



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

**Quantification of hippocampal metabolites with in vivo proton magnetic resonance spectroscopy at 9.4 T in an animal model of depression**

Autor: Sarah Violetta Biedermann  
Institut / Klinik: Zentralinstitut für Seelische Gesundheit Mannheim (ZI)  
Doktorvater: Prof. Dr. A. Sartorius

Recent evidence suggests that alterations of the hippocampal neurotransmitters glutamate and  $\gamma$ -aminobutyric acid (GABA) are associated with the pathomechanism of depression and treatment effects of electroconvulsive therapy (ECT), one of the most effective antidepressant treatment strategies. Thus, proton magnetic resonance spectroscopy ( $^1\text{H}$  MRS) at a 9.4 T animal system seems a promising tool to study underlying mechanisms since it allows for an accurate quantification of metabolites with distinction of glutamate, GABA and glutamine, as well as separation of taurine from choline in the living brain. Therefore, this work established absolute quantification with the help of waterscaling and brain tissue segmentation in a well validated animal model of depression, the congenital learned helplessness (cLH) in rats, resulting in good intra- and inter-individual reliability. Subsequently, the technique was applied for a comparison of antidepressant treatment strategies, namely electroconvulsive shocks (ECS), the equivalent of ECT in rodents, and the tricyclic antidepressant clomipramine, in different strains with respect to depressive-like behaviour. Comparing naïve cLH and wild type (WT) rats significantly lower hippocampal glucose and higher taurine concentrations were found. These alterations were partly reversed by ECS-treatment. Moreover, acute ECS-treatment significantly elevated concentrations of hippocampal glutamate in cLH and WT rats and choline in cLH rats. A positive correlation of learned helplessness (LH) behaviour and hippocampal glutamate in naïve cLH rats was observed. In ECS treated cLH rats, GABA concentrations correlated inversely with LH-behaviour. The findings of decreased hippocampal glucose concentrations and increased taurine concentrations in cLH rats as well as partly diverging effects of ECS in cLH and WT rats indicate a dysregulated hippocampal metabolism in cLH rats. Acute ECS-treatment tends to ameliorate this dysregulation. Even though not immediately leading to improvements in LH-behaviour, an important ECS effect seems to be an early increase of the excitatory neurotransmitter glutamate, which was not observed in pharmacologically treated rats. This initial increase of hippocampal glutamate could be a necessary temporal prelude of an increase of the inhibitory neurotransmitter GABA, since glutamate is a direct precursor of GABA synthesis. In contrast to its neurotoxic effects, glutamate also stimulates neurotrophic pathways. The idea of stimulated plasticity through ECS-treatment is supported by increased choline concentration in ECS treated cLH rats, indicating increased membrane turnover. Longitudinal studies and correlation of  $^1\text{H}$  MRS data with histological and molecular methods are needed to further analyse cerebral characteristics of cLH rats and the mechanism of action of ECS with the aim of gaining a deeper understanding of the pathomechanisms of depression.