

DISCOVER PRESENTS

# MEDICAL MYSTERIES

## THE SECRETS OF SLEEP

*Forever Night: The Terrors Of Insomnia, Narcolepsy, Sleep Eating, And More*

**ANDREW WEIL**  
How to Heal Yourself

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DISPLAY UNTIL SEPTEMBER 30, 2007

# Secrets of Sleep

We all lead double lives: More than a third of our hours are spent asleep. If we're lucky, we take this dual existence for granted. Yet many poor souls are tormented by sleep disorders. Tossing and turning into the wee hours is the least of it. Some of these sufferers, like tragic characters in a fairy tale, may spend weeks at a time in slumber. Others, while fast asleep, get behind the wheel of a car, gorge themselves on snacks, or even kill. At the same time, the basics of sleep remain biological mysteries: why we need it, how much we need, and why so many suffer from insomnia and other disorders. As the accounts of these waking wounded reveal, our nocturnal second lives can be wilder and weirder than anything our waking minds may imagine.

**By Kathleen Mc Auliffe**  
**Painting by Tina Gauthier**





# Wide Eyes Open

Sleep seems like a distant memory to Marilu Trobough. “I used to be high spirited and had great energy,” says the 49-year-old teacher from Pacific Palisades, California, her voice wistful for better days. That was a decade ago, before sleep—in her words—became “an unending quest.”

Trobough has no problem falling asleep; it’s her inability to stay asleep that torments her. A few hours after dozing off, with almost clockwork regularity, she awakens, then lies in bed, her mind racing till dawn. She stumbles through day after day, often on just a few hours of sleep, exhausted sometimes to the point that her body shakes. She’s tried yoga, hypnosis, listening to soothing tapes at bedtime, psychotherapy for anxiety, and virtually every gadget and sleeping potion, yet restful nights still elude her. “It’s gotten so bad at times,” says Trobough, “that I’ve had anxiety attacks from it—I’ve gotten that desperate and preoccupied by the need to sleep.”

“Desperate” is an oft-repeated word of the sleepless—and there are legions of them. About 30 to 50 percent of the population is afflicted by episodes of occasional insomnia, either trouble falling asleep or staying asleep. Another 7 to 17 percent suffer a more severe, chronic form of the condition that can last several weeks to years at a stretch. For those with this more persistent variety, the toll on lives can be devastating. Indeed, chronic insomniacs rank their overall quality of life to be as poor as those with severe depression or congestive heart failure.

As if insomniacs did not have enough worries keeping them awake at night, new studies have linked the condition to a raft of health problems, from depression and anxiety to high blood pressure and susceptibility to infectious disease. Insomnia may even contribute to obesity by altering the production of hunger-controlling hormones like leptin and ghrelin, according to Michael Thorpy, director of the Sleep-Wake Disorders Center at Montefiore Medical Center in New York City.

One of the challenges of treating the condition is identifying what is precipitating the problem in the first place. That’s no easy task, given the myriad environmental and personal factors known to disrupt sleep. Insomnia is a well-recognized side effect of a broad range of widely prescribed medications, including Ritalin and other stimulants, antihypertensive drugs like beta-blockers, and respiratory medicines like theophylline. Common substances in our diets can also rob us of sleep—caffeine in coffee and soft drinks being a notorious example. Less widely recognized as an enemy of insomniacs: alcohol. “It makes

sleep, but their circadian rhythms are also more likely to have shifted backward. Starting around age 40, most of us are transformed from night owls to morning larks, and with each decade that passes, we tend to go to bed and to rise earlier and earlier. By our sixties or seventies, reports Ancoli-Israel, it’s common to get sleepy between 6 and 8 o’clock at night and wake at 3 or 4 a.m. “These individuals may be getting plenty of rest, but because they’re awake when everyone else is asleep, they view their problem as insomnia,” she says. Older adults also spend less time in the deepest stage of sleep, so the least noise or

## **New studies have linked insomnia to health problems from depression and anxiety to high blood pressure—even obesity**

you sleepy, but several hours later, as the alcohol leaves the bloodstream, you’re more likely to wake up,” says Sonia Ancoli-Israel, a professor of psychiatry at the University of California at San Diego School of Medicine and director of the Sleep Disorders Clinic.

In addition, insomnia often goes hand in hand with anxiety, depression, and substance abuse, although whether it causes or is triggered by these is murky. Disturbed sleep may also be a fact of life for anyone suffering from diabetes, congestive heart disease, emphysema, heartburn, or prostate problems. Other culprits include jittery limbs in the p.m., a key symptom of restless leg syndrome. Sleep apnea, in which breathing temporarily stops dozens or hundreds of times a night, may also prevent restful sleep.

As might be suspected, aging may get in the way of a good night’s rest. Not only are the elderly more prone to illnesses that can disrupt

disturbance is more likely to awaken them.

Not all cases of insomnia, however, have an obvious cause. About 15 percent of cases are referred to as primary insomnia because they cannot be easily linked to any apparent underlying disorder, like a medical or psychiatric condition. This type is usually long-standing and afflicts individuals with anxious dispositions who come from families with a high incidence of insomnia, says Karl Doghramji, director of the Sleep Disorders Center at Thomas Jefferson University in Philadelphia. Trobough, a self-described worrywart, seems to fit the bill. She has eight siblings and says half her family, including her mother, are “poor sleepers.” People with primary insomnia, sleep experts now believe, may have inherited a “hyperaroused” nervous system—and a growing body of evidence supports that view.

*Right: Art by Sebastiaan Bremer/Roebling Hall Gallery.*



Insomniacs who match this profile, recent studies show, have elevated blood levels of the stress hormone cortisol. Compared with normal sleepers, they usually also have an increased heart rate as well as a faster body metabolism as measured by their rate of oxygen consumption. In addition, people with primary insomnia have a greater number of fast brain waves, which may be the basis for the perception of many insomniacs that they are more actively engaged in thinking during sleep.

Brain-imaging studies of chronic insomniacs re-



Sleep expert Sonia Ancoli-Israel.

## Some who come from families with a high incidence of insomnia may have inherited a “hyperaroused” nervous system

veal telling details. In insomnia patients, the brain’s arousal centers—the brain stem, hypothalamus, and emotion-activation systems—don’t shut off as would normally be expected during sleep, according to a team of psychologists, brain-imaging experts, and psychiatrists led by Daniel Buysse and Eric Nofzinger at the University of Pittsburgh. During wakefulness, these areas of the brain were more active than in normal sleepers. At the same time, chronic insomniacs showed a daytime tendency toward less metabolic activity in the frontal cortex—an area of the brain involved in organizing, planning, and prioritizing. People who are sleep deprived from other causes don’t show the same pattern of changes. “That might explain why people with insomnia complain of difficulty concentrating, focusing, and attending to a task,” says Buysse. “It also implies that they may have to work harder to achieve the same level of cognitive functioning as everyone else.”

