rhythms will be important. Taking the investigation to the cellular level in examining what must be a fundamental homeostatic regulation of activity with metabolism underlying the sleep-wake cycle will be key before understanding these principles at a systems level.

Editor: You have spent most of your research career in Canada. Can you talk about some of the differences between a research career in Canada and the United States? How favorable is the scientific environment these days for Canadian sleep scientists?

BEJ: I was drawn to Montreal because of my training and living in France, which I so enjoyed, and was able to establish my research career at McGill University in Montreal, which is an English university in a majority French city and province. I was also fortunate to join the Montreal Neurological Institute (MNI), an internationally renowned neuroscience research center based upon the interaction of basic and clinical scientists. The intimate atmosphere of mutual support and collaboration at the MNI was a very positive environment for me to develop my laboratory and research. Across Canada, research is conducted upon a smaller scale than in the United States with smaller grants and smaller individual laboratories, a system which I have found quite suitable to my own style. On the other hand, most scientists are concerned that the current level of funding for basic research in Canada is low and needs to be increased for Canadian scientists to remain competitive.

Editor: In your mind, what scientific achievements in your career stand out for you?
BEJ: One of the great pleasures in research is exploring new projects with new students. I have worked very closely with a small number of students at any one time through my career. I enjoy interacting in the development of a new project exploring new questions with new techniques while simultaneously introducing the new student to the rapidly expanding fields of neuroscience and sleep research.

Editor: What kind of guidance can you give to young basic sleep scientists? In your view, what are the keys to a successful career in research?

BEJ: Curiosity and wonder of learning and discovering new things. Always asking questions and seeking clear answers while maintaining the confidence that we will continue to understand a bit more each day and maybe even the most important secrets of the sleep-waking cycle some day.

APSS 2009 Recap: Beyond NIH: Diversifying Your Research Funding Sources

At SLEEP 2009, the Sleep Research Society in conjunction with the APSS Program Committee initiated a new Grantsmanship/Research Opportunities track. One of the presentations in this track, Co-Chaired by Terri Weaver, PhD, RN, FAAN, Professor and Chair, Biobehavioral and Health Sciences Division, University of Pennsylvania and James Walsh, PhD, Executive Director and Senior Scientist, Sleep Medicine and Research Center at St. Luke’s Hospital, was devoted to exploring funding sources beyond the National Institutes of Health.

Dr. Weaver informed the standing room only audience about the funding structure at the American Lung Association, which has an interest in respiratory-related sleep issues such as obstructive sleep apnea. As detailed on the website (http://www.lungusa.org/site/c.dvLUK900E/b.486859/k.6F8D/Awards_and_Grants_Program.htm), the Career Investigator Award is designed for mid-career scientists, while seed monies are provided through the Biomedical Research Grant, Clinical Patient Care Research Grant, and Social-Behavioral Research Grant. Trainees can submit proposals for the Senior Research Training Fellowship and there is also a Lung Health Research Dissertation grant. These grants along with several grants aligned with other organizations would be an excellent opportunity to explore how pulmonary disease and altered breathing patterns affect sleep and whether sleep deprivation alters outcomes in chronic pulmonary disease.

Dr. Charles Amlaner, Vice President for Research and Dean of the Graduate College at Kennesaw State University, gave a wonderful overview of funding available through the National Science Foundation. He described funding possibilities for both pre- and post-doctoral applicants. Program areas include biological sciences, particularly for instrument development, integrative activities for the development of research infrastructure, and social, behavioral, and economic sciences. Further information can be found at: http://www.nsf.gov/funding/.

Although the Centers for Disease Control and Prevention does not provide funding for sleep research, Janet Croft, PhD, Epidemiologist, CDCP, stated that utilization of several of their large data bases, such as the Health Risks in the United States Behavioral Risk Factor Surveillance System (BREFFS), was a great resource for secondary data analyses and pilot data. The BREFFS contains several sleep questions as well as other health information. There is also a page within the Chronic Disease Division dedicated to sleep disorders: http://www.cdc.gov/sleep/.

Max Hirshkowitz, PhD, Associate Professor of Psychiatry, Baylor College of Medicine, described the funding opportunities within the Veterans Administration. There are several mechanisms of support for scientists working in the VA system. Additionally, the VA Medical Centers, with their electronic medical record, is an excellent network for multisite studies.

Finally, David Dinges, PhD, Professor, Chair, Division of Sleep and Chronobiology, Department of Psychiatry, Director, Unit for Experimental Psychiatry, University of Pennsylvania School of Medicine, described potential sources of support through the Department of Defense (DOD). Dr. Dinges has been successfully funded by the DOD for several projects and emphasized the importance of speaking with the DOD before submitting an application. Information about their funding can be found at: http://researchfunding.duke.edu/detail.asp?OppID=1547.

Terri Weaver, PhD, RN, FAAN
University of Pennsylvania
The 14th Annual Trainee Day Symposium series held at SLEEP 2009 was once again a great success and extremely well attended, with over 300 trainees registered for the event. The series offered trainees an opportunity to network with peers and leaders in the field of sleep research, as well as attend scientific and career development sessions.

The day began with an exceptional Keynote address by Dr. Derk-Jan Dijk entitled “Training for Translation: From Sleep Models to Sleep Genes and Society.” This inspiring address set the stage for the rest of the symposia.

Trainees then attended a series of small workshops with topics ranging from career advice to the application of genetics in sleep research. Forty-eight of the field’s leaders volunteered their time to teach and interact with the trainees.

New to this year’s symposia were two, half-day workshops on grant mechanisms entitled, “Getting your NIH Postdoctoral Grant Funded: F-31/F-32 Mechanisms” presented by Dr. Alan Pack and multiple other faculty members and “Getting your NIH Career Development Award Funded: K-award Mechanism” presented by Dr. Jennifer Martin. These workshops were well attended and received excellent feedback by the trainees. Trainees particularly liked breaking into small groups during lunch to have discussions about their own project aims, grant writing, and future career goals. A special thank you to NIH personnel who volunteered their time to speak to the trainees about NIH infrastructure, funding, and other useful topics.

As with previous years, trainees were given the opportunity to present their research to their peers and research leaders who were moderating the session. Trainees had the opportunity to ask questions and receive feedback on presentation content, format, and style.

Trainee Day ended with the career development fair at which trainees mingled with lab groups and heads of labs and were able seek out potential job and training opportunities. Approximately 25 labs were represented at the career development fair, making for another very successful event.

The feedback from trainees regarding all aspects of Trainee Day was a resounding sense of positive engagement, highlighting how enjoyable and beneficial the day’s experiences were for sleep trainees. From my own experience, I can say I have not attended another professional meeting that has met and exceeded all my expectations for welcoming new trainees in the field and encouraging their growth by investing so much in their training.

**Acknowledgements**

The Trainee Education Advisory Committee (TEAC) is instrumental in the planning of the Trainee Day Symposium Series. Thank you to the members of TEAC: Jennifer Martin, Ph.D. (chair), Phillip Gehrman, Ph.D. (vice-chair), Jason Ellis, Ph.D., Ronald Harper, Ph.D., Lisa Meltzer, Ph.D., Allan Pack, Ph.D., MBChB, Amy Wolfson, Ph.D., Ronald Harper, Ph.D., Eliza Van Reen, Ph.D. (Trainee Member-at-Large), and Janet Mullington, Ph.D. (Board Liaison). Furthermore, thank you to Nick Cekosh, Annie Walker-Bright, and Anna Quintanilla for their administrative support. Thank you to the members of the Trainee Day subcommittee who helped select the topics and speakers for the symposia. The trainee day subcommittee was led by Eliza Van Reen, Ph.D. and other members included: Michelle Rissling, Leisha Smith, Maria Gardani, Leila Tarokh, Tyish Hall, Rebecca Bernert, Jennifer Accardo, Allison Brager, and Megan Ruiter.

Sara Nowakowski, M.S.
Trainee Member-At-Large
Clifford B. Saper received his M.D. and Ph.D. degrees and performed 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 where he served from 1981-1985 as Assistant and then Associate Professor of Neurology and Anatomy and Neurobiology. He then moved to the University of Chicago, where from 1985-1992 he was an Associate Professor, then William D. Mabie Professor of Physiology and Neurology, and Chairman of the Committee on Neurobiology. In 1992, he moved to his present position at Harvard Medical School, where he is the James Jackson Putnam Professor of Neurology and Neuroscience and Chairman of the Harvard Department of Neurology at Beth Israel Deaconess Medical Center. Since 1994, Dr. Saper has also served as the Editor-in-chief of the *Journal of Comparative Neurology*, the oldest basic neuroscience journal in the English language. He also serves on the Editorial Boards of *Neurology* and *Physiological Genomics*. Dr. Saper has received a Javits Neuroscience Investigator Award from the National Institutes of Health, and was named one of the 100 most frequently cited neuroscientists by the Institute for Scientific Information. He has served as Vice President and Councillor of the American Neurological Association, and has served on the Publications Committee and has chaired the Program Committee of both that organization and the Society for Neuroscience. Dr. Saper 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 (London). Dr. Saper’s research has explored circuitry of the brain that controls basic functions such as wake-sleep cycles, brain responses to immune stimulation, and the brain’s control of the cardiovascular and respiratory systems. Dr. Saper has been a member of the SRS Board of Directors since 2006.

