Title:	Deciphering the role of CASY-1, an ortholog of mammalian Calsyntenins in the C. elegans locomotory circuit
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Keywords:	Biological Sciences Mammalian Calsyntenins Functions of Calsyntenins Glutamate Monoamines
Issue Date:	1-Sep-2018
Publisher:	IISERM
Abstract:	Behavioral outcome of an organism is an integrated response of exposure to several distinct environmental stimuli. Locomotion is one of the most prominent behavioral output in C. elegans. Neural circuits that produce coordinated dorso-ventral sinusoidal bends allow normal locomotion in C. elegans. Locomotory behavior is synchronized at multiple levels and involves the integration of diverse sensory cues that are processed by the interneurons and ultimately cause changes at the neuromuscular junctions (NMJ). An important principle that maintains locomotion is a coordinated balance between the excitatory (E) and inhibitory (I) signaling at the NMJ. In my work, I characterize the function of a cell adhesion molecule CASY-1, an ortholog of mammalian calsyntenins in regulating this excitation-inhibition balance at the NMJ. In the first aspect of my work, I demonstrate that casy-1 mutants have an increased synaptic signaling at the NMJ which can be significantly rescued by expressing shorter isoforms of CASY-1: CASY-1B and CASY-1C specifically in GABAergic (inhibitory) motor neurons. Using pharmacological, behavioral, electrophysiological, optogenetic and imaging approaches I establish that GABA release is compromised at the NMJs in casy-1 mutants. Further, I demonstrate that CASY-1 functions in the transport of GABAergic synaptic vesicle (SV) precursors through a possible interaction with the SV motor protein, UNC-104/KIF1A. In the second part of my work, I report mechanisms by which the longer CASY-1A isoform affects excitatory cholinergic signaling at NMJ by modulating the activity of sensory neurons. Mutants in casy-1 appear to have hyperactive sensory neurons resulting in accelerated locomotion and motor circuit activity. These sensory neurons mediate increased motor activity via enhanced glutamate release. Using genetic, pharmacological and optogenetic manipulations, we establish that CASY-1A is required to monitor the activity of these neurons. The findings of this thesis illustrates a novel neuromodulatory role of CASY-1- mediated signaling in regulating the excitation-inhibition balance of the motor circuit

URI:	http://hdl.handle.net/123456789/968 (http://hdl.handle.net/123456789/968)
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