第76回　生体制御学セミナー

パート1

Importance of the Neuronal Environment: Role of the Neighboring Astrocytes in Brain Activation

Dr. Anne-Karine Bouzier-Sore

Center of Magnetic Resonance in Biological System, France

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講演内容

The hemodynamic and metabolic responses to brain activation have been the subject of intense investigations in the past twenty years. However, we still do not understand clearly the mechanisms at play. Considering the development and widespread use of brain imaging techniques, it remains of importance to provide valid explanations for the signals monitored in order to provide correct interpretations. In this context, the existence of intercellular lactate shuttling between astrocytes and neurons is of utmost importance. Indeed, in the astrocyte-neuron lactate shuttle (ANLS), it is proposed that astrocytes, the cells in the close environment of neurons, increase their glucose consumption in response to neuronal activation. Using in vivo localized ^{1}H-NMR spectroscopy and functional MRI (fMRI), we were able to follow metabolic fluctuations during brain stimulation and to visualize the activated area, the somatosensory cortex area, also called the barrel field (S1BF). We found that lactate increases in the S1BF during whisker stimulation. Using genetically-modified rats, down-regulated for the lactate transporters (MCTs), we were able to demonstrate that 1) the lactate increase linked to brain activity is lost and 2) no more positive fMRI signal is observed. These results strongly suggest that lactate shuttling is mandatory for brain activation. To go further, if lactate is an important fuel for neurons, we investigated its potential neuroprotective role in a hypoxic-ischemic pup model (rat). We will present results showing that lactate (and not pyruvate or glucose) administrations lead to early brain lesion regression as well as nearly complete motor and memory recoveries at later time. This presentation will therefore illustrate the importance of cerebral lactate shuttling, from physiological situation to therapeutic application.

問い合わせ先：塚原伸治(内)4352

stsuka@mail.saitama-u.ac.jp