I was forced to interrupt my work in the laboratory in the middle of the afternoon and proceed home, being affected by a remarkable restlessness combined with a slight dizziness. At home I lay down and sank into a not unpleasant intoxicated-like condition, characterized by an extremely stimulated imagination. In a dreamlike state with eyes closed . . . I perceived an uninterrupted stream of fantastic pictures, extraordinary shapes with intense, kaleidoscopic play of colours.

—Albert Hofmann, the discoverer of LSD, reflecting on the day he took a sample of the drug LSD: My Problem Child (1980)
On an April afternoon in 1943, Albert Hofmann, a research chemist at Sandoz Pharmaceuticals in Basel, Switzerland, went home early from work, unaware that his fingertips had made contact with an extremely minute trace of a new synthetic chemical he had been testing that day. The chemical was lysergic acid diethylamide (LSD), and, as the opening passage indicates, Hofmann unknowingly experienced history’s first “acid trip.”

Three days later, having pieced together the origin of his strange experience, he decided to try a more deliberate experiment. He chose a dose of 0.25 mg, a concentration that could not, so he thought, possibly be effective. His plan was to start with this dose and gradually increase it to see what would happen.

The dose Hofmann had considered inadequate was actually about five times greater than an average dose for LSD. As he later recalled his experience,

My condition began to assume threatening forms. Everything in my field of vision wavered and was distorted as if seen in a curved mirror. I also had the sensation of being unable to move from the spot.

A little while later, his experience worsened:

The dizziness and sensation of fainting became so strong at times that I could no longer hold myself erect, and had to lie down on a sofa. My surroundings had now transformed themselves in more terrifying ways. Everything in the room spun around, and the familiar objects and pieces of furniture assumed grotesque, threatening forms. . . . I was seized by the dreadful fear of going insane. I was taken to another place, another time.

His experience then became pleasant:

Kaleidoscopic, fantastic images surged in on me, alternating, variegated, opening and then closing themselves in circles and spirals. . . . It was particularly remarkable how every acoustic perception, such as the sound of a door handle or a passing automobile, became transformed into optical perceptions. Every sound generated a vividly changing image, with its own consistent form and colour.

Hofmann’s vivid memories are presented here at length because they succinctly convey some of the major facets of a hallucinogenic drug experience: the distortions of visual images and body sense, the frightening reaction that often occurs when everyday reality is so dramatically changed, and the strange intermingling of visual and auditory sensations. These effects will be considered later in more detail as this chapter explores the bizarre world of hallucinogenic drugs.

Like many of the drugs that have been examined in the preceding chapters, hallucinogenic drugs such as LSD and several others have a story that belongs both in our contemporary culture and in the distant past. Hofmann worked in the modern facilities of an international pharmaceutical company, but the basic material on his laboratory bench was a fungus that has been around for millions of years. It has been estimated that as many as 6000 plant species around the world have some psychoactive properties.

This chapter will focus on a collection of special chemicals called hallucinogenic drugs or simply hallucinogens, often pharmacologically dissimilar to one another but with the common ability to distort perceptions and alter the user’s sense of reality.

A Matter of Definition

Definitions are frequently reflections of one’s attitude toward the thing one is defining, and the terminology used to describe hallucinogens is no exception. For those who view these drugs with a “positive spin,” particularly for those who took LSD in the 1960s, hallucinogens have been described as psychedelic, meaning “mind-expanding” or “making the mind manifest.” In cases where a spiritual experience has been reported, such as with the ingestion of ayahuasca, hallucinogens have been called entheogenic, meaning “generating the divine within.” On the other hand, for people who view these drugs with more alarm than acceptance, the popular descriptive adjectives have been psychotomimetic, meaning “having the

### by the numbers . . .

| Approximate number of LSD doses in one ounce (28 grams) of pure LSD, based on 50 micrograms as a typical LSD dosage level | 566 990 |
| The number of documented cases of deaths due to LSD ingestion alone, since 1960 | 1 |

appearance of a psychosis,” psycholyptic, meaning “mind-dissolving,” or even worse, psycholytic, meaning “mind-dissolving.”

As a result of all this emotional baggage, describing these drugs as hallucinogenic, meaning “hallucination-producing,” is probably the most even-handed way of defining their effects; that is the way they will be referred to in this chapter. Some problems, however, still need to be considered. Technically, a hallucination is the reported perception of something that does not physically exist. For example, a schizophrenic patient might hear voices that no one else hears, and therefore we must conclude (at least the nonschizophrenic world must conclude) that such voices are not real. In the case of hallucinogens, the effect is more complicated because we are dealing with a perceived alteration in the existing physical environment. Some researchers have suggested using the term illusionogenic as a more accurate way of describing drugs that produce these kinds of experiences.

We also should be aware of another qualification when we use the term hallucinogen. Many drugs that produce distinctive effects when taken at low to moderate dose levels turn out to produce hallucinations when either the dose levels are extremely high or drug use is extended over a period of time. Examples of this possibility appeared in Chapter 4 with cocaine and amphetamines, and will appear in Chapter 13 with inhalants. Here the category of hallucinogens will be limited to those drugs that produce marked changes in perceived reality at relatively low dosages and over a relatively short time interval.

### Classifying Hallucinogens

The term hallucinogen comes from the Latin word alucinari, which means “to wander in mind, talk idly, or prate.” It is relatively easy to define what hallucinogens are by virtue of their effects on the users, but classifying them can be complicated. In general, most hallucinogens can be classified in terms of the particular neurotransmitter in the brain (see Chapter 3) that bears a close resemblance to the molecular features of the drug. This is the first step in determining how the drug works at the synapse. Generally, hallucinogens work on one major family of receptors, including serotonin, norepinephrine, acetylcholine, glutamate, and GABA receptors.

Table 6.1 shows the overall four-group classification scheme. The first three categories are (1) indolamine hallucinogens that are chemically similar to serotonin (LSD, psilocybin, morning glory seeds, DMT, and harmine), (2) phenethylamine hallucinogens that are...
Major categories of hallucinogens (continued)

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>SOURCE</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenethylamine hallucinogens related to norepinephrine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mescaline</td>
<td>the peyote cactus in Mexico and the U.S. Southwest</td>
<td>5-HT₂ agonist</td>
</tr>
<tr>
<td>2,5-dimethoxy-4-methylamphetamine (DOM or, more commonly, STP)</td>
<td>a synthetic, mescaline-like hallucinogen</td>
<td>5-HT₂ agonist</td>
</tr>
<tr>
<td>MDMA (Ecstasy) and MDA</td>
<td>two synthetic hallucinogens</td>
<td>5-HT₂ agonist</td>
</tr>
<tr>
<td>Miscellaneous hallucinogens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscimol</td>
<td>Amanita muscaria mushrooms</td>
<td>GABA₄ agonist</td>
</tr>
<tr>
<td>Ibotenic acid</td>
<td>Amanita muscaria mushrooms</td>
<td>NMDA agonist</td>
</tr>
<tr>
<td>Phencyclidine (PCP)</td>
<td>a synthetic preparation, developed in 1963, referred to as angel dust</td>
<td>NMDA agonist</td>
</tr>
<tr>
<td>Ketamine (K)</td>
<td>a PCP-like hallucinogen</td>
<td>NMDA antagonist</td>
</tr>
<tr>
<td>Salvia divinorum or salvia</td>
<td>a hallucinogenic Mexican herb, in the mint family</td>
<td>D₂ agonist and kappa opioid agonist</td>
</tr>
</tbody>
</table>

TABLE 6.1


Chemically similar to norepinephrine (mescaline, DOM, MDMA, and MDA), and (3) hallucinogens that are chemically similar to acetylcholine (atropine, scopolamine, and hyoscyamine). The fourth category comprises five hallucinogens (muscimol, ibotenic acid, PCP, ketamine, and Salvia divinorum) that are chemically different from the categories above; these drugs will be called miscellaneous hallucinogens. Most of these drugs have natural botanical origins (see four examples in Figure 6.1).

FIGURE 6.1

Botanical sources for four hallucinogenic drugs: (a) Claviceps tulasne (ergot), (b) Amanita muscaria (muscimol and ibotenic acid), (c) Atropa belladonna (atropine), and (d) Datura stramonium, called jimsonweed (atropine, scopolamine, and hyoscyamine). These sources are not shown to the same scale; actually, they differ in size.

Sources: [to come]


**Lysergic Acid Diethylamide (LSD)**

The most widely known hallucinogen is LSD, which does not exist in nature but is synthetically derived from ergot, a fungus present in moldy rye and other grains. One of the compounds in ergot, lysergic acid, is highly toxic, inducing a condition called ergotism. Historians have surmised that widespread epidemics of ergotism (called St. Anthony’s fire) occurred periodically in Europe during the Middle Ages, when extreme famine forced people to bake bread from infected grain.