Whatever the origin, most people with insomnia get some relief through better “sleep hygiene.” By that doctors mean using the bedroom for sleep and sex only, getting regular exercise, and going to bed and rising at the same time each day. That

strategy is more effective when combined with cognitive behavioral therapy (CBT). Unlike traditional insight therapy, CBT does not delve into troubling issues in a person’s past. Pragmatic in focus, CBT helps insomniacs counter overblown fears about the negative impact of losing sleep and discourages spending time in bed when awake. “That’s critical,” says Buysse. “Otherwise the insomniac may come to think of the bed as a place of torment, further increasing arousal and the inability to sleep.”

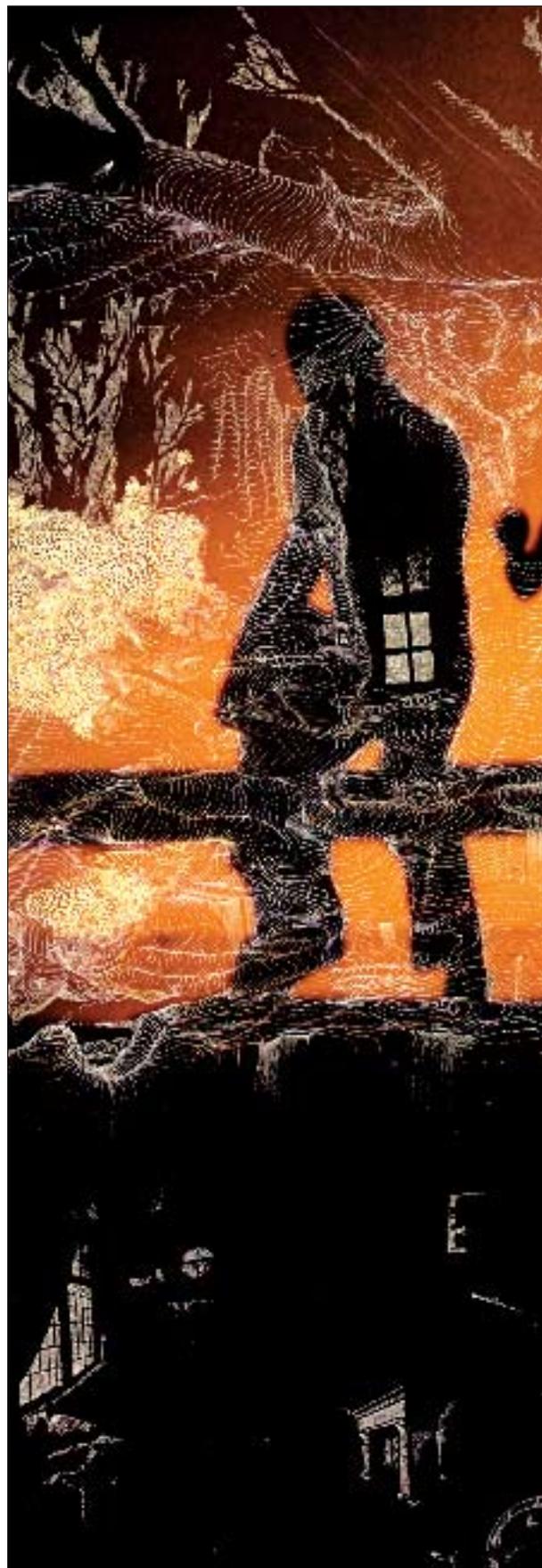
Together, research shows, good sleep hygiene and CBT offer the most effective long-term relief from insomnia. But in practice, most doctors combine behavioral and pharmacological approaches. “I favor this two-pronged approach, especially if sleep is interfering with work,” says Doghramji of Thomas Jefferson University. “It produces quicker results, and then when the cognitive program becomes ingrained, drugs may be phased out.”

Reassuringly, insomnia may not be as dire as sufferers imagine. Even in the worst cases, researchers say, it’s rare for anyone to go more than a day or two without a wink of sleep. “Almost all insomniacs underestimate the amount of sleep they actually get,” says Thorpy of Montefiore Medical

Center. In an extreme version of this misperception, some individuals suffer from paradoxical insomnia, in which they claim to be exhausted from lack of sleep; yet in a sleep laboratory they are shown to get a full eight hours of shut-eye. About 5 percent of people classified as insomniacs fall into this category. No one knows why one man’s insomnia may be another’s solid night’s rest. “It’s a great puzzle,” says Thorpy.

Perhaps a tendency to catastrophize is a core symptom of insomnia. If so, that raises the classic chicken-versus-egg conundrum of which came first: a lack of sleep or a grumpy, negative outlook? As Trobough knows all too well, it’s easy to lose perspective when plagued by fretful slumber night after night. “Believe me,” she says, “it’s enough to make anyone agitated.” With the aid of a sleeping pill, she’s now able to get a few good nights of rest a week. That’s undeniable progress in her struggle with insomnia. She’s recently been able to return to work as a substitute teacher and tutor—on a flexible schedule, just in case her tormenter returns. Ω

Right: Art by Sebastiaan Bremer/Roebling Hall Gallery.





# They Walk In The Night

While sleeping overnight at a hotel in 2006, Canadian tennis star Peter Polansky saw a dark figure with a knife standing by the doorway to his room. Still asleep, the 17-year-old athlete bolted out of bed, and in an effort to escape the phantom intruder, kicked the glass out of his window and jumped out. He plummeted three stories and landed in a courtyard, miraculously escaping death.

Though stories like these are rare, as many as 9 percent of adults are affected by so-called parasomnias, in which a person, technically asleep, engages in complex and bizarre activity. Parasomnias come in many forms, among them sleepwalking, sleep talking, and night terrors. Researchers still do not understand the origins of these odd behaviors. With rare exceptions, no one has been able to trace parasomnias to an obvious problem, such as an anatomical fault or chemical imbalance in the brain. Nonetheless, sleep disorder experts have been able to provide some help, mostly through the use of sedative drugs.

Although many parasomnias are exotic, one is very familiar: sleep talking. As anyone privy to such utterances knows, people who talk in their sleep rarely generate complete sentences, and the strings of words often make no sense. "Even in a sleep lab," says Mark Mahowald, a sleep expert and professor of neurology of the University of Minnesota, "we've never picked up someone expounding at length on any topic."

Sleepwalking is also common and well known. Here, too, the normal daytime activity is garbled and distorted. A typical sleepwalking episode in an adult man might lead him to get up because of a full bladder, take a wrong turn, go to the closet, and urinate in a shoe. A woman might instead sit down and urinate in a wastepaper basket. Other



frequently reported variations of sleepwalking include moving furniture around, banging on the piano, or going for a stroll.

