Neuropharmacology of alcohol addiction.

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Despite the generally held view that alcohol is an unspecific pharmacological agent, recent molecular pharmacology studies demonstrated that alcohol has only a few known primary targets. These are the NMDA, GABA(A), glycine, 5-hydroxytryptamine 3 (serotonin) and nicotinic ACh receptors as well as L-type Ca(2+) channels and G-protein-activated inwardly rectifying K(+) channels. Following this first hit of alcohol on specific targets in the brain, a second wave of indirect effects on a variety of neurotransmitter/neuropeptide systems is initiated that leads subsequently to the typical acute behavioural effects of alcohol, ranging from disinhibition to sedation and even hypnosis, with increasing concentrations of alcohol. Besides these acute pharmacodynamic aspects of alcohol, we discuss the neurochemical substrates that are involved in the initiation and maintenance phase of an alcohol drinking behaviour. Finally, addictive behaviour towards alcohol as measured by alcohol-seeking and relapse behaviour is reviewed in the context of specific neurotransmitter/neuropeptide systems and their signalling pathways. The activity of the mesolimbic dopaminergic system plays a crucial role during the initiation phase of alcohol consumption. Following long-term, chronic alcohol consumption virtually all brain neurotransmission seems to be affected, making it difficult to define which of the systems contributes the most to the transition from controlled to compulsive alcohol use. However, compulsive alcohol drinking is characterized by a decrease in the function of the reward neurocircuitry and a recruitment of antireward/stress mechanisms comes into place, with a hypertrophic corticotropin-releasing factor system and a hyperfunctional glutamatergic system being the most important ones.

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