In one particularly deadly episode in 944, an outbreak of ergotism claimed as many as 40,000 lives. The features of this calamity were two-fold. One form of ergotism produced a reduction in blood flow toward the extremities, leading to gangrene, burning pain, and the eventual loss of limbs. The other form produced a tingling sensation on the skin, convulsions, disordered thinking, and hallucinations.

Even though the link between this strange affliction and ergot in moldy grain has been known since the 1700s, outbreaks of ergotism have continued to occur in recent times. A major outbreak occurred in Pont-Saint-Esprit, a small French village, in 1951. Hundreds of townspeople went totally mad on a single night:

> Many of the most highly regarded citizens leaped from windows or jumped into the Rhône, screaming that their heads were made of copper, their bodies wrapped in snakes, their limbs swollen to gigantic size or shrunken to tiny appendages... Animals went berserk. Dogs ripped bark from trees until their teeth fell out.

Albert Hofmann’s professional interest in lysergic acid centred on its ability to reduce bleeding and increase contractions in smooth muscle, particularly the uterus. He was trying to find a nontoxic chemical version that would be useful in treating problems associated with childbirth. The LSD molecule was the twenty-fifth in a series of variations that Hofmann studied in 1938, and his creation was officially named LSD-25 for that reason. He thought at the time that the compound had possibilities for medical use but then went on to other pursuits. He returned to these investigations five years later, in 1943, the year of his famous LSD experience.

**The Beginning of the Psychedelic Era**

Sandoz Pharmaceuticals applied for U.S. Food and Drug Administration (FDA) approval of LSD in 1953. As was common practice at the time, the company sent out samples of LSD to laboratories around the world for scientific study. The idea was that LSD might be helpful in the treatment of schizophrenia by allowing psychiatrists to gain insight into subconscious processes, which this drug supposedly unlocked. One of the researchers intrigued by the potential psychotherapeutic applications of LSD was psychiatrist Humphrey Osmond of the University of Saskatchewan, who coined the word “psychedelic” to describe its effects and whose interest also extended to other hallucinogens, such as mescaline.

In 1953, Osmond introduced British writer Aldous Huxley to mescaline, and Huxley later reported his experiences, under Osmond’s supervision, in his essay *The Doors of Perception* (see Portrait—Erika Dyck). Prior to 1960, LSD was being administered to humans under fairly limited circumstances, chiefly as part of research studies in psychiatric hospitals and psychotherapy sessions in Saskatchewan. As would be revealed later in court testimony in the 1970s, there were also top-secret experiments conducted by the U.S. Central Intelligence Agency (CIA), which was interested in LSD for possible application in espionage work. Word of its extraordinary effects, however, gradually spread to regions outside laboratories and hospitals. One of those who picked up on these events was a young clinical psychologist and lecturer at Harvard University named Timothy Leary.

Leary’s first hallucinatory experience (in fact, his first psychoactive drug experience of any kind, other than alcoholic intoxication) was in Mexico in 1960, when he ate some mushrooms containing the hallucinogen psilocybin. This is his recollection of his response:

> During the next five hours, I was whirled through an experience which could be described in many extravagant metaphors but which was above all and without question the deepest religious experience of my life.

Back at Harvard, his revelations sparked the interest of a colleague, Richard Alpert (later to be known as Baba Ram Dass). The two men were soon holding psilocybin sessions with university students and whoever else.

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**ergot (ER-got):** A fungus infecting rye and other grains.

**ergotism:** A physical and/or psychological disorder acquired by ingesting ergot-infected grains. One form of ergotism involves gangrene and eventual loss of limbs; the other form is associated with convulsions, disordered thinking, and hallucinations.
was interested, on and off campus. At first these studies retained some semblance of scientific control. For example, a physician was on hand, and objective observers of behaviour reported the reactions of the subjects. Later, these procedures were altered. Physicians were no longer invited to the sessions, and Leary himself began taking the drug at the same time. His argument was that he could communicate better with the subject during the drug experience, but his participation seriously undermined the scientific nature of the studies.

In 1961 Leary, Alpert, and other associates turned to LSD as the focus of their investigations, in their homes and other locations off the Harvard campus. Although these experiments were technically separate from the university itself, public relations concerns on the part of the Harvard administration were mounting. Leary further aggravated the situation through his increasingly incendiary writings. In a 1962 article published in the *Bulletin of the Atomic Scientists*, he suggested that the Soviets could conceivably dump LSD into the water supply and that, to prepare for such an attack, Americans should dump LSD into their own water supply so that citizens would know what to expect. Needless to say, the U.S. government was not amused.

In 1963, after a Harvard investigation, Leary and Alpert were dismissed from their academic positions, making it the first time in the twentieth century that a Harvard faculty member had been fired. As you can
Imagine, such events brought enormous media exposure. Leary was now "Mr. LSD, and suddenly the public became acquainted with a class of drugs that had been previously unknown to them."

For the rest of the 1960s, LSD became not only a drug but also one of the symbols for the cultural revolt of a generation of youth against the perceived inadequacies of the established, older generation. Leary himself told his followers that they were "the wisest and holiest generation" and advised them to "turn on, tune in, and drop out." The era has been described in this way:

There were psychedelic churches, ashrams, rock festivals, light shows, posters, comic books and newspapers, psychedelic jargon and slang. Every middle-sized city had its enclaves, and there was a drug culture touring circuit. . . . Everyone had his own idea of what was meant by turning on, tuning in, and dropping out—his own set and setting—and the drug culture provided almost as many variations in doctrine, attitude, and way of life, from rational and sedate to lewd and violent, as the rest of society."

In congressional hearings on LSD use by the nation’s youth, scientists, health officials, and law-enforcement experts testified to a growing panic over the drug. Newspaper stories emphasized the dangers with alarmist headlines: "A monster in our midst—a drug called LSD" and "Thrill drug warps mind, kills," among them. Sandoz quietly allowed its LSD patent to lapse in 1966 and did everything it could to distance itself from the controversy. Hofmann himself called LSD his "problem child."

In 1966, LSD was made illegal in the United States. In Canada in 1967, LSD was added to the Food and Drug Act as a substance that would carry penalties for sale and distribution. The consequence of LSD experimentation, even for scientific research, became potential jail time and a criminal record. Research on LSD came to an abrupt halt. By the 1970s, LSD had become entrenched as a street drug, and taking LSD had become a component of the already dangerous world of illicit drugs. The story of LSD will be updated in a later section, but first it is important to understand the range of effects that LSD typically produces.

**How LSD Works at the Synapse**

LSD closely resembles the molecular structure of serotonin (Figure 6.2). Therefore, it is not surprising that LSD should have agonistic effects on receptors in the

![Multicoloured images such as these, inspired by the LSD experience, epitomized the psychedelic era of the 1960s.](image)
brain that are sensitive to serotonin (see Chapter 3). As a result of research in the 1980s, it turns out that the critical factor behind LSD’s hallucinogenic effects lies in its ability to stimulate a special subtype of serotonin-sensitive receptors called serotonin-2A (5-HT\(_2A\)) receptors. To date there have been 15 subtypes of serotonin receptors discovered, which are classified into seven main receptor subtypes: 5-HT\(_1\)-, 5-HT\(_2\)-, and 5-HT\(_3\)-subfamilies of receptors are all linked to G-proteins and act on the adenylate cyclase second messenger system or the phosphoinositide second messenger system, respectively (see Chapter 3 for review).

In fact, many hallucinogens, even those drugs whose structures do not resemble serotonin, have the ability to excite these receptor sites. Drugs that specifically block 5-HT\(_2A\) receptors, leaving all other subtypes unchanged, will block the behavioural effects of hallucinogens. In addition, the ability of a particular drug to produce hallucinogenic effects is directly proportional to its ability to bind to 5-HT\(_2A\) receptors.\(^{13}\)

**Acute Effects of LSD**

LSD is considered one of the most powerful psychoactive drugs known. Its potency is so great that effective dose levels have to be expressed in terms of micrograms (millionths of a gram), often called *mikes*. The typical street dose ranges from 50 to 150 micrograms, though sellers often claim that their product contains more. The effective dose can be as small as 10 micrograms, with only one-hundredth of a percent being absorbed into the brain. You can appreciate the enormous potency of LSD by comparing these figures to the fact that a single regular-strength aspirin tablet contains 325 000 micrograms of aspirin.\(^{14}\)

Taken orally, LSD is rapidly absorbed into the bloodstream and the brain, and its effects begin to be felt within 30 to 60 minutes, reaching a peak in about two to four hours. Within four to 12 hours, LSD effects are over.\(^{15}\)

Surprisingly, given its extreme potency, the toxicity of LSD is relatively low. Generalizing from studies of animals given varying doses of LSD, we can estimate that a lethal dose of LSD for humans would have to be roughly 300 to 600 times the effective dose, a fairly comfortable margin of safety. To this day, there has been only one definitive case in which a death has been attributed solely to an LSD overdose.\(^{16}\)

Street forms of LSD may contain colour additives or adulterants with specific flavours, but the drug itself is odourless, tasteless, and colourless. LSD is sold on the street in single-dose “hits.” It is typically swallowed in the form of powder pellets (microdots) or gelatin chips (windowpanes), or else licked off small squares of absorbent paper that have been soaked in liquid LSD (blotters). In the past, blotters soaked with LSD have been decorated with pictures of mystical symbols and signs, rocket ships, or representations of Mickey Mouse, Snoopy, Bart Simpson, or other popular cartoon characters.

