

When the Brain Disrupts the Night

By *ERICA GOODE (NYT)*

Awake, Jim Smith was an amiable and popular man.

As the director of public works in the small town of Osseo, Minn., he could be counted on to make house calls day or night, attending to burst pipes or broken water mains.

In fall, he hunted deer with buddies, who affectionately called him Smitty. In summer, he took his family pan fishing for crappie.

It was only when Mr. Smith fell asleep that something changed.

Wrapped in slumber, he would shout obscenities, kick the walls, punch the pillows. Sometimes, he hit his wife, Dee, in the back or grabbed her by the hair. One night, dreaming that he was putting a wounded deer out of its misery, he came close to breaking his wife's wrist.

"I just didn't sleep real sound," Mrs. Smith recalled. "Once he started talking or swearing, I would be afraid that the next thing, he would be swinging his fists."

In an earlier century, Mr. Smith might have undergone exorcism to expel the demons that possessed him when his eyes closed. In the 1960's, psychiatrists might have traced his problem to repressed aggression and prescribed a sojourn on the analytic couch.

But in the last two decades, researchers have begun to systematically investigate a variety of disorders -- called parasomnias -- involving odd or dangerous behavior during sleep. One is called REM behavior disorder, in which people act out their dreams.

This was the diagnosis Mr. Smith received in 1987 when he sought treatment at the Minnesota Regional Sleep Disorders Center in Minneapolis.

Parasomnias are more common than was once thought, researchers are finding. They can be successfully treated, and most have nothing to do with mental illness.

At the same time, research on such sleep problems is challenging basic assumptions about sleep and wakefulness, showing that the borders between the two states are far from clearly demarcated. And in the case of REM behavior disorder, one of the most studied parasomnias, investigators are finding surprising links to physical illness.

For example, at the annual meetings of the Associated Professional Sleep Societies in June, Dr. Carlos H. Schenck, a psychiatrist and senior scientist at the Minnesota sleep center, and Dr. Mark W. Mahowald, a neurologist and the director of the clinic, will present findings indicating that of 26 otherwise

healthy patients in whom REM behavior disorder was diagnosed in the 1980's, 17 went on to develop Parkinson's disease.

Other studies, at the Mayo Clinic and elsewhere, have found associations between the sleep disorder and other neurodegenerative diseases related to Parkinson's, including a form of dementia known as Lewy body disease and an illness called multiple system atrophy.

Mr. Smith, now 72 and retired, learned in May 2001 that he had Parkinson's.

The connection between REM behavior disorder and Parkinson's is the latest twist in a story that began 20 years ago, when a retired grocer named Donald Dorff came to Dr. Schenck complaining of what he called "violent moving nightmares." In one such dream, Mr. Dorff, believing he was a quarterback heading for a touchdown, ran forcefully into his bedroom dresser.

Wiring his new patient up in the sleep laboratory, Dr. Schenck discovered that Mr. Dorff's violent behavior occurred during periods of rapid eye movement, or REM, sleep, a stage that accounts for 20 to 25 percent of nighttime repose in humans and that shows up on electroencephalogram recordings as a pattern of electrical activity similar to that seen during waking. Most dreaming takes place in REM sleep.

During REM, the brain dispatches signals to the muscles, telling them to perform the movements that would be appropriate if the person were awake.

In most sleepers, however, another brain circuit also kicks into action during REM to prevent the dreamer from carrying out those instructions. Nerve cells transmit chemical messages that paralyze all muscles in the body except the diaphragm, one small muscle in the ear and the muscles that move the eyes.

Mr. Dorff's problem appeared to be that the normal paralysis of REM was missing. The same was true for four other elderly patients, described by Dr. Schenck and his colleagues in a 1986 report documenting the first human cases of the disorder. In fact, the researchers realized, the patients were acting a lot like a group of laboratory cats studied in the mid-1960's by a French sleep expert, Dr. Michel Jouvet.

Trying to locate the regions of the brain responsible for REM sleep, Dr. Jouvet and his colleagues destroyed cells in an area of the brainstem called the pons. Even with this damage, the cats still entered REM sleep, the scientists found. But instead of lying

still, they stood up, looked around and sometimes stalked imaginary prey.

Subsequent studies, by Dr. Adrian R. Morrison at the University of Pennsylvania School of Veterinary Medicine, showed that the extent of the behavior exhibited by the animals during REM depended on where in the pons the lesions were made. For example, when the cell damage encompassed nerve pathways extending from the amygdala, a brain structure involved with emotion, the cats would attack humans or other cats.

As with Mr. Dorff, who died in 1999, and Mr. Smith, studies show that more than 80 percent of patients who show up at sleep disorder clinics with REM behavior disorder are men, middle-aged or older, and most, Dr. Schenck said, are noticeably placid and good-natured in their waking life. Many display rhythmic movements of their legs even during non-REM or slow-wave sleep.

Most patients also report unusually vivid dreams (sometimes beginning long before they start acting them out) in which they are being threatened or attacked or engaging in active sports.

One man dreamed that his boss was chasing him with a hatchet; another that he was being pursued by a lion, said Dr. Bradley F. Boeve, a neurologist at the Mayo Clinic who studies REM behavior disorder and Parkinsonian illnesses.

Sometimes, Dr. Schenck said, a husband will awake from a dream in which he is protecting his wife from danger, only to find that in fact he has been pummeling her.