People even have sex during sleep (for firsthand accounts, go to [www.sleepsex.com](http://www.sleepsex.com)). To be sure, this behavior has not been documented in a laboratory setting, where people sleep solo. Still, researchers deem these stories highly credible. In most of these anecdotes, the behavior is initiated by the man—his partner may find out only later that he was asleep during the event. Experts say snoring during sex—they jest not—is a tip-off.

We may walk or talk in our sleep at any age, but sleep terrors, another form of parasomnia, particularly afflict children. During these distressing episodes, the sleeper sits up in a panic and

about to happen.” This frequently takes the form of a single fragmentary image—a monster face, a collapsing ceiling, or engulfing flames. “One man in the midst of a sleep terror bolted out of bed, grabbed his baby from the crib, and ran out of the house,” says Neubauer. “He thought a bomb was about to go off.”

Although sleepwalkers may appear to be dreaming, this is rarely the case, laboratory studies have shown. That’s because rapid eye movement (REM) sleep, when we dream, also paralyzes our limbs, Siegel explains. As REM sleep begins, the cortex becomes as active as when we’re awake—a sign that our imaginations are running riot in those fits of nightly madness we call dreaming. Yet the pons, an area of the brain just above the spinal cord, pre-

## People even have sex during sleep. Experts say snoring during sex—they jest not—is a tip-off

may launch into piercing screams, usually sweating and breathing heavily, with eyes wide open and pupils dilated. He or she may thrash around or bolt out of bed. During such episodes, both children and adults are often inconsolable and impossible to awaken. “All you can do is direct them back to bed, and they usually will calm down on their own after a few minutes,” says David Neubauer, associate director of the Sleep Disorders Center at the Johns Hopkins University School of Medicine. Why children are especially prone to this problem is unclear. “If you simply sit a child up in bed, it’s much easier to induce sleepwalking than in an adult,” says Jerome Siegel, professor of psychiatry at the University at California at Los Angeles.

Someone waking up from a nightmare can usually describe a complex plot. Night terrors, on the other hand, have no narrative—they are an experience of fear, pure and simple. People rarely recall anything. When they do, says Neubauer, “they report a crystallized sense of something terrible

vents motor neurons, the controllers of muscles, from activating movements. We are rendered as limp as wet noodles as we dream away, prevented from screaming or thrashing about no matter how intense our dreams become.

In non-REM sleep, by contrast, our muscles are functional, although people who walk or talk while asleep are a bit like automatons: They have no conscious awareness, and most have total amnesia about such episodes. “Sleep is not a whole-brain phenomenon,” explains Mahowald. “Part of your brain may be awake enough to engage in complicated behaviors while other parts are asleep, so you’re not aware of what you’re doing or responsible for your actions.”

That’s important to bear in mind, he says, since on rare occasions, parasomnias take a dangerous turn. Sleepwalkers have been known to switch on stoves and cook, fall off balconies, and even get behind the wheel of a car. Some deaths classified as suicides result from circumstances similar to

the ones that preceded the near-fatal fall of tennis star Peter Polansky, Mahowald believes.

A physical cause has been uncovered for one rare sleep disorder, known as REM sleep behavior disorder. This parasomnia is believed to arise from damage to pathways that block motor impulses to the limbs during REM sleep. As a result, the sleeper’s muscles are not paralyzed during REM, and she or he may literally “act out” dreams.

An individual with REM sleep behavior disorder may dream of being in a fight and slam his fist into the bedside table, says Helene Emsellem, medical director of the Center for Sleep and Wake Disorders in Chevy Chase, Maryland. In one case reported in the medical literature, a man dreamed that he was trying to snap the neck of a deer and woke up to his wife’s screams in response to his hands wrenching her neck. “When someone is prone to REM-related behavioral disorder, I often caution their sleep partners to get out of bed, turn on the lights, and call from the doorway,” says Emsellem, author of *Snooze . . . or Lose!*, a book on improving teenagers’ sleep habits. “Otherwise, there’s the danger that the partner will be incorporated into the dream and could be injured.” Mahowald believes people with this disorder may even be capable of killing in their sleep, although he’s the first to admit that it would be impossible to prove after the fact.

Why are some people more prone to parasomnias than others? Sleep apnea, in which breathing repeatedly stops during the night, is correlated with an increased incidence of REM sleep behavior disorder. Sleep deprivation due to jet lag or shift work is also a well-known trigger of all sorts of parasomnias. Genetics may also contribute, since the problems often run in families. Yet another cause may be alcohol or, paradoxically, sleep-promoting agents like Ambien, Halcion, and Restoril. Indeed, the Food and Drug Administration recently warned that in some cases, these drugs may be linked to sleep driving. Representative Patrick Kennedy, Democrat of Rhode Island, blamed Ambien when he crashed his car near the nation’s capital last year.

The good news is that benzodiazepines, a class of tranquilizing compounds, can often curb sleepwalking urges and related parasomnias. But psychotherapy may not help. “Contrary to popular perception,” says Mahowald, “the vast majority of parasomnias are unrelated to any kind of psychiatric disturbance.”

Fortunately, even in someone prone to sleepwalking, violent or self-injurious behaviors while asleep tend to be isolated events, never to be repeated. By the same token, that’s what makes them so scary. Despite technology that allows us to peer inside the brain, such episodes are not only mystifying but also—in Mahowald’s words—“frighteningly unpredictable.” Ω



# Narcolepsy

## The Weary Load

Harold Poertner used to fall asleep at the drop of a hat. “I’d be taking a bite of pie and my head would crash onto my plate,” says the 63-year-old retired educator and administrator from Emporia, Kansas. At other times, he’d be wide awake, but his body behaved as if it were asleep. “I’d be lying in bed, paralyzed,” he says. “It’s the scariest thing—I’d try to move my arms and legs, but they didn’t respond.” A joke or excitement could also trigger paralysis. “I could see you and hear you,

but I couldn’t move my upper limbs or talk,” he says. “I’d be paralyzed from the waist up for seconds or sometimes even minutes.” Occasionally, Poertner experienced hallucinations so vivid they made him doubt his sanity.