LSD initially produces an excitation of the sympathetic autonomic activity: increased heart rate, elevated blood pressure, dilated pupils, and a slightly raised body temperature. There is an accompanying feeling of restlessness, euphoria, and a sensation that inner tension has been released. There may be laughing or crying, depending on one’s expectations and the setting.\(^{17}\)

Between 30 minutes and two hours later, a “psychedelic trip” begins, characterized by four distinctive features. The best way to describe these effects is in the words of individuals who have experienced them:\(^{18}\)

- Images seen with the eyes closed.

*Closing my eyes, I saw millions of colour droplets, like rain, like a shower of stars, all different colours.*
An intermingling of senses called synesthesia, which usually involves sounds being perceived as hallucinatory visions.

I clapped my hands and saw sound waves passing before my eyes.

Perception of a multilevel reality.

I was sitting on a chair and could see the molecules. I could see right through things to the molecules.

Strange and exaggerated configurations of common objects or experiences.

A towel falling off the edge of my tub looked like a giant lizard crawling down. When my girlfriend was peeling an orange for me, it was like she was ripping a small animal apart.

During the third and final phase, approximately three to five hours after first taking LSD, the following features begin to appear:

Great swings in emotions or feelings of panic.

It started off beautifully. I looked into a garden . . . and suddenly, it got terrible . . . and I started to cry. . . . And then, my attention wandered, and something else was happening, beautiful music was turned on. . . . Then suddenly I felt happy.

A feeling of timelessness.

Has an hour gone by since I last looked at the clock? Maybe it was a lifetime. Maybe it was no time at all.

A feeling of ego disintegration, or a separation of one’s mind from one’s body.

Boundaries between self and nonself evaporate, giving rise to a serene sense of being at one with the universe. I recall muttering to myself again and again, “All is one, all is one.”

Whether these strong reactions result in a “good trip” or a “bad trip” depends heavily on the set of expectations for the drug, the setting or environment in which the LSD is experienced, and the overall psychological health of the individual.

### Patterns of LSD Use

The enormous publicity surrounding Timothy Leary and his followers in the 1960s made LSD a household word. As many as 50 popular articles about LSD were published in major newspapers and magazines between March 1966 and February 1967 alone. By 1970, however, the media had lost interest, and hardly anything was appearing about LSD. Even so, while media attention was diminishing, the incidence of LSD abuse was steadily rising.

It should be noted that today’s LSD users are different from those of a previous generation in a number of ways. Typical LSD users now take the drug less frequently. And because the dosage of street LSD is presently about one-fourth the level common to the 1960s and 1970s, they remain high for a briefer period of time. Their motivation behind using LSD is also not the same. They report using LSD as a club drug, simply to get high, rather than to explore alternate states of consciousness or gain a greater insight into life. For current users, LSD no longer has the symbolic significance that it had in an earlier time.

### Facts and Fiction About LSD

Given the history of LSD use and the publicity about it, it is all the more important to look carefully at the facts about LSD and to unmask the myths. It is useful to examine six basic questions that are frequently asked about the acute and chronic effects of this drug.

### Will LSD Produce Substance Dependence?

There are three major reasons why LSD is not likely to result in drug dependence, despite the fact that the experience at times is quite pleasant. First, LSD and other hallucinogens cause the body to build up a tolerance to their effects faster than any other drug category. As a result, one cannot remain on an LSD-induced high day after day, for an extended period of time. Second, LSD is not the drug for someone seeking an easy way to get high. As one drug expert has put it,

> The LSD experience requires a monumental effort. To go through eight hours of an LSD high—sensory bombardment, psychic turmoil, emotional insecurity, alternations of despair and bliss, one exploding insight upon the heels of another, images hurtling through the mind as fast as the spinning fruit of a slot machine—is draining and exhausting in the extreme.

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**synesthesia:** A subjective sensation in a modality other than the one being stimulated. An example is a visual experience when a sound is heard.
Third, the LSD experience seems to control the user rather than the other way around. It is virtually impossible to “come down” from LSD at will. Besides, the unpredictability of the LSD experience is an unpopular feature for those who would want a specific and reliable drug effect every time the drug is taken.

**Will LSD Produce a Panic Attack or Psychotic Behaviour?**

One of the most notorious features of LSD is the possibility of a bad trip. Personal accounts abound of sweet, dreamlike states rapidly turning into nightmares. Perhaps the greatest risks are taken when a person is slipped a dose of LSD and begins to experience its effect without knowing that he or she has taken a drug. But panic reactions may also occur when a person is fully aware of having taken LSD. Although the probability of having a bad trip is difficult to estimate, there are very few regular LSD abusers who have not experienced a bad trip or had a disturbing experience as part of an LSD trip. The best treatment for adverse effects is the companionship and reassurance of others throughout the period when LSD is active. The Health Line box includes some specific procedures for dealing with LSD panic episodes.

Despite the possibility of an LSD panic, there is no strong evidence that the panic will lead to a permanent psychiatric breakdown. Long-term psychiatric problems are relatively uncommon; one study conducted in 1960 showed that there was no greater probability of a person attempting suicide or developing a psychosis after taking LSD than when undergoing ordinary forms of psychotherapy. The incidents that do occur typically involve people who were unaware that they were taking LSD, showed unstable personality characteristics prior to taking LSD, or were experiencing LSD under hostile or threatening circumstances.

The possible link between the character of LSD effects and certain symptoms of schizophrenia also has been examined closely. It is true that on a superficial level, the two behaviours show some similarities, but there are important differences. LSD hallucinations are primarily visual, are best seen in the dark, and, as we noted earlier, are more accurately characterized as illusions or pseudohallucinations; schizophrenic hallucinations are primarily auditory, are seen with open eyes, and qualify as true hallucinations. Individuals taking LSD are highly susceptible to suggestion and usually try to communicate the experience to others, whereas the schizophrenic individual is typically resistant to suggestion and withdrawn from his or her surroundings. Therefore, it is unlikely that LSD is mimicking the experience of schizophrenia (see Chapter 15).

**Will LSD Increase Your Creativity?**

The unusual visual effects of an LSD experience may lead you to assume that your creativity is enhanced, but the evidence indicates otherwise. Professional artists and musicians creating new works of art or songs while under the influence of LSD typically think that their creations are better than

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**Health Line**

**Emergency Guidelines for a Bad Trip on LSD**

- Stay calm with the individual. Do not move around quickly, shout, cry, or become hysterical. Any sense of panic on your part will make an LSD panic worse. Speak in a relaxed, controlled manner.
- Reassure the individual that the situation is temporary and that you will not leave until he or she returns to a normal state. Encourage the individual to breathe deeply and calmly. Advise him or her to view the trip as though watching a movie or TV program.
- Reduce any loud noises or bright lights, but do not let the individual be in the dark. Darkness tends to encourage hallucinations in a person under the influence of LSD.
- Allow the individual to move around without undue restrictions. He or she can sit, stand, walk, or lie down if this helps the situation. You can divert attention from the panic by encouraging the individual to beat time to music or by dancing.
- If your assistance does not produce a reduction in the panic, seek out medical attention immediately.

anything they have yet produced, but when the LSD has worn off, they are far less impressed. Controlled studies generally show that individuals under LSD feel that they are creative, but objective ratings do not show a significant difference from levels prior to the LSD.\textsuperscript{22}

**Will LSD Damage Your Chromosomes?**

In March 1967, a study published in the prestigious scientific journal *Science* described a marked increase in chromosomal abnormalities in human white blood cells that had been treated with LSD in vitro (that is, the cells were outside the body at the time).\textsuperscript{23} Shortly after, three other studies were reported in which chromosomal abnormalities in the white blood cells of LSD abusers were higher than those of people who did not use drugs, whereas three additional studies reported no chromosomal effect at all.

By the end of that year, a second study was published by the people whose report had started the controversy in the first place. They wrote that 18 LSD abusers had two to four times the number of chromosomal abnormalities in their white blood cells, when compared with 14 control subjects. Interestingly, the subjects in this study were not exactly model citizens. Every one of them had taken either amphetamines, barbiturates, cocaine, hallucinogens, opioids, or antipsychotic medication, and some had abused more than one of these substances.