James K. Walsh earned his undergraduate degree from Lewis University (1972) in Romeoville, Illinois, and Masters (1975) and Doctoral (1978) degrees in experimental psychology from St. Louis University. He served as a visiting assistant professor of psychology at the Illinois Institute of Technology in 1978-1979, and in 1979 assumed the position of Assistant Director of the Sleep Disorders Center at the University of Cincinnati.

In 1981 he founded the Sleep Disorders and Research Center at Deaconess Hospital in St. Louis, where he served as Director until 1993. Dr. Walsh founded the Sleep Medicine and Research Center affiliated with St. John’s Mercy Medical Center and St. Luke’s Hospital in St. Louis in December, 1993, and currently holds the position of Executive Director and Senior Scientist. Additionally, Dr. Walsh holds the appointments of Clinical Professor in the Department of Psychiatry and Adjunct Professor of Psychology at St. Louis University.

Since 1975, Dr. Walsh has published over 170 scientific articles, book chapters and monographs dealing with sleep and its disorders. He co-authored the text *Sleep: A Scientific Perspective*. Currently, his primary research interests include the function of slow wave sleep, pharmacological treatment of insomnia and sleepiness, consequences of insomnia, and the relation of sleep loss to behavior and cognitive function.

As a member of the American Sleep Disorders Association’s (now the American Academy of Sleep Medicine) Board of Directors from 1982-1993, he has been a significant contributor to the development of the field of sleep medicine and research. Dr. Walsh held the ASDA offices of Secretary/Treasurer in 1989-1991, President in 1991-1992, and Chair of the Committee on Government Affairs and Public Policy from 1993-1996. He has been an advocate for the sleep field at local and national levels including presentation of testimony on numerous occasions to US Congressional Committees about the significance of sleep disorders in America. He has served as Chairman of the Board of the National Sleep Foundation from 2001-2005 and has been a member of that organization’s Board of Directors since 1998. In 2005 he was elected to the Board of Directors of the Sleep Research Society and he continues in that capacity currently. Other professional activities include serving on the Editorial Board of the journal *Sleep* as a reviewer for more than twenty professional journals, and as a special advisor to the National Commission of Sleep Disorders Research from 1988-1992. From 1994-1997 he was a member of the Sleep Disorders Research Advisory Board for the National Center for Sleep Disorders Research of the National Institute of Health, and was the Chair of the Board’s Education Subcommittee during that time.

Awards received include the ASDA’s 1995 Nathaniel Kleitman Award for Distinguished Service, the Lewis University Alumni Achievement Award in Psychology in 1994, the ASDA’s Senator Mark Hatfield Public Policy Award in 1998, and the 2006 and Lifetime Achievement Award from the National Sleep Foundation.
SRS BULLETIN

DIRECTORS AT LARGE

Sean P.A. Drummond, PhD, has been part of the sleep research community since he was an undergraduate at the University of Arizona and volunteered in the Sleep Research Laboratory there. He completed his PhD in Clinical Psychology in the SDSU-UCSD Joint Doctoral Program under the mentorship of Chris Gillin. Throughout his career, he has had the pleasure of working with and learning from several outstanding mentors, including Chris Gillin, Michael Perlis, Richard Bootzin, and Sonia Ancoli-Israel. Currently, Dr. Drummond is on faculty in the Department of Psychiatry at UCSD and the Psychology Service in the VA San Diego Healthcare System. His primary program of research examines the effects of various forms of experimental and clinical sleep deprivation on cognition and brain function. Dr. Drummond’s research has been funded by NIH, the Department of Defense, the National Science Foundation, and other organizations. Clinically, he runs the Behavioral Sleep Medicine Program and the Cognitive Behavioral Interventions Program (a mood disorders clinic) within the VA. Within those clinics, he trains graduate students, psychology interns, and fellows. He is also the Co-Director of the UCSD-VA Psychology Internship Training Program. Finally, Dr. Drummond has been actively involved in serving the SRS since he 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 every Trainee Symposia Series held 1996-2007; c) the Trainee Member-at-Large to the SRS Board, 1997; d) the Committee for Animal Research Ethics, 1999-2003; e) TEAC, 2003-2007, including the last 3 years as committee Chair; f) the Trainee Organizing Committee for Worldsleep07; and g) the SRS 50th Anniversary Task Force, 2008-present.

Gina R. Poe, Ph.D., serves on the graduate faculty in the University of Michigan’s Neuroscience Interdepartmental program. She is an Associate Professor in the Department of Anesthesiology and the Department of Molecular and Integrative Physiology at the University of Michigan. Dr. Poe has served the last 3 years as the Basic Sleep section head for the SRS and was the Trainee representative to the SRS Board of Directors in 1991. She has recently served the SRS on the Presidential Task Force (2007-8) and was a member of the Sleep Disorders Research Advisory Board of the National Council for Sleep and Sleep Disorders Research at the National Institutes of Health (2004-6) and served on the Vision 20/20 Task Force for the future of the SRS (1998-2000). She now serves the NIH as a regular study section member (IFCN-III, Learning and Memory, 2008-2011) and is a member of the Society for Neuroscience’s Committee on Women in Neuroscience (2008–present). She received a doctoral degree in Neuroscience from the University of California at Los Angeles in 1995 and did her postdoctoral studies at the University of Arizona in the laboratory of Carol Barnes, Neural Systems, Memory and Aging.

Gina Poe holds R01 grants from the NIH to study the physiological events that serve learning and memory consolidation during sleep.

David Rye M.D., Ph.D., is Professor of Neurology within the Emory University School of Medicine and Director of Emory Healthcare’s Program in Sleep. Dr. Rye received his doctorates in neurobiology and medicine from the University of Chicago’s Pritzker School of Medicine. Here he trained in Neurology and was Chief Resident 1991-1992. Since moving to Emory University in 1992 he has helped establish and build a clinical and research program in Sleep Medicine with an emphasis on movement disorders in sleep including Restless Legs Syndrome, Parkinson’s disease, and the role of dopamine in normal and pathological wake/sleep states. His work in rodents, non-human primates, and humans spans a spectrum from systems neurobiology to animal models of disease and human genetics. He is board certified in both Sleep Medicine and Neurology, recipient of several federal and non-federal grant awards, and has been awarded several institutional and national awards for his contributions. He is past chair of the Restless Legs Syndrome Foundation’s Medical Advisory Board, and has served on the editorial boards of Sleep Medicine, Sleep Medicine Reviews, Experimental Neurology, Neurology, and is a Deputy Editor for Sleep. He has been a member of the SRS for 3 years.

TRAINEE MEMBER-AT-LARGE

Sara Nowakowski is a Clinical Psychology Intern specializing in Behavioral Medicine at The Warren Alpert Medical School of Brown University and is a student in the Joint Doctoral Program in Clinical Psychology at San Diego State University and the University of California at San Diego (UCSD) under the mentorship of Dr. Barbara L. Parry. Sara is presently working with Dr. Mary Carskadon examining sleep, mood, and genetics in adolescence transitioning into their first year of college. Sara’s research interests focus on sleep, mood disorders, and cognitive functioning among women. She has authored a number of abstracts featured in the journal SLEEP, authored and co-authored several peer reviewed manuscripts and book chapters, taught several psychology courses and received numerous awards for her work. Sara has been an enthusiastic member of the Sleep Research Society (SRS) for the past eight years, attending seven trainee days and APSS conferences. Sara is presently serving as SRS Trainee Member-At-Large and has served as a member of the SRS Trainee Subcommittee to Trainee Education and Advisory Committee from 2007-08, and as a trainee member on the SRS Communications Committee from 2006-08.

More than 25 years ago, basic principles of how sleep timing and duration are regulated in humans were captured in the seminal two-process model of sleep regulation. The regulatory processes featured in this model are 1) a homeostatic process, which keeps track of time spent awake and time spent asleep, and 2) a circadian process, which keeps track of time of day. It has been shown that these processes predict waking neurobehavioral function under conditions of total sleep deprivation. However, recent sleep dose-response studies revealed that the two-process model does not accurately capture the cumulative performance impairments observed over days of chronic sleep restriction. This suggests the existence of an additional process, modulating the homeostatic process over the long term (days to weeks). An attempt was made to implement such a modulating process in the framework of the two-process model, but the approach taken initially was not successful in simultaneously predicting performance during total sleep deprivation and across days of sleep restriction. McCauley and colleagues in the Sleep and Performance Research Center at Washington State University Spokane extended the effort, and discovered a modeling solution to this problem that may have some far-reaching implications for understanding the effects of sleep loss on neurobehavioral functioning.

