

The Peril and Promise of Hallucinogens

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The hallucinogen class of drugs can be defined as any drug that causes a distortion of your perception, or drugs for which perception distorting effects are stronger than other effects. Three types of perceptual alterations are caused by three different subgroups of hallucinogens. The first subgroup is the classic psychedelics. Members of this subgroup are lysergic acid diethylamide (LSD), *N,N*-dimethyltryptamine (DMT) from ayahuasca, psilocybin from certain mushrooms, and mescaline from peyote cactus. Tetrahydrocannabinol (THC) from cannabis/marijuana is sometimes considered a member of the classic psychedelics group. The second subgroup is dissociatives. This group causes reduced perception of the environment and includes ketamine, phencyclidine (PCP), nitrous oxide, salvia, and dextromethorphan (DXM). The third subgroup is deliriants. Delirium can be caused by atropine and scopolamine.

Many hallucinogens have structures similar to those of natural human brain chemicals and temporarily modify the action of either these neurotransmitters or of the receptors that binds the neurotransmitters. The different subgroups of hallucinogens affect different neurotransmitter systems. Most classic psychedelics are thought to produce their perception altering effects by impacting the action of the neurotransmitter, serotonin, although THC acts on the endocannabinoid neurotransmitter receptors. Most dissociative hallucinogenic drugs interfere with the action of the neurotransmitter, glutamate. Many deliriant hallucinogens interfere with the action of the neurotransmitter, acetylcholine.

In recent years, there has been an expanding legalization of marijuana as well as a number of jurisdictions in the United States decriminalizing psychedelics. It is worth-

while to understand the potential impact of the hallucinogen class of drug on human welfare. Many hallucinogens do not cause addiction symptoms, although several can. In the past year, 2.5% of adults — nearly 6 million people — experienced marijuana use disorder. Likewise, repeated use of PCP can lead to tolerance and a substance use disorder with withdrawal symptoms. Ketamine users can develop signs of tolerance and craving for the drug as well.

Besides addiction, two other negative long-term effects have been associated with use of classic psychedelics, although these effects are rare. Hallucinogen persisting perception disorder (HPPD) is a condition in which certain visual effects of the drug recur even after the drug has worn off. These flashbacks may occur within a few days or more than a year after drug use. These symptoms are sometimes mistaken for other disorders, such as stroke or a brain tumor. Another condition that is associated with exposure to psychedelics is persistent psychosis. Psychosis involves visual disturbances, disorganized thinking, paranoia, and mood changes. For example, heavy cannabis users are more likely to have psychosis than nonusers. The higher the level of use, the greater the chances for psychosis. Researchers are not sure yet whether THC actually causes psychosis, or if there is some other explanation for the link.

Another type of harm caused by this class of drugs is a condition that has been in the news lately called E-cigarette/Vaping Associated Lung Injury (EVALI). Data shows that vaping products containing THC that are obtained off the street or from other informal sources have played a major role in the national outbreak. Vitamin E acetate, an ingredient found in many legal/illegal vaping products, is also strongly linked to the EVALI outbreak. Thankfully, in the months since its peak in September 2019, emergency room visits related to vaping have started to decline.

Despite the potential problems with using

hallucinogens, the drugs and derivatives from them also have some therapeutic potential. Most common is the use of nitrous oxide (aka laughing gas) in dentistry. Ketamine has some veterinary as well as human anesthetic uses. Several cannabis-related products are approved by the Food and Drug Administration (FDA) for certain causes of nausea. Cannabidiol (CBD), a naturally occurring cannabis-derived drug from the same biochemical pathway as THC, has been also approved by the FDA for treatment of certain rare seizure disorders. Further, a specific extract of cannabis was approved as a botanical drug in the United Kingdom for people with multiple sclerosis.

The hallucinogen class of drugs may be effective for psychiatric conditions. A form of ketamine has been FDA approved for treatment resistant depression. In addition, small studies have shown that three additional hallucinogens, LSD, ayahuasca, and psilocybin also hold promise for alleviating depression. In addition, psilocybin shows promising preliminary results in treating obsessive compulsive disorder.

There is emerging evidence that some drugs in this class may be helpful with addiction. Two small studies found significant improvements in abstinence and craving for alcohol and nicotine in dependent individuals after treatment with psilocybin along with psychotherapy. Reductions in alcohol and nicotine use remained significant after six months in both studies.

In each of the coming months, we will discuss individual hallucinogens so we can explore in more detail how it is that a simple molecule can exert such profound effects on our perception of reality.

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