washingtonpost.com

The Peace Drug

Post-traumatic stress disorder had destroyed Donna Kilgore's life. Then experimental therapy with MDMA, a psychedelic drug better known as ecstasy, showed her a way out. Was it a fluke -- or the future?

By Tom Shroder
Washington Post Staff Writer
Sunday, November 25, 2007; W12

THE BED IS TILTING!

Or the couch, or whatever. A futon. *Slanted*.

She hadn't noticed it before, but now she can't stop noticing. Like the princess and the pea.

By objective measure, the tilt is negligible, a fraction of an inch, but she can't be fooled by appearances, not with the sleep mask on. In her inner darkness, the slight tilt magnifies, and suddenly she feels as if she might slide off, and that idea makes her giggle.

"I feel really, really weird," she says. "Crooked!"

Donna Kilgore laughs, a high-pitched sound that contains both thrill and anxiety. That she feels anything at all, anything other than the weighty, oppressive numbness that has filled her for 11 years, is enough in itself to make her giddy.

But there is something more at work inside her, something growing from the little white capsule she swallowed just minutes ago. She's subject No. 1 in a historic experiment, the first U.S. government-sanctioned research in two decades into the potential of psychedelic drugs to treat psychiatric disorders. This 2004 session in the office of a Charleston, S.C., psychiatrist is being recorded on audiocassettes, which Donna will later hand to a journalist.

The tape reveals her reaction as she listens to the gentle piano music playing in her headphones. Behind her eyelids, movies begin to unreel. She tries to say what she sees: Cars careening down the wrong side of the road. Vivid images of her oldest daughter, then all three of her children. She's overcome with an all-consuming love, a love she thought she'd lost forever.

"Now I feel all warm and fuzzy," she announces. "I'm not nervous anymore."

"What level of distress do you feel right now?" a deeply mellow voice beside her asks.

Donna answers with a giggle. "I don't think I got the placebo," she says.

FOURTEEN YEARS AGO, Donna Kilgore was raped.

When the stranger at the door asked if her husband were home, she hesitated. Not long, but long enough. That was her mistake.

"That was it," Donna, 39 now, is saying. "He pushed in. I backed up and picked up a poker from the fireplace. I was screaming. He says, 'I've got a gun. If you cooperate, I won't kill you.' He unzipped his jacket and reached in. I thought, this is it. This is how I'm going to die. My life didn't flash before my eyes. I wasn't thinking about my daughter. Just that one cold, hard fact. I checked out. I could feel it, like hot molasses pouring all over my body. I went completely numb."

She dropped the poker.

Afterward, she stayed strong. She wasn't going to make the classic victim's mistake of blaming herself for provoking the attack. She had no doubts about that. She'd screamed and screamed until the police came through the door. (They later reported that her attacker jumped up, clutching for his pants, saying, "She said I could!")

And, bottom line, she'd survived. She'd be fine, she told herself. She was wrong.

"It was what it must feel like to have no soul," she says. She quit all her hobbies. A passion for tennis died. Devastating nightmares woke her in the dark, her heart racing and palms slick. She dreamed of explosions, tornadoes, bears eating people.

"Psychologists will tell you to go to your happy place," she says. "Well, my happy place had bears in it."

Five years passed. Whatever went wrong, or right, in her life, it felt like it was happening to someone else. She found a wonderful, loving man -- she could still recognize those qualities, even though she couldn't respond to them fully -- and remarried. She had more kids. But even her family felt alien. It was "almost like going overseas and being an exchange student, living with someone else's family . . . I didn't like being close to people, and my children didn't understand that. Mommy was always busy." She was often irritable, and felt an unaccountable anger, which sometimes morphed for no obvious reason into a heavy-breathing, sweat-streaming rage. Almost worse, she couldn't feel the love she knew surrounded her. "I was afraid it was gone -- when you look at your child and say, 'I would die for that child in a heartbeat,' I didn't feel it -- and I was afraid I would never get it back."

As she says this, she never breaks eye contact. Talking about her trauma and her treatment is a decision she's made, she says. "It's important." But it is also, obviously, hard, and she looks a little pale as she explains what it was like for those five years: "I would put my finger on my arm, and it would be like touching a dead body."

Incredibly, she didn't see a connection to the rape. Then, one evening, she was sitting on her couch watching a disaster show on TV -- she calls her interest in the genre "an addiction"-- when her apartment door opened. Something about the angle of it seemed odd. As she looked at the door, the room began to swirl. "It was kind of like a whirlwind, make-you-dizzy moment, and I saw the whole thing, that man pushing through the door, the warm molasses pouring down, my body going numb. I call it, 'when I left my body.'"

Now she understood: She had left her body -- and never come back.

The panic attacks began at work one Friday. She felt butterflies in her stomach, then couldn't breathe. "I thought: 'Oh my God, I'm dying. I'm having a heart attack.'"

It passed, but she was shaken, especially because she'd also been having fainting spells and migraine headaches. She went to a neurologist "sure they were going to find a brain tumor."

The doctor was getting ready to order an MRI scan when Donna just blurted it out: "Things don't feel real to me."

The doctor turned. "Oh? There's a word for that," she remembers him saying. The word is dissociation, which happened to be a prime symptom of post-traumatic stress disorder, or PTSD.

