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ゼブラフィッシュを用いた新規脳梗塞モデルの作出とグルタミン酸神経系の関与

Establishment of a novel cerebral infarction model using zebrafish and involvement of the glutamate nervous system

○久米 利明[1]
○Toshiaki Kume[1]

1. 富大院薬
1. Grad Sch Pharm Sci, Univ Toyama

Cerebral infarct is caused by cerebrovascular occlusion and results in brain damage. Stroke, including cerebral infarct, is major cause of death in the world. Development of therapeutic agent and further investigation of pathology is required because drug development based on neuroprotection is not enough. Reperfusion-induced neuronal dysfunction plays an important role in pathological process. There is a need for new disease models that contribute to the development of therapeutic agents based on various strategies. Therefore, we started a study using zebrafish because embryos and larvae were transparent and easy to observe in a live state. Although it has been reported that hypoxia causes brain cell damage in adult zebrafish, effects on blood vessels and blood flow are not known. Thus, the effect of hypoxia on blood flow was examined. Focusing on DA, as the trunk blood vessel, and MMCtA, as the brain blood vessel for quantification, it was found that MMCtA stopped blood flow significantly earlier than DA. These results suggested that reoxygenation immediately after the blood flow of MMCtA was stopped causes the reperfusion of the cerebral blood vessels. In fact, cerebral blood vessels reperfused after a certain period of time by performing reoxygenation immediately after the blood flow of MMCtA was stopped. Furthermore, in zebrafish, it was found that cerebral parenchymal cells were damaged by cerebral ischemia-reperfusion and astrocytes were activated. Treatment with MK-801, an NMDA receptor antagonist, and edaravone, a radical scavenger, suppressed brain cell death. These results indicate that this model reflects important elements of cerebral infarction pathology, such as NMDA receptor and ROS-mediated neuronal damage, and activation of astrocytes.