Cellular Mechanisms and Regulation of Stretch Feedback in the heart of *Homarus Americanus*

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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 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).

In order to maintain homeostasis in response to changing sensory inputs, there is often modulation as well as internal and external feedback that is responsible for the underlying flexibility of this neuronal network. The stretching of the heart activates a positive feedback pathway in which contraction frequency increases. The stretch of CG dendrites carries information about the filling of the heart to the rest of the CG. Extrinsic modulation via neuromodulators, especially peptides, plays a key role in achieving flexibility. However, the extent to which the heart's feedback system is modulated is still unknown.

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), are of particular interest in looking at the stretch feedback response. A previous study has shown SGRN and GYS 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).

Preliminary work investigating this prediction looked at the effects of the neuromodulators on stretch, using reduced preparation with just muscles under small cells. 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. In this study, the response to stretch during the hold period in control saline was measured by the bursting pattern generated by the CG, including the interburst interval and burst duration. During the hold period, the pattern reflected an increase in the interburst interval and a decrease in burst duration compared to the control before the stretch (Qu, 2017). 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 inhibited 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. This was done by recording the changes to the burst duration and interburst interval during a series of stretches induced on a reduced preparation of the isolated CG, muscle, and stretch-sensitive dendrites while in saline and also with the two neuropeptides SGRN and GYS. It was found that there GYS and SGRN both decreased the change in interburst interval that naturally occurs during stretch, thus both had an inhibitory effect on the interburst interval during stretch feedback. There were no significant changes in the burst duration for both experiments with GYS and SGRN.

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