A set of differential equations for the homeostatic process was formulated, representing two underlying biological subprocesses interacting dynamically with each other (and with the circadian process) during wakefulness and during sleep. One subprocess is characterized by time constants in the order of hours, the other by time constants in the order of days, and their reciprocal interactions involve positive feedback. The neurobiological underpinnings are not fully known, and many systems and substrates are likely to be involved. One hypothesis involves adenosinergic mechanisms: the subprocess with the shorter time constants would reflect changes in (extracellular) concentrations of adenosine, and the subprocess with the longer time constants would reflect up- and down-regulation of adenosine receptors. Upregulation of adenosine receptors occurs in response to sleep loss, and in turn increases sensitivity to sleep loss. It is precisely this kind of system that the model of McCauley and colleagues suggests causes the build-up of neurobehavioral impairment across days of sleep restriction. Such a mechanism implies that, besides trait vulnerability to sleep deprivation, a person’s sensitivity to sleep loss is determined by his/her sleep history—as was recently demonstrated experimentally.

Analysis of the model’s dynamics as a function of sleep dose yielded a surprising finding: the two interacting homeostatic subprocesses showed fundamentally different overall behavior under conditions of total sleep deprivation and severe sleep restriction (less than 4 hours sleep per day) than under conditions of less or no sleep restriction. This so-called “bifurcation” effect provided an integrated prediction framework for the ostensibly different neurobehavioral effects of total sleep deprivation vs. chronic sleep restriction as observed in the laboratory. The bifurcation was confirmed by the data of the two major published dose-response studies of sustained sleep restriction: for restriction to 8 hours or less, down to 4 hours, time in bed per day, performance deficits increased over days but eventually appeared to converge to an equilibrium state of stable, suboptimal performance; whereas for restriction to 3 or 0 hours time in bed per day performance deficits escalated rapidly and did not converge to an equilibrium state. See Fig. 1.

Assuming further validation efforts will be successful, the model of McCauley and colleagues makes a number of notable predictions. Simulations driven by the model show that one or two nights of recovery sleep should suffice for neurobehavioral recuperation after a period of acute total sleep deprivation, but several more recovery nights may be needed to overcome the cumulative effects of sustained sleep restriction. Moreover, although “sleeping in” to...
overcome the effects of prior sleep loss would accelerate recuperation, this strategy is predicted to be neither necessary nor sufficient to restore performance to baseline levels. The model also predicts that an extended recovery night after a period of chronic sleep loss should result in more performance improvement the greater the amount of prior sleep loss. However, if the pattern of sleep restriction is repeated after the recovery night, then the performance improvement will dissipate quickly—after just a few days it would seem as if the recovery night never took place. Preliminary data from a laboratory study at the University of Pennsylvania appear to support this prediction. The hours of service implications in extended work environments could be profound, as is illustrated for a hypothetical medical residency program in Fig. 2.

Figure 2—Illustration of model predictions for daytime averages (09:00–19:00) of performance lapses (reaction times > 500 ms) on a psychomotor vigilance test (PVT), expressed relative to baseline, across three different 4-week rotation schedules in a hypothetical medical residency program. The House Staff schedule (circles) involves 5 hours time for sleep from Monday through Saturday and 8 hours time for sleep on Sunday. The Elective 1 schedule (diamonds) involves no time for sleep every fourth day, 10 hours time for (recovery) sleep on the day thereafter, and 5 hours time for sleep on the remaining week days and 8 hours time for sleep on the remaining weekend days. The Elective 2 schedule (squares) involves 4 hours time for sleep from Monday through Friday and 9 hours time for sleep during the weekend. All three schedules have an average of 5.43 hours of time for sleep per day, and are predicted to result in cumulative performance impairment due to the sustained sleep restriction across the 4-week rotation (despite intermittent performance improvement following the days with the longer sleep periods). However, the grand average daytime level of performance impairment is predicted to be noticeably greater for the Elective 1 schedule, making this hypothetical schedule the least efficient in terms of performance relative to time invested in sleep.

A schedule with sustained sleep restriction to, say, 4 hours time in bed daily produces considerable cumulative performance deficits, as shown in Fig. 1. Yet, if such a schedule is followed by one or more days with more modest sleep restriction, then the prediction is not that there will be more modest additional degradation of performance, but rather that some improvement will occur. Although subjective experience might support this prediction, it is counterintuitive from a cumulative “sleep debt” perspective. Indeed, the new model does not substantiate a “sleep debt” account of the neurobehavioral consequences of sleep loss. Instead, the model dynamics imply that the effects of sleep restriction and sleep extension on performance should be interpreted in terms of physiologic balance shifts that depend on the prevailing ratio of total wake time to total sleep time. In this view, interestingly, the seemingly irresolvable question of “which components of sleep are most important for recuperation” is, at least in a practical sense, largely irrelevant.

References

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15. Peter McCauley M.A., Mark E. McCauley, Hans PA. Van Dongen Ph.D. Sleep and Performance Research Center, Washington State University Spokane
A Grander Scale for Sleep Medicine Research: Promoting Sleep Research Networks

Over the past decade, there has been tremendous progress in understanding the pathophysiology of sleep homeostasis and of sleep and circadian rhythm disorders. As has been accomplished for other complex, chronic diseases such as diabetes and atherosclerosis, the availability of high through-put technologies now also provides the means to discover genetic variants for sleep disorders, sleep homeostasis, chronotype, sleep patterns, circadian rhythms, and individual susceptibility to inadequate sleep and to circadian misalignment. Recent epidemiological studies also have highlighted the high prevalence and co-morbidities of many sleep disorders, and clinical laboratories have expanded to accommodate large increases in diagnostic and therapeutic services. However, unlike many other conditions, few rigorously controlled and well-powered clinical trials have been conducted that evaluate the role of alternative approaches for preventing, managing, or treating sleep disorders, resulting in large uncertainties in disease management. Studies of the human genetics of sleep disorders as well as definitive clinical trials both require large sample sizes and multi-disciplinary expertise that often necessitate cross-center collaboration. For advances in sleep medicine to keep pace with those in other scientific disciplines, as well as to identify the impact of sleep interventions on sleep disorder-related morbidities, demands a shift in sleep research from relatively small, single site investigations to large-scale research with coordinated data collection and analyses across many clinical sites and research cores. In response to these challenges, four new complementary initiatives have been launched: 1) Sleep Research Society-sponsored Task Forces on Genetics and on Academic Sleep Centers; 2) Establishment of a national Clinical and Translational Science Award (CTSA) Sleep Research Network; 3) Establishment of the Academic Alliance for Sleep Research (AASR); 4) National Center for Research Resources-supported sleep informatics development.

Sleep Research Society (SRS) Task Forces. In 2007, SRS President Eric Nofzinger, MD, convened two Presidential Task Forces of relevance to the development of sleep research networks.

The Task Force on Academic Sleep Centers, chaired by Ruth Benca, MD, PhD, aimed to better define the structures of current academic sleep centers. As an initial step, questionnaires were sent to the sleep centers associated with medical schools that have been awarded CTSA. Over 30 questionnaires were returned, and the data are being analyzed regarding the varying structures of academic sleep centers and how many of them might meet the criteria for Type III Academic Sleep Centers as defined in the IOM report on sleep medicine.

The Genetics Task Force, chaired by Allan Pack, PhD, MBChB, was charged with recommending approaches for developing a “sleep gene chip” for standardizing phenotype definitions and for coordinating sleep research data needed for gene discovery. The vision that the Task Force adopted was to establish a National Biobank for study of the genetics of sleep and its disorders. This Biobank is modeled on the Autism Genetic Resource Exchange (www.agre.org). If implemented, it will provide investigators access to data from well-phenotyped subjects and patients, together with DNA for their investigations. This will permit investigators to use different genotyping strategies, an area that is rapidly evolving. Moreover, it will facilitate investigators with expertise in human genetic studies to become involved in the field of sleep and its disorders. To make the vision a reality, the Task Force identified the following needs:

1. Obtain large cohorts of well-characterized patients with different sleep disorders based on the definitions and phenotyping strategies.
2. Obtain large cohorts of subjects at the extremes of novel variants in sleep—timing of sleep, sleep duration, response to sleep deprivation, etc.
3. Establish a national biobank of DNA from all these subjects and consider establishing cell lines. This biobank would be centrally located, e.g., under the auspices of NIH.
4. Establish a complementary biobank of serum and plasma samples for these subjects for future biomarker studies.
5. Establish a distributed or federated information system for clinical information and other data that will be available to investigators (i.e., clinical information being held locally but being able to be accessed centrally).
6. Establishing a steering committee to oversee the effort with members from both the sleep research community and the human genetics research community.