The picture was confused, to say the least. Not only were many of these studies never replicated, but many were methodologically flawed in the first place. Most importantly, when studies actually looked at the chromosomes of reproductive cells themselves for signs of breakage from exposure to LSD, the results were either ambiguous or entirely negative. By 1971, after nearly 100 studies had been carried out, the conclusion was that LSD did not cause chromosomal damage in human beings at normal doses, and that there was no evidence of a high rate of birth defects in the children of LSD users.\textsuperscript{24} Yet, in the highly politicized climate of the late 1960s, the media tended to emphasize the negative findings without subjecting their validity or relevance to any scrutiny. The public image of LSD causing genetic (mutation-generating) damage still persists, despite the lack of scientific evidence. This is not to say, however, that there is no basis for exercising some degree of caution. Women should avoid LSD, as well as other psychoactive and many nonpsychoactive drugs, during pregnancy, especially in the first three months.\textsuperscript{25}

**Do Flashbacks Occur?**

One of the most disturbing aspects of taking LSD is the possibility of reexperiencing the effects of the drug long after the drug has worn off—sometimes as long as several years later. These experiences are referred to as hallucinogen persisting perception disorder (HPPD), or simply “flashbacks.” The likelihood of LSD flashbacks is not precisely known. Some studies estimate its rate of incidence as only 5%, whereas others estimate it as high as 33%. It is reasonable to assume that the range of estimates is related to differences in the dosage levels ingested. Flashback effects could be frightening and at other times can be quite pleasant; they can occur among LSD novices or “once-only” drug takers, as well as among experienced LSD abusers. They can appear without warning, but there is a higher probability that they will occur when the individual is beginning to go to sleep or has just entered a dark environment.\textsuperscript{26}

Because they are not common to any other psychoactive drug, the reason why LSD flashbacks might occur is not well understood and has raised questions about the existence of flashbacks and HPPD. Flashbacks can occur in the general population who have never taken a hallucinogen, and are more common in people with anxiety disorders. Therefore, a reported flashback, or persistent visual symptom (as they can also be called), may not be due to past LSD use at all, and could be due to another underlying issue. Evidence against flashbacks also comes from large-scale studies examining psychedelic use in the United States that found no association between flashbacks and hallucinogen use in a sample of over 21,000 users.\textsuperscript{27}

Whether LSD produces major long-term deficits in the behaviour of the user remains unknown, but seems unlikely. Memory problems and visuospatial impairments have been reported in some studies but not in others. Unfortunately, several problems persist in research studies examining long-term effects of LSD. Often, they have included either individuals with a history of psychiatric disorders prior to LSD ingestion or regular users of other illicit drugs and alcohol. As a result, it has been impossible to tease apart the long-term effects of LSD alone from other factors.\textsuperscript{28}

Chapter 6  LSD and Other Hallucinogens

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Will LSD Increase Criminal or Violent Behaviour?

As noted in Chapter 2, it is very difficult to establish a clear cause-and-effect relationship between a drug and criminal or violent behaviour. In the highly charged era of the 1960s, stories related to this question were publicized, and conclusions were drawn, without any careful examination of the actual facts. Take, for example, the 1964 case of a woman undergoing LSD therapy treatment who murdered her lover three days after her last LSD session. The details of the case, overlooked by most subsequent media reports, reveal that the woman had been physically abused by the man, he had caused her to have an abortion, and the woman already had a serious mental disorder before going into treatment. The fact that the homicide took place well after the LSD had left her body indicates that the murder was not pharmacologically based (see Chapter 2). Other cases in which violent behaviour appeared to be associated with an LSD experience turned out to be associated with the use of other hallucinogenic drugs, or other underlying psychological problems instead.

LSD as a Medical Treatment

Interestingly, the first experiments on LSD performed by medical researchers Osmond and Hoffer in Saskatchewan looked at its potential to help with alcoholism (see Portrait—Erika Dyck). The results of all of these studies were never analyzed as a whole, in a meta-analysis. However, in 2012, two Norwegian researchers examined six trials where LSD was administered to a total of 536 participants. They both performed an independent analysis and both found that there was a significant effect of LSD—it decreased alcohol misuse: “A single dose of LSD, in the context of various alcoholism treatment programs, is associated with a decrease in alcohol misuse.” However, there are still many issues, legal and moral, surrounding the use of LSD as a treatment for addiction.

Psilocybin and Other Hallucinogens Related to Serotonin

The source of the drug psilocybin is a family of mushrooms native to southern Mexico and Central America. Spanish chroniclers in the sixteenth century wrote of “sacred mushrooms” revered by the Aztecs as teonanacatl (roughly translated as “God’s flesh”) and as capable of providing extraordinary visions when eaten. Their psychoactive properties had been known for a long time, judging from stone-carved representations of these mushrooms discovered in El Salvador and dating back to as early as 500 b.c.e. Today, shamans in remote villages in Mexico and Central America (see Chapter 1) continue the use of psilocybin mushrooms, among other hallucinogenic plants, to achieve healing on both physical and spiritual levels.

In 1955, a group of Western observers documented the hallucinogenic effects of the Psilocybe mexicana in a native community living in a remote mountainous region of southern Mexico. Three years later, samples worked their way to Switzerland, where Albert Hofmann, already known for his work on LSD, identified the active ingredient and named it psilocybin. As was his habit, Hofmann sampled some of the mushrooms himself and wrote later of his reactions:

Thirty minutes after my taking the mushrooms, the exterior world began to undergo a Mexican character. . . . I saw only Mexican motifs and colours. When the doctor supervising the experiment bent over me to check my blood pressure, he was transformed into an Aztec priest.

An interesting question is whether the Aztec character of these hallucinogenic effects was simply a result of suggestion, given the social context in which the drug-taking behaviour was occurring, or, alternatively, Aztec designs may have been inspired over the centuries by the effects of psilocybin.

Once ingested, psilocybin is enzymatically converted into psilocin, making it more fat-soluble and more easily absorbed into the brain. Psilocin is the actual psychoactive compound that works on the brain. Because LSD and psilocin are chemically similar, the biochemical effects are also similar. Cross-tolerance will occur (see Chapter 3). If you develop a tolerance to LSD, you have become tolerant to psilocybin effects, and vice versa.

**meta-analysis:** A method that combines and analyzes results from different studies to look for a general effect of a treatment.

**psilocybin (SIL-oh-SIGH-bin):** A serotonin-related hallucinogenic drug originating from some species of psychoactive mushrooms.

**psilocin (SIL-oh-sin):** The active ingredient that is enzymatically converted from psilocybin. It is a serotonin receptor agonist.
Chapter 6  LSD and Other Hallucinogens

Psilocybe mexicana mushrooms, the source of psilocybin.  
Source: Science Picture Library/Photo Researchers, Inc.

Far less potent than LSD, psilocybin is effective at dose levels measured in the more traditional units of milligrams, rather than in micrograms. At doses of 4 to 5 mg, psilocybin causes a pleasant, relaxing feeling; at doses of 15 mg and more, hallucinations, time distortions, and changes in body perception appear. A psilocybin trip generally lasts from two to five hours, considerably shorter than an LSD trip.

Individuals who have experienced both kinds of hallucinogens report that, compared to LSD, psilocybin produces effects that are more strongly visual, less emotionally intense, and more euphoric, with fewer panic reactions and less chance of paranoia. On the other hand, experimental studies of volunteers taking high doses of psilocybin have established that the drug produces drastic enough changes in mood, sensory perception, and thought processes to qualify as a psychotic experience.

Like LSD, psilocybin (often called simply “shrooms”) has become increasingly available as a drug of abuse.

**Lysergic Acid Amide (LAA)**

In addition to their reverence for psilocybin mushrooms, the Aztecs ingested locally grown morning glory seeds, calling them *ololuiqui*, and used their hallucinogenic effects in religious rites and healing. Like many Native American practices, the recreational use of morning glory seeds has survived in remote areas of southern Mexico. In 1961, Albert Hofmann (once again) identified the active ingredient in these seeds as *lysergic acid amide* (LAA) after having sampled its hallucinogenic properties. As the chemical name suggests, this drug is closely related to LSD.

The LAA experience, judging from Hofmann’s report, is similar to that of LSD, although LAA is only one-tenth to one-thirtieth as potent, and the hallucinations tend to be dominated by auditory rather than visual images. Commercial varieties of morning glory seeds are available to the public, but to minimize their abuse, suppliers have taken the precaution of coating them with an additive that causes nausea and vomiting if they are eaten.

**Dimethyltryptamine (DMT)**

The drug *dimethyltryptamine* (DMT) is obtained chiefly from the resin of the bark of trees and nuts native to the West Indies as well as to Central and South America, where it is generally inhaled as a snuff. This was first synthesized in a laboratory by Canadian, Richard Manske, in 1931. An oral administration does not produce psychoactive effects, but it is active when inhaled. DMT is structurally related to LSD and the serotonin-like hallucinogens (Figure 6.2). The similarity of this drug’s effects to those of LSD and its very short duration gave DMT the reputation, during the psychedelic years of the 1960s, of being “the businessman’s LSD.” Presumably, someone could take a DMT trip during lunch and be back at the office in time for work in the afternoon.

An inhaled 30-mg dose of DMT produces physiological changes within 10 seconds, with hallucinogenic effects peaking around 10 to 15 minutes later. Paranoia, anxiety, and panic also can result at this time, but most symptoms are over in about an hour. A chemical found in *Bufo* toads is similar to DMT (see Health Line).

