Astrocyte Calcium Signal and Gliotransmission in Human Brain Tissue

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Abstract

Brain function is recognized to rely on neuronal activity and signaling processes between neurons, whereas astrocytes are generally considered to play supportive roles for proper neuronal function. However, accumulating evidence indicates that astrocytes sense and control neuronal and synaptic activity, indicating that neuron and astrocytes reciprocally communicate. While this evidence has been obtained in experimental animal models, whether this bidirectional signaling between astrocytes and neurons occurs in human brain remains unknown. We have investigated the existence of astrocyte-neuron communication in human brain tissue, using electrophysiological and Ca\(^{2+}\) imaging techniques in slices of the cortex and hippocampus obtained from biopsies from epileptic patients. Cortical and hippocampal human astrocytes displayed spontaneous Ca\(^{2+}\) elevations that were independent of neuronal activity. Local application of transmitter receptor agonists or nerve electrical stimulation transiently elevated Ca\(^{2+}\) in astrocytes, indicating that human astrocytes detect synaptic activity and respond to synaptically released neurotransmitters, suggesting the existence of neuron-to-astrocyte communication in human brain tissue. Electrophysiological recordings in neurons revealed the presence of slow inward currents (SICs) mediated by NMDA receptor activation. The frequency of SICs increased after local application of ATP that elevated astrocyte Ca\(^{2+}\). Therefore, human astrocytes are able to release the gliotransmitter glutamate, which affect neuronal excitability through activation of NMDA receptors in neurons. These results reveal the existence of reciprocal signaling between neurons and astrocytes in human brain tissue, indicating that astrocytes are relevant in human neurophysiology and are involved in human brain function.

Key words: gliotransmission, glutamate, human astrocytes, intracellular Ca\(^{2+}\), neuron-glia communication