Multiple Mechanisms of Gain Modulation in the Serotonin System

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The serotonin neurons of the dorsal raphe nucleus (DRN) are the main source of serotonergic input to the forebrain and key regulators of behaviour. The spiking features of DRN serotonin neurons depend on complex interactions between their intrinsic excitability, local feed-forward inhibition by somatostatin (SOM)-expressing GABAergic interneurons, and long-range cortical and subcortical inputs. In order to get a dynamical understanding of these interactions, we fitted augmented generalized integrate-and-fire (GIF) models to serotonin and SOM neurons and used them to create experimentally-constrained models of the DRN network. In addition to optimally reproducing the spike trains of individual neurons, augmented GIF models captured the distinguishing characteristics of serotonin neurons highlighted by our electrophysiological experiments, including low excitability and the presence of a prominent voltage-dependent transient potassium conductance. In network simulations, DRN ensembles exhibited strongly amplified responses to fast-changing inputs. Importantly, our simulations indicate that endocannabinoid-regulated feed-forward inhibition previously described in the DRN and the transient potassium conductance found in serotonin neurons provide mechanisms to independently regulate: 1) the selective amplification of fast-changing inputs and; 2) the overall output gain of the network. These results begin to define the network-level operations performed by the DRN and how they may ultimately contribute to regulating behaviour.