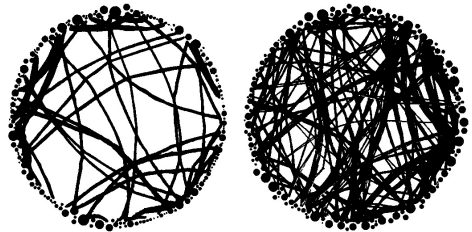


Psychedelic Drugs: Science and Society

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Cover image is a visualization of brain connections
on psilocybin (right) and not on psilocybin (left)



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Psychedelic Drugs: Science and Society

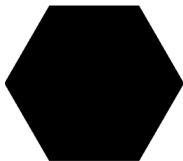
Chapter 1 of Part 1 of DMT: The Spirit Molecule

by Rick J. Strassman, MD
(an unauthorized reprint)

Psychedelics Encyclopedia (Berkeley, CA: Ronin Press, 1992).

12. Methyl groups, which consist of a carbon and three hydrogens, are themselves the simplest possible addition to an organic molecule.

13. 5-MeO-DMT is the active ingredient in the secretion from the venom glands of the Sonoran desert toad, *Bufo alvarius*. The drug is not obtained by licking these toads, as inaccurate media reports would have it. Rather, intrepid users catch a toad and painlessly “milk” the venom onto a glass slide. They release the toad, dry the secretions, and smoke them in a pipe. See Wade Davis and Andrew T. Weil, “Identity of a New World Psychoactive Toad,” *Ancient Mesoamerican* (1988): 51–59.



of plants, such as jimsonweed, cause hallucinations and altered thinking processes. However, they do so in the context of a confused, delirious state, with dangerous disturbances of cardiac function and temperature control. Oftentimes one remembers little, and serious toxicity, including death, may result from taking “a little too much.” On the other hand, there are no cases of psychedelic drugs being directly fatal.

Drugs like ketamine (“K” or “special K”) and phencyclidine (PCP or “angel dust”) also produce psychedelic effects. However, they first saw use as general anesthetic agents and cause unconsciousness at higher doses. The “classical” psychedelic drugs such as LSD or mescaline don’t cause general anesthesia.

In addition, ketamine, PCP, and nightshade-based drugs exert their psychoactive effects through pharmacological mechanisms different from those of LSD, psilocybin, and DMT. For our purposes I will limit my discussion of “psychedelics” to those with similar structures and pharmacological properties. For a review of any and all substances
52 with psychedelic properties, see Peter Stafford,

The history of human use of plants, mushrooms, and animals for their psychedelic effects is far older than written history, and probably predates the appearance of the modern human species. Ronald Siegel and Terence McKenna, for example, suggest that our apelike ancestors imitated other animals by eating things that caused unusual behavior. In this way, they discovered the earliest mind-altering substances.

There is growing physical evidence that many ancient cultures used psychedelics for their effects on consciousness. Archaeologists have uncovered ancient African images of mushrooms sprouting from a human body, and recent discoveries of prehistoric northern European rock art strongly suggest the influence of psychedelically altered consciousness.

Some authors have proposed that language developed out of psychedelically enhanced appreciation of, and associations with, early 1 hominid mouth sounds. Others suggest that

psychedelic states formed the basis of humans' earliest awareness of religious experience.

The visions, ecstatic states, and flights of imagination made possible by psychedelic drugs gave these substances an important role in many ancient cultures. Hundreds of years of anthropological research have demonstrated that these societies used psychedelics to maintain social solidarity, aid the healing arts, and inspire artistic and spiritual creativity.

New World aboriginal people used, and continue to use, a wide range of mind-altering plants and mushrooms. Most of what we know about psychedelics comes from investigating chemicals first found in Western Hemisphere materials: DMT, psilocybin, mescaline, and several LSD-like compounds.

- 2 The depth and breadth of psychedelic plant use by New World residents surprised and alarmed European settlers. Their reaction may have been due to the relative lack of

9. Stanley Schachter and Jerome E. Singer, "Cognitive, Social, and Physiological Determinants of Emotional State," *Psychological Review* 69 (1962): 379–99.

10. In addition to spawning so many names, psychedelics have inspired quite a following. I know of no other drugs, except perhaps marijuana, with as many organizations dedicated to educating about them, and promoting their use. There are dozens of psychedelic organizations with thousands of dues-paying members. They publish magazines, newsletters, journals, and Web sites. They organize and sponsor conferences and publish and distribute books. The late Dr. Freedman from UCLA, an early LSD researcher and a driving force behind my study, coined the term *cultogen*, referring to this zeal with which advocates and enemies of their use rushed in with simple, one-sided descriptions of their effects. Opiate, cocaine, or solvent users don't organize in such an effective manner. What is so unique about psychedelics that they provoke such evangelical responses?