PTSD is usually triggered by combat, rape, childhood abuse, a serious accident or natural disaster -- any situation in which someone believes death is imminent, or in which a significant threat of serious injury is accompanied by an intense sense of helplessness or horror. Not all or even most trauma victims

develop PTSD, but enough do so that nearly 24 million Americans, or 8 percent of the population, have suffered from it at some point in their lifetime. It is estimated that in any given year, more than 5 million Americans have active PTSD -- a costly problem in humanitarian and economic terms. Drug and alcohol abuse are all-too-frequent consequences of PTSD, as is loss of productivity and the need for expensive, long-lasting medical treatment.

The ever-lengthening Iraq war will count among its other costs a legacy of thousands of veterans in need of psychiatric treatment. The government estimates that already more than 50,000 soldiers -- about 4 percent of those who have been deployed to Iraq and Afghanistan -- have been treated for symptoms of PTSD. Many more might actually have it: Military studies put the number at 12 to 20 percent of those returning from Iraq and 6 to 11 percent of those returning from Afghanistan. And the news gets worse.

"Vets with PTSD are particularly costly to the [Veterans Affairs] system," says Linda Bilmes, a lecturer in public policy at Harvard's Kennedy School of Government. "They constitute 8 percent of the claims, but 20 percent of the payments." Bilmes, who has studied the ongoing costs of the wars, estimates that treating Iraq vets with PTSD over the next 50 years will cost taxpayers $100 billion. This is based on findings that one-third of vets with PTSD will remain unemployable, and all suffering with PTSD will have a much higher than normal likelihood of needing treatment for physical ailments. And that's just the direct costs to the budget. "Assuming that the war continues, though with lower deployments, through 2017," she says, and assuming the rate of PTSD isn't being underreported, the cost of lost economic productivity to the U.S. economy will be in excess of $65 billion.

Whatever the cause, the symptoms of PTSD are fairly consistent, and Donna's -- which rated severe on a standard diagnostic test -- were typical. Her prognosis was not great. Some antidepressants can diminish symptoms, and various forms of psychotherapy can, long term, sometimes untangle the psychological knot at the root of the problem. But the nature of PTSD makes therapy problematic. The very symptoms -- acute anxiety, heightened fear, diminished trust and inability to revisit the trauma -- are a direct roadblock to healing. At least one-third of people with PTSD never fully recover.

On that day of Donna's first diagnosis, the doctor sent her up to the seventh floor, the psych floor, to begin years of therapy and medication, none of which helped much, Donna says.

And then she found Michael Mithoefer and became the first to take one of his little white capsules.

THE CAPSULES RESIDE IN A SAFE, armed with an alarm and bolted to the floor of Mithoefer's office, a 1950s-vintage cottage on the road between downtown Charleston and Sullivans Island. It's been tastefully remodeled to create a softly lit, high-ceilinged sanctuary in the back, scattered with art and furnished with, among other things, the ever-so-slightly inclined futon where Donna got crooked.

The elaborate security is occasioned by what is inside the capsules: MDMA, a synthetic compound that is a chemical cousin to both mescaline and methamphetamine. Unabbreviated, MDMA is a real mouthful -- 3,4-methylenedioxymethamphetamine -- but it is far better known by its street name, ecstasy, millions of doses of which are synthesized in criminal labs from the oil of the sassafras plant. At one point, Mithoefer recounts, agents of the Drug Enforcement Administration, there to inspect the security arrangements, inquired about the therapist who rents the office adjoining the safe room.

"I guess they were concerned she might drill through the wall into the safe and steal the MDMA," Mithoefer says. "Though there's such a small amount in there, and it's so readily available on the street in such large quantities, I don't see how that would be worth the effort, even if she were so inclined."

Mithoefer became a psychiatrist in 1991, after a decade as an emergency room doctor -- he had found himself less interested in the bodily traumas his patients suffered than the psychological traumas that so often preceded their appearance in the emergency room. He's got that mellow, empathic vibe that they just can't teach at therapy school. He always seems moments away from a sympathetic chuckle, an understanding murmur or a sage observation. A fit 61, with a brown ponytail and relaxed dress code,

Mithoefer has become the accidental point man of a movement to revive medical research into psychedelic drugs. His Food and Drug Administration-approved PTSD study that began with Donna Kilgore in April 2004 is now nearly completed, with 18 of 21 subjects having undergone the double-blind sessions. Two Iraq veterans with war-related PTSD, the study's first, are cleared to begin. Close behind are similar studies in Switzerland and Israel. At Harvard's McLean Hospital, researchers are set to evaluate MDMA therapy as a way to alleviate acute anxiety in terminal cancer patients. In Vancouver, Canada, the effectiveness of an ongoing program to treat drug addiction with another potent psychedelic drug, ibogaine, is under scrutiny. There is a proposal, based on case histories, to study the ability of LSD to defuse crippling cluster headaches.

All of these studies are directly or indirectly funded by a surprisingly robust organization whose roots stretch back 40 years to the psychedelic movement of the 1960s. Before Harvard lecturer Timothy Leary started channeling aliens and urging college kids to turn on and drop out, an intense cadre of doctors and researchers had come to believe that psychedelic drugs would revolutionize psychiatry, providing those with a wide spectrum of psychological problems -- or even just ordinary life difficulties -- the ability to, basically, heal themselves.

But Leary's bizarre career, which morphed from doing research on psychedelics to cheerleading their widespread abuse, obscured whatever medical potential the drugs may have had. Instead, authorities focused on the risks, and often exaggerated them. Richard Nixon famously called Leary "the most dangerous man in America." After a slow start, regulators and legislators cracked down hard. Millions of dollars in enforcement efforts were unable to end abuse of psychedelic drugs, but they effectively stamped out sanctioned research into their healing potential.

