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The effects of nitric oxide on the modulation of the cardiac system of the American lobster, *Homarus americanus*, via a peptide (GYSDRNLRFamide)

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The central pattern generator (CPG) is a neural network that controls the rhythmic patterned outputs, which generate locomotion as needed. The lobster provides a good model to study CPGs because it has a relatively simple CPG. The lobster CPG, or cardiac ganglion accommodates for a range of activities and changes in the environment (Cooke, 2002).

The small lobster CG is made up of nine neurons that control the neurogenic heart. The lobster CG is located on the inner dorsal wall of the heart and forms long neurites that branch onto the heart muscle. The CG, through an intrinsic mechanism, generates patterned and rhythmic bursts to the heart (Cooke 2002).

The *H. americanus* CG sends information to the heart muscle to regulate the heart beat. The patterned bursts from the CG need to be adjusted in response to changing demands, for example, activity level or blood volume. Two general mechanisms, intrinsic feedback and extrinsic neuromodulation, have been identified to facilitate this adjustment. Through an intrinsic feedback mechanism, the muscle sends information back to the CG via a positive pathway and a negative pathway. In the positive pathway, stretch-sensitive dendrites of cardiac neurons increase the frequency of heart contractions when stretched (Cooke 2002). In the negative pathway, nitric oxide (NO), produced by the cardiac muscle, slows the frequency (Mahadevan et al. 2004). The interplay between the negative and positive feedback pathways regulates the output of the CG. An extrinsic mechanism has also been identified to regulate the CG output. Chemical neuromodulators that are released either locally or as hormones signal to the heart or CG to modulate ganglion activity. The intrinsic and extrinsic mechanisms affect the contraction amplitude and frequency of the heart.

Within this simple invertebrate organism, a complex layering of control exists. Studies of the effects of various extrinsic modulators suggest that these modulators may alter how the feedback pathways operate. I examined what effect the neuromodulator GYSDRNLRFamide (GYS), a peptide found in the lobster nervous system, has on the balance between the positive and negative pathways (Ma et al., 2008). Recent experiments have demonstrated that when GYS was applied at high concentrations in the whole heart, the frequency decreased. This suggests that GYS may play a role in the intrinsic feedback pathways, and likely enhances the negative pathway.

I looked at if nitric oxide altered the modulation of the heartbeat frequency when enhanced by the extrinsic modulator, GYS. Based on previous experiments, I hypothesized that GYS allows the NO, or negative pathway to predominate. In order to test my hypothesis, I examined the effects of GYS when I removed nitric oxide, which allows the negative pathway to exist. I compared the characteristics of the heartbeat when saline was run through the heart to when GYS was run through the heart. I also compared the characteristics of the heartbeat when the NO inhibitor, L-NA, was applied to when GYS was applied in the presence of L-NA. I finally compared the changes in frequency between these two comparisons. I found a significant difference between the change in frequency of the heart perfused with GYS in saline as opposed to perfused with GYS in L-NA. GYS had a greater negative effect without L-NA. These results demonstrate that NO is likely the cause of the observed decrease in frequency.

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