TWO

MDMA

Heart Medicine

Substance: MDMA (3,4-methylenedioxymethamphetamine), a.k.a. Molly, ecstasy, X, E, XTC, Adam.

Schedule: I[*6]

The psychoactive medicine 3,4-methylenedioxymethamphetamine (MDMA) is presently used primarily as a recreational drug—because it is illegal to use it for its most important purpose: psychotherapy. Effects include significantly increased empathy, mild euphoria, personal insight, and heightened sensations including sexual sensations. When taken by mouth, effects begin after thirty to forty minutes and last two to four hours.

MDMA increases the release and slows the reuptake of the neurotransmitters serotonin, dopamine, and norepinephrine in parts of the brain.

MDMA was first synthesized in 1912. It was used to improve psychotherapy beginning in the 1970s and became popular as a street drug in the 1980s. In 2014 up to 29 million people between the ages of fifteen and sixty-four used ecstasy.

MDMA is generally illegal in most countries. Researchers are investigating whether a few low doses of MDMA may assist in treating severe, treatment-resistant post-traumatic stress disorder. In November 2016, Phase III clinical trials for PTSD were approved by the United States Food and Drug Administration to assess effectiveness and safety.

A Cherubic Cheerleader for Psychedelic Research

Our first interviewee, Rick Doblin, PhD, is by far the world's foremost—and, if I may add, cherubic—cheerleader for psychedelic research. When I met him in 1985 at Esalen, he was full of enthusiasm for his dream. He planned on going to Harvard, getting a PhD, and then founding a pharmaceutical company that would fund research around the world into psychedelics. He accomplished all of these things and more. His insights into MDMA in the following interview are invaluable.

Drawing a Map from "X" to Rx

Rick Doblin, PhD

March 5, 2013 (with excerpts from August 18, 2015)

RICK DOBLIN, PHD, is the founder and executive director of the Multidisciplinary Association for Psychedelic Studies (MAPS). He received his doctorate in public policy from Harvard's Kennedy School of Government, where he wrote his dissertation on the regulation of the medical uses of psychedelics and marijuana. His professional goal is to help develop legal contexts for the beneficial uses of psychedelics and marijuana, primarily as prescription medicines but also for personal growth for otherwise healthy people, and eventually to become a legally licensed psychedelic therapist.

The Long Road to the Pentagon

RLM: Rick, welcome to *Mind, Body, Health & Politics.*

Rick Doblin, PhD (RD): Richard, it's a pleasure.

RLM: How are you?

RD: Really good. Super excited actually. On Monday I'm going to an appointment at the Pentagon to meet various Department

of Defense officials, and later that afternoon I'm going to the Senate. We're proposing a demonstration project with active-duty military with post-traumatic stress disorder [PTSD], where we would train the therapists, they would provide the active-duty military, and we would do MDMA-assisted psychotherapy.

They would have their own independent raters evaluating the patients, and we hope they can fund additional studies if they can see it work. If we get permission for this first study, it would be a tiny little nonprofit, MAPS, giving a grant to the Department of Defense.[*7]

Coming of Age in a Time of Change

RLM: Let us back up just a little bit. Over twenty-five years ago, Dr. Rick Doblin—well, he wasn't *Dr.* Rick Doblin when we first met in the early 1980s at the Esalen Institute—started MAPS, the Multidisciplinary Association for Psychedelic Studies, which supports pioneering, groundbreaking research on the psychoactive substances MDMA, ayahuasca, DMT, ibogaine, ketamine, LSD, mescaline, peyote, psilocybin, and salvia divinorum.

Research into these substances has been virtually nonexistent and has been suppressed by the United States government for the last fifty years. We're going to find out from Rick how he managed to start MAPS in the face of this governmental and political suppression. Why did you start MAPS over twenty-five years ago?

RD: Let's go back a little bit further. In 1972, when I was eighteen years old, I had my first experiences with LSD. I had been educated to believe one dose of LSD made you permanently crazy, and I was fearful of these drugs, but I also had a lot of questions about the accuracy of the information I was being taught. I read *One Flew Over the Cuckoo's Nest*, by Ken Kesey, and a friend of mine told me after I'd read it that Kesey wrote part of it under the influence of LSD. I'm thinking, "That can't be possible—this is such a fantastic book." When I tried

LSD, I felt like it started doing what my bar mitzvah was supposed to do.

RLM: Turned you into a man?

RD: Yeah, it was an existential challenge—it was opening up my emotions. I felt something fundamentally deep and profound was impacted. For a lot of us, traditional rituals, religious services, and rites of passage are more intellectual than deep and profound. So I woke up to the incredible value of psychedelics, just as the backlash from the sixties was coming into full power.

RLM: 1972—Nixon got elected.

RD: It was disheartening to see the potential of these [now illegal] substances. I'd also been aware of the Holocaust—born in 1953, growing up Jewish—and of how people project outward, disown their shadow, and put it on others. I felt the problems of survival had a lot to do with psychological factors. The technological advancement we've enjoyed through the incredible development of the mind—just miraculous technology—has outstripped our emotional and spiritual capabilities to handle it wisely. So we have global warming, we have the threat of nuclear weapons, and all sorts of environmental devas-tation. I felt that—both for me as an individual and for society—we needed to become more balanced with the emotional-spiritual side of ourselves.

Also, I had a very difficult time with the LSD and went to the guidance counselor at my college, New College in Sarasota, Florida, and he gave me a manuscript copy of *Realms of the Human Unconscious* by Stanislav Grof, which was inspiring. It wasn't philosophy. It wasn't basic science. It was therapy. It focused on how to actually help people, in a way, as reality testing. So I decided to devote myself to psychedelic research, spirituality, values, and reality testing of therapy. But everything was shut down, and I felt like I didn't have any opportunities. I needed to work on myself more so that I would be capable of handling all of these energies. Then ten years later, in 1982, I

went back to school and was able to do my first semester back, at Esalen, during a monthlong workshop with Stanislav and Christina Grof. During that time, somebody came by and started talking about MDMA, which was legal at the time.

A New Tool for Self-Discovery

RLM: Tell us what MDMA stands for please.

RD: MDMA is methylenedioxymethamphetamine, more popularly known as ecstasy, or Molly. It's a semisynthetic drug, so it is not found in nature by itself in that form, but it comes from sassafras—safrole—and is somewhat modified chemically. It is gentler than the classic psychedelics. Some people have tried to give it other names, like entactogen or empathogen, because you don't get the classic visual impacts on your train of thought—the flow, or emergence, of the unconscious—that happens under classic psychedelics or in dream states. MDMA is gentler than that, and it opens up emotional capabilities. It reduces fear and anxiety. It promotes a sense of self-acceptance and peace, and it can be used in many different ways.

I learned there was a tradition of therapists and psychiatrists continuing to work with substances, particularly MDMA, in a quiet, underground way. But some people who had used it therapeutically realized there was a major market for other uses, so they turned it into ecstasy, which started being sold in recreational contexts, attracting the attention of the government. It felt like I had a chance to do history all over again in that I had learned about MDMA before the crackdown, but it was clear that the crackdown was coming; this was the rise of Nancy Reagan's "Just Say No" and the drug war in full flower.

I felt like we needed to organize and prepare for the crackdown, so I had an incredible opportunity to work with psychiatrists and psychologists, and I also worked with Robert Muller, who was the assistant secretary general of the United Nations. He'd written a book, *New Genesis: Shaping a Global*

Spirituality, about how the United Nations exists to help mediate conflicts between countries, but how many conflicts go deeper, to religious conflicts. They felt we needed a mystical sense that people could come together with unity while still appreciating all the differences and uniqueness of religions. He realized psychedelics could be a tool in studying religion and spirituality, and so he decided to help me bring back psychedelic research.

RLM: This was before MDMA was made illegal, in the early ‘80s.

RD: I worked with Brother David Steindl-Rast, and Rabbi Zalman Schachter, and others who were lifelong Zen meditators. They were willing to use MDMA in small, roughly half-doses in meditation, which they found could facilitate deeper learning. Students could practice on their own, making progress in ways that they had not been able to do before.

The DEA Schedules MDMA

RD: Starting in 1984, the Drug Enforcement Administration [DEA] finally decided to criminalize MDMA. When they criminalize a sub-stance, they have to file something in the Federal Register, and then there are thirty days to file an appeal. We were prepared for that. We’d even done a safety study in around thirty-two people on Stinson Beach for the first study ever of MDMA, which we kept quiet. Just looking at blood pressure and heart rate and various other . . .

RLM: That’s the study that Dr. Jack Downing was involved with?

RD: Yes, that was the first study ever on MDMA.

RLM: Yes, I remember that. My therapist Robert Kantor gave me MDMA as part of my therapy in 1982 and 1983, while it was still legal. And Leo Zeff, PhD, aka the Secret Chief, whom I think you knew . . .

RD: He was in charge of handing out the MDMA at the experiment.

RLM: Leo lived four doors away from me in Kensington, California, at the time, so I was a regular subject of his.

RD: Lucky.

RLM: Very lucky.

RD: So we completely took the DEA by surprise. They had become aware of ecstasy, but the code name for MDMA was Adam when it was used in these therapeutic settings, and about half a million doses had been distributed and used since the mid ‘70s to the early ‘80s, and the DEA had no knowledge of that. There were no problems from it. It didn’t come to public attention—so they just thought they were criminalizing a recreational drug, and they were shocked when I walked in the door in Washington and handed them a petition with pro bono legal representation from a major DC law firm, and testimony from Harvard Medical School psychiatrist Lester Grinspoon and George Greer and others who had experience with MDMA and were willing to say, in public, that they thought that it should remain available to psychiatrists and therapists.

We were able to have what’s called an administrative law judge hearing in front of a DEA administrative law judge, arguing it was premature to criminalize it, and that it should remain available as a therapeutic tool. To our astonishment and to my great faith now in parts of the American political system, we won the lawsuit. The judge recommended that MDMA be made illegal for recreational use but that it remain available legally for therapeutic use. These administrative law judges make recommendations to the head of the agency that they’re working in. So this went to the administrator of the DEA who decided that this was a recommendation that he didn’t want to accept, and he rejected the recommendation. That was heartbreaking for us—we won the lawsuit and then the DEA rejected the recommendations.

Then we decided to sue in the appeals courts, and we won several times, but eventually the DEA was able to satisfy the court that they had a set of criteria that would criminalize MDMA completely, and that would be that.

How to Start a Psychedelic Pharmaceutical Company

The Only Way Is through FDA

RLM: You still had not started MAPS at that point.

RD: Right. For a long time we had an international strategy to try to start research everywhere else in the world, because we were blocked in the United States. Once it became clear that the United States could manipulate things around the world, we had to go back and start inside the United States with the Food and Drug Administration [FDA]. It became clear that the only way to bring it back was not through lawsuits that we had won but then lost, but through the FDA. At the time I had this naive hope, because there were hundreds of thousands—eventually millions—of people using MDMA, and I thought that if they all just donated a dollar or two then we would have the funds necessary to do the research. In 1986 I started MAPS as a nonprofit pharmaceutical company trying to develop psychedelics and marijuana into FDA-approved prescription medicines.

RLM: So, in effect, you formed a pharmaceutical company.