Poertner has narcolepsy, a sleep disorder that affects between 25 and 50 people in 100,000. Medication has kept these symptoms largely under control—a good thing, since narcolepsy can cause some odd behavior. Poertner’s former tendency to

take a nosedive into his pie is a classic sign of the disease, but the condition often manifests in lesser-known symptoms like paralysis, hallucinations, or “automatic behavior,” in which a person appears to be functioning normally but has no awareness of what he or she is doing. Because of these strange and unpredictable phenomena, sufferers

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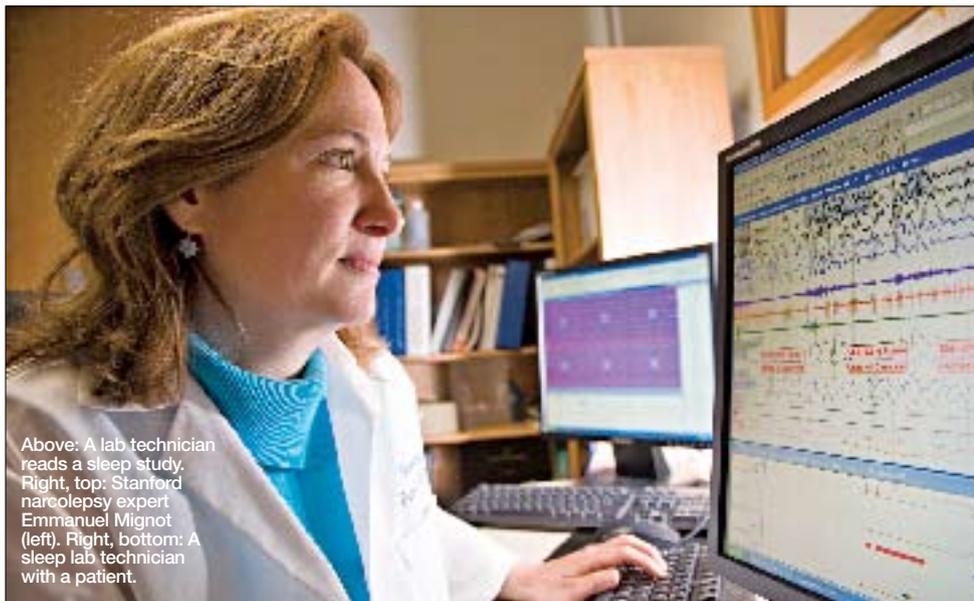
*Photograph by Erwin Blumenfeld. From the estate of Erwin Blumenfeld/Art+Commerce.*

often appear to be drunk or delusional rather than just extremely sleepy. Why the disease has such a wide range of effects isn't completely understood, but in recent years a potential cause—the loss of hormone-producing neurons, possibly through an autoimmune response—has been identified. That knowledge in turn promises to pave the way for more precise treatments and stronger relief from narcolepsy's debilitating symptoms.

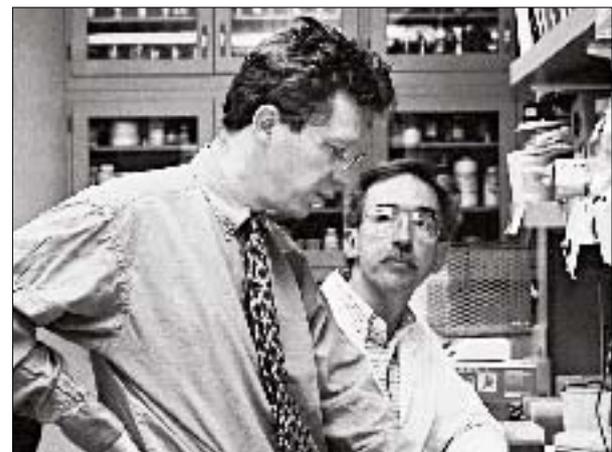
their propensity for nodding off, even while in the middle of doing something else. What's more, says Thorpy, fragments of REM—paralysis, for example—may intrude at inappropriate times. And because they can slide rapidly into REM at any time, people with narcolepsy are prone to hallucinations—or what sleep researchers refer to as hypnagogic imagery—when falling asleep. “A normal individual would be sound asleep

pen or not? A dozen times I had to remind myself that I was not Mick Jagger's girlfriend.”

Scannell believes her confusion stems from her memory of dreams being every bit as detailed and vivid as real events. Her intuition may be correct and could have a physiological explanation, says Emmanuel Mignot, a Howard Hughes Medical Institute investigator and director of the Center for Narcolepsy at Stanford University. “In normal indi-



Above: A lab technician reads a sleep study. Right, top: Stanford narcolepsy expert Emmanuel Mignot (left). Right, bottom: A sleep lab technician with a patient.



## Narcolepsy may manifest as paralysis, hallucinations, or “automatic behavior,” in which a person acts normally but has no awareness of what he or she is doing

For a narcoleptic, it's a great struggle just to stay awake. He or she may appear to be alert to others but be in a dream state, explains Michael Thorpy, director of the Sleep-Wake Disorders Center at Montefiore Medical Center in New York City. The narcoleptic's strange behavior is related to his or her highly fragmented, chaotic REM sleep, a hallmark of the disorder. Normal individuals typically slide into REM (rapid eye movement) sleep about an hour and a half after initially losing consciousness. Not narcoleptics. They often go from being wide awake to REM in 15 minutes or less—sometimes mere seconds. They also spend less time in continuous slow-wave sleep, the deepest phase, from which it is hardest to be aroused.

Because their sleep at night is disjointed and marked by frequent awakenings, narcoleptics tend to be exhausted during the day, increasing

when weird imagery starts floating across his mind,” says Thorpy.

Such vivid visions are nothing new to Joyce Scannell, 51, of North Kingstown, Rhode Island. “Since I was a kid, I'd have hallucinations while falling asleep or waking up that I thought were real because I didn't know I had narcolepsy,” she says. “This lurker in my closet moved around my toys and tickled my feet. To this day I have to sleep with my feet under the covers because of the lurker.”

Like many narcoleptics, before treatment Scannell also had an extraordinary memory of her dreams, so much so that it was sometimes a struggle to distinguish their plot lines from reality. “I had a fight with Mick Jagger, then we made up and started making love on stage in front of the world, at which point I woke up,” she says. “For four hours afterward, it was like, God, did this hap-

viduals, REM is not only associated with paralysis but also suppression of memory consolidation, which is why most people can't remember their dreams,” he says. “But there's some evidence that this suppression may be less powerful in narcoleptics. Their dreams may be laid down in memory in the same way as other events during the day. In rare cases this may even cause a schizophrenia-like problem in which the individual mistakes dreams for reality.”

Another curious feature of narcolepsy is cataplexy. Any strong emotion—sadness, elation, laughter, fear—can cause an attack to come on: The narcoleptic's muscles slacken and his or her face or body may become weak and begin to sag. In some cases, he or she may even collapse on the ground in a heap but still remain alert and aware of surroundings. Why powerful

## The Sage of Sleep

All of us sleep, and none of us knows why. Giulio Tononi, a psychiatrist and neuroscientist at the University of Wisconsin, has a theory: Sleep is the price we pay for being able to learn and remember.

### Why study sleep?

Every creature, with a few very strange exceptions, sleeps. That means sleep fulfills a very basic function, yet it is still an unsolved mystery. If you wake somebody up from deep stage-four sleep, they will usually have nothing to report about the experience. And yet the brain is not any less active than in waking. Where does consciousness disappear to during sleep?

### Will we ever find a way to go without sleep?

We don't know yet. We do know that if you stay awake longer and longer, sleep becomes impossible to avoid. Soldiers have actually fallen asleep while marching. Driving when sleep deprived can cause impairment at the wheel, much like alcohol consumption. Yet people who are sleep deprived think they are doing just fine, even though their brain function is temporarily deteriorating.

