Ambulatory Pickup from 2003 Preliminary Program
The National Institutes of Health (NIH) recently announced several initiatives that reconsider the research and business aspects of the NIH. The most notable change has been the introduction by Dr. Elias Zerhouni, NIH Director, of the NIH Roadmap on September 30, 2003. This initiative will undoubtedly offer many opportunities for our field.

The Roadmap was created to identify major opportunities and gaps in biomedical research that no single institute at the NIH could tackle alone but that the agency as a whole must address to make the biggest impact on the progress of medical research; the goal of this initiative is to facilitate the conduct of studies and the development of interdisciplinary technologies. It was constructed after consulting over 300 of the nation’s biomedical leaders from academia, government and the private sector. Through these consultations, three major themes emerged: “New Pathways to Discovery” (new technologies), “Research Team of the Future” (new, more interdisciplinary research teams), and “Re-engineering the Clinical Research Enterprise” (improve clinical research infrastructure).

Funding allocated to this effort will increase rapidly from the current level of $125 million per year in FY2004 to $2 billion per year in five years. As a result, a number of funding opportunities are available and are listed at http://nihroadmap.nih.gov/grants/index.asp. Further, several specific initiatives of the Roadmap can be used to increase funding in sleep research.

While most of these initiatives pertain to the development of large collaborative networks, some are also relevant to individual investigators. In the paragraphs below, I will briefly outline these themes and comment on how they may benefit SRS members.

New Pathways to Discovery

The goal of this initiative is to facilitate the creation and integration of new technologies in the conduct of health-related research. The initiative calls for the creation of centers for bioinformatics or nanomedicine and an NIH bioactive small molecule library, which could be used to screen for sleep active compounds. It also calls for the development of technology pertaining to imaging and the study of proteins or metabolism. While these areas are only marginally relevant to the sleep area, they may provide resources for future sleep research.

Research Teams for the Future

The scale and complexity of current biomedical research increasingly demands that scientists move beyond the confines of their own discipline and explore new organizational models for team science; the sleep field is a model of the need for bringing together people of different backgrounds. Additionally, innovative science or areas that are new (like sleep research and medicine) are often more difficult to review fairly and therefore fund. The Roadmap recognizes the difficulty in finding solutions to these problems in the context of our current academic and governmental structures and establishes several programs to address this. In one, the NIH Director will directly grant “innovator awards” that will provide support to individuals who have the potential to make extraordinary contributions. These awards will not be project-directed, but investigator-directed. The applicants will be evaluated on creative abilities, potential for ground-breaking discovery and evidence of focused and perseverant exploration.

Other awards will aim to establish interdisciplinary research centers and collaborative training initiatives. An example is a request for application advertised as “Exploratory Centers for Interdisciplinary Research.” In these Centers, groups of individuals will be asked to develop interdisciplinary strategies to solve significant biomedical and/or behavioral research problems. These exploratory Centers are intended to lay the foundation for submitting subsequent applications through an interdisciplinary research consortium. This mechanism is clearly applicable to many unsolved clinical and basic research sleep problems— for example, finding the cause of Restless Leg Syndrome or the function of sleep—and we encourage SRS members to consider developing programs using this mechanism. This program is also uniquely suitable to the study of rare sleep disorders, especially if a combined epidemiological and pathophysiological approach is used.

The training of researchers in interdisciplinary research is also well represented in the Roadmap. Three requests for applications having direct funding potential for our field have been released: “Interdisciplinary Health Research Training Programs,” “Curriculum Development Awards in Interdisciplinary Research,” and “Short Programs for Interdisciplinary Training.” The first program, a postdoctoral National Research Training Award, focuses on training postdoctoral fellows across disciplines. Genetic or Neuroscience PhDs interested in expanding the scope of their work to include sleep might be eligible for a program developed in this area. The second aims at the development of formal courses and other educational tools in interdisciplinary research. Educational programs in basic and clinical sleep research could be developed using this mechanism. The third, Short Programs for Interdisciplinary Training, seek to promote interdisciplinary programs for scientists at all levels of their careers. These programs offer unique training opportunities for our field and we encourage SRS members to apply.

Other requests for applications in similar areas are likely to appear soon on the NIH Roadmap Web site. Of special interest to our field will be efforts to remove structural barriers to interdisciplinary research as these may complement an initiative the SRS has started to develop in...
Re-engineering the Clinical Research Enterprise

The rapid pace of discovery in biomedical research has not sufficiently translated into clinical practice. This state of affairs is partially due to the disappearance of medical doctors with a strong research orientation (Duyk, 2003). Additionally, ongoing research efforts are often not well-integrated with patient care organizations, even in leading universities. Finally, there is also a lack of application of current knowledge to general public health problems. For example, the public and the medical profession are poorly informed regarding research developments in sleep medicine and in our understanding of the impact of sleep deprivation.

To address this issue, new partnerships among patient communities, community-based physicians and academic researchers will be developed. The NIH has also issued a request for applications inviting institutions to establish programs for training clinicians early in their career in the design, conduct and analysis of clinical research. The Roadmap will also promote the formation of better integrated networks of academic centers that will work jointly on clinical problems and include community-based physicians. A special emphasis will be placed on the consistent gathering and storage of clinical data and biological material in databases for large-scale studies. Sharing of these resources will be facilitated by the creation of a revolutionary program called the National Electronic Clinical Trial and Research Network (NECTAR). The NIH also intends to issue RFAs for technologies that improve clinical outcome assessments and for regional research centers; these initiatives are likely to be applicable to various aspects of sleep medicine.

Conclusion

The Roadmap will lead to a significant shift in the way the NIH conducts research and spends its resources. The doubling of the NIH budget has ended with a more modest 3.7% increase predicted for FY2004. The effect of the slowing of the NIH budget growth on traditional research grants will be mitigated by a significant decrease in building and facility budgets and by the investment in the Roadmap. In this context, however, more applied patient-oriented research is likely to be funded. A stronger emphasis on the development of new technologies that may have future clinical application is apparent. Finally, small studies led by a single investigator will be complemented by larger, interdisciplinary collaborative studies. Small case series studies from one center may become more difficult to fund. These initiatives may benefit the sleep field but will require SRS members to team up and collaborate.

The recognition by NIH of the importance of interdisciplinary research is an asset for areas such as ours. As your President, I recently sent a letter to Dr. Zerhouni encouraging him to consider sleep of primary importance in the replacement of Dr. Lenfant as head of NHLBI, the Institute that hosts the National Center on Sleep Disorders Research. I am pleased to report that his reply was very supportive, which highlights the interdisciplinary nature of sleep. He also stated the importance of the revised national research plan (http://www.nhlbi.nih.gov/health/prof/sleep/res_plan/) and his intent to work with the SRS to implement the plan’s content.

These developments are further illustration of the importance of our field and potential for future growth and development.

Emmanuel Mignot, M.D., Ph.D.


Editor’s Column

by Larry D. Sanford, Ph.D.

This issue of the Bulletin illustrates a number of activities undertaken in the advancement of sleep research. Emmanuel Mignot’s President’s Message (pages 4-5) focuses on the impact of the National Institutes of Health (NIH) Roadmap for medical research in the 21st century. I join Dr. Mignot in encouraging our members to visit the NIH web site to learn more about the Roadmap and the opportunities it affords sleep researchers. Carl Hunt, M.D., Director of the National Center on Sleep Disorders Research at the National Heart, Lung and Blood Institute, NIH, provides a summary of sleep related activities within the Center (pages 6-8). This issue also introduces the new SRS Research Committee (page 18), gives an overview of the inaugural Pfizer Lectureship in Sleep at the University of Michigan (page 19) and highlights sleep research activity in India (pages 20-22).

One of the great things about the current environment for sleep research is the potential for advancing the field. The scientific method provides formalized rules for inquiry and modern technology provides incredible tools for application to the questions that interest us. This, of course, was not the case when Thomas Ball wrote his doctoral dissertation on The Causes and Effects of Sleep in 1796 at the University of Pennsylvania, a “classic” paper included in this issue of the Bulletin (pages 12-16).

It is interesting to put Ball’s writings into a temporal perspective. In physical science, the fundamental contributions of Volta (invention of battery, 1800), Ampere (properties of magnetic field produced by electricity, 1800), Ohm (Ohm’s law, 1827) and Faraday and Henry (current produced in a wire moved near a magnet, 1831) that would eventually make a polygraph possible had not been made. As for what would become biology, psychology and neuroscience, Flourens, who pioneered experimental brain research, had just been born (1794) and basic concepts of the nervous system (e.g., the Bell-Magendie Law and recognition of sensory and motor pathways, 1822) had not yet been formulated.

Thus, it is not surprising that Ball’s writing contains some quaint notions. One can only speculate how future scientists will view our science today. However, our concerted efforts to understand the fundamental nature of sleep should make its future a bright one.

SRS Web Site
www.sleepresearchsociety.org

The site was designed to be a resource for members and to educate and inform the public. We suggest you visit us at www.sleepresearchsociety.org to view our recent upgrades and updates. Your suggestions and comments are welcome.
INTRODUCTION

Congress established the National Center on Sleep Disorders Research (NCSDR) in 1993. The stated goals were to enhance sleep disorders awareness, facilitate government-wide coordination of sleep research and training, and develop integrative multidisciplinary research and education programs to fill gaps in existing knowledge. The NCSDR is an office within the National Heart, Lung, and Blood Institute (NHLBI). The NCSDR coordinates sleep-related interactions within the National Institutes of Health (NIH) Institutes and Centers involved in sleep related research, and with other federal agencies with interest in sleep, sleep disorders and associated research and education activities. The NCSDR also partners with non-government organizations in a wide range of professional and community education and public health activities.

