the student, the professor and the birth of modern

SLEEP RESEARCH

story by Lynne Lamberg
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A­rnold Aserinsky offered up a handwritten sheet of notebook paper from a stack in his suburban Philadelphia home. “Look here,” he said. “It’s my father’s record of one of my nights in the sleep lab. I was 8 years old.”

The notes were jotted down more than a half century ago, when Arnold Aserinsky was the first subject of his father Eugene’s research at the University of Chicago. The nascent research led to a breakthrough in the study of sleep — pioneering work that continues to this day at Chicago, still a leader in the field.

“We now know the intrinsic importance of sleep to health,” said Eve Van Cauter, current director of Chicago’s Research Laboratory on Sleep, Neuroendocrinology and Chronobiology. “Today we’re studying a wide range of sleep-related health issues, especially with regard to sleep deprivation. But today’s studies owe an enormous debt to the science conducted here a half century ago.”

In 1953, Eugene Aserinsky, then a Chicago graduate student in physiology, reported that rapid eye movements (REMs) occurred regularly during sleep. Their paper, published in the journal Science, summarized Aserinsky’s doctoral dissertation research, the first documentation of REMs during sleep. Sleepers who were awakened during or soon after REMs usually recounted detailed dreams with visual imagery; the same sleepers, awakened while sleeping that affect an estimated 40 million Americans of all ages.

Sleep research in its infancy

Kleitman opened the world’s first sleep lab at Chicago in 1925, soon after he joined the faculty. He was the first scientist ever to make the study of sleep his primary work. Born in 1895 in what is now Moldova, Kleitman emigrated to the United States in 1915. After completing degrees from the College of the City of New York and Columbia University, he earned a PhD in physiology summa cum laude from the University of Chicago in 1923, exploring in his dissertation the effects of prolonged sleeplessness in humans.

A consummate scholar, Kleitman appraised 1,434 scientific studies, the whole of the world’s sleep literature at the time, in his 1939 book, Sleep and Wakefulness: His ability to read languages other than English, he noted apologetically, was “limited” to French, German, Italian and Russian.

Aserinsky arrived on Kleitman’s doorstep in 1949, at age 27, with, in his own words, “a motley background.” At Brooklyn College, he had switched majors from social science, to Spanish, to pre­­med. After three years, without graduating, he gained admission to dental school at the University of Maryland in Baltimore, but later dropped out. He was drafted into the Army in 1943, the same year his son Armond was born, and was sent to England, where — despite being legally blind in one eye — he served as a high-explosives handler until 1945. On returning to Baltimore, he worked as an employment counselor for Maryland’s department of employment security.

Deciding to make use of the GI Bill to complete his education — and with enough pre-war college credits to gain admission to graduate school — Aserinsky sought a degree in organ physiology. Chicago accepted him. Throughout his life, his son Armond remembered, “he was grateful to the U of C for its flexibility and willingness to evaluate a student on his real assets and not just on whether he had gotten his ticket punched in all the ‘right’ places.” Since other physiology department faculty members focused on cellular physiology, Kleitman, by default, was his only hope for a sponsor. Sleep was “perhaps the least desirable of the scientific areas I wished to pursue,” Aserinsky wrote in a 1996 memoir.

At the time, Kleitman was investigating sleep and activity in infants, using a device attached to the crib mattress that recorded body movement. He asked Aserinsky to see whether infants’ eye blinks stopped abruptly or gradually at sleep onset. Unable to differentiate blinks from quivers of babies’ eyelids, Aserinsky asked to study instead the presence or absence of any lid movement. Months of tedious observation showed sleeping babies had roughly 20-minute periods each hour with no eyelid movements.

Evidently pleased with results of the baby project, Kleitman encouraged Aserinsky to pursue a doctoral degree without writing a master’s thesis. Casting about for a dissertation project, Aserinsky proposed exploring whether adults had similar 20-minute sleep episodes and, if so, assessing physiological variables that occurred simultaneously. He hoped he might find some new aspect of brain function.
Moreover, when sleepers’ eyes darted, their hearts beat faster and breathing quickened, signs of emotional arousal. He started waking sleepers when he saw REMs, asking, “Did you dream? What did you see?”

