Module 1 - Basic Concepts and Context

Unit: What are psychedelics?

Definitions

The word “psychedelic” comes from the ancient Greek psychē (ψυχή, meaning “soul” or “mind”) and dēloun (δηλοῦν, which translates as “revealing” or “manifesting”).

It literally means “mind-manifesting” and it is used to describe a number of specific plants, fungi, substances and products and the consciousness experience they facilitate. The experiences they create have been described as mind-expanding, an altering of perception and a heightened sensory awareness that can reveal unexpected aspects of the mind.

The term was coined in 1956 by the psychiatrist **Humphrey Osmond** in a letter to his friend and author **Aldous Huxley** (1).

In science, the non-ordinary mental state induced by psychedelic substances is often referred to as an **altered state of consciousness (ASC)**, and in popular culture as a “trip.” This state is routinely assimilated to the concept of a “trance,” in which one’s reactions to external stimuli are distinct from those experienced normally, eventually accompanied by psychological, visual, auditory, or other sensory alterations such as synesthesia.

Generally, psychedelics act in relation with the neurotransmitter serotonin, particularly as agonists of the brain’s serotonin 5-HT2A receptor. Psychedelics, or hallucinogens, are:

> psychoactive substances that powerfully alter perception, mood, and a host of cognitive processes. They are considered physiologically safe and do not produce dependence or addiction. Their origin predates written history, and they were employed by early cultures in a variety of sociocultural and ritual contexts.
>
> David E. Nichols (2)

Psychedelics, entheogens or hallucinogens?

The plants, fungi, molecules and products known as psychedelics are sometimes referred to under distinct names such as “hallucinogen,” “fantastica,” or as “psychotomimetic,” “deliriogenic,” “entheogen,” “psychotogenic,” “empathogenic” or “dissociative” substances (1).

Of these, “**hallucinogen**” is particularly common. The National Institutes of Health (NIH) defines “hallucinogens” as:

> *Drugs capable of inducing illusions, hallucinations, delusions, paranoid ideations, and other alterations of mood and thinking. Despite the name, the feature that distinguishes these agents from other classes of drugs is their capacity to induce states of altered perception, thought, and feeling that are not experienced otherwise.*
>
> National Institutes of Health (2)

“Hallucinogen” continues to be relied upon in a number of areas of policy and research. However, the term may not be the most accurate: It derives from “hallucination,” yet not all psychedelics, and not all doses, generate perceptive alterations which can be characterised as “hallucinations.”

In the 21st century, the term “**psychedelics**” is increasingly preferred, since it seems to better reflect the particularity of these substances by not placing too much emphasis on

the objective phenomenon of distorted perceptions (hallucinations) while the ASC induced by psychedelics is a much more multi-faceted, subjective state, than only an hallucination (3). The term “psychedelic” also encompasses substances such as MDMA, whereas “hallucinogen” does not.

The term “**entheogen**” is a term introduced in 1979 (4) also sometimes used. Meaning “the divine within” and is often used when referring to spiritual, religious, or sacramental uses of psychedelics.

Psychedelics vs. “drugs”