### Why do you think we sleep?

Our hypothesis, which is most likely wrong in some of its details, says there is a cost to all the learning we do while awake. It says that sleep is the price we must pay for such an expensive and fantastic learning instrument as the brain. For its weight, the brain is already the most energy-expensive organ by far, and it is always buzzing along—unlike the muscles, it never really rests. Most of the energy is spent at synapses—connections between neurons. When you are awake, you learn a lot, whether you realize it or not. Memories are stored by changing the strength of many synapses—mostly, we think, by making them stronger. Stronger synapses are thirstier and consume more energy, besides being larger and occupying more space. So by the evening, even when the brain is running idle, it consumes more energy than in the morning, faces a real estate crisis, and requires more supplies. That means you can't keep learning day after day unless you can fix the situation. This is where sleep comes in. The very special slow waves your brain produces during non-REM sleep [80 percent of our sleep] enforce a kind of diet for synapses, we think. You don't lose all the memories you gained during the day, but you do reduce the overall strength of the synapses to the level at which you started in the morning. By the time you wake up, the brain is ready to learn again.

### Does every animal sleep?

One might think that dolphins and other sea creatures who are constantly in motion would be an exception, but dolphins literally sleep with one eye open. They sleep with one brain hemisphere asleep. They are safe night drivers. It would be nice if we could do the same.

By Jill Neimark with additional reporting by Jessica Kovler.

feelings can trigger cataplexy in some narcoleptics is not well understood.

Nonetheless, researchers have made great progress in elucidating the underlying causes of the disorder. The first big advance occurred in the early 1990s, when epidemiological studies revealed that 90 to 95 percent of individuals with the disorder carry a genetic marker associated with autoimmune disease—self-inflicted damage that occurs when the body mistakes its own tissues for a foreign invader and attacks them.

The next big clue came when Mignot of Stanford University tracked down a gene for narcolepsy in dogs and discovered it caused a mutation in a receptor for hypocretin, a neuropeptide involved in prodding the central nervous system awake and maintaining alertness and good muscle tone. Although humans with narcolepsy do not possess the same genetic mutation, this finding still proved instrumental in unraveling the disease's fundamental cause. In most human cases, as research by Mignot and his colleague Seiji Nishino soon showed, the sufferer is deficient in hypocretin. Further sleuthing revealed that the cells that normally produce it in the brain seem to have been destroyed in narcoleptics.

That knowledge, coupled with evidence that narcolepsy in humans might be an autoimmune disorder, has led many researchers to suspect that sufferers have immune systems that are genetically predisposed to attack and destroy hypocretin-producing cells. "That's just a theory," says Mignot. "We've not been able to prove it, but it's our best hunch for now."

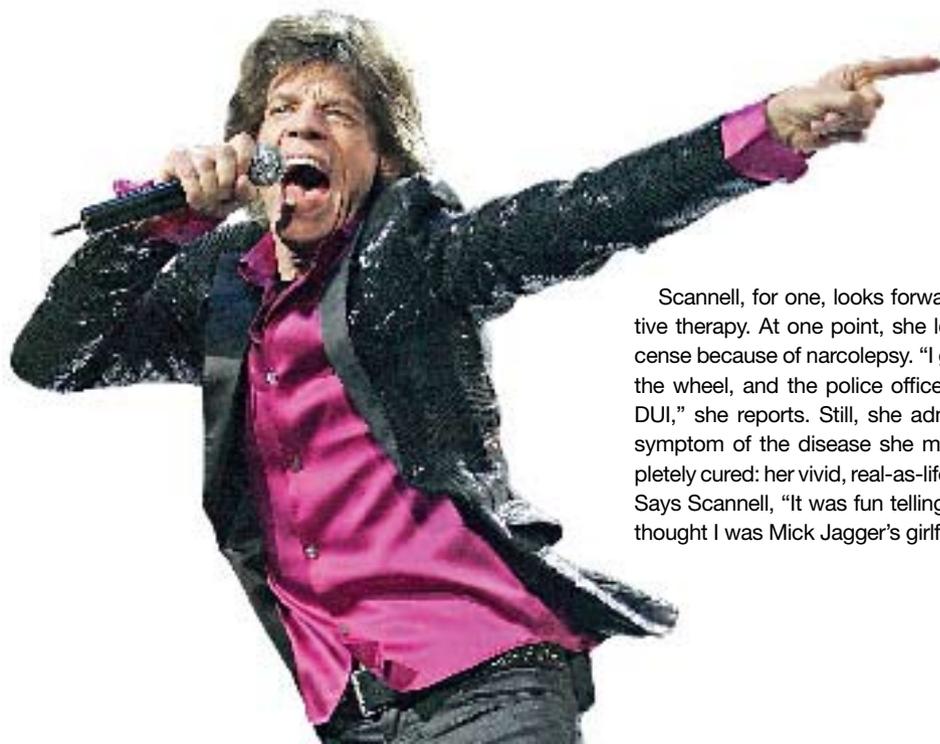
These revelations about the underpinnings of the disease have in turn led doctors to rethink the prevalence of the disorder. In recent sleep lab studies of 600 people age 30 or older, Mignot was surprised to find that 1 percent—or 20 times as many as with classic narcolepsy—suffered from inordinate sleepiness, had a high

frequency of the autoimmune marker linked to narcolepsy, and went very rapidly into REM when they napped. Yet none reported cataplexy. Even when the researchers took into account shift work and other environmental causes of daytime fatigue, the association held up. "It may be that a mild form of narcolepsy happens much more often than we realize and is an unappreciated cause of excessive sleepiness in the general population," says Mignot.

The treatment of narcolepsy, once a highly debilitating condition, has improved markedly. Stimulants and other drugs such as modafinil are often very effective in helping narcoleptics fend off sleepiness during the day. And experts report that Xyrem, a central nervous system depressant, has revolutionized the treatment of cataplexy. The drug consolidates the narcoleptic's sleep into a few blocks, preventing it from occurring in a scattered fashion throughout the day. "Just why that improves cataplexy we're not sure, but there's no question that it helps," says Michael P. Biber, medical director of the Neurocare Center for Sleep near Brookline, Massachusetts. At his center, the drug completely relieved cataplexy attacks in all 18 subjects who took the drug as part of an experimental trial, including one person who had experienced 220 episodes one week prior to treatment.

