

# HEROIN AND RELATED OPIATES

DAVID J. NUTT

Psychopharmacology Unit, Bristol University

Heroin is a derivative of morphine and both belong to a large family of drugs called the opiates, that were originally extracted from the resin of the opium poppy and which have been used by humans for millennia. They have strong pain-relieving actions and play a prominent role in the management of severe traumatic and post-operative pain, as well as in terminal care. When used in other circumstances, their profound ability to produce a state of inner tranquility and euphoria can lead to their misuse. Addiction to opiates is due to the often overwhelming desire to re-experience this mental state, and on repeated use many individuals become physically dependent on these drugs. This dependence leads to an unpleasant and sometimes dangerous withdrawal state when drug use is stopped, and the avoidance of this withdrawal helps to maintain drug use.

Opiate painkillers include drugs such as morphine and heroin, as well as the much-used codeine and powerful synthetic analgesics such as fentanyl and buprenorphine. In the brain there are a number of pathways in which endogenous opioid peptides (the endorphins and enkephalins) act as transmitters. Opiate drugs act on the same receptors as natural opioid peptides, but in some circumstances they can produce excessive stimulation of these receptors, leading to great pleasure but also a great risk of dependence and addiction.

Many factors increase the risk of opiate addiction, but the most important factor is the speed with which the opiate gets to the receptors in the brain. Over many centuries of use there has been a series of developments to produce opiates that get into the brain ever more rapidly. Heroin itself is a version of morphine designed to enter the brain faster, but once there it is converted back to morphine. Other ways of accelerating brain-entry involve bypassing the gastrointestinal tract. Taking opiates by smoking or by the intravenous route gets the drug into the blood and brain very quickly, producing much higher levels of stimulation for a shorter period. This pattern of extreme peaks and troughs of opiate action in the brain underpins many aspects of addiction, including the intense degree of craving and drug-seeking behaviour. Intravenous use is also a major cause of secondary illness, especially infections such as hepatitis and HIV.

Understanding of the pharmacology of opiates has helped design and optimize interventions for the treatment of addicts. Some, such as methadone, replace the chaotic use of heroin with the controlled and regulated use of a similar drug, with a longer brain action and a better use profile. Other drugs, such as naltrexone, act to block the effects of heroin in the brain, so making its use pointless. However, the low acceptance of this approach by street addicts means that it is rarely used except in special patient groups such as doctors and pharmacists. Buprenorphine is a new drug that acts partially like an opiate to encourage compliance with treatment and partly like an antagonist to block the effects of heroin should it be taken on top. It has become the main treatment of heroin addiction in France, and is now being used in the UK.

## SUMMARY

- Heroin is easily classified as a hard drug because repeated use often leads to physical dependence and there is a dangerous withdrawal syndrome. Also, overdose can cause death.
- The degree of addictiveness is determined by the speed at which the opiate gets to the receptors in the brain. Therefore, smoking or intravenous use of heroin often leads to addiction, while oral use of opium derivatives poses less of a problem.
- A pattern of peaks and troughs of opiate action in the brain contributes to the craving and drug-seeking behaviour that characterise addiction.
- There are considerable risks related to the route of drug administration. Intravenous use can result in overdose and lead to infections such as hepatitis and HIV. There is virtually no risk of overdose with smoking, but there are risks associated with lung damage.
- There is a potentially lethal dose threshold with full agonists like morphine and heroin. Partial agonists like buprenorphine blunt the activity of the full agonist, making it impossible to exceed this threshold.
- Methadone is used as a heroin substitute rather than a treatment.
- Antagonists like naltrexone stop the agonists working completely, but they are not popular with addicts because they have not even partial heroin-like effects, unlike buprenorphine.

## CONCLUSION

- A growing understanding of opiate action is leading to the development of better treatments. Currently several different combinations of agonists and antagonists are being developed, in an effort simultaneously to improve compliance and reduce heroin use.

## QUESTIONS AND ANSWERS

### **What are agonists and antagonists?**

Agonists are chemical substances which act to mimic and enhance the action of naturally occurring chemicals in the brain. Antagonists act to block the action of such chemicals on the brain's receptors.

### **How are antagonists used to block the effects of heroin?**

Naltrexone is generally taken orally on a daily basis, but it can be implanted under the skin. It blocks the effects of heroin completely. However, individuals experiencing trauma can still be treated for pain whilst taking naltrexone, as some painkillers and anesthetics are still effective. Naltrexone does not block the effects of cocaine.

### **What are the ethical challenges associated with making conformance to treatment with an antagonist a bail condition?**

There are other examples of similar bail conditions that are considered ethical. For example, drink-drivers are offered incentives (shorter ban/smaller fine) if they agree to attend alcohol-dependency programmes and educational courses. The drawback is that most medications only work well with compliance, and those addicts who are willing to comply are likely to be those that least need to take medication to come off the drugs.

