

A Neuromodulator Exerts Antagonistic Effects on the Network State of *Aplysia californica*

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Network states are prevalent in virtually all behaviors. In most cases, they are established by the actions of neuromodulators. To produce articulate behaviors, neuromodulators upregulate the modules involved in one behavior and inhibit their behavioral antagonists. An interesting question is what occurs when one neuromodulator exerts antagonistic effects on the same module. What are the consequences for the generation of behavior? This question was explored in the marine mollusk *Aplysia californica*. The *Aplysia* feeding central pattern generator produces ingestive behaviors whose strength and duration depend on the network state at the moment of stimulation. Activating the command neurons CBI-2 and CBI-3 releases neuromodulators that configure ingestive motor outputs. Likewise, repeated stimulation of CBI-2 primes the network to produce ingestive outputs. Here, it was found that the CBI-3 neuromodulator, APGWamide, reduces the excitability of motor neurons involved in ingestion, despite also upregulating the activity of these cells through their synaptic inputs. Notably, this does not drive motor output antagonistic to the ingestive network state. Rather, motor output remains strongly ingestive. Here, it is postulated that APGWamide cancels the persistent modulatory effects of CBI-2 peptides which drive ingestive priming. Therefore, when CBI-2 and CBI-3 are stimulated together, CBI-2 induced ingestive priming does not occur. This finding may have implications in the study of the Pre-Bötzinger complex, an area critical for the generation of breathing, where the actions of one neuromodulator are contingent on the presence of the other neuromodulators in the network.

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