RD: Yes, I wasn't quite aware of it at the time, but there had never been a nonprofit development of a drug. That changed in 2000. The first example of a successful nonprofit drug development was the abortion pill, Mifepristone, produced by the Population Council with funding by the Rockefeller family, Warren Buffett, who donated over $5 million to it, the Pritzker family, and others. They teamed up and took a drug that was highly controversial and that pharmaceutical companies would not research because their other products would be boycotted, and brought it to market. The FDA was willing to work with a nonprofit organization, and that was a success.

I didn't know that it had never been done when I started MAPS, but I felt that it could be done and should be done and that it was the only way forward. I believed in science. I really did believe in the scientific process, and I respected the work

that was done by the FDA to evaluate drugs. The genesis of MAPS was trying to gather together all the people that were having these profound personal experiences that were beneficial to them and to say, let's all put our resources together and try to fund studies that will satisfy the skeptics and critics and the regulators at the FDA.

The Mission to Legalize MDMA as Prescription Medicine

RLM: And your mission . . .

RD: Primarily, it was to develop MDMA into a prescription medicine. But of course I broadened it to all psychedelics and marijuana. MAPS is also chartered to look at non-drug techniques as well, like holotropic breathwork, hyperventilation, meditation, and spirituality. MAPS can actually do a large number of things consistent with our articles of incorporation, but the core element was to work politically and scientifically. Then I was an undergraduate, wanting to become a PhD in clinical psychology in order to do psychotherapy-outcome research with MDMA and LSD—to show that it really was helpful.

In 1987, when I graduated, I tried to get into various clinical psychology PhD programs, telling them I was interested in doing MDMA research, which was still illegal. The crackdown that began in the mid '60s was complete by the early '70s. By the mid '80s, research was still squashed and researchers were locked out of the laboratories. You couldn't do any science.

It was frustrating. So I sat down and I thought about it, and I realized that I wanted to do the science, but the politics were in the way. And I had this insight: maybe I should just switch my focus and study the politics.

I had read an interview in *Harper's Magazine* with a fellow named Mark Kleiman and several others who were drug-policy experts, and they mentioned the lawsuit that I had been

involved in. I decided to call up Mark Kleiman, who turned out to be a professor at the Kennedy School of Government at Harvard. I told him my situation—that I only had one class in politics, and that was a class about suing the DEA—everything else was in psychology. But I asked him if he would be my mentor, and he said he would and he encouraged me to apply. So I ended up getting a master's and a PhD from the Kennedy School of Government at Harvard with my dissertation focused on regulation of the medical use of psychedelics and marijuana.

RLM: Meanwhile, you had already started MAPS in the mid '80s. You were already starting to get donations. Had you already funded any research by then?

RD: No, since all the research was still blocked.

Overcoming the Global Suppression of Research

RLM: When you say research on psychedelic materials was squashed, what immediately comes to mind is that trip, to Israel, I had the good fortune of joining you on. We consulted with Israeli officials about the possibility of using MDMA with their PTSD patients, because so many Israeli citizens there had witnessed horrific events during the Intifada. We were told by the government of Israel that they would love to do the MAPS research study but they couldn't, because if they did the research, the United States government would sanction them. That was the first time in my life I came face-to-face with how the United States government squashes research around the planet. Now is that still the case? Where are we now with regard to other countries doing psychedelic medicine research?

RD: That was so disheartening. It really was. We had to start MDMA–PTSD research in the United States before we could get started in Israel, because it is so dependent on the security of the United States. Once we started it in the United States, however, they were still nervous, until we began a second

study at Harvard Medical School with MDMA for cancer patients with anxiety. That helped the Israelis realize that they weren't going to get any pressure from the United States for doing things that were already happening in the United States.

We have a study at the largest mental hospital in Israel with the former chief psychiatrist of the Israel Defense Forces as the principal investigator. Interestingly enough, one of the meetings that we had, when you and I were in Israel, was with the Israeli antidrug authority; so not only did we have to get approval from the Ministry of Health, we had to get approval from the antidrug authority. Just recently the Israeli government eliminated the antidrug authority—defunded it completely—so we're seeing a worldwide recognition that prohibition has gone too far and that one of the consequences of prohibition was to restrict research of beneficial uses of medicines that were prohibited, such as marijuana, MDMA, and LSD. Now that the zeal for prohibition is declining, and we're seeing movements toward the legalization of marijuana and an opposition to mass incarceration, we are able to do research with MDMA in almost any country in the world. It looks like next week I'll be going to Israel, and we are starting our MDMA–PTSD study there, in association with the Ministry of Health in the Israel Defense Forces.

RLM: What is it, ten years later from our trip to Israel?

RD: Yes.

RLM: But you persist. You persist, Rick, and it is so wonderful that you continue to persevere.

MAPS: The Intersection of Politics, Science, and Psychedelics

RLM: It is over twenty-five years from when you started MAPS in 1985. Tell us about the research that MAPS is sponsoring in these various psychedelic medicines that I listed.

RD: The good news is that there is now more psychedelic research taking place around the world than at any time in the last forty years. We're basically combining science, politics, and psychedelics. We've realized that because these drugs and their users are stigmatized we have to be very strategic about which drug and which patient population we start doing the studies with. Our resources are limited, and we want to do work that will have the biggest appeal to the American public.

I got my master's from 1988–1990, and I got a Presidential Management Fellowship for people who want careers in the federal government and applied for a job at the FDA. In 1990 the group at the FDA with the authority to regulate psychedelics and marijuana switched to a new group, and they wanted to put science before politics. That's where things really started.

Two Phases Down, One More to Approval

RD: It's been almost twenty-three years since then. We started from what are called Phase I studies—working in a healthy population to evaluate what the drug does—to get a sense of the risk and to get a sense of the potential patients. Phase II is where you can start working with patients, and Phase III are the large-scale, definitive studies.

We're in the middle of the Phase II stage all over the world—working with patients. Of the patients we've chosen—again for these political reasons—the first are those with PTSD. People are very sympathetic to those who have been victimized: those who have survived childhood sexual abuse, adult rape and assault, or particularly now veterans and soldiers with PTSD from the wars in Iraq and Afghanistan; or those in Israel from wars and terrorism, all over the world.

Our primary focus is MDMA, because it's a gentler psychedelic than the rest. We've actually heard from a lot of people who had difficult psychedelic trips with LSD or psilocybin or mescaline during the '60s or '70s—during their youth—who have been unable to work through them, and

when they smoke marijuana it brings it back. A fair number of people I know don't use marijuana because it brings back difficult psychedelic trips from the past; and we worked with some of these people and have found that MDMA can help them integrate these difficult psychedelic experiences.

I think MDMA will be the first drug that will be integrated into our culture, and I think PTSD is likely to be the first clinical indication, and we're seeing lots of support. That's why we're being invited to go to the Pentagon to present this proposal. Combining these two directions—both the politics of drug regulation and also psychotherapy—has led me to conclude that MDMA has an excellent chance of making it through the regulatory system.

Maximizing Benefits and Minimizing Risks of MDMA-Assisted Therapy

The Session: How Often Is Too Often?

RLM: Is there a negative effect of frequent use of MDMA, and what is frequent use?

RD: Every drug has its risks, and MDMA is not a magical drug that has no risks. Our model is a male/female co therapist team in a therapeutic setting. It's roughly a 3.5-month treatment process, and there are initially three weekly, non-medicine, ninety-minute sessions to build the therapeutic alliance between the therapist and the patients—to come to understand the history of each one's trauma and of how each patient has reacted.

Then there is an MDMA session, which starts at around 10 a.m. and goes to 6 p.m.—an eight-hour session. Then patients spend the night in the treatment center. The MDMA sessions are then followed by a non-medicine therapy session the next day, after which the patients receive phone calls every day for a week, followed by weekly non-medicine psychotherapy for a month.

The MDMA sessions in our therapeutic setting are three to five weeks apart. In our first study, we did a series of very complicated and expensive neurocognitive studies, because the claim has been that MDMA will reduce serotonin if it's done too frequently or at too-high doses, and then people will supposedly have cognitive deficiencies. We tested that and found no evidence at all. In our therapeutic setting, with pure MDMA spaced out once a month—three times—there's no evidence that it's harmful.

Now, if people were to do it every other day, I think that would be too frequent. I have seen some people that have done it too frequently, and they get the opposite of what they were looking for. They're looking for a heightened emotionality, deeper feelings of peace and love; but when you just continue to do it too frequently you kind of get muted in your emotions. You become much more washed out and drained.

RLM: On the other hand, Rick, I've had patients—couples—who have done it once a week, every single week for up to a year, and they report very beneficial effects.

RD: Yeah. There is so much individual variability.

RLM: I see.

Integrating the Experience

RD: In terms of frequency, the key part is for me is whether the patient integrated what happened before. So if you're just looking for the experience itself and not thinking about what you bring back from it, and how you adjust and grow in your daily non-drug life . . .

RLM: Non-medicine life, shall we say?

RD: Yeah, I think that's a healthy way to say, "Okay, I'm going to have this experience. It's for the experience itself, but it's also for what I bring back from it—what I've learned from it." And then once you've integrated it, then I think you're ready if you want to do it again.

RLM: That's true of all the psychedelic medicines, isn't it? That the key is bringing the information back over the line, into daily life?

RD: Yeah, that's exactly right.

RLM: Whether it's ayahuasca, LSD, ibogaine—with all of the psychedelics—there's an opportunity for gigantic learning; but then we are challenged to bring that gigantic learning right back into, quote, "the real world."

RD: Yeah. These are tools to help enhance our non-drug life. This is a voyage that you take—like a vacation you take—but you come back to your life, and then hopefully you feel refreshed and rejuvenated. I think there's something to the serotonin changes that government-funded researchers have highlighted or exaggerated. But in the therapeutic doses that we use, and for many people using even larger doses in recreational settings, they don't see these problems.

Not Too Much, Not Too Little: Finding a "Goldilocks" Dose

RLM: What is the therapeutic dose that you've been using with MDMA?

RD: We use 125 milligrams, and then between 1.5 and 2.5 hours later we administer a supplemental dose of half the initial dose.

RLM: And what is considered a large dose?

RD: Sometimes people outside of clinical settings will take two pills—or 250 milligrams—or sometimes even more.

RLM: Do we have any negative effects on record of people taking very large doses and something not good happening to them?

RD: There are rare instances, yes, of people in recreational settings that take MDMA and are engaged in vigorous dancing while not drinking adequate fluids, and they'll overheat—hyperthermia.

RLM: Thus, we have artifacts affecting results because it's not the medicine that causes negative effects, rather it is taking the medicine in what Jim Fadiman would say is the improper setting, one which itself causes hyperthermia—such as taking hot baths or other factors—which the MDMA exacerbates.

RD: MDMA has pharmacologically built-in safeguards against abuse. The classic addictive drug is one that you take a lot and you build up a tolerance to it, and so then you just up the dose. Before you know it, you're taking these huge doses and you're dependent on the drugs. With MDMA, if you take it very frequently and lose the feeling—the depth of it—you try to take a higher dose, but it doesn't work. You get more of the amphetamine, more of the speedy part of it, but not the peaceful part of it. It doesn't encour-age the traditional pattern of an addictive drug with tolerance and ever-larger doses.

RLM: I read a study indicating that some people actually do better on a smaller dose. What can you tell us about MDMA dosage and boosters?