### **There are severe ups and downs associated with the use of heroin. Do those who take heroin and manage to live productive lives still have these same usage kinetics?**

All heroin users will experience the highs and lows of addiction over a similar time course, but controllability is a major factor. Some users can maintain a productive life with less marked downs, due to maintenance of supply. The fear of withdrawal increases the motivation for the drug, so the user will seek it more desperately. Maintenance of supply lessens the compulsive behaviours associated with satisfying the habit, thereby cutting crime and unproductive preoccupations.

### **Is it a good idea to prescribe heroin to addicts?**

The Dutch and Swiss experiments suggest that there are benefits to the individual, but with costs to society because of the expense of "shooting galleries." The question is not whether shooting-up is bad, because it obviously is, but whether it is more cost-effective than other methods of treatment. Preventing people fighting and stealing to feed their habits is bound to be beneficial to society but there are other factors, such as cost, involved in its potential as a treatment. To make it less expensive a 'take-home' arrangement is needed, so that addicts come in only once a day for the dosage and then do the rest at home. However, this option has generally been considered politically unfeasible. Some have recommended that for certain individuals the use of prescribed heroin can be the best treatment.

### Is the vaporisation of diamorphine a potential treatment for heroin addiction?

It is virtually impossible to overdose by smoking, but there is likely to be some lung damage. If the heroin is pure, smoking is the preferred means of administration by users. However, due to the impurity of illegal drugs, many addicts prefer to inject as smoking the impure substance is ineffective. It is very difficult to get addicts who are used to injecting to switch to smoking. Once the IV route has been experienced, secondary reinforcers become so powerful that it is difficult for addicts to go back to the inhalation route.

### What is the role of opioid receptors in addiction?

Studies have shown a relationship between the degree of cocaine-craving and opioid receptor activity. Endogenous opioids may well be important mediators of the addictive potential of other drugs, including cannabis.

### Heroin and other Opiates

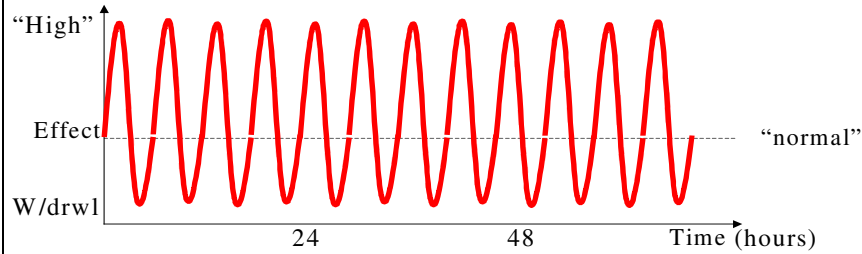
- Derived from poppy sap
- Used for several millennia to reduce pain and alter consciousness
- Active component – morphine
- Mimic natural brain chemicals – the endorphins – have roles in pain and stress
- Act at mu opioid receptors in the brain

### Speeding up brain entry

Faster brain entry → more “rush” and more addiction

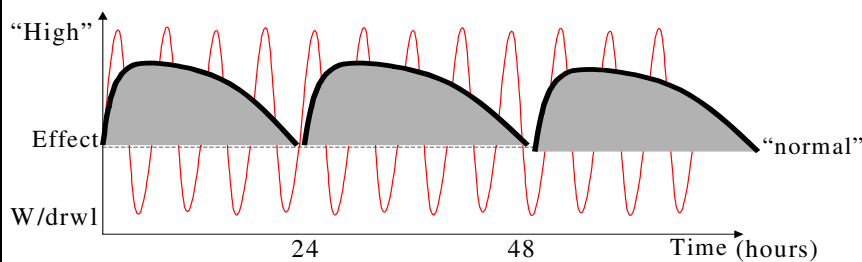


## Heroin - dosing principle



**Heroin** – short half life means brain levels fall fast so user loses effects and gets withdrawal → repeated use

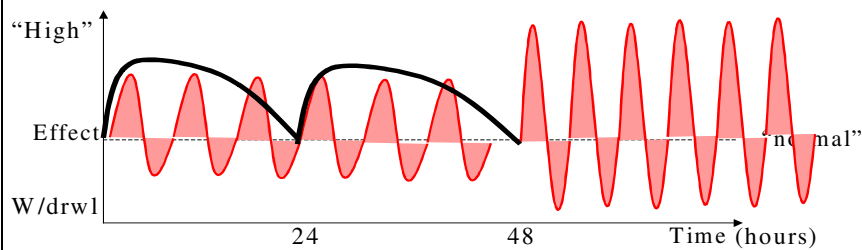
## Slower kinetics → reduced abuse



### Methadone

- slower to peak → less rush
- slower offset → less withdrawal -

## Methadone blocks “on top” heroin



**week end**

### Methadone

- when in brain blocks actions of heroin