**III. HALLUCINOGENS**

A few drugs have, as their primary action, the ability to induce altered perceptual states reminiscent of dreams. Many of these altered states are accompanied by visions of bright, colorful changes in the environment and by a plasticity of constantly changing shapes and color. The individual under the influence of these drugs is incapable of normal decision-making because the drug interferes with rational thought. These compounds are known as hallucinogens or psychotomimetic drugs.

1. **Lysergic acid diethylamide**

Multiple sites in the CNS are affected by lysergic acid diethylamide (LSD). The drug shows serotonin (5-HT) agonist activity at presynaptic 5-HT1 receptors in the midbrain, and it stimulates 5-HT2 receptors. Activation of the sympathetic nervous system occurs, which causes pupillary dilation, increased blood pressure, piloerection, and increased body temperature. Taken orally, low doses of LSD can induce hallucinations with brilliant colors. Mood alteration also occurs. Tolerance and physi- cal dependence have occurred, but true dependence is rare. Adverse effects include hyperreflexia, nausea, and muscular weakness. High doses may produce long-lasting psychotic changes in susceptible indi- viduals. Haloperidol and other neuroleptics can block the hallucinatory action of LSD and quickly abort the syndrome.

1. **Tetrahydrocannabinol**

The main psychoactive alkaloid contained in marijuana is ∆9-tetrahy- drocannabinol [tet-ra-HY-dro-can-NAB-i-nol] (THC), which is available as dronabinol [droe-NAB-i-nol]. This product is prescribed to treat emesis and to stimulate the appetite. Depending on the social situation, THC can produce euphoria, followed by drowsiness and relaxation. In addi- tion to adversely aff ecting short-term memory and mental activity, THC decreases muscle strength and impairs highly skilled motor activity such as that required to drive a car. Its wide range of eff ects includes appetite stimulation, xerostomia, visual hallucinations, delusions, and enhancement of sensory activity. THC receptors, designated CB1 recep- tors, have been found on inhibitory presynaptic nerve terminals that interact synaptically with pyramidal neurons. CB1 is coupled to a G pro- tein. Interestingly, like the endogenous ligands of the opioid system, endocannabinoids have been identifi ed in the CNS. These compounds, which bind to the CB1 receptors, are membrane derived and synthe- sized on demand, and they may act as local neuromodulators (Figure 10.11). The action of THC is believed to be mediated through the CB1 receptors, but this is still under investigation. The eff ects of THC appear immediately after the drug is smoked, but maximum eff ects take about 20 minutes. By 3 hours, the eff ects largely disappear. Dronabinol is administered orally and has a peak eff ect in 2 to 4 hours. Its psychoac- tive eff ects can last up to 6 hours, but its appetite-stimulant eff ects may persist for 24 hours. It is highly lipid soluble and has a large volume of distribution. THC itself is extensively metabolized by the mixed-func- tion oxidases. Elimination is largely through the biliary route. Adverse eff ects include increased heart rate, decreased blood pressure, and red- dening of the conjunctiva. At high doses, a toxic psychosis develops (Figure 10.12). Tolerance and mild physical dependence occur with con- tinued, frequent use of the drug. Dronabinol is indicated as an appe- tite stimulant for patients with acquired immunodeficiency syndrome who are losing weight. It is also sometimes given for the severe emesis caused by some cancer chemotherapeutic agents. The CB1-receptor antagonist, rimonabant [ri-MOH-nah-bant], is effective in the treatment of obesity and has been found to decrease appetite and body weight in humans. Rimonabant is not currently available in the United States because, during clinical trials, it was found to induce psychiatric distur- bances, such as anxiety and depression, which may limit its use.

1. **Phencyclidine**

Phencyclidine [fen-SYE-kli-deen] (also known as PCP, or “angel dust”) inhibits the reuptake of dopamine, 5-HT, and norepi nephrine. Phencyclidine has anticholinergic activity but, surprisingly, produces hypersalivation. Phencyclidine, an analog of ketamine, causes dissocia- tive anesthesia (insensitivity to pain without loss of consciousness) and analgesia. In this state, it produces numbness of extremities, staggered gait, slurred speech, and muscular rigidity. Sometimes, hostile and bizarre behavior is seen. At increased dosages, anesthesia, stupor, and coma may result but, strangely, the eyes may remain open. Increased sensitivity to external stimuli results, and the CNS actions may persist for a week. Tolerance often develops with continued use. Phencyclidine has no therapeutic applications, and manufacture of the drug in the United States is illegal.