A small group of psychedelic researchers and therapists willing to break the law continued their work clandestinely. A much larger group did not flout the law, but waited in the wings and is now emerging. Experience had convinced these therapists that psychedelics, along with significant risks, had potential for even more significant benefits.

This may have been especially true of MDMA.

Mithoefer states the case in an article he wrote for a book of scholarly essays, *Psychedelic Medicine: Social, Clinical and Legal Perspectives*:"The reported results [of early therapeutic use] include decreased fear and anxiety, increased openness, trust and interpersonal closeness, improved therapeutic alliance, enhanced recall of past events with an accompanying ability to examine them with new insight, calm objectivity and compassionate self-acceptance."

In short, a therapist's dream. Or is it a hallucination?

THE PROMISE OF A BLOCKBUSTER TREATMENT, one that doesn't just address symptoms but defuses underlying causes, is a particularly seductive vision right now. A report issued last month by the National Academy of Sciences' Institute of Medicine emphasizes the uncertain effectiveness of current PTSD treatments, and the urgent need of returning soldiers who will suffer from it.

To a non-scientist, the very preliminary results of Mithoefer's study would suggest that MDMA might be just what the doctors ordered. Of the subjects who have been through both the MDMA-assisted therapy and the three-month post-experiment follow-up tests, Mithoefer reports, every one showed dramatic improvement.

But scientists are a cautious lot. "It's potentially nice to hear those things," says Scott Lilienfeld, an associate professor of psychology at Emory University. But until results are statistically analyzed and peer-reviewed for publication, "you can't really judge them. The plural of anecdote is not data." Especially with a drug that has considerable risk, Lilienfeld cautions, it pays to be skeptical.

A.C. Parrott, a psychologist at Swansea University in Britain who has devoted a large part of his career

to studying the dangers of MDMA, is far more than skeptical. "MDMA is a very powerful, neurochemically messy and potentially damaging drug," he says. The government "should never have given it a license for these trials. Certainly I would not give it a license for any further trials."

But one of the nation's premier PTSD researchers, Roger K. Pitman, a professor of psychiatry at Harvard Medical School, disagrees. Morphine is a powerful, potentially damaging drug, Pitman says, "and we use it to treat the pain of cancer patients. Sound medical reasons should trump."

Current treatment for PTSD is "partial at best," he says. "There's a lot of room for improvement, and we need to be looking for novel treatments."

Though Pitman calls the MDMA study "a fringe hypothesis" -- "I've never heard anybody talk about it at any PTSD meeting I've ever attended in 25 years" -- he also observes that, based solely on a description of the preliminary results, "this seems worth further study. A lot of new ideas meet with rejection and skepticism, and we need to be careful not to be prejudiced against something just because it seems wacky. If it has a 5 percent chance, or even a 1 percent chance, of being effective in treatment of PTSD, it's worth pursuing."

AS THE SESSION TAPE ROLLS TOWARD THE FIRST HOUR, the giggles have passed. Donna Kilgore is still on the crooked couch, but she sounds very level. She's talking about her husband. Her voice is clear, calm, but you can hear something in it, something rising in the throat like water from a newly tapped spring.

"I just have a deep feeling of gratitude for all the love and understanding he's shown. I know it's been tough on him, not understanding what I've been going through and not knowing how to help. But if it wasn't for him, I don't think I'd be here."

The study protocol requires that a hospital crash cart and a trauma doctor be present during all therapy sessions, in case the drug precipitates a medical emergency. They are waiting a room away, a reminder that this is a test of a potent experimental drug, though you'd never know that from the calm, sober tenor of the conversation. It's really more of a monologue: Michael Mithoefer and his wife, Annie, a nurse and co-therapist, mostly listen, only occasionally murmuring supportively. This is their treatment plan: Construct a reassuring, protective environment and "let the drug do its work."

"He used to spend a lot of time laughing and cutting up," Donna continues about her husband, "but things have gotten so serious. I love him with all my heart, but there just hasn't been that warm fuzzy feeling, how you get excited every time you see him. It's put a damper on it. I don't fully enjoy anything. I don't enjoy my kids. I don't enjoy my dog.

"It's frustrating, just going through the motions day after day after day. I don't get any joy out of it."

She stops talking, and you can hear the faint strain of music coming from her headphones. She takes a deep breath. The blood pressure cuff, on a five-minute timer, starts to inflate.

"It sucks to just exist, and not live," Donna announces.

FIRST SYNTHESIZED IN 1912 -- A BYPRODUCT IN THE MANUFACTURE OF A DRUG TO SUPPRESS BLEEDING -- MDMA was little known until a former Dow Chemical researcher named Alexander Shulgin tried it himself in 1977. Shulgin had made his reputation, and made Dow millions, by inventing the first biodegradable pesticide. After that success, he was able to work on whatever he chose. He chose psychedelic drugs, based on a transforming experience he had with mescaline in the late 1950s. "I understood that our entire universe is contained in the mind and the spirit," he wrote. "We may choose not to find access to it, we may even deny its existence, but it is indeed there inside us, and there are chemicals that can catalyze its availability."

Shulgin made it his business to find those chemicals. In a New York Times profile in 2005, when Shulgin was 79, he estimated that he'd synthesized 200 psychoactive compounds and tested them on himself. Their effects ranged from paralyzing him with fear to granting him ecstatic visions. With MDMA, he was convinced that he'd found something special.

