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Title: C. elegans Locomotion: Finding Balance in Imbalance

 $Authors: \qquad Thapliyal, Shruti \ (/jspui/browse?type=author\&value=Thapliyal\%2C+Shruti)$ 

Babu, Kavita (/jspui/browse?type=author&value=Babu%2C+Kavita)

Keywords: Excitation

Inhibition Acetylcholine GABA C. elegans

Issue Date:

2018

Publisher: Springer New York LLC

Citation: Advances in Experimental Medicine and Biology, 1112, pp. 185-196

Abstract:

The excitation-inhibition (E-I) imbalance in neural circuits represents a hallmark of several neuropsychiatric disorders. The tiny nematode Caenorhabditis elegans has emerged as an excellent system to study the molecular mechanisms underlying this imbalance in neuronal circuits. The C. elegans body wall muscles receive inputs from both excitatory cholinergic and inhibitory GABAergic motor neurons at neuromuscular junctions (NMJ), making it an excellent model for studying the genetic and molecular mechanisms required for maintaining E-I balance at the NMJ. The cholinergic neurons form dyadic synapses wherein they synapse onto ipsilateral body wall muscles allowing for muscle contraction as well as onto GABAergic motor neurons that in turn synapse on the contralateral body wall muscles causing muscle relaxation. An alternating wave of contraction and relaxation mediated by excitatory and inhibitory signals maintains locomotion in C. elegans. This locomotory behavior requires an intricate balance between the excitatory cholinergic signaling and the inhibitory GABAergic signaling mechanisms. Studies on the C. elegans NMJ have provided insights into several molecular mechanisms that could regulate this balance in neural circuits. This review provides a discussion on multiple genetic factors including neuropeptides and their receptors, cell adhesion molecules, and other molecular pathways that have been associated with maintaining E-I balance in C. elegans motor circuits. Further, it also discusses the implications of these studies that could help us in understanding the role of E-I balance in mammalian neural circuits and how changes in this balance could give rise to brain disorders.

URI: https://link.springer.com/chapter/10.1007%2F978-981-13-3065-0\_14

(https://link.springer.com/chapter/10.1007%2F978-981-13-3065-0\_14) http://hdl.handle.net/123456789/2281 (http://hdl.handle.net/123456789/2281)

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