Reversal of age related learning deficiency by the vertebrate pituitary adenylate cyclase activating polypeptide (PACAP) in *Lymnaea*

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The common pond snail (*Lymnaea stagnalis*) has been extensively used as a model system for studying the cellular and molecular mechanisms of associative learning and memory [1]. The main advantage of this system is that animals can learn after a single trial food reward conditioning and the memory can be recalled even after 3 weeks [2]. However this robust, "flash-bulb" like memory can only be induced in young adults (3-4 months old); aged snails (over 6 months) can not learn the association after only one training trial [3]. Recently we have shown that the homolog of the vertebrate PACAP and its receptors (PAC1-R, VPAC1 and VPAC2) exist in *Lymnaea* and PACAP activates the adenylate cyclase enzyme [4], just like in the vertebrate nervous system. We first tested the hypothesis that PACAP plays an important role in the formation of robust LTM after classical food-reward conditioning. Our earlier findings provided the first evidence that PACAP is both necessary and instructive for fast and robust memory formation after reward classical conditioning in young animals [5]. Here we tested the role of PACAP in learning in aged animals by looking at its effect on the formation of long-term memory after single trial appetitive conditioning. Our new results show that systemic injection of synthetic PACAP 1h before training boosts memory formation in old animals. Since PACAP is a highly conserved molecule, our results indicate that it has an important role in learning and memory in general and it can also be used as a memory "rejuvenating" agent during normal biological ageing.

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