"I feel absolutely clean inside, and there is nothing but pure euphoria," he wrote in his field journal. "The cleanliness, clarity, and marvelous feeling of solid inner strength continued . . . through the next day. I am overcome by the profundity of the experience."

It's not well understood why MDMA, or any psychedelic drug, can produce extraordinary experiences. But in MDMA's case, the crude explanation seems to involve a drug-forced rush of serotonin in the brain. Serotonin assists in the transmission of nerve impulses and plays a role in regulating a wide range of sensations and impulses, from mood, emotion, sleep and appetite to sensation, pleasure and sexuality. One recent study pointed out physiological similarities between a brain under the influence of MDMA and the post-orgasmic state, also known for producing emotional closeness and euphoria.

Whatever the cause, Shulgin saw in the overwhelming positive feelings the drug engendered huge potential as an aid in the psychotherapeutic process. "I made samples of it for a good therapist friend of mine, Leo Zeff, which brought him out of retirement and into the enthusiastic task of making it available internationally with his psychotherapy friends," Shulgin recalls in an e-mail. "Its popularity spread in part by his enthusiasm, but in part by the fact that its ability to open the doors of communication made it widely popular as a social drug."

BY MULTIPLE ACCOUNTS, MDMA EMERGED AS A STREET DRUG IN 1984 at a new and instantly hot Dallas nightclub called Starck. Sold at $12 a hit, MDMA -- which Zeff's crowd had nicknamed Adam, for its presumed potential to return man to innocent bliss -- became ecstasy. Part of the drug's appeal was that it made dancing feel great, and staying up all night easy. But there was more. Here's an account of first-time ecstasy use from that period, recalled in the Austin Chronicle in 2000:

"The street lights got brighter, I could see the stars, car lights, even the shadows in this alley were, you know, *more so*. And I felt this tingle that began in my fingers and spread all over my body, coming in waves, just this indescribable feeling of aliveness. It was as if the nerves in my skin had been dormant all these years and were just now waking up and stretching. Just like that. And after this initial rush of pleasure came an overwhelming -- and I mean *over-[expletive]-whelming*-- feeling of total and complete positivity. Any and all fears I had harbored about doing my first drug were waylaid instantly. It was pure bliss, but it didn't knock me off my feet, or feel scary in any way.

"My girlfriend . . . and I . . . lay in the wet grass and watched the stars and cuddled. And we talked. We talked for hours. We talked about everything. Everything. It was probably the best, most open and honest conversation I've ever had with anyone in my entire life."

Word-of-mouth reviews such as that fueled an explosion of recreational use. From 1984 to 2001, the graph line for the number of first-time users of MDMA in the National Survey of Drug Use and Health quickly shot up, reaching a peak of nearly 2 million new users in 2001 alone. Concern about the drug, spurred by a spike in emergency room visits from rave bars and MDMA-related deaths, went up right along with it. Ecstasy use has since tapered off, though it is still substantial. The 2005 survey estimated that 11.5 million Americans had used ecstasy, and 615,000 had tried it for the first time that year. The average age skewed young. In 2001, 5.2 percent of eighth-graders and 11.7 percent of high school seniors had tried ecstasy (both numbers have been roughly cut in half in the most recent, 2006 survey).

When Zeff began his mission to spread the MDMA gospel in therapeutic circles, the drug was perfectly legal. But federal drug enforcement officials, who had taken half a decade to ban LSD, weren't about to delay on ecstasy. Within months of the rave boom in Dallas, officials announced they intended to list MDMA as Schedule I, the category reserved for dangerous drugs with high potential for abuse and no accepted medical use.

Rick Doblin was waiting for them.

LIKE A LOT OF OTHER PEOPLE, Doblin had discovered psychedelic drugs in college in the early '70s. By his own description a somewhat awkward, searching kid, he tried LSD in 1971 at New College of Florida, then a small, experimental liberal arts school in Sarasota. Very liberal and very experimental. "There was this tradition of all-night dance parties, until sunrise, under the palm trees, using psychedelics," Doblin says. It was bacchanalian, yes, but Doblin found something else in the experience, something "therapeutic and spiritual."

"I was like, man, this is the kind of energy, the kind of psychic stuff" that could lead him to the personal growth he had been yearning for. Ironically, says Doblin, "this was right as research into therapeutic uses was pretty much being shut down."

Doblin's world was legally circumscribed in another way as well. He was a draft resister. "What could I possibly do with my life, because I couldn't be a licensed anything, doctor, teacher a professional of some sort. All that was closed to me because I was a criminal."

As long as he was already an outlaw, Doblin reasoned, be might as well be one of those who disregarded drug criminalization and worked underground as a self-trained psychedelic therapist. When he encountered MDMA in 1982, he became convinced that he'd found the perfect therapeutic tool, one that had an LSD-like power to hurdle psychic roadblocks but lacked the frightening disorientation. Plus, it was still legal, and by then, so was Doblin -- President Jimmy Carter had pardoned draft resisters in 1977. Now Doblin had a vision: He would return to the mainstream and bring psychedelic therapy with him.

When, in 1985, prohibition of MDMA came, as everyone knew it would, Doblin had already prepared his case with a coalition of like-minded pro bono lawyers, researchers and therapists. He even won a round -- an administrative law judge ruled that MDMA met the standards for having a legitimate medical application and being safe enough for medical use. But the DEA rejected that recommendation and MDMA remained banned.