Acquisition of a standard model 4-channel Grass EEG provided more reliable recordings than the dynograph. Unaware that eye movements were periodic — and not wanting to waste the costly EEG paper — Aserinsky initially sampled only a few minutes of sleep each hour. Because of the sampling technique, he missed most first REM periods, which typically started 90 minutes after deep onset, but last only five minutes or so. He reported erroneously in the Science paper that “an eye movement first appears about 3 hours after going to sleep.” Moreover, he missed REMs completely in four of the 26 people he observed. Kleitman, unfortunately, was among those four, on at least one night. This experience, Aserinsky wrote, “did not instill [Kleitman] with confidence.”

The science paper, written in the dispassionate language of scholarly reports, provides no hint of the binary-eyed nights required to complete the study, the challenges of fiddling with primitive machinery or the anxiety over whether the research was going anywhere. Living on his meager salary in drafty former Army barracks that served as campus housing with wife Sylvia, Armond and daughter Jill, born in April 1952, Aserinsky knew he was taking a big gamble: “An unremarkable research program would continue to leave me without any degree,” he wrote in a 1996 memoir, “and I would be a perennial (and senescent) student.”

Like winning the lottery

In the fall of 1952, one of Kleitman’s lectures sparked the interest of William Dement, then a junior-year medical student. Kleitman assigned Dement to help Aserinsky record eye movements which is found only in sleep and may be associated with dreaming. He described dreams as a sudden transition from a relatively quiet sleep to a period of intense mental activity, characterized by vivid imagery and emotional intensity. His work was groundbreaking and contributed to the understanding of sleep and dreaming.

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Not having seen REMs himself, Kleitman handed Aserinsky a home movie camera and asked him to film sleepers’ eyes. Later, Kleitman insisted Aserinsky use Kleitman’s daughter Esther as the subject in a sleep session he personally observed. Aserinsky thought Kleitman unduly skeptical. Not until many years later did Aserinsky appreciate his adviser’s quip: An awake subject could easily pretend to be asleep and fake REMs; the EEG records would look the same.

Finally, Aserinsky had results Kleitman deemed sufficient: He had recorded REMs in all but four of 26 subjects. In 10 subjects, 27 REM awakenings elicited 20 reports of complex visual dreams. The same people, awakened 23 times during periods of no eye movement, recalled dreams only twice.

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The media-savvy Kleitman met alone with a representative from the university’s public relations department to discuss the forthcoming talk, an act Aserinsky found “unconscionable.” Kleitman, Aserinsky claimed, asked Aserinsky to listen from behind his office door and report any misstatements later.


These papers set off no fireworks in scholarly circles. Aserinsky, by his own account, divorced himself from sleep study for about a decade after his original research. That decade was deeply traumatic for him and his family: His wife, Sylvia, after several hospitalizations for mental illness, killed herself in 1957. By then, Aserinsky was at Jefferson Medical College in Philadelphia, where the new chair of the physiology department evinced little interest in sleep.

Attending a sleep meeting in the early 1960s, Aserinsky was surprised and pleased to be recognized for his pioneering work, said son Armond, now 61 and a clinical psychologist in North Wales, Pa., near Philadelphia. He set up a sleep lab and conducted studies on eye movements and respiration, but Aserinsky remained a “lone ranger,” his son said, a liability in an age of growing multidisciplinary collaboration. “He could have easily used a biomedical engineer,” Armond said. “He hated to have to ask for help with statistics.”

Aserinsky published only 20 papers and a few book chapters in ensuing years. After 22 years at Jefferson, he was promoted to professor, but passed over for appointment as department chair. He left to become chair of physiology and pharmacology at...
Marshall University, Huntington, W.Va., and retired in 1987. Aserinsky died in 1998 at age 77, when his car swerved off the road and hit a tree.

Continuing the work

In the summer of 1953, Dement, still a medical student, studied 17 people with chronic insomnia and 18 healthy medical students at Manteno (Ill.) State Hospital. Knowing Freud viewed dreams as a mental “safety valve,” he thought psychotitic patients might not have REMs in sleep. As Dement found, however, they had REMs as often as healthy subjects.

In early studies, the Chicago team explored whether people had voluntary control over dreaming, whether dreaming occurs outside of REM sleep and how medications affect REM sleep.