RD: We've tried that, and that hasn't worked. Part of my dissertation was about how to do double-blind studies with drugs like MDMA, where it's pretty easy to tell if you've got an inactive placebo or the full dose. The approach I arrived at after a lot of thought was a "dose–response," meaning everybody knows they're going to get MDMA, but they don't know what the dose will be. If you show a dose–response relationship, then that would be sufficient. The low doses in the neighborhood of 25 to 30 milligrams seem to have had an antitherapeutic effect. People get activated, but they don't get the peacefulness—the reduction of fear—so they're actually confronting their negative emotions or their trauma without the support that they would need. So that's antitherapeutic. And when you start getting higher and higher, we discovered something absolutely surprising, which is that the 75 milligram dose is doing remarkably well, to where the responses are really indistinguishable from full doses.

Supplementing MDMA to Reduce Fatigue

RLM: I want to read to you an email I got from a psychiatrist friend, Dr. Bruce Africa. He says:

> Please let Rick Doblin know that I have immensely appreciated his efforts in bringing intelligent, rational thought to the subject of psychedelic drugs and their place in society. But I also have a question about the negative effects, and if there are side effects, such as fatigue? What can be taken along with the MDMA, in advance, in order to ameliorate this fatigue? And what are the other negative effects you might mention?

RD: The first thing to say is that many people, myself included, feel exhausted the day after taking MDMA. In our therapy, we take advantage of that as a reason to talk about this as a two-day experience, where the second day is for people to rest, reflect, and integrate what happened the first day. When we do our therapy, people are required to spend the night in the treatment center. They can have a significant other come and spend the night if they want, and then the next day they have a leisurely morning. They have several hours of non-drug integration of psychotherapy. They can't drive home—somebody else has to come take them home—and they're encouraged to rest.

Then we call them every day on the phone for the first week. This exhaustion, when there is such a rush in our modern world, is a rather novel occurrence for a lot of people, and so we've woven that into the therapy. Also, to answer your question: we are trying to figure out what MDMA does by itself, so we don't administer any substances, before or after, to help ease this exhaustion or to increase the depth of the experience. However, people have talked about 5-HTP, which is a serotonin precursor that can be taken either before and/or after: before to try to make the experience deeper and after to try to recover more quickly from the exhaustion.

RLM: I've heard reports that 5-HTP has been helpful, and it's an over-the-counter medicine.

RD: Yeah. It's just a serotonin precursor, and it's something that a lot of people say does help with the exhaustion.

RLM: What about tyrosine, lysine, tryptophan? Any report on those?

RD: No, you really need to go to Erowid.org, where there are all sorts of personal accounts of people that have combined various things with MDMA for different purposes. Even though there is massive experience from tens of millions having done MDMA, all of that has taken place outside of the experimental context, so we don't have any scientific information about it. When we negotiate with the FDA or the European Medicines Agency we've been instructed to just assume we know nothing and then start from the beginning—the ground up, so to speak. We needed to see how strong the side effects actually were, and it turns out in our model it's not much of a problem. People are more exhausted when they take it at night during a party and then go do stuff the next day and don't eat or drink properly. We find that people welcome the time-out the next day to reflect, and it is an integral part of our treatment. There is a lot to learn in regard to combinations, but we don't have any direct information.

One of the concerns that was expressed thirty years ago about MDMA was that one dose causes permanent brain damage—that people would be suffering significant and severe functional consequences. But nobody was at the time, and so they reasoned that this is the kind of thing that's going to show up over time: "We can't see it right now, but as people age they're going to start showing all these symptoms. Their brains will decline, and the symptoms that are covered up by redundancy in the brain are going to be showing up later." Now we have people that have aged, and we don't see these symptoms. That whole time-bomb theory of MDMA neurotoxicity has been discredited.

RLM: It's certainly been discredited in my life. My therapist, Dr. Robert Kantor, gave MDMA to me during our sessions in the early '80s—I know I've taken it over a hundred times—and

while I do misplace my keys and glasses quite often, I think I'm still able to talk to you coherently.

Evidence of Safety in Clinical Setting

RLM: You said tens of millions of people have taken MDMA. We do not have reports coming in from all over the United States, as we did with cocaine and heroin, about emergency room admittances from MDMA overdoses. Tens of millions of people use this medicine with very few negative effects. We humans know when a substance is dangerous. I mean, if you ingest a bit of rat poison, or a little tiny bit of arsenic, or a little tiny bit of something that gives you the runs, and you know it immediately.

When you have something that's ingested by the public for ten, twenty, thirty, or fifty years with no negative results—that counts as part of science, is referred to as anecdotal evidence over time, and deserves to be taken very seriously. In my work at Wilbur Hot Springs, where people have been taking the medicinal waters for 150 years, there has never been one complaint to a health department. That record means a great deal, because when people sit in water, some of it goes in their mouths and other bodily orifices. If there's something in the water that will make them sick, it would eventually get reported and certainly we would be aware of the danger after ten, twenty, or thirty years, let alone 150 years. Anecdotal evidence over 150 years tells us this Wilbur Springs medicinal water has no unwanted complications, aka harmful side effects. How does this evidence of tens of millions of people safely using this MDMA medicine—along with tens of millions of people using marijuana and LSD—fail to positively affect the public, the psychiatric profession, and the law-making politicians? Does this massive amount of use without harm not influence in any way how the government acts?

RD: Well, it doesn't influence it directly. To make drugs into medicine you need data from FDA-approved studies. But it does make the FDA comfortable about MDMA or marijuana in

ways that they're not comfortable about any other drug ever approved, because when pharmaceutical companies try to get a drug through, at the most there will be ten thousand subjects. There are usually several thousand or even several hundred subjects studied to get a drug approved as a medicine.

Once the drugs are released into the market, then you have the one-in-one-hundred-thousand side effect or the one-in-a-million side effect. That's where you see a lot of drugs withdrawn from the market—*after* it seemed to the FDA and the pharmaceutical industry that they were sufficiently safe. With MDMA and these substances that have been used by tens of millions of people, we know the one-in-a-million side effects: we know that sometimes people can overheat and die when they're dancing all night without adequate fluid replacement. We know that sometimes people can die from taking MDMA and drinking too much water, causing hyponatremia.

"Ecstasy" Off the Street

RLM: Is there a difference between MDMA and ecstasy?

RD: There shouldn't be. Ecstasy, when it originally came out, was another name for MDMA, but now I almost never use the word *ecstasy* to describe what we're doing because it's impure. Recent studies have shown that most drugs sold as ecstasy or Molly are not pure MDMA—you usually get MDMA mixed with stuff or no MDMA at all. We had the eighth employee at Microsoft, Bob Wallace, donate about $100,000 for an ecstasy pill-testing program in order to protect and give some knowledge to the people who were purchasing it illegally. It turned out that over half of the samples had no MDMA in them at all, and there were all sorts of adulterants—methamphetamine, ketamine, caffeine. Ecstasy was a term meant to refer to MDMA, but now it's very difficult to say what's really in it.

RLM: Understood. So it's the difference between a real pharmaceutical-grade chemical and something off the street, where you have no idea what it is.

RD: Exactly. It's hard to say what the risks of pure MDMA are, but there have been over 1,100 people that have taken MDMA in a controlled, therapeutic, clinical research setting without any reported lasting negative consequences. Most of these people are healthy volunteers, not patients.

Early Treatments: End-of-Life Suffering, PTSD, and Addiction

The Tremendous Need for End-of-Life Care

RLM: I just got a letter here that I want to read to you, Rick. This man writes in and says:

> I have a sister, sixty years old, who was diagnosed with stage 3.5 primary peritoneal cancer three years ago. She underwent debulking surgery, and then extensive chemo treatments for six months afterward. She coped well with the surgery and the chemo, and the cancer is still in remission. But she is miserable and suicidal. Her husband of forty years is beside himself with what to do.
>
> She has undergone electroconvulsive therapy and has rejected every medication she has been given from benzodiazepines to SSRIs to opiates. She's really losing her mind, and has already attempted suicide once, maybe more. She needs help, and I'm curious if you think there is anything you could suggest for her. I'm curious [this is where you come in, Rick] if there are any psychedelic-treatment studies you might be aware of that could be tried with her?

RD: Yes. There are two studies that are recruiting subjects, currently—one at NYU[*8] and one at Johns Hopkins.[†2] And so she could consider applying to be a subject in both of those

studies. I'm not sure if they would screen her out because of suicidality, but they might be willing to enroll her in the study.

RLM: I'm certainly willing to give it a shot. I'll send this gentleman an email with these two ideas.

RD: This work with end of life is very important as well. This is politically well chosen because everybody is going to be in that situation. Most people are more scared of dying than they are of drugs, so if you can show that psychedelic medicines can be helpful to them, they will listen. When people are facing anxiety from end of life, a lot of their anxiety has to do with their health status, and that change is independent of the therapy, so there is this other variable going on.

The other scientific challenge with the work we're doing—and with helping people be more peaceful about this existential "getting ready to die"—is that this kind of change is not so clearly mapped onto the current measures of anxiety that the FDA has used to approve drugs. We have to get these drugs approved by the FDA and the European Medicines Agency and then get insurance companies to cover it. So we still have a lot of challenges.

Measuring Benefits of MDMA for PTSD

RD: So there are some methodological challenges with this independent variable—the health status of the participants for the LSD and psilocybin work with end of life. It's easier to show therapeutic progress with MDMA for PTSD—the measure developed by the Department of Veteran Affairs [VA], called the Clinician Administered PTSD Scale [CAPS], does a great job of measuring PTSD symptoms.

There's so much need, it's incredible. We have over 250 people on the waiting list for the study with MDMA for post-traumatic stress in Charleston, and we have over fifty people on the waiting list for the Boulder study, and we haven't even started the study yet.[*9] Once the FDA evaluates the data, its head would be permitted to approve MDMA. We say we've noticed that MDMA reduces activity in the amygdala, or the

fear-producing portion of the brain, and it increases activity in the frontal cortex, where we put things in association. It stimulates serotonin, dopamine, and norepinephrine, and it also releases oxytocin and prolactin—the hormones of nurturing and bonding. In contrast, PTSD reduces activity in the frontal cortex and increases activity in the amygdala.

There are only two drugs approved by the FDA for PTSD—Zoloft and Paxil—and they have marginal benefits. There is a large number of people that drop out of traditional non-drug psychotherapies—different estimates say 25 to 50 percent find traditional psychotherapy for PTSD to be retraumatizing rather than healing, because you have to relook at the trauma, and people are emotionally reactive or numb to it and avoid it.

At the same time, because of our foreign policy, we have a large number of veterans with PTSD that have failed to obtain relief from the currently available medications or psychotherapies that are being provided by the VA. Last year, the VA spent in the neighborhood of $6 billion just on disability payments to about thirty thousand veterans with PTSD. That's an annual figure that increases over time. These are young people, mostly, who are going to continue to grow and live for the next forty or fifty years. So there's an enormous moral debt that Americans feel toward these veterans. In addition, there is a growing awareness of the prevalence of childhood sexual abuse and adult rape and assault. People are realizing that there are way more people with PTSD from those causes than even from war-related PTSD. There was a terrific article in *Marie Claire*[†3] about our MDMA and PTSD research, and it highlighted some of the women subjects in our studies.