The Sleep Research Network. In the spirit of promoting cross-institutional and transdisciplinary research, a CTSA-sponsored initiative led to the establishment of a national Sleep Research Network. The University of Pittsburgh Sleep Medicine Institute, under the direction of David J. Kupfer, MD, serves as the secretariat for the network, responsible for coordinating and implementing its administrative and logistical tasks. Strategic planning and oversight are by a Steering Committee elected by CTSA Principal Investigators (Allan Pack PhD, MDChB, (Chair); Ruth Benca, MD, PhD, Charles A Czeisler, MD, PhD, Emmanuel Mignot, MD, PhD, Susan Redline, MD, MPH, Viren Somers, MD, PhD, and Patrick Strollo, MD.) Each CTSA Principal Investigator was asked to nominate a representative to attend national meetings held in June 2008 and March 2009. 28 individuals from 38 CTSA institutions participated in these meetings which: a) identified scientific priorities focusing on sleep and sleep disorders; b) established working groups to actively develop projects targeting those priority areas; c) shared information about the resources and capacity of each of the participating organizations to take part in these projects; and d) discussed multi-site training opportunities in sleep medicine. The four working groups are: Genetics and Biomarkers (Co-Chairs: E Mignot and A Pack); Clinical Trials and Outcomes (Co-Chairs: R Benca and S Redline); Research to inform Public Policy (Co-Chairs: C Czeisler and P Strollo); and Pediatrics (chair to be named). Network goals include:
1. To advance our clinical and translational research through multi-institutional studies.
2. To be a vehicle for obtaining funding to support these studies.
3. To develop relevant cores to support these studies.
4. To give institutions with CTSA’s, but not a strong academic research program in sleep, the opportunity to develop and enhance their sleep research profile.
5. To provide a vehicle for training the next generation of translational researchers in sleep, including at institutions with currently limited intellectual resources in sleep research.

On Oct 29-30, a third Sleep Research Network Meeting will be held in Bethesda MD. A key goal of this meeting will be for each of the four working groups to develop plans for pilot projects to demonstrate the feasibility and importance of multi-center collaboration for advancing sleep research. Similar to prior meetings, each CTSA Principal Investigator will be asked to nominate one institutional representative to the meeting. Additional individuals may participate, according to room availability, and at their own expense. Individuals interested in participating in the next meeting or wanting to learn more about the Sleep Research Network should contact: Jeanie Knox-Houtsinger Administrator, Sleep Research Network at Western Psychiatric Institute and Clinic 3811 O’Hara Street, Suite E279 Pittsburgh, PA 15213 (USA) Telephone: 412-246-6784 FAX: 412-246-6780 Email: knoxjv@upmc.edu.

Additional details about the upcoming meeting in Bethesda can be accessed at www.sleep.pitt.edu until the Sleep Research Network is operational.

Academic Alliance for Sleep Research (AASR) - The AASR is a cooperative effort of four academic sleep programs that were selected by Respiroinc Inc. to receive start-up funding to support multi-institutional research to advance sleep medicine. The four AASR institutions are:
- Division of Sleep Medicine, Harvard Medical School
- Stanford Center for Sleep Sciences, Stanford University
- Penn Sleep, University of Pennsylvania
- Center for Sleep Medicine and Sleep Research, University of Wisconsin

The steering committee includes Drs. Ruth Benca, Charles Czeisler, Emmanuel Mignot, Allan Pack, and James Walsh. The goals of AASR are:
- To develop the necessary research infrastructure, establish cooperative research protocols, and collect pilot data to obtain sustained support from NIH or other agencies, and
- To conduct multi-institutional sleep research that will advance the practice of sleep medicine to include preventative and personalized approaches.

Start-up funding, received early in 2009, is viewed as an initial investment toward these goals and AASR plans to insure that there is a return on this initial investment. AASR activities to date have been conducted by task forces with representatives from all four sleep programs. Some of the ongoing activities include: creation of an internet-accessible clinical evaluation questionnaire to be used in clinical sleep facilities affiliated with the four participating institutions. The common clinical information will produce database capabilities which allow local access to the AASR clinical databases and will facilitate phenotyping of patients across institutions. AASR also envisions internet-accessible instruments for patient management (e.g., sleep diaries, health outcomes). Work has begun on the development of procedures to establish a shared biobank and biosample registry for genetic and biomarker studies of sleep and its disorders. All four sleep programs have active local informatics projects and AASR is beginning to examine AASR-wide informatics needs. Finally, a number of cooperative grant applications are in progress or are in early stages of discussion.

Sleep Informatics Platform for Clinical and Translational Research - In response to the need for improved informatics tools to assist with cross-institutional data sharing, the National Center for Research Resources (NCRR) developed a pilot program and awarded three CTSA institutions and their collaborating partners contracts to develop novel informatics tools to support clinical and translational research. Case Western Reserve University, in collaboration with the University of Michigan, the University of Wisconsin (Madison) and Marshfield Clinic, were awarded a contract to develop “Physio-MIMI,” a web-based informatics platform specifically designed to meet the unique needs of the sleep researcher, including development of an initial ontology of sleep terms, and tools for: de-identifying complex physiological records for the purposes of data sharing, querying clinical and physiological data across multiple databases and across institutions, and assembling de-novo datasets of physiological records linked with clinical terms. Such work promises to provide improved standardization for defining sleep phenotypes, as well as flexible tools for incorporating distributed data models into sleep research. The open-source tools from this project are expected to be made publicly available by January 2010.

In summary, the integrated efforts of these programs promise to overcome many of the barriers sleep researchers have faced in coordinating the collection and collaborative analysis of high quality and well-defined data derived from potentially fertile clinical sources (including the many sleep laboratories) and research studies. The SRS has played an active role in supporting a dynamic dialogue among sleep researchers who have enthusiastically endorsed the need for coordinated clinical and translational sleep research data collection and for embarking on studies of a grander scale than in the past. In parallel, the support of the CTSA’s, NIH-NCRR, and industry in promoting cross-center collaboration, integration of modern informatics tools and work toward development of biobanks has provided an ideal environment for this latest maturational stage in sleep medicine research. However, the actual functionality of a Sleep Research Network is still only partially realized, and will require the continued hard work and active engagement of the entire sleep community, as well as NIH support, to blossom and produce the critically needed data to address the burning questions regarding disease etiology, susceptibility and management.

Susan Redline, Allan Pack, and James Walsh, for the Sleep Research Network and Academic Alliance for Sleep Research
FRANCIS S. COLLINS, MD, PHD NEW DIRECTOR OF NIH

Francis S. Collins, MD, PhD was officially sworn in as the 16th Director of the National Institutes of Health (NIH) on August 17, 2009. Dr. Collins, a physician-geneticist noted for his landmark discoveries of disease genes and his leadership of the Human Genome Project, served as Director of the National Human Genome Research Institute (NHGRI) at the National Institutes of Health from 1993-2008. This remarkable international project culminated in April 2003 with the completion of a finished sequence of the human DNA instruction book. In addition to his achievements as the NHGRI Director, Dr. Collins' own research laboratory has discovered a number of important genes, including those responsible for cystic fibrosis, neurofibromatosis, Huntington’s disease, a familial endocrine cancer syndrome, and most recently, genes for adult onset (type 2) diabetes and the gene that causes Hutchinson-Gilford progeria syndrome.

Dr. Collins received a B.S. in Chemistry from the University of Virginia, a Ph.D. in Physical Chemistry from Yale University, and an M.D. with Honors from the University of North Carolina. Prior to coming to NIH in 1993, he spent nine years on the faculty at the University of Michigan, where he was an investigator of the Howard Hughes Medical Institute. He has been elected to the Institute of Medicine and the National Academy of Sciences, and was awarded the Presidential Medal of Freedom in November 2007.

SLEEP 2010 LETTER OF INTENT TO SUBMIT A SESSION PROPOSAL

The APSS Program Committee requests early submission of a brief letter of intent to submit a postgraduate course, symposium, clinical workshop or discussion group proposal for the SLEEP 2010 24th Annual Meeting of the Associated Professional Sleep Societies, LLC. The letters of intent will be used by the Program Committee to identify gaps in the scientific program that need to be filled. The deadline to submit a letter of intent is Thursday, October 15, 2009.

The information required in each letter of intent includes:
(i) Session proposal type (half-day postgraduate course, full-day postgraduate course, symposium, clinical workshop or discussion group)
(ii) A suggested session title
(iii) A 2-3 sentence description of the session objectives
(iv) A list of potential speakers and the possible titles of their talks.

Note: potential speakers do not need to be contacted at this time.

A template for the letter of intent is available on the SLEEP 2010 Web site at www.sleepmeeting.org

The letter must be submitted via e-mail to Amber Josi, Meeting Planner, at ajosi@aasmnet.org ajosi@aasmnet.org by October 15, 2009. A final version of the session proposal must be submitted online via the SLEEP 2010 Web site by Tuesday, December 1, 2009.

