The cystine/glutamate antiporter as a potential novel target to modulate the stress response

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Research question and background

In modern society, stress is a major causative factor for a variety of psychiatric disorders. Depression, one of the main causes of disability worldwide, is a multimodal disease with chronic stress considered as a 'trigger' for depressive episodes. Depression and comorbid anxiety are usually related to a malfunctioning monoaminergic system, nowadays however compelling evidence points at an important role of glutamate in the etiology of the 'depressed/anxious brain'. Being the major excitatory neurotransmitter in the central nervous system, glutamate can potentially have important excitotoxic effects. System xc- is the cystine/glutamate antiporter and the major source of extrasynaptic glutamate in some important depression-related brain areas, where it can be an interesting new target for improved psychopharmacological treatment.

Methods and tissues used

In our recent investigation, we have obtained some promising results concerning the role of system xc- in our genetic mutant mouse strain, lacking functional system xc-. Furthermore we are determining the protein expression levels of glutamate transporters in our preclinical animal models for depression. Next to the ample results from animal studies, we aim to look further into the clinical aspects of psychiatric disorders. To unveil the expression levels of system xc- in human patients, we obtained post-mortem hippocampus and cingulate cortex tissue of depressed patients and non-demented controls from the NBB.

Results and conclusion

We are currently processing these tissues to analyze the protein expression levels of the glutamate transporters and compare the results with our previous data.