11. Drugs from other chemical families also may be psychedelic, but only within a narrow dose range. For example, compounds in the nightshade family⁵¹

6. Historians often contrast Leary's freewheeling take-all-comers approach to the use of psychedelics with Huxley's view that their use must be limited to a small elite of leaders and artists. The fact remains, however, that without the relatively lawless approach of Leary (see Timothy Leary, *Flashbacks* [New York: JP Tarcher, 1997]) and Ken Kesey (see Paul Perry, *On the Bus* [St. Paul, MN: Thunder's Mouth Press, 1997]), it is unlikely many of us would have had the opportunity to encounter these drugs.

7. Rick J. Strassman, "Adverse Reactions to Psychedelic Drugs. A Review of the Literature," *Journal of Nervous and Mental Disease* 172 (1984): 577-95.

8. Later revelations of CIA involvement in dosing unsuspecting citizens and Army recruits with LSD and other psychedelics added shame and embarrassment to this already painful assortment of feelings. See Martin A. Lee and Bruce Shlain, *Acid Dreams: The Complete Social History of LSD, the CIA, the Sixties, and Beyond* (New York: Grove Press, 1986); and Jay Stevens, *Storming Heaven: LSD and the American Dream* (New York: Grove Press, 1998), for thorough reviews of this remarkable chapter in American domestic national security operations.

psychedelic plants and mushrooms in Europe. Just as important was the association of mind-altering substances with witchcraft. The Church effectively suppressed information about the use of those materials in both the Old and New Worlds and persecuted bearers and practitioners of that knowledge. It is only in the last fifty years that we have realized that Mexican Indian use of magic mushrooms did not entirely die out in the sixteenth century.

In Europe, there was little interest in, or access to, psychedelic plants or drugs until the end of the late 1800s. Some authors described their own "psychedelic" reactions to opium or hashish, but the amount required for psychedelic effects was difficult to consume, excessive, or dangerous. This situation began to change with the discovery of mescaline in peyote, a New World cactus.

German chemists isolated mescaline from peyote in the 1890s. The more literary among those exploring its effects hailed its ability

to open the gates of an “artificial paradise.” However, medical and psychiatric interest in mescaline was surprisingly restrained, and researchers published only a limited number of papers by the end of the 1930s. The unpleasant nausea and vomiting that often occur with mescaline may have had something to do with the lack of interest in it.

Another reason for the minimal enthusiasm about mescaline may have been that there was no scientific or medical context in which to understand its effects. Freudian psychoanalysis was that era’s predominant force in psychiatry. While Freud himself was strongly attracted to mind-altering drugs such as cocaine and tobacco, his students were less so. In addition, Freud distrusted religion and believed spiritual or religious experience was a defense against childish fears and wishes. This attitude probably did little to encourage investigation of mescaline, with its trappings of

4 Native American spirituality. Then LSD made its revolutionary appearance.

releases a neurotransmitter, which then attaches to specialized receptor sites on the receiving cell. This docking of transmitter to receptor begins a sequence of events ending in the release of the receiving cell’s own neurotransmitter, and the process continues down the line. Other well-known neurotransmitters include norepinephrine (noradrenaline), acetylcholine, and dopamine.

3. For a sense of the vast amount of information accumulated during those years, see Abram Hoffer and Humphrey Osmond, *The Hallucinogens* (New York: Academic Press, 1967). Remarkably, almost forty years after its publication, this remains the best available textbook on these drugs.

4. For an excellent review of the scientific basis for psychedelic-assisted psychotherapy, see Walter N. Pahnke, Albert A. Kurland, Sanford Unger, Charles Savage, and Stanislav Grof, “The Experimental Use of Psychedelic (LSD) Psychotherapy,” *Journal of the American Medical Association* 212 (1970): 1856–63.

5. Aldous Huxley, *Doors of Perception and Heaven and Hell* (New York: HarperCollins, 1990).

of *Artificial Paradise* (New York: EP Dutton, 1989); Terence McKenna, *Food of the Gods* (New York: Bantam, 1993); and Paul Devereux, *The Long Trip: A Prehistory of Psychedelia* (New York: Penguin, 1997).

Wasson's work is the most exhaustive regarding early spiritual functions of psychedelic natural substances—see R. Gordon Wasson, Carl A. P. Ruck, and Stella Krammrisch, *Persephone's Quest: Entheogens and the Origins of Religion* (New Haven, CT: Yale University Press, 1988).

For in-depth discussions of specific plants and their roles in aboriginal societies, see Richard E. Schultes and Albert Hofmann, *Plants of the Gods* (New York: McGraw Hill, 1979). For the chemistry of those plants, see Richard E. Schultes and Albert Hofmann, *The Botany and Chemistry of Hallucinogens*, 2nd ed. (Springfield, IL: Charles C. Thomas, 1980); and Jonathan Ott, *Pharmactheon* (Kennewick, WA: Natural Products Co., 1993). Albert Hofmann's tale of discovering LSD never fails to delight—*LSD: My Problem Child* (New York: McGraw Hill, 1980).

In 1938 the Swiss chemist Albert Hofmann was working with ergot, a rye fungus, in the natural products division of Sandoz Laboratories, even then a major pharmaceutical company. He hoped to find a drug that might help stop uterine bleeding after childbirth. One of these ergot-based compounds was LSD-25, or lysergic acid diethylamide. It had little effect on the uterus of laboratory animals, and Hofmann shelved it. Five years later, “a curious presentiment” called Hofmann back to examine LSD, and he accidentally discovered its powerful psychedelic properties.