The NCSDR web site (http://www.nhlbi.nih.gov/sleep) identifies the current programs in which NCSDR is engaged and provides direct links to numerous resources of relevance to sleep researchers, sleep medicine clinicians, and lay audiences seeking sleep-related information.

SLEEP RESEARCH

NIH funding for sleep research has more than doubled since the creation of the NCSDR and release of the first research plan in 1996, reaching $175,022,000 in FY 2002. In addition to $45,155,000 in sleep research funding by NHLBI, substantial sleep research programs are also supported by the other nine Institutes/Centers participating with NHLBI in the Trans-NIH Sleep Research Coordinating Committee (SRCC). Please go to the NCSDR web site for a direct link to the Trans-NIH SRCC Annual Report for a complete listing of the members and contact information, and a summary of grants funded each year by Institute/Center.

2003 National Sleep Disorders Research Plan

The legislation to establish the NCSDR included a requirement for development of a National Sleep Disorders Research Plan. The first Plan was released in 1996 and called for strengthening existing sleep research programs, creating new programs to address important research gaps and opportunities, applying state-of-the-art techniques and technologies to the study of sleep, and developing strategies for better understanding daytime sleepiness and reducing its negative impact on society. Since 1996, new research and knowledge have vastly expanded the array of questions to be addressed, and new technologies have yielded tools and mechanisms for highly interdisciplinary broad-based sleep research.

The 2003 Revision summarizes the specific sleep research achievements since 1996, identifies present gaps in our knowledge and understanding, and concludes with prioritized recommendations for future research. The Plan is envisioned as a dynamic springboard for the creativity of individual scientists. These recommendations should contribute in substantial ways to advancing the frontiers of biomedical knowledge related to sleep, improving timely diagnosis and effective treatment, and improving the health of our nation through community-based public health education and intervention programs.

The following are some of the research recommendations given the highest priority in the 2003 Plan.

- An improved understanding of all aspects of the neurobiology and functions of sleep
- Enhancement of our understanding of the impact of reduced or restricted sleep on behavior and neurobiological and physiological functions across the age spectrum from childhood through old age
- Improvement in our understanding of the processes that lead to specific sleep disorders in children and adults—specifically, insomnia, restless legs syndrome and periodic limb movement disorder, sleep disordered breathing, disorders of ventilatory control, and primary disorders leading to hypersomnolence
- An assessment of normal human sleep phenotypes and the normal range of variation in this phenotype in adults and children including sleep duration, sleep stage distribution, sleep timing, sleep disruption, sleep quality, and other variables by which sleep and sleepiness can be quantitatively evaluated
- Development of new treatments for sleep disorders
- Further investigation of the relationship between the processes of sleep and the development and progression of diseases of both neural and non-neural tissues.
- Better understanding of the neurophysiology of sleep and the neuropathology of sleep disorders in women and in underserved populations.

The 2003 National Sleep Disorders Research Plan is available in HTML format at http://www.nhlbi.nih.gov/health/prof/sleep/res_plan/index.html and a PDF can be downloaded at no charge. If preferred, whenever requested the NCSDR can mail a hard copy of the Plan.

TRANSLATION

In addition to the substantial portfolio of basic research related to the neurobiology of sleep, circadian rhythms, and sleep disorders, the member Institutes/Centers of the Trans-NIH SRCC also support a substantial portfolio of “bench to bedside” clinical research. The critical final step, however, is translating what we now know about sleep and sleep disorders in a timely manner into cost-effective clinical practice programs leading to improved public health and quality of life. NCSDR is therefore actively engaged in a number of translational efforts to disseminate knowledge about sleep and sleep disorders and to implement programs to improve public health.

Garfield ‘Star Sleeper’ Campaign

The Garfield campaign, launched in 2001, is sponsored by Paws, Inc., the corporate entity for Garfield the Cat. Co-sponsors for the campaign
include the American Academy of Pediatrics and the National Association of Elementary School Principals. Garfield serves as the campaign’s official “spokescat” for healthy sleep in a multi-faceted educational program for elementary school-aged children, their parents and teachers, and pediatricians. The key message is that getting a good night’s sleep is important for children to do their best at whatever they do, and that most children need at least nine hours/night on a consistent basis in order to be well rested.

The web site is designed to help educate children and their parents, teachers, and pediatricians about the importance of getting a good night’s sleep. The goal is to reach children at a time when many of the habits affecting their life-long health, well-being, and productivity are still developing and before they learn bad habits. The web site provides direct access to multiple fun activities for children with sleep education messages, and corresponding guides for parents, teachers, and health care providers.

National Sleep Conference, March 29-30, 2004
http://www.nhlbi.nih.gov/meetings/slp_front.htm
or
www.sleeptranslation.com

Dramatic expansion of new knowledge about the importance of sleep, the health consequences of chronic sleep deprivation, and sleep disorders has occurred in recent years. Chronic sleep loss and untreated sleep disorders have a profound and diverse impact on health, behavior, and quality of life. The health consequences of sleep disorders, sleep deprivation and excessive daytime sleepiness annually affect 50 to 70 million Americans, add approximately $15 billion to our national health care bill, and cost industry $50 billion in lost productivity.

The National Sleep Conference is an innovative two-day program that will assemble health care providers, public health and education experts, policy makers, patient advocacy organizations, sleep medicine specialists, and other stakeholders. The Conference will address how information about sleep and sleep disorders can translate into cost-effective, comprehensive, and broadly-applied strategies to improve all aspects of sleep-related health care. Registration is free, but it is necessary to register to ensure access to the main auditorium and for the concurrent action group panels. Either of the above web sites will provide general information about the conference, the agenda, and registration and hotel information.

Our challenge is bridging the gap between knowledge and effective care. Sleep disorders are not identified in many affected individuals and many patients are therefore not receiving effective treatment.

To address this challenge, the Conference will capitalize on the unique interdisciplinary expertise of all participants to develop an action plan with high potential for improving public health and quality of life. The action plan will include steps for immediate implementation of the plan and a strategy for post-Conference monitoring.

EDUCATION/CURRICULUM DEVELOPMENT

Sleep Academic Award Curriculum
http://www.aasmnet.org/MEDSleepprogram.htm

The Sleep Academic Award program was established in 1996 and funded curriculum development programs in 20 medical schools. The program was developed to improve the quality of medical education, stimulate the development of patient & community education programs, and facilitate curriculum development at the undergraduate and postgraduate level in medical schools and curriculum development for continuing medical and nursing education. More than 70 sleep curriculum resources have been developed by grantees in this program.

Through a partnership with the American Academy of Sleep Medicine, any interested health care professionals can access the MEDSleep web site from the NCSDR web site or directly from the URL above and can download any of the slide presentations, interactive cases, or other curriculum resources that are available. In addition, one can search according to author, topic, curriculum, format and target group by linking directly to the MEDSleep educational resources at http://www.aasmnet.org/MEDSleep/SAAResources.asp

NIH ROADMAP
http://nihroadmap.nih.gov/

Science is changing rapidly and NIH needs to change too, according to Dr. Elias Zerhouni, NIH Director. “The current structure of NIH with its separately funded Institutes and Centers does not facilitate trans-NIH initiatives,” Dr. Zerhouni told a joint Senate/House hearing. Yet science today “is converging as the result of the discovery of unifying concepts, methods, and biological mechanisms that link apparently disparate diseases.” Also, “the way clinical research is conducted must be updated. We need to more quickly translate discoveries into practice,” Dr. Zerhouni states.

The Roadmap plan calls for more cooperation between NIH Institutes and Centers, and nearly $130 million has already been pledged for the fiscal year that began October 1, 2003.

Detailed descriptions of each Roadmap initiative can be obtained using the URL listed above. Several of these initiatives may have direct applicability to sleep investigators, especially as related to interdisciplinary and multidisciplinary research and research training. Some of these initiatives are listed below:

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<th>Receipt date</th>
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<th>Council</th>
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<td>February 11, 2004</td>
<td>DK-04-003 Short Interdisciplinary Research Programs R13</td>
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<td>February 24, 2004</td>
<td>GM-04-003 Curriculum Development Award in Interdisciplinary Research K07</td>
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<td>February 24, 2004</td>
<td>RR-04-002 Exploratory Centers for Interdisciplinary Research (P20)</td>
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<td>March 10, 2004</td>
<td>DK-04-002 Training for a New Interdisciplinary Research Workforce (new T mechanism)</td>
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<td>March 23, 2004</td>
<td>HD-04-006 K12 Multidisciplinary Clinical Research Career Development Award</td>
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OTHER RESOURCES

National Heart, Lung, and Blood Institute (NHLBI)
http://www.nhlbi.nih.gov

NHLBI Funding Opportunities
http://www.nhlbi.nih.gov/funding/index.htm

This site provides funding, training and grant policy information specific to NHLBI programs and initiatives, including those pertaining to sleep and sleep disorders.

Sleep Disorders Information (General Public)*
Sleep Disorders Information (Health Professionals)*

*These two links provide a range of free and downloadable information about sleep disorders for both health professionals and the general public, including sleep apnea, insomnia, restless legs syndrome, narcolepsy, and problem sleepiness.

National Institutes of Health (NIH)
Grants and Funding Opportunities
http://grants1.nih.gov/grants/index.cfm

This website provides current information and resources for NIH funding opportunities across all NIH Institutes and Centers, including: CRISP — (Computer Retrieval of Information on Scientific Projects) is a searchable biomedical database of federally-supported proposed research conducted at universities, hospitals, and other research institutions.

NIH Guide for Grants and Contracts — The Guide is the official document for announcing the availability of NIH funds for biomedical and behavioral research and research training and disseminating policy and administrative information.

