



Tom Shroder



# Earthquakes and Rainbows

## an excerpt from *Acid Test: LSD, Ecstasy, and the Power to Heal*

TOM SHRODER

NO ONE WAS MORE DISAPPOINTED than Rick Doblin that Strassman's breakthrough research on DMT hadn't been a trigger for the explosion of psychedelic research they had both hoped would follow. But Rick wasn't conceding anything. For him, the conflict between the irrational territory to which psychedelics sometimes seemed to point and the rational process of science was no conflict at all. That was the beauty of the reality test, the carefully controlled clinical trial, in which people with psychological issues—measurable deficits in their ability to lead happy, productive lives—would undergo psychedelic therapy and either get better... or not.

If only he could put it to the test.

From the moment the DEA overruled the administrative judge in 1985 and declared MDMA a poison with no redeeming value, he'd been trying to play the hand he'd been dealt, pursuing the painfully slow, measured course of the FDA process required to get approval for research with a Schedule I drug.

The problem was not just the background difficulty of getting psychedelic research approved. Since the idea that LSD damaged human genetic material had been discredited, few continued to claim that traditional psychedelics caused long-term harm to brain tissue. But MDMA was different. Even as Strassman was granted permission to study DMT and do a pilot study on psilocybin, MDMA stood out as a potential instigator of brain damage, the real problem child.

For Rick, that was a big problem. He had become convinced that MDMA's potential as a therapeutic drug exceeded any other psychedelic. For one thing, it tended not to induce the kinds of extreme experiences—machine-elf extreme—that had so upset Strassman. Plus the feelings of closeness, connectedness, and fearlessness it so often produced made it seem as if MDMA had been specifically engineered to work wonders in a therapeutic relationship, in which an alliance between patient and therapist was known to be an essential precursor to healing, and an ability to look at existentially threatening realities without turning away in fear preceded almost any significant breakthrough.

To Rick, this wasn't merely theoretical. He had seen it work before his eyes, watched as MDMA and talk had saved the life of his suicidal friend. What's more, he had taken it himself often enough, and with enough friends, that he had a strong intuitive sense that it had done neither them nor their brains any damage.

For the same reason, if it did cause damage, he definitely wanted to know.

What was lacking was any good science on the matter. Basing a judgment on toxicity from results with MDA, a related but entirely different drug, was pointless. The body could react to drugs that were even more similar than MDA and MDMA in radically different ways. (MDMA was also chemically similar to mescaline, and nobody was saying mescaline damaged brain neurons.)

Rick's typically, and somewhat counter intuitively, direct solution to the need for better science on the topic: make common cause with the man who had done the research that had instigated the whole brain damage idea to begin with.

Charles Schuster had since become director of the government's National Institute on Drug Abuse, but Schuster's protégé, the researcher who had done the hands-on work on the MDA rat studies, was the neurologist George Ricaurte, whose research had earlier been cited by the DEA during the court hearings on whether to add MDMA to Schedule I of the Controlled Substances Act. Ricaurte had gone on to do studies with MDMA itself, but still with rats, which were not always a reliable indicator of how humans react. Rick called him and offered to have MAPS buy Ricaurte some monkeys to do MDMA primate studies, the next best thing to testing on humans. Ricaurte was amenable, and the two, about the same age, entered a friendly partnership. Rick even attended Ricaurte's wedding to a research colleague and future collaborator in his MDMA studies, Una McCann.

Ricaurte took delivery of Rick's monkeys, then gave them 5 milligrams of MDMA per kilogram of body weight orally. This would be the rough equivalent of the upper range of what

a human heavy user might take recreationally. Tests conducted two weeks after the dose showed that while most brain regions had suffered no damage to serotonin receptors, in two specific areas, the thalamus and the hypothalamus, receptors had been reduced by about one-fifth, without any apparent functional or behavioral consequences.

Since the MDMA dosage Ricaurte had tested was about three times the average therapeutic dose equivalent—1.7 milligrams per kilogram—Rick urged him to do another test at a lower dosage to determine if, at any point above the therapeutic dosage, MDMA would show no long-lasting effect on serotonin neurons anywhere in the brain.

That point came at 2.5 milligrams per kilogram, still 50 percent above the usual therapeutic dosage. Eight doses of that size were administered over four months (one dose every two weeks), after which there was no detectable damage to neurons. Rick was greatly relieved, since that would be the key to persuading the FDA that it would be safe enough to conduct human therapeutic trials.