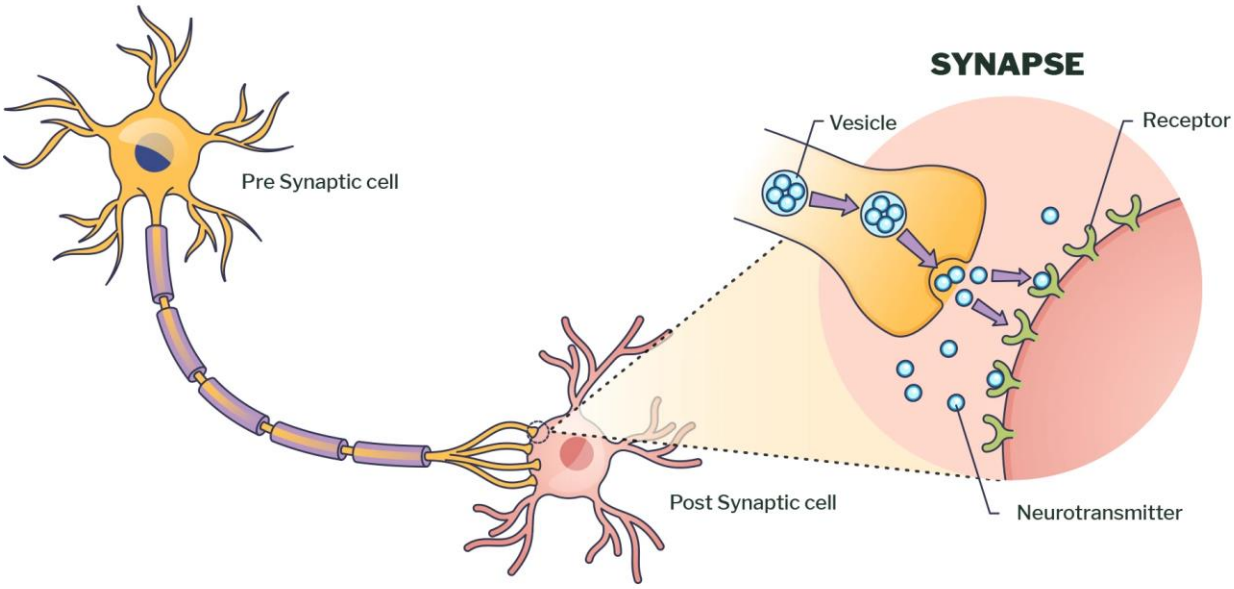
The plants, fungi, and products, substances or products known as psychedelics have been shown to have limited toxicity and behavioural harms to self and others. They have little liability to addiction (chronic uses are extremely limited), and provide a unique experience which can hardly be classified among either stimulant or depressant (or sedative) substances (1).

For this reason, many experts refuse to amalgamate psychedelics with other “drugs” – understood as “substances of abuse,” e.g., alcohol, cannabis, cocaine, opiates or tobacco (2).

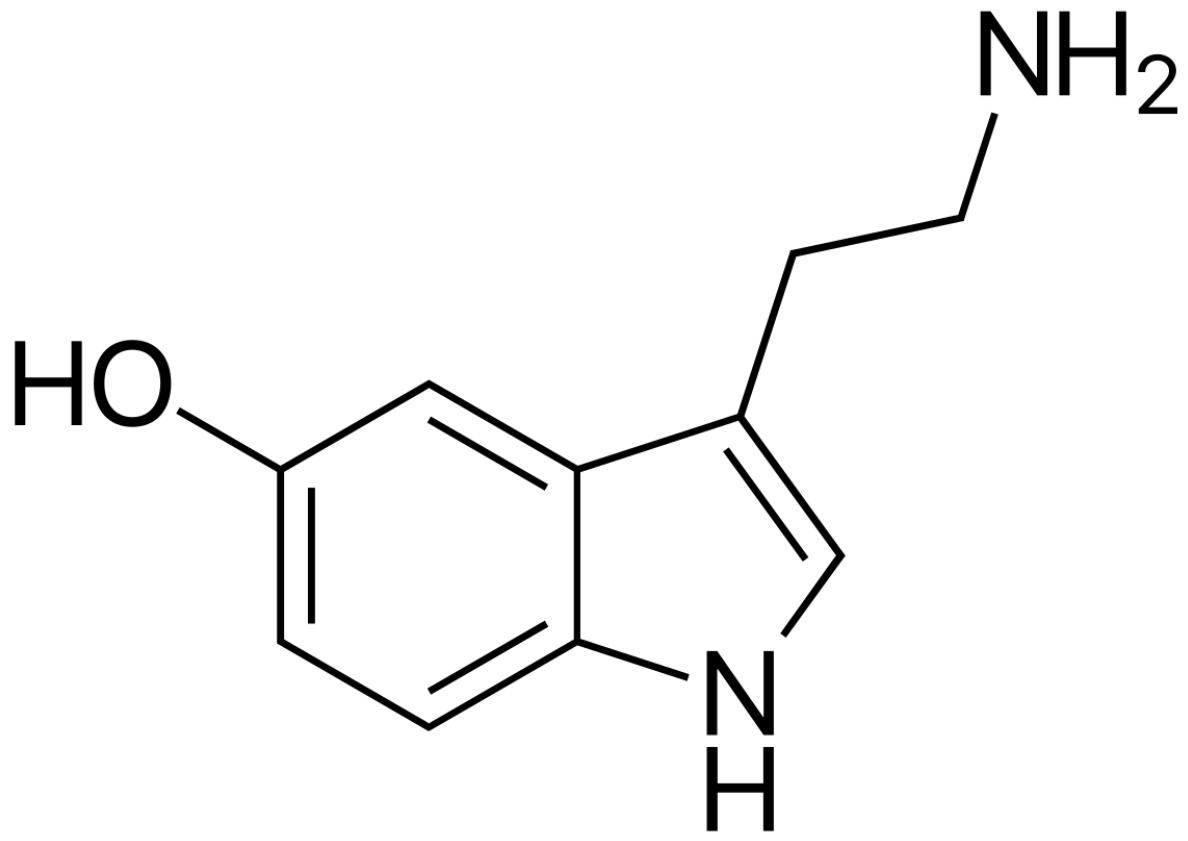
Yet, psychedelics are very often subject to legal limitations of being controlled or scheduled substances, similar to other controlled “drugs,” despite lacking an ample list of evidence-based criteria of harmful effects to justify its control (3). As psychedelics began to face increasing controls in the second half of the 20th century, the terms “narcotic” and “psychotropic” became more common to describe these substances.

