



The Stanford Center for Sleep Sciences

Exploring New Frontiers in Human Health

THE
STANFORD
CHALLENGE

Seeking Solutions, Educating Leaders

“Sleep is one of the most important predictors of how long you will live—as important as whether you smoke, exercise, or have high blood pressure or cholesterol. ... Unhealthy sleep remains American’s largest, deadliest, most costly, and least studied health problem.”

William C. Dement, MD, PhD

DIRECTOR EMERITUS, STANFORD SLEEP MEDICINE

LOWELL W. AND JOSEPHINE Q. BERRY PROFESSOR OF PSYCHIATRY AND BEHAVIORAL SCIENCES

“Sleep restores not only the brain but also the entire body, and sleep disorders have important connections with all areas of medicine.”

Emmanuel Mignot, MD, PhD

DIRECTOR, STANFORD CENTER FOR SLEEP SCIENCES

CRAIG REYNOLDS PROFESSOR OF SLEEP MEDICINE

The Stanford Center for Sleep Sciences

Exploring New Frontiers in Human Health

Seventy million people suffer from chronic, severe sleep disorders in the United States alone. For example, no other chronic disease afflicts more Americans than sleep apnea, a potentially fatal condition that causes people to stop breathing sometimes several hundred times a night.

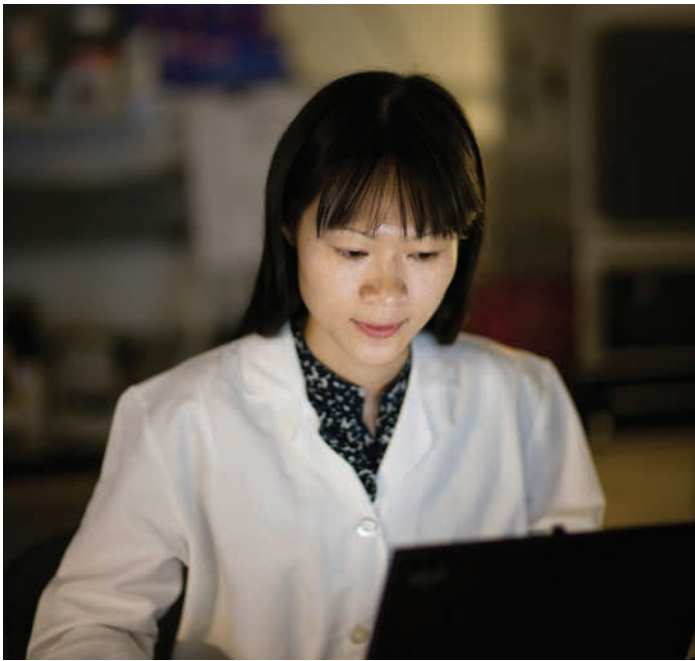
Crippling sleep deprivation is just one result of these disorders (and of our cultural bias against getting enough sleep). In addition to devastating careers and relationships, sleep deprivation causes accidents responsible for countless injuries and deaths.

Unhealthy sleep is linked with heart disease, depression, obesity, and lower life expectancy. Financially, the cost of sleep disorders and sleep deprivation in the United States is in the hundreds of billions of dollars per year. Moreover, at least 80 percent of sleep disorders go untreated. This is an urgent but poorly understood challenge.

As the birthplace of sleep medicine, Stanford has driven considerable growth in sleep research and treatment. Unfortunately, however, the field is still young and less widely recognized than more established areas of medicine. Vital work is needed, but funding from traditional sources is extremely limited.

Now Stanford is seeking private support to expand sleep research and patient care. Stanford’s advantages in this area include a medical center that integrates research and treatment to an unusual degree, and a high level of collaboration with other scientists and engineers all over campus. These are vital strategies in a subject as complex and a field as new as sleep.

Because sleep encompasses some of the greatest remaining mysteries in the biological sciences, breakthroughs in this area will constitute some of the foremost advances in human health in this century.