**Harmine**

Among Native tribes in the western Amazon region of South America, the bark of the *Banisteriopsis* vine yields the powerful drug harmine. A drink containing harmine, called *ayahuasca*, is frequently used by

**lysergic acid amide (LAA)** (lye-SER-jik ASS-id A-mide): A hallucinogenic drug found in morning glory seeds, producing effects similar to those of LSD.


**harmine (HAR-meen)**: A serotonin-related hallucinogenic drug frequently used by South American shamans in healing rituals.
local shamans for healing rites. It is chemically similar to serotonin, like LSD and the other hallucinogens examined so far. Its psychological effects, however, are somewhat different. Unlike LSD, harmine makes the individual withdraw into a trance, and the hallucinatory images (often visions of animals and supernatural beings) are experienced within the context of a dreamlike state. Some preparations of ayahuasca can also contain DMT. Reports among shamans refer to a sense of suspension in space or of flying, falling into one’s body, or experiencing one’s own death.

Hallucinogens Related to Norepinephrine

Several types of hallucinogens have a chemical composition similar to that of norepinephrine. As you may recall from Chapter 4, amphetamines are also chemically similar to norepinephrine. Consequently, some of the norepinephrine-related hallucinogens are capable of producing amphetamine-like stimulant effects. This is the case with MDMA (Ecstasy) but not with mescaline or DOM (short for 2,5-dimethoxy-4-methylamphetamine).

Mescaline

The hallucinogen mescaline is derived from the peyote plant, a spineless cactus with a small, greenish crown that grows aboveground and a long carrot-like root. This cactus is found over a wide area, from the southwestern United States to northern regions of South America, and many communities in these regions have discovered its psychoactive properties. Given the large distances between these groups, it is

Bufotenine and the Bufo Toad

Bufotenine is a drug with a strange past. Found in a family of beans native to Central and South America, bufotenine is better known as a chemical that can be isolated from the skin and glands of the Bufo toad, from which it gets its name. As noted in Chapter 1, Bufo toads figured prominently in the magical potions of European witches. Evidence also exists that Bufo toads were incorporated into the ceremonial rituals of ancient Aztec and Mayan cultures. Largely as a result of these historical references, it has been widely assumed that bufotenine was the primary contributor to the psychoactive effects of these concoctions and that bufotenine itself is a powerful hallucinogen.

It turns out that these conclusions are wrong. The few studies in which human volunteers were administered bufotenine indicate that the substance induces strong excitatory effects on blood pressure and heart rate but no hallucinatory experiences. Some subjects report distorted images with high dosages of the drug, but this might well occur as oxygen is cut off from parts of the body, particularly the optic nerve carrying visual information to the brain. It is likely that whatever hallucinogenic effects Bufo toads may produce are brought on by another chemical also found in these toads that functions similarly to the hallucinogen DMT.

Despite the confusion about which substance is responsible for its psychoactive properties, Bufo toads continue to fascinate the public. Wildly exaggerated and frequently unsubstantiated accounts of “toad licking” and “toad smoking” periodically circulate in the media. Reportedly, a small group calling themselves Amphibians Anonymous was formed in the late 1980s; the group’s motto was “Never has it been so easy to just say no.”

The bottom line, however, is that the dangers of consuming toad tissue are substantial. Besides the extreme cardiovascular reactions, toxic effects include a skin condition called cyanosis (literally, “turning blue”). Actually, that description may be an understatement. Skin colour has been observed to be closer to an eggplant purple.

Sources:

Bufotenine (byoo-FOT-eh-neen): A serotonin-related drug obtained either from a bean plant in Central and South America or from the skin of a particular type of toad.
Cyanosis (SIGH-ah-NOH-sis): A tendency for the skin to turn bluish purple. It can be a side effect of the drug bufotenine.
Mescaline (MES-kul-leen): A norepinephrine-related hallucinogenic drug that comes from the peyote cactus.
Peyote (pay-YOD-tay): A species of cactus that is the source for the hallucinogenic drug mescaline.
remarkable that they prepare and ingest mescaline in a highly similar manner. The crowns of the cactus are cut off, sliced into small disks called buttons, dried in the sun, and then consumed. An effective dose of mescaline from peyote is 200 mg, equivalent to about five buttons. Peak response to the drug takes place 30 minutes to two hours after consumption. Mescaline is still used today as part of religious worship among many Native Americans in the United States and Canada (see Drugs... in Focus).

The psychological and physiological effects of mescaline are highly similar to those of LSD, though some have reported that mescaline hallucinations are more sensual, with fewer changes in mood and the sense of self. Nonetheless, double-blind studies comparing the reactions to LSD and mescaline show that subjects cannot distinguish between the two when dose levels are equivalent. Although the reactions may be the same, the mescaline trip comes at a greater price, as far as physiological reactions are concerned. Peyote buttons taste extremely bitter and can cause vomiting, headaches, and, unless the stomach is empty, distressing levels of nausea.38

Today mescaline can be synthesized as well as obtained from the peyote cactus. The mescaline molecule resembles the chemical structure of the ritual of taking Holy Communion, or drink peyote tea. It is considered sacrilegious to take peyote outside the ceremonies in the church. In 2005, a study found that peyote use among church members does not result in impairments on tests of memory, attention, and other aspects of cognitive functioning.

Canadian law allows the use of peyote for religious practices, and allows possession of peyote plants and seeds that are not for the purposes of consumption. Mescaline, on the other hand, is illegal and listed as a Schedule III substance.


Among Native Americans, the ritual use of peyote buttons, called peyotism, can be traced to the eighteenth century, when the Mescalero Apaches (from whom the word mescaline was derived) adopted the custom from Mexican Indians who had been using peyote for more than 3000 years. By the late 1800s, peyotism had become widely popular among tribes in the United States from Wisconsin and Minnesota to the West Coast. It was not until the early twentieth century, however, that peyotism became incorporated into an official religious organization, the Native American Church of North America, chartered in 1918 and registered later in Canada in the 1930s.

The beliefs of the Native American Church membership, estimated to include anywhere from 50 000 to 250 000 Native Americans in the United States and Canada, combine traditional tribal customs and practices with Christian morality. To them, life is a choice between two roads that meet at a junction. The Profane Road is paved and wide, surrounded by worldly passions and temptations. The Peyote Road is a narrow and winding path, surrounded by natural, unspoiled beauty; it is also a path of sobriety (since alcohol poisons the goodness of the body), hard work, caring for one’s family, and brotherly love. Only the Peyote Road leads to salvation. In their weekly ceremonies, lasting from Saturday night until Sunday afternoon, church members swallow small peyote buttons as a sacrament, similar to
norepinephrine (Figure 6.3) but stimulates the same serotonin-2A receptors as LSD and other hallucinogens that resemble serotonin. As a result, mescaline and LSD share a common brain mechanism.\(^{39}\)

**DOM**

A group of synthetic hallucinogens have been developed that share mescaline’s resemblance to amphetamine but do not produce the strong stimulant effects of amphetamine. One example of these synthetic drugs, DOM, appeared in the 1960s and 1970s, when it was frequently combined with LSD and carried the street name of STP. To some, the nickname was a reference to the well-known engine oil additive; to others the letters stood for “serenity, tranquility, and peace” or, alternatively, “super terrific psychedelic.” It is roughly 80 times more potent than mescaline, though still far weaker than LSD. At low doses of about 3 to 5 mg, DOM produces euphoria; with higher doses of 10 mg or more, severe hallucinations result, often lasting from 16 to 25 hours. Though similar to LSD in many respects, DOM has the reputation of producing a far greater incidence of panic attacks, psychotic episodes, and other symptoms of a very bad trip. Cases have been reported of STP being added as an adulterant to marijuana.\(^{40}\)

**MDMA (Ecstasy)**

Another synthetic norepinephrine-related hallucinogen, (3,4-methylenedioxy-N-methylamphetamine) MDMA, was first synthesized by a scientist named Anton Kollisch, and patented in 1914 by the Merck pharmaceutical company. The original goal of Kollisch was to create a drug that could be used in wars to suppress the appetite of soldiers. It was put on the shelf for a long period of time, and regained interest in the middle of the 1970s when a number of psychiatrists started to use the drug as part of their therapy, believing that MDMA had a special ability to enhance empathy among their patients. In fact, some therapists at the time suggested the name *empathogens* (meaning “generating a state of empathy”) to describe MDMA and related drugs. It is now considered an *entactogen*, which is a compound that increases introspection and the internal feelings of the external world. It is currently listed as a Schedule I drug in Canada, because of its similarity to amphetamine. In recent years, a small number of research laboratories have received permission to produce MDMA and study its effects under closely supervised circumstances. In the United States the treatment of post-traumatic stress disorder among veterans of the wars in Iraq and Afghanistan has been identified as a potentially useful therapeutic application. In 2012, Health Canada approved the use of MDMA in clinical trials for the treatment of post-traumatic stress disorder. Dr. Ingrid Pacey, a Vancouver-based clinician and researcher, and psychologist Andrew Feldmár will begin to assess the benefit of MDMA in therapy.\(^{41}\)

“*What the MDMA does, because of the physiological effects, it means you are in a present, fearless state—able to look at those events without being re-traumatized, and healing in the present what was the trauma of the past.*” —Dr. Pacey

“It brings you into the present. You don’t worry about the past or the future. It opens your heart; you don’t feel any shame. Something horrible is done to you, and an alarm starts ringing. You just don’t know how to turn it off. Even though the war is over, or no one is torturing you, or no one is hurting you, the alarm is still ringing. With the help of MDMA and good therapy, good connection and good company, the alarm can be stilled.” —Mr. Feldmár.\(^{42}\)
Assorted Ecstasy tablets.