The remarkable thing about LSD was that it brought on psychedelic effects at doses of *millionths* of a gram, which meant that it had more than one thousand times the strength of mescaline. In fact, Hofmann nearly overdosed himself with what he thought was too small a quantity to possibly be mind-altering: a quarter milligram. Hoffman and his Swiss colleagues were quick to publish their findings in the early 1940s. Because of the highly altered state

48 2. Neurotransmitters allow chemical communication among nerve cells in the brain. A transmitting cell

of mind LSD produced, and the traditional psychiatric context in which researchers explored it, scientists decided to emphasize its “psychosis-mimicking” properties.¹

The years after World War II were exciting ones for psychiatry. In addition to LSD, scientists also discovered the “antipsychotic” properties of chlorpromazine, or Thorazine. Thorazine made it possible for severely mentally ill patients to improve enough that they could leave asylums in unprecedented numbers. This and other antipsychotic medications finally allowed doctors to make progress in treating some of our most disabling illnesses.

The contemporary field of “biological psychiatry” was born in those years. This discipline, which studies the relationship between the human mind and its brain chemistry, was the child of these two strange bedfellows: LSD and Thorazine. And serotonin

6 was the matchmaker.

this way in the 1960s. His opinion was that it was “just slightly faster” than

smoking it.

3. William J. Turner Jr. and Sidney Merlis, “Effect of Some Indolealkylamines on Man,” *Archives of Neurology and Psychiatry*

81 (1959): 121–29.

Notes

1. For reviews of historical data regarding naturally occurring psychedelics’ importance, see Marlene Dobkin de Rios, *Hallucinogens: Cross-Cultural Perspectives* (Albuquerque, NM: University of New Mexico Press, 1984); and Peter Furst, *Flesh of the Gods: The Ritual Use of Hallucinogens* (New York: Waveland, 1990).

For more speculative musings regarding these 47 issues, see Ronald Siegel, *Intoxication: Life in Pursuit*

studies in which researchers gave psychedelic drugs to humans in this manner. However, there is a report describing

direct administration of LSD into the cerebrospinal fluid using a spinal tap. Since the cerebrospinal fluid bathes the

brain, it allows direct access to it. In this case, LSD effects began “almost instantly.” See Paul Hoch, “Studies in Routes

of Administration and Counteracting Drugs,” in *Lysergic Acid Diethylamide and Mescaline in Experimental Psychiatry*, edit-

ed by Louis Cholden (New York: Grune & Stratton, 1956), 8–12.

2. There were people who had used IV DMT in non-research, or recreational, settings. One of the men I interviewed in the

In 1948 researchers discovered that serotonin carried in the bloodstream was responsible for contracting the muscles lining veins and arteries. This was vitally important in understanding how to control the bleeding process. The name for serotonin came from the Latin *sero*, “blood,” and *tonin*, “tightening.”

A few years later, in the mid-1950s, investigators discovered serotonin in the brain of laboratory animals. Subsequent experiments demonstrated its precise localization and its effects on electrical and chemical functions of individual nerve cells.

Drugs or surgery that modified serotonin-containing areas of an animal’s brain profoundly altered sexual and aggressive behavior as well as sleep, wakefulness, and a diverse array of basic biological functions. The presence and function of serotonin in the brain and in animal behavior clinched its role as the first known neurotransmitter.²

At the same time, scientists showed that LSD and serotonin molecules looked very much like each other. They then demonstrated that LSD and serotonin competed for many of the same brain sites. In some experimental situations, LSD blocked the effects of serotonin; in others, the psychedelic drug mimicked serotonin's effects.

These findings established LSD as the most powerful tool available for learning about brain-mind relationships. If LSD's extraordinary sensory and emotional properties resulted from changing the function of brain serotonin in specific and understandable ways, it might be possible to "chemically dissect" particular mental functions into their basic physiological components. Other mind-altering drugs with comparably well-characterized effects on different neurotransmitters could lead to a decoding of the varieties of conscious experience into their underlying chemical mechanisms.

Dedication

1. Jean Toomer and Rudolph P. Byrd, *Essentials* (Athens: University of Georgia Press, 1991), 27.

Acknowledgments

1. National Institutes of Health grants funded the melatonin project (RR00997-10), the DMT and psilocybin studies (R03

DA06524 and R01 DA08096), and general operations of the Clinical Research Center (M01 RR00997).

Prologue

1. The most direct way to get DMT into the brain, of course, is to inject it straight into this sensitive organ. I know of no

ended an extraordinarily rich human research endeavor.

It was into this seething matrix of conflict, ambivalence, and controversy that I looked for a point of traction and a clear line of sight in order to formulate my own research agenda. Where could I get a toehold? In which direction should I look? I needed a key with which to open the lock keeping psychedelic research buried.

