Athophysiological findings in age-related brain disorders in small animals

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The incidence of age-related brain disorders tend to increase in human medicine and also in veterinary medicine. It has been widely accepted that free radicals play an important role in these disorders and also in ischemia/hypoxia-induced neuronal cell death by their severe cytotoxic effects, such as lipid peroxidation and protein denaturation in cell membrane followed by the alteration of the membrane fluidity, enzyme properties, and iron transport.

To elucidate mechanisms of free radical-induced neuronal cell death, lipid peroxidation measured as thiobarbituric reactive substances (TBARS), three antioxidative enzyme activities (superoxide dismutase, glutathione peroxidase, and catalase), and cytosolic free Ca2+ (Ca2+i) were examined in rat hipocampus-derived cell (HV16–4) exposed to free radicals generated by hypoxanthine-xanthine oxidase system. The viavility of cells decreased with an increase in numbers of free radical positive cells in a dose-dependent manner of xanthine oxidase. The protein-bound TBARS did not change, whereas free TBRS increased. No remarkable change was observed in antioxidative enzymes. Cytosolic Ca2+ increased after exporsure followed by cell death. The addition of Co2+ or nonspesific Ca2+ blocker, delayed the increase of Ca2+i and subequent cell death. Thses results suggested that the increase of Ca2+ influx played a crucial role for neuronal cell death induced by free radicals.

On the other hand, adenosine A1 or benzodiazepine receptor is considered to be an available marker for the neuronal cell conditions. To elucidate changes of the distribution of these receptors in cat brain with experimentally induced ischemia, positron emmision tomography (PET) was carried out using selective ligands against these receptors. On the PET images before the middle cerebral artery occulusion, the highest of the distribution volume was observed in the cerebral cortex and lowest was found in the mid brain on both adenosine A1 and benzodiazepine receptors. After the occulusion, no remarkable changes of both distribution volumes were observed in the cat brain. However, both distribution volumes decreased in the infarction areas confirmed by the magnetic resornans imaging. These results suggested that adenosine A1 and benzodiazepine receptors are closely related to neuronal cell death caused by ischemia.

References

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