To ensure that Sections encompass the primary areas of sleep research and to create more equal distribution of members among Sections, SRS Section titles and descriptions have been updated. Current Sections are: Basic Sleep Research, Circadian Rhythms Research, Sleep and Behavior Research and Sleep Disorders Research. Please contact the membership department at srsmembership@srsonline.org to confirm your Section affiliation.

**Basic Sleep Research**
Members of the Basic Sleep Research Section have research interests in areas such as neuroscience, genetics, cell biology, endocrinology and physiology. From these perspectives, animal and/or human research is aimed at understanding the molecular, neurophysiological or neuronal mechanisms controlling the sleep-wake cycle and states. Research also comprises the phylogeny, ontogeny and general physiology of sleep.

**Circadian Rhythms Research**
Members of the Circadian Rhythms Research Section have research interests in interactions between sleep and biological rhythms. These interests range from elucidating the molecular, genetic, neural and physiological nature of these interactions to understanding how these processes interrelate across development and aging. Research also includes human circadian studies in healthy individuals and circadian sleep disorder patients.

**Sleep and Behavior Research**
Members of the Sleep and Behavior Research Section have research interests in sleep and wakefulness throughout the life cycle. Sleep deprivation and sleep loss, development, aging, pharmacological influences on sleep, gender differences, sleep and performance, and dreaming are among the interests of this Section.

**Sleep Disorders Research**
Members of the Sleep Disorders Research Section have research interests in the epidemiology, cause, effect or treatment of sleep disorders. Members include those studying adult or pediatric sleep disorders (i.e., sleep apnea, narcolepsy, restless legs/periodic limb movement syndrome, parasomnias, insomnia) and those studying sleep in medical and psychiatric illnesses. Research may be conducted in humans or using animal models of sleep disorders.
SRS TO CO-SPONSOR NATIONAL SLEEP CONFERENCE

The SRS is a co-sponsor of the National Sleep Conference, an innovative two-day program that will address the challenge of bridging the gap between knowledge and effective clinical care as sleep disorders are not identified in many individuals and many patients are not being diagnosed or receiving effective treatment. The Conference is March 29-30, 2004, on the NIH Campus in Bethesda, Maryland. There is no charge for admission to the conference, but attendees must register in advance. Learn more at http://www.sleep-translation.com.

MEMBERSHIP RENEWALS

The SRS has mailed invoices to members for the 2004 membership dues. Membership renewal notices have been sent to the address provided in each member’s records; please contact the membership department at (708-492-1093) as soon as possible if your contact information has recently changed. Members may also review their membership online at http://www.sleepresearchsociety.org/about/membership.php. Members should renew their membership as soon as possible to avoid interruption of their member benefits.

SLEEP SCIENCE AWARD

The American Academy of Neurology invites all sleep specialists to apply for the Sleep Science Award, which is intended to stimulate and reward individuals in the pursuit of basic or clinical research in sleep. The recipient of the award is invited to attend the American Academy of Neurology’s 56th Annual Meeting held April 24 to May 1, 2004, in San Francisco, California, and will receive a certificate of recognition and $1,500 prize. The guidelines and application are available online at www.aan.com/professionals/awards/index.cfm.

ANA PRESENTS F.E. BENNETT MEMORIAL LECTURESHIP AWARD

Emmanuel Mignot, M.D., Ph.D. and current President of the Sleep Research Society, was selected as the 2003 recipient of the American Neurological Association’s F.E. Bennett Memorial Lecture ship award. A special lecture to commemorate this award was given during the Association’s October 19-22 2003 annual meeting in San Francisco. The award recipient is selected by the American Neurological Association Scientific Program Committee. Since 1969, this award has recognized outstanding researchers and educators in neurology. Dr. Mignot is known internationally for discovering that the sleep disorder narcolepsy is associated with hypocretin abnormalities in both humans and animals.

PAGE CHARGES TO JOURNAL SLEEP POSTPONED

The APSS Board of Directors met via conference call to discuss page charges in the journal SLEEP. A related editorial is posted on the Web at www.journalsleep.org.

On behalf of the Sleep Research Society, President Emmanuel Mignot, M.D., Ph.D., presented Michel Jouvet a plaque in recognition of his seminal discoveries and theories in the area of paradoxical sleep. The plaque was presented during the September 2003 international conference in Lyon, France honoring Michel Jouvet, The Paradox of Sleep: An Unfinished Story.

Dr. Claude Lenfant Credits Sleep Community

On August 30, 2003, Dr. Claude Lenfant retired from his position as Director of the National Institute of Health National Heart, Lung and Blood Institute. Under his leadership, the Institute initiated countless innovative educational and research programs advancing scientific discoveries and improving public wellness. SRS President Emmanuel Mignot thanked Dr. Lenfant for his efforts and contributions on behalf of the sleep community. An accomplishment of particular note was the establishment of the National Center on Sleep Disorders Research. The Center has been instrumental in conducting and supporting research, training, health information dissemination and other activities relating to sleep and sleep disorders. The 1996 Sleep Disorders Research Plan improved the health, safety and productivity of Americans by promoting basic, clinical and applied research on sleep and sleep disorders. The plan strengthened existing sleep research initiatives by creating new programs to address gaps in knowledge and identify opportunities for advancement. Under his guidance, the 2003 plan which will further advance the profession was developed. Following is Dr. Lenfant’s September 3 response to Dr. Mignot’s letter.

Dear Dr. Mignot,

This is to thank you and your colleagues of the Sleep Research Society for your letter and nice comments. I appreciate them very much. However, the reality is that much of the credit is due to the “sleep” community who supported me and the Institute to the fullest.

In addition, I consider this line of research as critically important because of the need for public health it addresses. Please convey my thanks to your colleagues.

Very best regards,
Claude Lenfant, M.D.
Former Director of NHLBI
Society-based scientific journals face a number of challenges these days as they try to both attract the best science in their particular field while meeting the needs of the associated society(s). Attracting science is a difficult undertaking for a specialty journal such as SLEEP as we must compete with the established basic science journals for the more fundamental research, and with the primary specialty journals (neurology, pulmonary, psychiatry, etc.) for the clinical papers. In competing, we can promise and deliver rapid reviews, quick publication, editorials, and prominent placement in the Journal. However, at the end of the day, impact factor is what attracts science. For those who don’t live and breathe this number, the impact factor for a journal is calculated based on the number of citations each paper in that journal receives over the first two years after the paper is published. Thus you take every paper published in SLEEP, determine the number of times each was cited over the first two years following publication, and calculate the average. Currently our citation index is 3.71 meaning that, on average, a paper in SLEEP is cited 3.71 times over the first two years after it is published. The question then becomes, how can one influence or improve the impact factor of a journal.

Substantially improving the impact factor is not easily accomplished and trying to do so can importantly impact the journal. The most straightforward way to improve the impact factor of a journal is to publish only very important cross-cutting papers that are likely to receive substantial attention. For most journals, including SLEEP, this could only be accomplished by substantially reducing the number of papers published. We simply don’t receive 15-20 such papers every 4-6 weeks. The logical extreme of this concept would be to carefully identify the single best paper received each month and publish only that one paper. This would almost certainly lead to a high impact factor, but would mean in reality that the journal itself had very little actual “impact” scientifically and the needs of the society(s) would not be met. The clinicians would not learn about sleep and its disorders while the scientists would not improve their understanding of the mechanics of sleep and circadian biology. Thus a balance must be struck between publishing the very best, most visible science and publishing enough good papers for both scientists and clinicians to steadily learn about our field. We are still, at this time, trying to define this balance.

It is also not always easy to predict which papers will turn out to be scientifically important and which will never be cited. Even in the very best journals there is substantial variability in the number of citations a paper will receive. Virtually all major journals publish many low impact papers. The journal still maintains a high impact factor because it has enough “winners” (i.e. very high impact papers) that the “losers” can be accommodated. However, just because a paper is published in a prestigious journal does not mean the paper will turn out to be important. On the other hand, papers published in low impact journals may turn out to be quite important.

Paper selection is not the only way to influence impact factor. High quality reviews addressing important clinical and basic science topics are commonly cited frequently. This applies to consensus conferences, papers addressing scientific techniques or definitions, and clinical practice guidelines. Documents such as these also meet the needs of most members of our societies and thus serve several purposes. As a result, publishing reviews is planned. On the other hand, industry-sponsored journal supplements can generate substantial income for the society but tend to drag down the impact factor as these papers are rarely cited. As a result, we have, to date, decided not to publish such supplements.

Thus what is the journal SLEEP doing to maximize its impact factor while meeting the needs of the SRS/AASM?

1. We are always trying to attract high profile articles by providing rapid, quality reviews. This has been greatly improved by our electronic review process (ScholarOne).
2. We now make papers available on our web site almost immediately after acceptance which is well before the print copy comes out. Thus the articles have several months of exposure prior to print publication.
3. We have started our rapid publication process and have thus far published two important papers.
4. I have solicited a number of important reviews and these have begun to be submitted. Thus they will be published in the months ahead and should be of superb quality.
5. I am soliciting 3-5 editorials for each issue of the journal to bring focus on a number of the papers we publish.
6. We have not currently made formal decisions regarding what percentage of papers should be accepted and published. To date we are publishing all papers that the reviewers and Associate Editors deem appropriate for publication. However, the number of submissions to SLEEP has increased substantially and we will either have to tighten up our acceptance standard or publish more than the current nine issues per year. This will be discussed at length at a meeting of the Associate and Deputy Editors at the end of January 2004.
7. We have not solved the problem of ready access to our Journal web site (and thus our papers) for non-members of our societies. We have attempted to provide all subscribing libraries with access for all individuals at the associated university. However, we have only been partially successful with this and need broad electronic access to our journal. Thus other approaches will have to be pursued.

