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Mechanosensation circuitry in *Caenorhabditis elegans*: A focus on gentle touch

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ABSTRACT

Forward or reverse movement in *Caenorhabditis elegans* is the result of sequential contraction of muscle cells arranged along the body. In larvae, muscle cells are innervated by distinct classes of motorneurons. B motorneurons regulate forward movement and A motorneurons regulate backward movement. Ablation of the D motor neurons results in animals that are uncoordinated in either direction, which suggests that D motorneurons regulate the interaction between the two circuits. *C. elegans* locomotion is dictated by inputs from interneurons that regulate the activity of motorneurons which coordinate muscle contraction to facilitate forward or backwards movement. As *C. elegans* moves through the environment, sensory neurons interpret chemical and mechanical information which is relayed to the motor neurons that control locomotory direction. A mechanosensory input known as light nose touch can be simulated in the laboratory by touching the nose of the animal with a human eyebrow hair. The recoil reaction that follows from light nose touch appears to be primarily mediated by glutamate release from the polymodal sensory neuron ASH. Numerous glutamate receptor types are found in different neurons and interneurons which suggest that several pathways may regulate the aversive response. Based on the phenotypes of mutants in which neuropeptide processing is abolished, neuropeptides play a role in circuit regulation. The light touch response is also regulated by transient receptor channel proteins and degenerin/epithelial sodium channels which modulate the activity of sensory neurons involved in the nose touch response.

Introduction

The detection of mechanical stimulation is conserved in a variety of organisms, however our understanding of how organisms with complex nervous systems detect and respond to different magnitudes of mechanical stimulation remains a mystery. The diversity in mechanoreceptors and the intricacy of the nervous system within mammalian models has proven difficult to characterize. Insight into the neuronal circuitry underlying the sensation of touch has proceeded far more rapidly within the nematode *Caenorhabditis elegans* due to the presence of a relatively simple nervous system (302 neurons), an established neuronal connectivity map [73], and ease in analyzing behavioral responses. Despite the evolutionary distance, many of the proteins and signaling molecules mediating mechanosensation in *C. elegans* are broadly conserved among vertebrates and invertebrates.

In their natural habitat, *C. elegans* must navigate through soil to avoid predators and unfavorable environments while foraging. Although locomotory patterns are influenced by diverse environmental stimuli, the organisms are persistently exposed to mechanical stimulation. Consequently, the sensation of touch is highly important. The composition of the nematode nervous system reflects the significance of touch as 10% of its neurons are thought to be mechanoreceptors [27]. However, in the regulation of gentle nose touch response, mechanosensory neurons appear to work in combination with polymodal (multi-functional) neurons [9]. *C. elegans* thus provides a useful model for characterizing the neuronal circuitry underlying differing degrees of mechanostimulation.

The gentle nose-touch/mechanosensory signaling pathway requires the contribution of specific neurons and their associated receptors, gap junctions, and chemical/neuropeptide signaling molecules (Table 1). Mechanosensory neurons communicate with each other in either a stimulatory or inhibitory fashion through their signaling components. A map of the interconnections

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Table 1
List of neuron, gene and protein abbreviations.

Sensory neurons	
Neuron abbreviation	Description
ASH	Anterior amphid neuron with single ciliated endings
ASE	Anterior amphid neuron with single ciliated endings
FLP	Anterior multidendritic neuron with ciliated endings
OLQ	Anterior outer labial neuron, ciliated endings
ALM	Anterior lateral microtubule cell
AWC	Amphid wing "C" cells, ciliated sheet-like sensory endings
AQR	Anterior neuron with small cilium exposed to body cavity fluid
PQR	Posterior neuron with small cilium exposed to body cavity fluid
ADL	Anterior amphid neuron with dual ciliated sensory endings
ADF	Anterior amphid neuron with dual ciliated sensory endings
CEP	Anterior neuron of cephalic sensilla exposed to body cavity fluid
Interneurons	
Neuron abbreviation	Description
AVA	Anterior ventral cord neuron
AVD	Anterior ventral cord neuron
AVE	Anterior ventral cord neuron
AVB	Anterior ventral cord neuron
PVC	Posterior ventral cord neuron
AIB	Anterior amphid neuron
AIY	Anterior amphid neuron
RIH	Anterior neuron
DVA	Posterior interneuron
Motor neurons	
Note that all neuron cell bodies are located in the ventral cord the "D" refers to dorsal synapse at the neuromuscular junction. Thus, DB is "Dorsal B type motor neuron" meaning that it has a neuromuscular junction on the dorsal side. While VB is "Ventral B type motor neuron	
Neuron abbreviation	Description
DB	Ventral cord dorsal B-type neuron
VB	Ventral cord ventral B-type neuron
DA	Ventral cord dorsal A-type neuron
VA	Ventral cord ventral A-type neuron
DD	Ventral cord dorsal D-type neuron
VD	Ventral cord ventral D-type neuron
Neurons with multiple roles	
Neuron abbreviation	Description
NSM	Pharyngeal neurosecretory and motor neuron
IL1	Sensory, motor, and interneuron of inner labial sensilla
RIM	Anterior interneuron and motor neuron
URX	Anterior sensory and ring interneuron; flattened, non-ciliated endings exposed to body cavity fluid
Neuropeptides	
Protein abbreviation	Description
NLP-1	Neuropeptide-like peptide
NLP-12	Neuropeptide-like peptide 12 of the LQFamide neuropeptide family
FLP-1	FMRF-like peptide 1
FLP-18	FMRF-like peptide 18
FLP-21	FMRF-like peptide 21
INS-1	Insulin like peptide orthologous to human insulin
Neuropeptide receptors	
Protein abbreviation	Description
NPR-1	Neuropeptide Receptor 1
NPR-2	Neuropeptide Receptor 2
NPR-3	Neuropeptide Receptor 3
NPR-5	Neuropeptide Receptor 5
NPR-9	Neuropeptide Receptor 9
CKR-2	Cholecystokinin receptor
Neurotransmitter receptors	
Protein abbreviation	Description
LGC-55	Ligand-gated ion channel, Tyramine gated chloride channel
NMR-1	NMDA-type ionotropic glutamate receptor subunit
NMR-2	NMDA-type ionotropic glutamate receptor subunit
GLC-1	Alpha subunit of a glutamate-gated chloride channel
GLC-2	Beta subunit of a glutamate-gated chloride channel
GLC-3	L-glutamate-gated chloride channel subunit
GLC-4	Glutamate-gated chloride channel
AVR-14	Alpha-type subunit of a glutamate-gated chloride channel
AVR-15	Two glutamate-gated chloride channel subunits
GLR-1	AMPA-type ionotropic glutamate receptor subunit
GLR-2	AMPA-type ionotropic glutamate receptor subunit
GLR-3	AMPA-type ionotropic glutamate receptor subunit
GLR-4	AMPA-type ionotropic glutamate receptor subunit
GLR-5	AMPA-type ionotropic glutamate receptor subunit
GLR-6	AMPA-type ionotropic glutamate receptor subunit
GLR-7	AMPA-type ionotropic glutamate receptor subunit