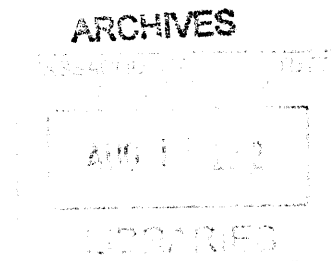


The Twitching Eye:
REM Sleep and the Emotional Brain

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Submitted to the Program in writing and Humanistic Studies in Partial Fulfillment of the
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ABSTRACT

Sleep and emotion have been linked since the discovery of rapid eye movement (REM) sleep sixty years ago. Sleep, in particular REM sleep and the dreams it harbors, seems to modulate mood, restoring stability to the weary mind. Scientists have struggled to understand this link through the biological study of the brain, the psychological study of dreaming, and the clinical study of how sleep is affected by psychiatric illness.

This thesis examines the history of sleep research in terms of its relationship to emotional processing, both from the physiological and the psychological perspective. We are introduced to the scientists who discovered REM in 1953, to those who tracked the links between the biochemistry of mood and of sleep, and to contemporary researchers who are exploring the link between sleep and mood using brain-scanners and electrodes to study the dreaming brain, and the sleep and dreaming of patients with mood disorders.

On our journey we will experience both the progress sleep research has made this century, and the enduring mystery of why humans sleep and dream.

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Introduction

Think of the commonest dreams: You are falling. You are giving a speech, when you realize you are naked. You are being chased—by a robber, a lion, a dragon. Someone you love is angry with you, and you don't know why. This nocturnal flood of emotion may be crucial for regulating our moods, the latest sleep research suggests. Dreams and the brain-state that houses them seem to re-calibrate our emotional registers each night, to refresh us emotionally for a new day—and to be broken in mood disorders, when stormy dream sleep comes to invade the deeper sleep earlier in the night, ruining sleep and exacerbating moodiness. The question is: How do our brains dream, and why?

* * *

I'm going to take you on a journey to find out why we dream. The trip will take us back in time and across the world, into many bedrooms and laboratories, from Vienna to Chicago, from Lyon and Harvard cat-labs to Berkeley brain scanners. We will meet frogs with disembodied beating hearts, cats who act out their dreams, doctors and therapists who believe the secret of curing mood disorders lies in dream-sleep. We will go back in time to the beginning of sleep science, to see how the twitching eye was discovered, and we will go inside the brain, to see the chemicals that drive our dreams and our moods. We will see the brain-scanners used today to image the dreaming brain—and to uncover the link between mood and the twitching eye of dreaming.

We begin where we will end, here in 2012, at the edge of the science of sleep.

SLEEP 2012

Pictures of brains faced a crowd of sleep scientists and doctors watching a debate on why we dream. The sleep-scientists munched box lunches at this final debate of *Sleep 2012*, the 26th annual meeting of the scientists and medical doctors who study sleep, on June 12. The title of the debate was a hot topic in sleep today: “REM Sleep and Dreaming: Cause or Consequence of Emotion?”

Sleep is a huge conference, reflecting what a major health problem and scientific mystery sleep is: Why do we need sleep? Why does a healthy human spend roughly a third of his life sleeping, and almost a quarter of this time dreaming? Why is sleep so difficult for so many people? How does sleep loss affect the body and mind—and what does sleep do in healthy brains to keep us well? 14,000 sleep specialists in fields ranging from psychology to pulmonology crowded into Boston’s Hynes Convention Center from June 9 to the 12th. The swarm of sleep specialists presented data and discussed why humans sleep and dream, and what goes wrong when sleep goes awry. Insomnia, apnea, metabolic problems and overeating; depression, anxiety and bipolar disorder—all are tied to disordered sleep. But here on the final day of the conference, the focus turned to the magic that happens in our heads at night: Dreaming.

Sleep science today is like an elephant. Scientists from different fields, like blind men, touch different parts, and imagine a different animal. But data from a variety of fields is converging lately on a picture of sleep and emotion, suggesting that REM sleep and dreams nightly restore stability to emotion, like medicine for the moody mind. Before we can understand this picture, though, we have to know how we got here, where sleep science comes from. This story takes us first to Vienna in 1900.

* * *

From Dreaming to Anatomy and Back Again

Sigmund Freud (1853-1939), the Austrian neurologist who founded psychoanalysis, brought scientific attention to dreams with his 1899 book *The Interpretation of Dreams*. Indigenous cultures from the ancient Greeks to the Iriquois had believed that dreams “were coming from gods, from this magical place called the soul, wherever that was,” says Matt Walker, director of the Sleep and Neuroimaging laboratory at the University of California, Berkeley. “What Freud did was to place dreaming solidly in the brain.” Oracles and shamans made predictions of the future from dream symbols. But Freud popularized the idea that dreams could be understood scientifically, as produced by the unconscious brain. Freud argued that dreams were platforms for people to act out unconscious desires: the job of the analyst was to help patients interpret their dream symbols, to recognize and deal with primitive desires.

Freud’s “wish-fulfillment” theory dramatically influenced 20th century art and culture, but has less lasting sway on the modern science of sleep and dreaming. What has lasted is Freud’s conviction that dream sleep is linked to emotional health.

* * *

Nathaniel Kleitman was the first scientist to devote his career to studying sleep. The curmudgeonly Russian immigrant, who lived to be 104, trained the first generation of sleep researchers. Kleitman got his Ph.D. in physiology at the University of Chicago, then joined the faculty there in 1925 where he set up the world’s first sleep lab. Kleitman was so obsessively devoted to studying sleep that he once lived for a month in a Kentucky cave, to see whether the body’s daily cycle, when removed from environmental cues, could be shifted to either a twenty-one-hour or a twenty-eight hour day (He found

that no, our body's internal clock is naturally set to between a twenty-four and twenty-five hour day).

Meanwhile, in the 1930s, Hans Berger, a German physiologist and contemporary of Kleitman's at Harvard, invented the electroencephalogram (EEG), a device used to record brain activity from the scalp. Kleitman and his students soon used the machine to see what happens in the brain during sleep. What they saw was that the brain slows down when we fall asleep: brainwaves recorded from the scalp synchronize into a slow pulse, as opposed to the fast, shallow buzz of wakeful brainwaves. This led Kleitman to think of sleep as an "off" state for the brain to recuperate from waking and to restore the body. By 1939, when Kleitman published *Sleep and Wakefulness*, the first textbook on sleep, it seemed that sleep had become the province of physiology. But a mid-century discovery by one of Kleitman's students would lead some researchers down a path back to dreams.

