

第76回 生体制御学セミナー

パート 2

Sensing Environmental Energy Needs: Astrocytic Glutamate Uptake Drives Brain Glucose Utilization

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講演内容

As part of the Astrocyte-Neuron Lactate Shuttle (ANLS) hypothesis proposed 25 years ago, it was postulated that astrocytes detect neuronal activity at glutamatergic synapses. The mechanism involves glutamate uptake via high affinity Na⁺-dependent glutamate transporters which is necessary for recycling glutamate and maintaining glutamatergic neurotransmission. As these active neurons need energy, in parallel, it leads to enhanced glucose utilization by astrocytes and release of lactate as a supplementary energy substrate. Such a concept bears an important corollary for brain imaging techniques based on the measurement of glucose consumption rate using the analog deoxyglucose. It predicts that such functional brain imaging techniques indirectly highlight neuronal activation by measuring in reality a surrogate marker for this activity, which is glucose consumption by astrocytes (and not by neurons). In vivo evidence supporting this hypothesis and obtained by two distinct strategies will be presented. In the first case, transgenic mice in which glial glutamate transporters are invalidated have been used to perform cerebral activation visualized by 14C-2-deoxyglucose autoradiography. Results show that following stimulation of the animal whiskers, the normal enhancement in glucose utilization observed in the corresponding barrel cortex of wildtype mice is strongly reduced in knockout mice. In the second approach, using 18Fluorodeoxyglucose (18FDG) and Positron Emission Tomography (PET), it was observed that injection of Ceftriaxone (an antibiotic that was found to stimulate the activity of the glial glutamate transporter GLT1) in adult rats caused an enhancement in the 18FDG signal proportional to the density of glial glutamate transporters. These results obtained in vivo establish that astrocytes represent the primary source of signal for functional brain imaging techniques based on the measurement of glucose consumption rate. Moreover, they suggest that astrocytes might play a critical role for brain function by providing lactate as a necessary energy substrate to sustain certain forms of neuronal activity.

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