Psychedelics and the brain

All psycho-pharmacologically active (also known as “**psychoactive**”) medicines exercise their effects by acting on the neurons in the brain. **Neurotransmitters** are substances that travel between neurons using receptors near the end of the neuron, the synapse, that serve a messenger function to control the passing of information from one neuron to another.

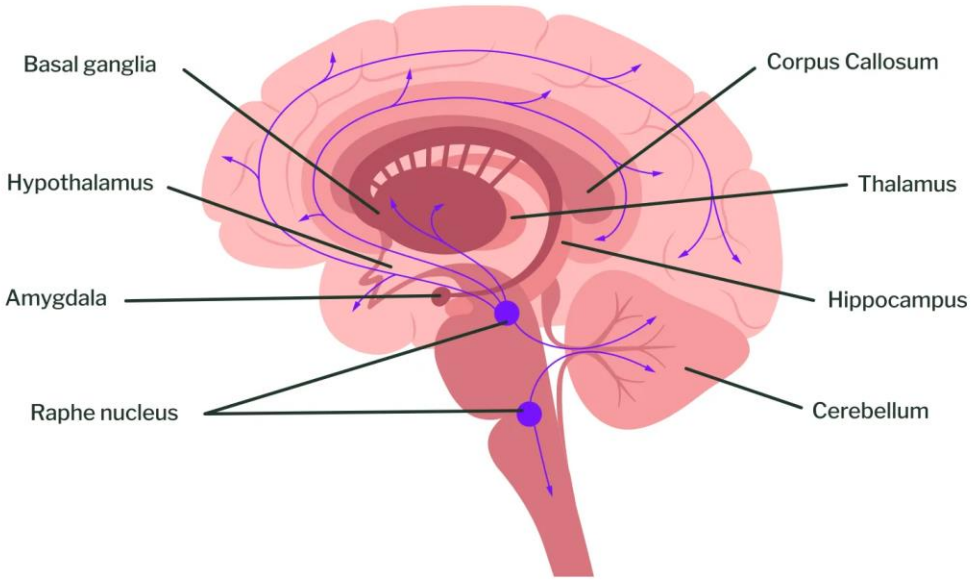


On a chemical and structural level, psychoactive substances are similar to the neurotransmitters that naturally occur in the brain. Because of this resemblance, psychoactive substances can bind to the same neuron receptors and hence alter the transmission of information, thus producing the mind-modifying effects.



SEROTONIN 5-HT

The primary feature of psychedelics is their similarity to the neurotransmitter **serotonin** (5-HT), and their capacity to trigger the serotonergic system of neurons, located in the cerebral cortex. In particular, the action of psychedelics as agonists of the 5-HT2A receptor (often referred to as the 2A receptor) is central to their unique mind-modifying effects.



An abnormal or suboptimal functioning of the serotonergic brain system has been identified as playing a role in a number of medical conditions (e.g., anxiety, depression, PTSD…). The medical potential of psychedelics, in large part, derives from that particular body of research.

