Excitatory amino acid transporters (EAATs) restrain nucleus tractus solitarii (nTS) activity induced by ionotropic and metabotropic glutamate receptor activation

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Introduction: Glutamate (Glu) is the primary excitatory amino acid neurotransmitter released from visceral afferents in the nTS. Glu binds to postsynaptic ionotropic glutamate receptors (iGluRs, AMPA or NMDA) to induce rapid phasic synaptic currents and depolarization. Glu also binds to metabotropic glutamate receptors (mGluRs), including postsynaptic Grp I receptors to induce a slower depolarization, or alternatively presynaptic Grp II or III receptors to limit terminal activity and attenuate release of Glu via autoreceptor mechanisms. The timing and effect of iGluR and/or mGluR activation is guided not only by the concentration and spatial distribution of these receptors in the synaptic and extrasynaptic space, but also their position relative to uptake transporters that remove extracellular Glu and thus limit receptor activation. Thus excitatory amino acid transporters (EAATs) are critical to preventing over-excitation and maintaining synaptic efficacy.

Objective: To examine the contribution of EAATs on nTS activity induced by iGluRs and mGluRs.

Methods: We recorded synaptic currents and membrane activity in rat nTS slices before and after antagonism of iGluRs and mGluRs.

Results: We showed that EAAT1 and EAAT2 are localized to nTS astrocytes. EAAT block with TBOA increases the static and afferent-induced, phasic release of nTS Glu. The increase in Glu depolarized neuronal membrane potential, induced inward currents and enhanced action potential discharge that are dependent on AMPARs and NMDARs, with a moderate contribution of Grp I mGluRs. Enhanced nTS discharge amplified network-induced spontaneous excitatory synaptic currents (EPSCs). Conversely, antagonism of EAAT and resulting Glu attenuated the amplitude of afferent (TS)-driven EPSCs. The latter reduction was due to activation of mGluR II/III and reduction in presynaptic calcium.

Conclusion: Taken together, our data demonstrate EAATs critically limit activation of ionotropic and metabotropic GluRs, and thus neuronal and synaptic activity. These effects likely influence cardiorespiratory homeostasis and reflex responses to a variety of stimuli.

Keywords: Excitatory amino acid, transporters, nucleus tractus solitari, glutamate, receptor activation

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