Is stretch feedback in the heart of *Homarus americanus* modulated by neuropeptides*?*

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Central pattern generators (CPGs) are neuronal networks that produce a consistent rhythmic motor output to generate behaviors such as eating, walking, and breathing. One central pattern generator is the cardiac ganglion (CG), which controls the heart of the American lobster and is responsible for generating patterned bursts of action potentials, each of which results in a contraction of the heart. The cardiac ganglion includes four premotor and five motor neurons, as well as stretch-sensitive dendrites, which extend from the CG neurons (Cooke, 2002).

Two intrinsic feedback pathways modulate the bursting pattern of the CG. A negative feedback pathway using nitric oxide decreases contraction frequency, while feedback from the stretch-sensitive dendrites generally increases contraction frequency. The stretch of CG dendrites carries information about the filling of the heart to the rest of the CG. In addition, extrinsic modulation via neuromodulators plays a key role in achieving flexibility. However, the extent to which the heart's feedback system is modulated is still unknown. Here, we asked whether neuromodulators alter the positive stretch feedback system itself.

One family of modulatory peptides that modulate the CG is the FMRFamide-like peptides. In *Homarus americanus*, two FMRF-amide-like peptides, SGRNFLRFamide (SGRN) and GYSDRNYLRFamide (GYS), have been found to alter contraction amplitude and frequency by actions at multiple sites. Data suggest that they may alter feedback as well, with SGRN favoring positive feedback and GYS favoring negative feedback (Dickinson, et. al., 2015).

Though it was predicted that SGRN enhanced feedback, whereas GYS inhibited feedback in the muscle (Dickinson, et. al., 2015), preliminary data looking into these effects has suggested that both SGRN and GYS inhibit the stretch response by decreasing the changes in burst characteristics elicited by stretch (Dickinson, et. al., 2015, Qu, 2017). With these contradictory results, the goal of this study was to further look into how these two neuropeptides, SGRN and GYS, modulate the response to stretch in order to understand whether or not feedback itself is modulated.

To investigate this prediction of the effects of the neuromodulators on stretch, a reduced preparation with just the muscle surrounding the premotor neurons was used. The muscle and stretch-sensitive dendrites were subjected to rounds of stretch characterized by an increase in stretch, a hold period, and a release from stretch. The changes to the burst duration and interburst interval during a series of stretches was recorded extracellularly, while in saline and also with the two neuropeptides SGRN and GYS. In response to stretch, cycle frequency most often increased, while burst duration decreased. However, the responses varied considerably across preparations, with some stretches inducing an excitatory response, and others inducing an inhibitory response.

It was found that application of GYS appeared to decrease the changes in the burst duration and interburst interval elicited by stretch, resulting in a significant decrease in variation in the presence of the peptide compared to the control. GYS thus may reduce positive feedback, favoring negative feedback, as was previously predicted. SGRN did not enhance feedback, as we had predicted, but instead also generally decreased the variation of change in burst duration and interburst interval elicited by stretch. The effects of SGRN on feedback were more variable, suggesting that any change in the balance of positive and negative feedback elicited by the peptide is more likely mediated by the negative feedback pathway.

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