Discovering a New Continent of the Brain

One night in December 1951, an eight-year-old boy fell asleep in his father's lab. Chemicals spurted across a synapse in the boy's brainstem that night, as they typically do in the human brain about ninety minutes after falling asleep. In response to this tidal shift in brain-juices, the boy's eyes began to twitch; his mind awoke while he slept. He dreamed.

What was new that night was that someone was watching sleeping eyes and brain waves at the same time. The boy's father, Eugene Aserinsky, a 30-year-old physiology graduate student at the University of Chicago, was recording eye-movements and electrical activity from his son's sleeping brain in search of a doctoral project.

Eugene's pregnant wife, Sylvia, cared for their son, Armond, in a chilly dormitory, renovated from a World War II barracks. Sylvia battled manic depression while her husband toiled in the lab at night. They were poor, and Eugene Aserinsky was a name no one knew. Aserinsky's boss, Nathaniel Kleitman, the world's preeminent authority on sleep at the time, believed that sleep was the brain's off state - a period of rest to recuperate the body. "Sleep is to waking as ice is to water," Kleitman would say. But on this night in the basement of Abbot Hall, our view of the sleeping brain changed.

When Eugene Aserinsky saw Armond's brainwaves spiking in rapid jerks on the EEG, he thought the boy must have woken up. Ink-pens wiggled in time with the boy's brainwaves, making a soft scribbling sound, the output of the machine recording electrical activity from electrodes on his scalp. Wavy lines appeared on a spool of white paper, as his neurons fired in synchrony. Slow-moving waves meant deep sleep. When the pens scribbled fast, it usually indicated the boy was awake. But then Eugene noticed Armond's eyes: lids closed, rapidly moving back and forth. The brain looked awake, but not the boy.

Since sleep scientists like Kleitman only expected to see two stages—"Awake" and "Asleep," like the brain's on and off modes—they had never recorded far past sleep onset, when the brain slowed down. They assumed the rest of the night would look the same: the synchronous brain peacefully fluctuating like an ocean, slow waves rhythmically lapping up on the shore of the scalp from the depths of sleep. But that night in Chicago, when Eugene Aserinsky watched his sleeping son's brainwaves over a longer period, he glimpsed a new territory no one had seen before: the time at night when the brain awakes while we sleep, the eyes move and we dream. In the world where Armond

Aserinsky woke up, his father had discovered what he called *rapid eye movement (REM)* sleep, and a new field of science was born.

Two years later, in 1953, Aserinsky and Kleitman published their findings in *Science* and sleep scientists around the world were intrigued. The discovery of REM sleep was like finding “a new continent” in the brain, a third state of consciousness apart from waking and sleep, wrote Michel Jouvet, the French neurosurgeon and sleep researcher. “Paradoxical sleep” is what Jouvet called it: a waking brain in a sleeping body.

In the following few years, Aserinsky and Kleitman released a series of papers, along with William Dement, the young psychiatry M.D./Ph.D. student who joined the lab in 1952. They found many ways the body is turned on during REM: heart rate increases by an average of ten percent, breathing by twenty percent; genitals fill with blood: bodily signs of emotion.

They also found that dream intensity seemed to track the eye movements: the emotionality, vividness, and length of dream reports correlated with the eyes’ twitching. Dement, who went on to establish the sleep research center at Stanford, was the first to describe the cyclical nature of nocturnal sleep in a 1957 paper, after making continuous recordings of brain and eye activities throughout the night. He was the one to name the main sleep stages: Stage I (sleep onset); Stage II; slow wave sleep (also called deep sleep, or Stages III and IV); and REM. This cycle of sleep stages is evident from EEG readings.

When we are awake, our EEG brainwaves look like jerky, shallow squiggles. This is because large groups of neurons don't tend to fire in synch when the brain is awake.

When we are awake, patterns of neurons across the brain's cortex are processing varied signals at once, reflecting the busy cacophony of daily life. During deep sleep, on the other hand, the brain is unconscious—electrical activity fluctuating in slow, coordinated pulses across the brain. So sleep scientists can distinguish conscious states by eyeballing brain waves.

During Sleep Onset (Stage I sleep), the faster brainwave rhythms of waking give way to the slower “theta” rhythm characteristic of deep relaxation: four to eight hertz, or peaks per second, on the electroencephalogram. At the same time, eyelid-movements also cease. A low-tech way to determine when someone has fallen asleep is thus just to watch the twitching of his eyelids: when the twitches stop, the person is asleep.

Next comes Stage II sleep, which takes up half of sleep, the gaps between deep-sleep and dreaming. It is recognizable by waves called *k-complexes* and *spindles*, two large spikes associated with suppressing outside noises and with learning. Spindles in particular are thought to convert recent “procedural learning,” like guitar playing, into memories.

Deep sleep, or slow-wave sleep, fills between twenty and twenty-five percent of sleep nightly in a healthy adult, and comes after Stage II in the cycle. Deep sleep is the restorative part of sleep—the stage most hungered for after sleep loss—which is lost by older people as they age. After a period of sleep deprivation, a person will plunge quickly into slow wave sleep, and stay in this phase longer, to replenish nutritious slow waves. During slow-wave sleep, the pituitary gland secretes its peak amount of human growth hormone (HGH), which is involved in repairing body tissue, restoring energy levels for a new day. This is also the sleep stage when “memory replay” happens in the brains of

birds and rats, and when researchers believe human experiences are initially laid down as memories. It is a largely unconscious stage of sleep, when dreaming is extremely uncommon.

REM sleep, when dreaming most often occurs, comes after deep sleep in the cycle, and takes twenty-percent to a quarter of the night. Dreams are common during this stage, reported in about 80 percent of awakenings in Dement's original 1957 experiment. So the average human spends about two hours per night dreaming: Over the course of a life-time of eighty years, at 720 hours of REM per year, that's more than *six years* of dreaming.

Dreaming is the one situation outside waking life when mental experience is busy. When a person passes into REM sleep, brainwaves suddenly shift from the regular pulse of slow-wave into a jerky pattern that looks a lot like waking, as the eyes jerk back and forth rapidly in a repetitive motion.

Once we fall asleep, the brain cycles through the three main stages - Stage II or light sleep; Slow-Wave deep sleep; and REM Sleep, in that order - about every ninety minutes. The first cycle from waking to REM takes between fifty and seventy minutes, and REM returns about every ninety minutes. During the first half of the night, for healthy sleepers, deep sleep predominates and REM periods are as brief as ten minutes. As the night progresses, non-REM sleep grows lighter and the REM periods last longer, extending from twenty minutes to as much as one hour in the early-morning hours. By the fourth or fifth REM period in a healthy night's sleep of eight and a half hours, most of the cycle is REM.