COMMON SLEEP DISORDERS AND IMPACT ON OVERALL HEALTH

At some point in their life, at least three-quarters of all adults will suffer from one or more of the approximately 90 different diagnosable sleep disorders. (By comparison, Alzheimer's disease affects about 4 million Americans.) Stanford sleep research and treatment focuses on disorders including the following:

INSOMNIA debilitates no fewer than 14 percent of Americans. It has been shown to be one of the strongest predictors of depression later in life. But new therapies, including some that do not require medication—such as sleep restriction, light therapy, better sleep habits, and cognitive therapy—bring 80 percent to 90 percent satisfaction even in severe cases.

OBSTRUCTIVE SLEEP APNEA afflicts 30 million Americans, or 10 percent of the population. Soft tissue in the airway stops breathing repeatedly during sleep, preventing deep sleep, causing low oxygenation, and resulting in sleep deprivation. Apnea is now accepted as the leading treatable cause of hypertension and is a strong predictor of stroke and heart disease. Difficulty with memory, intimacy, and attention are common.

CENTRAL SLEEP APNEA, a less common type of sleep apnea, affects several million Americans. Although people with central sleep apnea seldom snore, symptoms and results are much the same as the obstructive type—a deprivation of oxygen and poor sleep. About 40 percent to 60 percent of persons with heart failure have central sleep apnea.

RESTLESS LEGS SYNDROME (RLS) afflicts 12 million Americans. An uncontrollable urge to move the legs, often associated with painful sensations, seriously disrupts sleep. The genetic basis of RLS has just been discovered. RLS is also associated with depression, anxiety, and heart disease.

NARCOLEPSY AND IDIOPATHIC HYPERSOMNIA (disabling daytime sleepiness) shatter more than 200,000 lives in the United States. In addition to sudden, unpredictable sleeping, they can cause cataplexy, a muscular collapse brought on by emotional excitement. Lifelong treatment with stimulants or powerful sedatives is often required but brings only partial relief. Although the cause of narcolepsy is now established, almost nothing is known regarding idiopathic hypersomnia and its treatment.

SLEEP DEPRIVATION

- In the United States, a car accident occurs approximately every minute due to drowsy driving.
- Sleep-deprived medical interns make 36 percent more serious medical errors than those on a schedule that eliminates extended work shifts.
- Sleepiness was a strong contributor or the major cause of the Three Mile Island radiation leak, the *Exxon Valdez* oil spill, and the Bhopal, India, chemical release.
- Stanford tests of reaction times established that people who are tired because of disrupted sleep perform about as poorly as subjects who are legally drunk.
- Although more than \$300 million is spent every year on public education to prevent drunk driving, which kills 14,000 Americans per year, less than \$300,000 is spent annually on public education to prevent drowsy driving, which kills about 8,000 Americans every year.



STEVE FISCH



DALE HIGGINS PICTURES

MILESTONES IN SLEEP MEDICINE

For centuries, sleep was thought to represent the body shutting down and the brain turning off. The advent of the electroencephalogram (EEG) revealed just how active the brain is during sleep. In 1953, Nathaniel Kleitman of the University of Chicago used EEG to discover rapid eye movement (REM) during sleep. One of his students, William Dement, showed that REM sleep occurs as one of several distinct phases in the sleep cycle.

Dement came to Stanford in 1963 and by 1970 established the Stanford Sleep Medicine Center, the world's first accredited sleep center. He and his close associate Christian Guilleminault, MD, went on to conduct the first major research studies on sleep disorders. Over the years, Stanford has been the site of numerous advances in sleep, such as:

- **1973:** Guilleminault coins the term “obstructive sleep apnea.”
- **1978:** Mary Carskadon, PhD, invents the multiple sleep latency test, a measure of sleepiness now used routinely in diagnosing narcolepsy and idiopathic hypersomnia.
- **1980:** Dement and Carskadon document the shift in circadian rhythms in early adolescence, showing sleep deprivation is a major factor in teen mood disorders and drug use.
- **1985:** Nelson Powell, MD, performs the first surgery to treat sleep apnea.
- **1989:** Sharon Keenan, PhD, establishes the first course on sleep medicine.
- **1999:** Rachel Manber, PhD, launches the first group therapy program for insomnia.
- **1999:** Emmanuel Mignot finds the cause of narcolepsy: a lack of the neurochemical hypocretin, most likely caused by an autoimmune attack.
- **2001:** Mignot and others identify a genetic marker for sleep apnea. The marker is also associated with Alzheimer’s and cardiovascular diseases.
- **2004:** Shahrhad Taheri, MD, PhD, reports an association between short sleep, the appetite regulatory hormone leptin, and obesity.
- **2005:** Clete Kushida, MD, PhD, begins the largest-ever study of the long-term effects of “CPAP,” the main treatment for sleep apnea.
- **2007:** Mignot identifies a genetic mutation in zebrafish associated with insomnia.