Before he graduated from medical school in 1955, Dement had recorded sleep continuously and divided it into non-REM (NREM) stages 1-4, six lightest to deepest sleep, plus REM, categories still used today. In 1957, he and Kleitman charted the normal human sleep cycle, showing that REM and NREM periods alternate about every 90 minutes and that REM periods grow longer as sleep progresses. His findings in cats, together with research by neurophysiologist Michel Jouvet of Claude Bernard University in Lyon, France, prompted recognition of REM sleep as a third state of existence, distinct from both sleep and wakefulness — a major finding.

After receiving his PhD from Chicago in 1957, Dement — described by Kleitman as “my pride pupil” in a 1989 interview with this writer — went to New York City to work with Charles Bliwise (PhD ’82, behavioral sciences), now a professor of neurology at Emory University Medical School, coordinated that study. Once, Bliwise recalled, he arrived late at the airport to pick up Kleitman, then 90. Returning to Stanford, he found Kleitman had made his own way there, after negotiating three bus transfers. Kleitman bragged that, with his senior citizen’s discount, the trip had cost him only a dime.

Today, on the M3 corridor of the hospital, a plaque provided by the Sleep Research Society last June commemorates the 50th anniversary of the Discovery of REMs. This past summer, sleep specialists from around the world celebrated the anniversary at the annual meeting of the Associated Professional Sleep Societies in Chicago.

For more than four decades, the Chicago sleep research lab grew under the leadership of neurologist Allan Rechtschaffen, who directed it from 1958 to 1999. Soon after Rechtschaffen arrived, psychiatrist Edward Wolpert, who had worked with Dement on dream studies, invited him to observe a sleeping subject.

“Watch. I’m going to wake this person, and he’ll have a dream,” Wolpert said, and the sleeper did, “Now Wolpert said. ‘Now I’m going to wake him again, and he won’t. I thought that was a fantastic way to study the mind/body problem.”

Cats, rats and alligators

In the late 1950s, the rapidly increasing Chicago sleep group outgrew the Abbott Hall laboratory and moved to a three-story, gray-brick row house at 5743 Drexel Ave., later expanding into 5739. Those buildings were torn down in 2001 to make way for the Interdivisional Research Building, where researchers from the biological and physical sciences will pursue collaborative projects. In early studies, the Chicago team explored whether people had voluntary control over dreaming (they found little), whether dreaming occurs outside of REM sleep (it does, but NREM mental activity tends to be less vivid and emotional than that of REM sleep) and how medications affect REM sleep (amphetamines, to scientists’ surprise, suppressed it). Chicago researchers found that people with narcolepsy have REM episodes at sleep onset, an early clue to identification of narcolepsy as a disorder in which REM sleep intrudes into wakefulness, causing sudden bouts of muscle weakness. They also conducted the first sleep lab study of insomnia, finding insomniacs were physiologically aroused while they slept, which probably contributed to their underestimation of the amount of sleep they actually got.

“In the early days, sleep was wide open territory. We knew nothing about it,” Rechtschaffen said. “At one time we were running humans, cats, rats, alligators, tortoises and lizards in the sleep lab. We tried to study fish, but were unsuccessful.”

For almost two decades, Rechtschaffen and colleagues Bernard Bergmann, Samuel Refetoff and several graduate students explored the biological functions of sleep by studying effects of chronic sleep deprivation in rats.

The researchers developed a study paradigm involving a pair of rats, both allowed to move freely in their cages and to eat and drink as they desired. One rat could sleep when it wished. Whenever the other rat started to sleep, it was required to walk on a slowly rotating disk to avoid getting wet, an experience rats resist. Rats deprived entirely of sleep ate more then usual but lost weight. The increased energy expenditure was apparently in response to both a huge increase in heat loss and a dramatic decrease in food intake, an effect that increased significantly as the rats’ feeding time. The data might not have REMs in sleep. As Dement found, however, they had REMs as often as healthy subjects.

