

NIH Funding of Sleep Research: A Prospective and Retrospective View

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WHILE REMARKABLE STRIDES HAVE BEEN MADE IN UNDERSTANDING FUNDAMENTAL NEUROSCIENCE OVER THE LAST DECADE, insights into mechanisms underlying sleep and its disorders have come more slowly. In recognition of the need to focus upon sleep research, the National Institutes of Health (NIH) established the National Center on Sleep Disorders Research (NCSDR) within the National Heart, Lung and Blood Institute (NHLBI). The NCSDR was mandated by Congress: *to support research, training, health information dissemination and other activities with respect to sleep disorders, including biological and circadian rhythm research, basic understanding of sleep, chronobiological and other sleep-related research, and to coordinate the activities of the Center with similar activities of other Federal agencies, including the other agencies of the NIH, and similar activities of other public and nonprofit entities.*

The legislation further provided for establishment of a Sleep Disorders Research Advisory Board composed of non-federal experts and ex officio federal members and it mandated development of a National Sleep Disorders Research Plan (www.NHLBI.PHS.gov/NHLBI/sleep/sleep.htm). The Plan, released by NIH Director Harold Varmus, is broad and multidisciplinary in recommending the strengthening of existing sleep research programs and creating new programs that address important research gaps and opportunities. The major themes of the Plan's recommendations include the need to apply today's most advanced techniques and technologies to the study of 1) basic science, and patient-oriented research in sleep and its disorders, and 2) daytime sleepiness, so as to reduce its negative impact on society.

Needs and opportunities receiving special emphasis in the Plan include:

- Understanding the cellular, molecular and genetic basis of sleep and its disorders.
- Determining the epidemiology of variations in sleep and sleepiness in health and disease.
- Identifying the effects of sleep loss on the waking function of the brain, other systems, and behavior.
- Elucidating the pathophysiology and optimal management of common sleep disorders and developing new technologies to accomplish this task.
- Learning to manage sleep-wake function to optimize health and performance in the 24-hour society, including developing new technologies to address evaluation, diagnosis and prevention of the causes of sleepiness.
- Determining the functions of sleep.
- Training investigators to expand the pool of sleep researchers.

In seeking to facilitate implementation of the Plan, the Board identified a number of new directions. The NCSDR with its partners at the NIH has initiated several workshops, Program Announcements (PAs) and Requests for Applications (RFAs), including those on the Basic and Clinical Research on Sleep and Wakefulness, Molecular Approaches to the Study of Sleep, Neuroscience Technology Development, Obstructive Sleep Apnea in Children, Genetic Architecture of Complex Phenotypes, Phenotypic Characterization of Sleep in Mice, Basic and Clinical Research in Fibromyalgia, the Sleep Institutional National Research Service Award, and the Sleep Academic Award.

In order to assess the distribution of NIH-funded research in sleep prior to implementation of the Plan, a subcommittee of the Board evaluated the distribution of sleep grants funded by NIH in fiscal year 1995, the funding period preceding release of the National Sleep Disorders Research Plan. This subcommittee comprised Drs. Tom Roth (analysis coordinator), Tim Roehrs, Allan Pack, Fred

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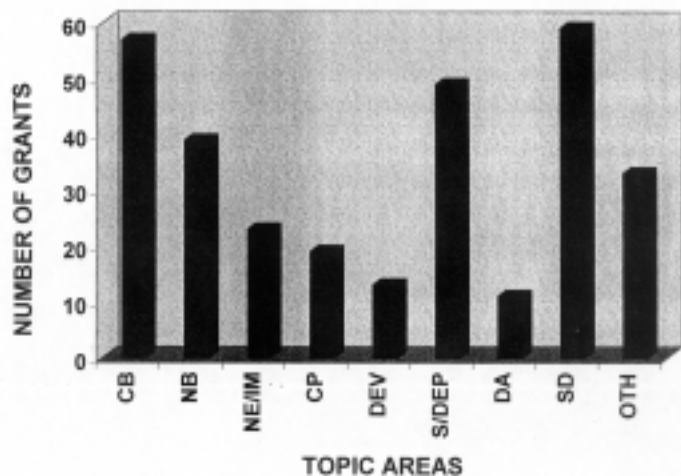


Figure 1—Number of grants by topic areas for all NIH funded grants in fiscal year 1995. CB-Circadian Biology, NB-Neurobiology, NE/IM-Neuroendocrine/Immune, CP-Cardiopulmonary, DEV-Devices, S/DEP-Sleep/Depression, DA-Drug Abuse, SD-Sleep Disorder, OTH-Other

Turek, Barbara Phillips, Chris Gillin and Martha Gillette (Chair). The intention was to provide a profile of NIH-funded research selected strictly by peer-review for reference in future years.