Stanford pursues research side by side with patient care. The university’s sleep clinics treat more than 5,000 adults and children each year, including patients from all over the world. More than 100 doctors, research faculty, staff, and students are dedicated to the study and treatment of sleep at Stanford.

Few medical centers conduct any sleep research at all. At Stanford, sleep research spans multiple scientific and medical specialties—from seeking the genes associated with sleep disorders, to studying the neurological and chemical systems that regulate sleep and waking, to conducting clinical trials of promising drugs and devices.

William Dement, MD, PhD, has studied sleep in animals, students, psychotics, even Rockettes. Along the way, he’s become nationally known as the “father of sleep medicine.” Dement founded the American Academy of Sleep Medicine and the American Board of Sleep Medicine. He chaired the National Commission on Sleep Disorders Research, in response to which Congress created the National Center on Sleep Disorders Research. It’s partly because of him that today there are more than 1,400 sleep clinics across the country, many staffed by people he mentored at Stanford. Dement’s *Sleep and Dreams* became the most popular course at the university, taken by nearly 20,000 students. Every one of them remembers the call to action with which he tirelessly champions public education on the dangers of sleep debt: “Drowsiness is red alert!”

DROWSINESS IS RED ALERT!

Drowsiness is the last step before falling asleep, not the first. It means you are seconds away from sleep. If you’re behind the wheel, that could mean seconds away from death.



Watch a video tribute to Dr. Dement: Visit [youtube.com](https://www.youtube.com) and search “dement tribute”



STANFORD'S GOALS

We still don't know exactly how the brain produces sleep and wakefulness. For that matter, we don't know why all species need sleep. Evolution may have favored sleep as a means of conserving energy and avoiding night's dangers; as a way of restoring cellular function; or, as many studies now suggest, as a time to consolidate learning and memory.

We do know sleep is intimately connected with serious health problems. For instance, studies show that insomnia correlates with depression and mood disorders. Others suggest sleep deprivation increases overall mortality by 21 percent for women and 26 percent for men.

The crucial importance of sleep and its disorders warrants a far greater effort. To pursue the most promising research, give new hope to patients, and spread national awareness of sleep disorders, Stanford must expand its sleep medicine programs. At the same time, the university seeks to integrate research and treatment even more closely.

DID YOU KNOW?

- We all have our own daily sleep requirement. Lost sleep accumulates as a larger and larger sleep debt, which can only be reduced by sleeping over and above your daily requirement for days or even weeks.
- About half the people who snore during sleep and feel tired during the day have sleep apnea.
- A recent study showed a fivefold increase in cardiovascular deaths in sleep apnea patients over a period of 18 years.
- Although sleep apnea is more common in men, it also occurs in women and children, where it often goes undiagnosed.
- REM sleep behavior disorder (acting out during dreams, often violently) is often a precursor to Parkinson's disease.
- During REM sleep, the whole body is paralyzed. In "sleep paralysis," the sleeper awakes but is briefly unable to move.
- People sleepwalking or having "night terrors" are not dreaming. These problems have a genetic predisposition, but can also be caused by sleep apnea and anxiety.
- At the onset of sleep, many of us experience a brief body jolt, known as a "hypnic jerk."

