5. Addiction
   A. Definition of addiction
      a. An addiction is a disorder characterized by a loss of control of intake of a particular substance and demonstrates psychological dependence (craving) and physical dependence on (physical withdrawal symptoms upon abstinence) the substance.
      b. Some experts argue that psychological and/or physical dependence may not be prerequisites for addiction.
   B. Role of neurotransmitters in addiction
      a. Drugs that are frequently abused (alcohol, cocaine, opiates, nicotine, marijuana) release dopamine in the nucleus accumbens.
      b. Brain imaging studies show alcohol activates the medial temporal lobe (hippocampus and amygdale), the septum and the nucleus accumbens.
      c. Alcohol acts to stimulate the reward cascade causing the release of serotonin, which activates release of endorphins and ultimately releases dopamine.
      d. Decreased dopamine D2 receptor activity in the nucleus accumbens and hippocampus is associated with dysphoria, craving, and compulsive drug self-administration.
   C. The development of an addiction
      a. Compulsive drug use is a hallmark of addiction.
      b. Most people who use drugs do not become addicts. Genetics, stress, life circumstances, and drug availability all play a role in the development of addiction.
      c. Koob and LaMoal (1997) proposed the hedonic homeostatic dysregulation model of addiction which maintains alterations in the reward pathway explains how addiction develops.
         1. This theory holds addiction as a downward spiral that proceeds from an initial failure to self-regulate to a large-scale breakdown of self-regulation.
         2. This model is based on three stages through which addicts cycle: preoccupation-anticipation, binge-intoxication, and withdrawal-negative affect.
         3. As addicts enter the preoccupation-anticipation stages dopamine, endorphin, and stress hormone levels increase to produce pleasure and serve as positive reinforcement, a stimulus that increases the probability of the behavior that precedes it.
         4. The withdrawal-negative affect stage is characterized by reduced levels of dopamine and endorphins and increased levels of stress hormones that result in negative emotions and withdrawal symptoms and serve as negative reinforcement or increase the probability of a behavior by removal of something like withdrawal symptoms when the drug is re-administered.
      d. Tolerance and resetting of an addict’s hedonic set point to higher levels contribute to addiction.
d. Glutamate activity has also been implicated in the development of addiction. Altered gene function appears to increase the availability of glutamate receptors in the ventral tegmental area causing an increase in dopamine release and may explain sensitization observed in some addicts.

e. Stress and increased stress hormone activity are thought to contribute to addiction by increasing drug seeking behavior and symptoms associated with drug withdrawal.

D. Treatment for addiction

a. Early pharmacological interventions focused on alleviating drug withdrawal, however, drug cravings persist long after withdrawal symptoms subside and recent treatments focus on decreasing craving.

b. Drugs that increase dopamine D2 receptor activity, endorphins, or serotonin may promote abstinence.

c. Anti-anxiety drugs, which increase GABA activity, have been used to attenuate withdrawal symptoms.

d. Glutamate antagonists, like acamprosate, may be effective in reducing