

# ***Impromptu Seminar***

Venue: Medical University Vienna, Center for Physiology and Pharmacology,  
Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna, "Leseraum".

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Tuesday 16.4.2013 11:00 s.t. **Laszlo Heja** (host: H. Sitte )  
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***„Controlling synaptic function by glial GABA transporters”***

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Abstract.

Several studies demonstrated the ability of astrocytes to sense, respond to and regulate neuronal function. Importantly, astrocytes possess the complete set of membrane proteins to detect GABA, the major inhibitory neurotransmitter of the brain. In addition to ionotropic and metabotropic GABA receptors, astrocytes also express GABA transporters the role of which has long remained uncertain. In this lecture I will present evidence that activation of the glial glutamate transporters by their endogenous substrates triggers the reversal of the closely localized glial GABA transporter subtypes GAT-2 or GAT-3 and lead to an increase of the extracellular GABA level. GAT reversal is initiated by the elevation of the local intracellular Na<sup>+</sup> concentration that subsequently turns back the driving force for the GABA transporters. In addition, we explored the potential physiological and pathophysiological role of the Glu/GABA exchange process in freshly isolated hippocampal slices and in the hippocampus *in vivo*. We demonstrated that the glutamate uptake-induced release of putrescine-derived GABA through astrocytic GATs has a direct impact on the excitability of pyramidal neurons in the hippocampus. The released GABA significantly contributes to the tonic inhibition of neurons in a network activity-dependent manner providing a tuneable, *in situ* negative feedback. We prove that the Glu/GABA exchange mechanism is functioning in the hippocampus under physiological conditions *in vivo*. Importantly, blockade of the mechanism increases the duration of seizure-like events and frequency of glial Ca<sup>2+</sup> spikes in the low-[Mg<sup>2+</sup>] *in vitro* model of epilepsy, demonstrating that the negative feedback control of astrocytes on neuronal excitability offers significant neuro- and glioprotection in pathophysiologically overactivated states.