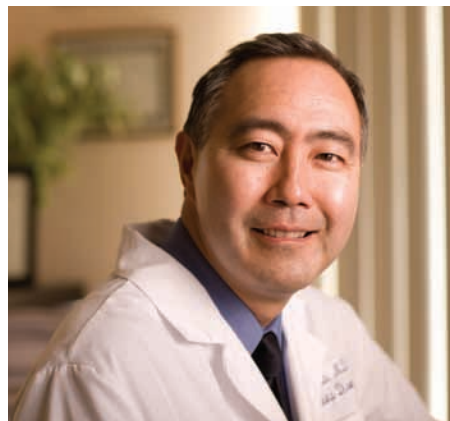


Blanton Hamilton was a perfectly healthy boy until age 7, when he began having seizures. It took a year to identify them as cataplexy, the episodes of muscular collapse associated with narcolepsy. Pediatric sleep disorders are more common than most people realize, with impacts on children's development and their whole families' lives. Narcolepsy in particular "is a cruel disorder," says Blanton's father, Blanton, Sr. In addition to overwhelming sleepiness during the day and (paradoxically) trouble sleeping at night, any intense feelings can trigger cataplexy: For instance, if Blanton, Jr., laughs too hard, he collapses.

After their son's diagnosis, his parents brought Blanton to Stanford, which his dad calls "the mecca of sleep centers." Today, a sophisticated blend of medications allows their son to play three sports and do well in school. "Now he's a happy, normal kid, and we owe a lot to Stanford for that," says his dad. The Hamiltons have become generous supporters of sleep medicine at the university "We give as much as we can possibly afford," adds Blanton, Sr. "The more we help scientists and doctors unlock the secrets of the brain, the better off we're all going to be."



TED ELDEN



MARK TUSCHMAN

CLETE KUSHIDA, MD, PHD, STUDIED SLEEP WITH BILL DEMENT AS A STANFORD UNDERGRADUATE. TODAY, AS AN ASSOCIATE PROFESSOR OF PSYCHIATRY AND BEHAVIORAL SCIENCES, HE DIRECTS THE STANFORD SLEEP DISORDERS CLINIC AND SERVES AS PRESIDENT OF THE AMERICAN ACADEMY OF SLEEP MEDICINE.

THE NEW **STANFORD SLEEP CLINIC**, PART OF A NEW STANFORD MEDICAL FACILITY IN REDWOOD CITY (RIGHT), WILL PROVIDE MORE BEDS AND BETTER COORDINATION BETWEEN RESEARCH AND PATIENT CARE.

FROM BENCH TO BEDSIDE: USING RESEARCH TO PERSONALIZE MEDICINE

At this stage in the development of sleep medicine, findings are coming fast and treatments are continually being piloted and refined. For this reason, Stanford places great emphasis on clinical research: This is where basic science, which uncovers the fundamental mechanisms of sleep and waking, intersects with applied science, where such knowledge leads to new treatments.

The evaluation of new therapies in clinical settings should feed vital information back to the basic research scientists at the beginning of the process. At Stanford, the PhD at the laboratory bench and the MD at the bedside are often one in the same person.

The latest research can also be used to tailor the treatment of individual patients. For example, lab science is revealing genetic and biological markers associated with sleep disorders, such as genes that correlate with apnea and RLS, and variations in EEG signals or levels of hypocretin linked with narcolepsy. Compiling data from many patients will guide lab science toward ever more detailed genetic patterns associated with specific disorders and even with the effectiveness of particular treatments.

Connecting the cycle of research and treatment depends on new systems that bridge the two, so that the flow of data from basic research is combined with continuous monitoring from clinical settings. Stanford's goal is to establish gold-standard protocols for patient evaluation, treatment, and outcome research, and to disseminate those protocols across the nation.

