論 文 要 旨

The pivotal role of pituitary adenylate cyclase-activating polypeptide for lactate production and secretion in astrocytes during fear memory

Background Pituitary adenylate cyclase-activating polypeptide (PACAP) plays an essential role in the modulation of astrocyte functions. Although lactate secretion from astrocytes contributes to many forms of neuronal plasticity in the central nervous system, including fear learning and memory, the role of PACAP in lactate secretion from astrocytes is unclear.

Methods The amygdala and hippocampus of PACAP (+/+) and PACAP (-/-) mice were acquired one h after memory acquisition and recall in the passive avoidance test. The concentration of glycogen and lactate in these regions was measured. The concentration of lactate in the hippocampus's extracellular fluid was also measured by microdialysis during memory acquisition or intracerebroventricular administration of PACAP.

Results We observed that memory acquisition caused a significant decrease in glycogen concentration and increased lactate concentration in the PACAP (+/+) mice's hippocampus. However, memory acquisition did not increase in the lactate concentration in PACAP (-/-) mice's hippocampus. Further, memory retrieval evoked lactate production in the amygdala and the hippocampus of PACAP (+/+) mice. Still, there was no significant increase in lactate concentration in the same regions of PACAP (-/-) mice. In vivo microdialysis in rats revealed that the hippocampus's extracellular lactate concentration increased after a single PACAP intracerebroventricular injection. Additionally, the hippocampus's extracellular lactate concentration increased with the memory acquisition in PACAP (+/+) mice, but not in PACAP (-/-) mice.

Conclusions PACAP may enhance lactate production and secretion in astrocytes during the acquisition and recall of fear memories.

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