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An Active, Purposeful Machine That Comes Out at Night to Play

By BENEDICT CAREY

The task looks as simple as a "Sesame Street" exercise. Study pairs of Easter eggs on a computer screen and memorize how the computer has arranged them: the aqua egg over the rainbow one, the paisley over the coral one — and there are just six eggs in all.

Most people can study these pairs for about 20 minutes and ace a test on them, even a day later. But they're much less accurate in choosing between two eggs that have not been directly compared: Aqua trumped rainbow but does that mean it trumps paisley? It's hazy.

It's hazy, that is, until you sleep on it.

In a study published in May, researchers at Harvard and McGill Universities reported that participants who slept after playing this game scored significantly higher on a retest than those who did not sleep. While asleep they apparently figured out what they didn't while awake: the structure of the simple hierarchy that linked the pairs, paisley over aqua over rainbow, and so on.

"We think what's happening during sleep is that you open the aperture of memory and are able to see this bigger picture," said the study's senior author, Matthew Walker, a neuroscientist who is now at the University of California, Berkeley. He added that many such insights occurred "only when you enter this wonder-world of sleep."

Scientists have been trying to determine why people need sleep for more than 100 years. They have not learned much more than what every new parent quickly finds out: sleep loss makes you more reckless, more emotionally fragile, less able to concentrate and almost certainly more vulnerable to infection. They know, too, that some people get by on as few as three hours a night, even less, and that there are hearty souls who have stayed up for more than week without significant health problems.

Now, a small group of neuroscientists is arguing that at least one vital function of sleep is bound up with learning and memory. A cascade of new findings, in animals and humans, suggest that sleep plays a critical role in flagging and storing important memories, both intellectual and physical, and perhaps in seeing subtle connections that were invisible during waking — a new way to solve a math or Easter egg problem, even an unseen pattern causing stress in a marriage.

The theory is controversial, and some scientists insist that it's still far from clear whether the sleeping brain can do anything with memories that the waking brain doesn't also do, in moments of quiet contemplation.

Yet the new research underscores a vast transformation in the way scientists have come to understand the sleeping brain. Once seen as a blank screen, a metaphor for death, it has emerged as an active, purposeful machine, a secretive intelligence that comes out at night to play — and to work — during periods of dreaming and during the netherworld chasms known as deep sleep.

“To do science you have to have an idea, and for years no one had one; they saw sleep as nothing but an annihilation of consciousness,” said Dr. J. Allan Hobson, a psychiatry professor at Harvard. “Now we know different, and we’ve got some very good ideas about what’s going on.”

The evidence was there all along. Infants make sucking motions when asleep, and their closed eyelids quiver, as if the eyeballs beneath had a life of their own. But it wasn’t until the early 1950s, in a lab at the University of Chicago, that scientists recorded and identified what was happening.

Eugene Aserinsky, then a graduate student in physiology, reportedly was monitoring sleep and waking in his 8-year-old son, using electronic leads stuck to the boy’s head, connected to a brain-wave detecting machine. He had attached two leads to the boy’s eyelids as well, so he could tell whether his son woke up. One night he noticed percolating wave patterns that showed the boy had awoken. But he hadn’t.

Dr. Aserinsky confirmed the activity in others, and in 1953 he and his adviser, Nathaniel Kleitman, published the finding in a now-famous paper in Science. They later called the odd, unconscious state rapid eye movement, or REM, sleep.

“This was really the beginning of modern sleep research, though you wouldn’t have known it at the time,” said Dr. William Dement, then a medical student in Dr. Kleitman’s lab and now a professor of psychiatry and sleep medicine at Stanford University. “It took years for people to realize what we had.”

Dr. Dement, infatuated with Freud’s theories about dreams, quickly threw himself into the study of REM. He found that it was universal and occurred periodically through the night, alternating with other states. He gave them names: Stages 3 and 4, or deep sleep, when electrical waves roll as slow as mid-ocean swells; Stage 2, an intermediate stage between REM and deep sleep; and Stage 1, light sleep.

He also confirmed the link between REM and dreaming, and for a time hopes for sleep research — and money for it — soared.

Yet Drs. Dement, Hobson and others found in their studies scant evidence to confirm that dreams were the disguised, forbidden wishes described by Freud. They found instead a tangle of apparent anxieties, fantasy and vivid, often nonsensical replays of events that showed few verifiable patterns or measurable function.