Doblin, decided he couldn't win in the courts and switched his crusade to the lab. He would focus on fostering the science that would prove the benefits of psychedelic therapy outweighed the risks. In 1986, he founded a nonprofit organization -- the Multidisciplinary Association for Psychedelic Studies -- to raise money for the research. (Knowing he would need to navigate through the obstacle course of federal bureaucracy, he entered Harvard's Kennedy School of Government and, in 2001, received a PhD in public policy.) On the elaborate MAPS home page -- alongside a psychedelic research library, the organization's financial statements, elaborate news updates and notices of psychedelic art for sale -- is a splash box featuring the MAPS "Rites of Passage Project." It's an extended pitch for the idea that "within responsible limits" parents can sometimes find great benefit in doing psychedelic drugs with their adolescent children, and includes an archive of testimonials with taglines such as "Mother-Son Peyote Ritual . . . a beautiful rite of passage a mother shared with her teenaged son, strengthening his family connection, his sense of self, and his bond with nature."

Doblin is frank about his passionate desire to defuse the drug war, which he believes is counterproductive and an assault on personal liberties. He doesn't think the government should be able to tell Americans what to put in their bodies, and he has even volunteered in interviews that he sometimes finds it useful to consider important personal and strategic issues with psychedelic assistance. He acknowledges that his outspokenness caused a schism in the original coalition that fought against relegating MDMA to Schedule I -- many of his colleagues wanted to stress their support for the criminalization of any nonprescription use. He has seen it jeopardize one of his most prized accomplishments -- MAPS funding of the Harvard MDMA-cancer study almost killed it. Doblin had to withdraw MAPS as a sponsor and persuade a donor to give the money directly to Harvard instead. He must realize he is handing his critics a potent argument, i.e.: Don't be fooled by the careful science and limited goals of the current studies; the real goal is unrestricted use of psychedelic drugs.

So, why does he do it? "Sometimes, it's just a relief to say, 'This is what I believe,'" Doblin says.

His honesty has apparently been no impediment to soliciting cash from fellow believers, which, fortunately for MAPS, include some entrepreneurs with a high regard for the psychedelic experience -- and a distaste for government drug policies -- who struck it rich in the tech boom. Last year, MAPS donations topped $1 million.

MAPS continues to fund Mithoefer's study, which is estimated to cost $900,000 through completion. And Doblin will raise money to support the much more expensive next step -- Phase III trials, which involve multiple sites and multiple therapists who will treat hundreds of people suffering from PTSD. If it proves safe and effective, MDMA would be certified as a prescription drug. That all could take five years and $5 million, Doblin says. "But if it took twice that long and cost twice that much, it would be worth every penny."

Mithoefer speaks far more cautiously of his eventual goal. "If MDMA indeed proves an effective treatment for PTSD," not only should the drug require prescription, but it should be administered only in licensed clinics with specially trained therapists, "like methadone," he says. Regarding Doblin's controversial views, Mithoefer says: "I respect his openness. I think it's a good thing that there's nothing sneaky about Rick, but that's not what I'm oriented toward. I'm oriented toward doing medical research. There are real patients suffering with real problems, and I'm trying to learn through good science if there are some methods to help people heal."

MITHOEFER DOES NOT WANT TO TALK ABOUT HIS PERSONAL EXPERIENCE WITH MDMA, except to say that it occurred when the drug was legal. But it must have stuck with him. "I was working in the emergency department, looking for some deeper way to address people's problems," he recalls. "Stan Grof's work really got my attention."

Stanislav Grof, a Czech psychiatrist and one of the first to research therapeutic uses of LSD, believed that the West had lost touch with the healing potential of non-ordinary states of consciousness. When psychedelic drugs became illegal in the United States, Grof created an alternative called holotropic breathwork. The idea was that hyperventilation, combined with music and a ritualistic setting, could foster an altered consciousness, through which patients could be guided into insight and problem resolution. Mithoefer went to California to train with Grof, then began to use breathwork in his own practice. And though he says it is often effective, he wondered how much more could be accomplished using MDMA. In 2000, Mithoefer approached Doblin to ask if he knew of a country in which a study of MDMA-assisted therapy might be permitted.

"You can do it here," Doblin said. "And we'll help."

Doblin says his optimism was based on a change in leadership and culture in the federal bureaucracy. When he first founded MAPS, Doblin says, "the FDA was refusing to permit all the studies we proposed," even one attempting to use MDMA therapy to ease the fears of a dying cancer patient who had found solace using the drug before it was banned. "The FDA said, 'No, we have to protect him from brain damage,'" Doblin says.

Then in 1992, after six years of refusals, the FDA approved a MAPS-funded human safety study. Safety studies are required before any drug can move on to Phase II -- studies of a specific medical application. In MDMA's case, this was particularly important because many believed the drug to be so toxic. Even *talking* about the possibility of therapeutic benefits would only make more people want to try it, some believed, and that would inevitably lead to more emergency room visits. And deaths.

More than 200 fatalities involving ecstasy use in the United States were reported to the Substance Abuse and Mental Health Services Administration from 1994 to 2001. Many of these deaths were related to traffic accidents and the use of other drugs and alcohol or other incidental causes. Of deaths directly related to ecstasy, most were caused by heatstroke. MDMA exerts a stress on the body similar

to strenuous exercise and increases core body temperature, so dancing all night in a hot, crowded bar can quickly go from fun to deadly. More rarely, some ravers, paranoid about hyperthermia, have reportedly consumed so much water, many gallons, that the water itself became toxic and killed them.