"She wants to know why he's beating up on her and he says, 'I'm not, I'm beating up this man,'" Dr. Schenck said.

In other cases, patients have no memory of what stirred them to action. On a hunting trip, for example, Mr. Smith leaped abruptly from bed and began singing "God Bless America," to the amusement of his bunkmates. But he could not recall the dream that inspired this burst of patriotism.

An increasing number of studies link REM behavior disorder to neurological disease. The damage to the pons that in animals suspends paralysis during REM sleep is not regularly found in humans with the disorder. And it is not yet entirely clear how the sleep problem is connected to neurodegenerative illnesses later in life.

But recent work by Dr. Jerome Siegel at the University of California at Los Angeles offers another piece of the puzzle and may help explain a possible connection to Parkinsonian diseases.

Neurons in particular areas of the midbrain, just above the pons, have a potent effect in suppressing muscle tone, Dr. Siegel has found. In rats, damage to those areas produces muscle movements during REM similar to those seen in human patients with the sleep disorder. And the nerve cells in those regions are very close to, and interconnected with,

neurons in a midbrain center known to suffer cell damage in Parkinson's.

"Given the connection between REM behavior disorder and Parkinson's," Dr. Siegel said, "the hypothesis that we're pursuing is that the degenerative process that causes Parkinson's may spread to the region responsible for inhibiting muscle tone" or vice versa.

Brain scans of patients have added to the suspicion that the sleep disorder in some way signals the beginning of Parkinsonian disease. In 2000, Dr. Ilonka Eisensehr of the University of Munich reported finding a kind of "Parkinsonian fingerprint" -- a reduction in the enzyme that transports the messenger chemical dopamine in the striatum, the region of the midbrain where Parkinson's originates -- in the brain scans of patients with REM behavior disorder who did not yet have any other signs of neurological disease.

In a development that experts call troubling, sleep clinics are also seeing a number of patients who develop some symptoms associated with REM sleep disorder while taking Prozac, Zoloft or others of the newer generation of antidepressant drugs called selective serotonin reuptake inhibitors or S.S.R.I.'s

A 1992 study by scientists at the Minnesota sleep clinic found that 20 of 41 patients taking Prozac for depression or obsessive-compulsive disorder exhibited "extensive, prominent eye movements" during light non-REM stages of sleep, a phenomenon the researchers have called "Prozac eyes." In one patient, the eye movements were still present 19 months after the man stopped taking the antidepressant.

Other reports suggest that some people taking the drugs experience muscle jerks or other movements during sleep or waking.

Dr. John Winkelman, the medical director of the sleep health center at Brigham and Women's Hospital in Boston, said he had seen a number of patients who developed REM behavior disorder while taking S.S.R.I.'s.

"A couple of people threw themselves out of bed," Dr. Winkelman said.

No one yet knows how common such side effect are, or their implications -- if any. And other drugs -- barbiturates and stimulants, for example -- can also contribute to REM behavior disorder. But the findings, the experts say, should encourage doctors to prescribe responsibly.

"The drugs are very effective," Dr. Mahowald said. "But it's the physician's responsibility to make sure the patient's condition is severe enough to warrant prescribing a neuroactive agent."

On the other hand, some psychiatric drugs are effective in treating the sleep disorder. Dr. Boeve said he found the antidepressant Seroquel helpful for some patients.

What eventually kept Mr. Smith from inflicting further damage on his wife was clonazepam, a tranquilizer that Dr. Schenck and other experts have

shown almost always calms patients' turbulent nights.

"It helped right away," Mrs. Smith said.

REM behavior disorder is the only parasomnia routinely associated with violence. But sleepwalkers have also been known to stab their relatives, molest children or confidently stride out of third-story windows, in states varying from confused wakefulness to partial arousal to the deepest stages of non-REM or slow-wave sleep.

Other sleep disorder patients, who suffer from a condition called nocturnal dissociative disorder, awaken and leave their beds to re-enact scenes of physical or sexual abuse, sometimes cutting themselves with razors or banging their heads against the wall. Afterward, they remember nothing about their nighttime behavior.

Reports of violence during slumber date back to the ancient Greeks.

In Homer's "Odyssey," Elpenor, the youngest of Odysseus' crew, wakes suddenly from a drunken nap and runs off the roof of a house, breaking his neck.

Simon Fraser, a 19th-century Scot who killed his 18-month-old son by dashing him against the wall,

said he did so while dreaming that a wild beast had jumped on the bed and was attacking the boy. "I am guilty in my sleep, but not guilty in my senses," he insisted.

More recently, the defendants in several murder cases have used sleep as a defense, in one instance successfully: a Canadian, Kenneth Parks, was acquitted after experts testified that he was in a somnambulistic state when, in May 1987, he drove 14 miles to the house of his in-laws, where he stabbed his mother-in-law to death and nearly killed his father-in-law.

Such cases, Dr. Mahowald said, make it clear that sleep and waking are hardly distinct states.

In many normal people, he said, detailed neurophysiological studies of the brain show that the signs of sleep persist for an hour after awakening, though an EEG indicates that the person is already fully awake.

"Most people's concept is that the entire brain is in one state of being, and that's just not true," Dr. Mahowald said. "You can have parts of the brain that are awake while others are asleep."

