

## Cannabinoids and drugs of abuse

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### Introduction

Derivatives of *Cannabis sativa*, such as marijuana and hashish, are the most widely consumed illicit drug: almost half of all 18-year olds in the USA and in most European countries admit to having tried it at least once, and 10% of that age group are regular users. There have been many subjective accounts of the cannabis 'high'. A typical 'high' is preceded initially by a transient stage of tingling sensations felt in the body and head accompanied by a feeling of dizziness or light-headedness. The 'high' is a complex experience, characterized by a quickening of mental association and a sharpened sense of humor, sometimes described as a state of "fatuous euphoria". As reported by Atha and Bianchard [1] in a survey of 1333 young British cannabis users the most common benefit reported were relaxation and relief from stress, insight/personal development and euphoria, but 21% of the users also described some adverse effects, including impaired memory, paranoia and amotivation/laziness. As with other intoxicant drugs, little is known about the brain mechanisms that underlie the cannabis high. The intoxicant effects are clearly mediated via CB<sub>1</sub> receptors. In a well-controlled study in 63 healthy cannabis users [2] who received either a CB<sub>1</sub> receptor antagonist (Rimonabant) or placebo and smoked either a  $\Delta^9$ -tetrahydrocannabinol ( $\Delta^9$ -THC)-containing or placebo marijuana cigarette, Rimonabant blocked the acute psychological effects of the active cigarettes. Moreover, self ratings of cannabis intoxication correlated most markedly with increased blood flow in the right frontal region as demonstrated using positron emission tomography (PET) to measure changes in cerebral blood flow.

The potential ability of cannabis derivatives to produce dependence in humans is still a controversial issue. Earlier clinical literature (for reviews see [3–5]) suggested that tolerance also occurs after repeated administration of  $\Delta^9$ -THC in humans, although many of these studies were poorly controlled. But for many years cannabis was not considered to be a drug of addiction. Withdrawal of the drug did not lead to any obvious physical withdrawal syndrome either in people or in animals, and animals failed to self-administer the drug, a behavior usually associated with drugs of addiction.

Attitudes have changed markedly in recent years. According to the Diagnostic and Statistical manual of Mental Disorders (DSM IV) [5a] criteria