But, even in the context of uncontrolled doses and settings, deaths from MDMA are relatively infrequent events, considering the estimated tens of millions of doses taken.

Perhaps of even greater concern was the possibility that MDMA could cause permanent brain damage. Though research is ongoing and hotly debated, it's clear that test animals injected with high doses experienced lasting deformation of serotonin receptors in the brain.

There were worrisome human studies as well: In some, long-term recreational users of ecstasy performed more poorly on tests for short-term memory and some other cognitive functions than control groups, though the meaning of these results is complicated by the fact that most long-term ecstasy users also use other dangerous drugs.

The new safety study was not testing the dangers of MDMA under the conditions of illegal use. Eighteen people were given dosages similar to those that would be used in psychotherapy sessions, and the settings were comparable to the calm of a psychiatrist's office. The gist of the findings: MDMA given under those circumstances produced no acute harm or evidence of brain impairment. These results were bolstered by a Swiss study in which people who had never before taken MDMA were given brain scans before and after being given a single therapeutic-range dose of the drug. Comparison of the before and after scans showed no damage.

Given those results, Doblin figured the time was right for persuading regulators to approve Mithoefer's proposal, a placebo-controlled, double-blind study (meaning that neither doctor nor patient would be told who got the real drug). The safety study, and others done elsewhere, had made the case: Many valuable medicines have been developed from far more problematic drugs.

Doblin and the Mithoefers spent 18 months developing an elaborate protocol for the study: Research subjects would be limited to people who'd struggled with the disorder for years, and whom conventional treatments hadn't helped. The cases would be relatively severe, as scored on the standard diagnostic test, and subjects would be required to undergo multiple non-drug therapy sessions with the Mithoefers before and after the two MDMA sessions to prepare them for the experience and to help them process it afterward. The protocol dealt with such details as what kind of touching would be permitted (supportive, non-sexual), and what kind music would be played on earphones (soothing).

Submitted to the FDA in October 2001, it was approved a month later.

Then, in September 2002, the institutional review board engaged to guarantee the study's ethics -- de rigueur for human medical research -- abruptly withdrew its support. A study published in Science magazine found that relatively small doses of MDMA had created severe damage to the dopamine system in the brains of squirrel monkeys and orangutans. Dopamine damage could put human users at risk of developing Parkinson's disease, among other problems. In the case of the primate test subjects, the Science article said, the drug was so toxic that two of 10 animals died, and two more were in such bad shape that the researchers didn't give them a planned third injection.

After 2 1/2 years of work, the PTSD study appeared to be doomed.

A year later, Science printed a retraction: The vials containing the drugs that so damaged the monkeys' brains had been mislabeled. It wasn't MDMA after all, but methamphetamine. A new review board quickly signed on to support Mithoefer's study, but the irony of the wasted year wasn't lost on him: The misidentified drug that had been deemed too toxic to evaluate for medical use, the drug that was far more toxic than MDMA, was *already* a prescription drug.

Meanwhile, in the four years the MDMA study lingered between concept and reality, Donna Kilgore had been driven to the brink. She took "every anti-depressant you can name," tried a dozen therapists and an almost equal number of therapeutic approaches. But nothing made that numbness, panic and rage recede.

"I was getting to the point," she recalls, "where it was either go sit on a mountaintop or go dive off a cliff."

That's when a therapist told her about the Mithoefers' experiment. She applied, and became patient No. 1.

DONNA SPENDS A LOT OF HER TIME ON THE CROOKED COUCH holding the Mithoefers' hands, one on each side. She needs that reassurance now, recalling the rape.

"I was backed into a corner, nowhere to go, desperate. I kept telling him I wouldn't tell anybody," she says.

Can she feel that desperation now?

"A little bit, yeah."

Minutes pass. On the tape, you can hear the blood pressure cuff whir to life as the amplified beat of her heart thumps faintly in the background.

Finally she speaks, her voice rising with conviction.

"I feel protected. I do. I feel completely protected. I don't feel like I'm hanging out there anymore . . . It feels good to be loved. It feels good to be protected."

Minutes pass. She is lost in a vision, she will say later. She can *see* herself standing on a ridge, high above a valley shrouded in mist. Down in the valley, she knows, is a battlefield, containing all kinds of terrors. Her terrors. She knows they are there, but can't see their shape through the fog. Now the fog is lifting. Now she can begin to see.

"You're right," she says, as if in response to an assertion that hasn't been made. "I am angry. I'm angry at myself. It changed from being afraid to being mad at myself, that I allowed it to happen . . .

"And not just that," she says. There's a sudden, involuntary intake of breath. "I think that a lot of this baggage I'm carrying around is really stuff that I put in there myself. I stacked the luggage. Either in disappointment in myself or self-blame. Don't get me wrong. Under no circumstances do I think that I deserved it or I asked for it or that I did something to bring that on. I don't feel that way at all . . . It's like you take your base line [which is] fear, and you throw some self-doubt on top of that, and then you throw some desperation on top of that, and, before you know it, you got a seven-layer burrito going there. I mean I can feel every one of them. I don't know how to express it, but I can feel them . . . just one right on top of the other, and maybe I've done that for so long, that when the rape happened, that was maybe the straw that broke the camel's back, and my mind said, 'Okay, that's enough, you're cut off, no more.' There's no more room on the pile."

The Mithoefers murmur sympathetic words as Donna continues unburdening herself.