The first step in the analysis was conducted by program administrators of the sleep portfolios of eight trans-NIH Institutes represented on the Sleep Disorders Research Advisory Board (National Heart, Lung and Blood Institute, National Institute of Neurological Diseases and Stroke, National Institute of Mental Health, National Institute on Aging, National Institute of Child Health and Human Development, National Institute of Alcohol Abuse and Alcoholism, National Institute of Nursing Research, and the National Institute of Drug Abuse). Program officers used key words (*) to search the CRISP system (Computer Retrieval of Information on Scientific Projects). The list of grants identified by the key words/CRISP search was compared with the list of sleep-related projects provided by the Institutes to generate the final list of sleep grants funded during FY95 for analysis.

Next, information was compiled regarding grant number, which encodes the funding instrument, principal investigator, institution, title and total dollar amount of the award, and then the abstracts were collated. Each member of the Sleep Grant Evaluation Subcommittee was assigned roughly 50 grants near their area of expertise for primary review. Additionally, every twelfth grant on the list (10% of the total) was assigned at random to a committee member for a secondary review, to cross-check scoring patterns. The scoring system applied during this evaluation was developed by Martha Gillette in consultation with the full Sleep Disorders Research Advisory Board. It permitted categorization of each grant according to the general topic area within the sleep field, the sleep disorder addressed, the levels of inquiry utilized by the research (from molecular to

epidemiological), the organismic state under assessment (from normal/diseased, genetic variant or age of the subject) and the methodology/assessment mechanisms. Score sheets were analyzed and cross-checked by Tim Roehrs, who was blind to the information in grant abstracts. General findings are summarized here.

The total number of sleep grants funded in FY95 was 341, ~5 % of the nearly 7,000 total new and competing NIH grants. Dollars committed to sleep research totaled \$72.8 million, ~7.7% of the \$9.4 billion total for NIH grants. The range of funding instruments, from ROIs and FIRST awards to Program Projects and Clinical Trials, was included in this analysis. There was general agreement by committee members that these grants were appropriately categorized as sleep-related grants. Recognizing the success of this identification process, the committee asked the program officers of the Institutes that participated in the gleaning process to provide them with the list of key words used in identifying these grants, in order that the same criteria could be used to identify awards in the broad area of sleep when this exercise is repeated in the future, but noted that the key words alone provide only a partial accounting of all NIH sleep-related research. Further, evaluation of the cross-checking process revealed a good correlation between reviewers in the scoring process. Thus, the scoring matrix applied by the subcommittee was judged useful for the evaluation process and recommended for use in future evaluations of sleep grants.

It is important to note that grants funded in 1995 were written and, for the most part, reviewed before 1995. Therefore, this analysis provides a profile of the range and foci of funding before the Sleep Research Plan was published, and before announcements of directed sleep research initiatives. Thus, this analysis provides a profile of sleep research that was initiated by investigators and competitive in the general peer review process prior to dissemination of the Research Plan.