We hope our current approach will bring a balance of quality science yet broad coverage of most research areas thereby meeting the needs of our scientists and clinicians. However, this balance is likely to evolve over time as I and my Associate and Deputy Editors learn our roles and observe the trends in papers submitted to our journal.
Planning for the 2004 APSS Annual Meeting is well underway, and the Program Committee is developing a scientific program which will present the best and most recent basic and clinical sleep science. This year, our scientific keynote speaker is Clifford Saper, M.D., Ph.D. who will address, “Brain Circuitry Regulating Sleep and Circadian Rhythms.”

The deadline for submission of postgraduate course and symposia/discussion group/clinical workshop proposals was December 1, 2003. The abstract submission deadline was December 15, 2003. In order to streamline the abstract submission process, abstracts were submitted and are being reviewed through Abstract Central, a Web-based system operated by ScholarOne.

All notices concerning the status of abstracts and symposia/discussion group/clinical workshop submissions will be sent on approximately February 1, 2004. Also, watch your mail in March for the Preliminary Program, which will include details on program content and registration information.

For the latest updates regarding the APSS 18th Annual Meeting, please visit www.apss.org or contact the National Office at (708) 492-0930. Mark your calendar to attend the largest gathering of sleep professionals in the world, June 5-10, 2004 in Philadelphia, Pennsylvania.

The Sleep Research Society Club Hypnos social has become a tradition at the Society for Neuroscience annual meeting. This year’s reception was a resounding success with approximately 200 individuals attending the event at the Sheraton New Orleans! Attendees included sleep researchers and other interested neuroscientists from around the globe. During the one-and-a-half hour event everyone was treated to a taste of New Orleans - seafood gumbo, red beans and rice, jambalaya, muffaletas and much more.

Club Hypnos was conceived as a social event to provide an informal setting for collegial discussions away from the hectic scientific schedule characteristic of Society for Neuroscience meetings. Over the years the event has grown, as evidenced by the record number of individuals that attended the Club Hypnos reception in New Orleans. The social event also provides opportunity for non-SRS members to learn about the activities of the society and the benefits of membership, and is a good venue for recruiting new SRS members. This year we had available for distribution past issues of the *SRS Bulletin* and SRS membership applications. We also displayed samples of SRS promotional items.

After the Club Hypnos reception, the crowd moved next door for the Sleep and Circadian DataBlitz. DataBlitz is sponsored by the National Heart, Lung, and Blood Institute of the National Institutes of Health and other organizations interested in sleep and circadian rhythms research, including the SRS. It derives its name from the fast-paced presentations given during this event. Speakers are allowed one minute and one slide to summarize their most important findings. Such a venue is entertaining and informative. DataBlitz presentations covered a wide range of topics, from the molecular and genetic basis of sleep disorders to interactions between sleep regulatory and circadian systems. The highlight of the evening was a two-minute “plenary” lecture titled “Seeing the Light” given by Dr. Rae Silver of Columbia University. All-in-all, the Club Hypnos reception followed by DataBlitz provides a fitting way for members of the sleep research community to discuss the newest data presented at the Society for Neuroscience meeting and to catch up with friends and colleagues.
This dissertation was submitted to the examination of the Rev. John Ewing, STP, Provost, the Trustees and Medical Professors of the University of Pennsylvania, on the Seventeenth day of May 1796 for the degree of Doctor of Medicine by Thomas Ball of Virginia, member of the Philadelphia Medical Society.

The dissertation was printed by Budd and Bartram of No. 58 North Second Street in Philadelphia in the year 1796.

To doctor William Davis of Virginia and to doctor Benjamin Say, fellow of the College of Physicians of Philadelphia and corresponding member of the Medical Society of London, etc.

Gentlemen,

In dedicating this Dissertation to you, I at once follow the strong impulse both of duty and inclination. Receive, therefore, my grateful acknowledgments for the kind attention and useful instruction that I have received from both; and be assured, that what medical knowledge I may possess, the sources from when it sprung cannot be effaced from my recollection; nor shall my humble supplications be wanting to the throne of mercy for your health, prosperity, and future happiness. I am, with due respect, your much obliged, and very affectionate pupil.

Thomas Ball

INTRODUCTION

When I survey the wonderful works of our Creator — I view with pleasure the various productions of the vegetable and mineral kingdoms.

With silent astonishment, I behold the order, magnificence and splendor of the heavenly bodies; but, at the fight of man, I almost forget every other part of the creation, and gaze in ignorant silence on him alone, especially when I think on what a slender thread human life is suspended and how very easily it may be divided. When I recollect how very complicate his wonderful machine is, and how easily disorganized; when I view the many accidents that might befall him, from the time of conception to his birth, the innumerable dangers that he is exposed to from infancy to manhood, the ills that await him, the dangers that surround him, and the pains and diseases which attend him during this whole life, I am lost in inquisitive amazement, and think it a wonder that man should ever live as many days as he does years. When we recollect that the outlets to human life are so very numerous, so wide, and so very unguarded, and how few, straight and narrow the paths of good health — nothing less than that Omnificent Power, which first created us, could possibly conduct us through life’s dark and dangerous road: — yet if the Lord is with us who can be against us? “Yea, though I walk through the valley of the shadow of death, I will fear no evil, for thou art with me.”

In compliance with the rules of this university, I submit (though with diffidence) to the examination of the medical professors, an inaugural dissertation, on the causes and effects of sleep, hoping the inconvenience and darkness of this metaphysical and physiological subject will procure me the indulgence, both of the medical faculty and of the public, for its imperfections.

AN INAUGURAL DISSERTATION ON THE CAUSES AND EFFECTS OF SLEEP

CAUSES OF SLEEP

Salutary sleep depends on the excitement being raised, until a certain degree of indirect debility is produced.

“As the immediate cause of sleep consists in a suspension of volition, it follows, that whatever diminishes the general quantity of sensorial power, or derives it from the faculty of volition, will constitute a remote cause of sleep; such as fatigue from muscular or mental exertion, which diminishes the general quantity of sensorial power, or an increase of the sensitive motion, as by attending a soft music, which diverts the sensorial power from the faculty of volition; or lastly, by an increase of the irritable motion, as by wine, or food, or warmth, which not only by their expenditure of sensorial power diminish the quantity of volition, but also by their producing pleasurable sensations (which occasion other muscular or sensorial motions in consequence) doubly decrease the voluntary, and thus more forcibly produce sleep.”

Sleep may be produced by excessive direct or indirect debility; but such sleep is not salutary or refreshing, but what is termed morbid.

Sleep then is the effects of the actions of the day at first giving always more and more excitement, but less and less in proportion to the continuance of the operation, but in such sort as always to add some excitement, till the matter at last come to a point where the degree of excitement necessary to constitute the waking state no longer exists.

This state of indirect debility, which constitutes refreshing sleep, is commonly produced by the action of the various stimuli through the course of the days on the different senses, wearing out the excitability and raising the excitement to the sleep-giving point.

Particular pleasing sounds have the effect of producing sleep; such as the gentle tumbling of water over a cascade, the long continued sound of the falling of rain on the house, the buzzing of bees, vocal and instrumental music, and many other things that fix the attention for some time, so as to prevent it from changing to any other object, all constitute remote causes of sleep, and produce the effect in the same way that fatigue from muscular motion does, that is, by wafting the excitability and raising the excitement to such degree of indirect debility, which alone can give calm and refreshing sleep.

I cannot pass by the causes of natural sleep; without taking some notice of the power of habits in producing it. So great is its influence in sleep, as well as in all other things, that it has been justly termed a second nature; for instance, tobacco, that powerful narcotic and noisome weed; by use, becomes inoffensive, and, by long habit, even a luxury.

We know that, by a continued use, our most powerful medicines lose their effects in a great measure, as we daily see in practice. In giving of opium we are oft obliged to increase the dose as we continue the use of it, or we fail in the wished for effects.

One grain of opium would have a greater effect on me, who have never taken two grains in my life, than one hundred would on Doctor Bouchie,* a French physician, who has taken as much as one hundred
grains of opium and a pint of æther a day; here the very large quantity of one hundred grains of opium, by habit, became too little to ease the pains of a colic; for, in conjunction with it, he was obliged to take as much as a pint of æther also to procure ease to himself. (* case related by Dr. Sush, in his lectures*)

Dr. Say informed me that he had a patient who kept opium by her bedside, and chewed it until ease was obtained, which sometimes was to a considerable quantity; and another who takes from ten to fifteen teaspoonfuls of liquid laudanum in a day, having been long in the habit of using it.

I could mention many other instances of the surprising power of habit; bit I take it for granted, that those already mentioned will be sufficient to convince the impartial reader; if they should not, I must request him to recollect for a moment how many things he does daily, almost entirely owing to the force of habit, viz. we eat two, three, or four times a day. If we go to sleep for two days, at a certain hour, we are sure to be sleepy on the third day, at the same time.

Farther, so great is the power of habit that the miller does not find it difficult to sleep, while the mill is grinding, without being awakened by the noise. Dr. Zimmerman observes that “the soldier sleeps, even amidst the thunder of cannon.”

I do not wish to be thought here to insinuate that sleep depends alone on habit-no-I only wish to take this good opportunity of observing, how very cautions mankind ought to be of getting into any idle or injurious habit, since we see and know, how great and how irresistible is the power thereof.

In health we are not sensible of the good effects of sleep; but who has not experienced its health restoring, life prolonging effects, after having been denied its sweet repose for two, three, or four days together, by an acute disease, or some other sleep forbidding cause.? It appears to me that there is no part of our existence in which we enjoy more pleasure, and from which we derive more beneficial effects, than we do from sleep, and yet I may say that there is no part, in which mankind in general are not as well or better acquainted with themselves, than what they are during this state.

