

# DRUGS AND THE BRAIN

Most of the psychological and behavioural effects of psychoactive drugs is due the interaction they have with the nerve cells in the CNS (which includes the brain and peripheral nervous system). To understand how drugs affect the CNS, we will first examine briefly how the brain works under normal conditions.

The human brain is made up of billions of nerve cells. There is a wide variety of shapes and sizes of brain cells (or neurons), but most consist of:

- the cell body, which directs all the activities of the neuron
- dendrites, like a series of antennae, which receive chemical signals from other cells and relay them to the cell body
- the axon, which has fine nerve terminals. The axon sends messages from the cell body to other neurons, via their dendrites

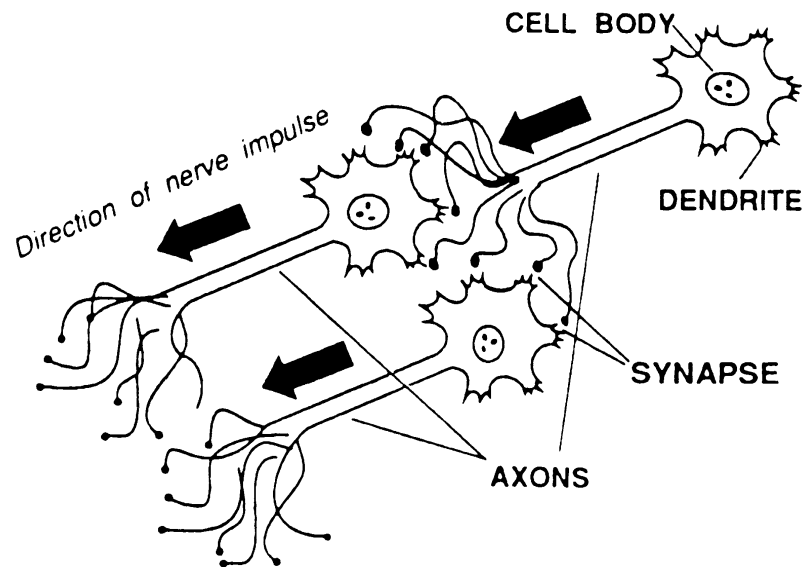
Communication between brain cells is not a simple matter of direct contact between the axon terminal of one cell and dendrites of the next. There is a very small gap between the axon terminal and the dendrites of the adjacent cell, called a synapse. Brain cells communicate when one cell sends an electrical current through the axon. This causes the release of chemicals called neurotransmitters into the synapse. From there they attach (bind) to molecules on the dendrites called receptors. Depending on the type of cell it is and the amount of receptors that bind to the neurotransmitter, this will either trigger or prevent an electrical impulse that causes the brain cell to release (or not) its neurotransmitters, and so on.

Most brain cells produce and release either one or more types of neurotransmitter. Each type of neurotransmitter plays a precise role in the functioning of the brain. Most neurotransmitters can only bind to a specific matching receptor – in the same way as a key can fit into only one type of lock.

Under normal operation, once the chemical communication has occurred, neurotransmitters are either:

- reabsorbed into the original cell, and recycled (reuptake), or
- broken down and deactivated

The following diagram illustrates brain cell activity:



## How drugs effect the central nervous system

Most drug's effect on the brain through their ability to mimic or displace the naturally occurring neurotransmitters. This disrupts or distorts the normal flow of information across the synapses. Some of the ways that drugs are thought to exert their effects are:

- by blocking receptors and preventing neurotransmission
- by inhibiting the production of a neurotransmitter
- by causing a neurotransmitter to be broken down more quickly than normal
- by affecting the receptor site in exactly the same way as a neurotransmitter (opiates and LSD work this way)
- by causing more of neurotransmitter to be produced (amphetamines work this way)
- by inhibiting the breakdown of neurotransmitter, which leads to an artificial build up of the natural substance (cocaine works this way, by preventing 'reuptake' of certain neurotransmitters)

## Homeostasis

When we consume a drug, it alters the levels of neurotransmitters in the synapse. There are a number of biological responses that attempt to restore the rate of neurotransmission to normal levels. This mechanism of regulating neurotransmission and returning it to normal function is called homeostasis.

Homeostasis is a complex set of mechanisms to counteract the effects of the drug. In a single episode of drug use by an occasional user, normal functioning rapidly returns through the reduction in the amount of drug in the body and the action of homeostatic mechanisms.

This may take from a few minutes to a few hours and it depends on the half-life of the drug. Half-life is the time it takes for a drug to fall from its highest level in the blood to half the peak level. This in turn depends on how long it takes the body to process and excrete the drug.

In fact our bodies are constantly making all sorts of adjustments to maintain optimal functioning, such as sweating or '*goose flesh*' when it gets too hot or cold.

## Neuroadaptation or tolerance

The more often a drug is used, the more accustomed the brain becomes to its effects, and the more established its pattern of homeostatic responses to the drug's presence becomes. This is called neuroadaptation. The common effect of neuroadaptation is an increased tolerance to the drug.