The findings of the grant analysis were unambiguous and provide an interesting profile. Noteworthy observations include:

- Fully half of sleep grants were clinical in nature, while 30% addressed basic research and 20% applied sleep research.
- The distribution of topic areas was broad. The largest numbers of grants were in the category of sleep disorders (19%), followed closely by circadian biology and sleep/depression. The fewest grants were identified as addressing drug abuse and sleep, devices, cardiopulmonary, and neuroendocrine/immune issues, which together comprised 21% of the total. The relative distributions across topic areas are presented in Figure 1.
- The predominant experimental paradigm involved behavioral analysis. Fifty per cent of the studies were con-

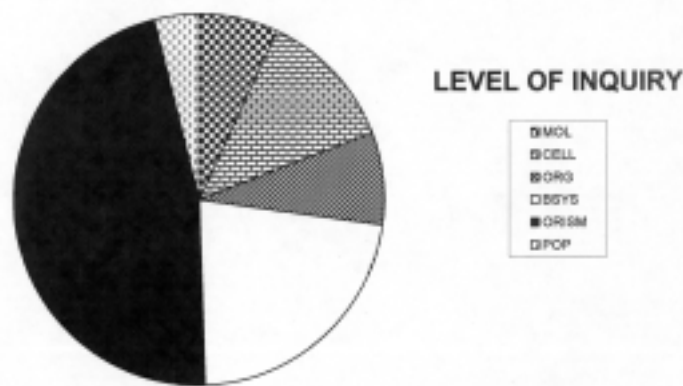


Figure 2—Level of inquiry employed by all NIH-funded grants in fiscal year 1995. MOL—Molecular, CELL—Cellular, ORG—Organ, BSYS—Body System, ORISM—Organism, POP—Population

ducted on humans. This is a very different focus than in many areas of NIH research. Furthermore, although the percentage of grants focusing upon human subjects was high, few studies were epidemiological in their approach.

- Research at the organismic level was by far the most prevalent level of inquiry. Studies of organisms were nearly twice those analyzing sleep at the level of body systems, the next highest category. Basic sleep science, particularly non-human, was substantially under-represented with respect to model systems, as well as molecular and genetic approaches. Again, this sets sleep research apart from other research areas in which cellular, molecular and genetic bases of brain function and disorders are better understood. Figure 2 presents the aggregate data on levels of inquiry summed over all the grants. Because many grants proposed multiple approaches, this total exceeds that of the total awards.

- Among the sleep disorders, significant numbers of grants were supported in sleep apnea and insomnia. There were, however, extremely limited numbers of grants investigating other disorders, in particular, restless legs syndrome, narcolepsy, and issues of pediatric sleep disorders.

A subset (225) of these grants was analyzed for demographics of the Principal Investigators. The age distribution of these awards was as follows: <36 yr = 15 grants, 36-45 yr = 71 grants, 46-55 yr = 92 grants, > 55 yr = 36 grants, with 11 awards unclassifiable using this criterion.

The Sleep Disorders Research Advisory Board has considered the broad profile of this investigator-initiated body of funding. Interestingly, the development and dissemination of the Sleep Research Plan highlighted a number of scientific gaps that this analysis identified independently. Obviously under-represented areas have become the targets for developing special initiatives to encourage submission

of grant applications so directed.

Finally, this exercise has pointed to additional strategies for fostering sleep research. These include more targeted training opportunities, proactive measures to accomplish the goals of the Sleep Research Plan, communicating research needs to epidemiologists, a "blitz" approach of information dissemination, particularly regarding research gaps, to both established and young investigators, and novel strategies to recruit new investigators and implement the Plan. Additionally, public awareness will be enhanced through the development of informative materials for dissemination via radio, physician's offices, and the public schools.

Director Varmus envisioned the Plan "not as a blueprint, but as a dynamic springboard for the creativity of individual scientists, whose insights and initiative underlie research progress". We urge you to heed this call and seize the opportunity to participate in this mandate to provide a solid foundation of understanding of sleep, sleep disorders and sleepiness. We all will reap the benefits of improvement in the health and well-being of the nation.

For further information on sleep and sleep disorders research, contact the National Center on Sleep Disorders Research, NIH (301-435-0199) or email comments to NCSDR@NIH.GOV.

** Sleep, Sleep Deprivation, Sleep Regulatory Center, Circadian Rhythm, Wakefulness, REM Sleep, Apnea, Sudden Infant Death Syndrome, Respiratory Center Dysfunction, Respiratory Airflow Disorder, Consciousness, Attention, Arousal, Narcolepsy, Bed/Bedding, Biological Clock, Chronic Fatigue Syndrome, Dream, Fatigue, Relaxation, Rest, Reticular Formation.*