"It's not just about the rape. It's not just about any one thing. It's so many different things . . . All I can remember feeling, as far as I can remember, is fear. Heart-stopping, gut-dropping fear . . . I've kept all this inside for so long, and it feels so heavy . . . these emotions -- it's like I've been trained to be this way as long as I can remember -- to be seen and not heard. Just from that point on, I've tried to make myself as small and inconspicuous as possible. And then the rape happened, and you're headline news . . . I

was ashamed."

The study protocol calls for the therapists to periodically ask the subjects to rate their level of distress on a scale of zero to 10.

"Zero," Donna says quickly. Another pause. "No, that's not entirely true. That's a lie. I would say about a two. It's a disturbing revelation, I guess you could say."

Once again, she pauses.

"I feel calmer, a whole lot calmer," she says. "Kind of putting it all together, rather than just throwing it all in a box."

"OH, MAN, I'M IMPRESSED," SAYS MARK WAGNER, a clinical psychologist on faculty at the Medical University of South Carolina in Charleston, an expert in psychological testing and an independent evaluator conducting the before and after PTSD assessments in Mithoefer's study. "I didn't know much about the clinical use of MDMA before this," Wagner says, "But I've seen each and every one of these patients, and, just as a clinical psychologist, it is impressive to see the degree of treatment response these folks have had. There are a couple of areas in medicine, like hip replacement, where one day you are bedridden, and the next you're out playing tennis. Or with Lasik surgery, you're blind, and then you can see. Nothing in psychology is like that. But this was dramatic."

Lilienfeld, the Emory psychologist, is less enthusiastic. "These subjects knew if they got the drug or the placebo," he says. "Particularly when you have a very dramatic and powerful intervention, people may change but not in a longstanding way."

Wagner points out that two subjects who got the placebo were convinced they had gotten MDMA, and others who did get it weren't sure. The people who wrongly believed they'd gotten the drug initially showed improvement, but quickly relapsed. "The chance that a placebo effect would last for three months is very slight," Wagner says. "And for it to last for a year or more, which anecdotally we believe might be the case here, would be extremely remote."

But if MDMA does work, the question remains, why? "Patients in our study had a fear of the fear," Wagner says. "Something about the MDMA made it possible for them to approach the feared thought, the feared 'place' in their mind -- and when they got there, it wasn't as terrible as they thought. A lot of these people, the light bulb went off, they had the insight, but there's still a lot of work to do. They've had this for years, it's shaped their lives, and now they have to rebuild them."

In Mithoefer's *Psychedelic Medicine* article, he theorizes that the breakthroughs came from having the psychic calm -- the feeling Donna had of being protected -- that allowed subjects to meaningfully reexperience and reassess the events that traumatized them, and at the same time be able to feel a powerful new connection to positive aspects of their lives. In Donna's case it was the love of her husband and children. Another patient told Mithoefer: "I had never before felt what I felt today in terms of loving connection. I'm not sure I can reach it again without MDMA, but I'm not without hope that it's possible. Maybe it's like having an aerial map, so now I know there's a trail."

For some subjects, the most significant part of the experience seemed to be a physical release of mental anguish. In Mithoefer's article, he says one subject exclaimed: "I can relax! Forty-three years of fear and not being able to feel my body. Now I can feel my body without pain."

Another subject, a 50-year-old woman named Elizabeth, had one of the more dramatic physical releases. "I thought it was supposed to be talk therapy, that I was supposed to talk about things, but it doesn't have to be," she says. "The drug itself will do the work."

Her trauma centered on a stepfather who viciously abused her and her brother from an early age. She

describes him as "a truck driver, ignorant, uneducated, Southern, moonshine-drinking, swearing, wife-beating idiot. He thought kids were there for his entertainment, amusement and personal use."

From an early age, Elizabeth was stuck in a grim survival mode. "Doesn't matter what you do to me, you will never touch me," is how she described it. "It was a feeling, all self-defense, all self-protection, nobody gets in."

Her whole life evolved, pathologically, from that premise. Running away as an adolescent from the horrors at home, she was raped, twice, by men who picked her up as she hitchhiked. With no real concept of love and nurture, she got involved in a series of physically and emotionally abusive relationships. When something triggered memories of her abuse, she froze in a nearly catatonic state, caught between fight and flight, unable to do either.

During her MDMA session, Elizabeth says, she remembered that after her mother divorced her stepfather, she'd confided to Elizabeth that he had been the best lover she'd ever had.

As she talked about how that made her feel, Elizabeth recalls, Mithoefer "was pushing me verbally. I was mad, and he was pushing me, provoking me to feel it. I just kept getting madder and madder, hitting the bed. Then the drug just took me and slammed me down. I was sitting one second, then down on my back in the next. I became very rigid, the tension was so powerful. I remember lying on the bed where I slammed down, looking at Dr. Mithoefer . . . like I'm mad at him for putting me through this, and this wave of energy just slammed through me, and it was just a release of a tremendous amount of this negative energy. It was powerful, and it was explosive. I felt like I'd been through something significant . . . *My mother traded my childhood for sex!*"

In the weeks following the therapy sessions, Elizabeth says, she would be standing in the kitchen, or just sitting in a chair at work, and without warning that powerful release would move through her body. Afterward, she says, "I felt at ease, a level of ease I was not familiar with, just being comfortable within myself, within my body."