SLEEP 2010 CALL FOR ABSTRACTS AND SESSION PROPOSALS NOW AVAILABLE ONLINE!

The APSS Program Committee invites you to become an integral part of SLEEP 2010 by submitting an abstract or coordinating and submitting a session proposal. This is your opportunity to ensure that the SLEEP 2010 program includes the latest educational content and scientific developments that are important to the fields of sleep medicine and sleep research. The Program Committee relies on your commitment and volunteer efforts to create a program that stimulates interest in the field from the seasoned professional to researchers and clinicians just entering the realm of sleep research and sleep medicine.

This unique meeting is only possible with the submission of high-quality session proposals and abstracts from individuals practicing in the fields of sleep research and sleep medicine. Please refer to the SLEEP 2010 Call for Abstracts and Session Proposals or visit the SLEEP 2010 Web site at www.sleepmeeting.org for details on abstract and session guidelines.

All abstracts and session proposals must be submitted online via the SLEEP 2010 submission site. The site will be live beginning October 30, 2009. The deadline to submit session proposals is Tuesday, December 1, 2009. The deadline to submit abstracts is Tuesday, December 15, 2009. Questions can be directed to the APSS Meeting Department at (708) 492-0930.

RECENT NIH FUNDING OPPORTUNITIES

a. Pilot Studies for Studying the Mechanisms of Improvement in Type 2 Diabetes and Cardiovascular Risk Factors or in Cardiovascular, Lung, or Sleep Diseases after Bariatric Surgery (RO1)

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Heart, Lung, and Blood Institute have announced a new research program (RO1) to determine the optimal research design and pilot test the feasibility and implementation of a randomized clinical trial that will ascertain the effects of bariatric surgery on type 2 diabetes and cardiovascular risk factors in people with type 2 diabetes or in cardiovascular, lung and sleep diseases in people. For more information please visit: http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-09-012.htm

b. Nutrition and Physical Activity Research to Promote Cardiovascular and Pulmonary Health

This FOA encourages Research Project Grant applications that propose research on the roles of nutrition and physical activity in the development, prevention, and management of cardiovascular diseases (CVD) or pulmonary diseases. In particular, the FOA aims to (1) improve knowledge of the contribution of diet and physical activity
to these conditions and how sleep influences these relationships, (2) increase the evidence base for refining public health recommendations and clinical guidelines regarding these lifestyle behaviors, and (3) develop and test strategies to improve the adoption of these recommendations.

This FOA will utilize the NIH research project R01 grant mechanism (PA-09-243: http://grants.nih.gov/grants/guide/pa-files/PA-09-243.htm) and runs in parallel with a FOA of identical scientific scope that encourages applications under the R21 grant mechanism (PA-09-244: http://grants.nih.gov/grants/guide/pa-files/PA-09-244.htm).


The Sleep Research Society is excited to announce the new, fully peer reviewed, SRS Basics of Sleep Guide, second edition is now available for purchase on the SRS website (http://www.sleepresearchsociety.org/Products.aspx).

The newly revised SRS Basics of Sleep Guide, Second Edition has been expanded in both scope and content, including the addition of 10 new chapters authored by international experts covering all fields of basic and applied sleep research. Each of the original Basics of Sleep Guide chapters has also been revised to reflect ‘state of the art’ knowledge. Many of the chapters now include ‘Sleep Pearls’ and chapters and figures have also been coordinated with the SRS Slide Sets (v1.1).

**New NIH Tool Makes Funding Data, Research Results and Products Searchable**

Comprehensive funding information for NIH grants and contracts is now available on the NIH Research Portfolio Online Reporting Tool (RePORT) thanks to a new, user-friendly system called the RePORT Expenditures and Results, or RePORTER. RePORTER combines NIH project databases and funding records, PubMed abstracts, full-text articles from PubMed Central, and information from the U.S. Patent and Trademark Office with a robust search engine, allowing users to locate descriptions and funding details on NIH-funded projects along with research results that cite the NIH support. RePORTER is the newest tool on the RePORT website, NIH’s comprehensive online repository of reports, data and analyses of research-related funding. RePORT provides a wealth of data on NIH’s research-related grant and contract funding, including general reports and statistics, funding by research, condition and disease categories, new data visualization tools, and more. Dynamic reports and geographic mapping tools offer unparalleled access to information on NIH’s Recovery Act grant funding on an individual project, state or national level. RePORT is available at RePORT.nih.gov. The project search tool, RePORTER, is available through the RePORT site or by going directly to ProjectRePORTER.nih.gov.

**Circadian Rhythms and Metabolic Disease Workshop**

The National Institute of Diabetes and Digestive and Kidney Diseases has announced a workshop on the link between circadian rhythms and human health and disease to be held April 12-13, 2010 at the North Marriott Conference Center in Bethesda, Maryland. A particular emphasis will be on the influence of both central and cellular clocks on the physiology of behavior and metabolism, specifically effects on overall energy balance and obesity.

For more information on this workshop please visit: http://www3.niddk.nih.gov/fund/other/circadian2010/index.htm

**Applications for Sleep Science Award Due November 2**

Be recognized for your efforts in sleep science; apply now for the Sleep Science Award, sponsored by the American Academy of Neurology (AAN). The award recognizes an individual who has made significant contributions to basic and/or clinical research in sleep.

The recipient will be recognized at the 62nd AAN Annual Meeting in Toronto, April 10 through 17, 2010, and will receive a certificate of recognition and $1,500 prize, complimentary registration for the Annual Meeting, and recognition at the Awards Luncheon. To be eligible, you must have made significant contributions to clinical or basic research in the neurology or neuroscience of sleep. Young and middle level investigators who are MDs or PhDs are eligible to apply.

Complete award details and application are available at www.aan.com/view/sleepaward. Award application deadline is November 2. A variety of other scientific and nonscientific awards are also available, for more information, visit www.aan.com/2010awards.
On May 5, 2009, Drs. Clif Saper, James Walsh, Michael Vitiello, and Terri Weaver descended on Washington for two days of research advocacy. Developed by the Research Advocacy Board Subcommittee and coordinated by SRS staff member Nicholas Cekosh and Executive Director Jerry Barrett, the team spent the first day on Capitol Hill meeting with nearly 20 members of Congress or their staff. The objective of this day was to acquaint members of Congress with the Sleep Research Society and the significant contributions made by the knowledge generated through sleep research. Handouts that were provided demonstrated the critical research being conducted by SRS members. Also stressed was the importance of continued funding for government agencies, including the National Institutes of Health. We thanked them for the bolus to NIH funding provided by the American Recovery and Reinvestment Act and stressed the importance of significantly funding NIH beyond that initiative. A concern that we expressed was the boom or bust cycles of Congressional funding. We requested sustained increases in NIH support in line with the Biomedical Research and Development Price Index and requested a 7% increase in funding for fiscal year 2010.

The second day of our visit was devoted to meeting with Directors of NIH Centers and Institutes with the similar objective of promoting sleep research and acquainting them with the SRS as a source of information and connection to sleep research and investigators. Background materials were provided about the SRS, as well as a listing of SRS members funded by their Institutes. In addition to meeting with Dr. Michael Twery and his staff at the National Center for Sleep Disorders Research, the team also met with Dr. Story Landis, Director of the National Institute of Neurological Disorders and Stroke; Dr. Duane Alexander, Director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development; Dr. Richard Hodes, Director of the National Institute on Aging; and Dr. Patricia Grady, Director of the National Institute of Nursing Research. The discussions were stimulating and will hopefully lead to new initiatives in the area of sleep research.

The team felt that the two days were highly productive. It is difficult to actually measure the success of such a venture, but we felt that we increased the awareness of members of Congress regarding the importance of funding sleep research and developed and strengthened relationships with key directors of NIH Institutes. The Subcommittee recommended that, to have maximal impact on research advocacy, the next step would be to develop relationships between investigators and their local Representatives and Senators. This would create the opportunity for investigators to provide talking points, information, and presentations regarding issues important to the SRS, particularly to Congressmen on key committees. The Subcommittee also recommended that future connections with NIH be less of a team effort, but rather that individual investigators meet with the Director of the Institute supporting their research to advocate for particular programs that the SRS would like to see initiated. As the Subcommittee has now completed its work, future advocacy activities will be undertaken by the newly formed Advocacy Committee, which will continue promoting investment in sleep research.

Terri Weaver, PhD, RN, FAAN
University of Pennsylvania
On behalf of the World Association of Sleep Medicine, I am delighted to invite you to our 3rd International World Sleep Congress in Sao Paulo from November 7-11, 2009. The congress is an international forum inviting professionals to advance current thinking, improve sleep health, and encourage prevention and treatment of sleep disorders. The congress will bring together leading experts to discuss, debate, and disseminate knowledge amongst sleep clinicians and researchers for the advancement of sleep health worldwide.

