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

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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.