Introduction
What constitutes a hallucinogenic agent; what is the definition of hallucinogen? What effects are commonly produced by hallucinogens? How are hallucinogenic agents classified? Chemically, what are the structural requirements for hallucinogenic activity? How do hallucinogenic agents work? Interestingly, and perhaps counterintuitively, these questions are roughly listed in descending order of difficulty. Actually, there is more agreement today on how hallucinogens work than on a definition of the term hallucinogen.

Hallucinogens: A Definition
In his book Chemical Psychoses, Hollister (1968) stated that “one can scarcely get any agreement upon the term used to describe this class of drugs” (p. 18). According to Brimblecombe and Pinder (1975), there is “no clear definition or even agreement as to what constitutes [hallucinogenic] action” (p. 1), categorizing hallucinogens into hallucinogenic poisons or agents that produce toxic psychoses (e.g., ethanol, carbon tetrachloride), deliriants (e.g., atropine, hyoscine, benztropine), and psychotomimetics (e.g., lysergic acid diethylamide or LSD). Szara (1994) has argued that the various names for hallucinogens, for example, phantastica, psychotomimetic, psychogenic, psychedelic, hallucinogen, have largely lost their usefulness and may even be misleading. Szara proposes that these agents be termed psychoheuristics. In this chapter, the term hallucinogen is used because it is readily recognized and commonly accepted. How, then, do we define hallucinogenic? The most inclusive definition of hallucinogen was proposed by Hollister (1968). A hallucinogenic agent (Hollister actually favored the term psychotomimetic) meets the following criteria: (1) in proportion to other effects, changes in thought, perception, and mood should predominate; (2) intellectual or memory impairment are minimal at doses that produce the effects just mentioned; (3) stupor, narcosis, or excessive stimulation is not an integral effect; (4) autonomic nervous system side effects are neither disabling nor severely disconcerting; and (5) addictive craving is minimal. These criteria are specific and encompass a wide variety of agents. Using these criteria, Hollister (1968) narrowed the field of “psychotomimetics” to seven categories that include (1) lysergic acid derivatives, such as LSD, (2) phenylethylamines, (2) indolealkylamines, (4) other indolic derivatives (including harmala alkaloids and ibogaine), (5) piperidyl benzilate esters, (6) phenylethylhexyl compounds (including phencyclidine or PCP), and (7) miscellaneous agents (including cannabinoids, kawain, and dimethylacetamide). Using this
definition, it has been possible to pare down psychoactive agents to a more circumscribed group. Nevertheless, this group of agents is still quite broad, and is also heterogeneous with respect to the actions of the agents. It would appear that hallucinogenic agents do not represent a behaviorally homogeneous class of agents.

Within the past decade, the term \textit{classical hallucinogen} has evolved. No formal definition has yet been provided for this class of agents. However, the term may further aid in restricting the types and classes of agents to be considered and might, from this perspective, be useful. It is quite clear that certain agents, such as PCP, THC (\(\Delta^2\)-tetrahydrocannabinol), and LSD do not produce identical effects (Hollister, 1984). In fact, PCP is thought to act via PCP receptors, tetrahydrocannabinol may act via cannabinoid receptors, and such agents are discussed separately in other chapters of this book. Using the Hollister definition as a starting point, classical hallucinogens may be considered those that also possess a basic nitrogen atom and that produce little to no cholinergic or anticholinergic effects. This extension of the original definition essentially eliminates agents such as the piperidyl benzilates (which are potent anticholinergic agents), and the cannabinoids, kawain, and dimethylacetamide (which lack a basic nitrogen atom). Perhaps the best working definition of a classical hallucinogen is an agent that (1) binds at 5-HT\(_2\) serotonin receptors, and (2) is recognized by animals trained to discriminate 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) from vehicle in tests of stimulus generalization (Glennon, 1996).

\section*{Hallucinogenic Agents: Classification}

Classical hallucinogens can be grouped into two broad categories: indolealkylamines and phenylalkylamines. As shown in Table 1 both categories consist of several subclasses of agents; the indolealkylamines include N-substituted tryptamines, \(\alpha\)-alkyltryptamines, ergolines, and, most likely, \(\beta\)-carbolines, whereas the phenylalkylamines consist of the phenylethylamines and the phenylisopropylamines. The phenylethylamines and the phenylisopropylamines differ only in the presence or absence of an \(\alpha\)-methyl group; for example, removal of the \(\alpha\)-methyl group of the phenylisopropylamine DOM results in the phenyl-

\begin{table}[h]
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\caption{Categories of Arylalkylamine Classical Hallucinogens}
\begin{tabular}{|l|l|l|}
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Category & Subcategory & Examples* \\
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Indolealkylamines & N-Substituted Tryptamines & Dimethyltryptamine (DMT)  \\
& & 5-Methoxy DMT  \\
& & 4-Hydroxy DMT (Psilocin)  \\
& & N,N-Diethyltryptamine (DET)  \\
& \(\alpha\)-Alkyltryptamines & \(\alpha\)-Methyltryptamine (\(\alpha\)-MeT)  \\
& & 5-Methoxy-\(\alpha\)-methyltryptamine  \\
& Ergolines & Lysergic acid diethylamide (LSD)  \\
& & 1-Acetyl LSD  \\
& \(\beta\)-Carbolines & Harmaline  \\
& & Harmine  \\
Phenylalkylamines & Phenylethylamines & Mescaline  \\
& & \(\alpha\)-Desmethyl DOM  \\
& Phenylisopropylamines & 2,4,5-TMA  \\
& & DOM  \\
& & DOB  \\
& & DOI  \\
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\end{tabular}
\footnote{For additional examples, see Nichols and Glennon (1984).}
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