Since the early 1990s, MDMA has become prominent among the new club drugs (see Chapter 1), and especially popular at dance clubs and all-night “rave” parties. Widely available under names such as Ecstasy (not to be confused with the stimulant Herbal Ecstasy), E, XTC, X, Essence, Clarity, and Adam, MDMA has the reputation of having the stimulant qualities of amphetamines and the hallucinogenic qualities of mescaline.

The consequences of Ecstasy use are debatable because many pills contain added active ingredients other than MDMA. Ecstasy that is purchased on the street is likely very different than pure MDMA. As a result, the physical health concerns with respect to street Ecstasy centre on its short-term and long-term toxicity. The principal acute effect is severe hyperthermia (and heatstroke), which can be lethal when one ingests Ecstasy while engaged in the physical exertion in an already overheated environment. The dehydration associated with hyperthermia causes an elevation in blood pressure and heart rate and places a strain on kidney functioning. These problems are compounded by the highly risky practice of “Ecstasy stacking,” in which multiple Ecstasy tablets are taken at once or Ecstasy is combined with LSD, alcohol, marijuana, or other drugs. Ecstasy use also has been linked to long-term cognitive impairments and emotional difficulties; however, there have also been recent studies showing no impairments in cognitive functioning. In general, women show greater behavioural effects from chronic Ecstasy use than do men. It is a common recommendation that pregnant women do not take Ecstasy.43

The use of pure MDMA is much less dangerous than street Ecstasy. Dr. Perry Kendal, the provincial Health Officer for British Columbia, recently stated that pure MDMA is “safe” when used under appropriate conditions and dosages. The reason that MDMA is commonly considered a dangerous drug is because street gangs cut up pure MDMA with a variety of other drugs and impurities, which makes Ecstasy dangerous and unpredictable. In British Columbia, an average of 20 deaths per year are linked to Ecstasy. Royal Canadian Mounted Police advise strongly against taking street Ecstasy because it is very hard to know what is in the tablet, and there are a wide variety of individual reactions to these drugs. However, pure MDMA that is manufactured in legitimate laboratories may help treat some mental health disorders in the future.

Hallucinogens Related to Acetylcholine

Of the acetylcholine-related hallucinogens, some enhance the neurotransmitter and some inhibit it. Examples include atropine, scopolamine, and hyoscyamine.

The Hexing Drugs and Witchcraft

A number of natural plants contain chemicals that share a common feature: the ability to block the parasympathetic effects of acetylcholine in the body. The drugs with this ability, called anticholinergic drugs, produce specific physiological effects. The production of mucus in the nose and throat, and of saliva in the mouth, is reduced. Body temperature is elevated, sometimes to very high fever levels. Heart rate and blood pressure go up, and the pupils dilate considerably. Psychological effects include a feeling of delirium and confusion, and a loss of memory for events occurring during the drugged state.44 The amnesic property is one of the primary reasons for the minimal street appeal of these drugs.

The principal anticholinergic drugs are atropine, scopolamine (also called hyoscine), and hyoscyamine. They are found in various combinations and relative

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atropine (AT-tro-peen): An anticholinergic hallucinogenic drug derived from the Atropa belladonna plant. It is an antagonist at muscarinic acetylcholine receptors.

scopolamine (scoh-POL-ah-meen): An anticholinergic hallucinogenic drug. Also called hyoscine or levo-duboisine. It is an antagonist at M1 muscarinic acetylcholine receptors.

hyoscyamine (HEYE-oh-SEYE-eh-meen): An antagonist of muscarinic acetylcholine receptors that is found in mandrake, henbane, and various species of the datura plant. Also called daturine.
Atropine is principally derived from the *Atropa belladonna* plant, also called deadly nightshade. It acts on both the peripheral and central nervous systems and antagonizes muscarinic acetylcholine receptors. Its lethal reputation is quite justified, since it is estimated that ingesting only a dozen or so berries is sufficient for death to occur. Through history, atropine has been associated with poisoning, either accidental or not. In the eleventh century, Scottish forces succeeded in destroying an opposing army (English or Scandinavian, records are unclear) by atropine-adulterated shipments of meal. At lower, more benign dose levels, plant extracts can be applied to the eyes, causing the pupils to dilate. Egyptian and Roman women used this technique to enhance their beauty or at least improve their appearance. The term “belladonna” (“beautiful lady”) originates from this specific application. The psychological effects of atropine are generally associated with the anticholinergic effects of heart-rate acceleration, light-headedness, and general arousal.

The *mandrake* plant is an oddly shaped, potato-like plant with a long forked root that has traditionally been imagined to resemble a human body. In ancient times, mandrake was considered to have aphrodisiac properties. According to medieval folklore, mandrake plants supposedly shrieked when they were uprooted, understandably driving people mad.

Mandrake contains a combination of atropine, scopolamine, and hyoscyamine. Because low doses act as a depressant, mandrake has been used as a sedative-hypnotic drug to relieve anxiety and induce sleep. At higher doses, it produces bizarre hallucinations and muscular paralysis.

*Henbane* is a strong-smelling herb, native to widespread areas of the Northern Hemisphere, with purple-veined, yellowish flowers and hairy leaves. Its English name, meaning “harmful to hens,” originates from the observation that henbane seeds were toxic to chickens and other birds. The lethal possibilities for henbane potions have been described by writers since the days of the Roman Empire. Hamlet’s father in Shakespeare’s play was supposedly murdered with henbane poison. Lower doses of henbane, however, have been used in a more benign way, as an anesthetic and painkiller. We now know that the predominant drugs in henbane are scopolamine and hyoscyamine.

Various species of the datura plant, containing a combination of atropine, scopolamine, and hyoscyamine, grow wild in locations throughout the world. In the United States, one particular species, *Datura stramonium*, is called jimsonweed, a contraction of “Jamestown weed” (the name given to it by early American colonists). Consumption of the seeds or berries of jimsonweed produces hypnotic and hallucinogenic effects, together with disorientation, confusion, and amnesia. At high doses, jimsonweed is quite toxic. In recent years, there have been occasional reports of hospitalizations and even deaths among teenagers who have eaten jimsonweed seeds as an inexpensive way to get high.45

During medieval times, mixtures of deadly nightshade, mandrake, and henbane were responsible for the psychoactive effects of witches’ potions, producing a disastrous combination of physiological and psychological effects. Satanic celebrations of the Black Mass centred on the ingestion of such brews. Atropine, in particular, produced a substantial elevation in arousal, probably leading to the feeling that the person was flying (or at least capable of it), while the hallucinogenic effects enabled the person to imagine communing with the Devil. According to fourteenth-century reports, witches were described as preparing these mixtures as ointments and rubbing them on their bodies and on broomsticks, which they straddled while naked. The chemicals would have been easily absorbed through the skin and the membranes of the vagina. The considerably sanitized Halloween image of a witch flying on a broomstick has been with us ever since.46

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**Atropa belladonna (a-TROH-pah BEL-ah-DON-ah):** A plant species, also called deadly nightshade, whose berries can be highly toxic. It is the principal source of atropine.

**mandrake:** A potato-like plant containing anticholinergic hallucinogenic drugs atropine, scopolamine, and hyoscyamine.

**henbane:** An herb containing anticholinergic hallucinogenic drugs scopolamine, and hyoscyamine.

**Datura stramonium (duh-TOOR-ah strah-MOH-nee-um):** A species of the datura family of plants with hallucinogenic properties because they contain atropine, scopolamine, and hyoscyamine. In North America, the plant is called jimsonweed.
Miscellaneous Hallucinogens

Five hallucinogens are referred to as miscellaneous hallucinogens because they do not have any chemical resemblance to serotonin, norepinephrine, or acetylcholine. They are ibotenic acid, muscimol, phencyclidine, ketamine, and *Salvia divinorum*.

Amanita muscaria

The *Amanita muscaria* mushroom, also called the fly agaric mushroom because of its ability to lure and sedate flies and other insects, grows in the upper latitudes of the Northern Hemisphere, usually among the roots of birch trees. The mushroom has a bright red cap speckled with white dots; the dancing mushrooms in Walt Disney’s film *Fantasia* were inspired by the appearance (if not the hallucinogenic effects) of this fungus (see Figure 6.1b).