They had hit a wall, and sleep research, like its nocturnal subjects, dropped from REM excitement back into a void. “You had this great excitement, basically followed by 40 years of nothing; it was just horrible,” said Robert Stickgold, a cognitive neuroscientist at Harvard. “Just a period of darkness.”

The sun came up in 1994, in Rehovot, Israel. There, a research team led by Avi Karni found that depriving people of REM sleep undermined memory of patterns they had learned the day before, while depriving them of deep sleep did not.

This result raised more questions than it answered — Were the participants simply sleepy, or stressed? Why just REM? What was the purpose of the other sleep states? — but it was an invitation to researchers interested in sleep.

“I called Karni immediately, and he sent me all his protocols, everything,” Dr. Stickgold said.

Others called, too. The field was waking up, and now turning its focus to a long-neglected area: learning and memory.

Since then the study findings have come almost too fast to digest, and they suggest that the sleeping brain works on learned information the way a change sorter does on coins. It seems first to distill the day's memories before separating them — vocabulary, historical facts and dimes here; cello scales, jump shots and quarters over there. It then bundles them into readable chunks, at different times of the night. In effect, the stages of sleep seem to be specialized to handle specific types of information, the studies suggest.

On a recent Monday afternoon in Dr. Stickgold's lab at Beth Israel Deaconess Medical Center in Boston, a postdoctoral student, Matthew Tucker, was running a study of the effect of naps on memorized words. In a neighboring room, a Boston University student was cramming on a list of 48 word-pairs; in another, a stubbly University of Massachusetts student had finished studying and was reclining for a nap, his face covered with electrode patches, like leeches sprouting antenna.

"College students are always ready for nap; we have no problems there," Dr. Tucker was saying, as he moved back and forth, checking his watch, timing one student's nap and the other's study period.

He sat down for a moment. "We are finding that if a person takes a nap that contains slow-wave sleep — deep sleep — that performance on declarative memory tasks, which require the memorization of fact-based information like word-pairs, is enhanced compared to a person who doesn't take a nap," Dr. Tucker said.

Previous studies of nocturnal sleep have found the same thing. Memory of learned facts, whether they are names, places, numbers or Farsi verbs, seems to benefit in part from deep sleep. Healthy sleepers usually fall into deep sleep about 20 minutes or so after head meets pillow. They might spend an hour or more in those lolling depths early in the night, and typically less time later on. When cramming on facts, in short, it may be wiser to crash early at night and arise early, than to burn the candle until 2 a.m., the research suggests.

REM sleep, the bulk of which comes later in the night, seems important for pattern recognition — for learning grammar, for example, or to bird-watch, or play chess.

In one 2003 study, Sara Mednick, then at Harvard and now at the University of California, San Diego, led a team that had 73 people come into the lab at 9 a.m. and learn to discriminate between a variety of textured patterns. Some of the participants then took a nap of about an hour at 2 p.m. and the others did not.

When retested at 7 p.m. the rested group did slightly better. When tested again the next morning, after everyone had slept the night, the napping group scored much higher. The naps included both REM and deep sleep.

"We think that a nap that contains both these states does about the same for memory consolidation as a night's sleep," when it comes to pattern recognition learning, Dr. Mednick said.

Not that Stage 2 is an empty corridor between destinations. In series of experiments that he began in the early 1990s, Dr. Carlyle Smith of Trent University in Canada has found a strong association between the amount of Stage 2 sleep a person gets and the improvement in learning motor tasks. Mastering a guitar, a hockey stick or a keyboard are all motor tasks.

Musicians, among others, have sensed this for ages. A piece that frustrates the fingers during evening practice often flows in the morning. But only in recent years has the science caught up and given their instincts a practical shape.

For instance, Dr. Smith said that people typically got most of their Stage 2 sleep in the second half of the night.

"The implication of this is that if you are preparing for a performance, a music recital, say, or skating performance, it's better to stay up late than get up really early," he said in an interview. "These coaches that have athletes or other performers up at 5 o'clock in the morning, I think that's just crazy."

For all these nighttime fireworks, memory researchers have yet to work out a complete picture of how all the pieces fit together. Each has a theory, but they differ: Dr. Smith focuses on Stage 2, others on deep sleep, still others on REM or a combination of REM and deep sleep. And no one knows how individual differences, between night owls and early birds, for instance, affect nighttime learning.