Unit: Psychedelics and the law

National psychedelics control

Psychedelics are often distinguished from other “drugs” (such as alcohol, cannabis, cocaine, opiates or tobacco).

Nevertheless, psychedelics are routinely regulated under the strict narcotic or psychotropic laws and policies (“drug control”). The legal status of psychedelics varies importantly depending on the country and on the substance considered. An important number of psychedelics are listed in the international drug control law, that's generally followed by the vast majority of countries (1).

This involves the placement of psychedelics in the schedules, tables lists, or annexes of laws on narcotic drugs or psychotropic substances, which usually translate into important limitations over the production, trade, possession and use. As a result, medical research in the field is subject to extremely strict enforcement measures. The thin line between “doctor and drug dealer” (2) makes research and clinical practice with psychedelics a delicate and risky endeavour in many countries (3).

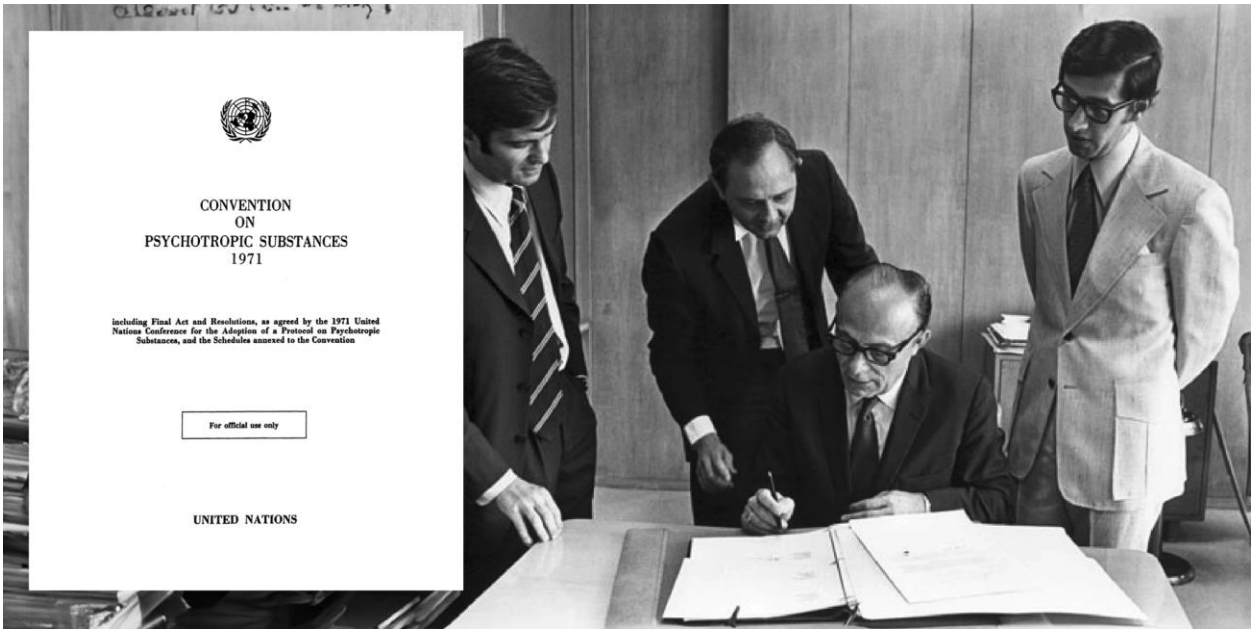
However, there are a large number of countries home to indigenous psychedelic plant and fungi species, often growing wild and protected by cultural or religious laws. Therefore, many of these countries have never placed some of their local psychedelics under drug control. For example, this is the case in Jamaica (for psilocybe mushrooms), Mexico (for salvia and other plants and fungi) and Peru (ayahuasca and San Pedro).

In some instances, countries like Brazil only consider the pure psilocybin molecule to be a controlled substance, leaving the psilocybe “magic mushroom” fungi in a grey area of de facto legality (4). Similarly, in specialised retail shops in the Netherlands, the sale of a number of psychedelics such as the “magic truffles” (a subterranean fungi) is tolerated, but not psilocybin mushrooms. Policy reforms are ongoing in a number of jurisdictions worldwide.

