Drug Dependence and social impact

Physical Dependence

Physical dependence is marked by withdrawal symptoms that occur when drug use is ceased or an antagonist is administered. Withdrawal symptoms vary in intensity and duration depending on the drug's pharmacokinetic properties. The mechanisms underlying withdrawal are well-characterized for opioids but apply similarly to cocaine and ethanol withdrawal.

At the cellular level, opioids inhibit cAMP formation, and withdrawal results in a rebound increase in cAMP due to 'superactivation' of adenylyl cyclase. This leads to increased protein kinase A (PKA) activity, enhanced adenosine levels, and activation of cAMP r**esponse element-binding protein (CREB)**. These changes increase the excitability of nerve terminals and neurotransmitter release, including GABA, contributing to withdrawal symptoms (Bagley et al., 2005). Specifically, opioids reduce GABAergic inhibition in the VTA, leading to increased dopamine release. During withdrawal, the sudden removal of the drug's inhibitory effects results in a hyperactivation state. The increased GABA release, though typically inhibitory, now acts as part of a rebound mechanism, exacerbating the discomfort and physiological stress associated with withdrawal. Additionally, the enhanced extracellular levels of adenosine, acting on presynaptic A1 receptors, inhibit glutamate release at excitatory synapses. This action helps counteract the neuronal hyperexcitability that occurs during drug withdrawal. However, this compensatory mechanism is not yet fully understood in clinical practice, and the potential therapeutic use of adenosine agonists in treating drug dependence remains under investigation (Bagley et al., 2005). CREB, which is up-regulated in the nucleus accumbens by prolonged administration of opioids or cocaine, plays a key role in regulating various components of cAMP signalling pathways, and transgenic animals lacking CREB show reduced withdrawal symptoms

Psychological Dependence

Psychological dependence involves emotional and cognitive changes during drug withdrawal, including irritability, stress, anxiety, low mood, and diminished pleasure responses. These changes drive individuals to retake the drug to escape negative emotional states. Craving, a powerful driver of relapse, is triggered by stress or cues associated with prior drug use, such as specific environments or drug paraphernalia (Weiss, 2005; Robbins et al., 2008).

The reward pathways play a central role in psychological dependence. Virtually all major dependence-producing drugs activate the mesolimbic dopaminergic pathway, which extends from the VTA of the midbrain to the nucleus accumbens and limbic regions. These drugs increase dopamine levels in the nucleus accumbens, enhancing the rewarding experience (Koob & Volkow, 2016). Memory of previous drug-induced experiences can be intense and long-lasting, contributing to craving and relapse even after prolonged abstinence. Drugs enhance memory formation by altering synaptic plasticity, a cellular basis for memory. For example, cocaine, morphine, nicotine, and ethanol enhance long-term potentiation (LTP) in the VTA by increasing AMPA receptor expression, while cocaine also induces long-term depression (LTD) in the nucleus accumbens (Hyman et al., 2006).

Genetic and Environmental Factors

Genetic factors account for about 50% of the risk of drug dependence, with the remainder attributed to developmental and environmental influences. Adolescents are more at risk than adults, and factors such as stress, social pressures, and drug availability also play significant roles. Genetic

polymorphisms, such as those affecting ethanol metabolism, can influence an individual's susceptibility to addiction.

Understanding the neurobiological mechanisms and genetic factors contributing to dependence is crucial for developing effective interventions and treatments for addiction. This includes addressing both the physical and psychological components of drug dependence to provide comprehensive care for affected individuals.

Comment on the Use of Addictive Drugs in Present-Day Society

Nicotine and Alcohol

Nicotine and alcohol are legal and culturally accepted substances, despite their significant health risks. Nicotine, primarily consumed through smoking, is linked to cancer, respiratory diseases, and cardiovascular issues. Public health campaigns and smoking bans have reduced smoking rates, but it remains a global health burden. Alcohol, associated with liver disease, cancer, and cardiovascular problems, also contributes to social issues like domestic violence and accidents. Efforts to promote moderate consumption and address binge drinking are ongoing, but alcohol abuse continues to be a major public health concern.

Illicit Drugs (e.g., Heroin, Cocaine, Methamphetamine)

Illicit drugs such as heroin, cocaine, and methamphetamine are illegal and highly addictive, carrying severe health risks including overdose and infectious diseases (HIV) from needle sharing. These substances often lead to criminal behaviour to support addiction, exacerbating societal problems. Despite strict law enforcement and public health initiatives like harm reduction programs, illicit drug use remains a pressing issue. The opioid crisis, particularly in North America, underscores the need for comprehensive strategies combining prevention, treatment, and policy reform.

Cannabis

Cannabis's legal status varies widely; it is legalized for medicinal and recreational use in some regions while remaining illegal in others. Legalization is driven by evidence of medicinal benefits and societal shifts towards liberal drug policies. However, concerns about potential abuse, especially among adolescents, and long-term mental health effects persist.

In summary, the use of addictive substances in society is shaped by cultural norms, legal frameworks, and public health efforts. Addressing the harms of legal substances like nicotine and alcohol, while combating the challenges posed by illicit drugs, requires multifaceted strategies and support for those affected by addiction.