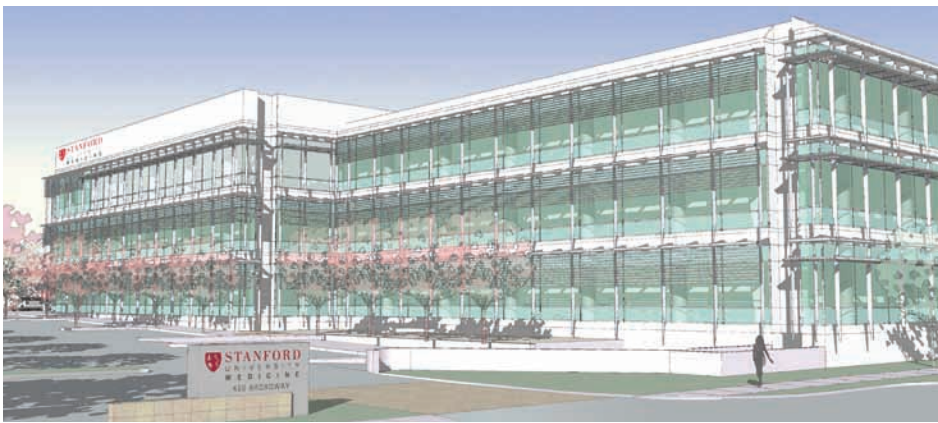
A STATE-OF-THE-ART SLEEP CLINIC

In 2009, the Stanford sleep clinic will move to a state-of-the-art facility in the new Stanford Medicine Outpatient Center in Redwood City. The new clinic will provide the cutting-edge setting for laboratory and clinical research to be more closely linked: all of the clinic's medical records will be electronic, and data collected from patients (with proper consent) will be integrated with data from research.

The clinic will also expand the number of research and clinical beds from 12 to 18, with the potential to increase to 24. Overnight, in-depth sleep recording, which is still required for positive diagnosis, will remain an important capability, but the clinic will be able to take advantage of much more ambulatory home monitoring without requiring overnight stays, an important trend in sleep medicine.

The clinic will also improve coordination among the various specialties involved in treating patients, with a clinic staff that combines psychologists, psychiatrists, neurologists, pulmonary specialists, dentists, surgeons, and pediatricians.

There is not yet a cure for narcolepsy. But the discovery in 1999 by **Emmanuel Mignot, MD, PhD**, of the gene that causes the disease in dogs was a major breakthrough. After 10 long years of sequencing canine DNA, Mignot found a gene that forms a receptor for the neurochemical hypocretin. He later established that a lack of hypocretin in the brain causes the disease in humans. Progress continues: "We now have evidence that the cause is an autoimmune attack against the hypocretin-containing cells in the brain," says Mignot, the Craig Reynolds Professor of Sleep Medicine and the director of the Stanford Center for Sleep Sciences. "Our goal now is to use this knowledge to find new treatments." In addition to lab research, Mignot is active in patient care, specializing in such disorders as idiopathic hypersomnia and Kleine-Levin syndrome. With narcolepsy, he is determined to find a cure. As he once told *The New York Times*, "I don't care if it's going to take a long time. I'm ready to cross deserts."



MARK TUSCHMAN



THE STANFORD CENTER FOR SLEEP SCIENCES

Not only in the clinic, but also throughout the university, Stanford is coordinating the myriad researchers and physicians involved in sleep. This field touches not only many traditional medical disciplines and specialties, such as those noted above, but also hybrid areas such as bioengineering, genetics, and biochemistry. Therefore, integrating research and treatment requires reaching across traditional academic boundaries to take an interdisciplinary approach.

Stanford's Division of Sleep Medicine has historically been based within the School of Medicine in the Department of Psychiatry and Behavioral Sciences. Today, with the rapid growth of the field and the exciting potential for discoveries, the division has a new mandate as the Stanford Center for Sleep Sciences. This interdepartmental structure will promote and coordinate sleep research and medicine throughout the medical school and across the university.

Once it is fully funded, the sleep center will provide seed grants for pilot studies, help affiliated faculty to prepare outside grant applications, and provide the structure for much needed cross-fertilization across the university. Crucially, the division will design and implement the systems that link researchers all along the cycle from basic science through clinical care.

In addition, the sleep center will coordinate sleep education for Stanford undergraduates, medical students, other graduate students, and postdoctoral fellows. The center will also expand Stanford's outreach efforts to primary care physicians and their patients, an essential ingredient in the national effort on sleep medicine, which the university is helping to lead.

THE STANFORD ADVANTAGE

The Center for Sleep Sciences makes Stanford one of only five institutions that meet the Institute of Medicine's recommendations for comprehensive sleep centers. These stipulate that sleep research be interdisciplinary and extend from basic science through clinical trials, and that sleep centers provide treatment, professional training, and public education.