I may here observe, that although natural sleep is produced by the stimuli acting on the excitability, in such a manner as to diminish that and to raise the excitement to that degree which affords refreshing sleep; yet if these be too long continued and in too violent a degree, the excitement will be raised above the sleeping point, and must be reduced before salutary and refreshing sleep can be obtained. This must be done by giving of sedatives just strong enough to reduce the accumulated excitement to the natural sleeping point, or by using sedatives more powerful, and at once reducing the system into excessive direct debility, which produces morbid sleep of the most dangerous kind. I may further add, that an excess of the same cause that produces sleep will produce its opposite state, viz. watchfulness.

I have before observed, that sleep may be and oft is produced by very different causes; it is likewise attended with very different effects, as I shall show hereafter when speaking of the effects of sleep.

Hitherto I have only mentioned the natural causes of sleep. I shall now proceed to mention others that are very different, but that are indispen-sably necessary to be used at times: these are first, stimulants; second, sedatives. First, of stimulants: when the excitement is too low to provably necessary to be used at times: these are first, stimulants; second, sedatives. First, of stimulants: when the excitement is too low to

The remedies that are to be made use of are such as produce sedative effects: the most effectual for this purpose that I have ever seen, are:

First, blood-letting. This should be preferred to all other depleting remedies; because we have it more under command than any other. We can open a vein at any time, take as much as the case requires, or as our judgment directs; which may be known by feeling the pulse previous to benefaction, and by keeping our fingers on the pulse while the blood is flowing; by doing this we judge rightly of the quantity to be taken, by the pulse becoming softer and by the abatement of symptoms, such as pain, etc. but in order to effect this, sometimes in very violent cases I have seen it necessary to bleed as oft as four, five, or even six times, before the excitement would be sufficiently reduced to admit of sleep; but in less violent cases I have seen one bleeding act like an anodyne.

Second, purging. This acts nearly in the same way that blood-letting does, by depleting; but there is this disadvantage attending it, we have it not so much under our command as blood-letting, and if one will answer, we should prefer benefaction - but we oft find it necessary to use both, and with the happiest effect, in reducing the accumulated excitement to the sleeping point.

Third, vomits. These have the same effect, though they do not operate the same way exactly that a purge does, though they both deplete, if the evacuation is to be made from the stomach instead of the bowels, as is often the case; emetics answer best and frequently act like an anodyne.

Fourth, clysters. These are oft used with bloodletting, when it is improper to give purges, and they are oft used by themselves, with very good effects, where there is an irritation in the rectum from any cause; or where the excitement is but little too high, these acts as all other depleting remedies, though in a less degree than many others.

Fifth, cold bath. This has sometimes very wonderful effects in reducing the excitement, and keeping up an equilibrium in the system.

Sixth, cool air and cool subacid drinks. I have sometimes seen these effectual in reducing the excitement, and causing sleep, when there has
been but a very small accumulation of excitement.

Seventh, cold local applications, such as ice, or cloths dipped in cold water, or vinegar and water, and applied to parts partially affected, such as affections of the head, or other local inflammations. I have seen these attended with very good effects, in taking down the excitement and inducing sleep.

Eights, blisters have been very serviceable, when applied to parts locally affected, in reducing the system to the sleeping point.

Ninth, the sedative passions, such as fear, grief, etc. all act the same way that other sedatives do; that is, by reducing the excitement and procuring sleep.

Tenth and last, salvation. This may be used with advantage when most of the others have failed. I think there are very few in the practice of the healing art, who have not seen the good effects of mercury. Dr. Sush has called it the Sampson of the Materia Medica, and I think with propriety. But it is chronic cases that call for this remedy mostly; in but few others should it be used, especially when the lancet, which is a certain specific for accumulated excitement, can be employed.

I have now mentioned (in as few words as the importance of the subject would admit) the natural and artificial causes of sleep, I shall next take some notice of the sleep of children, and then proceed to the cause of vegetable sleep.

“The reason why children sleep so much, has been supposed to be owing to their want of reflex sensation. May not the phenomenon of sleep in children, be explained upon other physical causes and not upon the want of reflex sensation? That the excitability of children is more abundant, cannot or will not, I imagine, be denied, and from this I may justly infer, that the waking and sleeping state of children, do more easily run into each other than they do in adults: their excitability, therefore, is more susceptible of the action of stimuli of every kind, and the sleep-inviting point is consequently produced or brought on sooner in children, by fewer causes in a given time, than in adults.”

It appears to me probable, that the want of reflex sensation in children is a powerful cause of their sleeping so much: at this early period, their abundant excitability is powerfully wrought on by the weaker stimuli, which soon raise their tender excitement to the sleeping point; and as they have no reflex sensation, there is little or no counter action in their system: they at once sweetly fall away into that pleasing, death-like state, called sleep.

By the time they begin to acquire reflex sensation, they are capable of using exercise, either of crawling or walking, the fatigue of which makes up for the former want of reflex sensation, and sleep is still produced. We may observe, that their little minds, at this early period, are incapable of thinking long on any one subject; hence the reason why they change their amusements so often; and as every new amusement adds a new stimulus to the mind, the excitability is worn down in proportion as the state, called sleep.

Eights, blisters have been very serviceable, when applied to parts locally affected, in reducing the system to the sleeping point. We appear to enter life through the doors of sleep, and in natural death make our exit the same way: out of sleep we have awoke into time; and in time we come to an appointed for its change of place and mode of existence.

I suppose the foetus goes on, waking oftener as it advances to the time of its conception: it indeed, that its sensibility is thus suspended by sleep, or it would have more to suffer than its little nature could bear. This is the way in which this way I suppose the foetus continues, until weary of being so long in one position, it is again roused by the stimulus of its uneasy posture, it moves and instantly returns to its former destined state; happy for it, indeed, that its sensibility is thus suspended by sleep, or it would have more to suffer than its little nature could bear. This is the way in which I suppose the foetus goes on, waking oftener as it advances to the time appointed for its change of place and mode of existence.

We appear to enter life through the doors of sleep, and in natural death make our exit the same way: out of sleep we have awoke into time; and out of sleep we shall awake in eternity.

Second, I am now to mention the good effects of sleep to infants; that is, after their births. Here indeed, at this early period of life, human nature, in undergoing so great a change, stands in need of the softening influence of sleep.

I suppose this to be the case with vegetables; in the morning their irritability is much greater than in the afternoon or evening, because it is dissipated by the action of the stimuli through the course of the day; but during the silence of the night, all stimulus being withdrawn, they sleep, and during that state of repose their irritability is accumulated, which is again wafted by the action of stimuli the succeeding day; such as light, heat, air their voluntary and involuntary motions (which are very remarkable in some vegetables, viz. Mimosa, berberis vulgaris, cistus helianthemum, etc.) all which assist in wafting their irritability, and reducing them to that degree of indirect debility which constitute salutary sleep.

“We may lay it down as a pretty constant and certain axiom, that the sleep of vegetables is more or less profound in proportion to their vigour or debility. During the continuance of this sleep the appearance of the plants is so much changed, that the most experienced botanist is sometimes at a loss to know them, without a very minute examination, though as any other time the plants would be quite familiar to him.”

But as great as the difference is, in vegetables, between the sleeping and waking states, in man, that difference is far greater. (Dr. Benjamin S. Barton, professor of Materia Medica, Natural History and Botany.)

If we view man while awake and in action, his figure is majestic – his actions pleasing–his speech communicative–and his countenance portends something heavenly and divine.

But if we view him while asleep, how greatly is the scene changed! his majesty is flown–his actions ceased–his speech has failed–his countenance, the index of his very soul, is now neutral–and his sparkling eyes, half equal to his tongue for expression, while awake, is now closed in death-like darkness.

“The connection of causes and effects–traced in the vegetable world, and compared with those of the animal kingdom, point out the striking analogy between the two, and proclaim that nature is uniformly the same in all her works.”

**EFFECTS OF SLEEP**

The effects of sleep may be divided into good and bad. I shall begin with the good and point out its effects,

- First. To the foetus in utero.
- Second. The good effects of sleep to infants.
- Third. I shall mention the good effects of sleep, both to children and adults, in preserving health.
- Fourth and Last. It’s good effects in restoring health, when lost.

First. Of the good effects of sleep to the foetus in utero. I hope that it will not be thought presumptuous in me to suppose that the foetus in utero passes nearly the whole time of its gestation sweetly encircled in the soft arms of balmy sleep: that during the three or four first months of its conception it does not awake once. I suppose that, until this time, the liquor amnii is so mild and bland as not to give the least irritation to the tender embrio of human nature, which is as yet unable to bear the slightest injury with impunity; that after the third or fourth month the liquor amnii or something else, does irritate the foetus so as to rouse it for a moment from its lethargic state; but, happily for it, it soon falls away again into its former state of insensibility—that state intended by Providence as most suitable for its ease and most favourable for its growth. In this way I suppose the foetus continues, until weary of being so long in one position, it is again roused by the stimulus of its uneasy posture, it moves and instantly returns to its former destined state; happy for it, indeed, that its sensibility is thus suspended by sleep, or it would have more to suffer than its little nature could bear. This is the way in which I suppose the foetus goes on, waking oftener as it advances to the time appointed for its change of place and mode of existence.

We appear to enter life through the doors of sleep, and in natural death make our exit the same way: out of sleep we have awoke into time; and out of sleep we shall awake in eternity.

OF VEGETABLE SLEEP

Sleep is a function inherent in all living matter, and, for ought we know, may be attended with similar effects in all. May not the sleep of vegetables depend on the same cause that it does in animals, viz. indirect debility.