A person can be said to have developed a tolerance to a drug when:

- the same dose no longer produces the effect that it used to
- increased doses of the drug are needed to get the same effect

Tolerance becomes known as dependence when not having the drug begins to produce a negative response: the user needs to take the drug to feel '*normal*' rather than to get the effect they first began taking the drug for.

Tolerance often develops to one effect of a drug, but not another. If a tolerance develops to a desired drug effect but not to a harmful effect, this can have very important consequences. This is the case for the heavy user of sedatives/hypnotics. The user takes increasing amounts in order to overcome the tolerance to the CNS depressant effects of sedation and disinhibition or other psychoactive effects – that is, to overcome tolerance to the desired effects. But they have not been developing the same level of tolerance to the respiratory-depressant effect of the drug. So when they increase their dose to maintain the psychoactive effects they want, they may inadvertently take enough to cause respiratory arrest, that is they stop breathing.

## Withdrawal: reversal of neuroadaptation

Withdrawal refers to the physical and mental effects of reducing or ceasing consumption of a drug when a person has developed a tolerance to it.

When regular drug use stops, or is reduced, the altered neuroadaptation balance starts to revert to its original state. This can cause withdrawal symptoms that last until homeostatic mechanisms restore balance (or until consumption of the drug is resumed). In some circumstances, normal functions can be restored in a few days, but in others complete restoration may take a considerable time, or may never be possible (as with the damage caused by long-time heavy alcohol use).

Withdrawal symptoms tend to be the opposite of the effects produced by the presence of the drug in the body. For example the normal effect of amphetamines is stimulation, so the effect of sudden withdrawal is emotional depression. The normal effect of benzodiazepines is relief from anxiety, so the effect of withdrawal is increased anxiety.

The severity of drug withdrawals varies greatly with individuals and circumstances. In extreme cases, and with certain drugs (such as alcohol or benzodiazepines)

withdrawal may require medical intervention as it can be life threatening. The pace of withdrawal will be influenced by:

- the qualities of the drug (including its half-life)
- how much the user has been taking each day
- the length of time the drug has been used
- how frequently the user has been taking the drug
- the user's expectations of the experience
- the physical and psychological well being of the user
- the setting in which withdrawal takes place.

While a small number of people will go through severe or obvious withdrawal, a larger number will go through more subtle experiences, which may include symptoms such as anxiety, confusion, insomnia and depression. Figure 4 illustrates the withdrawal process:

## Tolerance & withdrawal

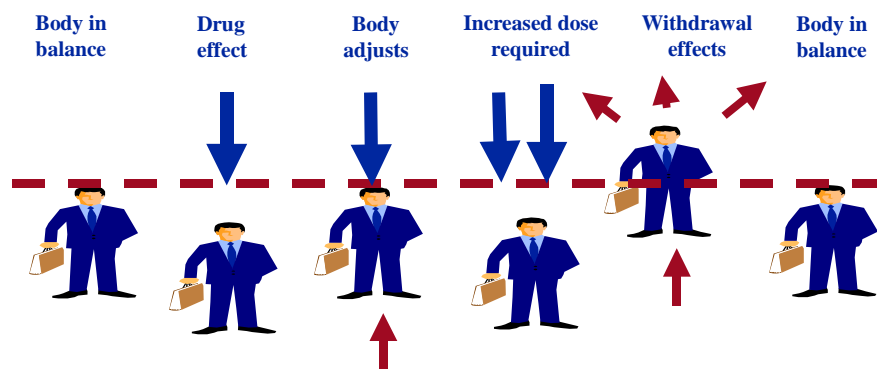


Figure 4. Tolerance and withdrawal

## Overdose

An overdose is the accidental or intentional use of a drug in an amount that is higher than is normally used (subject to tolerance). This type of intoxication presents some degree of physical or psychological harm. The effects of overdose vary with different drugs. An overdose of CNS stimulants will cause anxiety, extreme excitability and a rising of the body's core temperature. An overdose of CNS depressants may cause increased activity initially because of the disinhibiting effects, but will lead to sedation and stupor. In extreme situations, this can progress to unconsciousness and cessation of breathing then cardiac arrest and death.

# FACTORS INFLUENCING THE EFFECTS OF DRUGS

Although people are usually very interested in the effects of different drugs, it needs to be realised that the effects of drugs on the CNS and the effect seen in the user are often two quite different things.

It is true to say that stimulants stimulate the CNS, depressants depress it and hallucinogens distort its perceptions, and that the first two categories are referred to as 'uppers' and 'downers' generally. But it is by no means certain that the same drug will provide the same boost or the same calming effect for two different people.

Factors that influence the effects of drugs are:

## The individual

- the user's state of neuroadaptation to the drug
- their physical health status, for example liver problems
- their age and sex
- psychological factors such as expectations, mental states, social status, motives, personality, current mood and past experiences

## The substance

- the amount, strength and purity of the drug
- any other drugs taken at the same time

## The setting

- where the user is
- who they are with
- their cultural background
- changes in the setting during use.

## The route of administration

As described before, there are five main ways a drug can be taken (orally, by injection, by inhalation, absorption via mucous membranes and skin patches) and this has a significant impact on the effects of the drug in terms of:

- onset (how soon the effects of the drug are felt)
- intensity (how strong the effects of the drug are)
- duration (how long the effects of the drug last)