Aserinsky and Kleitman as physiologists were more interested in the biology of

sleep than in dreaming. But William Dement, the young psychiatrist who joined their lab, was trained in psychoanalysis and focused on dreaming. By the late 1950s, Dement had established a link between REM sleep and dreaming. He found that more REM sleep awakenings produce dream reports, as compared to awakenings during sleep periods when the eyes are not moving.

Dream studies later confirmed that dreams are more common in REM, but percentages varied depending on what is defined as a dream: Is a dream any image or thought you remember when you wake, or only a visual story with a narrative plot? People report dreams after 75-95 percent of REM awakenings, while non-REM awakenings produce reports less than half the time. Dreams reported after non-REM awakenings also tend to be flatter and less emotionally intense: mundane replays of recent waking experience, rather than the fanciful, sexual, or nightmarish fantasies of REM. So although dreams do occur outside of REM—mostly in Stage I and Stage II sleep, which takes up half the night, rather than the 25 percent of the night in deep sleep—these dreams have a different character: shorter, less bizarre, and less emotional than REM dreams.

This aspect of REM dreams—the emotion—is what first drew researchers to find a link between dream-sleep and emotional health. One of the first to look into this link was a colleague of William Dement's in Chicago named Rosalind Cartwright.

The Dream Queen

Rosalind Cartwright began doing dream research in Chicago shortly after REM was discovered there in 1953. The Dream Queen, as she is known in the sleep research

community, earned her nickname by studying divorced people's dreams. Her goal was to discover what role dreams play in lifting depression after a traumatic event. Dreams, Cartwright believes, can update a person's shattered sense of self, healing depression naturally, without therapy or meds.

Rosalind Cartwright stands not much over five feet tall but remains energetic, talkative and red-haired today, at the age of ninety. The walls of her 11th floor Lakeshore Drive apartment are covered in abstract-expressionist paintings by her deceased brother-in-law, including one in the living room called "Queens Shall Reign." Last year Cartwright published her fourth book, *The Twenty-Four Hour Mind: The Role of Sleep and Dreaming in Our Emotional Lives*, and she is now working on a memoir, using the iPad her daughter gave her for Christmas. Her new book will describe her contributions to both dream research on emotion-regulation and to sleep-apnea treatments, her lifetime's worth of sleep science.

Cartwright first heard of rapid eye movement sleep in 1952 from her secretary, Pat, who dated Bill Dement, then a young medical student working in Kleitman's lab.

"One day Pat burst in all breathlessly, plopped down in the chair next to me, and said: 'Do you know the eyes move while dreaming?'" A few years later, Cartwright found herself searching for a new area of research after her mentor, the psychotherapist Carl Rogers, left to take a new job at the University of Wisconsin. She realized she was "sitting right in the heart of a new field" in Chicago. Back then, she laughs, the whole field was so small they could fit around "a single conference table at Bill's."

Bill Dement had shown, in a 1960 *Science* paper called "The effect of dream deprivation", that sleepers respond to being deprived of REM by getting more of it the

next time they sleep. We “hunger” for dream sleep, Cartwright and Dement found, and replenish it when we’ve been starved of REM. Trained as a clinical psychologist, Cartwright was curious to apply this REM treatment to people with mood disorders—to see how depriving REM sleep might affect their moods.

In 1961, Cartwright left the University of Chicago to take a new job at the University of Illinois in Chicago. There she worked with Allan Rechtschaffen, who would later write the sleep-stage manual that set the standards for distinguishing REM from slow-wave sleep. But at the time Cartwright met him, Rechtschaffen was just beginning his career. Critically, Rechtschaffen was a psychologist, not a physiologist or a medical doctor like Aserinsky, Kleitman, and Dement, so his lab became one of the first bases for psychological work on REM sleep and dreaming. Rechtschaffen taught Cartwright how to use a small 4-channel EEG machine, a little old-fashioned device that Cartwright called her Model T. Once she became proficient, Cartwright scoured the campus for space to start her own lab. The spot she found was a converted men’s restroom: her first dream lab.

Cartwright’s first dream research focused, like Dement’s, on REM deprivation—what effect depriving REM sleep has on healthy people and those with disorders. In 1978, she moved from the University of Illinois to found the Sleep Disorder Service and Research Center at Rush School of Medicine, where she focused her work on clinical sleep disorders like apnea and sleepwalking, and on emotional processing during sleep. The sleep lab at Rush has eight beds equipped for polysomnography, used seven nights a week: six are used to diagnose sleep disorders, while the last two are used for research.

When Cartwright began her dream research on depression in 1983, she was aware

of previous work by David Kupfer, showing that the REM cycles of depressed patients differ from than those of healthy adults.

At the University of Pittsburgh, when Kupfer ran the depression unit at the hospital, he had all his patients sleep-monitored every night they were in-patients. The patients were weaned off antidepressant drugs when they arrived in the hospital, so Kupfer could see what their sleep looked like in natural conditions, and how it responded to medication. Kupfer and his colleagues collected sleep data for about ten years, allowing them to see how REM sleep is influenced both by depression and the antidepressant drugs used to treat it.

Sleep in depression, they saw, shows a pattern: the first REM period generally comes too early in the night - after less than sixty-five minutes, rather than the usual ninety. Depressed dream-sleep often comes immediately after light stage II sleep, skipping the first slow-wave period of the night. This first REM in depression is longer than normal - as long as twenty minutes, rather than the usual five to ten - and stormier: filled with dense volleys of rapid-eye movements.

REM earliness seems to be a marker of genetic vulnerability to depression. Depressed people's first-degree relatives, who are not depressed themselves, tend to show the same pattern. Not all depressed people have early REM, but those who do are the ones who tend to respond to antidepressant medications: after the drugs move REM back later in the night (most antidepressant drugs suppress REM sleep), the depression remits. REM earliness in depressed people tends to correlate with behavioral symptoms of depression: the earlier a person's first REM arrives, the more likely he is to report loss of interest in hobbies, decreased energy, pervasive feelings of tiredness, poor appetite and

weight loss, decreased drive, social withdrawal, unreasonable feelings of guilt and worthlessness, difficulty concentrating and making decisions, and suicidal thoughts. These are the hallmarks of clinical depression, as measured by the psychiatrists' guidebook, the Diagnostic and Statistical Manual of Mental Disorders IV (DSM IV).

