

## Awakened by a Sleeping Pill?

BY Dave Andrusko

"We have always been told there is no recovery from persistent vegetative state—doctors can only make a sufferer's last days as painless as possible. But is that really the truth? Across three continents, severely brain-damaged patients are awake and talking after taking ... a sleeping pill."

From "Reborn," written by Steve Boggan, which ran in the British publication *The Guardian*, September 12

Steve Boggan's remarkable and dramatic account appeared in the well-left-of-center *Guardian*. "Reborn" is breathtaking not so much for breaking new ground, but for having brought together in one place a number of remarkable stories documenting the almost miraculous impact of the sleeping pill Ambien [known also as zolpidem] on patients with severe brain injuries. These include men and women diagnosed to be in a "persistent vegetative state" (PVS), the label affixed (incorrectly, according to her parents) to Terri Schindler Schiavo.

Since the column is a delightful read and easily accessible on the web, let me just highlight a couple of considerations. [The story can be read in full at [www.guardian.co.uk/medicine/story/0,,1870279,00.html](http://www.guardian.co.uk/medicine/story/0,,1870279,00.html)]

As I perused the manner in which patient after patient, diagnosed as utterly without hope, had awakened, I instantly thought of a scene from *Lord of the Rings: The Two Towers*. You'll remember that Saruman's surrogate, Wormtongue, has woven a spell on the noble King Theoden. He is barely conscious, his face ashen and lifeless.

When Gandalf exorcises Theoden, the color returns to his cheeks, his countenance comes alive, and his voice, previously a mere rote whisper, grows strong and vibrant. It is as if Theoden has leaped away from death's doorstep.

That is precisely the picture that emerges of Louis Viljoen, who was "cruelly described by a doctor as 'a cabbage.'" Prior to his daily medication, "there is a droop to one side of his mouth and brow because of brain damage. His right arm is twisted awkwardly into his side."

Nine minutes after taking a dose of zolpidem, "the grey pallor disappears and his face flushes," Boggan writes. "He starts smiling and laughing. After 10 minutes he begins asking questions. ... A couple of minutes later, his right arm becomes less contorted and the facial drooping lessens. After 15 minutes he reaches out to hug [his mother] Sienie."

After the South African media publicized Viljoen's remarkable improvement, Dr. Ralf Claus, a physician of nuclear medicine, called his doctor, Wally Nels, to suggest carrying out a brain scan.

"The results were so unbelievable that I got other colleagues to check my findings," Claus told Boggan. "We did scans before and after we gave Louis zolpidem. Areas that appeared black and dead beforehand began to light up with activity afterwards. I was dumbfounded—and I still am."

How this works is a mystery. Why would a sleeping medicine—a depressant—“wake up the seemingly dead brain cells”? Their hypothesis is far beyond my ability to fully grasp or explain, but the gist of it goes something like this.

Following a severe trauma, a chemical known as Gaba closes down brain functions to save energy and preserve surviving brain cells. Nels and Clauss speculate that after a long time in a dormant state, the “receptors in the brain cells that respond to Gaba become hypersensitive.” Since “Gaba is a depressant, it causes a persistent vegetative state.”

But, again, why would zolpidem, a sleeping pill, awaken these patients? “It is thought that during this process [of dormancy] the receptors are in some way changed or deformed so that they respond to zolpidem differently from normal receptors, thus breaking the hold of Gaba.”

I asked a friend, a professor of neurology, to speculate. Harkening back to basic principles of pharmacology, he explained that more than one chemical may “compete” for a receptor on a cell, “like two ships heading for a docking slip that can fit either of them. One might displace the other. Its action may be stronger [Gaba] or weaker [zolpidem].”

Switching metaphors, it’s like “a wrestler (Gaba) who forcefully subdues an opponent (the brain cell). A second, gentler wrestler (zolpidem) comes along and knocks the stronger wrestler off the opponent [an example of competitive binding]. The hold is resumed, but much lighter, allowing the opponent (the brain) more freedom of action—to wake up.”

What matters most is captured in the last paragraph of Boggan’s story. The patient, George Melendez, had been in a car accident in 1998 and said to be “clinically dead,” according to his mother, Pat Flores. “After three weeks he suffered multi-organ failure and they said his body would ultimately succumb. They said he would never regain consciousness.”

But he survived and four years later his mother gave him a sleeping pill “because his constant moaning was keeping her and her husband, Del, awake in their shared hotel room,” she told Boggan. The next thing you know he sat up, wide awake, asking and answering questions. He continues to improve.

“It is difficult to describe how it feels to get someone back who you were told you had lost for ever,” Flores told Boggan. “There is a bond that has been restored and it validates our absolute belief that all along George was locked inside there somewhere. It tells us that we were right and the doctors were wrong. George, and his personality, were in there the whole time”.