Out of this virtual swamp emerged one small obscure molecule: DMT. Its call was one I could not ignore, even though I had little idea of how I might get to it. Nor could I possibly expect where it would lead me once I found it.

Endnotes

Dozens of investigators around the world administered a dizzying array of psychedelic drugs to thousands of healthy volunteers and psychiatric patients. For more than two decades, generous government and private funding supported this effort. Researchers published hundreds of papers and dozens of books. Many international conferences, meetings, and symposia discussed the latest findings in human psychedelic drug research.³

Sandoz Laboratories distributed LSD to researchers so they might induce a brief psychotic state in normal volunteers. Scientists hoped such experiments might shed light on naturally occurring psychotic disorders like schizophrenia.

Sandoz also recommended giving LSD to psychiatric interns to help them establish a sense of empathy for their psychotic patients. These young doctors were amazed by this temporary encounter with insanity. The raw encounter with their own previously unconscious

memories and feelings led these psychiatrists to believe that these mind-loosening properties might enhance psychotherapy.

Numerous research publications suggested that the normal mechanisms of talk therapy were much more effective with the addition of a psychedelic drug. Dozens of scientific articles described remarkable success in helping previously untreatable patients suffering from obsessions and compulsions, post-traumatic stress, eating disorders, anxiety, depression, alcoholism, and heroin dependence.

The rapid breakthroughs described by researchers using “psychedelic psychotherapy” spurred other investigators to study these drugs’ beneficial effects in despairing and pain-ridden terminally ill patients. While there was little effect on the underlying medical conditions, psychedelic psychotherapy in these patients had striking psychological effects. Depression
10 lifted, requirements for pain medication fell dramatically, and patients’ acceptance of their

We experience others influencing our minds or bodies—in ways that are beneficial or frightening. The future is ours for the taking, or fate has determined everything and there is no point in trying.

Psychedelics affect every aspect of our consciousness. It is this unique consciousness that separates our species from all others below, and that gives us access to what we consider the divine above. Maybe that’s another reason why the psychedelics are so frightening and so inspiring: They bend and stretch the basic pillars, the structure and defining characteristics, of our human identity.

These are the psychedelic drugs. There exists a complex and rich context for viewing them, a perspective that few appreciate.

They are not new substances, and we know an enormous amount about them. They ushered in the modern era of biological psychiatry,⁴³ and their highly publicized abuse prematurely

the same time. Emotional conflicts become more painful, or a new emotional acceptance takes place. We have a new appreciation of how others feel, or no longer care about them at all.

Our thinking processes speed up or slow down. Thoughts themselves become confused or clearer. We notice the absence of thoughts, or it is impossible to contain the flood of new ideas. Fresh insights about problems come, or we become hopelessly stuck in a mental rut. The significance of things takes on more importance than the things themselves. Time collapses: in the blink of an eye, two hours pass. Or time expands: a minute contains a never-ending march of sensations and ideas.

Our bodies are hot or cold, heavy or light; our limbs grow or shrink; we move upward or downward through space. We feel the body no longer exists, or that the mind and body have separated.

42

We feel more or less in control of our “selves.”

disease and its prognosis improved markedly. In addition, patients and their families seemed able to address deep-seated and emotionally charged issues in ways never before possible. The rapid acceleration of psychological growth resulting from this new treatment appeared quite promising in these cases where time was of the essence. Some therapists believed that a transformative, mystical, or spiritual experience was responsible for many of these “miraculous” responses to psychedelic psychotherapy.⁴

In addition, it soon became apparent that the experiences described by volunteers under deep psychedelic influences were strikingly similar to those of practitioners of traditional Eastern meditation. The overlap between consciousness alteration induced by psychedelic drugs and that induced by meditation attracted the attention of writers outside of academics, including the English novelist and religious philosopher Aldous 11 Huxley. Huxley underwent his own remarkably

positive mescaline and LSD experiences under the watchful eye of the Canadian psychiatrist Humphrey Osmond, who visited him in Los Angeles in the 1950s. Huxley soon wrote about his drug sessions and the musings they inspired in him. His writings on the nature and value of the psychedelic experience were compelling and eloquent, inspiring many individuals' attempts to attain, and researchers to elicit, spiritual enlightenment through psychedelic drugs. Despite that fact that his ideas stimulated a massive movement toward popular experimentation with the psychedelics, Huxley was a staunch advocate of the theory that only an elite group of intellectuals and artists should have access to them. He did not believe that the common man or woman was capable of using psychedelics in the safest and most productive ways possible.⁵

However, terminal illness studies and discussions of similarities between psychedelic
12 drug effects and mystical experiences brought religion and science together in an uneasy mix.

always, are primary. Objects in our field of vision appear brighter or duller, larger or smaller, and seem to be shifting shape and melting. Eyes closed or open, we see things that have little to do with the outside world: swirling, colorful, geometric cloud patterns, or well-formed images of both animate and inanimate objects, in various conditions of motion or activity.

Sounds are softer or louder, harsher or gentler. We hear new rhythms in the wind. Singing or mechanical sounds appear in a previously silent environment.