Treatment of Addiction Reveals the Mechanism of Recovery

RD: The third main area that we're trying to research is the treatment of addiction. It's a problem from a political point of view in that the addict is "the other." In terms of social change, it's not as powerful to develop treatments for the addict as

working with people who are dying or with PTSD, but it offers this other opportunity to show that it's not about the drug.

The fundamental problem with our drug policy is that it ascribes good and bad qualities to drugs themselves—"this is a good drug, that's a bad drug"—when really it's the relationship that you have with the drug that determines the value of it and whether it's harmful or helpful. I think it was Paracelsus who said that the difference between a drug and a medicine—or a drug and a poison—is the dose. So by doing work with psychedelics with people who are struggling with dependence and addiction, we're able to demonstrate to people that psychedelics considered by the law to be drugs of abuse can help people overcome drug addiction in the proper circumstances. Bill W., who founded Alcoholics Anonymous [AA], used LSD in the 1950s and found it to be very helpful. It offers the two things that we know are important principles of Alcoholics Anonymous.

First is this idea of making amends and coming to terms with what you've done and overcoming denial. Psychedelics have this way of changing the mind in such a way that the things that people are repressing and denying and putting down come to the forefront. Sometimes people call it a "bad trip," or as we try to call it a "difficult trip," but you can learn from it. The second part of AA is this whole spiritual model and a higher power. So psychedelics in the treatment of addiction offer the opportunity for people to address and see what they have been trying to avoid and at the same time give them an opportunity for this unitive mystical experience of connection, from which they can draw strength to aid in their recovery.

Finding Common Ground with Psychedelics as well as Non-Drug Techniques

RD: There is also a series of studies being done on basic neuroscience and consciousness research asking what these drugs do in the brain. There is even a series of studies looking

at the merging of religion and science in this forum in the sense of meditation, and this is extremely exciting for me. In the early ‘70s when the crackdown came, there was a large group of people who said, “We don’t really need drugs—they’re illegal. Let’s explore non-drug alternatives.” People have done that for the last forty years or so, and among the alternatives are yoga and meditation and various different techniques. People in their sixties are recognizing that they were inspired by their psychedelic experiences. Now there is a return to psychedelics—not in a frequent-use way, but in an inspirational way. We’re working on starting research in Switzerland that would look at lifelong meditators who would be administered psilocybin in a meditation retreat.

Roland Griffiths at Johns Hopkins looked at whether people had mystical experiences. They were taking religiously inclined people—not just clergy, but people who have a religious or spiritual practice of some sort. An ideal experiment would be to take people in clergy from different religious traditions and have them go through whatever normal training they go through, and then also have a subgroup go through their normal training with the additional opportunity of psychedelic experiences. You could then compare how the people did with their peers in their own religion, and then you can look at the content of their experiences and compare a content analysis across all the different religions and look for the commonalities. I think we would find an awful lot of them. Eventually, people will be able to do this.

RLM: Fascinating.

RD: We believe it’s not just about medical uses, it’s about integrating psychedelics. In particular, it’s about integrating the full range of consciousness into our mainstream society such that people have these profound senses of spiritual connection that I would equate to what astronauts who went to the moon felt when looking back at Earth.

RLM: Yes.

RD: If we can understand and appreciate our commonality, then we can all together face these incredible life-threatening changes happening to the planet, and we can appreciate differences rather than be scared of them.

RLM: Hear, hear, Rick. I think that's a perfect place to stop: to appreciate differences in each other rather than be afraid of them.

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My next interview on MDMA is with one of the first scientists to conduct government-approved psychobiological research on MDMA, Charlie Grob. I had the privilege of first meeting Charlie Grob at my home, in the early 1990s, during something called the "Friday night meetings," which were started by the Jungian analyst Dr. John Perry. These monthly meetings were an opportunity for researchers in the psychedelic community, from far and wide, to socialize and share ideas. Among many others, psychedelic pioneers Sasha and Anne Shulgin were regular attendees. It is a great honor to include this interview with Charlie Grob.

Pioneering Government-Approved Research

Charles Grob, MD

Excerpt from November 29, 2011

CHARLES S. GROB, MD, is director of the Division of Child and Adolescent Psychiatry at Harbor-UCLA Medical Center and Professor of Psychiatry and Pediatrics at the UCLA School of Medicine. In the early 1990s he conducted the first government-approved psychobiological research study of MDMA, and he was the principal investigator of an international research project in the Brazilian Amazon studying ayahuasca (see chapter 4). He has also completed an investigation of the safety and efficacy of psilocybin treatment in advanced-cancer patients with

anxiety and published his findings in the January 2011 issue of the *Archives of General Psychiatry* (see chapter 3). He is the editor of *Hallucinogens: A Reader* (2002) and the coeditor (with Roger Walsh) of *Higher Wisdom: Eminent Elders Explore the Continuing Impact of Psychedelics* (State University of New York Press, 2005). He is a founding board member of the Heffter Research Institute.

The MDMA Neurotoxicity Scandal

RLM: You did the first government-approved psychological research study of MDMA. Please tell us about what you found.

Charles Grob, MD (CG): My initial involvement came after reading an article in the *Archives of General Psychiatry* in 1989 alleging that MDMA could cause permanent neurotoxic changes in the brains of human users. My colleagues and I felt there were some serious flaws in the article. The methodologies seemed somewhat questionable, so we published a letter to the editor critiquing the article's conclusions.

Shortly after, I received a call from Rick Doblin, whom I did not know at that time. Sasha Shulgin had shown him our letter to the editor that was published in the *Archives*. Rick contacted me and a colleague of mine when I was at UC Irvine and asked us if we were interested in submitting a protocol to the FDA on an application for MDMA. We wrote a protocol that would examine the effects of MDMA on a population of terminal cancer patients with anxiety, focusing on the anxiety and also pain.

The FDA examined our protocol and informed us that they could not approve a treatment study at that point because there had been no normal volunteer Phase I study. So we then went back to the drawing board, rewrote our protocol for normal volunteer human subjects, and later conducted that study between 1993 and 1995 at Harbor-UCLA Medical Center.[*10] We studied eighteen individuals in the clinical research unit at Harbor-UCLA Medical Center utilizing pure,

government-grade MDMA. Individuals came in on three occasions: on two occasions they received different dosages of MDMA and on one occasion they received an inactive placebo. The order of these differing drug conditions was randomized. Both the subjects and our research team were blinded for the condition at each experimental drug session.

Physiological Effects, Side Effects, and Complications

CG: We measured physiological reactions, including blood pressure and heart rate. We took blood from an indwelling intravenous catheter every thirty minutes to study pharmacokinetics and neuroendocrine secretion, and we utilized a variety of psychological instruments as well. And at the end of the day we found that our subjects tolerated the MDMA experience very well. Two individuals of the eighteen people did have high blood pressure reactions. This is something one has to be wary of. One was an older individual who simply had labile blood pressure [hypertension]. His baseline blood pressure was normal, but under the influence of the MDMA he did have a significant rise.

The other subject was interesting because he was in his third session, so on at least one other occasion he had received MDMA, and on this third occasion his blood pressure shot up, whereas during the previous two occasions his blood pressure had remained normal. When I asked him if there was anything different about this morning than the previous occasions, he said that although there had been something different he didn't want to bother us by telling us. He went on to say he had stayed at a friend's house overnight who lived close by, to get to the hospital early in the morning. His friend had a cat. The subject was allergic to cats and had some trouble breathing in the morning, so his friend gave him some of his asthma medications. So we learned that interactions with particular medications can potentially be somewhat risky, and individuals do need to be apprised of that.

The Power of the Placebo

CG: We also had one individual who appeared to have experienced an adverse psychological reaction. He got very anxious and said that the hospital was not the right place to be on this kind of drug and that he was picking up on all the bad vibes of the hospital. We talked him down and told him that he could drop out of the study. This was his first session; he could drop out of the study but he had to spend the night in the hospital because he had agreed to that for safety reasons. When he left in the morning he decided he was going to withdraw from the study. So we decided to break the blind to see how much MDMA we had given him to cause such an anxious and fearful kind of response, and to our amazement it turned out we had given him a placebo. So never underestimate the power of the placebo response. The guy had simply psyched himself out.

Initial Results Bode Well for Safety

RLM: You talked about the subjects that had a little difficulty. What about the ones who did not have difficulty?

CG: The nineteenth subject, who never got MDMA, just got the placebo and dropped out. The others did remarkably well. They physiologically tolerated the experience well. Psychologically they had very upbeat, positive experiences. The only other problem I ran into was one day the head nurse on the research unit took me aside and complained that her nurses were spending too much time with my subjects and not enough time with their other patients. I thought they were just enjoying talking with our subjects and almost getting a contact high, or perhaps our subjects were so empathetic and interested in the lives of the nurses that perhaps that made it alluring for them to just spend that time.

But our subjects did very well. We published our results. Although our group at that time did not go on to do any therapeutic studies with MDMA—this had been a normal

volunteer study—Michael Mithoefer's group in South Carolina did move the MDMA field forward by doing his controlled studies with chronic PTSD patients.

What's Keeping MDMA Underground?

Lack of Government Funding

RLM: It is interesting to note that the medicine MDMA is called "ecstasy" on the street. The public knows that it has had widespread use and not just in this country but around the world. But on the other hand, we don't really hear about widespread sub rosa use of Prozac. You don't hear of thousands of people going to parties and taking Zoloft, for example. MDMA has been referred to as an empathogen, given that it has the capacity for enhancing empathy, and an entheogen—bringing on a kind of religious experience. Was the government not impressed enough with this research to want to facilitate or support more research?

CG: We've had success since the early '90s with obtaining government regulatory approvals. They often take some time, and there's often a lot of back and forth, but at the end of the day we've found the regulatory agencies to be fairly reasonable. The limiting step is funding. The national health funding agencies are not prioritizing therapeutic research with psychedelics, so the money has to be raised from private sources. We've completed the studies we've had funding for, and now we are looking at our depleted funding accounts and trying to raise additional funding, but it is a painstakingly laborious process.

Suppression of Doctors' Personal Experience

RLM: In a previous interview you were asked, "Have you ever taken MDMA?" I imagine it would be very tempting for many researchers, when they come across something like MDMA that enhances empathy, to want to take it.

I'm not going to ask if you've ever taken it, but instead I'm going to quote your response, because I think it is terrific: "My response to that sort of question is usually along the lines of 'I'm damned if I have and I'm damned if I haven't.'"

This is very accurate: "If I have taken ecstasy then my perspective as a researcher would be discounted due to my own personal-use bias, and if I haven't taken it I would be discounted because I would not truly understand the full range of experience the drug can induce."

I imagine that's an issue for all research, as in all of these various medicines, isn't it?

CG: Yes, I've taken the tack of not responding to those questions but rather just pointing out the dilemma that each answer would lead to.

RLM: Yes, of course. Since I'm not a researcher in the area I can tell you that I was given MDMA in my doctor's office back before it was scheduled, and it had a very helpful effect on me. I had repeated sessions with him. Your quote about how it may induce profound psychological realignments that could take decades to achieve on my therapist's couch without it was absolutely correct; it was a huge benefit. I could immediately see the benefits for people all over the world, undoubtedly. It was so obvious, and so it has been painful to see how little research is going on.