Cartwright was also following the work of her friend and former colleague in the Reschaffen lab, psychiatrist Gerald Vogel, head of the Sleep Lab at Emory University School of Medicine. He decided in 1975 to try depriving depressed people of REM sleep, to see what would happen if you changed the dose of REM sleep in a depressed person's brain. His formula was simple: for three weeks, a depressed patient would sleep in his lab, hooked up to an EEG. Whenever the sleeper began to enter REM, Vogel and his assistants would wake him up. Up to thirty times in a single night, the subject would be awakened from dream-sleep and forced to fall back into non-REM sleep. The seventh night of every week was a "rebound" night, when the subject was allowed to sleep undisturbed to catch up on the six nights of missed REM sleep. A control group of other depressed patients was awakened the same number of times each night, but from non-REM sleep instead. If, after the three weeks, a patient's depression had remitted, he was released, and a new depressed patient was cycled into the experiment to fill his spot.

What Vogel discovered was that REM deprivation, in about half of his patients, had an antidepressant effect. The six nights of REM loss caused a binge in REM on the seventh night, as the psychologists expected from previous studies. But in half of his patients, REM not only increased, it was also regularized in terms of sleep structure: REM sleep came mostly at the end of the night, and slow-wave sleep mainly at the beginning, in the normal pattern. And the depression lifted.

REM deprivation was not a cure for depression. The REM-redistribution trick only worked for half of Vogel's patients and even those typically needed antidepressants to maintain stability after the sleep treatment. But Vogel's work, coupled with Kupfer's, did suggest that REM sleep is related to depression.

With Kupfer and Vogel's having shown the link between depression and REM sleep, Cartwright wanted to find out if there was a relationship between depression and the dreams themselves that occur during REM sleep. Might there be something different about the REM dreams of the depressed people who recover from the blow of a breakup, as compared to the dreams of those who get stuck in a depressive rut?

The dreamers, in a series of experiments Cartwright ran at Rush School of Medicine in Chicago, were men and women who had recently lost their spouses through divorce. Each dreamer came to sleep in Cartwright's lab multiple times soon after the divorce. Each time the subject was evaluated for depression using the Structured Clinical Interview for DSM Disorders, or SCID, the standard test for mental illness. By comparing her subjects' dream reports, Cartwright could see what differed in the dreams of people after trauma, whether depressed or not, and whether anything in the dreams of future remitters (people who would grow past their depression naturally, without medication or therapy) differed from those who stayed stagnant in depression.

This picture emerges from a series of experiments, the most recent published in 2006. Twenty divorced people entered the study depressed, while ten, although fresh from a divorce, were not clinically depressed. Each person slept in the lab three separate times - Month 1, Month 2, and Month 4 after the divorce. In each session, Cartwright measured the person's mood before and after a night of sleep, and awoke the sleeper

during each REM period to ask, "What was going through your mind?" Afterward, the dream reports were rated - by the dreamer himself and by a judge blind to the dreamer's status, for the emotional intensity of the dream and the appearance in the dream of twelve "current concerns," emotional factors in the dreamer's recent life. Cartwright's team also recorded the length of each dream report, and whether or not it referenced experience from the past or the future.

By the third visit, twelve of the twenty depressed patients had recovered, while eight were still depressed. So Cartwright could see, looking back on the reports, what was different about the dreams of those who recovered. Cartwright hypothesized that it might be dreams about the trauma - about the ex-partner or the divorce - which aided the recovery. But she found that all her subjects dreamed of their exes. What mattered, she discovered, was not just dreaming about the trauma, but experiencing strong emotion and associating the recent trauma to older memories.

Dreams of the people who recovered were longer and more emotional, with more dramatic plots, higher numbers of scene changes, more characters, and a mix of recent experience with older memories. The dreams of the "control" patients, the ones who were never depressed, and those in recovery, tended to show a shift from dark to happy dreams across REM cycles, whereas the depressed people's dreams stayed flat, or negative, across the night.

Cartwright's work suggests that the dreaming process of those who emerge from depression after trauma somehow inter-relates recent emotional experience with past memories, and this integration seems to help soften traumatic blows by associating them with previous challenges that have been overcome. The emotional content of dreams, for

these people, seems to function as the brain's built-in psychotherapy.

“Negative dreams at the beginning of the night and positive at the end of the night” Cartwright asserts, is the indication of successful natural dream therapy, a sign that the brain is processing the trauma on its own. The evolution of dreams across the night, she believes, plays a role in de-toxing memories of their traumatic tone, and when this process of dream-evolution fails, a continuing clinical depression is the result.

“If you've got a trauma, that's new to you - you get hit by a car as you're crossing the road, your wife breaks up with you - something that's never happened to you before, it's unexpected,” Cartwright says, and you are forced to update your sense of self and your place in the world. Cartwright believes dreams are the brain's way of stitching emotional experiences like these into the fabric of our sense of self. Our brains may assimilate such traumatic experiences by free-associating them to other events in our personal memory, to other times we were challenged but survived; or to memories of movies or books where the tragedy ultimately resolved, where what seemed like the end of the world turned out not to be. This is why Cartwright thinks dreams over REM cycles tend to move from literal replays of experience to medleys of the present and past, as our dreams rebuild new aspects of who we are.

Dream studies based on subjective report, like Cartwright's, raise challenges. Since dreams can't be measured outside a person's head, we don't know if dream reports are true descriptions of what a person remembers seeing in his sleep. The flat reports of depressed patients might spring from lack of energy or enthusiasm for the research, rather than differences in their actual dreams. Conversely, other subjects may try to please

researchers, while the researchers themselves may seek confirmation of their theories. For these reasons, other sleep researchers have tried to understand what happens during REM sleep biologically, in experiments where results can be physically measured and evaluated. But in order to understand the REM research of modern neuroscientists, we must understand some of the basic chemistry of the brain.

Dreaming Chemistry

The chemical story of dreaming began with a scientist dreaming of chemistry.

The night was Easter Sunday, 1921, thirty years before REM sleep was discovered. Otto Loewi (1873 –1961), a German-born pharmacologist, was a professor in Graz, Austria, while Sigmund Freud developed his dream theories of wish fulfillment in nearby Vienna. Freud's *The Interpretation of Dreams*, published two decades before, was still the leading theory of dreaming at the time. But Loewi, through chemistry, was about to crack open a new window into the dreaming brain.