The skin is more or less sensitive to touch. Our ability to taste and smell becomes more or less acute.

Our emotions overflow or dry up. Anxiety or fear, pleasure or relaxation, all feelings wax and wane, overpoweringly intense or frustratingly absent. At the extremes lie terror or ecstasy.⁴ 1 Two opposite feelings may exist together at

happen after taking a psychedelic drug on any particular day. Nevertheless, we will generalize about their subjective effects because we must gain a sense of a “typical” response. We can do this by averaging all of our own and others’ experiences, all of the “trips” that have gone before us. (By “trip” I mean the full effects of a typical psychedelic drug like LSD, mescaline, psilocybin, or DMT. A trip is difficult to define, but we certainly know when we are having one!)

The following descriptions do not apply to “mild” psychedelics such as MDMA or usual-strength marijuana, nor do they describe responses to low doses of psychedelics, for which effects are similar to those of other non-psychedelic drugs, like amphetamine.

Psychedelics affect all of our mental functions: perception, emotion, thinking, body awareness, and our sense of self.

40

Perceptual or sensory effects often, but not

The research was moving further away from Sandoz’s original agenda.

Complicating things further was LSD’s escape from the laboratory in the 1960s. Reports of emergency room visits, suicides, murders, birth defects, and broken chromosomes filled the media. The highly publicized abandonment of scientific research principles by Timothy Leary, Ph.D., and his research team at Harvard University ultimately resulted in their dismissals. These events reinforced the growing suspicion that even the scientists had lost control of these powerful psychoactive drugs.⁶

The media exaggerated and emphasized psychedelic drugs’ negative physical and psychological effects. Some of these reports resulted from poor research; others were simply fabricated. Subsequent publications cleared psychedelics from serious toxicity, including chromosome damage. However,¹³ these follow-up studies generated much less

fanfare than did the original damaging reports.

Papers in the psychiatric literature describing “bad trips,” or adverse psychological reactions to psychedelics, also multiplied, but are similarly limited. In order to address these concerns in my own study, I read every paper describing such negative effects and published the results. It was clear that rates of psychiatric complications were extraordinarily low in controlled research settings, for both normal volunteers and psychiatric patients. However, when psychiatrically ill or unstable individuals took impure or unknown psychedelics, combined with alcohol and other drugs, in an uncontrolled setting with inadequate supervision, problems occurred.⁷

In response to the public’s anxiety about uncontrolled LSD use, and over the objections of nearly every investigator in the field, the United States Congress passed a law in 1970
14 making LSD and other psychedelics illegal.
The government told scientists to return their

processes: cardiovascular, hormone, and temperature regulation, as well as sleep, feeding, mood, perception, and motor control.

Now that we’ve looked at what psychedelics “are” and “do” in the worlds of objective and measurable data, let’s turn our attention how they feel to us, for it is only in the mind that we notice their effects.

It is important to remember that while we understand a great deal about the pharmacology of psychedelics, we know nearly nothing about how changes in brain chemistry directly relate to subjective, or inner, experience. This is as true for psychedelics as it is for Prozac. That is, we are far from comprehending how activating particular serotonin receptors translates into a new thought or emotion. We don’t “feel” a serotonin receptor blockade; rather, we feel ecstasy. We don’t “see” frontal lobe activation; instead, we observe angels or demons.

It is impossible to predict accurately what will

effects on the brain's serotonin system. Animal research, in contrast to human studies, has continued over the last thirty years and has established conclusively this neurotransmitter's crucial role.

Serotonin has reigned as the royal neurotransmitter for decades, and there's little sign of change. The new, safer, and more effective antipsychotic medications all have unique effects on serotonin. The new generation of antidepressants, of which Prozac is the most famous, also specifically modify the function of this neurotransmitter.

We now believe that psychedelics mimic the effects of serotonin in some cases and block them in others. Researchers are now concerned with determining which of the twenty or so different types of serotonin receptors psychedelics attach to. These multiple docking sites for serotonin exist in high concentrations
38 on nerve cells in brain areas regulating a host of important psychological and physical

drugs, paperwork requirements for obtaining and maintaining new supplies of psychedelics for research became a time-consuming and confusing burden, and there was little hope for new projects. Money for studies dried up and researchers abandoned their experiments. With the new drug laws in place, interest in human psychedelic research died off almost as rapidly as it had begun. It was as if the psychedelic drugs became "un-discovered."

Considering the intense pace of human research with psychedelics just thirty years ago, it is amazing how little today's medical and psychiatric training programs teach about them. Psychedelics were *the* growth area in psychiatry for over twenty years.

Now young physicians and psychiatrists know nearly nothing about them.

By the time I was a medical student in the mid-1970s, less than ten years after the drug
15 laws changed, psychedelics were the topic of

just two lectures in my four years of study. Even this may have been more information than students received at most other medical schools, because there was a research group performing animal studies at the Albert Einstein College of Medicine in New York City, where I trained. In the mid-1990s, I taught a psychedelic drug research seminar to senior psychiatric residents at the University of New Mexico—probably the only one of its kind in the country in decades.