Advice for Personal Experimentation

RLM: You and I differentiate between a material used as a medicine and the exact same material used as a drug. We know that there are people using LSD, MDMA, and psilocybin recreationally, and we also know that people are using the same exact materials as medicines—like it or not, whether the government likes it or not, and whether we are concerned about these folks or not. This is going on, and it's happening on a widespread scale. Many listeners are experimenting in their own lives. What can you say, in terms of caution or

encouragement, to the people who are going to do this regardless of what you or the government have to say?

CG: It certainly would be a lot easier to have these compounds thoroughly examined and vetted for treatment modalities if there was no recreational use going on, but that's not the real world we live in. There are a lot of people who are drawn to these compounds for a variety of reasons. They need to understand that they could get into serious difficulty. There are significant adverse medical effects that can occur with MDMA or ecstasy use.

These effects are aggravated by common settings where it's taken. People are exercising vigorously at dances, in crowded or stuffy environments. They forget to replace body fluids, and you can get the malignant hyperthermia catastrophes. On the flip side, individuals who are not exercising but are drinking copious quantities of water, particularly women, may expose themselves to a life-threatening water intoxication syndrome.

I'm a big supporter of the harm-reduction model. You take it as a given that individuals are going to be inquisitive, so you just try to provide them with essential information that will lessen the likelihood that they could harm themselves. You want to help people be more risk avoidant.

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My next interview regarding MDMA is with another person I consider a friend, Phil Wolfson, MD. Wolfson is a psychiatrist, researcher, author, political activist, and gardener. His book, *The Ketamine Papers,* was the subject of a recent TV-and-radio interview we did together. I am pleased to present here Phil's insights into his work with MDMA.

Demonstrating MDMA's Safety and Efficacy in Treating End-of-Life Anxiety

Phil Wolfson, MD

PHIL WOLFSON, MD, earned his BA at Brandeis University. He went on to medical school at New York University School of Medicine and began practicing psychotherapy and psychiatry in the Bay Area in 1977. He is licensed to practice medicine in California and Washington, DC. Dr. Wolfson has been an assistant clinical professor of psychiatry at the University of California San Francisco and has taught at several graduate schools. He was one of the founding members of the Heffter Research Institute, which is another psychedelic research organization, along with MAPS, the Multidisciplinary Association for Psychedelic Studies. He is the author of *Noe: A Father-Son Song of Love, Life, Illness, and Death* and is editor/contributor of *The Ketamine Papers.*

Dr. Wolfson is the principal investigator of a double-blind, placebo-controlled Phase II study located in Marin, California, which is in the middle of its work concerning the safety and efficacy of MDMA-assisted psychotherapy for anxiety in eighteen subjects diagnosed with a life-threatening illness. The study has received coverage in the *San Francisco Chronicle* and on KQED Radio's *Forum* with Michael Krasny as well as in media around the globe, and it is bringing more mainstream attention to the topic of psychedelic medicines, psychedelic psychotherapy, and legalization.

Called to Help and Be Helped

Early MDMA Treatments for the Chemically Wounded

RLM: Dr. Phil Wolfson was recently granted FDA approval to use MDMA legally in his psychotherapy practice. Tell us about that please, Phil.

Phil Wolfson, MD (PW): I was running an alternative psychiatric unit in Contra Costa County called I Ward, which was based on the notion that people in altered states of consciousness

could benefit from work with their actual state of psychosis, using family members and supportive teams, and going through the course of their mental alteration. This would apply to first-break schizophrenia and to some degree bipolar illness. I had a very difficult patient who had been seriously wounded, chemically, by mega dosages of the neuroleptic drugs in use at the time. I was looking for an alternative substance when I was introduced to Sasha Shulgin, the great psychochemist. I visited him, and he suggested the use of MDMA. As it was legal in those days, he and his wife Anne gave me a session with my wife. I began to see its utility as what we came to call an empathogen—a substance that elicited warmth, closeness, and an ability to better handle negative emotions and to find compassion for self and others.

A large number of psychotherapists and psychiatrists, including myself, began to use MDMA in our clinical practices, which was in many respects a revolution in psychotherapy and psychiatry, because you had to sit with people for long periods of time. You could do open work with process, and the sessions could last anywhere from three to five hours, or longer, and you had to stay with people until their process concluded. It was a fantastic opportunity, really, to get to know people and elicit new kinds of consciousness and reactions.

A Family Copes with Tragedy

RLM: What can you tell us from your memory of your first session with MDMA when Shulgin and his wife administered it to you?

PW: I was not a naive subject—I had done my first trip with LSD in 1964 while in medical school. MDMA was quite a bit different. It was not hallucinogenic; it was warm. It was relatively easy to work with, to stay in touch, and in many respects it was what came to be called a love drug. It was an exciting way to be with people—to be deeper in oneself and to handle negativity, judgments, and reactions that might have been obsessional or interfering with relationships. My session was a very close and warm session with people I hardly knew,

who were just generous, thoughtful people. It was very helpful to my wife and me.

RLM: Did you and your wife go on to use it together after that?

PW: Well, unfortunately, I had a terrible experience in my life. My eldest son Noah contracted leukemia when he was nearly thirteen. That was the year after that session. I had begun using MDMA in therapy, especially with couples and occasionally with families. During the course of my son's four-year illness, we as a family—the parents, not the children—would have sessions with MDMA in order to bring about a sense of family unity and process, which I actually wrote about in my book about my son's life and illness. So it was very valuable episodic support to our lives and our ability to cope with a terrible illness.

RLM: Please remind us of the name of the book that you wrote about yourself and your son?

PW: It's called *Noe: A Father-Son Song of Love, Life, Illness, and Death.*

DEA Shuts the Lid on MDMA Research

How MDMA Got a Bad Reputation

RLM: You were a licensed psychiatrist using MDMA legally in your practice in California, and then George Ricaurte publishes an article in the very prestigious journal, *Science,* in which he says that MDMA causes neurotoxicity in primates after a common recreational dose regimen. What happened after that?

PW: My memory is a little different, Richard. We were working with larger numbers of people, and MDMA was spreading in a relatively small way when the DEA got into the act in 1984 and insisted on scheduling the drug. The DEA appointed an administrative law judge to have a hearing. We had national press, and a lot of us got up and talked about the merits of

MDMA. In fact, the judge found in favor of scheduling MDMA in a still-accessible schedule—Schedule II—within the Federal Regulatory statute. The DEA overruled that—their own judge—and made MDMA illegal in 1985. Subsequently, there was a vast explosion of use. As usual, illegalization had the impact of increasing interest in it.

Ricaurte came later. He was doing so-called science, and he came to the periphery of the group and then toward MAPS, which had formed to scientifically develop an argument against the DEA's scheduling by showing the utility, scientifically and clinically, of MDMA. In that process, Ricaurte, as with others before him, had been making a reputation by basically doing pseudoscience and cultivating a negativity that would give him a reputation through the Drug Enforcement Agency and give him authority, money, and position.

As it evolved, he came toward us looking for experienced subjects that he could test in a variety of ways. As he was writing negative stories about the serotonergic problems with MDMA, he gained stature among the naysayers and war-on-drugs folks, and then he published in *Science* after getting that stature.

It turned out that he and his group were so-called "mistakenly" using methamphetamine in their studies—at least two of them, but I believe there were others—and he was forced to retract the data that implicated MDMA. Unfortunately, dirty work persists and dirty minds have an effect, and the negativity toward MDMA continued.

What was not talked about—it is always interesting to me—is that methamphetamine is a dopaminergic substance. It works on the dopamine neurotransmitter primarily, whereas MDMA worked on the serotonin neurotransmitter primarily, and secondarily norepinephrine and perhaps dopamine. So here he was writing about the serotonergic effects of methamphetamine, which doesn't have any; so the whole thing was a terrible abuse of science and caused quite a stir.

RLM: It caused a tremendous stir and it left the public with the impression that MDMA is far more hazardous than it turned out

to be. Both Congress and the former director of the National Institute of Drug Abuse, Alan Leshner, came out strongly about how dangerous MDMA was even after Ricaurte was forced to retract his entire mistaken article. British scientists went on record expressing their concerns, Phil. I have a quote: “It’s an outrageous scandal,” Leslie Iverson said, “It’s another example of a certain breed of scientist who appears to do research on illegal drugs mainly to show what the governments want them to show. They extract large amounts of grant money from the government to do this sort of biased work.”[*11] That’s quite an indictment.

PW: You beat me to the quote. I had that in front of me. When I was in med school in the heyday of LSD, there was a guy at New York University making a reputation by finding chromosomal breaks caused by LSD, which was bogus work. He did very well by giving the negative camp ammunition and then eventually that was retracted. There were no chromosomal breaks. But the impression still lingers—unfortunately. So there is a long history of toady sycophants working to make money and a reputation within science. You always have to look at science with a grain of salt and look at who is sponsoring whom, and who is going where.

RLM: It’s intimidating.

PW: And fascinating.

RLM: And fascinating at the same time. One of the things I didn’t tell the listeners about you is that you’re also a Buddhist practitioner. So these words of wisdom that come out when I say it’s intimidating, and you say it’s fascinating, are also delightfully and beautifully from your Buddhist background, which I very much appreciate.

PW: You are very sweet to me, thank you.

RLM: Well you’ve always been very sweet to me as well, Phil.

The Bay Area MDMA Study with End-of-Life Anxiety

RLM: I want to move on to a discussion of the historic study that you're going to be doing, please tell us about it.

PW: Sure, it's an exciting study. We—MAPS—were given a grant by a man, who unfortunately died, to explore the effects of MDMA-assisted psychotherapy on anxiety in people with life-threatening illnesses who are at risk for relapse or recurrence, or death itself. We've designed the study to maximize the possibility of observing the effects of MDMA. We have FDA approval that allows us to do a Phase II study.

There are three phases on the path from science to the prescription. This is an orphan drug—it has no patent, because it was first patented in 1914 and that expired many decades ago. Phase I is for assessing toxicity of a substance. Phase II is to assess both safety and efficacy in small numbers. Phase III entails a much wider study, which sets the stage for prescriptions by MDs worldwide.

We're in Phase II with MAPS, moving toward Phase III, particularly with studies directed toward post-traumatic stress disorder. Our study in the Bay Area is the first one with MDMA here, and it is attempting to look at anxiety in people who have had a terrible illness and are fearing recurrence, relapse, or death itself, but have a life expectancy ahead of them. We hope that anxiety will be reduced by MDMA-assisted psychotherapy. So it's a very complex approach to working with MDMA in a thoughtful and integrated psychotherapy practice.

This study is probably going to take one and a half to two years because it's complex and involves a randomization—sorting people into groups of subjects who will receive placebos and then go on to MDMA sessions as well as subjects that receive the MDMA from the start. We've designed it so that it includes people who are not terminally ill—who have a life-threatening illness but are not acutely ill. The study, which will take at least four months for each person, can

go on without being severely impacted by people's declines or illnesses that may inevitably occur during the study, unfortunately; so the study has a large therapy component. We go through a screening process to accept people, and then we do a series of preliminary sessions followed by overnight sessions. Participants will be at my home for twenty-four hours, where they have a very comfortable and intense experience.

We are working with two institutional review boards. We finished with one and almost with another, and we're waiting for the DEA to come inspect the premises. I've had to put a safe in my house, and we've wired the place because the DEA requires stringent security mechanisms to protect the MDMA that is shipped to us in bulk. We have a formulating pharmacist who makes placebos and identical capsules containing MDMA, which are tracked by computer. I am blinded to their contents —only the computer knows and randomizes. The computer and MDMA stay in the safe, and the DEA is very concerned about security for that.