Unfortunately, Ricaurte had already published the results of the 5 milligram trials that did show some nerve damage, and they had gotten splashy coverage in the press and been incorporated aggressively in campaigns against illicit Ecstasy use—a giant red flag waving in the FDA's face.

Rick says he urged him to publish the new results showing no effect, but Ricaurte refused, saying a single new data point wasn't enough to justify a new publication. Rick says he ultimately persuaded Ricaurte to write a memo to the FDA informing them of the new result. He urged him to conclude the memo on a note he felt the data merited: that it would be safe to move on to human trials. Ricaurte wouldn't go that far.

Once again Rick refused to be discouraged. If they couldn't yet test MDMA on humans in a lab, they could bring humans who had done a lot of MDMA into a lab and test them. Rick happened to know people who had done a lot of MDMA, and he could try to recruit them for the study.

Not that that would be easy. At the time, in 1988, the only way to test brain serotonin levels in humans, short of an autopsy, was to remove spinal fluid through a scary spinal tap procedure. To assure himself that he could persuade his acquaintances in good faith, Rick offered himself as subject number one. As he sat on the examination table, his back open in one of those paper hospital gowns, waiting for a gigantic needle to be plunged between two vertebrae into his spinal column, he tried to think of himself as a soldier, a soldier in the War on Drugs, only on

the other side—or, rather, on the side of truth and rationality and individual liberty. To anyone who knew Rick, it wouldn't be a surprise to learn he actually thought in those terms. He was fighting for a cause, and soldiers took risks and accepted pain and discomfort. Then, as the needle went in and he felt a disorienting and uncomfortable sensation, he switched to imagining the pain that all mothers go through for the cause of bringing a life into the world; what he was bringing into the world was his spinal fluid so that someday people could legally seek therapy with MDMA.

Anyway, he got through it. Now it was time to persuade friends and acquaintances—heavy MDMA users all—to follow him. Instead of urging them to think of themselves as soldiers or mothers, he incentivized them by promising to fly them to San Francisco and put them up at the luxurious Red Victorian bed-and-breakfast on Haight Street. The procedure would be done at Stanford medical facilities, then they'd all go down to Esalen and sit in the clothing-optional hot tub as a reward.

It worked. About twenty people, mostly friends from New College, all braved the big needle and gave up their fluid for science. None expressed concern that the results would indicate brain damage; all felt in good mental and physical health after years of, in some cases, very heavy use of MDMA and other drugs. On average, each member of the group had taken MDMA ninety-five times.

Ricaurte compared their spinal fluid to levels in a control group that had never taken MDMA. He found that the average presence of serotonin metabolites—what was left after serotonin was excreted and broken down in the body—in the spinal fluid of the user group was 32 percent lower than in the control group.

That was less dramatic than it sounded. For one thing, individual serotonin levels in healthy individuals varied widely; the normal range varied by as much as 100 percent. Still, the 32 percent average was statistically significant:

it was very unlikely to be just a coincidence that the MDMA-taking group tested that much lower on average. But it wasn't necessarily due to the MDMA itself. Most of the subjects had also taken many other psychoactive drugs in their lives. So it could be due to one of the other drugs, or the combination.

Or none of the above: about this time, an unrelated study determined that people who had lower serotonin levels also tended to score on the high end of tests for risk-taking behavior. Since drug taking was generally perceived as risky behavior, it would follow that the low serotonin levels could have led to MDMA use rather than the other way around.

There was another factor that Ricaurte didn't explore.

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No serotonin decrease had yet been linked to any negative behavioral consequences in animal studies, and even years into their frequent MDMA use, Rick and his wide-ranging group of friends were all apparently high-functioning and physically healthy. Beyond that, in a decade of widespread abuse—millions upon millions of recreational doses of MDMA taken in uncontrolled circumstances—no epidemic of any serious brain dysfunction had appeared. Given all of the above, Rick thought looking strictly at serotonin levels would be a myopic waste of resources. As long as he'd recruited this group of willing test subjects, he wanted them to undergo cognitive testing as well to determine how they matched up against a normal baseline in broad measures of brain function.