We know that vegetable in general possess most irritability in the morning – man’s excitability is greatest at the same time. Vegetables sleep most in the spring, which is the morning of their lives, because their irritability at this time is most abundant. Man also sleeps most at the commencement of life: for at this time I suppose his excitability is in the highest degree possible, to admit of good health; and also at this time being so very easily acted on by any stimulus, it is much sooner wafted and the excitement raised to the sleeping point, and by this death-like state it is again accumulated for the necessary purpose of life.
hand of a supreme being to shield their tender bodies from external injuries, which are as yet so exquisitely sensible—and what could have been found out to answer the purpose better than sleep? By this they are at once defended and refreshed. It moderates all the tumultuous motions in the human body.

“Thus the heart is gradually restored, from its quick and almost feverish pulsation, to the slow and calm condition we find it in the morning; the breathing, in sleep, becomes slower and smaller, the peristaltic motion of the stomach and intestines, the digestion of the aliment, the sense of hunger, and the progression of the faces, are all diminished at the same time; the thinner juices move more slowly on, while the more gross and sluggish are collected together; and the fat being poured out is accumulated in the cellular substance; the viscid, aluminous humours, for the nourishment of the parts, adhere more plentifully to all sides of the fibres and small vessels; the consumption of the spirits, the attrition of the blood, and the quantity of perspiration, are all diminished. Thus, while the quantity of the nervous spirits continues to be secreted, with less consumption, it is by degrees accumulated in the brain, so as to fill and distend the collapsed nerves, that both the internal and external organs return to action by the approach of some small stimulus, by which they are restored to vigilance.”* (*Haller’s Physiology.)

This is the time in which I suppose animals to grow, most particularly young ones; because during sleep the secretory organs perform their respective functions; and as all volition and voluntary motion is suspended, of course there cannot be so great a consumption of the secreted fluids, during the refreshing moments of balmy sleep; consequently more must go to the nourishment and growth of the body, especially during the infantile state, as there is less muscular motion and mental exertion, and more sleep, than at any future period of life.

Third. I am now, in the third place, to mention the good effects of sleep, both to children and adults, in procuring health. Few, very few, I believe, arrive to the years of knowledge who are not sensible of its good effects, especially after much fatigue either of body or mind. As the hungry soul seeketh food, and as the thirsty panteth for the cooling streams, so the wearied soul seeketh rest and refreshment from the down bed of balmy sleep; she findeth it and thereby health is preserved.

The wearied body of the playful child, or the industrious labourer, would soon grow sick and faint, if it was not for the restorative power of sleep.

The good effects of sleep are not confined to the body alone; but extends its heavenly influence also to the mind—and here let us for a moment pause, and contemplate the good effects there produced. The mind that refused to recollect or ever to think at all, while the body was languid for the want of refreshing sleep, as soon as it has been gratified with it, appears to be at once endowed with new powers of almost every kind.

Sleep, like many other blessings of heaven, if rightly and moderately used, is a source of much pleasure and of great good; but if misused and misapplied may be and is the cause of much evil.

Fourth. I am now, in the last place, to speak of the good effects of sleep in restoring health, when lost. Such is the nature of our constitutions, that whatever is habitual, nature accommodates herself to, and at length it becomes, as it were, natural to us; so that we cannot break off suddenly from any one habit with impunity, neither can suddenly take up any one, without risking the same. As sleep is both natural and habitual to us, of course there must be a greater danger from wandering out of that path which nature hath pointed out, and which habit hath made us acquainted with. This we are sensible of by experience; if we pass twenty-four hours without sleep, as we are accustomed to spend a part of that time in that pleasing state, we suffer from it both in body and mind, in a small degree; but if we pass the succeeding twenty-four hours likewise without it, we are much more sensible of the loss of sleep; our bodies feel dull, our heads ache, our appetites fail, our ideas are darkened, our imagination clouded, and our judgment weakened; in short, our whole bodies are disordered. In all such cases, natural, salutary sleep is the only true specific for us.

If from fatigue of body or mind, nature stands in need of the cordial power of balmy sleep, to restore us to our wanted health; and if, in many cases, sleep appears to act like a charm in dispersing indisposition and restoring health; I need scarcely hint how much may be learned from a patient, during sleep, by an attentive and skillful physician.

We may sometimes learn more of the true state and every cause of the disease, during sleep, by an attentive observation, than we can at others by inquiry while awake. How indispensably necessary then must it be, for every physician, to be well acquainted with the appearance, etc. of patients in different diseases, as well as in health, while asleep?

“Sound and uninterrupted sleep refreshes the body and mental powers, by accumulating or bringing back the greatly wafted excitation, to the stimuli of the preceding day, and preparing of fitting it for the operation of the exciting powers, of the succeeding day.”

Having now enumerated, as briefly as possible, the good effects of sleep, I shall proceed to mention the bad effects. First, in health. Second, in sickness.

Sleep, when continued long, induces debility, and this predisposes to diseases; for we know that the system is much more liable to disease, when debilitated by any cause, and we find by daily observation, that sleep, when continued long, always induces debility. Hence the reason why diseases attack so much oftener in the night than in the day, particularly inflammatory diseases: and in general, they attack in the latter part of the night, or in the morning, when sleep has ceased to be refreshing and invigorating, but, on the contrary, is morbid and debilitating.

“Sleep, continued for too great a length of time, disposes to all the disorders that attend a slow circulation; to fatness, drowsiness, weakness, and cachexies; and is, at the same time, highly detrimental to the memory.” I doubt not but that sleep, too long continued, has oft been the cause of fatuity and idiocy.

I imagine that six or seven hours of sleep at farthest is a sufficient length of time for an adult. I rather suppose, that sleep is seldom refreshing, when continued longer than that time; and we know, that as soon as it ceases to be refreshing, by its long continuance, it becomes very debilitating, not only to the body but also to the mind. If mankind were more attentive to their hours of sleep, and would break themselves of the idle and pernicious habit of sleeping ten or twelve hours, as some do, they would enjoy better community health and would be much more useful to community. No man that sleeps half his time, can ever become eminent in any thing, that will be of advantage to himself or to his country.

I do not conceive, that mankind, after arriving to the years of knowledge, were every intended by their Creator, to spend nearly half of their lives in a vegetable state (for man, during found sleep, is but little more) he was made for a nobler purpose than to spend the half of his life useless to his fellow mortals, useless to his Maker, and useless, nay, ungenerous to himself. I scarce see how it is possible for man, who enjoys good health, to be void of thinking, while the spacious earth and seas, by the light of day, present innumerable resources of knowledge, to the physician, as well as philosopher, for investigation; and the heavens, though veiled in the sable curtains of the night, display dazzling beauties, to this our earth, for the wonder of the ignorant and the observation of the wise.

I am now, in the second and last place, to mention the bad effects of sleep in sickness.

The bad effects of sleep, are most evident in diseases of excessive direct or indirect debility; in these cases, the effects of long continued sleep tend to death, by entirely exhausting the excitement. In many diseases, patients are apt to sleep very much, this is likewise morbid, and if long continued is highly injurious: they ought not to be suffered to sleep long: they should be waked regularly to take their medicines, and it is sometimes even necessary, to wake them as oft as two or three times of a night, to take some nourishment.

Patients, labouring under the convalescent state of diseases, ought to be very particular as to their sleep, as well as their diet: they should not sleep too much, for that is very debilitating, even in health; they should not set up too late at night, and they should rise early in the morning, for
this is the healthiest, as well as the pleasantest part of the day.

In the morning, the feathered songsters warble forth their enchanting notes to please the ear; the vegetable world mingle their rich odors, and saturate the morning zephyrs, with healthy perfumes to please the nose; and the variety and simplicity of nature please the eye more than all the laboured improvements of art.

Think of these things, O ye lovers of long sleep! and let them keep you from your pillows late, and let them raise you from your beds early, so shall you enjoy good health, while you view the beauties of nature in full perfection.

THE THOMAS BALL SLEEP AWARD

Catesby J. Ware, Ph.D.
Sleep Disorders Center
Eastern Virginia Medical School

Who are Richard Allen, Lynn D’Andrea, Jack Edinger, Robert Kowatch, Vaughn McCall, Charles Morin, Walter Mendelson, Samuel Pitolichio, Pamela Stubbs, Paul Suratt, Robert Vorona, Catesby Ware, Thomas Wehr and Maria Winn, and, what do they have in common? Those listed above are a select group of sleep clinicians and researchers who have won the Thomas Ball Sleep Award. This award is presented annually to a member of the Chesapeake Bay Sleep Society (CBSS) in recognition of his or her efforts to understand sleep. Unlike the highly organized and professionally run AASM and SRS, the CBSS has no budget, no dues, no meeting registration fee and no treasurer. What it does have is members from Virginia, North Carolina, the District of Columbia and Maryland who are interested in understanding sleep and sleep disorders.

Thomas Ball, the Virginian for whom the award is named, knew little about sleep by today’s standards when he completed a dissertation on the Causes and Effects of Sleep for his Doctor of Medicine degree in 1796. He did not talk about REM sleep, sleep apnea, and stimulus control techniques. He would not have been able to answer any of the basic sleep questions that today’s medical students may be asked when they take Part I of their board examinations. However, he was curious about what occurred during sleep and the effects of sleep. In this dissertation, Dr. Ball gives hints of things to come years later. The Thomas Ball award recognizes this spirit of inquisitiveness.

NEW MEMBERS

As the Sleep Research Society grows, we strengthen the impact of the profession by offering members unique education and research opportunities and keeping members abreast of current sleep research and topics. Information regarding membership can be found on the SRS Web site, www.sleep-researchsociety.org or from Judy Milton, SRS Coordinator at jmilton@aasmnet.org.

