2-LBS-21 LBS**Involvement of central L-lactate and AMP-activated protein kinase in fear memory in diabetic mice**

Aimi Yamagishi¹, Daiki Ueda¹, Naomi Yonemochi¹, Junzo Kamei², Hiroko Ikeda¹

¹Dept. Pathophysiol. Ther., Hoshi Univ Sch. Pharm. Pharmaceut. Sci., ²Dept. Biomol. Pharmacol., Hoshi Univ Sch. Pharm. Pharmaceut. Sci.

The prevalence of mental disorders in diabetes mellitus is reported to be higher than that in general population. However, its mechanism is unclear. Since glucose is metabolized to L-lactate in the astrocytes of the brain and L-lactate suppresses AMP-activated protein kinase (AMPK), we investigated whether L-lactate and AMPK in the brain are involved in fear memory in streptozotocin (STZ)-induced diabetic mice. In the conditioned fear test, L-lactate injection increased freezing. In addition, injection of the AMPK inhibitor compound C also increased freezing. Freezing induced by both L-lactate and compound C was inhibited by the AMPK activator AICAR. We next examined the levels of L-lactate and AMPK in the amygdala and the hippocampus, which are known to play important roles in fear memory. L-lactate was increased in the amygdala and the hippocampus in STZ-induced diabetic mice. In contrast, phosphorylated AMPK, which is an active form of AMPK, was reduced in the amygdala and the hippocampus in STZ-induced diabetic mice. In addition, the increase of freezing in STZ-induced diabetic mice was suppressed by AICAR. These results suggest that L-lactate production is increased in the amygdala and the hippocampus in diabetes, which enhances fear memory through inhibition of AMPK.