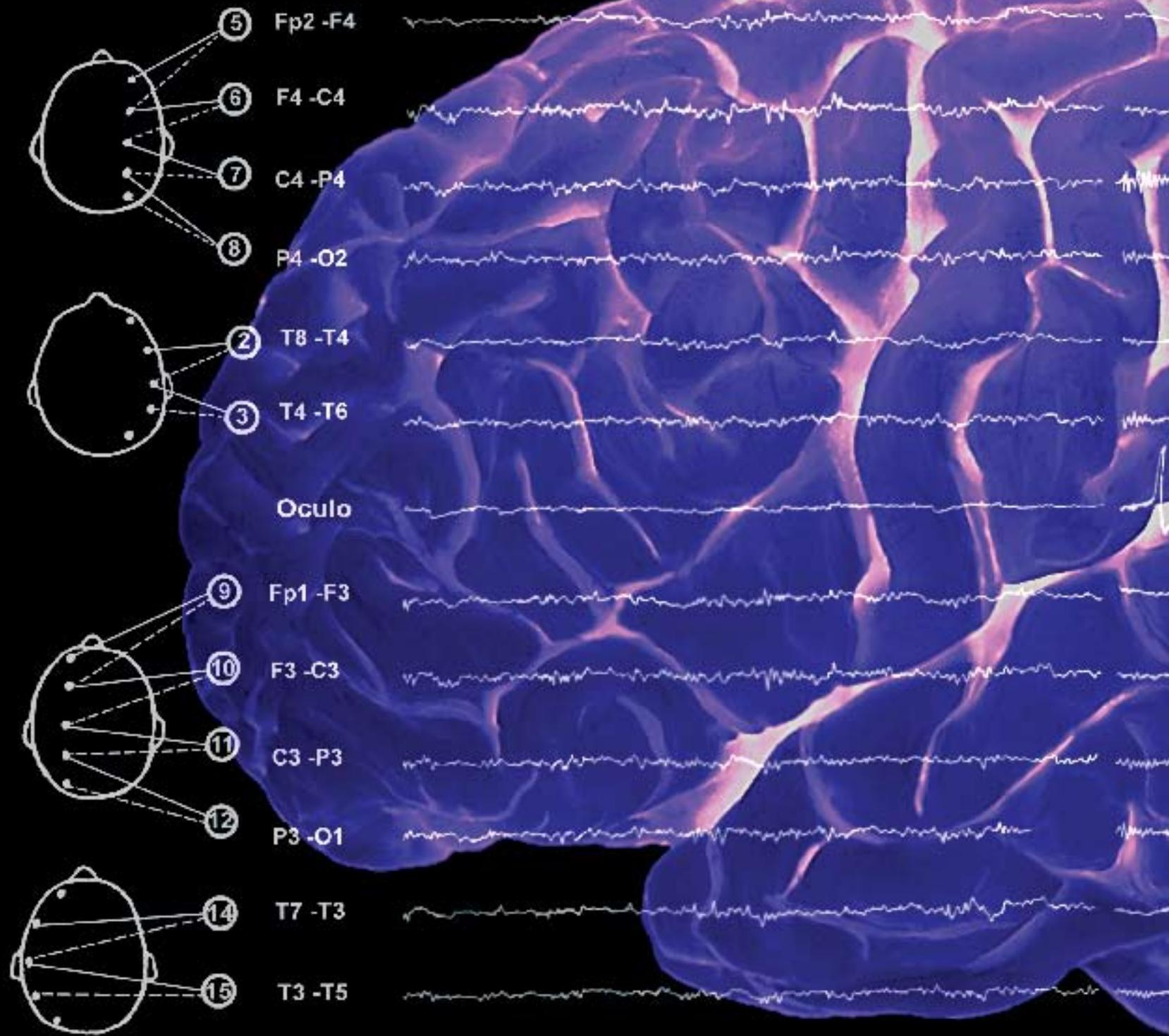
Meanwhile, pharmaceutical companies are racing to design new narcolepsy drugs based on the discovery of hypocretin's central role in the disorder. Unfortunately, hypocretin itself is too large to pass directly from the bloodstream into the brain, which is the way most neuroactive drugs work. So drug developers are attempting to design compounds that mimic the neuropeptide's action but are still small enough to get inside the brain. "This is a very fertile area of research," says Mignot. "It could bring about a big shift in how we treat the disorder in future."

Scannell, for one, looks forward to more effective therapy. At one point, she lost her driver's license because of narcolepsy. "I got woozy behind the wheel, and the police officer assumed I was DUI," she reports. Still, she admits, there is one symptom of the disease she might miss if completely cured: her vivid, real-as-life recall of dreams. Says Scannell, "It was fun telling coworkers that I thought I was Mick Jagger's girlfriend." Ω



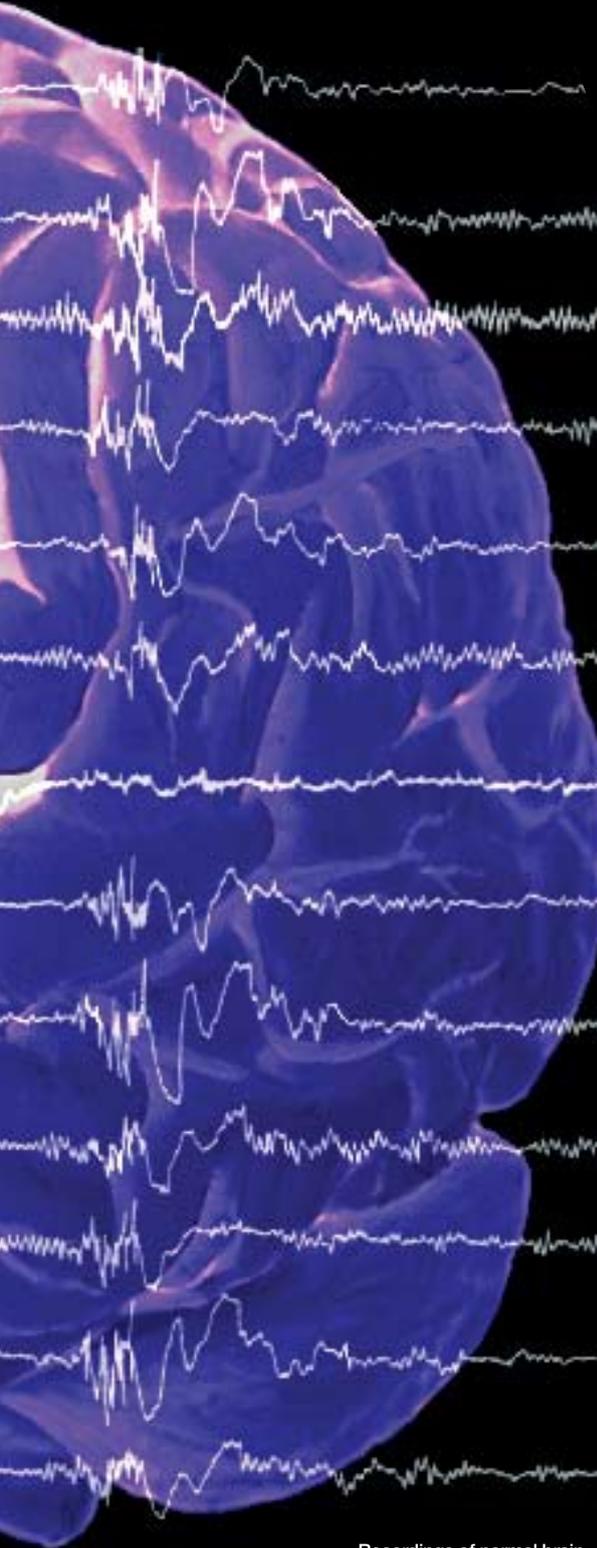
# SOMNOLENCE

EY



# Sleep

## Eaters



Recordings of normal brain electrical activity transitioning from sleep to awakening (above), overlaid on a 3-D image of an MRI.