Amanita mushrooms are one of the world’s oldest intoxicants. Many historians hypothesize that this mushroom was the basis for the mysterious and divine substance called soma that is celebrated in the Rig-Veda, one of Hinduism’s oldest holy books, dating from 1000 B.C.E. It is strongly suspected that amanita mushrooms were used in Greek mystery cults, and were the basis for the legendary “nectar of the gods” on Mount Olympus.  

The effects of amanita mushrooms can be lethal if dose levels are not watched very carefully. They produce muscular twitching and spasms, vivid hallucinations, dizziness, and heightened aggressive behaviour. It was briefly mentioned in Chapter 1 that Viking warriors were reputed to have ingested amanita mushrooms before sailing off to battle. The drug-induced strength and savagery of these “berserk” invaders were so widely feared that a medieval prayer was written especially for protection from their attacks: “From the intolerable fury of the Norseman, O Lord, deliver us.”

Muscimol is the active ingredient in amanita mushrooms, whereas ibotenic acid is not thought to be responsible for the sedative/hypnotic effect until it is metabolized and becomes muscimol. Muscimol acts specifically at GABA_A receptors on the GABA binding site to open their Cl^- channels, and acts independently of normal GABA release. This is in contrast to drugs like benzodiazepines and barbiturates that bind to a different binding site and still need normal GABA neurotransmission to be effective.

Although ibotenic acid is not considered to have hallucinogenic properties on its own, it is converted to muscimol in the body after amanita mushrooms are consumed. It is also commonly used in its non-modified form in research as an agent to produce chemical lesions. This is because ibotenic acid is a potent neurotoxin that acts to increase excitatory glutamatergic neurotransmission, partially by agonizing N-methyl-D-aspartate (NMDA) receptors. When NMDA receptors are opened for long periods of time there is an excess of Ca^{2+} ions that trigger cell death (apoptosis). Thus, the insertion of ibotenic acid via a cannula can nonspecifically destroy neurons in the brain area of interest. This allows researchers to examine what is missing in the animal’s behaviour, which may explain the function of destroyed brain area.

Phencyclidine (PCP)

Perhaps the most notorious of all the hallucinogens is *phencyclidine* (PCP), commonly known as *angel dust*. Technically, PCP is a synthetic depressant, and it was originally introduced in 1963 as a depressant drug by the Parke-Davis pharmaceutical company, under the brand name of Sernyl. It was marketed as a promising new surgical anesthetic that had the advantage of not depressing respiration or blood pressure or causing heartbeat irregularities, as some other anesthetics do. In addition, PCP had a higher therapeutic ratio than many other anesthetics available at that time. By 1965, however, it was withdrawn from human applications after reports that nearly half of all patients receiving PCP showed signs of delirium, disorientation, hallucinations, intense anxiety, or agitation. PCP is now classified as a Schedule I controlled substance and is still used as an anesthetic for animal surgery.

The weird combination of stimulant, depressant, and hallucinogenic effects makes PCP difficult to classify. Some textbooks treat the discussion of PCP in a chapter on hallucinogens, as is done here, whereas others include it in a chapter on stimulants because

![Amanita muscaria (a-ma-NEE-ta mus-CAR-ee-ah): A species of mushroom containing the hallucinogenic drugs ibotenic acid and muscimol.](image1.png)

Muscimol: A selective GABA_A receptor agonist that causes a sedative/hypnotic effect. It is the active ingredient in amanita muscaria mushrooms.

Ibotenic acid: Found in the amanita muscaria mushroom, this compound is most commonly used for research purposes. It is an excitatory neurotoxin that acts on NMDA receptors.

Phencyclidine (PCP) (fen-SIGH-klih-deen): A dissociative anesthetic hallucinogen that produces disorientation, agitation, aggressive behaviour, analgesia, and amnesia. It has various street names, including angel dust.
some features of PCP intoxication resemble the effect of cocaine. A growing consensus of opinion has it that PCP should be described as a dissociative anesthetic hallucinogen, because it produces a feeling of being dissociated or cut off from one’s environment.

PCP acts primarily on NMDA receptors as a non-competitive antagonist. It acts to block the ion channel in the NMDA receptor and prevents any movement of Na$^+$ and Ca$^{2+}$ ions into neurons. This means that even if glutamate binds to the NMDA receptor, if PCP is also bound, there will be no effect. Since there are many NMDA receptors in the cerebral cortex and hippocampus, it makes sense that PCP alters memory and many aspects of cognitive processing.

**Acute Effects of PCP**

PCP can be taken orally, intravenously, or by inhalation, but commonly it is smoked either alone or in combination with other drugs. Whatever its mode of administration, the results are extremely dangerous, with an unpredictability that far exceeds that of LSD or other hallucinogens. The symptoms may include manic excitement, depression, severe anxiety, sudden mood changes, disordered and confused thought, paranoid thoughts, and unpredictable aggression. Because PCP has analgesic properties as well, individuals taking the drug often feel invulnerable to threats against them and may be willing and able to withstand considerable pain. The mechanism behind PCP effects appears to be the blocking of a specific subtype of glutamate receptor in the brain (see Chapter 3).

Hallucinations also occur, but they are quite different from the hallucinations experienced under the influence of LSD. There are no colourful images, no intermingling of sight and sound, no mystical sense of being “one with the world.” Instead, a prominent feature of PCP-induced hallucinations is the change in one’s body image. As one PCP abuser has expressed it:

*The most frequent hallucination is that parts of your body are extremely large or extremely small. You can imagine yourself small enough to walk through a key hole, or you can be lying there and all of a sudden you just hallucinate that your arm is twice the length of your body.*

Individuals under the influence of PCP also may stagger, speak in a slurred way, and feel depersonalized or detached from people around them. A prominent feature is a prolonged visual stare, often called “doll’s eyes.”

The effects of PCP last from as little as a few hours to as long as two weeks, and they are followed by partial or total amnesia and dissociation from the entire experience. Considering these bizarre reactions, it is not surprising that PCP deaths occur more frequently from the behavioural consequences of the PCP experience than from its physiological effects. Suicides, accidental or intentional mutilations, drownings (sometimes in very small amounts of water), falls, and threatening behaviour leading to the individual being shot are only some of the possible consequences.

**Patterns of PCP Abuse**

It is strange that a drug with so many adverse effects would be subject to deliberate abuse, but such is the case with PCP. Reports of PCP abuse began surfacing in 1967 among the hippie community in San Francisco, where it became known as the PeaCe Pill. Word quickly spread that PCP did not live up to its name. Inexperienced PCP abusers were suffering the same bizarre effects as had the clinical patients earlier in the decade. By 1969, PCP had been written off as a garbage drug, and it dropped out of sight as a drug of abuse.

In the early 1970s, PCP returned under new street names and in new forms (Table 6.2). No longer a pill to be taken orally, PCP was now in powdered or liquid form. Powdered PCP could be added to parsley, mint, oregano, tobacco, or marijuana, rolled as a cigarette, and smoked. Liquid PCP could be used to soak leaf mixtures of all types, including manufactured cigarettes.
which could then be dried and smoked. Many new users have turned to PCP as a way to boost the effects of marijuana. Making matters worse, as many as 120 different designer-drug variations of PCP have been developed in illicit laboratories around the country and the world. The dangers of PCP abuse, therefore, are complicated by the difficulty in knowing whether a street drug has been adulterated with PCP and what version of PCP may be present. Unfortunately, the common practice of mixing PCP with alcohol or marijuana adds to the unpredictability of the final result.

Ketamine

Ketamine, a drug chemically similar to PCP, is also classified as a dissociative anaesthetic hallucinogen. Like PCP, ketamine has a mixture of stimulant and depressive properties, though its depressive effect is more extreme and does not last as long as that of PCP. Ketamine also acts as a noncompetitive antagonist on NMDA receptors. Ketamine (brand name: Ketalar) was used as an emergency surgical anaesthetic on the battlefield in Vietnam as well as in standard hospital-based operations in which gaseous anaesthetics could not be employed. It has also been used occasionally in short surgical procedures involving the head and neck or in the treatment of facial burns where it is not possible to use an anesthetic mask. Adverse side effects, however, have limited its therapeutic use. These problems include unpredictable and sometimes violent jerking and twitching of the body, as well as vivid and unpleasant dreams during and after surgery. During recovery, patients may experience hallucinations and feelings of disorientation. Delayed effects of ketamine, such as nightmares, have been reported to occur for weeks or longer after surgery.

Ketamine abuse began to be reported in the 1980s. More recently, under the names “Special K” and “Vitamin K,” it has been included among current club drugs on the scene (see Chapter 1). Its popularity has increased among college students and patrons of dance clubs and all-night “rave” parties. Like PCP, ketamine produces a dreamlike intoxication, accompanied by an inability to move or feel pain. There are also experiences of dizziness, confusion, and slurred speech. As is the case with dissociative hallucinogens, ketamine produces amnesia, in that abusers frequently cannot later remember what has happened while under its influence. The primary hazard of acute ketamine ingestion is the depression of breathing. Little is known, however, of the chronic effects of extended ketamine abuse over time, except that experiences of “flashbacks” have been reported. As with PCP, the effects of ketamine are associated with the blocking of specific glutamate receptors.

