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SI Editorial

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Molecular mechanisms of astrocyte-neuron signaling

The mammalian central nervous system is comprised of neurons but also many other cell types. Among these, astrocytes and their involvement in determining synapse function, neuronal properties and network behavior have been the subject of increasingly intense research over the past decades. Especially the ability of astrocytes to sense neuronal and synaptic activity and to modify it in return sparked interest (Araque et al., 2001). Because a single astrocyte can contact on the order of 100 000 synapses (Bushong et al., 2002), bi-directional neuron-astrocyte signaling can powerfully modify the behavior of large synaptic and neuronal assemblies and thus shape their computational properties.

Intense research on the mechanisms of astrocyte-neuron interactions has uncovered a strikingly diverse set of signaling pathways that enable synaptic and non-synaptic astrocyte-neuron interactions (Rusakov et al., 2014). Because their effect on neuronal activity can be opposite even at the same model synapse/preparation it is sometimes unclear what the net effect is and how these mechanisms are coordinated or compartmentalized to provide a physiologically meaningful modulation of synapses and neuronal networks. In addition, these more recently discovered mechanisms of neuron-astrocyte interactions need to be conceptually integrated with classical functions of astrocytes such as neurotransmitter clearance and maintenance of extracellular ion homoeostasis. Given the many potential roles in physiological brain function it is intuitive that astrocyte dysfunction could also contribute to the development of brain diseases. A more subtle additional scenario is that astrocytes are not the primary drivers of brain pathology but amplify or maintain aberrant network activity (Henneberger, 2016).

The articles of this special issue focus on the questions and issues outlined above with emphasis on the relevant molecular mechanisms. A first set of articles is reviewing and presenting recent experimental evidence advancing the understanding of astrocyte glutamate uptake and potassium homoeostasis. Whereas *Rose et al.* give an overview of the mechanisms of glutamate uptake, *Dvorzhak et al.* discuss how their malfunction can contribute to pathway-specific alteration of synaptic transmission. Glutamate uptake is helped by the very negative membrane potential of astrocytes,