On the other hand, some psychedelics are not subject to international control at all, and often receive little scrutiny from national drug laws. This is for instance the case of iboga and ibogaine, which are not under international control, and are therefore only subject to national controls or prohibitions. (Currently only 13 countries apply such a status, including the U.S. and U.K.(5).)

The Convention on Psychotropic Substances of 1971

The international regulatory framework for psychedelics follows the **Convention on Psychotropic Substances of 1971**, which was adopted and opened for signature at a special United Nations Conference held in Vienna, Austria, in January and February 1971 (1).



In the Convention's annex, there are four Schedules that list the control substances to which specific mandatory or recommended measures of control apply, ranging from Schedule I (most restrictive measures) to Schedule IV (least restrictive) (2).
Psychedelics that fall under the 1971 Convention's control are listed either in Schedule I or II (3):
Schedule I includes drugs claimed to be dangerous, to create a serious risk to public health, and are labelled as having a doubtful or no therapeutic value at all. It is where most psychedelics are listed, and notably (with controversies):

- DMT and analogs

- LSD and a number of related compounds
- MDMA
- Mescaline
- Psilocybin and psilocin
- etc.

Schedule II mostly includes amphetamine-type stimulants and analgesics, but also some psychedelics such as 2C-B and related compounds, or PCP.

Schedule III and IV are lower levels of control, where no psychedelic substance is currently listed.

While mandatory control of substances listed in Schedule II are strict, but do provide leeway for researchers and clinicians, Schedule I establishes a notoriously rigorous regime because the aim was to provide a legal category for the “street drugs” that the Convention sought to ban (4).

Notably, the 1971 Convention only applies to pure, isolated molecules, and clearly excludes plants, fungi, and raw preparations from the scope of its regulations. This is distinct from another important treaty, the 1961 Single Convention, which establishes upfront control over the living plants and herbal materials of traditional psychoactive plant species like cannabis, coca and poppy (5).

While United Nations member states have been adding a number of new synthetic psychoactive substances to the Schedules of the 1971 Convention, among which some are psychedelics, an important number of psychedelics remain outside of international regulations on psychotropic substances. These include ketamine, salvia, iboga and ibogaine, etc (6).

Beyond the 1971 Convention, a number of treaties and international regulations may influence national approaches to psychedelics, for instance:

- Ketamine is listed in the WHO list of Essential Medicines.
- The use of psychedelics for religious purposes, as well as in the context of indigenous cultures and traditions, is protected by human rights instruments, like the Universal Declaration of Human Rights and the international Covenants on Civil and Political rights and on Economic, Social, and Cultural rights.
- Plant- and fungi-based psychedelics fall under international environmental and biodiversity law.

Classifications of psychedelics

Since psychedelics are often listed together at the highest levels of control in the same category or schedule — in both national as well as international laws — legal categorisations are often not very helpful when it comes to classifying and subdividing the category. Additionally, the scheduling of psychedelics is based on classes and classification criteria that don't rely on strong methodology (1) and don't correspond to the actual harms observed (2).

Most psychedelics are often classified into two families (3):

- **Tryptamines:** The most classical psychedelics, many of which are found in plants (e.g., LSD, psilocybin, DMT, ayahuasca) and in animals (some tryptamines are endogenous neurotransmitters of the human brain, like serotonin, melatonin or bufotenin). They principally exert their activity as agonists of the human 2A brain receptor. They are sometimes sub-divided into simple indolealkylamines, complex indolealkylamines and ergolines.
- **Phenethylamines:** This category of psychedelics, often called "empathogens" (which generate a state of empathy) or entactogens ("producing a touching within", (4)), act primarily as a serotonin-releasing agent and has effects that somewhat overlap but are substantially distinct from classic psychedelics. Examples include mescaline, MDMA, 2C-B.

Other categorizations can be found, for example **lysergamides** (psychedelics closely related to LSD, whose chemical structure may relate to both phenethylamine and tryptamine groups) and **complex tryptamines** (substances like ibogaine).

There are other substances often considered among the psychedelics, but which involve different mechanisms of action, and whose classification may vary depending on the jurisdiction, dose and usage, such as ketamine, scopolamine, or the compounds present in salvia and datura.