Types of Drug Research

Some psychologists study drugs to examine what they do to the brain, behavior, mood, and/or cognition to gain more information about the effects of the drugs. Basic research attempts to increase our understanding of fundamental principles of drug effects and how drugs produce these effects. This type of research can be done with both humans and nonhumans. Other psychologists study how drugs can help individuals. This is applied research, which uses our understanding of drugs and their effects to treat behavioral, cognitive, or emotional problems. By knowing the principles of how drugs produce their effects (e.g., increasing the availability of serotonin in the certain parts of the brain) researchers can then give the drug to humans to test whether it is effective in treating some condition (e.g., depression). With applied research, we have the goal of solving a problem to help an individual. The type of research that scientists do depends on a variety of variables, such as where and with whom they trained, how much and what type of resources are available, and the types of drugs they have access to study, just to name a few.

How do drugs get approved for human use to begin with? In the United States and other many other countries, drugs go through rigorous testing before they are approved for human use. We will briefly discuss the process of bringing a drug to market in the US. It takes between 10-15 years of testing and over $1 billion to bring a drug to the marketplace. Many people wonder why it takes so long and costs so much money.

Part of the reason is that for every 5,000-10,000 compounds screened only 250 of those enter the first stage of testing in nonhuman organisms, called preclinical testing. Of those 250 compounds, only five make it to testing with humans, called clinical testing, and of those five only one gets approval from the US Food and Drug Administration (FDA), the government agency that regulates prescription medications.

Before human testing can begin, for ethical reasons, researchers must test the safety of the drug on at least two species of mammals. This is termed *preclinical testing.* Drugs will be tested for things such as toxicity, for example, whether it damages organs or causes cancer, and even whether it can damage a fetus. The pharmaceutical companies must submit their data on the safety of the drug to the FDA before human testing can begin. Once the FDA approves of the safety of the drug based on the animal work, human testing can begin.

There are four phases of human clinical trials. In Phase I, a small number of healthy individuals (usually about 20-100) receive the drug. These are considered "safety" studies. The purpose is to determine the metabolic and pharmacological action of the drug in humans with different doses. Although this is officially the safety phase, researchers will still try to get a glimpse on whether or not the drug is also effective for the condition it is intended to treat (e.g., depression, high blood pressure). The official phase for testing efficacy is Phase II. In this phase, no more than a few

hundred people with the condition of interest (a particular patient population, such as those with depression) are tested in usually a double-blind, placebo-controlled study, a comparator-drug study, or both. In Phase III, the purpose is to demonstrate the safety and efficacy needed to assess the risk vs. benefit relationship for the intended use of the drug and to provide adequate data for the product package insert. In this phase, thousands of participants from multiple study sites receive the drug.

The package insert is important because it tells the consumer for which conditions the FDA approved the drug. It also contains all of the data from the research that was conducted prior to getting approval to market the drug. Phase IV occurs after the drug has been approved and sold to consumers, and its purpose is to gather data on long-term safety of the drug, as well as to compare its efficacy with drugs that have already been approved and in the marketplace. Once a drug is approved and in the marketplace, it is not guaranteed to remain there. If data gathered in Phase IV indicate a health threat, the FDA can pull the drug off the market and it has done so numerous times.

Additional Drugs

We discussed the general classes of drugs and the prototypical drugs in each category. This short section provides more information on a few select drugs.

MDMA

In addition the psychological effects of MDMA that Dr. Doblin discussed in our interview, the drug also produces a variety of physiological effects. These include increased blood pressure and body temperature, jaw clenching, dry mouth, teeth grinding, sweating, and other autonomic nervous system effects. Users of MDMA also report euphoria (a very positive mood), increased energy, lowered inhibitions, sensitivity to touch, and intensified emotional feelings. In the brain, MDMA induces acute (short-term) release of serotonin and dopamine, two neurotransmitters that are associated with mood and pleasure, among other things.

Phencyclidine (PCP) and Ketamine

Phencyclidine and ketamine are termed *dissociative anesthetics* because cause a dissociation of the individual from reality and their body (e.g., they can produce out of body experiences) and they reduce pain sensations (anesthesia). PCP is considered a dangerous hallucinogenic substance due to its unpredictable effects. Users report dramatic changes in body perception, prolonged confusion, bizarre hallucinations, and, as a result, they may become angry, dangerous, or even unmanageably manic. This can be problematic not only for the user, but also for those interacting with the user. This is especially troublesome for law enforcement or medical personnel because PCP is also an anesthetic. Therefore, the user may not respond to force used to control or subdue the user because he or she is

experiencing an anesthetic effect. Ketamine is used in veterinary practice, but it is also considered a "club" or "party" drug. It produces effects similar to those of PCP, but these effects are not as strong as those of PCP.

Inhalants

The class of drugs termed inhalants includes over 1,000 common household products. Inhalants are most often used and abused by young people, because they are easily accessible, but other populations, such as homeless people, abuse them as well. Inhalant use can result in immediate death, termed *sudden sniffing death*, brain damage, loss of muscle control, and damage to the kidneys, heart, liver, and bone marrow. The inhalants include volatile solvents, aerosols, propellants, gasses, anesthetics (such as nitrous oxide and ether), and nitrates. Signs and symptoms of inhalant use include drunken behavior, headaches, nausea, nosebleeds, watery and red eyes, and a rash around the mouth and nose.

Psychotherapeutics

In this lesson we covered drugs used as medicines, such as the benzodiazepines, that are used effectively as medicines but may also be abused. As we discussed earlier, the drugs that are used as medicines must earn FDA approval. These drugs are prescribed by physicians and psychiatrists to alleviate or reduce the symptoms experienced by those with mental disorders. Although there are a wide variety of these drugs for treating mental disorders, we will briefly discuss the antidepressants used for treating symptoms of depression.

Antidepressants

The antidepressants include three generations of drugs. First we have the monamine oxidase inhibitors (MAOIs). These work by increasing the amount of serotonin, norepinephrine, and dopamine available in certain brain regions. Although effective for some individuals, the MOAIs are not used as often today due to their side effects and toxicity. People who use these substances must avoid certain foods and drug in order to prevent severe and unwanted interactions.

The second generation of antidepressants includes the tricyclic antidepressants. In addition to other effects on neurotransmission, they block presynaptic norepinephrine and serotonin reuptake transporters, which in turn, allows for more availability of those neurotransmitters. These also block acetylcholine, which can result in mental confusion and impaired learning and memory. Although these substances reduce the severity of the depressive episodes as well as the duration, they are not effective for all people.

The newest class of antidepressants is the selective serotonin reuptake inhibitors (SSRIs). These are safer than the tricyclic antidepressants and they work by reducing the uptake of serotonin; this increases the availability of serotonin. The

SSRIs have been approved for major depression, dysthymia, panic disorder, obsessive-compulsive disorder, general anxiety disorder, post-traumatic-stress-disorder, and phobias. Some patients that abruptly stop taking the drug may experience serotonin discontinuation syndrome, a type of withdrawal effect.

Drug Treatment

There are a variety of drug treatment methods available for those who are psychologically and/or physically dependent, and the link below provides a summary of treatment options and strategies.

National Institute on Drug Abuse Drug Facts: Treatment Approaches for Drug Addiction.
http://www.drugabuse.gov/publications/drugfacts/treatment-approaches-drug-addiction