Our educational committee chaired by Drs. Max Hirshkowitz, Sergio Tufik, and Dalva Poyares are currently planning a series of plenary sessions and conference tracks designed for healthcare providers and sleep professionals.

The natural beauty, carnival-like atmosphere, the festive spirits, the rich culture, the enchanting beauty, the warm hospitality, the sights and sounds have attracted international tourists to repeatedly visit Brazil over the years. Some of the most beautiful spots on this planet, the Amazon rain forest, the most beautiful beaches and ecological paradise are within easy reach of Sao Paulo, the venue of the Congress and the largest and richest city of Brazil. The local Brazilian Sleep Society is planning several opportunities to experience the local Brazilian culture and allow our congress participants to network informally together.

Please join us in Sao Paulo and attend the 3rd International World Sleep Congress in November 2009 for an outstanding opportunity to exchange information and advance sleep health worldwide.

Best regards,
Dr. Sudhansu Chokroverty
President
World Association of Sleep Medicine

INVITED LECTURE TOPICS

COLIN E. SULLIVAN - Disorders of Sleep and Pregnancy
EVE VAN CAUTER - Sleep, Obesity, and Metabolic Function
KATHRYN A. LEE - Sleep and Menopause
ALFRED J. LEWY - Circadian Disorders
ERIC A. NOFZINGER - Portraits of Sleep and Sleep Disorders: Imagining the Brain
STANLEY FAHN - Wayne Henning Memorial Lecture

SYMPOSIA

1. Epidemiology of Sleep Disorders Around the Globe
2. The Evolution of Sleep and Its Disorders in Children
3. Sleepiness, Commercial Driving, and Transportation Safety
4. Pharmacotherapy: Novel Approaches
5. Restless Legs Syndrome - An International Perspective
6. Obstructive Sleep Apnea and the Heart
7. Tools of the Trade: Computerized Polysomnography, Cardiopulmonary Recorders, and Other Devices
8. Images of the Sleep-disordered Brain
9. Immune Function and Inflammation in Deprived and Disordered Sleep
10. Genetics of the Circadian Rhythm and Sleep
11. Sleep Deprivation in modern societies
12. Geriatrics and sleep

MEETING OVERVIEW

Jack Smith left us on June 11, 2009. Jack was a pioneer and pre-eminent authority in the development of digital polysomnography (D-PSG) systems. In the 1980s, his early work on D-PSG systems laid the groundwork for the emerging new field of D-PSG, onto which the world-wide sleep science and clinical endeavor happily piggy-backed. In the past two decades, Jack’s continuing innovations in D-PSG systems have been sine qua non for accelerated progress in sleep science and clinical work, without which the current sleep science and the clinical sleep endeavor would be embryonic in comparison.

Jack was born and raised in North Dakota and Minnesota, and moved to Los Angeles in his teens. Prior to enlisting in the Army in 1953, he attended Menlo College. His BS, MS, and PhD in Electrical Engineering were completed at the University of Southern California. He worked in the space and military industries before joining the University of Florida Electrical Engineering Department in 1964. At the university, Jack turned his attention to biomedical engineering, collaborating with the Department of Psychiatry on a variety of research projects in which the core data were brain waves (electroencephalograms). Principal collaborators were Ismet Karacan and Wilse B. Webb.

In the 1960s-1970s, sleep recordings were comprised of nightly recordings of brain waves, eye movements, and chin muscle tone, recorded by large, heavy, unwieldy vacuum tube-driven “polysomnographs” that produced piles and pounds of pen and ink recordings (“polysomnograms”) to be scored by hand by trained technicians, and subsequently stored in large rooms.

Jack immediately recognized that a major impediment to progress in sleep science was the lack of objective, fast, and reliable automated analyses of brain waves (EEG), eye movements (EOG), and muscle activity (EMG) collected during the typically lengthy (5-10 hours) nocturnal sleep recordings. So he went to work. By the 1970s, his recording and analysis programs were using integrated circuits and 16 bit microprocessors. His first of three academic sabbaticals was spent in Cassis, France, collaborating with researchers at the University of Marseille in the development of sleep instrumentation. In 1978, he collaborated with the late Jean-Michel Gaillard at the University of Geneva, Switzerland.

Upon his return to the States in the early 1980s, Jack switched his attention and efforts from the relatively low-frequency data of sleep to the very high frequency radio frequency spectrum. The result was the textbook Modern Communication Circuits, currently in its second edition and still widely used and referenced today.

The appearance of desktop computers in 1985 drew Jack back into sleep research. He quickly recognized the potential of the desktop computer as a catalyst in the development of D-PSG systems. A sabbatical with Kazuo Azumi and Suichiro Shirakawa at the Tokyo Metropolitan Research Institute in 1985 honed Jack’s integration of microprocessors with desktop computers in the automated analysis of sleep stages and events.

In 1986, Jack started his own company, Microtronics, which married the capabilities of the desktop computer to his innovations in polysomnographic hardware and software development. The result was the development of the Microtronics Sleep Analyzing Computer (SAC). In keeping with Jack’s ability to use the latest in modern technology to create innovative solutions for the sleep community, the Microtronics SAC system was essentially a modern computerized PSG system that used 1980s technology. The SAC system included a unique high-resolution black and white monitor to display waveforms, and a separate smaller monitor for reports and trending. For storage, it used a first-generation recordable optical disk drive. The amplifier specifications met or exceeded the specifications of sleep amplifiers sold today. The most important innovation was the real-time sleep stage analysis capability, based on Jack’s research and development effort up to that time. The system could identify sleep waveforms, display them on a computer monitor screen, and use the results to determine sleep stages based on the Rechtschaffen and Kales Scoring Manual. Recognizing the potential of Jack’s system, Oxford Medical Inc. purchased Microtronics, Inc., in 1990.

After the sale of Microtronics, Jack returned to the University of Florida, retiring as professor emeritus in 1994. During his last academic year, he served as a consultant to Motorola in Plantation Florida. In the mid-1990s, Jack founded Neurotronics, Inc., which developed “Polysmith,” the first native 32-bit sleep system. Polysmith offered the capability of acquisition and automated analysis of sleep EEG, EOG, chin EMG, EKG, leg movements, respiratory effort and airflow, and snoring. Based first on Window NT and later on Windows 95, the system took advantage of advances in computing technology to improve on the previous systems. Through the 14 years of subsequent development, the system has evolved into a complete sleep analysis and lab management solution, including a 5,000 parameter per record clinical database, synchronized digital
video, hospital EMR integration, remote access capability, and an open XML file format.

The development of these and other innovations were driven by Jack’s desire and ability to apply the latest technology to the field of sleep research. Polysmith has enjoyed great success, with well over 1,500 beds of sleep currently in use worldwide. The recent purchase of Neurotronics by Nihon Kohden, Inc., augurs well for the continuation of Jack’s legacy for many years to come.

In recognition of Jack’s seminal contributions to D-PSG systems, the American Academy of Sleep Medicine frequently invited Jack’s participation on several committees and study groups charged with the development of standardized rules for the scoring of sleep stages and events. In the past decade, Jack authored seminal articles and papers outlining sampling rate, bandwidth, and data display issues in D-PSG. A primary argument has been that if certain crucial steps are not taken to prevent frequency aliasing, the displayed data on a 30-second computer monitor screen will be a distorted, inaccurate representation of the original analog data. Other papers argued for the use of time domain analytic techniques rather than frequency-based analytic techniques in automated EEG analysis. Jack’s arguments of the past ten years have not gone unheeded, obviously having helped shape many aspects of the technical specifications section of the recently published *AASM Manual for the Scoring of Sleep and Associated Events* (2007).

As might be surmised from Jack’s professional accomplishments, he had high standards for himself. These high standards often carried over to his personal life, hobbies, and other non-professional endeavors. If an activity could be done, Jack engaged in the activity at its highest level of expression. For instance, Jack decided to learn to play chess. Within a few months he had entered into several tournaments. By the end of a few years, he was the amateur champion of Florida. He took up fishing. It was not enough to fish in our local lake, the Gulf, or the Atlantic. Jack fished in Iceland, Ireland, Belize, throughout the Caribbean, and the mountains of Mexico. Hunting? He maintained a rack full of the best guns, took up skeet shooting for practice, and frequently went on hunting trips in varied and exotic locales. Poker? A weekly game with friends, and the reason for extended trips to Los Vegas. When line poker evolved, Jack would play three of four games simultaneously when at his summer home in the Carolinas. In business pursuits, owning one company wasn’t enough. He had to have two.

Jack’s superior analytic cognitive armamentarium was tempered by a Midwestern agrarian background. He was a good old boy at heart. As a result, everyone was a friend until proven otherwise. Nature and the outdoors was the landscape, money was a convenience, and high society and its mores and adornments shallow. His range of friends was broadly nonpareil. Rich man, poor man, beggar man, thief, millionaire, mechanic, fishing guide, farmer, black, white, Korean, Japanese, male, female. Caste or class was an irrelevance.