That feeling of ease has given her a new relationship with her life, she says. Difficulties continue, but "I'm not having as much problem with the puzzle. I'm able to just keep slugging away. I don't feel so much like going to bed and sucking my thumb."

The problems don't disappear, Mithoefer says, they just become something that can be managed.

"All subjects have told us they found MDMA helpful," Mithoefer says in his article. "Some have felt the effect . . . was dramatic and even lifesaving: however, others have reported disappointment that MDMA was not a "magic bullet" to remove all their symptoms, or have said it would have been helpful to have one or a few additional sessions."

Parrott, the MDMA critic from Britain, worries that in some cases MDMA magnifies negative feelings instead of positive ones, and can bring up difficult memories that may be overwhelming. It's problematic, he says, that the outcome of therapy sessions can be so dependent on the skill of the therapist.

Mithoefer acknowledges that this is an issue and says that's precisely why he believes that, if MDMA is ever prescribed, it should be administered only in licensed clinics by specially trained therapists.

Still a problem, says Parrott. "Those patients who had good experiences on the drug would often want further-on MDMA sessions (just like many novice recreational users)," he writes in an e-mail. "This scenario is very worrying for many obvious reasons: reducing efficacy but increasingly adverse effects following repeated usage; drug seeking elsewhere when it stopped being forthcoming from the clinic etc; regular use leading to a variety of psycho-biological problems."

Wagner, who questioned all of Mithoefer's subjects in detail about their post-therapy attitudes, thinks Parrott is way off mark. "I didn't see a single individual who thought: 'Oh, yeah, this is great fun. I'm going to try to go out and use this for recreational use.' All of them took this very seriously and therapeutically. They saw it as hard, but important, work."

Amy, a woman in her 40s, is a case in point. She remembers being psychologically and physically abused by her father "from birth," culminating one winter when he locked her in the basement for three weeks. She had a reaction to MDMA very different from Donna's instant giggles. When the drug started to take effect, she says, "It just hit me, and it wasn't pleasant. I felt like I was going to throw up. So I said, *Okay, when's this happy, lovey feeling going to happen?* I went to lie down on the couch and waited to go higher, but the drug took me down instead. [Mithoefer] was taking notes. I felt like he was drawing circles around me, but he showed me his notes, and they were just notes. That's when I saw that my internal world and external world didn't match up, and I connected with that. I saw myself as a baby wrapped in a white blanket, my family members standing there, and I realized, *It wasn't my fault* . . . I was flooded with feelings of peace and safety. 'It wasn't my fault. I didn't do anything,' I kept saying. 'I was a little girl. I was a baby.'

"After the first session, I felt exhausted, like I had a really bad hangover. But everything continued to unfold. I started to make connections. Like going into the grocery store, I used to feel very alienated. I couldn't connect with the other shoppers. But after the first session, I realized I could look at the people, and I wasn't afraid, like they were going to hurt me. I made the connection between the way I was always sizing up my environment, the alienation and the numbness that I felt, and the abuse.

"It felt weird at first, but kind of nice, that I could look at someone, and they would look back, and we'd smile at each other."

But like several other of the test subjects, Amy also confronted difficult new terrain. "Sometimes to go forward you have to go backwards," she says. "I knew that, but it wasn't comfortable to go there, back into the basement, into the abuse, into the beatings. I was apprehensive. I had already started feeling more grounded, but I'd functioned so long on autopilot that feeling things was difficult."

Difficult, but also better. "So many things happened," she says. "Before, I never wore a seat belt. I would look at it but not wear it. It was self-sabotage. But after therapy, without even thinking about it, I just automatically started putting it on."

FOR A YEAR AFTER HER TWO MDMA SESSIONS, Donna Kilgore says now, she was symptom-free.

"To me, the biggest breakthrough -- it meant the world to me to be able to look at the fear, to look at the shame. I didn't know I was ashamed. It was like I'd been wearing the scarlet letter. It was so heavy. When I got out of that session, I felt a hundred pounds lighter.

"Before, I knew the path was through the battlefield, but I just could not get through it. [But during the MDMA therapy] I knew I could walk through it, and I wasn't afraid. The drug gave me the ability not to fear fear." Otherwise, she says, "I would have not been able to do it."

Donna's sense that she'd had a breakthrough was supported when she retook the evaluation test on which she'd rated as an extreme case just weeks earlier. Her score had declined dramatically -- Mithoefer says that he can't give an exact number before publication of results -- but if she had been taking the test for the first time, she would not have been considered to have PTSD at all.

It's now been more than three years since her MDMA sessions. Donna is "still extremely grateful for the experience," she says. But problems are starting to crop up again.

"I've had a lot of stressors recently," she says. Her husband got laid off from a good job; they had to

move; she had a difficult job at a dental practice for children.

Donna was doing paperwork in the office. "It wasn't in the best part of town," she says, "and I started to have catastrophic thinking again." It was the resurgence of the paralyzing, unreasonable fears characteristic of PTSD that she'd had before the MDMA sessions. "I just started being convinced that someone was going to come in with a gun and start shooting. And then I just couldn't listen to the children screaming in the next room . . ."

She says she had to quit the job. She begins to cry.

"I know I can work through it," she says, her voice breaking a little. "I know what I'm fighting now, and I can fight it."

Does she think it would help if she could have another MDMA therapy session?

"Yes," she says quickly. "But I can't. It's illegal."

Tom Shroder is editor of the Magazine. He can be reached at shrodert@washpost.com. He will be fielding questions and comments about this article Monday at noon at washingtonpost.com/liveonline.