Ricaurte was collaborating with a team from Yale on an analysis of how frequent MDMA users responded to a drug that challenged the serotonin system, so Rick hired a clinical psychologist from Yale named Charles Opsahl to test the volunteers who had agreed to make another long flight for that study, this time to New York. After suffering through the friendly skies and being injected with the challenge drug—which had a sedating effect—they underwent a battery of written, verbal, and tactile tests. The results were compared to a control group of local volunteers who had never taken MDMA. Opsahl reported the results in a letter to Rick dated July 5, 1988.

“By and large, these results are striking for the fact that most subjects evaluated had IQ scores in the above average range, or higher,” he wrote. Well, they were Rick's friends, so ... While there was some evidence of impairment in a test of short-term memory as well as a test in which the subjects had to assemble a block puzzle while blindfolded, Opsahl concluded, “It is quite possible [the slightly lower scores] are related to travel fatigue, being in a new environment, or being stressed in some way following the challenge testing that each subject performed.”

Rick breathed a sigh of relief. These were people who had been heavy MDMA users for years, and ultimately, regardless of serotonin levels, their cognitive testing results were no worse than what might be expected from people who had just flown across the continent to undergo a medical procedure with a sedating drug. It was another piece of evidence to help persuade the FDA to approve human MDMA studies.

But again Rick would be disappointed—“shocked” is how he remembers it—when Opsahl and his colleagues published their results, the first-ever assessment of MDMA and neurocognitive function. Although the authors concluded that, despite serotonin levels on the low side, none of the test subjects “reported depressed mood or met clinical criteria for an affective disorder at the time of testing,” it went on to emphasize the negative.

The cognitive test deficits—which, in his letter, Opsahl said could be no more than the result of travel and stress—instead became “a pattern of mild-to-moderate impairment” which “raise[s] concern about possible detrimental effects of MDMA use on neuropsychological function.” The letter contained no

mention of the adverse circumstances under which the tests were taken.

Rick struggled with his frustration: everything with MDMA seemed to be an uphill battle. What were basically positive results got reported as negative results, and even if you did take the most negative view, these were subtle dangers under discussion—potential subtle dangers—when drugs with far more certain and significant dangers sailed through FDA approval for clinical trials and became prescription medicines.

Rick had only one gear, and that was forward. If the cloud of potential neurotoxicity couldn't be dissipated, he had to focus on finding a way to test the benefits of MDMA that could be set against the hypothesized detriments. He knew from the therapeutic history of MDMA before it was criminalized that it had been found to effectively reduce depression and anxiety and could even make physical pain more tolerable in patients who were battling terminal disease. Of what concern would possible long-term serotonin depletion be to someone who had no long term to worry about?

Of course, he'd already tried that argument when attempting to treat his own grandmother who had been near death. And George Greer, a plaintiff named in the suit against DEA and one of the leading practitioners of MDMA psychotherapy before criminalization, had recently proposed a clinical study on terminal cancer patients and gotten nowhere. He had been told that “even dying people have the right to be protected against brain damage.”

But Rick thought it was time to try again. Of course, he was a political scientist, not a psychiatrist. He couldn't do medical research on his own. He needed someone with medical qualifications and credentials to work with, and just as he was struggling with the toxicity issue, he found one.

Rick noticed a letter in the Archives of General Psychiatry pointing out serious methodological flaws in one of Ricaurte's MDMA studies. The writer was Charles Grob, the University of California psychiatrist who would eventually conduct the study of sacramental ayahuasca users.

Grob had grown up in the sixties and, like so many of his cohorts, “had modest firsthand experience” in college with psychedelics—experiences at least impressive enough so that when, after leaving school, he found himself working as a late-shift technician in a dream research studies lab, he became fascinated with the library of psychedelic literature belonging to one of the researchers. He read to stay awake at night, and soon developed a passionate interest in psychedelic research—enough to motivate him to go to medical school and become a psychiatrist.

“Meanwhile,” Grob says in a familiar refrain, “all psychedelic research shut down.”

But Grob maintained his interest, and even published a speculative article on how to proceed “if the opportunity should arise to pursue sanctioned clinical research with these unique psychoactive substances.”

Of course, Rick Doblin noticed that article too. Rick decided to pay Grob a visit. When he suggested they develop a

protocol to present to the FDA on using MDMA to treat cancer anxiety in terminal patients, Grob felt he had come full circle.

