

# Mechanisms of cortical inhibition in alcohol-dependence and –withdrawal and its glutamatergic modulation

## 1. Introduction

Alcohol dependence is of utmost clinical and social relevance in Switzerland. There are approx. 300,000 persons in Switzerland who are alcohol dependent or at risk of becoming alcohol dependent (BAG). Efforts to treat alcohol addiction are hampered by high relapse rates.

There is however a shortage of neurobiological data concerning the understanding of the biological basis of alcohol dependence. The biological mechanisms of the psychoactive effects of alcohol and the central changes induced by chronic alcohol consumption are not yet fully elucidated. Various mechanisms are discussed in connection with the development of alcohol dependence.

At least two different neurobiological pathways which are involved in the development and maintenance of addicted behaviour have been identified. The first pathway involves the opioidergic system and probably the mesolimbic dopaminergic system and may induce alcohol craving and relapse due to the mood enhancing, positive reinforcing effects of alcohol consumption. A second pathway involves several components of the glutamatergic system (in particular NMDA receptors) and may induce alcohol craving and relapse by negative motivational states including withdrawal and stress. In particular conditioned withdrawal and stress-induced relapse are mediated by a hypertrophic glutamatergic system. The NMDA receptor modulator acamprosate is a synthetic compound structurally similar to the naturally occurring amino acid, homotaurine. Acamprosate has an anti-craving effect and is used in the prevention of alcohol relapse. Clinical trials have shown increases in abstinence rates compared with placebo when acamprosate use was paired with appropriate psychosocial and behavioral therapies (1, 2). The precise mechanism of acamprosate in the treatment of alcohol-dependent patients is unclear, it may restore the balance between inhibitory and excitatory neurotransmission in the central nervous system (3).