# PSYCHEDELICS

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Mankind has used psychedelic drugs for thousands of years. Originally, plant materials were discovered by many peoples to have the psychoactive properties now associated with known and often synthetic chemicals. In many ancient cultures, the use of these plant materials became incorporated into religious beliefs and practices, with the plants becoming sacraments used ceremonially and medicinally. Some of these sacramental practices continue to this day and are legally sanctioned.

In modern Western science, both the active components of plant materials and newly-synthesized psychedelics have been identified and studied. The isolation of mescaline and psilocybin as the active principals in peyote and magic mushrooms respectively, coupled with the discovery of the activity of lysergic acid diethylamide (LSD) and the synthesis of phencyclidine, has led to the recognition of four main chemical classes of psychedelics. Although each class exhibits unique pharmacological effects, the three types of classical hallucinogens that share major mechanisms of action are the phenalkylamines such as mescaline, the indolealkylamines such as psilocybin, and the ergot alkaloids such as LSD. The more psychotomimetic class of compounds, the NMDA antagonists exemplified by phencyclidine or ketamine, includes dissociative anaesthetics that produce a different profile of effects, overlapping to only a limited degree with the effects of the classical psychedelics.

The psychedelics differ from most other drugs that have been regulated by modern Western cultures as being "drugs of abuse". The most striking difference lies in the typical pattern of use of these drugs. While virtually all other legally defined drugs of abuse generally lead to frequent and uncontrolled consumption in humans and are self-administered by experimental animals, psychedelics are almost always ingested only occasionally by humans and are not self-administered by either rodents or monkeys. Coupled with the absence of any notable withdrawal phenomena associated with discontinuation of psychedelic exposure, these patterns of use indicate that the psychedelics are not "addictive" by virtually any definition of the term.

Scientific research regarding the nature and neurobiological mechanisms subserving the effects of psychedelics flourished briefly after the chemical identification of specific compounds and, especially, the discovery in 1943 of LSD. However, the societal disturbances associated with the widespread popularity of psychedelics in the 1960s led to their legal control and a cessation of most scientific investigations. The tremendous advances in basic neuroscience, and the recognition of the importance of drugs acting on serotonin receptors in the treatment of psychotic disorders, has prompted a revitalization of research involving these compounds in recent years. As a result, important new information is now available regarding the neurobiological systems involved in the profound behavioral effects of psychedelics

in humans as well as in experimental animals, with a particular focus on the neurotransmitter serotonin as a key player. The new insights drawn from this research have important implications for both the treatment of psychotic disorders and for the potential psychotherapeutic uses of the psychedelics themselves.

## SUMMARY

- Historically, psychedelic plant extracts have been used as religious sacraments. These traditions have been modernised by the use and production of LSD.

- There are three types of classical hallucinogens that share major mechanisms of action: the phenalkylamines, the indolealkylamines, and the ergot alkaloids.

- Psychedelics are not addictive - animals do not self-administer these drugs and humans who use them do so intermittently - a rapid tolerance stops continued use. Furthermore, there are no withdrawal symptoms.

- There is no strong evidence that the use of hallucinogenic drugs induces psychosis. Psychedelic states may resemble the very early stages of schizophrenia, but do not resemble the syndrome. Lasting psychoses appear to be associated with a predisposition to schizophrenia. Few enduring effects are seen in animals.

- Due to a lack of official support, there has been a poverty of research into the potential therapeutic applications of the psychedelics. There is little interest from drug companies as small doses are likely to be used on a one-off, or very infrequent basis, and such a limited therapy would not be financially viable for them.

- Serotonin has been identified as a key mediator of psychedelic action. There are different physiological mechanisms associated with serotonin receptor activation underlying different sets of the behavioural experience.

## CONCLUSIONS

- Psychedelics are ancient medicines that have received little scientific attention.

- Psychedelics are not addictive.

- Further studies could increase our understanding of a variety of mental states and potential therapeutics. Therefore, more research needs to be done on this very interesting category of compounds.