The two labored on the protocol, a complex document describing the design of the proposed study that had to be rigorous and overwhelmingly persuasive, both scientifically and politically. It took a frustrating two years to complete; Grob struggled to find the time among his other responsibilities, which kept increasing. Finally, in the spring of 1992, after countless revisions, they submitted it to the FDA for approval.

Once again Rick's timing was impeccable.

Almost immediately, the National Institute on Drug Abuse scheduled a policy summit on the issue of psychedelic research for mid-July, just weeks after the submission of Grob's protocol. NIDA hadn't considered psychedelics (they were still referring to the drugs generally as "hallucinogens" despite the fact that the visual perceptions the drugs provoked were rarely true hallucinations) for fourteen years, largely because there had been little research to consider. Now four currents had converged to change that. First was the fact that, despite ever tougher drug laws, the illegal use of various psychedelics only seemed to increase. Meanwhile, interest in human psychedelic research among researchers—primarily Rick Strassman's DMT study and Grob's proposed MDMA study, both inspired directly or indirectly by Rick—had begun to build. Finally, amidst frustration with the failure to find an effective treatment for opiate drug addiction, impressive reports of offshore success in treatment of addicts with ibogaine were increasingly hard to ignore.

Synchronistically, the FDA, which had neither approved nor rejected Grob's MDMA study protocol, had forwarded it—with a critique and suggested changes—to an advisory committee scheduled to meet the day after the NIDA psychedelic policy review ended.

So, seven years after MDMA had been placed on Schedule I—seven years of unceasing effort on Rick's part—he and Grob boarded a plane to Washington for two meetings in three days that would either open the door to human psychedelic research or nail it shut.

The NIDA and FDA meetings would take place in immense federal office buildings within two miles of each other in North Bethesda, a half hour northwest of the Capitol. Grob and Rick got a hotel room within brisk walking distance of both headquarters. When the NIDA meeting began on July 13, Rick braced for a hostile or at least fiercely skeptical atmosphere.

So he was surprised when the opening speaker, Stephen Szara, the retired chief of NIDA's biomedical research branch, began with a detailed and nuanced review of the history of psychedelic research, including its promise as a therapeutic aid.

Szara pointed out that from 1953 to 1973, before the clamp-down, the federal government had funded—not even counting the secret military research—at least 116 studies of LSD involving more than 1,700 subjects at a cost of about \$4 million. He even spoke about the studies that suggested that psychedelics, given in large doses, produced transcendent, cathartic, and even mystical experiences in subjects ranging from prisoners to priests.

Rick felt as if he had slipped into an alternate universe when Szara reached his conclusion: careful research into the mysterious workings of the brain with these uniquely useful psychedelic tools could yield new discoveries of significant potential.

Rick Strassman, his DMT research still ongoing, made a presentation whose subtext was unmistakable: with caution and proper screening, hundreds of doses of a powerful psychedelic could be safely administered to humans in a research setting.

But the emotional high point for Rick came when Sasha Shulgin, the chemist who had rediscovered MDMA, made a passionate argument for restarting human research. Even as DEA agents looked on, Shulgin didn't shy away from

talking about the hundreds of novel psychoactive compounds he had tested on himself and a team of twelve research associates—and not always in a strictly legal manner. If there was one overriding lesson from his decades of research, Shulgin said, it was that the variance in the psychoactive effects of closely related chemical compounds were unpredictable and could be determined only by human testing. He gave specific instances of data from animal studies that had been directly contradicted by human subjects. He referred back to Stephen Szara's talk of psychedelics' ability to produce religious experiences. Did the assembled experts think rats could provide sufficient data on that?

The laughter that followed felt to Rick like the beginning of a new era. ●

**Tom Shroder**, author of *Old Souls*, the classic study of the intersection between science and mysticism, is an award-winning journalist, writer and editor. As editor of *The Washington Post Magazine*, he conceived and edited two Pulitzer Prize winning feature stories. Shroder has edited humor columns by Dave Barry, Gene Weingarten and Tony Kornheiser, as well as conceived and launched the internationally syndicated comic strip, *Cul de Sac*, by Richard Thompson. His last book, written with former oil rig captain John Konrad, is *Fire on the Horizon: The Untold Story of the Gulf Oil Disaster*. His most recent editing project, *Overwhelmed: Work, Love, and Play When No One Has the Time* by Brigid Schulte was a New York Times bestseller.

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