As with other club drugs that produce depressive effects on the central nervous system, there is the dangerous potential for ketamine to be abused as a “date-rape” drug. Women who may unwittingly take the drug can be rendered incapacitated, without the ability to recall the experience. Just like PCP, ketamine is classified as a Schedule I controlled substance.

Salvia Divinorum

The Mexican herb Salvia divinorum (commonly referred to as salvia) has a long tradition as a shamanic treatment for diarrhea, headache, rheumatism, and abdominal discomfort. When smoked, chewed, or brewed as a tea, salvia produces intense visual hallucinations (resembling the effect of psilocybin-containing mushrooms), laughter, and an “out of body,” dissociative experience. Its potency approaches that of LSD, but the effects are very short-lived. In one recent study of salvia users, 85% reported salvia effects lasting less than 15 minutes.

Considerable media attention has been directed toward recreational use of salvia. At present, it has not been classified as a controlled substance under the federal Controlled Substances Act. Salvia remains legally available through numerous Internet websites. In a growing number of U.S. states and in countries around the world, salvia has been officially classified as an illicit drug, along with other hallucinogens.
According to the 2010 CADUMS, 1.6% of Canadians over the age of 15 have used salvia at some point in their lifetime. The majority of users are under the age of 24, with 6.6% of youth reporting trying salvia. There is significantly more use by young Canadians relative to adults (0.6%), which shows that salvia is more popular in the younger generation. This trend in use primarily in youth could be due to a few reasons. First, it is virtually certain that extensive media attention has dramatically increased the level of awareness about salvia and its legal availability through Internet sources, so that most adolescents and young adults have heard about it. Second, it is likely that salvia may be attractive to those experimenting with a hallucinogen but not particularly attractive to chronic drug users. The particularly intense and unpredictable character of the salvia experience, as well as its very short duration, will be unpleasant to many. A majority of the first-time salvia users in the college sample said they would not want to use it again.

A Summary of the Dangers of Classic Hallucinogens

When any substance is taken in high quantities, it can cause toxicity. There have even been reports of individuals who die because of drinking too much water. After the review of many hallucinogenic substances above, the question still remains, how dangerous are hallucinogens? If taken in very high quantities, they are capable of producing toxicity, but do users go to these extremes, and do so repeatedly? The risks of hallucinogen use remains a controversial topic; however, a recent study published by Norwegian authors Teri S. Krebs and Pål-Ørjan Johansen suggests that classical psychedelics such as LSD, psilocybin, and mescaline are not very dangerous. These researchers contacted over 21,000 individuals in the United States who had reported psychedelic use in previous national surveys. They found that lifetime psychedelic users were more likely to be “younger, male, white, Native American, or more than one race, male, have somewhat higher income and more education, not be married, like to test self by doing risky things, experienced an extremely stressful event, and to have used all classes of illicit drugs.” These researchers also looked at the prevalence of mental health issues in psychedelic users. They found “no relation between lifetime use of psychedelics and any undesirable past year mental health outcomes, including serious psychological distress, mental health treatment.” In fact, the use of psilocybin or mescaline at some point in life, or past year LSD use, was associated with a decreased rate of serious psychological distress. It is important to remember that this study only examined LSD, psilocybin, and mescaline use, and not other hallucinogens discussed in this chapter.

Quick Concept Check 6.2

Understanding PCP

Check your understanding of the effects of PCP by listing three major features of PCP intoxication that are significantly different from the effects of other hallucinogens.

Answer: Correct responses can include any of the following: analgesia, amnesia, prolonged stare, absence of synesthesia, absence of mysticism, unpredictable aggression, extreme disorientation, feelings of being cut off from oneself or the environment.

Summary

A Matter of Definition

- Hallucinogens are, by definition, drugs that produce distortions of perception and of one’s sense of reality. These drugs have also been called psychedelic (“mind-expanding”) drugs. In some cases, users of hallucinogens feel that they have been transported to a new reality.

Other classes of drugs may produce hallucinations at high dose levels, but hallucinogens produce these effects at low or moderate dose levels.

Classifying Hallucinogens

- Hallucinogens can be classified into four basic groups. The first three relate to the chemical
similarity between the particular drug and one of three major neurotransmitters: serotonin, norepinephrine, or acetylcholine.

- The fourth, miscellaneous group includes synthetic hallucinogens, such as PCP and ketamine, which bear little resemblance to any known neurotransmitter.

**Lysergic Acid Diethylamide (LSD)**

- LSD, the best-known hallucinogenic drug, belongs to the serotonin group. It is synthetically derived from ergot, a toxic rye fungus that has been documented as being responsible for thousands of deaths over the centuries.
- Albert Hofmann synthesized LSD in 1943, and Timothy Leary led the psychedelic movement that popularized LSD use in the 1960s.
- Although the LSD experience is often unpredictable, certain features are commonly observed: colourful hallucinations, synesthesia in which sounds often appear as visions, a distortion of perceptual reality, emotional swings, a feeling of timelessness, and an illusory separation of mind from body.
- It is now known that LSD effects are due to the stimulation of a subtype of brain receptors sensitive to serotonin, referred to as serotonin-2A receptors.
- In the early 1990s, there was a resurgence in LSD abuse, particularly among young individuals, a trend that began to reverse in 1997.

**Facts and Fiction about LSD**

- LSD does not produce psychological or physical dependence, and has only a slight chance of inducing a panic or psychotic state (provided that there is a supportive setting for the taking of LSD).
- LSD does not elevate one’s level of creativity. It does not damage chromosomes (though there remains a chance of birth defects if a woman ingests LSD when she is pregnant), and a relationship between LSD abuse and violent behaviour has not been established. Flashback experiences, however, are potential hazards.

**Psilocybin and Other Hallucinogens Related to Serotonin**

- Other hallucinogens related to serotonin are psilocybin, LAA, DMT, and harmine.

**Hallucinogens Related to Norepinephrine**

- Mescaline is chemically related to norepinephrine, even though serotonin-2A receptors are responsible for its hallucinogenic effects.
- Two synthetic hallucinogens, DOM and MDMA, are variations of the amphetamine molecule. MDMA (Ecstasy) is currently a popular club drug, but research studies indicate that it poses serious health risks to the user.

**Hallucinogens Related to Acetylcholine**

- A number of anticholinergic hallucinogens, so named because they diminish the effects of acetylcholine in the parasympathetic nervous system, have been involved in sorcery and witchcraft since the Middle Ages.
- These so-called hexing drugs contain a combination of atropine, scopalamine, and/or hyoscyamine. Sources for such drugs include the deadly nightshade plant, mandrake roots, henbane seeds, and the datura plant family.

**Miscellaneous Hallucinogens: Phencyclidine (PCP), Ketamine, and Salvia Divinorum**

- A dangerous form of hallucinogen abuse involves PCP. Originally a psychedelic street drug in the 1960s, PCP quickly developed a reputation for producing a number of adverse reactions.
- PCP reappeared in the early 1970s in smokable forms, either alone or in combination with marijuana. Extremely aggressive tendencies, as well as behaviours resembling acute schizophrenia, have been associated with PCP intoxication.
- Ketamine is popular as a club drug that produces a dream-like intoxication, accompanied by an inability to move or feel pain. Like PCP, ketamine produces amnesia and a potentially hazardous depression in breathing.
- *Salvia divinorum* (or simply salvia) is a Mexican leafy herb with short-duration hallucinogenic effects when smoked, chewed, or brewed as a tea. It is regarded as a “drug of concern,” considering its growing popularity as a recreational drug, although it is not presently classified as an illegal drug under the Controlled Drugs and Substances Act.
Key Terms

Amanita muscaria, p. xx
Atropa belladonna, p. xx
atropine, p. xx
bufotenine, p. xx
cyanosis, p. xx
Datura stramonium, p. xx
dimethyltryptamine (DMT), p. xx
DOM, p. xx
Entactogen, p. xx
ergot, p. xx
ergotism, p. xx
hallucinogens, p. xx
harmine, p. xx
henbane, p. xx
hyoscymine, p. xx
ibotenic acid, p. xx
ketamine, p. xx
lysergic acid amide (LAA), p. xx
lysergic acid diethylamide (LSD), p. xx
mandrake, p. xx
MDMA (Ecstasy), p. xx
mescaline, p. xx
meta-analysis, p. xx
muscimol, p. xx
peyote, p. xx
phencyclidine (PCP), p. xx
psilocin, p. xx
psilocybin, p. xx
Salvia divinorum (salvia), p. xx
scopolamine, p. xx
synesthesia, p. xx

Endnotes

2. Ibid., pp. 17–18.
3. Ibid., p. 19.
20. Ibid., p. 266.