Help us spread the word about the benefits of SRS membership and get a bonus! Each member who recruits a new Full Member will receive a coupon redeemable for an SRS coffee mug! The newly revised SRS membership application is posted on the SRS web site in PDF format.

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Linda Toth, D.V.M., Ph.D. represented the Sleep Research Society at the September meetings of the Board of Trustees (BOT) of the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International. Following is her report to SRS members.

On September 20, 2003, AAALAC Council and BOT members met for a question/answer session with representatives of the NIH Office of Laboratory Animal Welfare (OLAW), the USDA, and the FDA. The main focus of the session was reduction of regulatory burden. Issues raised and discussed included minimization of the burden associated with ensuring congruence between grant proposals and animal protocols, minimization of regulatory focus on process as opposed to outcome, and avoidance of the regulatory creation of new requirements through interpretation of legislation.

On September 21, 2003, the BOT met for the annual business meeting. AAALAC reported that most of the biomedical research “market” has already been tapped, as 97 of the top 100 NIH grantee institutions are AAALAC-accredited, and two of the remaining three are currently seeking accreditation; 85% of the top 200 NIH-funded institutions are accredited. AAALAC estimates that over 90% of the animals used in research in the United States, including rodents, are maintained in AAALAC-accredited facilities. At present, the BOT is comprised of 66 member organizations. The 32 member Council on Accreditation, supported by over 25 emeritus council members and 175 ad hoc consultants, conducted site visits of 223 institutions between October 2002 and September 2003. Major outreach efforts for future accreditation will focus on agricultural research institutions in the United States and on foreign institutions. The financial position of AAALAC is sound.

Business reviewed at the BOT meeting included:

- Discussion of accreditation categories, which have been revised to increase clarity.
- Discussion of the primary intent of the accreditation process. Two interpretations of accreditation are that it is intended primarily either to provide assurance of quality within accredited institutions, or, alternatively, that it is intended to stimulate improvement of quality for the purpose of gaining and maintaining accreditation.
- Discussion of the use of AAALAC deficiency lists by animal rights organizations as a rationale for increased regulation of animal-based research and as ammunition against the use of animals in research.

As part of the reorganization of its Committee structure, in 2003 the SRS established a new Research Committee to focus on the Society’s policies and activities relating to research. Membership of this new committee includes: Mary Carskadon Ph.D., Chiara Cirelli, M.D., Ph.D., Charles Czeisler, M.D., Ph.D. (Chair), David Dinges, Ph.D., Max Hirshkowitz, Ph.D., Robert McCarley, M.D., Mark Sanders, Ph.D., and Linda Toth, D.V.M., Ph.D., with Ruth Benca M.D., Ph.D. serving as Board Liaison.

The Research Committee is charged with facilitating support for sleep research by NIH and other Federal and private resources; advising the SRS Board on matters of research funding, coordinating professional responses to research issues, and addressing general research-related matters. In accordance with this charge, the Research Committee is investigating a system to notify SRS members regarding non-government research opportunities similar to the system that Dr. Michael Twery has developed for notifying the sleep research community regarding U.S. government-supported research opportunities. The Committee is also developing initiatives to assess the basic research needs of the profession, such as addressing research issues related to animal care, research ethics, and dissemination of research findings. Finally, the Research Committee has been charged with evaluating and administering the SRS Young Investigator Award and the Junior Faculty Development Program, and with developing new awards that highlight achievements in sleep science.

The Research Committee is planning to meet early in 2004 to develop recommendations for new research-related programs and activities for the Society. We would welcome your input and suggestions as to activities that the Research Committee might pursue in addressing the mission it has been given by the SRS Board to foster sleep research. Please email your comments or suggestions to jmilton@aasmnet.org.
On October 21-23, 2003, Dr. Giulio Tononi presented the inaugural Pfizer Lectureship in Sleep at the University of Michigan. The Pfizer Lectureship in Sleep is a joint effort between Pfizer Global Research and Development, the Department of Anesthesiology and the Neuroscience Graduate Program of the University of Michigan, and Henry Ford Hospital. The aim of this joint effort is to bring leaders in the field of sleep research and academic sleep medicine to the University of Michigan Ann Arbor campus.

As part of the Pfizer Lectureship in Sleep at the University of Michigan, Dr. Tononi presented a seminar for the neuroscience community entitled “Genes and Sleep.” This seminar focused on data obtained in collaboration with Dr. Chiara Cirella, also of the University of Wisconsin. Using a variety of techniques and models ranging from *Drosophila* to rodents and humans, Dr. Tononi has demonstrated changes in expression of groups of genes that correlate with wakefulness and sleep. The demonstration, using many mammalian criteria that *Drosophila* sleep, was also the topic of a roundtable discussion at the Pfizer Global Research and Development Ann Arbor campus.

The final event in the series was a dinner lecture held in the Pendleton Room of the historic Michigan Union building. After dinner, 90 basic scientists and physicians from southeast Michigan and northwest Ohio listened to Dr. Tononi speak on “The Mind and Consciousness.” During this presentation, Dr. Tononi addressed the problem of how activities of functionally specialized areas of the brain can be integrated to give rise to a unified conscious state.

Dr. Tononi, received his medical degree and specialized in psychiatry at the University of Pisa, Italy. After serving as a medical officer in the Italian Army, he obtained a Ph.D. in neuroscience as a fellow of the prestigious Scuola Superiore S.Anna, based on his work on the mechanisms and functions of sleep. From 1990 to 2000, he was a Senior Fellow in Theoretical and Experimental Neurobiology at the Neurosciences Institute, first in New York and then in San Diego. Dr. Tononi is currently Professor of Psychiatry at the University of Wisconsin, Madison, where he studies the mechanisms by which the brain gives rise to conscious experience and continues his work on the functions of sleep.

Dr. Tononi is a frequent lecturer and invited speaker at scientific symposia. He is the author of more than 120 scientific publications, co-editor of the volume *Selectionism and the Brain* (with Olaf Sporns), and author of two recent books on the neural basis of consciousness: *A Universe of Consciousness* (with Gerald M. Edelman) and *Galileo and the Photodiode*. It was an honor to have Dr. Tononi present the inaugural Pfizer Lectureship in Sleep.
Sleep Research in India
School of Life Sciences
Jawaharlal Nehru University
Birendra Nath Mallick, Ph.D., D.M.S., F.N.A.Sc.

It is an honor and privilege for me and I thank Dr. Larry Sanford, editor of the SRS Bulletin, for inviting me to participate in this feature of International laboratories on view. Although it is very difficult task to write about my own work, I will try to do with all humility. However, at the onset I must acknowledge the knowledge gained from all my teachers and the Ph.D. theses work done by my students, without which it would not have been possible to reach to this stage.

In India, like in several other countries, biomedical research is controlled primarily under two broad administrative organizations, the University and the Institute. In the case of the former, one remains amidst young, fertile minds and has to constantly interact with the ever-inquisitive students. Since I had a natural liking and bent of mind for teaching and research, I was happy to be selected (1986) for the Assistant Professor’s position at the School of Life Sciences, Jawaharlal Nehru University (JNU), New Delhi, India, a premier post-graduate University having emphasis on basic research. It was a coincidence that the post was advertised around the time I was submitting my Ph.D. thesis at the All-India Institute of Medical Sciences (AIIMS), New Delhi, India, a premier Medical Institute in the country. Because of my selection in the JNU, I requested Prof. Jerry Siegel, Ph.D., UCLA, USA to kindly allow me to join his lab as a post-doctoral fellow after a year. I am grateful that he was very kind to oblige me.

In the School of Life Sciences, JNU, I am involved in teaching courses on Cell Biology, Neurobiology and Physiology to the students enrolled for Master’s and Ph.D. degrees. The course contents are modified from time to time and the core course on Cell Biology was modified to include a section on Neural Cell Biology. At the time of my joining the JNU, neurobiology research was at a low level compared to that of research in other fields of science and sleep research was not there. However, I was fortunate that the School has a Central Instrument Facility (CIF) where heavy equipment is housed and can be shared by any member of the school. The CIF is the backbone for research in this school, especially for a new faculty. Although for studies using electrophysiological recording methods and for sleep studies there was only a four-channel polygraph and an oscilloscope, it was better quipped for biochemical and biophysical investigations. Gradually I have been able to compete and attract reasonable funding from various national-level funding agencies. At present, my lab is equipped to study behavioral sleep-wakefulness in animals using electrophysiological recordings and to correlate them with gross behavior as well as single neuronal activities in freely behaving animals. Micro-injection and micro-iontophoresis have been successfully used in the lab to understand the subtype of receptors present on neurons in specific regions in the brain and that are involved in sleep-wakefulness and thermoregulation. Furthermore, changes in other biochemical, micro-anatomical, immuno-histochemical correlates in relation to sleep-wakefulness and their deprivation are being studied in the lab. In addition, more recently the lab is set for molecular biology studies where cell-line cultures, as well as primary culture of neurons, are done to understand the cellular mechanism of such action at the intracellular microenvironment and molecular levels. Thus, my lab (along with the CIF) is reasonably equipped to understand Neural Mechanism and Functions of Sleep and REM sleep from behavioral to cellular to molecular levels. Our school is planning to acquire a proteomics facility while neighboring Institutes have electron microscopic and microarray facilities.

My research work can be divided primarily into two aspects. One is the investigation of where the neural mechanism (neurophysiological and neurochemical) Sleep-Wakefulness especially that of REM sleep; second is the study of the function and/or the physiological role of REM sleep and its possible mechanism of action.