The dream Loewi had that Easter night was of two frog hearts beating in a fluid. The dream, as Freud might say, fulfilled a wish of Loewi's: a scientific image that had eluded him.

When Loewi woke up, he dashed to the lab to try the experiment he had seen in his sleep. Loewi was studying the vagus nerve, the neuron that slows the heart beat. Scientists did not know then how nerves communicate. They assumed the link must be electrical, like wiring. Loewi had a hunch, though, that it was chemical: that neurons talk to the heart through messenger molecules. He couldn't think of a way to find any chemical messengers, though, until his Easter dream brought the answer.

When he got to the lab, Loewi stimulated one frog's vagus nerve with current: as usual, the heart started beating slower. Then he took the fluid around this first frog's heart and used it to bathe the heart of another frog. The second disembodied heart slowed its beating. Loewi had his proof: neural messages move through chemicals.

Though he didn't know its name yet, Loewi had found the first of the brain's chemical messengers, acetylcholine, now called a neurotransmitter—a discovery that secured Loewi the 1936 Nobel Prize in Medicine or Physiology. Loewi's work opened the door to a century of science revealing how chemicals run the racing of our hearts, our fears and anxieties, and how they switch our brains from waking to sleep to dreams.

In 1951, the same year Aserinsky discovered REM sleep in Chicago, Betty Twarog, a 25-year-old Harvard graduate student, was studying another chemical in the brains of clams. She was on the road to discovering the first proof that chemical talk happens not just in the heart, but in the brain. The molecule Twarog found in the brains of clams, and later in rats, dogs, monkeys, and humans, is today perhaps the most famous neurotransmitter, the one we associate with happiness and depression: serotonin.

The chemicals of mood and of dreams had now been discovered. The link between these two chemicals and sleep came later, from sleeping cats.

In 1959, in Lyon, France, neurosurgeon Michel Jouvet surgically disconnected the part of the cat's brain that normally paralyzes the muscles during REM sleep, and watched what happened. What he saw was startling. When the cats entered REM sleep, just like Aserinsky's son, their eyes would start twitching. But unlike Armond, whose body lay motionless on the bed while his mind took off into imaginary worlds, Jouvet's

cats would leap up and move about the lab. They pounced and clawed with their paws as if to capture imaginary mice. The cats seemed to be acting out their dreams.

Jouvet had discovered how the brainstem paralyzes the muscles during REM sleep—and what happens when this connection is cut. Jouvet's sleep-walking cats suggested that dreams may rehearse survival programs ingrained in the animal's genes: escape from threat; capture prey; pursue and copulate with mate. His experiments also paved the way for the discovery that sleep stages are triggered by chemical cues from the base of the brain.

The decoder of this chemical key to sleep was a student of Jouvet's. In 1963, Allan Hobson came to visit the French lab from Harvard, as a young psychiatry resident. After learning the techniques for recording from sleeping cat brains in Lyon, Hobson returned to Harvard and teamed up with fellow psychiatrist Robert McCarley in 1968. They started inserting electrodes into cats' brainstems to record from certain neurons across the sleep cycle. Their targets were neuromodulators: brain-chemicals secreted from the brainstem which soak the whole brain, turning on and off regions of cortex at once, like conductors directing the brain's orchestra.

REM sleep and deep-sleep, they found, are dueling neurochemical states. Sleep's two main stages, REM and slow-wave, are triggered by the firing of two separate groups of neurons in the brain-stem's pons, an ancient structure at the base of cortex. The pons acts as the brain's chemical pacemaker, by dousing the cortex in sequential blasts of neuromodulators. By 1975, after years of watching cats sleep, Hobson and McCarley had discovered the chemicals that turn on dream-sleep and the ones that turn it off.

“REM-on” and “REM-off” neurons - that is what they called the neurons that flip

the switch between REM and deep sleep. REM-on neurons, they found, spurt acetylcholine, the brain-chemical Otto Loewi discovered. When Aserinsky's son's eyes started twitching that night in Chicago in December 1951, the chemical that flowed from his brainstem to flood his cortex was acetylcholine. The chemical that made his eyes twitch, paralyzed his spinal cord to stop him from acting out his hallucinations, while drenching his cortex in dreams, was the same stuff that had slowed the beating hearts of Loewi's frogs thirty years before: Acetylcholine: heart-pacer, dream-maker.

REM-off neurons, on the other hand—the ones that turn off the tap of dreaming—use serotonin and noradrenaline. These are the same molecules that spur alertness, memory, and upbeat mood in waking brains, but are depleted in depression. They are at their lowest concentrations during REM sleep—when acetylcholine drenches the brain in levels twice as high as during waking. During deep sleep, the levels of serotonin and norepinephrine are at about half the waking level, but twice as high as during REM. So Hobson's sleeping cats at Harvard revealed that the brain shifts gears chemically from one sleep stage to another, using some of the same neurotransmitters psychiatrists target to treat depression.

The anti-depressant era had begun in the 1950s when the psychiatrist Nathaniel Kline published "The Serotonin Theory of Depression" in *Science*, launching the idea that depression is related to low levels of serotonin. The medications subsequently developed to treat depression, by raising serotonin—tricyclics, monoamine oxidase inhibitors, and serotonin-selective reuptake inhibitors (SSRIs)—also tended to block REM sleep.

Since REM sleep was triggered by a chemical wave welling up from the

brainstem, Hobson argued that dreams are merely an epiphenomenon: our mind's synthesis of the random emotions and images triggered by the firing brainstem.

According to Hobson's now famous activation-synthesis hypothesis, dreams may have meaning, but only what our conscious mind creates. The source of dreaming is simply biochemistry.

* * *

While neuroscientists continue to probe the biochemistry of dreaming, there is no proof yet that dreams have a biological function. But the Berkeley neuroscientist Matt Walker, for one, still suspects that dreams are more than just random images:

"I would find it remarkably surprising to find that dreams do not have a purpose," he says, pointing out that an activity like dreaming, combined with rapid eye movements, must be metabolically demanding. "That seems like a great amount of energy to spend for something that's not functional," he argues. But what might that function be? Walker's mentor at Harvard, a student of Allan Hobson's, has some ideas.

Dreaming as Digestion: Metabolism of Memory

Dr. Robert "Bob" Stickgold, a professor of psychiatry at Harvard Medical School and a leading expert on sleep has developed a theory of the function of dreaming. Stickgold's experiments using videogames to influence dream content have begun to show the link between waking experience, memory and dreams.