The lack of academic attention to psychedelics may have been partly due to the absence of any ongoing human research. However, it is common for physicians-in-training to learn about previously popular theories and techniques, even if they no longer are in favor. The psychedelic drugs, however, seemed to have dropped out of all psychiatric dialogue.

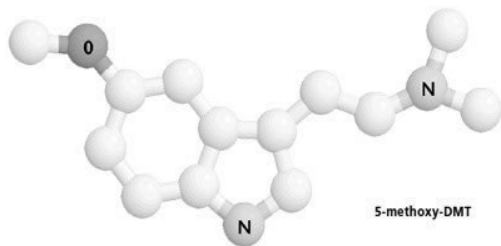
Most new theories, techniques, and drugs in the
16 clinical psychiatric field follow a predictable
course of evolution as they are introduced,

DMT and 5-MeO-DMT effects are remarkably rapid in onset and brief in duration. We gave DMT through a vein, or intravenously, in which case volunteers felt it within several heartbeats. They were “highest” at 1 to 2 minutes and were “back to normal” within 20 to 30 minutes.

LSD, mescaline, and ibogaine are longer-acting. Effects begin 30 to 60 minutes after swallowing them. The effects of LSD and mescaline may last 12 hours, ibogaine up to 24 hours. Psilocybin effects are slightly shorter; they begin within 30 minutes and last 4 to 6 hours.

Another more basic aspect of pharmacology is “mechanism of action,” or how drugs affect brain activity. This is a crucial issue, because it is by altering brain function that psychedelics change consciousness.

The earliest psychopharmacological experiments in humans and animals suggested that LSD, mescaline, DMT, and
37 other psychedelic drugs exerted their primary



Many of the plants, fungi, and animals containing DMT also possess 5- MeO-DMT. As with DMT, those who use 5-MeO-DMT usually smoke it.¹³

In addition to their chemical *structure*, psychedelics also possess *activity*. This is where chemistry becomes *pharmacology*, the study of drug action.

36 One way to describe psychedelics' activity is by how quickly they work and how long they last.

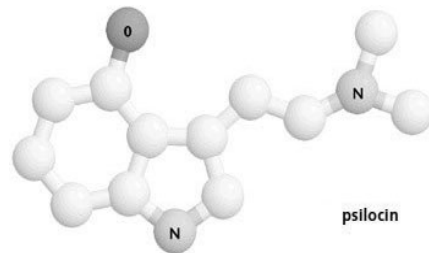
tested, and refined for further application. Therefore, it was not at all surprising that conflicting results began to emerge as more data accumulated during the first wave of human psychedelic research. Enthusiasm predictably slowed for claims that psychedelics could produce a “model psychosis” or “cures” in intractable psychotherapy cases. The natural process within psychiatric research is for scientists to refine research questions, methods, and applications. This never happened with the psychedelic drugs. Instead, their study went through a highly unnatural evolution. They began as “wonder drugs,” turned into “horror drugs,” then became nothing.

I believe that medical students and psychiatric trainees learn so little about psychedelic drugs not because research did end, but because of *how* it ended. This process deeply demoralized academic psychiatry, which then turned its back on psychedelic drugs.

Psychedelic research was a bruising and

humiliating chapter in the lives of many of its most prominent scientists. These were the best and the brightest psychiatrists of their generation. Many of today's most respected North American and European psychiatric researchers, in both academics and industry, now chairmen of major university departments and presidents of national psychiatric organizations, began their professional lives investigating psychedelic drugs. The most powerful members of their profession discovered that science, data, and reason were incapable of defending their research against the enactment of repressive laws fueled by opinion, emotion, and the media.

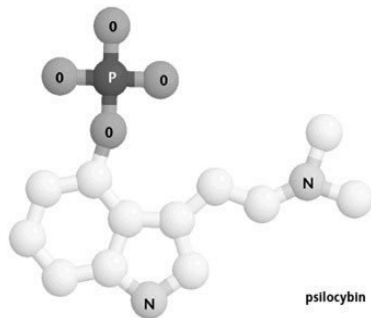
Once these laws passed, government regulators and funding agencies quickly withdrew permits, drugs, and money. The same psychedelic drugs that researchers thought were unique keys to mental illness, and that had launched dozens of careers, became feared and hated.



Psilocin differs from DMT by only one oxygen. I like to think of psilocybin/psilocin as “orally active DMT.”

Another important tryptamine is 5-methoxy-DMT, or 5-MeO-DMT. It differs from DMT by the addition of only one methyl group and one oxygen.

One of the best-known tryptamine psychedelics is psilocybin, the active ingredient of “magic mushrooms.”



When these mushrooms are ingested, the body removes a phosphorous atom from the
34 psilocybin, converting it to psilocin.

becoming an embarrassing source of contention even within psychiatry itself. Biology-based psychiatrists had little patience with colleagues who “found religion” and touted the spiritual effects of these drugs. These latter researchers viewed their brain-only associates as narrow-minded and repressed. Psychiatry has never been especially comfortable with spiritual issues, and in fact, an entirely new division appeared in the field to contend with results from psychedelic research: the “transpersonal” area of theory and practice. Thus, at least some psychedelic researchers may have been quietly relieved that they no longer had to face many of the complex, contradictory, and confusing effects these drugs produced in their patients, themselves, and their colleagues.