RLM: What do you mean when you say you've wired the house?

PW: We have to put an alarm system in, as well as for the room in which the safe is located.

Nonclinical "Anecdata"

RLM: Let me take you back to the time when MDMA was legal, and you were allowed to use it and you did use it as a psychiatrist in your practice. You also must have known other therapists who were using it in their practice. What was the usefulness or the dangers of this medicine back then, prior to its becoming illegal?

PW: It was in small-scale use. By that I mean tens of thousands of doses. Now one estimate has twenty-nine million users in one year, 2012. But it became renowned as a therapy drug. Quite a large number of people using it were practitioners, and

we formed some informal organizations to collaborate and exchange data. It was quite persuasive in its use for couples—helping relationships integrate—and people becoming more expressive. We had a lot of people get married on MDMA. We used to warn people not to get married on MDMA: “You’re in the glow! Take a little time see if the glow persists after use.” But people didn’t always listen, and I know of a few marriages that have survived over these decades after an MDMA set of sessions. We used it for individuals with depression, where it had wonderful effects—not 100 percent, but people often got better with a series of MDMA sessions in a psychotherapeutic context. Anxiety often improved. It was a short period, really, from 1982 to 1985—after which it became illegal and research could no longer continue with our informal network—but there were lots of publications, and many people were influenced by their experience with MDMA in a positive way.

Looking Critically at Risks

Side Effects, Dangerous Mixtures, and Overdose

RLM: People are hearing this, Phil, and they’re learning about thousands of people who took MDMA in their therapist’s office between 1979 and 1985. They are also learning that twenty-nine million people have used it recreationally in one year—in one year, twenty-nine million people! So people may be saying to themselves that this sounds like something they’d like to try. We have the responsibility to tell them what might happen that’s not very pleasant. Were there problems or negative side effects from using MDMA?

PW: It’s really important for people to be informed users. In general, the substance is quite safe. Mixing it with other substances has been the biggest cause of problems. In fact, most of the deaths attributed to MDMA are the result of a mix of substances ranging from alcohol to methamphetamine and other unspecified contaminants used to reduce cost to the dealer.

The number of actual deaths related to *pure* MDMA itself used in good settings can be characterized as truly rare, but still present, so there is some risk as with any substance. You want to be in a good set and setting. You want to be with people who are responsible and who can help you in case of emergency. An emergency almost never happens with a good set and setting. In our set of studies of over nine hundred people, there have been no significant medical problems. That's within the MAPS set of studies. So the things to watch out for are getting too hot—MDMA and MDA substances that are related to amphetamines or methamphetamines can cause a heat problem, so you want to cool off—and mixing substances can be problematic.

There are always minor side effects to begin with, such as jaw clenching and headache. Some people speak of a kind of emptiness or grayness, which can persist for a couple days, or even a mid-week low. I have never seen that in my extensive use, but it is reported. There is dehydration if you don't drink enough—and that was a source of problems that came up during the illegal period at raves where people were in high-heat environments and didn't drink properly. There were several deaths. And there was also the rare problem of overhydration. During the legal period, we saw one strange reaction I could not explain, in which a person on a known batch of MDMA ended up in the ICU with a neurological illness. She fully recovered, but there was no explanation for that. So, like with all drugs, there is a certain level of risk of idiosyncratic reactions.

There is also a question of whether there's such a thing as MDMA overdose. There has been an unverified report of a death in England of a young girl—a tragic death—of a fifteen-year-old who weighed one hundred pounds and took 500 milligrams, which is four times the usual dosage. There are issues of purity that come up as well. This girl apparently was in a group that got a powerful, new, and purer MDMA substance. The dilution of MDMA has been extreme in many cases, so people were getting pills and tablets that might have had 25 to 30 percent MDMA, or even less, with another

dilutant. One issue for consumers is to know what you're getting.

RLM: Can you recommend a place where people can send something they buy and get an honest analysis so they know what it is they're taking, since they're not allowed to buy it legally at the drugstore?

PW: Well, the most beneficial one is called DanceSafe, which does analyses. I'm not sure of the current status of other testing agencies. I can't recommend one, but DanceSafe was established to make sure that there was safety among users at raves and parties. It was done entirely for the benefit of people, without money being an issue. It's a worthy thing to look up, and you can purchase kits to assess the presence of many different substances. So you can examine for purity.

RLM: And there's also a website called Erowid.org that has intellectual content to read.

PW: If you really want to know about what you're doing and what you're taking, if you want to read user reports and get a sense of what's going on currently in the world of psychoactive drugs, go to Erowid. They are great people and they're doing a great service.

Controlling the Set and Setting

RLM: Earlier in the program you said that as long as the set and setting were appropriate, this is a very safe medicine. Please elaborate on the words *set* and *setting* and what they mean to our listeners?

PW: Well, setting is the obvious one. Be in a comfortable, safe place with support when you do substances. People I know who have gotten into trouble—kids and others—have been out in the world in places where heightened vigilance is necessary, because they're doing something that makes them more wary and puts them in the view of police, and so forth.

The set idea is what you bring to it—your own mental status, your own view of things, where you are with yourself. It's a very good practice before using a psychedelic substance to spend the day getting clear and clean, to prepare yourself to make it a sacred experience—one that recognizes the power of what you're going to do and doesn't just take it for granted. When you take that time—when you prepare yourself, when you meditate, when you do some exercise or yoga before, when you really set the stage, light candles, and create an environment that is conducive to your use—your exploration is going to go deeper and your safety will be much better.

RLM: So you're talking about the difference between creating an ambience, a setting, and preparing a mental set, so that you're taking the substance as *medicine* rather than "doing drugs."

PW: Yeah, I'd say that's a good idea. A vast number of people have gotten away with doing drugs and have gotten myriad benefits from it, but if you want to improve your odds, do it the way we just discussed.

RLM: Now given people are hearing this and they're going to perhaps experiment, some people suggest that when you do this in the privacy of your own home you should not do certain things such as answer the telephone or turn on the television set or go to the front door and start talking to people who happen to be in the neighborhood. How do you feel about those things and what other kinds of privacy or safeguards might you recommend?

PW: Well, it's good to turn the cell phone off. It's good to not get distracted by things that are silly. I think having great music is always a benefit. It's deepening to have instruments, where you might play drums or bells. I love bells. I think the sound of bells is penetrating and overcomes obsession and other preoccupations. Do not operate motor vehicles or heavy-duty machinery.

Take the time to make the space solid and take the time afterward to integrate. A lot of us talk about integrative work for

sessions after an experience. Take the time to look at your experience, remember it as best as possible, and take some notes for your own benefit, because memory does fade and it's sometimes hard to recover the memory of the experience.

MDMA's Relation to Amphetamines

RLM: We're going to take a caller here, Phil.

Caller: Hi, thanks for your program.

RLM: You're welcome.

Caller: I have heard of MDA [methylenedioxyamphetamine], and I would rather not have the side effects of methamphetamine, so I'm wondering if there is a pure substance that you are working with that works without the methamphetamine. Thank you.

PW: I can point out to you something that is easily confused—look at the chemical pictures of both methamphetamine and MDA if you can. MDA is amphetamine. The difference is that the MDA molecule has the amphetamine structure, whereas methamphetamine has the CH_3 group on another part of it. Neither the substance MDA nor MDMA resembles amphetamine or methamphetamine in side effects—only partially at best.

Amphetamine and methamphetamine both have pretty similar side effects. Hyperthermia, or too high of a temperature, and jaw clench are problems with both substances. So anything related structurally to amphetamine, such as methamphetamine, will have some of those side effects. That said, they are very different molecules and they have very different effects. Mescaline is in the same framework—there are myriad psychoactive substances that are related to those. If you look further you'll see that many of the spices on your shelf also have very similar structures; so the structural analysis of molecules and their effects on the mind is very intricate and not straightforward.

Emergency Room Visits from MDMA

RLM: When we had the last cocaine epidemic, which goes in cycles of about twenty years or so, there were reports from all over the United States of emergency room admissions of people taking overdoses of cocaine. You tell us that approximately twenty-nine million people used MDMA last year. Are we getting admission reports from emergency rooms as a result of this MDMA use, or not?

PW: There are some great statistics. There is a very interesting online group called the DEA.org [Davis Education Association], if you really want to look at statistics for the last period of reporting. I'm looking at it as we speak, and there were 5,542 visits to emergency rooms across the United States; that's in 2001. Apparently we don't have more recent data.

If you take a look at the SSRI Paxil [paroxetine], where I would imagine there is much less use, that's 8,932 use visits. For amphetamine, it lists 8,000. For nonsteroidals—ibuprofen, Naprosyn, Aleve, Advil, and so forth—the number is 22,000. For all antidepressants it's 61,000. Those MDMA numbers apply also to other drugs that are being used along with MDMA, so it's not a pure statistic. People go in for anxiety reactions and physical reactions of various sorts.

RLM: The 61,000 emergency room admissions for people on antidepressants sort of ties in with a guest we had a few weeks ago, Robert Whitaker, and his book *Anatomy of an Epidemic,* in which he talks about his research indicating that antidepressants are causing mental illness [see chapter 5].

Underworld Production of Synthetic Drugs

RLM: Let's take this call here. Welcome to *Mind, Body, Health & Politics*. You're on the air.

Caller: Where is ecstasy being produced? Is it coming from laboratories and then being black marketed, or are there people cooking it up in a back room?

PW: The production of ecstasy is across the world including the United States. Some is apparently coming in from China. There are stories of North Korea making drugs of various sorts, which I think could be true, and India is also a source. There are chemists within countries such as the United Kingdom—and all across our country and the globe.

RLM: So, if I understand you correctly, when it comes to illegal substances, until we analyze what we have before us we cannot know what we have; caveat emptor. Is MDMA difficult to make?

PW: MDMA is difficult. You need precursors, and precursors are tightly controlled. I'm not an authority on how easy or difficult it is to make.

RLM: And what about the use of MDMA concurrently with other psychedelic substances? We have a few minutes left. Please tell us a little about that.

PW: Sure. It's quite common for people to do an admixture; that is, to take more than one substance together to try to affect the nature of their individual effects. So it's common use, for instance, to take MDMA with LSD. MDMA is used with many other substances to make them a bit smoother.

Is MDMA a Sex Drug?

RLM: I have a question here that was handed to me. Is MDMA a sex drug?

PW: It depends who you talk to. MDMA is an extremely sensual substance. The general idea out there is that it doesn't lead to sex. I would argue with that—it may well lead to sex, and it may well lead to lovely sex. It's pretty difficult for people to have an orgasm on MDMA, but I'm sure some people have achieved that. When we did the first study of MDMA, which was in 1994 in a wonderful home in Stinson Beach, I was one of the people designing the study and not taking the

substance. It was very difficult to proceed with the neurological and mental statuses I was doing with the twenty or so subjects there, because they were just hugging and kissing and touching, so it was very hard to get attention.

RLM: Since it does affect blood pressure, what about the use of MDMA with Viagra and Cialis, which also lower blood pressure? Is that going to create a problem?