Dreams, Stickgold believes, process emotional experiences and integrate them with essential memories from the past. "Memory evolution," Stickgold calls this process, which he and Matt Walker explained in a 2010 review called "Overnight Alchemy."

Deep sleep early in the night, they suggest, is when recent memories are replayed and consolidated into memory.

Evidence for this “memory reactivation” comes from studies of sleeping rats: When MIT researcher Matt Wilson left electrodes in the brains of his lab rats after they ran a maze and fell asleep, he saw familiar sequences of neurons fire back to life. In the hippocampus, a brain-region involved in spatial navigation and episodic memory, the same series of neurons that were triggered when the rat ran a maze were “reactivated.” Later studies showed that “rewarded routes,” where the rat received chocolate, were played back more often. This suggests, as Stickgold believes, that emotional experiences are preferentially converted to memory by slow-wave sleep. REM’s job, on the other hand, he believes, is the extraction of meaning from memory: processing new experiences in the context of old memories: integration of new emotional learning.

Stickgold’s Tetris study, published in 2000 in *Science*, was the first study of dreaming published in that journal in thirty years. Focused on dreams at sleep onset, the “hypnagogic period,” the study showed that both healthy people and amnesics, after playing the repetitive shape-falling game *Tetris*, saw images of falling shapes in their dreams. These “day residues,” as Sigmund Freud called the bits of waking life that leak into dreams, were most common immediately after falling asleep.

In later dreams, these day-residue images became interspersed with older memories. Although the lab version of Tetris was black-and-white and silent, it inspired experienced video-gamers to dream of colored shapes and the theme music from the Nintendo version of Tetris. Similarly, in a later experiment using the ski videogame

Alpine Racer II before sleep, subjects dreamed of old experiences on ski slopes. Recent experience became incorporated into a web of older memories as the night progressed.

The role of REM sleep and the dreams it produces, Stickgold suggests, is to digest information: to sift through the events of our daily lives, tease out the “salient information,” and integrate this new knowledge into what we know.

* * *

Scientists don't know yet why we have multiple REM cycles during the night, or why healthy people have more deep sleep in the first half of the night, and more REM in the second. The fact that evolution designed sleep this way, though, and that mentally ill people have disturbed cycles, suggests the sleep cycle has a function. Deep sleep and dream sleep may play complementary roles—first slow-wave sleep, then REM, in sequence— to process our memories and moods.

“One of the most impressive abilities of the brain,” says Stickgold, who first proposed this serial-process view, “is to take new information and integrate it into larger networks.” The important experiences are the emotional ones, the events that we process and remember later, and it is these emotional events that Stickgold and other researchers believe are preferentially digested by REM sleep. “I think we do ninety-eight percent of this processing unconsciously,” Stickgold says, “and probably two-thirds of that during the night.” It is to this emotional processing, or nocturnal “therapy” that we will turn next.

Overnight Therapy

Here comes a picture of a bloody cut-off hand. Then a topless woman appears on

screen, followed by a baby with a grotesque goiter on its face. A snake appears, its pink mouth open, baring attack-ready fangs. Then a shark bursts out of the water. A knife. A burn. A pile of corpses.

These are the images you might have seen before sleeping if you were a volunteer at Matt Walker's Berkeley lab in the fall of 2009. What the sleep scientists there were trying to find out is how the brain response to emotional experiences is changed by a night of sleep. Walker believes that during REM sleep, when our brains are drenched in de-toxing chemicals, we relive our most painful memories, and they are softened.

Before their experiment, Walker and Els Van Der Helm, his 28-year-old Dutch graduate student, published "Overnight Therapy," a review paper in which they argued that sleep disturbance is a symptom in almost all mood disorders, from depression to bipolar disorder to PTSD, and that sleep must play a role in regulating mood. "There has been in the psychiatric world a notion that sleep abnormalities are present in mood disorders," Walker explains. "but they have largely been considered co-occurring, not causally related. I believe they are causally related, and I think we are going to find that evidence very soon."

Walker and Van Der Helm call their theory, "Sleep to remember, sleep to forget," meaning that one goal of sleep is to imprint useful information from new experiences on the brain, while stripping the memories of their toxic emotional tone. They point out that emotion might be useful for memory initially since feeling is what tags an experience to tell our brains what to remember later. Scary and sexy experiences are the ones we can learn from, the ones to be remembered later. But after an experience has been converted to memory, the brain's goal might be to keep the information it has learned, and lose the

disturbing mood. Walker believes sleep helps us achieve that detox and he thinks his experiment with the disturbing pictures supports his central claim: that dream-sleep strips emotional experiences of their reactive power by re-processing stressful memories in a chemically safe mental space.

The fMRI at Berkeley sits inside a trailer on a grassy quad, a short star-lit walk from Tolman Hall, the psychology building. Els van der Helm, who ran the brain scanner, remembers preparing their subjects for a night in the lab. She noticed that placing electrodes on the scalps of her subjects tended to make them sleepy, so they dozed off easily in the lab. Thirteen of her subjects viewed the disturbing images before they slept, while thirteen others got to sleep without seeing any scary pictures. All the subjects had their sleeping brains recorded by nineteen electrodes, glued with sticky gel to their scalp. The people who saw the pictures before sleep were shown them again in the morning, while their brain response was re-measured, and they clicked a button to show how emotionally disturbed they felt by each image, on a scale of one to five. Control participants saw the same pictures twice the following day, once in the morning and again after twelve hours of being awake. What the scientists wanted to find was: What is different about the emotional response of a rested brain? How does the brain refresh itself through sleep? Their results suggest that REM sleep in particular plays a role in regulating mood.

People who slept were less scared by the photos the next day than those who stayed awake. By looking at the fast brain-waves in the EEG data, Walker's team were able to measure how much the stress chemical adrenaline seemed to be tamped down during REM sleep in each of the thirteen sleepers. They found that people who were most

relaxed after sleep, the ones who were better able to regulate their emotions, also showed the greatest dip in adrenaline during REM. No other stage of sleep, and no other speed of brain wave, correlated with the emotional change, suggesting that REM sleep is the place where overnight therapy happens.

Adrenaline, in the noisy chattering front of the brain-- where thought and planning and worry come from-- is knocked out during REM sleep, as Allan Hobson discovered in his sleeping cats. This, Walker speculates, may be why Rosalind Cartwright's dream-work does its job of healing depression: Dreams are experienced in a chemical atmosphere without anxiety, where toxic emotions can be stripped from memories. This change in chemical brain-state, it seems from Walker's work, may divorce the scary experience from the emotional stew where it was born.

