

**Possible role for Serotonin and Octopamine as specific signals, during reinforcement learning, in the vertical lobe of *Octopus vulgaris*.**

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Octopuses uniquely combine vertebrate advanced behavior with a relatively simple invertebrate brain. This feature makes them an ideal preparation for comparative analysis of brain mechanisms evolved to mediate complex behaviors. In previous studies in the octopus vertical lobes (VL), a pivotal brain region in its learning system, we have demonstrated activity dependent synaptic plasticity mechanisms (LTP), analogous to suggested mechanisms for learning and memory in mammals<sup>1,2</sup>. Recently, we showed that serotonin is a facilitatory neuromodulator of synaptic transmission in the VL<sup>3</sup>. In the current research we found a similar effect by octopamine. However, in contrast to serotonin, which enhances induction of LTP by high frequency stimulation (HF-LTP), octopamine blocks induction of HF-LTP and depotentiates LTP when co-exposed with IBMX (increases intracellular cAMP and cGMP). Based on our previous and current work we hypothesized that serotonin and octopamine serve as specific reinforcement signals during learning, allowing the octopus to associate between a situation and its consequences. In conjunction with results in mammals and insects our research shows the universal importance of neuromodulators that, together with activity dependent plasticity, determine the computational properties of learning and memory networks in animals with complex behavior.

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- 2 Hochner, B., Brown, E. R., Langella, M., Shomrat, T. & Fiorito, G. A learning and memory area in the octopus brain manifests a vertebrate-like long-term potentiation. *J Neurophysiol* **90**, 3547-3554 (2003).
- 3 Shomrat, T., Feinstein, N., Klein, M. & Hochner, B. Serotonin is a facilitatory neuromodulator of synaptic transmission and "reinforces" long-term potentiation induction in the vertical lobe of *Octopus vulgaris*. *Neuroscience* **169**, 52-64, doi:10.1016/j.neuroscience.2010.04.050 (2010).