Above all, Jack was a family man. His wife Eileen, four children, two step-children, and swarms of grandchildren were his muses. He was never happier than when at his annual family week in the Florida Keys.

We have had the good fortune to have this remarkable guy in our midst.

*By Wilse B. Webb and Augustin de la Peña, with contributions by Eileen Smith, James Schubert, and Jake Johnson.*
Maria Manasseina, Pioneer Sleep Scientist

Last year we celebrated the 165th anniversary of the birth of Maria Mikhailovna Manasseina-Korkunova (1843-1903), also known as Marie von Manassein and Marie de Manacéine. Her name was well known at the frontier of the 20th century as a pioneer in physiological (biological) chemistry and experimental somnology but later, though not fully forgotten, her work was less frequently cited. Manasseina published scientific articles in Russian, French and German, and she is sometimes mistakenly referred to as a French or German scientist. In recent years, interest in her scientific contributions has increased significantly, but her life and personality remain largely unknown.

Maria M. Manasseina was the daughter of a well-known Russian historian and archeologist, a member of the St.-Petersburg Academy of Sciences, Professor M.A. Korkunov (1806-1858). After receiving an excellent education at home, Maria Korkunova became one of the first women in Russia to obtain a higher medical education. In 1865, she married V.A. Manassein (1841-1901), who became a professor of the Medical Military Academy, a publisher of the first Russian medical magazine “Vrach” (Physician), and a rather well-known person in the history of Russian medicine. In 1870-1871, Maria Manasseina spent six months training in the laboratory of J. Wiesner (1838-1894) at the Polytechnical Institute in Vienna, where she studied the process of alcohol fermentation. While studying there, she made a discovery of paramount importance that led her to become a founder of the new science of physiological chemistry (now biochemistry). She demonstrated that the process of fermentation is due to specific substances (so-called “unorganized enzymes”, using the terminology of the time), which could be isolated from yeast cells, but not the living yeasts per se. More than a quarter of a century had passed before these results were completely confirmed by German chemist Eduard Buchner (1860-1917) who, despite being aware of Manasseina’s work, failed to make any reference to it. Unfortunately, injustice triumphed: the name of Manasseina as a pioneer of biochemistry was forgotten, while Buchner received the Nobel Prize in 1907, four years after her death, for the discovery of the extracellular (chemical) nature of fermentation.

Soon after coming home, Maria Manasseina worked as a physician in the laboratory of professor I.R. Tarkhanov (originally Tarkhishvili, 1846-1908), a pioneer of the so-called skin-galvanic reflex (the “Tarkhanoff reflex”). Ivan Tarkhanov was extremely interested in sleep problems. Possibly under his influence, the assistant and disciple Maria Manasseina performed pioneering studies in dog puppies with prolonged deprivation of sleep. Her study, presented at the International Congress of Medicine in Rome (1894) [1], was performed on 10 puppies of 2-4 months old by keeping them in constant activity (forced walking and handling). She discovered that all the animals invariably perished within 5 days, and the younger the pup, the faster its death. During sleep deprivation, body temperature decreased and was 4-6°C lower than normal. Locomotor activity of the pups became slower and weaker, and red blood cell numbers decreased. However, the weight loss was relatively mild (5-13%). A macroscopic study of body organs revealed many local hemorrhages in the brain, impairment of cerebral blood vessels (probably including perivascular infiltrates) and “fat degeneration” in several brain “ganglia.” Manasseina came to the conclusion that the main effects of prolonged sleep deprivation originated in the brain and were very different from the brain changes associated with dogs dying of starvation after 20-25 days. Analyzing the results, Manasseina concluded that sleep is more important for an organism than food. She rejected “the strange opinion regarding sleep as a useless, stupid and even noxious habit” ([1], p.325).

Manasseina also performed interesting research on dreams. Over a period of five years she collected data on the dreams of 37 different people and came to the following conclusions: the educated and active brained dreamed more than the less educated; the dreams of the educated were more logical, complex and varied; journalists, chemists, schoolmasters and other “brain workers” had only 3 to 10 dreamless nights a month, whereas manual workers had from 8 to 5; and dreams became less frequent with age [2].

In 1889, M.M. Manasseina published a large book entitled “Sleep as one third of human life, or physiology, pathology, hygiene and psychology of sleep” (2nd Russian edition – 1892) [3]. Its revised and significantly expanded version was later published in English (1897) [4]. This book was the sleep encyclopedia of its time, where for the first time all knowledge on the sleep problem was presented in a popular statement. The book had tremendous success: it was also translated into Swedish and distributed in many European countries. According to Manasseina, “the scientists recognizing sleep for stopping or diastole of cerebral activity are mistaken, for during sleep the brain as a whole does not sleep at all, it does not stay idle entirely, but only those parts of it which constitute an anatomical basis, anatomic substrate of consciousness are under the process of sleeping” ([3], p. 43). “The sleep is a time for the rest of our consciousness”, - she wrote ([3], p. 36). This book on sleep was the best known of all Manasseina’s works and a number of positive reviews were published in the Russian and foreign press.

The works of Manasseina had a tremendous impact on sleep science. In 1896 two American psychologists, G.T.V. Patrick and J.A. Gilbert, clearly inspired by Manasseina’s pioneer work, performed the first study of sleep deprivation in humans [5], and in 1898 three Italian investigators, L. Daddi and G. Tarozzi from Pisa, and C.
Agostini from Perugia, also inspired by her studies, performed a more detailed investigation of sleep deprivation in dogs [6]. Thus, the main contribution of Manasseina to physiology is related to sleep. In fact, she was a pioneer of the experimental science of sleep.

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A full version of this paper has been published in The Journal of the History of the Neurosciences, 2009, 18(3): 312-319.

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Like those early explorers, the scientists of today don’t always know what lays ahead, but their pursuit of knowledge drives them ever closer to new, profound discoveries every day.

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Domestic Laboratory Spotlight

The Sleep and Chronobiology Research Center includes several sleep and chronobiology research programs, lead by different principal investigators, including Daniel J. Buysse, MD (insomnia, sleep and aging); Timothy Monk, PhD (chronobiology, sleep and bereavement); Martica Hall (stress, sleep, and health and functioning); Eric Nofzinger, MD (sleep neuroimaging); Ron Dahl, MD (pediatric sleep and affective neuroscience); Peter Franzen, PhD (sleep deprivation and emotions); Wendy Troxel, PhD (sleep and cardiovascular health); and Michele Okun, PhD (pregnancy, inflammation, and sleep). Other principal investigators and sleep researchers closely collaborating with the Sleep and Chronobiology Research Center include Patrick Strollo, MD, Charles Atwood, MD, Christopher O’Donnell, PhD, Mark Unruh, MD, Georgina Cano, PhD, Karen Matthews, PhD, and Anne Newman, MD.

This “Domestic Lab Spotlight” focuses mainly on research conducted by Dr. Anne Germain and her team on sleep and posttraumatic stress disorder (PTSD). For more information about ongoing research conducted by other sleep researchers in Pittsburgh, visit our website at http://www.sleep.pitt.edu.

Research Interests

The Sleep and PTSD Research Program is a clinical sleep research program focused on investigating the nature, pathophysiology, neurobiological correlates, and treatments of sleep disturbances comorbid with stress-related psychiatric disorder, with a special emphasis on posttraumatic stress disorder (PTSD). The research program includes two closely related branches. The first branch is aimed at investigating the psychophysiological and neurobiological correlates of sleep disturbances in PTSD and other stress-related psychiatric disorders, such as major depression and complicated grief. The second branch focuses on developing and testing the efficacy of new and established sleep-focused behavioral and pharmacological treatments for nightmares and insomnia comorbid with PTSD.

Pathophysiology of sleep in PTSD and other stress-related psychiatric disorders. Studies conducted in the first branch of our program focus on:

- Developing and validating new self-report questionnaires and methods to assess the nature and severity of sleep disturbances in PTSD and other psychiatric and sleep conditions and their relationship to daytime functioning;
- Developing and validating novel murine models of sleep disturbances in PTSD;
- Evaluating objective indices of sleep disruption and heightened central arousal during sleep and wakefulness in trauma-exposed adults with and without PTSD, with a primary focus on military veterans, using in-lab and ambulatory polysomnography, actigraphy, and quantitative EEG and ECG methods;
- Investigating functional neuroanatomical correlates of REM and NREM sleep relative to wakefulness in adults with and without PTSD using positron emission tomography (PET) sleep imaging methods.