Alternative Views

Not everyone agrees that REM sleep detoxes our traumatic experiences so we can adjust emotionally and move on. The month after Walker's work was featured in the December 2011 *National Geographic* with the headline, "Why Do We Dream? To Ease Painful Memories, Study Suggests." ABC news announced the results of a new study drawing the opposite conclusion: "Sleep Locks in Bad Memories, Emotions." Research at the University of Massachusetts, Amherst suggested that sleep consolidates not just memory, but emotional sting too: that REM hammers home not only our recollection of a shocking experience, but also the feelings that went with it. The authors' suggestion for treating trauma: Stay awake.

Edward Pace-Schott, one of the authors of the *Journal of Neuroscience* paper, has

published evidence that sleep mellows emotional response. His studies, like Walker's, use disturbing pictures to stimulate mood before and after sleep. But in Pace-Schott's studies, it is early-night deep sleep, rather than late-night REM, which is associated with emotional "detox." REM, in his studies, tends to have the opposite effect: to amplify both memory of emotional experiences and the emotional volatility that goes with them.

The new study found that sleep improved memory: people who slept remembered the pictures better later, especially the emotionally negative ones, as many studies have shown. But in contrast to Walker and Van der Helm's "Overnight Therapy" theory, the new study did not see REM sleep mellowing emotions. The more REM a person got in the third quarter of the night, the more negatively he rated the pictures the next morning.

"Our version of the story evolutionarily," explains Rebecca Spencer, who worked with Pace-Schott on the study, "is that over sleep you not only protect the memory, but you protect the emotional response." This makes sense, she reasons, because "way back when, when you were attacked by somebody, you not only needed to remember what the face looks like, but you should also have that same emotional fight or flight response, in order to behave appropriately when you see that person again... There's something helpful about sleep protecting emotion." Whereas the Berkeley group argues "Sleep to Remember, Sleep to Forget," Spencer believes it makes more sense that sleep burns on the brain not only information, but also emotion.

"One of the complicating things about Matt's theory," Pace-Schott points out, "is that intensification of REM is associated with depression." When people are depressed, they have *more* REM, earlier in the night, with denser eye-movements, crowding out the restorative deep sleep that usually dominates early in the night. "This could be the brain

attempting to moderate emotion and failing,” Pace-Schott concedes, if Walker’s Overnight Therapy theory is correct. But it could also be that REM isn’t the detox, but the poison: that REM sleep is amplifying feelings of guilt, sadness, and anxiety, while consolidating only the negative memories from a depressed person’s day, so his mind the next day is dominated by a darker autobiography. Vogel’s work, showing that REM deprivation can lift depression, and that antidepressant drugs suppress REM, may also support this view.

If slow-wave sleep early in the night relieves emotional stress, while REM sleep later amplifies it, why is the net effect of sleep to calm our moods? Why don’t slow-wave sleep and REM cancel each other out? It could be, Pace-Schott speculates, that “there is a successive effect of the sleep stages on emotion, as some have argued with memory.”

This theory of memory “evolution” during sleep was discussed by Robert Stickgold and Walker in an influential 2010 review paper in *Nature Reviews Neuroscience*. Stickgold and Walker argued that slow wave sleep early in the night converts new experiences into memory, while REM later processes and integrates this new information with the brain’s existing memory: Slow-wave and REM sleep perform complementary functions in converting our waking experiences into memories overnight.

Something similar could be happening with emotional digestion, Pace-Schott thinks. Since sleep overall has the effect of “overnight therapy” - people who have slept are less emotionally jittery than those who are sleep-deprived; insomnia and mood disorder often go hand in hand - it seems likely that both stages of sleep contribute to stabilizing mood and memory. But exactly how this nocturnal trick works is still not

completely understood.

“I don’t think we have the answer yet,” Stickgold says, after a long career in sleep research, working with Allan Hobson at Harvard, mentoring both Walker and Pace-Schott, and pursuing his own interest in dreams and learning. But, he adds, “I don’t see those [two results] as contradictory. What they are telling us is that sleep is not stupid.”

Sleep does not convert all experience into memory, removing the emotion from *all* traumatic memories indiscriminately. “Think of a child who touches a stove.” Stickgold says. “How long should the child be afraid of the stove?” The answer, he says, is until she understands why it burned her: When she knows how to avoid getting burned, she can quit being afraid of the stove. The purpose of REM, Stickgold believes, is to *process* experience, to evaluate what is essential in our experiences, extract the emotional and informational core, and discard the rest. “What sleep is doing is trying to optimize the information that it has managed to collect,” Stickgold says. “Classically, with emotional events, we tend to forget all the details and remember the core experience. But the brain won’t let go of the details until it is confident it has calculated what the core aspect is.”

Stickgold thinks the Walker and Pace-Schott studies may simply be seeing memories at different stages of evolution: the process of emotional detox may take more than one REM cycle, over more than one night, to resolve. He agrees with Pace-Schott that slow wave and REM sleep perform sequential roles in processing emotion.

“Slow wave sleep early in the night is involved in strengthening memories in the form in which they were initially encoded,” Stickgold speculates. “What REM sleep is about is the evolution beyond that: now we’ve got it, now what do we want to do with it?”

Meta-analysis of the data, once it's been stabilized: That's what REM sleep does." But Stickgold also acknowledges, "Looking for *the* function of dreaming is like asking what waking does."

Sleep Therapy

Sleep changes brain chemistry, which changes mood. Whatever sleep's main function is, researchers agree on its importance for health. Allison Harvey, an Australian sleep therapist, looks out her window at the foggy Berkeley mountains, as she explains why she believes sleep problems are the core of mood illness.

Harvey, the director of the Golden Bear sleep clinic at Berkeley, points out that sleep disturbances are common to psychological disorders such as depression, bipolar disorder, anxiety, PTSD, and even dementia and schizophrenia. Harvey is a clinical psychologist with a friendly demeanor and the upbeat lilt of an Aussie. She believes that sleep is central to mental health: that the imbalance in brain-chemicals caused by warped sleep contributes to most mood disorders, and that treating underlying sleep problems, from insomnia to apnea, may improve mood illnesses too.

"There's been a shift in thinking over the past ten years," Harvey says. "Prior to that, across psychiatry, people would assume that if you treat the main psychiatric disorder, then the sleep symptoms will go. But now we are finding that sleep is so important for mood: if you have a mood problem, then you're not going to be able to get as much sleep. And if you don't get enough sleep, that's going to impact your mood the next day. You're going to have an escalating vicious cycle, whereby mood and sleep are going to keep feeding into each other, making each other worse." If you treat both the

mood and the sleep problems, though, you make progress on both types of symptoms, Harvey claims.