Mechanism of Rapid Eye Movement (REM) Sleep Generation and Regulation

Cholinergic and norepinephrine (NE)-ergic neurons communicate for the generation of REM sleep. Studies during my one-year stay as a post-doctoral fellow in Prof. Jerry Siegel’s lab revealed that those neurons alter firing rates after REM sleep deprivation (Mallick et al., 1989, 1990). Those two are probably the only published reports where single neuronal activities in freely moving animals have been continuously monitored for 96 hrs. Since the NE-ergic REM-OFF neurons in the locus coeruleus (LC) cease firing during REM sleep and continue firing during REM sleep deprivation, it was hypothesized that cessation of those neurons is probably prerequisite for the generation of REM sleep. To prove that, the LC neurons were not allowed to cease firing by continuous but mild electrical stimulation (work by Dr. Sangeeta Singh, my Ph.D. student) which decreased REM sleep while there was rebound increase in REM sleep after the stimulation was stopped (Singh and Mallick, 1996). However, the questions that followed were (1) why do those neurons not cease firing during wakefulness, but do so only at certain depth of slow wave sleep, (2) why does REM sleep not follow every slow wave sleep episode, and (3) what is the neurochemical mechanism of cessation of firing of the REM-OFF neurons for the regulation of REM sleep?

My Ph.D. students Drs. Stephen Thankachan and Satvinder Kaur (presently both are at Dalhousie University, Canada) carried out the studies. Results showed that the wakefulness area in the brain activates the REM-OFF neurons but inhibits the REM-ON neurons (Thankachan et al., 2001), while the sleep area in the brain stem stimulates the REM-ON neurons (Mallick et al., 2004). Thus, it was shown that the wakefulness and the sleep areas in the brain modulate the REM-OFF and the REM-ON neurons for the regulation of REM sleep (for review, see Mallick et al., 2002).

Further, we showed that neurochemically GABA in LC regulated REM sleep (Mallick et al, 2001, Kaur et al., 1997, 2001, 2003) possibly inhibiting the REM-OFF neurons. Based on these results neuronal connections explaining the mechanism of cessation of the REM-OFF neurons for the generation and regulation of REM sleep have been modelled in Fig. 1. The model also explains why levels of NE increase in the brain
after REM sleep deprivation. As a mechanism of action it has been shown that there is increased synthesis of tyrosine hydroxylase within the NE-ergic neurons in the LC which then increases NE turnover in the brain (Majumdar and Mallick, 2003). This paper describes localization and quantification of the enzyme within a particular neuron.

It is known that the concentrations and activities of degrading enzymes would also modulate the levels of respective neurotransmitters. My student, Mahesh Thakkar Ph.D. (presently at Harvard University, USA), showed that REM sleep deprivation affects acetylcholinesterase (Thakkar and Mallick, 1991; Mallick and Thakkar, 1991, 1992) and monoamine oxidase (Thakkar and Mallick, 1993) activities. These results suggested that not only increased synthesis but also decreased breakdown of those neurotransmitters play a significant role in modulating acetylcholine and NE levels in the brain during spontaneous REM sleep and its deprivation.

**Function of REM Sleep**

My working hypothesis is that “one of the functions of REM sleep is to maintain brain excitability” and my lab is working towards understanding its possible cellular mechanism of action. The work has been carried out by Dr. Seema Gulyani, presently in the USA; Dr. Anupama Gopalakrishnan, presently at the University of Wisconsin-Madison, USA; and the late Md. Faisal, who unfortunately was killed in a tragic road accident. It has been shown that REM sleep deprivation increases ATPase activities, the primary factor responsible for maintenance of brain/neuronal excitability (Gulyani and Mallick, 1993; Mallick and Gulyani, 1993). REM sleep deprivation also affects neuronal responsiveness through changes in membrane fluidity (Mallick et al., 1995) and calcium concentrations (Mallick and Gulyani, 1996). As a mechanism of action it was found that the REM sleep deprivation induced increase in Na-K ATPase activity is mediated by NE acting on α-1 adrenoceptor (Gulyani and Mallick, 1995). The NE causes release of membrane bound calcium (Mallick and Adya, 1999) which then dephosphorylates the Na-K ATPase causing its activation (Mallick et al., 2000). Sequence of molecular to cellular to behavioural changes, induced by REM sleep deprivation, as possible mechanism of increased in brain excitability and disorder(s) thereof have been shown in Fig 2. Studies have also found that after REM sleep deprivation the increase in the Na-K ATPase activity is due to withdrawal of un-competitive inhibition (Adya and Mallick, 2000). Further, recently it has been shown that after REM sleep deprivation there is enhanced synthesis of the Na-K ATPase molecules in the brain (Majumdar et al., 2003).

Thus, isolated studies showed that normally the REM-OFF neurons cease firing, possibly by GABA, for the generation of REM sleep. During REM sleep deprivation since those neurons do not cease firing; there is increase in NE in the brain. This increased level of NE increases the Na-K ATPase activity in the brain. To confirm this, we blocked GABA in the LC for longer time in freely moving animals and showed that there was REM sleep loss and simultaneously there was increased Na-K ATPase activity in the brain (Kaur et al., 2003). Presently, using molecular biology tools, we are working on understanding the molecular mechanism of NE induced increase in the Na-K ATPase activity.

**Mechanism of Sleep-Wakefulness and Relation to Thermoregulation**

Work in this section was carried out by my Ph.D. students Dr. Md. Noor Alam (presently in UCLA, USA), Dr. M. M. Joseph (Presently in UCLA, USA) and Dr. Sushil K. Jha (presently in University of Pennsylvania, USA). The preoptic area in the brain regulates sleep-wakefulness and body temperature simultaneously and the two functions influence each other. I argued that the preoptic area has independent parallel pathways to regulate those functions and experimentally showed that regulation of the two functions may be dissociated, however, they go hand in hand to maintain the latter within phys-
iological limit, i.e., one of the functions of sleep is to maintain the body temperature (Mallick and Alam, 1991; 1993). It was also shown that the medial preoptic area is more effective than the lateral portion in modulating hypnogenesis and thermoregulation (Alam and Mallick, 1990, 1991, 1994). Subsequently, we explored the possible mechanism of action of one neurotransmitter, NE, acting on the same brain area, the medial preoptic area, for the regulation of sleep-wakefulness and body temperature. The observations unravelled a unique physiological regulatory mechanism that NE alters sleep, wakefulness and body temperature by acting on α-2, β and α-1 adrenoceptors, respectively (Mallick and Alam, 1992). This is unique in its concept as well as finding. It helps explain complex regulatory mechanism/s including NE induced preoptic area mediated simultaneous but independent effects on sleep-wakefulness and thermoregulation. Subsequently, at the cellular level Dr. Matsumura’s group in Japan and we microiontophoretically confirmed that sleep related neurons possess α-2 while the thermosensitive neurons possess α-1 adrenoceptors (Jha et al., 2001; Mallick et al., 2002), respectively. Further, we have also studied the role of cholinergic inputs into the preoptic area (Mallick and Joseph, 1997) and its interactions with adrenergic input for sleep-wakefulness and thermoregulation. These studies suggested that the cholinergic and adrenergic systems have parallel inputs into the preoptic area where they are integrated and the output is an algebraic sum of those inputs (Mallick and Joseph, 1998).

Marker Molecule for REM Sleep Deprivation Identification

Although REM sleep deprivation has very serious effects on our behavior, as of now there is no marker molecule for easy identification and quantification of the loss of REM sleep. Studies in our lab during the past five years have been able to identify a molecule in the rat. The molecule has been purified, the sequence has been determined and an antibody has been raised against it (unpublished work done by Bibhuti B. Mishra and Vibha Madan). The chemistry and physiology of the molecule are under study.

Changes in Cellular Morphology after REM Sleep Deprivation

The effects of REM sleep deprivation on brain neuronal morphology, cell structure and cytoskeleton have been studied. Results show that REM sleep deprivation facilitates apoptosis in the brain cells (manuscript under preparation, work by Dr. Sudipta Majumdar, presently in USA). The mechanism is under investigation. This could be one of the contributing factors for neuronal cell loss related diseases because REM sleep is reduced with aging.

Thus, at present my lab is equipped with facilities to carry out work from behavior to cellular to molecular levels. My efforts are to take a holistic view and attempt to unravel the mysteries one by one. We develop and adopt technique(s) as and when needed to find an answer to the problem raised. Science is fast developing and I am fully aware and recognize the need for collaboration for doing better science and I am open to such ideas.

Now it is more challenging to get major funding to sustain elaborate research. In recognition of my work, I have been conferred several National level awards by the Indian Council of Medical Research, Department of Biotechnology, Council of Scientific and Industrial Research, under the Government of India, to name a few. Several of my Ph.D. students received best-published paper awards.

However, the ride has not been smooth throughout. During the last several years, the animal activists particularly targeted my animal research, which had almost come to a halt for about three years. They were insensitive to any argument and logic, even those for the benefit of the animals. Finally, it has been resolved by the intervention of the Prime Minister of India. I am grateful to the PM for his vision and support for the cause of science. I am also thankful to all others who stood by my science during those trying moments.

Some of the problems in working here are that we primarily depend on the Ph.D. students and the post-doctoral culture is not very effective. The other disadvantage here, as compared to the USA, is that the overall system has to be geared up, e.g., obtaining chemicals takes at least one and a half month and often longer. However, I must accept that it has been much better than it was about a decade ago. Also, the administrative machinery of funding agencies has to be research-friendly in terms of the timely release of funds, etc. Notwithstanding, one positive aspect of my job here is that it is a permanent position and I do not have to constantly worry about my salary for survival, unlike several of my counterparts in other parts of the world as I am told. The positive aspect of such a position is that one has the freedom to think and work at will, of course, with responsibility and honesty. I believe, because of such freedom I have been able to carry on so far.
**SLEEP RESEARCH SOCIETY**

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