Aserinsky and Kleitman’s 1953 paper showed the notion that the brain merely idled during sleep and launched the contemporary field of sleep medicine. The REM study spurred the identification and treatment of 84 discrete disorders of sleeping and waking that affect an estimated 40 million Americans of all ages. But at the same time, the research prompted little publicity in the mainstream press. In fact, their findings only garnered a paragraph from The New York Times.
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— Eve Van Cauter, Director of the University of Chicago Sleep Lab

rise in preferred or “setpoint” temperature. The sleep deprived rats looked scrawny and sick. Their fur changed in color from creamy white to brownish yellow, looked disheveled and stuck together in clumps. Unique ulcerative lesions developed on the tail and soles of the feet. After two to three weeks, the sleep-deprived rats died. But sick rats, if allowed to sleep, recovered fully. The studies indicate that sleep serves important energy and thermoregulatory functions and that, at least in the rat, sleep is necessary for life.

No single theory of why we sleep has gained universal acceptance, said Rechtschaffen, who retired in 2001 and is now professor emeritus of psychiatry and psychology. Understanding the mechanisms of sleep also is evolving. “We still don’t have a clear picture,” he said, “of which structures and which chemicals operate in which sequence to produce sleep.”

Chicago’s Eve Van Cauter said that ongoing research aims at filling in some of those gaps in understanding.

“Our goals today are to understand the health implications of too little or poor-quality sleep,” she said, “especially in relation to chronic illnesses of older people, such as diabetes, high blood pressure, weight gain and memory loss.”

Van Cauter and her colleagues have conducted a series of studies that explore consequences of partial chronic sleep deprivation in humans, a growing concern in the United States. The typical American adult averages just under seven hours of sleep per day, compared to 8.25 hours that sleep specialists regard as optimal for adults. People who rotate shifts average less than five hours sleep, fell by about 75 percent. By age 45, most men experience little deep sleep. Van Cauter said, and thus likely secret little growth hormone.

Although the total nightly amount of sleep does not fall appreciably until after midlife, as people grow older, sleep becomes more fragile. People in their 60s and older awaken frequently. The Chicago research shows that men who get less sleep, at any age, secrete less growth hormone than peers who sleep longer.

Loss of growth hormone in older people increases fat tissue and abdominal obesity, reduces muscle mass and strength, and reduces exercise capacity. So far, attempts to replace growth hormone through drug therapy have been tried only in patients age 65 and older. The Chicago work suggests that such therapies might benefit people in early mid-life. Synthetic growth hormone injections have substantial adverse effects, however. Boosting sleep deep in adults by using novel drugs may trigger a proportional increase in secretion of growth hormone, Van Cauter suggests, a promising approach supported by recent studies at Chicago and elsewhere.

The possibility that curbing age-related changes in sleep quality might delay some hormonal consequences of growing older, Van Cauter said, “is tantalizing.”

In current research, Van Cauter and colleagues are exploring the impact of sleep loss on hunger and appetite. Findings so far, she said, show that people limited to four hours sleep always feel hungry and crave carbohydrate- and fat-rich foods. They also show changes in secretion of leptin and ghrelin, hormones that regulate hunger and appetite.

“We speculate,” Van Cauter said, “that sleep-deprived people are more likely to put on weight.” The general trend for people to sleep less, she suggests, thus may be implicated in the current worldwide epidemic of obesity.

In a sure sign that the research had touched the public consciousness, it recently was lampooned by humor columnist Dave Barry of the Miami Herald.

“According to the University of Chicago researchers,” Barry wrote, “men produce a hormone that causes them to develop muscle mass, which they need to perform masculine tasks that are biologically necessary for human survival, such as operating the remote control.”

“The thing is, men produce this particular hormone only during sleep. If they don’t get enough sleep, they become flabby.”

Barry’s column reflects the increased attention that the once-overlooked study of sleep now has gained. Beginning with Kleitman’s 1923 scrutiny of the effects of sleep loss in young adults, through the landmark 1953 Aserinsky/Kleitman report showing brain activity persists in sleep, to Rechtschaffen’s exploration of sleep loss in animals and Van Cauter’s present investigation of sleep and hormones, University of Chicago continues to generate eye-opening results.

Lynne Lamberg’s experience with sleep research started informally in the early 1970s at the University of Chicago. Since then, Lamberg has written hundreds of articles and five books on sleep, dreams and biological rhythms, including her most recent: The Body Clock Guide to Better Health.