Ruprecht-Karls-Universität Heidelberg
Medizinische Fakultät Mannheim
Dissertations-Kurzfassung

Neurobiochemistry and volumetry of the anterior cingulate cortex and the hippocampus during acute alcohol withdrawal

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Neurobiological alterations during acute alcohol withdrawal are expected to offer insights into basic principles of the development and maintenance of alcohol dependence and therefor provide targets for individualized treatment. The aim of the present thesis is to translate evidence of preclinical findings from in vitro and animal studies into clinical populations.
In a first step elevated glutamate levels during acute withdrawal in the anterior cingulate cortex, a region involved in motivation and choice, were measured in both humans and rats. Normalization after a few weeks was observed in both species. Glutamine, closely linked to glutamate in the glutamate cycle, was found to be reduced during alcohol withdrawal in rats, indicating elevated glutamatergic neurotransmission. So, this study successfully demonstrated translational evidence of glutamatergic dysfunction during alcohol withdrawal using MR spectroscopy.
In a second step brain volume shrinkage in human alcohol dependent subjects during acute alcohol withdrawal was investigated and compared to healthy controls. Previous reports on lower cortical volumes could be confirmed to be present during alcohol withdrawal. After two weeks of controlled abstinence there was substantial volume regain in several parts of the brain, indicating, that short periods of abstinence are sufficient to activate brain tissue recovery.
In a third study, evidence supporting excitotoxic effects of hyperglutamatergic states in the hippocampus was found in both human alcoholics and rats. MR spectroscopic markers of glutamatergic metabolism were negatively associated with hippocampal grey matter volumes. Furthermore, a reduction in N-acetylaspartate, a marker of neuronal osmosis and energy metabolism, was found during intoxication and vanished within short periods of time. However, in patients showing severe alcohol withdrawal, this recovery of neural integrity was impaired.
Taken together the work presented in this thesis translates preclinical evidence of the glutamate theory of alcoholism into clinical samples, by showing elevated glutamate concentrations during acute withdrawal and associations of higher markers of glutamatergic neurotransmission with reduced grey matter volume. Additionally it provides insights in neurobiological alterations in brain metabolism and brain atrophy during acute alcohol withdrawal in humans and recovery rates therein within a relatively short time of abstinence. By using a highly parallel approach in humans and rats, showing the practicability of the methods as well as new insights into temporal changes within metabolism, this work may inspire both clinical and preclinical research.