In addition, said Jerome Siegel, a professor of psychiatry at the University of California, Los Angeles, millions of people have taken drugs that suppress REM without reporting serious memory problems. "I wouldn't rule out the possibility that sleep contributes to learning and memory consolidation, but the claim is that it's essential, that it's doing something the waking brain won't, and the research hasn't shown that," Dr. Siegel said.

Even the college all-nighter provides evidence that some consolidation occurs during waking, he said. "College students know that the best way to learn stuff isn't to stay up all night because it's going to impair your judgment," Dr. Siegel said, "but it doesn't matter how good your judgment is if the information isn't in there. And students know from experience that a lot of it is."

One reason some neuroscientists are confident that the sleeping brain is actively working on the day's streaming video of information is because they have seen it with their own eyes — or heard it, at least.

In his lab at the Massachusetts Institute of Technology, Matthew Wilson has been studying rats and mice wearing what look like Carmen Miranda hats. These are ultralight implants through which researchers thread hairlike wires to record the activity of single cells deep in the brain, in the left and right hippocampus, where the day's memories are recorded.

Past research has shown that the hippocampus is spatially sensitive: it seems literally to pair the firing of individual neurons with locations outside the body. These systems are thought to function in similar ways in humans and rodents.

Computers record the cells' firing in real time and can broadcast it over speakers. "I would listen to this background music of the brain sometime when the animals were asleep, and I started hearing this section that sounded very much like the pattern when the animals were in the maze," Dr. Wilson said in an interview. "I recognized the firing pattern."

The maze route is an important memory for these animals; it's about all they know. In a paper published last December, Dr. Wilson and Daoyun Ji reported that in sleeping animals they had recorded chatter in neurons in the visual center of the neocortex, followed by an apparent response in the hippocampus — and not just any response, but a replay of the activity in the hippocampus that occurred during a maze task.

Dr. Wilson thinks of this as a kind of off-line conversation between the neocortex, which is involved in conscious learning during waking, and the hippocampus. "What we notice is that the light goes on in the neocortex a fraction of a second before it goes on in the hippocampus, as if the cortex is asking for information," he said.

He said that this process was probably similar to what goes on when people take a moment to reflect, without distractions, sifting through the experiences of the day, also flagging important details, replaying events. "The question is not whether this is an essential process; it is," Dr. Wilson said. "The question is whether there is something going on during this process that is unique to sleep."

Subimal Datta, a neuroscientist across the river at Boston University School of Medicine, thinks so. In his studies of animals, he has documented that during sleep the brain is awash in a chemical bath unlike any during waking. Levels of inhibitory transmitters increase sharply, and levels of many activating messengers drop, or shut down entirely.

Even before REM is detectable, Dr. Datta said, a small pocket of cells in the brainstem spurs a surge in glutamate — an activating chemical — which leads to protein synthesis and other changes that support long-term memory storage.

"During waking we have a thousand things happening at once, the library is filling up, and we can't possibly process it all," Dr. Datta said. While awake the brain is also gathering lots of valuable information subconsciously, he said, without the person's ever being aware of it.

"It's during sleep that we have this special condition to clear away this overload, and these REM processes then help store what's important," Dr. Datta said.

In the jargon of the field, the "signal to noise ratio" becomes much stronger. The neural trace of the trivia has weakened, and crucial details are replayed and reinforced.

Dreams still defy scientific measurement but they, too, have a place in the evolving theory of sleep-dependent learning.

It is likely during REM, some scientists argue, that the brain proceeds to mix, match and juggle the memory traces it has preserved, looking for hidden connections that help make sense of the world. Life experience is cut up and reordered, sifted and shuffled again. This process could account for the cockeyed, disjointed scenes that occur during dreams: the kaleidoscope of distilled experience is being turned.

It also might account for that golden gift often attributed to a night's sleep: inspiration.

To hear some people tell it, a night's sleep changed their world. It was reportedly during sleep that the Russian scientist Dmitri Mendeleev's periodic table of the elements tumbled into place. Friedrich August Kekule, a 19th-century chemist, said he worked out the chemical structure of the benzine ring — an important discovery — when he dreamed of a snake biting its tail. Athletes, including the golfer Jack Nicklaus, have also talked about insight coming during sleep.

Slight corrections in technique are revealed; sand traps are averted; mountains move.

"It does make sense these insights come during REM," Dr. Walker said. "I mean, what better time to play out all these different scenarios and solutions and ideas than in dreams, where there are no consequences?"

The problem, he and others say, is how to study it. That, most neuroscientists agree, will take some very creative thinking — both of the daytime and nighttime kind.