At Stanford, sleep medicine also takes place in the context of a university-wide Initiative on Human Health. This initiative reaches far beyond the School of Medicine to bring the physical sciences, engineering, and other fields to bear on complex health challenges.

Finally, Stanford's access to the entrepreneurial resources of Silicon Valley is one reason the university has an unparalleled record of converting new discoveries into useful applications. Advances here will help more people more quickly than work conducted anywhere else.

When **Barbara Corneille, '55**, first met Bill Dement back in the 1970s, she was riveted. Dement began his presentation to a group of Stanford alumni early one afternoon, and their conversation went on into the evening. "It was then I realized what an important subject sleep is," says Corneille. "It is universal. If you discover the cause of cancer, that affects some people. Sleep affects everybody." Since then, she's been a generous supporter of Dement's department. When Corneille's parents passed away her family foundation endowed a professorship for Dement in their memory. At one time, Corneille's own son had surgery to treat obstructive sleep apnea, a procedure developed at Stanford. But Corneille's goal in supporting the university has always been to help others: "To know that Stanford is working on sleep at such a pace, and just to be a part of it, makes me proud."



MARK TUSCHMAN

A window into the brain: Exploring sleep disorders will inevitably shed light on other problems. For example, the EEG technology used to monitor sleep yields a complex and detailed signal that can be used to explore brain activity, such as communication between the cerebral cortex and other parts of the brain. Variations in the EEG have been shown to have a strong genetic basis. Stanford researchers are seeking the genes responsible, which will likely correspond to previously unknown dysregulations in the brain. These markers could help diagnose and ultimately treat depression, anxiety, autism, schizophrenia, and Alzheimer's and Parkinson's diseases. Unlike other imaging techniques, the EEG can easily be collected from large numbers of individuals at home—as in typical sleep studies.



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THE ROLE OF PRIVATE FUNDING

Although the federal government supports a great deal of medical research, support for sleep medicine is limited. This is partly because it is a newer field and partly because of its interdisciplinary nature. Despite the creation of the National Center for Sleep Disorders Research within the National Institutes of Health, the agency does not have funding earmarked specifically for sleep.

This creates a unique opportunity for private donors to make a significant difference. The next decades' work in sleep medicine could have sweeping consequences for our entire society.

GIFT OPPORTUNITIES

ENDOWED FUNDS ESTABLISH PERMANENT INVESTMENTS AND PROVIDE A CONTINUING SOURCE OF SUPPORT.

ENDOWED PROFESSORSHIP \$4 MILLION
One of the highest honors in academia, the center wishes to establish named professorships in areas such as restless leg syndrome, sleep apnea, insomnia and basic sciences.

ENDOWED RESEARCH AND TRAINING FUND \$300,000 MINIMUM
Fund long-term research and education programs in perpetuity.

EXPENDABLE FUNDS ARE SPENT AS THEY COME IN AND MAY BE MADE IN SUPPORT OF SPECIFIC PROGRAMS, RESEARCH, OR PEOPLE OF THE DONOR'S CHOOSING.

FACULTY RECRUITMENT FUND \$750,000
In the fierce competition for the best and the brightest, Stanford offers start-up funding for new faculty laboratories.

INTERNATIONAL FACULTY SCHOLARSHIP FUND ANY AMOUNT
Sleep disorders are prevalent in every population around the world. This fund provides support for faculty visiting from countries with limited access to sleep medicine expertise.

SLEEP SCIENCE RESEARCH FUND ANY AMOUNT
Provide funding to support innovative studies in the sleep sciences.

ADVANCED TECHNOLOGY AND DATA PROGRAM FUND \$2.5 MILLION
Our new "sleep clinic of the future" is creating a program to establish computer protocols and a biological data bank to facilitate personalized patient care and clinical research.

PLANNED GIVING, INCLUDING BEQUESTS, LIVING TRUSTS, LIFE INSURANCE POLICIES, IRAS OR OTHER RETIREMENT PLANS, AND LIFE INCOME GIFTS, CAN PROVIDE A DONOR WITH CONSIDERABLE TAX SAVINGS AS WELL AS AN INCOME FOR LIFE.