

Neurobiological and genetic aspects of alcohol addiction: a special focus on acetaldehyde, the first metabolite of ethanol

Prof. Etienne Quertemont, PhD

Centre de Neurosciences Cognitives et Comportementales

Université de Liège, Belgium

Although alcoholism is one of the most common forms of addiction, its neurobiological mechanisms still remain unclear. The reinforcing properties of ethanol are mediated by the interaction of multiple neurotransmitter systems, including dopamine, serotonin, glutamate, GABA, endogenous opioids and endocannabinoids. Additionally, long term changes in these neurotransmitter systems are believed to promote the development of alcoholism, probably through specific alterations of brain regions involved in motivation. In humans, it has been clearly demonstrated that alcohol dependence is a genetically heritable disease, at least to some extent. Twin and adoptions studies indicate that 50-60% of the phenotypic variations in alcohol dependence are accounted for by a genetic component. Among the multiple genes that are possibly involved in the development of alcohol dependence and addiction, there is very strong evidence that genes related to the metabolism of ethanol play a major role. For example, genetic polymorphisms in alcohol and aldehyde dehydrogenase enzymes strongly affect alcoholism susceptibility in humans. In recent years, several studies have also provided evidence that acetaldehyde, the first metabolite of ethanol, contributes to alcohol abuse and alcoholism. In rodents such as rats and mice, low doses of brain acetaldehyde induce reinforcing and stimulant effects, although high concentrations of peripheral blood acetaldehyde produce adverse reactions. These results led to the controversial theory that acetaldehyde mediates or at least contributes to the reinforcing and addictive properties of ethanol.