Why would anyone want to lecture on this embarrassing chapter in academic psychiatry to an auditorium packed with two hundred sharp-witted medical students? This early group of psychedelic researchers was for the most part 19 professional scientists, not zealots. They knew

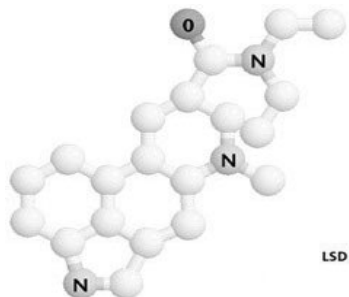
enough not to publicly criticize the behavior of their colleagues and benefactors. Better to live and learn.⁸

Now that we have reviewed some important background of the psychedelics, let's look at what they do.

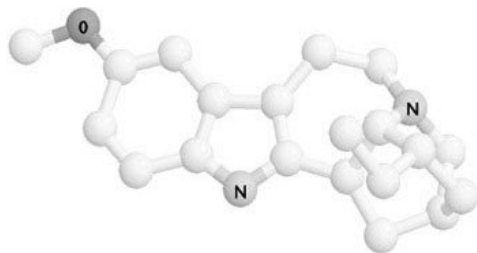
Psychedelics exert their effects by a complex blending of three factors: *set*, *setting*, and *drug*.

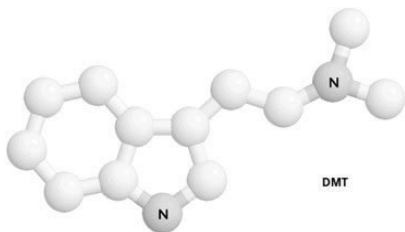
Set is our own makeup, both long term and immediate. It is our past, our present, and our potential future; our preferences, ideas, habits, and feelings. *Set* also includes our body and brain.

The psychedelic experience also hinges on *setting*: who or what is or isn't in our immediate surroundings; the environment we're in, whether natural or urban, indoor or outdoor; the quality of the air and ambient sound around us; and so on. *Setting* also partakes of the *set* of who is with us while we take the drug, whether



LSD





The “grandfather” of all modern psychedelics, LSD, contains a tryptamine core, as does ibogaine, the African psychedelic with highly publicized anti-addictive properties.

they be a friend or a stranger, relaxed or tense, a supportive guide or a probing scientist.

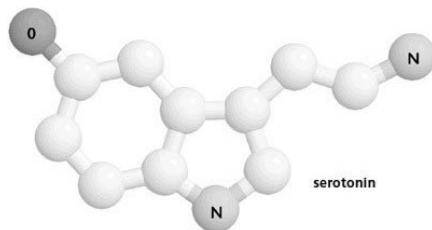
Then, there is the *drug*.

First, what do we call it? Even among researchers there is little agreement over this crucial point. Some don’t even use the word *drug*, preferring instead *molecule*, *compound*, *agent*, *substance*, *medicine*, or *sacrament*.

Even if we agree to call it a drug, look at how many different names it has: *hallucinogen* (producing hallucinations), *entheogen* (generating the divine), *mysticomimetic* (mimicking mystical states), *oneirogen* (producing dreams), *phanerothyme* (producing visible feelings), *phantasticant* (stimulating fantasy), *psychodysleptic* (mind-disturbing), *psychotomimetic* and *psychotogen* (mimicking or producing psychosis, respectively), and *psychotoxin* and *schizotoxin* (a poison causing psychosis or schizophrenia, respectively). 21

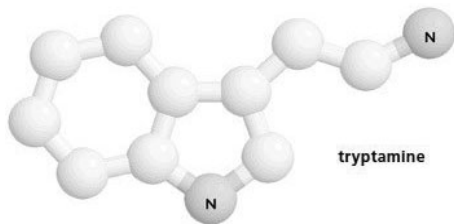
This focus on name is not trivial. If everyone agreed about what a psychedelic is or does, there certainly would not be so many words for the same drug. The multitude of labels reflects the deep-seated and ongoing debate about psychedelic drugs and their effects.

Scientists rarely acknowledge the importance of the name they give to psychedelics, even though they know how powerfully expectations modify drug effects. All undergraduate psychology students learn this in their introductory psychology courses when they review landmark studies published in the 1960s. These experiments injected volunteers with adrenaline, the “fight-or-flight” hormone, under different sets of expectations. Adrenaline caused a calm and relaxed state in volunteers told they were receiving a sedative. If told that the experimental drug was stimulating, volunteers felt the more typical anxiety and energy.⁹



DMT is also a tryptamine and is the simplest psychedelic. Simply add two methyl groups to the tryptamine molecule and the result is “dimethyl-tryptamine”: DMT.¹²

Thus, what we call a drug we take, or give,



Serotonin is a tryptamine—5-hydroxy-tryptamine, to be exact—but it is not psychedelic. It contains one more oxygen atom than does tryptamine.

influences our expectations of what that drug will do. It also modifies the effects themselves, and how we interpret and deal with them. No other drug's name feeds back so powerfully upon the responses they elicit as do the psychedelics, because they greatly magnify our suggestibility.