PW: I can't answer that question. I don't have enough information on that.[*12]

RLM: But as far as MDMA's raising blood pressure, that has not been a concern in leading to emergency room visits?

PW: Not that I'm aware of. There is a reliable and definite increase in blood pressure, pulse rate, and temperature with MDMA use, but generally without severity and with quick return to baseline.

Bottom Line: Get Educated

RLM: We're reaching the end of our interview. Is there any last-minute thing you might want to mention to our listeners about MDMA?

PW: For more information, our website at MAPS—the Multidisciplinary Association for Psychedelic Studies—is terrific. Erowid.org is also a great source of information. Be thoughtful about your use and remember, *it is still illegal*. We just passed Proposition 47 in California that really reduces penalties for possession. Look at the terms of Proposition 47 and understand that it's a major change in our drug prohibition policy, locally.

I have been delighted to be with you, Richard. Thank you so much.

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A Husband and Wife Team for MDMA Research

I met psychiatrist and researcher Michael Mithoefer, MD, ten years ago when he and I joined June Ruse, PhD, José Carlos Bouso Saiz, PhD, and Peter Cohen on a scientific trip to Israel organized by Rick Doblin, PhD, the founder of MAPS. The purpose of the trip was to ask the Israelis to allow research into the use of MDMA for PTSD, which they recently have allowed.

Here in the United States, Michael and his wife, Annie, were involved with some of the very first research on MDMA, which was sponsored by MAPS. The Mithoefers are currently conducting MDMA research at their facility in Charleston, South Carolina, and Michael is also the medical monitor for MAPS-sponsored clinical trials in Europe, the Middle East, Canada, and Colorado. I am pleased to include the following interview with them.

MDMA for Post-traumatic Stress Disorder

Michael Mithoefer, MD, and Annie Mithoefer, BSN

October 4, 2011

MICHAEL MITHOEFER, MD, spent a decade of his early career as a board-certified emergency medical physician. He is certified in internal medicine, and in 1991 he became certified in psychiatry. He and Annie Mithoefer, BSN, have a private practice of psychiatry in clinical research in Mount Pleasant, South Carolina. On November 2, 2001, Michael and Annie obtained FDA approval to run a clinical trial in the United States giving MDMA in combination with psychotherapy to treat chronic, treatment-resistant post-traumatic stress disorder. The first experimental session of this Phase II clinical trial happened in April of 2004. This is a historic, groundbreaking study.

Overcoming Research Suppression

Politics Triumphs over Science

RLM: Annie, how did you and Michael get interested in MDMA?

Annie Mithoefer, BSN (AM): We experienced MDMA with a therapist when it was legal and did some couples work and found it to be incredibly useful. We did holotropic breathwork training together and learned how you can use techniques to help people process things like trauma, which started our curiosity about it.

RLM: You had a personal experience while MDMA was still a legal medicine in this country, and you were so impressed with the value that you got from the medicine that it sparked your scientific interest; is that what you're saying?

AM: It did spark our scientific interest. We have also worked with many people who have had trauma or difficult times in their lives, and because of this we were constantly looking for something new to help people since many people are not helped by traditional therapies.

RLM: When did MDMA move from being a legal medicine to being categorized by our government as an illegal medicine; or, when did it get turned into what's called a "drug" instead of a medicine?

Michael Mithoefer, MD (MM): That was in 1985 when the DEA put MDMA in Schedule I. Actually, this was contrary to the recommendations of the administrative law judge who ran the hearings about MDMA, who recommended that it should be a prescription medicine. The DEA at that time overruled that recommendation and put it in Schedule I. It was first patented in 1914 by Merck, but they never used it for anything. It was used as an adjunct to therapy when it was legal in the 1970s, but in 1985 all legal use came to an end.

RLM: Annie and Michael, you both first experienced this medicine when you were patients in a therapist office while the medicine was legal, and you had a positive experience. I'll share with you that in 1983 I was administered MDMA in my therapist's office. I had it over a series of sessions and found that it was

profoundly helpful in my own personal growth and development. In your opinions, why did the government take this position on something that you, Annie, a psychiatric nurse, and you, Michael, a psychiatrist, and I, a doctor of clinical psychology, have all used to our benefit?

MM: I don't know the answer to that, but it must have been political rather than scientific. There was concern that use had spread to selling it in bars and for recreational use. And the government was, I'm sure, reacting in part to that. It was striking in the hearings—there were very reputable medical professionals testifying on its potential safe use in therapeutic hands, with Dr. Charlie Grob, a psychiatrist from UCLA, being one of those. There was no question in the hearings that there were reasons it should be further researched, so I can only conclude that it was a political decision.

There's a lot of fear, and also there is the drug-war mentality—some people are afraid of sending the wrong message. If you allow for the fact that some things may be dangerous when used unwisely but also may be very useful, healing, and even lifesaving when used by health professionals, that's a more complicated message than just "all drugs are bad."

RLM: Would you be willing to go a little further in your speculation as to what you mean by a political decision? Here we have something that, as far as I know, there have been very few if any incidences of emergency room admissions around the country, particularly when MDMA is used as a medicine. Was the risk theological? Where do you think they were coming from in the suppression, particularly of the research? It's really a head-scratcher.

MM: It is a head-scratcher. There was a lot of promising psychedelic research going on in the '50s and '60s and early '70s, but then President Richard Nixon took a strong position in favor of the drug war, and the government turned away from funding or even allowing most research with these compounds. It was very irrational from a medical point of view.

Suppressed but Not Banned

RLM: How is it that some of these medicines are not only researched but also are sold to the public and then some of them such as MDMA are selected out—not only are they made illegal for consumption, but research at the university level is also made illegal?

MM: It's fascinating. I scratch my head too, although the research hasn't actually been made illegal. It was more of a de facto thing. In fact, people couldn't get studies approved or funded for many years.

RLM: Fifty years later, and I stand corrected—you're right—it's not that the research was made illegal. It's just that the research was suppressed.

MM: Right. It just isn't tenable to say there is a group of potential medicines that might be very helpful for these people who aren't responding to the existing therapies, but we're not allowed to even look there. That's just not a tenable position for a physician or a psychologist or a nurse to be in. We need to look for anything that sounds like it might be promising without prejudice—according to scientific data, not political decisions.

RLM: Yes. In fact, not only are we not able to offer people these medicines, we're not even able to tell people where in the world they might go to obtain them. In other areas of medicine, you can send people to another country if they want to be on the cutting edge. But in this particular case, we can't even do that because the United States government suppresses the research in other areas of the world.

I had the good fortune to be with Michael Mithoefer some years ago as part of a small expedition of scientists that went to Israel to talk with their scientists about the use of MDMA with people suffering from PTSD—post-traumatic stress disorder—particularly during the Intifada, when there were body parts flying around and people were severely

traumatized. I'm sure you'll bear this out, Michael, that we were told that although the Israelis were interested in doing this research, they really couldn't until the United States gave them the go-ahead, because they could lose funding. Correct?

MM: I recall that. I don't recall if they said the exact reason. But they did make it clear that they wouldn't consider it until we had full approval for our research here.

RLM: Extraordinary suppression, as you said.

Hopeful Horizons

MM: The good news is that we have been allowed to do research now, and it is picking up. So as you say, we submitted our FDA application in the fall of 2001, in October, and then we got permission from the FDA within thirty days. It then took another two and a half years to get permission from an institutional review board and the DEA. But we were then able to do the first clinical study of MDMA to have been completed.

There were some other studies before us called Phase I trials. Charlie Grob at UCLA did the first of those. Then there were two others in the United States and some in Europe. There was some data about giving it to humans but not for treatment, and there had been one study started in Spain that was shut down. So ours was the first that was actually able to study MDMA as a treatment and be completed. We started in 2004, and one of the important things about this model is that we're not just doing a drug study, but rather we're studying MDMA-assisted psychotherapy. So people don't get MDMA to take home. They get MDMA two or three times, a month apart, in an all-day session with me and Annie as cotherapists.

RLM: This is a medicine that they took in the office with Dr. Mithoefer and his wife Annie, a psychiatric nurse—that's important. Also, the medicine was taken in conjunction with verbal psychotherapy. This was not a medicine that you swallowed and then immediately looked at the results.

MM: There was also careful screening to make sure people didn't have some underlying health problem that might make MDMA dangerous, because it does increase blood pressure and pulse. We monitored those things very carefully. So it is a very controlled setting.

Is MDMA Rightly Considered a Psychedelic?

Entheogens, Entactogens, and Empathogens

RLM: Michael, what do you mean when you refer to a medicine as psychedelic?

MM: Well, I wish we had a better term that was agreed upon. Psychedelic means mind-manifesting, and for many people it implies hallucinations and maybe very strong transpersonal or spiritual kinds of experiences—the kind that you associate with LSD or psilocybin.

RLM: But not with MDMA?

MM: MDMA is different. Some people have suggested other terms like entactogen, something that helps you touch within, or empathogen, something that increases empathy.

RLM: Or entheogen. It gives sort of a mystical, almost religious experience. But no one has pointed a finger at this particular medicine MDMA and accused it of being a hallucination- or schizophrenic-mimetic or anything like that.

MM: No—the terms are often used loosely but you're right. It's quite different and many of these compounds have great potential and need to be studied, and some are being studied; but I think MDMA in some ways is easier to work with clinically, in that it doesn't cause as much of a shift in consciousness as these others do.

Pharmacodynamics of MDMA

MM: MDMA is a molecule that looks something like methamphetamine and something like mescaline. It's a

medicine that's taken by mouth in capsule form, as a powder, and it has a wide range of effects on the brain and body.

It largely boils down to a lot of monoamine release—release of things like serotonin, dopamine, and norepinephrine, as well as a number of hormones like prolactin and oxytocin. Basically, it amounts to giving people an experience that's not quite psychedelic in the sense that people often mean—in that it doesn't cause hallucinations. But it does cause a real shift in consciousness that often involves greater insight, greater empathy for self or others, and greater connection with emotions in an interesting way.

It seems to allow people to access difficult emotions that they've been cut off from, but with the sense that they won't be overwhelmed by fear. It also allows access to positive emotions people have been cut off from. So it seems to modulate the emotions in a way that creates a state that's potentially very useful.

RLM: Does MDMA work on the neurotransmitters in the brain in a similar way that legal medicines such as the SSRIs, like Prozac [fluoxetine], Luvox [fluvoxamine], Zoloft [sertraline], Paxil, and so on, do?

MM: Part of the effect is similar in that it does cause changes in the serotonin system in blocking serotonin reuptake, but then there are all these other effects, and no one really understands how they all combine to cause this shift in consciousness.

RLM: We're on the cutting edge, in other words. We're learning about the way these different medicines interact with the neurotransmitters with brain function?

MM: Absolutely. There's a lot to be learned.

Overcoming Treatment-Resistant PTSD

Comparing Against Baseline Ineffective Treatment

RLM: Okay, let's come back to your study.

MM: The first study was with twenty participants, all of whom had treatment-resistant PTSD. And they had to have had prior treatment with both medications—Zoloft and Paxil—that are the two existing treatments approved by the FDA for PTSD or other medicines in the same class. They had to have had at least a course of treatment with these, but most of them had already had many different medicines. And they had to have had at least six months of psychotherapy, and most had more than that. They had to still show significant PTSD symptoms.

