S47-5 Development of glucose intolerance and neuronal damage in cerebral ischemic stress

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Hyperglycemia, one of the risk factors for cerebral stroke, is known to be induced by ischemic stress *per se*, while details remain unclear. Here, we focused on the relationship between ischemic neuronal damage and post-ischemic hyperglycemia. In addition, we examined the effect of known anti-diabetic drugs on the development of ischemic neuronal damage.

We performed 2 hr of middle cerebral artery occlusion (MCAO) in male ddY mice. At 24 hr after MCAO but not at 72 hr, fasting blood glucose levels were significantly elevated comparing to sham group. At the same time, insulin secretory activity or insulin receptor sensitivity was significantly decreased. On the other hand, the development of neuronal damage was observed at 24 hr and gradually increased up to 72 hr after MCAO. Interestingly, inhibition of post-ischemic hyperglycemia by insulin administration completely suppressed the neuronal damage observed at 72 hr after MCAO. Furthermore, anti-diabetic drug metformin, an AMP kinase (AMPK) activator, could also inhibit the post-ischemic hyperglycemia and neuronal damage when administered systemically. Although AMPK is expressed in brain as well as liver or skeletal muscle, central administered metformin did not effect at all, suggesting the important role of activation of peripheral AMPK.

These results indicate that the improvement of hyperglycemia or normalization of blood glucose levels after cerebral stroke is needed to obtain good prognosis in cerebral stroke.