As a young teen, Lynne Romano recalls awakening to find turned-over jars of ravioli sauce dripping down her dresser or mustard-smeared potato chips scattered around her room. How they got there was a total mystery to her. “Then my mother started getting mad at me for messing up the kitchen at night,” she says. “I had no idea I was getting up in my sleep and eating.”

The problem worsened with age. “I’ve woken up with candy wrappers all over my bedroom floor,” says Romano, now a 51-year-old mother of two living in Andover, Massachusetts. “I’ve found plates on the floor that I have to be careful not to step on when I get up.”

Except for the trail of crumbs and gooey messes that confront her in the morning—and a nauseous feeling from overeating—Romano has no memory of her nightly foraging. Once she awoke in the morning to a throbbing pain in her wrist. “I opened my eyes to see what was wrong, and I was burned,” she says. “I’d been cooking in my sleep!”

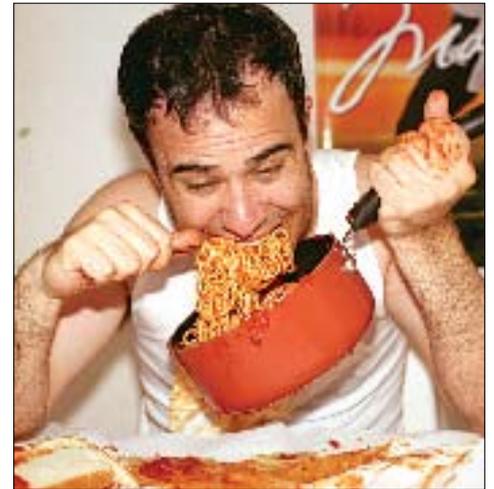
Romano suffers from a specialized form of sleepwalking called nocturnal sleep-related eating disorder (NSRED), a condition first recognized in 1991. It is a cross between a sleeping disturbance and an eating disorder. Unlike other parasomnias, NSRED often resembles a serious addiction, with sufferers frequently getting up several times a night. In this somnolent state they may scarf down voluminous quantities of food—and balloon up in weight.

For now, medical science has little to offer those whose lives are ruled by this inexplicable condition. But new research holds out hope that drugs developed to treat other neurological problems—notably epilepsy—could rein in the compulsive and blind drive to eat at the core of the disorder.

Sleep eating is often confused with the more common disorder known as night eating syndrome, in which individuals consume the bulk of their daily calories after 6 p.m. Night eating syndrome is most prevalent in people with mood dis-

turbances and involves a disruption in the circadian rhythms that govern appetite, shifting the urge to eat into the nocturnal hours. But unlike sleep eaters, night eaters are aware of what they’re doing, gorging themselves before even going to bed. If they snack in the middle of the night, they are awake and fully conscious of their actions.

By contrast, sleep eaters have minimal or no awareness, although “they usually do manage to find a way back to bed,” says Helene Emsellem, medical director of the Center for Sleep and Wake Disorders in Chevy Chase, Maryland. The disorder is also rare: Questionnaire responses suggest that



the problem affects from 0.5 to 1 percent of the population. But that’s a sketchy estimate based on a small sample, cautions John Winkelman, who conducted the survey as medical director of the Sleep HealthCenters at Brigham and Women’s Hospital in Boston. Because sufferers are often ashamed, many cases may go unreported.

“A lot of individuals with this problem start out as conventional sleepwalkers (see page 57) and then become fixated on food,” reports sleep expert Mark Mahowald of the University of Min-

nesota. “Why this happens we don’t know.” Doctors are not even sure whether it disproportionately affects people with daytime eating disorders. People seeking help for the problem at sleep clinics aren’t likely to have eating disorders while awake. But at eating-disorder clinics, many sleep eaters also suffer from daytime anorexia nervosa or bulimia.

However, hunger does not generally seem to be a motive, says David Neubauer, associate director of the Sleep Disorders Center at the Johns Hopkins University School of Medicine. “Episodes

resourceful in their quest for satisfaction. While still asleep, “one woman took scissors from her bedside table and chipped away at the wood around her lock,” reports Neubauer. “Or they go foraging and find the food they or others have tucked away in the garage.”

Still, Neubauer believes that sleep eaters may be able to exert some control over their compulsion. “A female patient was deathly afraid of snakes and succeeded in keeping herself from raiding the fridge at night by putting a large fake snake on the kitchen table,” he says.

## Except for the trail of crumbs and gooey messes in the morning—and a nauseous feeling—Romano has no memory of her nightly foraging



tend to occur within a few hours after they go to sleep,” he says, “and if you ask them why they do it, they don’t know.”

Sleep eaters usually make a beeline for high-calorie foods that are sweet, sticky, or gooey. Ice cream, chocolate sauce, peanut butter, and honey are favorites—even if the sleep eater shuns these foods when awake. Oddly, sleep eaters have been known to munch on buttered cigarettes, salt sandwiches, raw meat, even Brillo pads—virtually anything except vegetables. “I don’t know of any case of a sleep eater making a healthy green salad,” says Mahowald. “I guess people don’t like vegetables any more when asleep than when awake.” The attraction to inedible things, he admits, is harder to explain.

If a family member tries to stop the foraging, individuals who are not normally combative during the day may wage a major battle, thus discouraging others from intervening. Sleep eaters themselves have put bicycle locks on refrigerators or asked household members to lock them in their room or hide food. But these efforts usually fail, as sleep eaters may be persistent and

Some doctors will prescribe hypnotic medications to inhibit sleep eaters from getting out of bed in the first place. But that practice has become controversial due to the Food and Drug Administration’s recent warning that some of these drugs—notably Ambien—may actually trigger sleep eating in patients who did not previously have the problem.

Better treatments may soon be forthcoming. A recent trial at Brigham and Women’s Hospital suggests that the anticonvulsant Topamax, currently used to treat everything from migraines to obesity, may offer a more effective means of controlling the compulsion. Like many anticonvulsants, Topamax promotes sleep. It has been noted that, coincidentally, epileptics treated with the drug lost weight—possibly, says Winkelman, because it may suppress appetite. “We don’t know precisely how the drug acts,” he says, “but it’s certainly plausible that it might reduce episodes of nocturnal eating, so we decided to give it a try.” In his small pilot study—it involved only 30 patients—almost 70 percent of the participants experienced a significant reduction in sleep-eating episodes, and 28 percent lost more than 10 percent of body weight.