RLM: This is how you define "treatment resistant"—meaning they had these various other forms of treatment, and they did not get a significant enough improvement to feel healed or to have gained a sense of well-being.

MM: Right. Part of the study consisted of an independent rater who determined the participants' levels of PTSD before and then later. If people qualified for the study we would do several introductory sessions to get to know them and to prepare them for the experience. Then, after their all-day experience with us, they would spend the night in the clinic with a nurse on duty. We would meet with them the next morning for a ninety-minute session, and we would talk to them every day on the phone for a week. We would meet with them approximately every week for a month in between the sessions to help them integrate the experience.

This study was a double-blind, meaning people got either MDMA on two occasions, one month apart, or placebo on those two occasions, with all the same therapy—the same all-day sessions and the same follow-up treatment. So neither the participants, nor Annie and I, nor the testing psychologist knew who was going to get what. When we broke the blind after we measured their symptoms two months later, if it turned out they'd gotten a placebo then they could go through the whole thing again with MDMA in an open-label fashion so everybody knew what they were getting. That way we could compare how they did with the placebo and how they did when MDMA was added.

Active vs. Inactive Placebo

RLM: Did you use neutral placebos or active placebos?

MM: We used an inactive placebo on this first study.

RLM: The reason I brought that up is because Robert Whitaker, *Anatomy of an Epidemic,* and Irving Kirsch, *The Emperor's New Drugs,* have made some breakthrough studies comparing placebos to the SSRIs, and one of the things they found is that there was a significant difference in results when they used either active or inactive placebos—when they used active placebos, the placebos did much better than the SSRIs.

MM: Yeah. Now, in our current study with veterans, we are using an active placebo.

RLM: Michael is talking about a double-blind study. That means the person who is administering either the medicine or the placebo does not know what each subject is receiving. This procedure is used because it has been found that the mind is so powerful that when the person who hands the medicine to the patient in the study knows what they're giving, it actually has an effect. The person who's doing the administration must be blinded, that is, have no idea who's getting the placebo and who's getting the medicine.

Whitaker, Kirsch, and others have discovered that when you give a neutral, inactive placebo—a sugar pill that has no effect—to some, and you give a medicine to the other people, the people who get the placebo know they're getting the placebo because they feel that nothing happens. And the people who get the medicine know they're getting a medicine, because within a certain number of minutes they can feel something happening.

Therefore, the study itself is affected by our minds knowing, "Oh, I'm one of those who is getting the placebo," or, "Oh, I'm one of those getting the medicine." So these scientists have created placebos that give you a feeling of some kind—not a feeling that alters your mind in any way. It's just a feeling.

These placebos that create a feeling are called active placebos. Thus the subjects themselves can't tell which of them are on the medicine and which are on the placebo, because everybody's getting some subjective change in their feeling state.

MM: That's an important point, and we're addressing that in this current study. We felt for other reasons it was important to use an inactive placebo for the first study so that we could really document the differences in side effects. So people would have their two or three sessions, and then, two months after their last MDMA or placebo-assisted session, they would have the PTSD-symptom measures done again by the psychologist. Then we would break the blind, and if it turned out they had received the placebo, then they could go through the same thing again but with active MDMA, and we'd measure the results two months after that. We compared the placebo group and the MDMA group first, and then we also compared the original placebo group's placebo results to that same group's MDMA results.

Encouraging Results

RLM: And what did you discover?

MM: We had very strong, encouraging results. We had a significant effect with placebo in these all-day sessions with all the follow-up therapy. Two of the eight people who received randomized placebo had a very strong placebo response from just that. One of those was fairly short lived, but we did have two strong placebo responders, and the rest did not change or didn't change much. Some got slightly worse and some got a little better with the placebo, but overall the placebo did make a difference. The MDMA group had a much stronger response. In the MDMA group, 83 percent had a very strong clinical response compared to the 25 percent in the placebo group. Then when the placebo group crossed over and had MDMA, everyone had a significant response, including the ones that had no response to the placebo.

The Therapeutic Process: The Struggle Before the Healing

RLM: Annie, did any of the people have a negative response?

AM: No. Sometimes things can look worse at first, as you're digging deeper into the trauma and you're re-experiencing what it feels like to have emotions again. But that would be the only thing that may have been negative in that way. That is why we have so many integration sessions and phone calls every day for a week, because you're helping people move through the trauma.

RLM: And in terms of your measurements, did any of the people score as if they were worse off after the medicine than they were before?

AM: No, not in the PTSD measurements. What I'm talking about is an increase in anxiety a few days after they are back home, when they are thinking about what they talked about and thinking that maybe they shouldn't have talked about it.

RLM: Yes—the middle road before they get to the place of being healed.

MM: Yes, and that's why the integration sessions, we think, are so important to help people move through that period.

PTSD: The Nature of the Beast

RLM: I just realized we've been using the acronym PTSD—post-traumatic stress disorder—but I think it would be a good idea if you two would talk a little bit about PTSD and what it is.

MM: PTSD is a syndrome that sometimes occurs following severe trauma. In this first study it was mostly childhood sexual abuse or rape as an adult, and in the current study it is veterans with either war trauma or military sexual assault. Some people have symptoms but improve without treatment, while a certain percentage of people end up with this thing called PTSD.

The three symptoms clusters are: one, re-experiencing—they either have intrusive memories, flashbacks, or nightmares about the trauma; two, a physiological response to certain cues with hyperarousal, anxiety, startle response, sleep disturbance, and things like that; and three, avoidance—they avoid places and people that remind them of the trauma, or it can also be an inner avoidance, a kind of emotional numbing, i.e., they stay away from emotions because they're upsetting. It's always a combination of those things that we define as PTSD, and it can be very debilitating. Some of the people in the study hardly got out of their house and really could not function well at all. It interfered with their relationships and their physical health. There is very good evidence showing how much more medical morbidity there is in people with PTSD compared to those without it. Many are immobilized by fear and do not want to be with people.

Striking Results: Emotions as a Map to Healing

RLM: You've now gone through the first study. What can you share with the listeners regarding the efficacy of this medicine?

MM: Well, as scientists, we need to keep in mind that this was a small study, even though we found very statistically significant results. We don't want to get ahead of ourselves. We need to see if this can be replicated in larger studies. Having said that, the effect we've seen so far was very striking and encouraging. People have told us it changed their relationship with their emotions.

RLM: Say more about that, Annie. Please speak to that topic.

AM: They are usually so afraid to revisit the traumatic event or the emotions that are around it that they completely shut everything out. What sometimes happens in the MDMA session is that they have an experience of some emotion coming, and with your help, they can sit with it and they can realize they are able to deal with these feelings. I think another thing that happens for people is a template of feeling really

good and relaxed, like they have never felt in their whole life. Just having that template and helping people anchor that within themselves, then they can go back to it—like a map for this good feeling.

RLM: It makes sense. If I understand, you're saying that the traumatic experience was so powerful in one area of emotion that, as a protective device against the pain of that experience, all emotions were blanketed out. Is that what you're saying?

AM: Exactly.

RLM: So they're walking around in a state of constantly or automatically having to suppress one of the most vital aspects of the human condition, which is our emotional state.

AM: Yes.

RLM: And the medicine, with your guidance and help in therapy, allows subjective feeling and/or expression of an emotion, which then opens the door for an experience. Is that correct?

MM: Yes.

Climbing Down Ladders to Dark Feelings

Facing Anxiety without Being Taken Over

RLM: We've got another caller here. Welcome to *Mind, Body, Health & Politics.* You're on the air.

Caller: Good morning. What is it actually like to experience this chemical as it begins to affect you?

AM: For some people, when the drug comes on it can make them more anxious. There's a little bit of time when we talk people through that, and we have them use their breath. This is usually when the medicine is coming on initially. Then the positive effects of the medicine gradually set in, and they aren't as fearful—they aren't thinking about that anxiety. In the beginning, the effects focus patients and bring them into the

present moment in a way that they've never experienced before. It often brings up things from their childhood and positive things in their lives, such as surviving the trauma or having a family that loves them. And then it will open up—it's different for each person—and sometimes they will have very strong stories and pictures that go with their experience, where they have an animal that comes to them and talks them through it or there might be images such as looking in jars that hold the trauma.

MM: Some people would see images during their MDMA sessions. One was as if the trauma were down in this dark place, and the MDMA gave them ladders so they could descend into the feelings. It was painful, but they could go there; it allowed them to process and integrate these emotions without being taken over by them.

AM: And what Michael means by "being taken over by it" is the tendency for people to react with fear, anger, or rage to these memories.

MM: Sometimes there's a comfortable feeling in the body, so it can be quite affirming. People with PTSD often haven't felt comfortable in their body since the trauma. One person told us that after having been abused as a child, he had never felt happiness—he only deduced what it must be from watching other people's behavior. He felt happiness for the first time with MDMA. He realized it was actually a possibility for him. So there's that very comfortable, positive part of it.

But often it was very difficult, and a lot of people told us they didn't know why it was called ecstasy because a lot of time was spent revisiting trauma and having painful feelings that were still very difficult. In a nutshell, what's effective about MDMA is that people can revisit the trauma and not be emotionally cut off from it. They still have the pain. They still have to move through the feelings, but it gives them a sense that they can work through it. So the experience seems to be a combination of those affirming, positive, and comfortable

experiences with the more painful ones that they are able to process in a more helpful way.

RLM: I'll go back some twenty-eight years to the experience in my therapist's office. I recall that the experience I had, as this medicine saturated my system, was a feeling of connecting with what our Founding Fathers called divine providence. I was being lifted into some divine space, and it was ecstatic. I remember clearly a visual image I had while sitting there with Dr. Kantor of a shield in front of my heart that was melting. And as the shield melted away, my heart spoke. And I heard it speak in a different way than I'd ever heard before. It was a soft voice. It was the voice of my inner truth, and it felt very undefended—as if I were allowing my inner spirit to speak. It was a very powerful experience, and of course I wanted to come back to his office and do it again, which I was fortunate enough to be able to do.

The Need for More Research into Trauma and Addiction

Caller: The other half of my question is: How is MDMA used in treating alcoholism?

MM: There are no studies going on now—and I don't think there have been—but I think it would be a very good thing to study.

RLM: It would.

AM: We had one person that stopped smoking. We had a couple people that didn't drink caffeine anymore after our study. We had three people go back to work that had not been able to work. So we found a lot of things that could help.

RLM: Yes. Thank you, Annie. We have another caller here. *Welcome to Mind, Body, Health & Politics.* You're on the air.

Caller: Can you discuss the difference between people who cave in under the trauma and those where it passes over them?

Have you found the determining factor?

MM: Many people have been asking that question, and nobody really knows the answer. There is quite a lot of research—there is some association to early childhood trauma and later developing PTSD from a dull trauma. There is now some work suggesting genetic factors. I'm sure it has a lot to do with the kind of support the person has, such that we really don't know the answer to that.

RLM: Do we have time for one more question here? We can get one more in here. *Welcome to Mind, Body, Health & Politics,* you're on the air.

Caller: Thank you so much for the program. I wanted to relay to you and to the listening audience that MDMA was really a heart medicine for me. It was as if I came into the realm of pure love. The few people that I was around, I felt safe with. And I saw the beauty in them. I felt the angels were all there. I just came into a realm of pure love.

RLM: Thank you; and that, I think, is what you heard from Annie and Michael.

AM and MM: Yes.