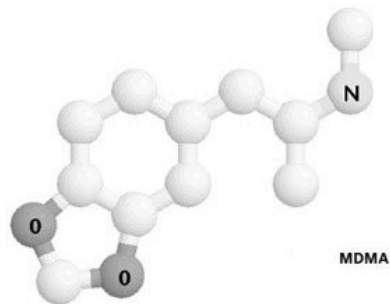
In addition to what we call psychedelics, the terms we apply to the people involved in their use also impact set and setting, and therefore drug response. As one who takes the drug, are we research subjects or volunteers? Clients or celebrants? As the one giving them, are we *guides, sitters, or research investigators? Shamans or scientists?*

Try this mental exercise: Consider how you might look forward to your day as a “research subject” under the influence of a “psychotomimetic agent.” Then reconsider: How would you feel about your role as a “celebrant” in a “ceremony” involving an²³ “entheogenic sacrament”? How would these

different contexts affect your interpretation of the hallucinations and intense mood swings brought on by the drug? Would you be “going crazy” or having an “enlightenment experience”?

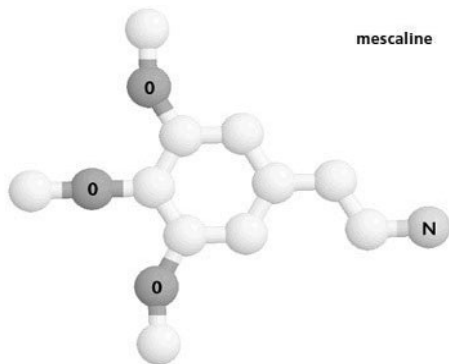
If you were administering psychedelics, what types of behavior would you anticipate in your research subject, and what sorts would you ignore? Much would depend upon whether you were giving a “schizotoxin” or a “phantasticant.” You might encourage an “out-of-body experience” in a “shamanic” context, but abort the same effects by giving an antipsychotic antidote in a “psychotomimetic” one.¹⁰

Hallucinogen is the most common medical term for psychedelic drugs, and it emphasizes the perceptual, mostly visual effects of these drugs. However, while perceptual effects of psychedelics are usual, they are not the only
24 effects, nor are they necessarily the most valued. The visions actually may be distractions



The other main chemical family of psychedelic drugs is the tryptamines. These all possess a nucleus, or basic building block, of tryptamine. Tryptamine is a derivative of tryptophan, an amino acid present in our diet.

American Southwest.



Another famous phenethylamine is MDMA, or “Ecstasy.”

from the more sought-after properties of the experience, such as intense euphoria, profound intellectual or spiritual insights, and the dissolving of the body’s physical boundaries.

I prefer the term *psychedelic*, or mind-manifesting, over hallucinogen. Psychedelics show you what’s in and on your mind, those subconscious thoughts and feelings that are hidden, covered up, forgotten, out of sight, maybe even completely unexpected, but nevertheless imminently present. Depending upon set and setting, the same drug, at the same dose, can cause vastly different responses in the same person. One day, very little happens; another day, you soar, full of ecstatic and insightful discoveries; the next, you struggle through a terrifying nightmare. The generic nature of psychedelic, a term wide open to interpretation, suits these effects.

Psychedelic has taken on its own cultural and linguistic life. It now can refer to a particular style of art, clothing, or even an especially

intense set of circumstances. When it comes to rational discourse about drugs, psychedelic also stirs up powerful 1960s-based emotions and conflicts over unrelated political and sociological issues. Many of us now think “counterculture,” “rebellious,” “liberal,” or “left-wing” when we see the term “psychedelic.” I will take my chances, however, and use it throughout this book. I think it is the best term we have. I hope not to offend anyone who finds the word objectionable.

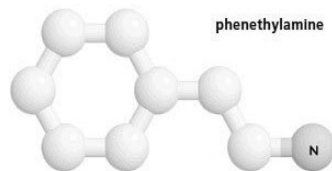
No matter what we call them, most of us agree that the psychedelic drugs are physical, chemical things. It is at this most basic level that we can begin to understand what they are and what they do.

The diagrams accompanying the following descriptions show the chemical structure of various psychedelic compounds. The balls represent atoms, the most common of which
26 is carbon, which is not labeled. “N” signifies nitrogen; “P,” phosphorous; and “O,” oxygen.

Numerous hydrogen atoms are attached to other atoms in the molecules; however, there are so many that they would unnecessarily clutter up the diagram, so I have not included them here.

There are two main chemical families of psychedelic drugs: the phenethylamines and the tryptamines.¹¹

The phenethylamines build upon the “parent compound” phenethylamine.



The best-known phenethylamine is mescaline,²⁷ which is derived from the peyote cactus of the