She cites a study by Rachel Manber's group at Stanford University that compared a group of depressives treated with the antidepressant drug escitalopram (trade-name, Lexapro; an SSRI drug in the same family as Prozac) to one that took Lexapro along with CBT-I, cognitive-behavioral therapy for insomnia. 61.5 percent of the patients who took both the drug and sleep therapy recovered from depression in the 12 weeks of the study, versus only a third of the patients who took Lexapro with a "sham" talk therapy that did not teach better sleep habits. Harvey's lab is pursuing a similar study now on teenagers, using talk-therapy instead of the antidepressant drug, to see if sleep therapy improves mood above and beyond regular talk-therapy for depression. So far, the results look the same: Sleep improves mood above and beyond the other treatments for depression.

Bipolar disorder, once known as "manic-depressive illness," is the mood sickness most linked to sleep: Depressive periods come with insomnia, while manic periods include reduced need for sleep. Bipolar affects 1.5 percent of the population, and is a focus of Harvey's lab's studies of sleep and mood. Bipolar patients' sleep is erratic. One study found that variability in a bipolar person's sleep and wake times across a week averages about three hours: the same as the time-difference between Boston and California: so bipolar patients are living in a state of perpetual jetlag, Harvey says. REM sleep is affected, too.

"No one really knows what the eye-movements are," Harvey says, referring to the rapid eye movements of REM sleep, "but one theory is that they are indicative of intensity of emotional processing." A 2009 study by Harvey and her Berkeley colleague

Lisa Talbot manipulated mood in bipolar patients, by having them listen to happy or sad classical music while recalling emotional memories. The rapid eye movements in the patients' next dream-sleep became more intense. The more stormy the emotional state of the sleeper, it seems, the more violent his eye-movement storms. Thus, dream-sleep seems central to balancing mood, and disturbed when emotions go out of control.

Sleep deprivation tends to be the trigger of both manic and depressive episodes. One group in Italy sleep deprived bipolar patients, and showed that this triggered mania in ten percent of them. Harvey speculates that even more would have tipped into mania if the sleep loss had continued for multiple nights—as it does in the lives of many bipolar patients. Their sleep problem springs in part, Harvey says, from a tendency to addictive behavior: Bipolar patients' brains respond more intensely to rewarding activities, so they tend to do these—videogames, TV, movies, eating or working—late into the night, instead of sleeping, as Berkeley psychologist Sheri Johnson has shown. Which tips the balance of chemicals in their heads, and often propels them into mania.

Harvey's current bipolar study is a collaboration with the University of Pittsburgh lab of Daniel Buysse, focused on forty-eight bipolar patients. Half the patients get training in sleep hygiene—regularizing bedtimes and wake times, limiting stimulation at night, using the bed only for sleep—while the other twenty-four receive a sham treatment that doesn't teach them about sleep. The results are provisional, but so far, the cognitive-behavioral insomnia treatment seems to be working: The bipolar patients who are taught to take better care of their sleep do better than those who are just treated with medications alone. Healthy sleep may have an effect as strong as medicine on bipolar people's mood.

* * *

Harvey prefers to treat sleep disorders with talk therapy rather than pills, whenever possible. “There’s so much that we can change in our biologies through our behaviors, and what we think, what we pay attention to. Psychology and biology are intimately linked and it’s possible that you can powerfully change your biology just by changing thought,” she says. Talk-therapy for sleep is simple, and takes only eight weeks to teach—and it changes the brain. “Our nervous systems are plastic,” Harvey argues. “When we change our behavior, we will be changing our brains.”

“We know what the behaviors are that encourage sleep,” Harvey says. “But how to get people to do them at the public health level is the big challenge.” Knowing what we do about the links between sleep and mood, Harvey says, “People are not prioritizing sleep in this ridiculous twenty-four seven society we live in.” The problem is to figure out how to motivate people to make these changes in behavior that affect their sleep, happiness, and emotional health. Harvey puts this in terms of New Year’s resolutions: How often do people follow through on what they commit to do?

Sleep is a public health emergency, Harvey believes, in need of better PR. Sleep researchers strive to get the message out to the public, in hopes that such information will motivate the behavior changes that bring us better sleep, and happier lives.

Afterword: SLEEP 2012

Matt Walker opened his speech at Sleep 2012 with a joke. Police sirens interrupted his British voice as he began to explain his theory. Walker deadpanned, “That

must be Immigration coming for me.” The crowd met Walker’s humor with the usual response: surprised laughter. So the audience was loosened up to hear the story Walker had to tell-- his usual story, that is: “Overnight Therapy”: How REM sleep might regulate emotion.

All scientists fall somewhere along the spectrum from empiricist to theorist—the tinkers who collect data, the dreamers who imagine new questions and see data in new ways. Walker, like most sleep researchers, is unapologetically a dreamer: an explorer at the edge of the still only partly mapped continent of sleep. His contribution to science is not only the data his lab gathers, but also the new theories he dreams up for framing sleep. Walker tells a good story—one that both looks compelling from his data, and inspires further questions, new experiments. It was he who first seduced me into studying sleep—and I was reminded, here at Sleep 2012, both of the seductiveness of the theory, and the remaining mysteriousness of the science of sleep.

Sleep research is full of clever talkers. Think of Bob Stickgold, Rosalind Cartwright, Allan Hobson, Allison Harvey. Each has his or her own story tell about what sleep and dreaming do for the mind: how sleep integrates experiences into memory, how dreams process emotional experiences; how disturbed sleep warps mood in disorders from depression to PTSD. All will admit though that sleep remains a world to be mapped: the exact link between sleep and mood is still unknown. The one consensus is that sleep is good for our health, and must have some function since evolution designed us to sleep.

“The best bridge between despair and hope is a good night of sleep,” Joseph Cossman once said, and sleep researchers today are coming to understand why.

Sleep research today still has more mysteries to offer than answers. But the very unknown of sleep offers space for imagination: for hypotheses, scientific storytelling. Why do we spend a third of our lives sleeping, and a quarter of that time dreaming? Why do our eyes twitch when we dream, and twitch more when we're emotionally disturbed? Why do the drugs that fix our depressions also delete our dreams? We don't know the answers yet, but sleep science continues to probe—and with each new question, sheds a bit more light on the twitching eye and the dreaming brain.

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