Lynne Romano was one of them. “On the drug,” she says, “I got up less frequently to binge and I lost a good 20 or so pounds. It wasn’t a miracle cure, but it sure helped.” That’s heartening news, because sleep eaters need all the help they can get. As droves of failed dieters can attest, resisting the urge to overeat takes an iron will—something hard enough to muster when awake, much less when asleep.

Winkelman is now recruiting subjects for a large placebo-controlled trial of Topamax. Sleep eaters who want to participate should contact him at [jwinkelman@sleephealth.com](mailto:jwinkelman@sleephealth.com). Ω



# Rip Van

The disease sounds as if it came straight out of Grimm’s fairy tales. Teens fall into a slumber, dozing weeks or even months at a stretch. Marathon sleeping spells come and go, cropping up intermittently for roughly a decade. Then, symptoms vanish as mysteriously as they first appeared.

Called Kleine-Levin syndrome, the condition is so rare that only a few cases have been reported in the world medical literature. Though the disorder is little known or understood, a flurry of recent research could change that. A few centuries ago, KLS might have been attributed to a witch’s curse. Now the hunt for its cause focuses on genes and infectious agents.

Stephen Maier is among the unlucky few who know the groggy misery of KLS firsthand. He developed the disorder at age 13, after what seemed like a severe case of the flu. “My parents couldn’t wake me up, and even when they succeeded, I



zombie. “You could drag me to the doctor, but I could barely string together a sentence,” Maier recalls. “Sometimes I’d speak in baby talk.”

Now a 33-year-old accountant in San Jose, California, Maier has not had a recurrence in five years. He hopes that’s the end of it—and he could be right. KLS typically comes on with a vengeance at puberty, gradually abates by the midtwenties, and vanishes altogether by about 30.

“Owing to its rarity, few sleep specialists have seen a single case of the disorder,” says Emmanuel Mignot, an authority on KLS at Stanford University. “For that reason there is skepticism about it in the medical profession, but KLS is without question a distinct disorder, with symptoms that are unique and very consistently manifested by those who fit the diagnosis.”

Like Maier, sufferers often report that the onset of the illness coincides with a flulike infection, leading many doctors initially to mistake the disorder for mononucleosis or viral encephalitis. At regular intervals after that the patient is afflicted by hypersomnia—a sleeping bout that typically lasts around 10 days. In one of the longest episodes on record, one young woman slept nearly a year.

During these periods of hypersomnia, patients usually get up only to shovel food into their mouths, bathe, and take care of bodily functions. Even then, they’re in a hazy, confused state. Light and sound may be irritating, and they have tremendous difficulty focusing. Reading or even holding a conversation is a challenge. A common complaint is that the world seems unreal or strangely off-kilter. “About the only thing I can do during episodes,

during a bout of hypersomnia is very different from that of someone in a coma or vegetative state, who typically exhibits severe EEG abnormalities. When wired up with electrodes at a sleep clinic, a person with KLS has the same sleep phases as a healthy person, says Mignot, “only they keep cycling on and on through the different stages of sleep,” rather than exiting the cycle and waking up. One hint about the disease’s underlying cause comes from functional magnetic resonance imaging (fMRI) studies, which capture pictures of the brain at work. In one study conducted in Taiwan, the researchers uncovered abnormal activity in the hypothalamus and thalamus—parts of the brain that play a critical role in regulating sleep, eating, and sex. “Sometimes changes were also seen in the cortex of these patients, which may explain some of the cognitive impairment,” says Mignot.

Heredity may play a role. A questionnaire sent to 100 patients and their parents revealed that KLS disproportionately affects Ashkenazi Jews. Given that the disease is frequently preceded by fever and other flulike symptoms, it seems that a combination of factors precipitates the illness. “My leading hypothesis,” says Mignot, “is that KLS is caused by a virus or bacterium that some individuals are more genetically susceptible to.”

Exploiting methods that he developed in his hunt for the gene responsible for narcolepsy, Mignot is now in hot pursuit of a KLS gene. He’s identified several families with a strong hereditary pattern of the disease and has begun searching for common genetic markers. At the same time, the KLS Foundation ([www.klsfoundation.org](http://www.klsfoundation.org)) is working with laboratories to collect blood samples from KLS patients and their families for a genetic study, and nasal swabs from patients during active episodes with the aim of isolating an infectious trigger. “We’re very encouraged that we will soon have some answers to an illness that has heretofore been a complete mystery,” says Neal Farber, father of a son and a daughter with KLS and co-president of the foundation.

For now, medicine has little to offer sufferers. “Stimulants can make KLS patients less sleepy, but they’re still in this weird fog and can become agitated or aggressive,” says Mignot. “That can be worse than simply sleeping.” Other treatments that have been tried with marginal or no benefit are lithium, antidepressants, anticonvulsants, and mood stabilizers. “Many doctors just want to act,” says Mignot, “but the best course of action may be to do nothing.”

No magic kiss from a handsome prince (or princess) will awaken sufferers from their long slumber. But in keeping with its fairy-tale symptoms, KLS does have a happy ending: Virtually everyone outgrows it.  $\Omega$

*Above left: Painting by Tina Gauthier.*

# Winkle Disease

was incoherent,” says Maier. “So they took me to an emergency room.”

Maier was subjected to a battery of tests, but they all came back negative. Two weeks later, he finally woke up and returned to normal life. But the bad dream wasn’t behind him: Extended sleeping episodes of about 10 to 20 days’ duration recurred about every six months throughout his teens. When they occurred, he would spend about 22 hours a day in a haze of sleep. He slept through his high school basketball team’s tournament and his senior prom. Like Rip Van Winkle, Maier emerged from these long spells in bed plagued by a sense of time warp. “Friends and family have to fill me in on what’s been going on in the world,” he says.

By his early twenties, the episodes gradually became less frequent, with his sleep time reduced to about 16 hours a day. During these relapses, though, even when he was awake, he felt like a

apart from sleep, is watch mindless videos that I’ve seen a dozen times,” says 17-year-old Eric Haller of Placentia, California, who has suffered bouts of KLS since age 12. “Anything new is too taxing on my brain.”

Another common feature of KLS, seen in about 60 to 70 percent of cases, is a ravenous appetite for sweets, potato chips, and other high-calorie comfort foods. A similar percentage of patients may also engage in inappropriate sexual behavior during episodes. During one of his first bouts of KLS, Maier recalls being dragged out to watch a basketball game, where he began groping his girlfriend directly in front of his parents and her parents. “I think the hypersexuality just comes down to the fact that you’re less inhibited in this fuzzy state of mind,” says Maier. “If it feels good, you just want to do it, regardless of the consequences.”

Just what causes KLS is unknown. Brain activity