

Nose-to-brain delivery of CGRP against fear memory retention in mice

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We previously reported that intracerebroventricular administration of calcitonin gene-related peptide (CGRP) effect on hippocampus-dependent fear memory in mice. Although CGRP plays an important role in central nervous system, it seems to be degraded before reaching the brain by intravenous administration. The intranasal route offers an alternative approach for drug delivery to the brain without the interference of the blood-brain-barrier. In this study, we evaluated the nose-to-brain delivery of CGRP to investigate the effects on fear memory retention by contextual learning test. 8-week-old male C57BL6J mice were examined to contextual fear learning test. Mice were given a 0.3 mA foot shock. After fear conditioning, mice were given saline or CGRP (0.5 nmol) by intranasal administration (i. n.). CGRP injections shortened the freezing time when compared to saline. Next we also evaluated *Bdnf* or *Npas4* mRNA in mice hippocampus. As same as intracerebroventricular administration, CGRP i.n. significantly increased the level of *Npas4* rather than saline treatment. *Bdnf* level were also significantly increased. These results suggest that nose-to-brain delivery of CGRP alleviate the fear memory with increases *Npas4* and *Bdnf* in mice hippocampus.