Treatments of sleep disturbances comorbid with PTSD and other psychiatric disorders. Studies conducted in the second branch focus on treatment development efficacy/effectiveness studies. These studies focus on:

- Comparative studies of the efficacy of cognitive-behavioral vs. pharmacological approaches for the treatment of nightmares and insomnia comorbid with PTSD and other deployment-related stress disorders;
• Adapting and testing the efficacy of brief behavioral treatments of insomnia and nightmares in adults with PTSD or older adults with comorbid insomnia;
• Developing evidence-based intervention protocols to mitigate the negative impacts of sleep disruption following trauma exposure and/or in high-stress environments;
• Developing behavioral/lifestyle interventions targeting regularization of sleep and social rhythms to augment psychopharmacological treatments in adults suffering from bipolar disorder;
• Investigating the sleep-specific clinical, physiological, and neurobiological predictors of sleep treatment response in adults with PTSD.

Current Research

Current research conducted in our group include four federally-funded studies, which include two clinical trials, and two sleep neuroimaging studies in military veterans with and without PTSD. The first clinical trial aims at comparing the efficacy and durability of the effects of prazosin (an alpha-1 antagonist) and a cognitive-behavioral intervention targeting insomnia and nightmares relative to placebo in military veterans (PRO54093). A second study aims at evaluating the predictors and functional neurobiological changes associated with sleep treatment response with prazosin and placebo using PET imaging methods during wakefulness, REM sleep, and NREM sleep (PT073961). The second clinical trial aims at evaluating the efficacy of a brief behavioral treatment for insomnia in returning military veterans compared to an information control condition (MH080696). Finally, a fourth ongoing study focuses on the functional neuro-anatomical correlates of REM sleep in military veterans with and without PTSD (MH083035).

Technical Capabilities

The N-CTRC offers a unique and extensive wealth of technical capabilities and expert resources to our research program. The N-CTRC is a clinical research center in the Department of Psychiatry at the University of Pittsburgh, located on the 13th floor of Western Psychiatric Institute and Clinic (WPIC). The N-CTRC is one component of the University of Pittsburgh Clinical and Translational Science Institute (CTSI; RR024153). All current studies of the Sleep and PTSD Research Program are conducted in the N-CTRC, which contains 3,500 sq. ft. of space. This space is divided into five bedrooms and two time isolation apartments, each with its own bathroom, audio/visual monitoring capabilities, TVs, VCRs, and PCs. In addition, there is a separate technical/control room, a nurse’s station, treatment room, subject preparation room, and lounge. Two of the bedrooms are equipped with ports which allow for IV administration of medications and blood sampling. All patient rooms are equipped to monitor EEG sleep, EKG, respiration, oxyhemoglobin saturation, periodic limb movements, heart rate and heart rate variability, core body temperature, skin temperature, and mood and performance. This laboratory also has the capability to perform studies requiring radionuclide injection for positron emission tomography (PET), and has the software and hardware necessary to conduct pupillometry studies.

The N-CTRC maintains close collaborations with other specialty resources, such as the Radiochemistry Laboratory included within the PET Facility, and MR center. The WPIC Pharmacy, Phlebotomy Laboratory, and Primary Care Laboratory all facilitate the conduct of clinical sleep research.

Clinical Activities

The UPMC Sleep Medicine Center offers clinical rotations for interns in Clinical Psychology, Residents in Psychiatry, as well as for Sleep Medicine Fellows.

Training Opportunities

Training opportunities are numerous within the Sleep and PTSD Research Program, as well as within other research programs lead by investigators of the Sleep and Chronobiology Research Center. Training opportunities are offered for undergraduate sleep research interns, clinical research internships for masters’ level social work students, and masters’ and PhD level students in Nursing, Neuroscience, Psychology, and related domains. Trainees at all levels are encouraged to contact Faculty for additional information on available training opportunities.

The research center also offers post-graduate training in Translational Research Training in Sleep Medicine (T32), funded by the National Heart, Lung, and Blood Institute, and aims to train clinical and basic researchers in a translational approach to Sleep Medicine. The primary focus of this training program is on post-doctoral training, with a secondary focus on mentored medical student research. For post-doctoral fellows, the program provides salary support and some additional funds to support research and pursue external training opportunities. Many other post-graduate training programs (T32) are also available for postgraduate fellows who are interested in sleep research.

Representative Publications

Although many aspects of sleep-wake regulation are genetically controlled, the mechanisms underlying trait- and state-like, inter-individual variation in sleep-wake functions are unknown. We are interested in genotype-dependent differences in sleep, waking performance and response to sleep and wake promoting pharmacological agents in humans. To elucidate molecular mechanisms of sleep-wake regulation in health and disease, we combine and integrate methods of human genetics, selective pharmacology, multi-channel EEG, neuropsychological/cognitive testing and brain imaging.

Adenosine and sleep

In a convergent series of studies, we established an important role for the adenosinergic neuromodulator/receptor system in homeostatic sleep-wake regulation in humans. We identified a genetic variation in the gene encoding the adenosine metabolizing enzyme, adenosine deaminase, that strongly modifies the duration of slow wave sleep and EEG delta activity during sleep. Subsequent pharmaco-genetic studies showed that a common variation in the gene encoding the adenosine A2A receptor modulates individual sensitivity to subjective and objective effects of caffeine on sleep. Moreover, we demonstrated that adenosinergic mechanisms contribute to inter-individual variation in neurobehavioral and cognitive functions during sleep deprivation. Taken together, the findings suggest that the adenosinergic system may provide new targets for pharmacological improvement of disordered sleep and vigilance, which are highly prevalent in society.

Aging and sleep

Analyses of local changes in the sleep EEG revealed that aging not only reduces global EEG activity in waking and sleep, but also causes frequency-specific alterations in sleep EEG topography. Other studies demonstrated prominent age-related alterations in healthy men in the vulnerability of neurobehavioral functions to impairment by sleep loss. These findings may have important implications for the prevention of sleep-related accidents, which are recognized today as a major public health issue associated with immense economic costs for society.

Cognition and sleep in health and disease

Supported by the Zürich Center for Integrative Human Physiology (ZIHP), we established a collaborative project together with research teams from the University Children’s Hospital (O. Jenni and

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From left to right: Valérie Bachmann, Katharina Hefti, Sereina Bodenmann, Hans-Peter Landolt (not pictured: Renate Wehrle, Federica Klaus, Shuyang Xu)
R. Huber), the Department of Neurology (P. Brugger and C. Bassetti) and the Institute of Pharmacology and Toxicology (P. Achermann), to investigate functional relationships between cognition and sleep in developing children, healthy adults and neurological patients. We examine whether high and lower cognitive abilities are associated with individual differences in sleep duration and distinct features of sleep. Sleep-wake regulation and EEG patterns are studied in cognitively well-characterized children and adults with distinct genotypes in neuromodulatory systems related to cognition and sleep, and in patients with cortical and thalamic stroke. The studies will show whether neuronal plasticity and sleep are functionally related in humans, and possibly contribute to improved patient care in the future.

**Medical diseases and sleep**

We are part of an inter-disciplinary network of neuroscientists and clinical researchers who are interested in sleep and waking functions in patients with psychiatric and neurological disorders. While the analysis of sleep EEG topography in moderately depressed patients revealed no changes when compared to healthy controls, other projects provided important new insights into sleep-wake disturbances in patients with sporadic Creutzfeldt-Jakob disease and narcolepsy. Ongoing studies in idiopathic hypersomnia and tetraplegia are spanning from the molecular level to sleep-wake behavior and cognitive task performance to clinical sleep neuropsychology, and aim to reveal possible pathophysiological underpinnings of disturbed sleep and wakefulness in these patients.

**Technical Capabilities**

The Human Sleep Psychopharmacology Laboratory is an independent part of the Section of Chronobiology and Sleep Research at the Institute of Pharmacology and Toxicology, University of Zürich. The human sleep research facilities (used together with the group of Prof. P. Achermann) consist of a 4-bedroom temporal isolation unit with subjects preparation room and kitchen, two bathrooms, and an adjacent recording room equipped for 32-channel long-term digital, polysomnographic recording including EEG, EMG, EOG, ECG, body and skin temperature, breathing variables, etc. The infrastructure provides complete isolation from any time information, noise, vibration and electromagnetic fields, and can be equipped for endocrine measurements. State-of-the-art polygraphs ensure high-quality waking and sleep EEG recordings and, together with a portable 128-channel high-density EEG system, are suitable for EEG mapping and ERP studies. Several portable recording systems are available for clinical and home recordings. Other resources include analysis software for sleep, EEG spectral analysis, and brain imaging data; actimetry devices to record wrist activity/light exposure; validated questionnaires and tests to assess neurobehavioral, neurocognitive and affective performance and state; and assays for genotype, pharmacokinetic and biochemical analyses.

**Training Opportunities**

Our group can offer trainee opportunities for PhD, MSc and MD students, and postdoctoral fellows. Enquiries are welcome.

**Selected Original Publications**


**Selected Reviews**


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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